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DR. LUIS RAZETTI

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Volumen 133 **Nº 3** **Julio-Septiembre 2025**

Í N D I C E

EDITORIAL
Consideraciones sobre el liderazgo médico
Enrique Santiago López-Loyo 653

CARTAS AL EDITOR
El síndrome de publicar o perecer en jóvenes investigadores: una carga silenciosa en la academia contemporánea
Edwin Gustavo Estrada-Araoz 658

Suspensión de agonistas GLP-1 en el manejo de la obesidad: ¿cuándo y cómo hacerlo con criterio clínico?
Jorge Andrés Hernández Navas, Luis Andrés Dulcey Sarmiento, Juan Sebastián Therán León, Jaime Alberto Gómez Ayala, Yerson Javier Villamizar Beltrán 661

Tratamiento de la osteopenia: enfoque integral y papel de los bifosfonatos en la prevención de fracturas
Jorge Andrés Hernández Navas, Luis Andrés Dulcey Sarmiento, Juan Sebastián Therán León, Jaime Alberto Gómez Ayala, Yerson Javier Villamizar Beltran 663

ARTÍCULOS ORIGINALES
Efecto de la terapia con inhibidores de la bomba de protones sobre los niveles séricos de vitamina B12 y los parámetros hematológicos en la sangre de pacientes con reflujo laringofaringeo
Muhammad Amsyar Akil, Uleng Bahrun, Foppy Puspitasari 666

Autocodificadores de grafos isomorfos versus firmados para la reconstrucción de redes de polimorfismos de un solo nucleótido de microARN en paisajes osteogenómicos periodontales
Sarvagya Sharma, Pradeep Kumar Yadalam, Carlos M. Ardila 675

Correlación entre la expresión y supervivencia del receptor del factor de crecimiento epidermal, la quinasa del linfoma anaplásico y el ligando-1 de la muerte celular programada en pacientes con adenocarcinoma pulmonar
Karen González Cabrera, Meribeth Henry Archbold, Rafael Vallejo Rodriguez, Astor Aguirre Santamaría, Alex Dominguez-Vargas, Henry J González-Torres 686

Comparación de la eficacia de la punción seca y el masaje de fricción profunda en el tamaño del punto gatillo, el nivel de dolor y el rango de movimiento en pacientes con dolor lumbar
Mujaddidah Yuharti, Aryadi Arsyad, Andi Ayandy, Meutiah Mutmainnah Abdullah, Andi Rizky Arbaim Hasyar 697

Autocodificadores variacionales condicionales para genes centrales generados en retrovirus endógenos humanos e inflamasoma periodontal
Pradeep Kumar Yadalam, Carlos M. Ardil 709

Factores de riesgo para la utilización de servicios de salud hospitalarios entre los afiliados a la Agencia de Seguridad Social para la salud en Liwuto, Baubau, Isla Makasar
Dwi Sumarningsih, Sukri Palutturi, Amran Razak, Muhammad Yusran Amir, Stang 715

Relación de las características antropométricas y síndrome de ovario poliquístico en mujeres en edad fértil pertenecientes a una universidad
Luisa Galeano-Muñoz, Raúl Polo-Gallardo, Sindy Ariza-Egea, Roberto Rebolledo-Cobos, Laura Ardila-Pereira, Martha Mendinueta-Martínez, Eulalia Amador-Rodero, Leslie Montealegre-Esmeral 724

Hepaticoduodenostomía laparoscópica versus hepaticoyeyunostomía abierta en quistes coledocianos pediátricos: estudio pionero colombiano
Diana Lopera Gómez, Pastor Thomas Olivares, Enrique Ramos Classon, Gennys Gutiérrez Ramírez, Aura Guevara Díaz, Jaime Plazas Román 734

Evaluación de la carga de síntomas en pacientes con EPOC tras un programa de rehabilitación pulmonar domiciliaria
Irmawan Andri Nugroho, Fatimah Ahmedy, Zulkhairul Naim bin Sidek Ahmad 744

Edad, resiliencia, habilidad del cuidador y tiempo de cuidado como predictores de la sobrecarga en cuidadores informales de pacientes con esquizofrenia y trastorno bipolar
Guadalupe Pérez Lezama, Marian Acosta, Victoria Bustamante 753

Evaluación de la Viabilidad y Fiabilidad de las Pruebas de Contacto en la Práctica Clínica Habitual
Maria Zofia Lisiecka 763

Polipéptido insulinotrópico dependiente de glucosa (GIP) y resistina como biomarcadores en la preeclampsia
Anita Israel, Elsa Camacho, María Gabriela Matos, Rafael Cortés 780

Desempleo y funcionalidad familiar en hogares escolares de Cartagena de Indias, Colombia
Eddie Del Carmen De Ávila Naraina, Verónica del Carmen Castro Bocanegra, Anderson Díaz Pérez, Sofía Del Mar Colón Arroyo, Silvia Del Mar Gómez Porto, Biana María Madera Fuentes, Raulis Jesús Olave De Arco, Natalia Daniela Villadiego Berrocal, Maricarmen Zambrano Pérez 791

Uso problemático de los videojuegos como predictor del desarrollo de habilidades sociales en estudiantes de educación básica
Katerin Valdez-Castro, Sadith Soncco-Champi, Edwin Gustavo Estrada-Araoz, Néstor Antonio Gallegos-Ramos 803

Una estrategia para mejorar el estancamiento de pacientes en el Servicio de Urgencias del Hospital General Dr. Wahidin Sudirohusodo mediante el uso de Lean Hospital
Michiko Inas Annisa Nasman, Indahwaty Sidin, Syahrir A Pasinringi, Dewi Rizki Nurmala, Fridawaty Rivai, Noer Bahry Noor, Irwandy, Adi Putra Pratama 813

Características de la adaptación psicofisiológica de los estudiantes extranjeros en las Universidades de Medicina
Aigul Chonkoeva, Ykyval Taalaibekova, Cholpon Zhaparalieva, Nurlanbek Mannap uulu, Aikerim Chonkoeva 829

Predictores de progresión de la infección por VIH en niñas, niños, adolescentes y jóvenes por transmisión materno infantil en una institución proveedora de servicios especializada, Montería
Lucelly de las Mercedes Benítez Cheij, Julia Susana Vidal Avilez, Luisa Fernanda Mendoza Villera, Yubis Yadith Ayazo Torres 843

ARTÍCULOS DE REVISIÓN

Autopsia psicosocial en casos de suicidio en poblacion de niños y adolescentes: Una revisión sistemática
María Laura Vergara-Álvarez, María Angelica Vivas Domínguez, Boris Sose Señas Sierra, Mónica Liliana Romero Jiménez, Juan Guillermo Macías Sánchez, Pavel Eduardo Rodríguez Durango, María Natividad Elvira-Zorzo 852

Cambios bioquímicos y metabólicos asociados a la depresión: Una revisión sistemática
Mariangel Carvajal-Vargas, Danitza Peñaranda-Reyes, Sandra-Milena Carrillo-Sierra, Astrid Rozo-Sánchez, Eliana María Ibañez-Casadiegos, Vivian Peña-Parada, Julio César Contreras-Velásquez, Valmore Bermúdez, Diego Rivera-Porras 870

De las nubes a la claridad: comprendiendo las verdaderas consecuencias de los cigarrillos electrónicos y EVALI
Carlos Silva Paredes, Marien Semprún, Juan Lauretta, Omar Ross, Jennifer Rojas, Luis Rincón, Valmore Bermúdez 889

Factores psicosociales asociados a la participación política juvenil: Una revisión sistemática
Beatriz-Milagros Mendoza-Rincón, Manuel Riano-Garzón, Daniel Cepeda-Pineda, Franlet Araque-Castellanos, Orlando González-Gutiérrez, Diego Rivera-Porras 910

Modelos predictivos de la conducta suicida basados en la autopsia psicosocial: Revisión sistemática de enfoques y evidencia reciente
María Laura Vergara-Álvarez, Liliana Margarita Meza Cueto, Jobana Fayine Agredo Morales, Martha Viviana Vargas Galindo, María Angelica Vivas Domínguez, Álvaro Enrique Loheste Charris, María Natividad Elvira-Zorzo 935

Efectividad del uso de la tecnología en el cuidado de enfermería: Revisión integrativa
Judith Cristina Martínez-Royert, Viviana Paola Franco Mejía, Adriana Marcela Mendoza Lubo, Saray Michell Redondo Orozco 947

La intervención con imágenes guiadas mejora la calidad de vida en pacientes con cáncer de mama: Una revisión bibliográfica
Sulasri, Andi Zulkifli, Kadek Ayu Erika 959

CASOS CLÍNICOS
Manejo de tejidos blandos en implante dental post-extracción con injerto de tejido conectivo. Informe de un caso
Enrique Nuñez, Suani Torres-Tom, Brian Espinosa-Segira, Antonio Diaz-Caballero 967

Linfoma de células grandes anaplásicas asociado a prótesis mamarias, a propósito del primer caso diagnosticado en Venezuela. Propuesta para la evaluación de las muestras
Enrique Santiago López-Loyo 973

HISTORIA Y BIOGRAFÍAS
Dr. José Gregorio Hernández (1864-1919): una nueva visión de la bacteriología
Tomás González, Cynthia Verónica Hernández Campuzano 989

VARIOS
La Gaceta Médica de Caracas hace… 100… 50… 25 años.
Enrique Santiago López-Loyo 996

Vida de la Academia, Resúmenes de los trabajos presentados y Notas Bibliográficas
Enrique Santiago López-Loyo 1001

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Volume 133 **No. 3** **July-September 2025**

I N D E X

EDITORIAL
Considerations on medical leadership
Enrique Santiago Lopez-Loyo 653

LETTER TO THE EDITOR
Publish or perish syndrome in early-career researchers: A silent burden in contemporary academia
Edwin Gustavo Estrada-Araoz 658

Discontinuation of GLP-1 agonists in obesity management: When and how to do it using clinical judgment?
Jorge Andres Hernandez Navas, Luis Andres Dulcey Sarmiento, Juan Sebastian Theran Leon, Jaime Alberto Gomez Ayala, Yerson Javier Villamizar Beltran 661

Osteopenia treatment: A comprehensive approach and the role of biphosphonates in fracture prevention
Jorge Andres Hernandez Navas, Luis Andres Dulcey Sarmiento, Juan Sebastian Theran Leon, Jaime Alberto Gomez Ayala, Yerson Javier Villamizar Beltran 663

ORIGINAL ARTICLES
Effect of proton pump inhibitor therapy on serum vitamin B12 levels and hematologic parameters in the blood of patients with laryngopharyngeal reflux
Muhammad Amsyar Akil, Uleng Bahrun, Foppy Puspitasari 666

Signed versus isomorphic graph autoencoders for microRNA–single–nucleotide polymorphisms network reconstruction in periodontal osteo-genomic landscapes
Sarvagya Sharma, Pradeep Kumar Yadalam, Carlos M. Ardila 675

Correlation between epidermal growth factor receptor, anaplastic lymphoma kinase and programmed cell death-ligand-1 expression and survival in patients with pulmonary adenocarcinoma
Karen Gonzalez Cabrera, Meribeth Henry Archbold, Rafael Vallejo Rodriguez, Astor Aguirre Santamaria, Alex Dominguez-Vargas, Henry J Gonzalez-Torres 686

Comparison of the effectiveness of dry needling and deep friction massage on trigger point size, pain level, and range of motion in low back pain patients
Mujaddidah Yuharti, Aryadi Arsyad, Andi Ayandy, Meutiah Mutmainnah Abdullah, Andi Rizky Arbaim Hasyar 697

Conditional variational autoencoders for generated hub genes in human endogenous retrovirus and periodontal inflammasome
Pradeep Kumar Yadalam, Carlos M. Ardil 709

Risk factors for the utilization of inpatient Health Services among Social Security Agency for health participants at Liwuto Community Health Center, Baubau, Makasar Island
Dwi Sumarningsih, Sukri Palutturi, Amran Razak, Muhammad Yusran Amir, Stang 715

Relationship between anthropometric characteristics and polycystic ovary syndrome in women of reproductive age attending a university
Luisa Galeano-Munoz, Raul Polo-Gallardo, Sindy Ariza-Egea, Roberto Rebolledo-Cobos, Laura Ardila-Pereira, Martha Mendinueta-Martinez, Eulalia Amador-Rodero, Leslie Montealegre-Esmeral 724

Laparoscopic hepaticoduodenostomy versus open hepaticojejunostomy for pediatric choledochal cysts: A pioneering colombian study
Diana Lopera Gomez, Pastor Thomas Olivares, Enrique Ramos Classon, Gennys Gutierrez Ramirez, Aura Guevara Diaz, Jaime Plazas Roman 734

Evaluation of Symptom Burden in COPD Patients Following a Home-Based Pulmonary Rehabilitation Program
Irmawan Andri Nugroho, Fatimah Ahmedy, Zulkhairul Naim bin Sidek Ahmad 744

Age, resilience, caregiver skill, and caregiving time as predictors of burden in informal caregivers of patients with schizophrenia and bipolar disorder
Guadalupe Perez Lezama, Marian Acosta, Victoria Bustamante 753

Evaluation of the Feasibility and Reliability of Contact Tests in Routine Clinical Practice
Maria Zofia Lisiecka 763

Glucose-dependent insulinotropic polypeptide (GIP) and resistin as biomarkers in preeclampsia
Anita Israel, Elsa Camacho, Maria Gabriela Matos, Rafael Cortes 780

Unemployment and Family Functionality in School Homes in Cartagena de Indias, Colombia
Eddie Del Carmen De Avila Naraina, Veronica del Carmen Castro Bocanegra, Anderson Diaz Perez, Sofia Del Mar Colon Arroyo, Silvia Del Mar Gomez Porto, Biana Maria Madera Fuentes, Raulis Jesus Olave De Arco, Natalia Daniela Villadiego Berrocal, Maricarmen Zambrano Perez 791

Problematic video game use as a predictor of social skill development among elementary school students
Katerin Valdez-Castro, Sadith Soncco-Champi, Edwin Gustavo Estrada-Araoz, Nestor Antonio Gallegos-Ramos 803

A Strategy To Improve Patient Stagnation In The Emergency Department of Dr. Wahidin Sudirohusodo General Hospital Using Lean Hospital
Michiko Inas Annisa Nasman, Indahwaty Sidin, Syahrir A Pasinringi, Dewi Rizki Nurmala, Fridawaty Rivai, Noer Bahry Noor, Irwandy, Adi Putra Pratama 813

Features of Psychophysiological Adaptation of Foreign Students in Medical Universities
Aigul Chonkoeva, Ykyval Taalaibekova, Cholpon Zhaparalieva, Nurlanbek Mannap uulu, Aikerim Chonkoeva 829

Predictors of progression of HIV infection in girls, boys, adolescents and young people by mother-to-child transmission in a specialized service provider institution, Montería
Lucelly de las Mercedes Benitez Cheij, Julia Susana Vidal Avilez, Luisa Fernanda Mendoza Villera, Yubis Yadith Ayazo Torres 843

REVIEW ARTICLES
Psychosocial autopsy in cases of suicide in child and adolescent populations: A Systematic review
Maria Laura Vergara-Alvarez, Maria Angelica Vivas Dominguez, Boris Sose Senas Sierra, Monica Liliana Romero Jimenez, Juan Guillermo Macias Sanchez, Pavel Eduardo Rodriguez Durango, Maria Natividad Elvira-Zorzo 852

Biochemical and Metabolic Changes Associated with Depression: A Systematic Review
Mariangel Carvajal-Vargas, Danitza Penaranda-Reyes, Sandra-Milena Carrillo-Sierra, Astrid Rozo-Sanchez, Eliana Maria Ibanez-Casadiegos, Vivian Pena-Parada, Julio Cesar Contreras-Velasquez, Valmore Bermudez, Diego Rivera-Porras 870

From clouds to clarity: Understanding the real consequences of e-cigarettes and EVALI
Carlos Silva Paredes, Marien Semprún, Juan Lauretta, Omar Ross, Jennifer Rojas, Luis Rincón, Valmore Bermúdez 889

Psychosocial factors associated with youth political participation: A systematic review
Beatriz-Milagros Mendoza-Rincon, Manuel Riano-Garzon, Daniel Cepeda-Pineda, Franlet Araque-Castellanos, Orlando Gonzalez-Gutierrez, Diego Rivera-Porras 910

Psychosocial autopsy-based predictive models of suicidal behavior: Systematic review of approaches and recent evidence
Maria Laura Vergara-Alvarez, Liliana Margarita Meza Cueto, Jobana Fayine Agredo Morales, Martha Viviana Vargas Galindo, Maria Angelica Vivas Dominguez, Alvaro Enrique Loheste Charris, Maria Natividad Elvira-Zorzo 935

Effectiveness of technology used in nursing care: An integrative review
Judith Cristina Martinez-Royert, Viviana Paola Franco Mejia, Adriana Marcela Mendoza Lubo, Saray Michell Redondo Orozco 947

Guided Imagery Intervention Improves the Quality of Life in Breast Cancer Patients: A Literature Review
Sulasri, Andi Zulkifli, Kadek Ayu Erika 959

CLINICAL CASES
Management of soft tissues in post-extraction dental implant with connective tissue graft. Case report
Enrique Nunez, Suani Torres-Tom, Brian Espinosa-Segira, Antonio Diaz-Caballero 967

Anaplastic large cell lymphoma associated with mammary prostheses, relating to the first case diagnosed in Venezuela. Proposal for the evaluation of the samples
Enrique Santiago Lopez-Loyo 973

HISTORY AND BIOGRAPHIES
Dr. José Gregorio Hernández (1864-1919): A new vision of bacteriology
Tomas Gonzalez, Cynthia Veronica Hernandez Campuzano 989

VARIOUS
The Gaceta Medica de Caracas 100, 50, 25 years ago.
Enrique Santiago Lopez-Loyo 996

Life of the Academy, Summary of the papers presented and the Bibliographic Notes
Enrique Santiago Lopez-Loyo 1001

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En la GMC se dará cabida a los trabajos realizados por profesionales de la medicina o especialidades conexas, presentados en la Academia, en los Congresos de Ciencias Médicas y los que sugiera la Corporación a través del Comité Científico, y aceptación final por la Dirección-Redacción. Los manuscritos enviados a la GMC —escritos en español o en inglés—, serán revisados por el Comité Editorial y— si reunen la calidad científica y cumplen con las normas de presentación necesarias— serán sometidos a un proceso de arbitraje externo, doble ciego, por personas con competencias similares a las de los productores del trabajo (pares) para su debida evaluación. Una vez recibida la opinión de los árbitros, el Comité Editorial tomará la decisión final de su aceptación para publicación. Queda entendido que el Comité Editorial puede rechazar un manuscrito, sin necesidad de acudir alproceso de arbitraje, si se incumple con lo establecido en las normas.

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Comunicaciones breves
Perlas de observación
Noticias y cartas al editor
Varios

Los trabajos enviados deberán cumplir con los requisitos que se describen a continuación.

EDITORIALES

Esta sección estará dedicada al análisis y la reflexión sobre los problemas de salud de la población, los distintos enfoques preventivos y terapéuticos, así como los avances logrados en el campo de la investigación biomédica y otros que considere la Dirección-Redacción.

ARTÍCULOS ORIGINALES

Deberán contener en la página frontal, el título conciso e informativo del trabajo; nombre(s) y apellido(s) de cada autor; grados académicos de los autores e institución en la cual se realizó el trabajo; nombre y dirección actual del autor responsable de la correspondencia; un título corto de no más de 40 caracteres (contando espacios y letras) y las palabras clave.

Los trabajos originales, revisiones sistemáticas y metanálisis deben tener un resumen estructurado, como se indica a continuación:

Debe contener un máximo de 250 palabras, y los siguientes segmentos:

- Introducción: ¿Cuál es el problema principal que motivó el estudio?
- Objetivo: ¿Cuál es el propósito del estudio?
- Métodos: ¿Cómo se realizó el estudio? (selección de la muestra, métodos analíticos y observacionales).
- Resultados: ¿Cuáles son los aspectos más importantes? (datos concretos y en lo posible su significancia estadística)
- Conclusión: ¿Cuál es la más importante que responde al objetivo?

Al final se anotarán 3 a 6 palabras clave.

Resumen en inglés

Debe corresponderse con el resumen en español.Se sugiere que este sea revisado por un traductor experimentado, a fin de garantizar la calidad del mismo.

Introducción

Incluir los antecedentes, el planteamiento del problema y el objetivo del estudio en una redacción libre y continua debidamente sustentada por la bibliografía.

Método

Señalar claramente las características de la muestra, el o los métodos empleados con las referencias pertinentes, de forma que se permita a otros investigadores, realizar estudios similares.

Resultados

Incluir los hallazgos importantes del estudio, comparándolos con las figuras estrictamente necesarias y que amplíen la información vertida en el texto.

Discusión

Relacionar los resultados con lo reportado en la literatura y con los objetivos e hipótesis planteados en el trabajo.

Conclusión

Describir lo más relevante que responda al objetivo del estudio.

Agradecimientos

En esta sección se describirán los agradecimientos a personas e instituciones así como los financiamientos.

Referencias

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Indicarlas con números arábigos entre paréntesis en forma correlativa y en el orden en que aparecen por primera vez en el texto, cuadros y pie de las figuras. En las citas de revistas con múltiples autores (más de seis autores), se deberá incluir únicamente los 6 primeros autores del trabajo, seguido de et al.,

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Fotografías

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En las microfotografías deberá aparecer la ampliación microscópica o una barra de micras de referencia.

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Artículos especiales

Son aquellas contribuciones que por su importancia el Comité Redactor considere su inclusión en esta categoría.

Casos clínicos

Deberán constar de resumen en español e inglés (máximo 100 palabras) en formato libre. Constará de introducción, presentación del caso, discusión, ilustraciones y referencias, con una extensión máxima de 10 cuartillas y apegadas a las instrucciones a los autores.

Historia y filosofía de la medicina

En esta sección se incluirán los artículos relacionados con aspectos históricos, filosóficos, bases conceptuales y éticas de la medicina. Aunque su estructura se dejará a criterio del autor, deberá incluir resúmenes en español e inglés (máximo 100 palabras) en formato libre, referencias bibliográficas citadas en el texto y en listadas al final del

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Actualidades terapéuticas

Se informará sobre los avances y descubrimientos terapéuticos más recientes aparecidos en la literatura nacional e internacional y su aplicación en nuestro ámbito médico. La extensión máxima será de cuatro cuartillas y con un máximo de cinco referencias bibliográficas. Deberá incluir resúmenes en español en inglés, en formato libre (máximo 100 palabras).

Información epidemiológica

Será una sección de información periódica sobre los registros epidemiológicos nacionales e internacionales, destacando su importancia, su comparación con estudios previos y sus tendencias proyectivas. La extensión máxima será de cuatro cuartillas y deberá incluir resúmenes en español en inglés (máximo 100 palabras), en formato libre.

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Serán considerados en esta sección, los informes preliminares de estudios médicos y tendrán la estructura formal de un resumen como se describió previamente (máximo 150 palabras). Se deberán incluir 10 citas bibliográficas como máximo.

Bioética

Se plantearán los aspectos éticos del ejercicio profesional y aquellos relacionados con los avances de la investigación biomédica y sus aplicaciones preventivas y terapéuticas. Su extensión máxima será de cuatro cuartillas y cuatro referencias bibliográficas, deberá incluir resúmenes en español e ingles (máximo 100 palabras) en formato libre.

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Consideraciones sobre el liderazgo médico

Enrique Santiago López-Loyo

El liderazgo del médico en el mundo contemporáneo ha trascendido en su contexto para asegurar una atención médica de calidad basada en su desarrollo profesional tradicional, considerando solo la capacidad técnica y académica. Ha habido una variación en la calidad del liderazgo entre las organizaciones corporativas, que ha conducido a fallos catastróficos en los estándares de atención que reciben los pacientes. Aunque hay una vinculación del liderazgo clínico con el rendimiento de las unidades, se promueve que esto se complemente con sus papeles de gerencia comenzando desde edades tempranas y continuando a lo largo de sus carreras. Este papel debe garantizarse en todo el sistema de salud, para que los médicos sean capaces de desarrollar valores personales y profesionales sólidos, al igual que una amplia variedad de habilidades no técnicas que les permitan mantener el liderazgo más allá de las fronteras profesionales, con una clara comprensión del entorno cada vez más complejo en el que se brinda la atención médica del siglo XXI. Para desarrollar todos estos atributos se requiere la aplicación de sofisticadas y diversas metodologías de aprendizaje, las cuales incluyen la mentoría, el coaching, el aprendizaje activo, el *networking*, además del uso racional de herramientas de inteligencia artificial (1).

Es fundamental la aplicación apropiada de los conceptos modernos de liderazgo en los procesos formativos del recurso humano en la medicina, lo cual es considerado determinante para el logro de buenos resultados educativos y en los aspectos clínicos en hospitales universitarios. El liderazgo en medicina y su orientación en la educación médica no ha sido suficientemente expandido en todos los continentes y el éxito en su aplicación va a depender del conocimiento de cada país con sus particularidades y de la aplicación de resultados de investigaciones originales para lograr un adecuado desarrollo curricular sobre el tema en el contexto nacional y local, sin perder de la mira la perspectiva global. El liderazgo no solo debe estar supeditado a los profesionales de la salud especialistas en gerencia o administración sanitaria, sino que cada egresado de la carrera médica debe contar con una formación básica como instrumento para su ejercicio futuro (2).

La práctica de la medicina ha ido aumentando su poder político en las sociedades contemporáneas. Por ello destacan los fenómenos de sectorización de la salud, en aspectos como lo que se dado en llamar "la invención de la infancia", el uso de los conceptos de la familia, la promoción de la higiene, el desarrollo conceptual de la salud pública, la creación y el diseño del hospital moderno, los conceptos de

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la tercera edad, los principios de salubridad de los espacios urbanos, hasta llegar a la práctica de campañas médicas sectorizadas a las clases populares, entre otros aspectos. Como resultado lógico de estos procesos, se ha llegado a una medicalización absoluta de la sociedad y a la identificación completa del problema de la salud en conjunción con los intereses de la economía. De allí han surgido los programas de asistencia y seguridad social. Todo termina sumergido en los vaivenes racionales del mercado y en los patrones de consumo que este genera. Esto ha llevado a que los sistemas de atención den prioridad a un proceso gradual de evaluación de los pacientes con citas ya tardías a la evolución natural de las enfermedades. Alejan las citas médicas de forma irracional al punto de que cuando llegan al nivel de atención especializada con complementación de estudios imagenológicos e intervencionistas de alta precisión, el paciente está en una situación de agravamiento de su cuadro clínico y por este motivo se realizan en la práctica cada vez más tardíos los diagnósticos (3).

Por otra parte, los médicos como dirigentes sociales han sido utilizados en tareas de carácter político disfrazados de elementos de refuerzo en países con supuestos problemas de cobertura de ese recurso humano en sus sistemas de atención, sobre todo en zonas de difícil acceso geográfico. Esa utilización de contingentes de médicos como agentes ideológicos con función de motorizar programas sociales se ha descrito con el objetivo de servir de inductores de transformación de conductas de pensamiento político. En este caso, la formación de esos profesionales de la salud se orienta a darle prioridad a la atención directa de las comunidades y también incluye profesionales de la odontología y bioanalistas, entre otros. Estos grupos son trasladados bajo contratación directa con los estados que ofertan el servicio y en muchos casos hay denuncias de que se trata de un "esclavismo moderno" porque del total de la remuneración contratada, el profesional recibe una mínima parte del sueldo. Este modelo puede funcionar en poblaciones apartadas de los centros urbanos y en conglomerados o barrios de la periferia de las grandes ciudades. En los países donde se ha establecido este sistema de "asistencia" se han producido acusaciones de injerencia de factores externos en las decisiones propias de cada país, donde chocan aspectos de culturas e idiosincrasias a veces antagónicas. El médico en algunos contextos sociales, sobre todo en países poco desarrollados, mantiene un liderazgo en la orientación de las comunidades, muy a la par con los liderazgos religiosos que actúan en el mismo entorno geográfico.

Los líderes médicos deben llevar adelante actividades generales de gestión y liderazgo, y deben procurar un equilibrio entre la gestión y la medicina, ya que estos médicos deben cumplir con los objetivos tanto de la organización como del personal médico. Para un desempeño eficaz, la credibilidad entre sus colegas médicos resulta ser un factor muy importante, seguido de una demostración de numerosas áreas de conocimiento, habilidades y actitudes. Se han identificado como barreras la ambigüedad de papeles y la falta de tiempo y apoyo al trabajo en equipo. Hay una reasignación de tareas fundamentales para la labor profesional médica; sin embargo, se pueden generar confusiones sobre dónde terminan y comienzan los papeles del médico y del gerente. En lo que sí existen opiniones muy claras es en la comparación que se realiza entre los resultados de la gestión de un médico al frente de la gerencia en relación con la labor de un profesional de la administración gerencial. El profesional de la administración se orienta a la obtención de buenos resultados financieros de las corporaciones, pero el médico busca en todo momento un punto medio de las políticas administrativas que den prioridad a la calidad y cobertura eficiente de la atención de los pacientes (4).

En el transcurso de las carreras médicas, tradicionalmente la enseñanza del principio de liderazgo no ha formado parte del desarrollo de las competencias tanto académicas como técnicas. Se requiere promover reformas en el perfil formativo de los futuros profesionales de la salud como una respuesta a los desafíos del sistema y a las mejoras en la salud pública. El ser médico requiere el manejo óptimo de la gestión profesional y de un liderazgo sólido, por lo cual la educación médica tiene la necesidad de transferir competencias a la comunicación y crear individuos con pensamiento crítico. Los estudiantes de medicina deben desarrollar habilidades para abordar y resolver conflictos, aprender a compartir ese liderazgo, preparar a otros para ayudarlos y reemplazarlos, así como

asumir la responsabilidad en equipo y discutir su desempeño para perfeccionarlo (5).

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Considerations on medical leadership

Enrique Santiago Lopez-Loyo

Physician leadership in the contemporary world has transcended its traditional context of ensuring quality healthcare, which was based solely on professional development that considered only technical and academic ability. There has been a variation in the quality of leadership across corporate organizations, which has led to catastrophic failures in the standards of care received by patients. Although clinical leadership is linked to unit performance, it is encouraged to complement this with their management roles, beginning at an early age and continuing throughout their careers. This role must be guaranteed throughout the healthcare system, so that physicians are able to develop strong personal and professional values, as well as a wide variety of non-technical skills that allow them to maintain leadership across professional boundaries, with a clear understanding of the increasingly complex environment in which 21st-century healthcare is provided. Developing all these attributes requires the application of sophisticated and diverse learning methodologies, including mentoring, coaching, active learning, networking, and the rational use of artificial intelligence tools (1). The appropriate application of modern leadership concepts in the training of medical personnel is essential, as it is considered crucial for achieving good educational and clinical outcomes in university hospitals. Leadership in medicine and its focus on medical education have not been sufficiently expanded across all continents. The successful application of this approach will depend on understanding each country's particularities and applying original research results to develop adequate curricula in the national and local context, while maintaining a global perspective. Leadership should not only be subordinated to health professionals specializing in health management or administration, but every medical graduate must have basic training as a tool for their future practice (2).

The practice of medicine has been increasing its political power in contemporary societies. For this reason, the sectorization of health care is prominent, in aspects such as what has been called "the invention of childhood," the use of concepts of family, the promotion of hygiene, the conceptual development of public health, the creation and design of the modern hospital, concepts of the elderly, principles of urban health, and even the implementation of targeted medical campaigns for the working class, among others. As a logical result of these processes, we have reached an absolute medicalization of society and a complete identification of the health problem in conjunction with economic interests. From this, social security and assistance programs

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have emerged. Everything ends up submerged in the rational fluctuations of the market and the consumption patterns it generates. This has led healthcare systems to prioritize a gradual process of assessing patients with appointments that are already overdue, based on the natural evolution of their illnesses. They irrationally postpone medical appointments to the point that by the time they reach specialized care with the addition of high-precision imaging and interventional studies, the patient's clinical condition worsens. For this reason, diagnoses are made increasingly late in practice (3).

Furthermore, physicians as social leaders have been utilized in political tasks, often disguised as reinforcements, in countries with purported coverage gaps of this human resource in their healthcare systems, particularly in areas with difficult geographical access. This use of contingents of physicians as ideological agents with the function of driving social programs has been described as serving as inducers of the transformation of political thought behaviors. In this case, the training of these health professionals is oriented to prioritize direct care of communities and also includes dental professionals and bioanalysts, among others. These groups are transferred through direct contracts with the states providing the service. In some cases, concerns have been raised regarding the total contracted compensation, as professionals may receive only a small portion of their salary. This model can work in populations far from urban centers and in conglomerates or neighborhoods on the outskirts of large cities. In countries where this "assistance" system has been established, accusations of interference from external factors in each country's own decisions have arisen, where aspects of cultures and idiosyncrasies, sometimes antagonistic, collide. In some social contexts, especially in underdeveloped countries, physicians maintain leadership in guiding communities, much like religious leaders operating in the same geographical area.

Medical leaders must carry out general management and leadership activities. They must strive to strike a balance between management and medicine, as these physicians must meet the objectives of both the organization and the medical staff. For effective performance, credibility among medical colleagues is a very important factor, followed by a demonstration of numerous areas of knowledge, skills, and attitudes. Role ambiguity and a lack of time and support for teamwork have been identified as barriers. There is a reassignment of fundamental tasks for professional medical work; however, confusion can arise about where the roles of the physician and the manager end and begin. However, there are very clear opinions regarding the comparison between the results of a physician's management role and those of a managerial administration professional. Administration professionals are oriented toward achieving good financial results for corporations, but physicians constantly seek a compromise in administrative policies that prioritize quality and efficient patient care (4).

In medical careers, teaching the principles of leadership has traditionally not been part of the development of both academic and technical competencies. Reforms in the training profile of future health professionals are needed as a response to the challenges of the system and improvements in public health. Being a doctor requires optimal professional management and strong leadership, so medical education needs to transfer communication skills and develop critical thinking skills. Medical students must develop skills to address and resolve conflicts, learn to share leadership, prepare others to assist and replace them, and assume team responsibility, discussing their performance to improve it (5).

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El síndrome de publicar o perecer en jóvenes investigadores: una carga silenciosa en la academia contemporánea

Publish or perish syndrome in early-career researchers: A silent burden in contemporary academia

Edwin Gustavo Estrada-Araoz

RESUMEN

El síndrome de publicar o perecer se ha convertido en una presión estructural dentro del sistema académico, afectando especialmente a los jóvenes investigadores. Este modelo prioriza la cantidad de publicaciones por encima de la calidad, generando ansiedad, agotamiento y distorsionando el sentido de la investigación. La urgencia por publicar moldea decisiones temáticas, metodológicas y éticas, favoreciendo prácticas cuestionables como la fragmentación de estudios o la publicación en revistas de baja rigurosidad. Además, empobrece la experiencia científica al desplazar la reflexión crítica, la innovación y el compromiso social. Frente a este panorama, es urgente que las instituciones revisen los criterios de evaluación académica, promoviendo un enfoque holístico que valore la relevancia, el impacto social y la ética del conocimiento generado. La ciencia debe ser una práctica responsable y humana, y su futuro dependerá del bienestar, la motivación y las condiciones de quienes la construyen en el presente.

Palabras clave: *Publicar o perecer, artículos científicos, jóvenes investigadores, carga silenciosa.*

SUMMARY

Publish or perish syndrome has become a structural pressure within the academic system, especially affecting early-career researchers. This model prioritizes the quantity of publications over their quality, generating anxiety, exhaustion, and distorting the true purpose of research. The urgency to publish shapes thematic, methodological, and ethical decisions, encouraging questionable practices such as the fragmentation of studies or publication in low-quality journals. Moreover, it impoverishes the scientific experience by displacing critical reflection, innovation, and social engagement. In light of this situation, it is urgent for institutions to revise academic evaluation criteria, promoting a holistic approach that values the relevance, social impact, and ethical integrity of the knowledge produced. Science must be a responsible and human practice, and its future will largely depend on the well-being, motivation, and working conditions of those who build it today.

Keywords: *Publish or perish, scientific articles, young researchers, silent burden.*

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Señor Editor

La comunidad científica ha alcanzado un punto de inflexión en cuanto a sus dinámicas de producción de conocimiento. El imperativo de "publicar o perecer" (*publish or perish*) se ha instalado con fuerza en la cultura académica contemporánea, transformándose en una presión sistémica que afecta a investigadores de todos los

niveles, pero con especial intensidad a aquellos que recién inician su carrera académica (1). Este fenómeno, silencioso pero persistente, se manifiesta en la necesidad constante de producir artículos científicos como requisito para lograr estabilidad laboral, ascensos, reconocimiento y acceso a financiamiento. Sin embargo, este modelo de exigencia cuantitativa, lejos de fortalecer la ciencia, amenaza con desvirtuar sus fines esenciales (2).

En particular, los jóvenes investigadores se ven atrapados en una lógica donde lo prioritario no es necesariamente la calidad del conocimiento producido, ni su pertinencia social o impacto transformador, sino la cantidad de publicaciones en revistas indexadas (3). Este mandato no solo moldea las prácticas de investigación, sino también las decisiones sobre qué investigar, cómo hacerlo y dónde publicar. Se privilegian temas "publicables" y rápidos de ejecutar, en detrimento de proyectos más complejos, interdisciplinarios o de largo aliento. La innovación, la reflexión crítica y el pensamiento profundo corren el riesgo de ser desplazados por la urgencia de obtener resultados publicables en el menor tiempo posible.

La consecuencia directa de este modelo es la normalización de un estado de ansiedad y agotamiento que afecta de forma significativa la salud mental de los jóvenes investigadores (4). Las jornadas extensas, la competencia desmedida, el temor al fracaso académico y la presión constante por cumplir con métricas impuestas —como el índice H, el factor de impacto o el número de publicaciones al año— generan un entorno poco saludable para el desarrollo científico y humano. Se ha documentado la prevalencia de síntomas de estrés, insomnio, inseguridad profesional, y hasta depresión, entre investigadores en formación y docentes universitarios jóvenes (5). Se ha creado, en efecto, un sistema que produce conocimiento al mismo tiempo que afecta negativamente a quienes lo generan.

Además de sus efectos psicológicos y personales, este modelo tiene implicancias éticas y epistemológicas preocupantes. El afán por publicar a toda costa ha fomentado prácticas como la fragmentación de investigaciones (*salami slicing*), la publicación redundante, el uso excesivo de coautorías sin justificación real, el plagio y autoplagio, e incluso la adhesión a revistas de escasa rigurosidad científica (6). Estas prácticas no solo comprometen la calidad del conocimiento difundido, sino que contribuyen a una inflación editorial que dificulta la identificación de trabajos realmente significativos en un mar de artículos repetitivos o irrelevantes. En otras palabras, la sobreproducción científica no necesariamente se traduce en progreso académico.

Resulta contradictorio que, en un sistema que valora tanto las publicaciones como indicador de excelencia, se genere simultáneamente un contexto que propicia la pérdida de sentido de la actividad investigativa. Publicar deja de ser un acto comunicativo y se convierte en una estrategia de supervivencia (7). La ciencia, que debería estar al servicio de la sociedad, corre el riesgo de volverse autorreferencial, cerrada sobre sus propias lógicas de validación interna. Es necesario recordar que el objetivo final de la investigación es producir conocimiento pertinente, ético y útil, y no simplemente llenar currículos o escalar posiciones institucionales (8).

Frente a esta realidad, es urgente que las universidades, centros de investigación, revistas científicas y agencias de financiamiento repiensen los criterios que rigen la evaluación académica. No se trata únicamente de revisar indicadores, sino de replantear el modelo de excelencia que orienta la actividad científica (2). Es imprescindible transitar hacia un enfoque más holístico, que no solo considere el número de publicaciones, sino también la relevancia de los aportes, el impacto social de los resultados, la coherencia metodológica y la integridad ética de los procesos (9). Asimismo, debe valorarse el trabajo en equipo, la participación en la formación de nuevos investigadores, la divulgación científica en lenguajes accesibles y la contribución a la construcción de ciudadanía crítica (7). Solo un sistema que premie el compromiso con el conocimiento y no la acumulación mecánica de productos permitirá fortalecer una ciencia verdaderamente responsable y sostenible.

La solución a este problema no debe centrarse en desalentar la publicación científica, sino por recuperar su sentido original. Publicar debe ser la consecuencia natural de una investigación bien concebida, no un fin en sí mismo ni una obligación basada en recompensas. En este proceso, es importante rescatar el valor del tiempo, del

debate académico y de la reflexión crítica como partes esenciales del quehacer científico. Los jóvenes investigadores necesitan un ambiente laboral que promueva el pensamiento riguroso y crítico, el trabajo colaborativo y el equilibrio entre vida personal y actividad académica. Solo así será posible formar nuevas generaciones de científicos comprometidos, creativos y éticamente responsables.

En conclusión, el síndrome del publicar o perecer se ha convertido en una carga silenciosa pero profundamente arraigada que puede debilitar tanto la salud mental de los investigadores como la integridad de la ciencia. Esta presión constante por publicar, sin considerar los tiempos necesarios del pensamiento, de la maduración metodológica y del análisis crítico, no solo empobrece la experiencia académica, sino que también distorsiona los fines fundamentales de la actividad científica. Por lo tanto, existe la necesidad de reconocer este problema y actuar en consecuencia, ya que no es únicamente una necesidad académica: es una responsabilidad institucional, ética y humana. Es indispensable crear condiciones más justas y sostenibles para el desarrollo profesional de los jóvenes investigadores, así como revisar los sistemas de evaluación que actualmente favorecen la cantidad por encima de la calidad.

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Suspensión de agonistas GLP-1 en el manejo de la obesidad: ¿cuándo y cómo hacerlo con criterio clínico?

Discontinuation of GLP-1 agonists in obesity management: When and how to do it using clinical judgment?

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Señor Editor:

Los agonistas del receptor del péptido similar al glucagón tipo 1 (GLP-1), como liraglutida y semaglutida, han transformado el abordaje farmacológico de la obesidad, gracias a su eficacia comprobada en la reducción ponderal, la mejora del perfil cardiometabólico y el control glucémico, incluso en pacientes sin diabetes. Su mecanismo de acción, que combina efectos sobre la saciedad, el vaciamiento gástrico y la homeostasis glucémica, ha sido validado por múltiples ensayos clínicos. No obstante, el uso extendido y sostenido de estos fármacos con fines exclusivamente metabólicos ha abierto una discusión necesaria sobre cuándo y cómo debe considerarse su suspensión en la práctica clínica (1).

Suspender un agonista del receptor GLP-1 no debe entenderse como una interrupción abrupta, sino como una fase planificada dentro de un proceso terapéutico integral. Esta decisión debe estar guiada por criterios clínicos bien establecidos. Un primer escenario en el que puede contemplarse la suspensión es cuando el paciente ha alcanzado una pérdida de peso clínicamente significativa (≥10 % del peso corporal inicial), sostenida por al menos seis a doce meses, y ha logrado adoptar cambios estables en el estilo de vida. En estas condiciones, una reducción gradual del fármaco puede plantearse, siempre que exista seguimiento médico riguroso para evitar la reganancia ponderal (1,2).

Un segundo escenario corresponde a la aparición de efectos adversos relevantes,

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como intolerancia gastrointestinal persistente, colelitiasis, pancreatitis, deterioro de la función renal o pérdida excesiva de masa magra. Aunque estos eventos son infrecuentes, su presencia debe motivar una reevaluación inmediata del tratamiento y, de ser necesario, la suspensión del mismo. En tercer lugar, cuando tras tres a seis meses de tratamiento a dosis terapéuticas no se ha logrado una pérdida de al menos el 5 % del peso corporal, se considera que el fármaco ha sido clínicamente ineficaz, lo cual justifica su retiro para evitar intervenciones inútiles y costos innecesarios (2).

Adicionalmente, el uso indefinido de agonistas de GLP-1 sin una estrategia de transición puede generar consecuencias clínicas y prácticas relevantes. Entre estas se incluyen el riesgo de dependencia farmacológica para el control del peso, la aparición de efectos adversos a largo plazo aún no completamente caracterizados, la desmotivación hacia intervenciones no farmacológicas, y una carga económica considerable tanto para el paciente como para el sistema de salud. Por ello, la planificación de la suspensión debe contemplar una transición segura, integrando otras alternativas farmacológicas o no farmacológicas según el perfil clínico del paciente (3,4).

En este contexto, pueden considerarse como opciones terapéuticas la combinación de naltrexona/bupropión de liberación prolongada en pacientes con trastornos del comportamiento alimentario o antecedentes afectivos, el uso de orlistat en quienes presentan intolerancia a terapias centrales, o incluso la introducción de tirzepatida, un agonista dual GLP-1/GIP, que ha mostrado beneficios superiores en la pérdida de peso y el control glucémico en estudios recientes. En casos de obesidad refractaria o severa, la evaluación para cirugía bariátrica debe formar parte del arsenal terapéutico (4,5).

El mantenimiento del peso logrado tras la suspensión del fármaco depende, en gran medida, de la implementación de un modelo de atención continua, multidisciplinaria y centrada en el paciente. Este modelo debe integrar seguimiento médico regular, apoyo nutricional, actividad física estructurada y acompañamiento psicológico. Solo de este modo se garantiza la consolidación de los logros obtenidos y se minimiza el riesgo de recaídas (5,6).

En conclusión, la decisión de suspender un agonista del receptor GLP-1 en el tratamiento de la obesidad debe basarse en criterios clínicos objetivos, abordarse desde una perspectiva individualizada y ejecutarse dentro de un plan terapéutico estructurado. Más que representar el final del tratamiento, esta etapa constituye una transición clave hacia el mantenimiento autónomo del peso y la consolidación de hábitos saludables. La experiencia clínica y la evidencia acumulada deben guiar este proceso con responsabilidad, sensatez y visión a largo plazo.

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Tratamiento de la osteopenia: enfoque integral y papel de los bifosfonatos en la prevención de fracturas

Osteopenia treatment: A comprehensive approach and the role of biphosphonates in fracture prevention

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Señor Editor:

La osteopenia ha sido durante años una condición subestimada tanto por profesionales de la salud como por los sistemas sanitarios en general. Considerada frecuentemente como una "fase intermedia" entre la masa ósea normal y la osteoporosis, ha recibido históricamente menos atención diagnóstica y terapéutica. No obstante, cada vez resulta más claro que la osteopenia representa una entidad clínica con implicaciones significativas en la salud pública, especialmente en el envejecimiento poblacional y en la prevención de fracturas por fragilidad (1).

La densidad mineral ósea (DMO), medida habitualmente mediante densitometría ósea, ha sido el pilar diagnóstico para categorizar los estados de masa ósea. En este contexto, la osteopenia se define por un puntaje T entre -1,0 y -2,5. Sin embargo, esta definición densitométrica, aunque útil, no refleja completamente el riesgo de fractura individual. De hecho, una proporción significativa de fracturas osteoporóticas ocurre en pacientes con DMO en rango de osteopenia, lo cual ha obligado a reconsiderar estrategias de prevención que no dependan exclusivamente de los valores densitométricos (1,2).

El abordaje de la osteopenia debe ser, ante todo, integral y centrado en el paciente. Esto implica no solo la medición de la masa ósea, sino una evaluación más compleja del riesgo de fractura, que considere variables clínicas adicionales como edad, sexo, antecedentes personales o familiares de fractura, uso de medicamentos que comprometan la salud ósea (como glucocorticoides), comorbilidades asociadas, historia de caídas y estilo de vida. Herramientas como FRAX® (*Fracture Risk Assessment Tool*), un modelo que permite predecir

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el riesgo absoluto de fractura osteoporótica en individuos de ambos sexos (tanto de cadera como vertebral, antebrazo y hombro) a 10 años; combina e integra factores clínicos de riesgo fáciles de obtener en la consulta diaria con la DMO del cuello femoral si está disponible, lo que resulta fundamental para tomar decisiones terapéuticas racionales (2,3).

En cuanto al manejo no farmacológico, existen pilares fundamentales que deben ser promovidos sistemáticamente en todos los pacientes con osteopenia. La adecuada ingesta de calcio y vitamina D es esencial para mantener el metabolismo óseo en equilibrio. Aunque estos nutrientes por sí solos no previenen fracturas en pacientes sin déficit, su deficiencia puede comprometer la eficacia de cualquier intervención posterior. La actividad física regular, especialmente ejercicios de resistencia y de impacto moderado, ha demostrado efectos positivos tanto en la densidad ósea como en la fuerza muscular, equilibrio y prevención de caídas. Igualmente, la modificación de factores de riesgo como el tabaquismo, el consumo excesivo de alcohol y el sedentarismo es parte inseparable de cualquier estrategia de prevención (2,3).

Ahora bien, el aspecto más debatido en el tratamiento de la osteopenia es el uso de farmacoterapia, especialmente bifosfonatos. Estos fármacos, inhibidores de la resorción ósea mediada por osteoclastos, han sido durante décadas el pilar del tratamiento de la osteoporosis. Su uso en osteopenia ha generado controversia, particularmente por el riesgo-beneficio en poblaciones sin fracturas previas ni osteoporosis densitométrica. Sin embargo, existe un consenso creciente en torno a la idea que los pacientes con osteopenia y riesgo elevado de fractura se benefician del uso de bifosfonatos, incluso en ausencia de osteoporosis establecida. Esta afirmación se apoya en evidencia clínica sólida, que ha mostrado reducciones significativas en el riesgo de fracturas vertebrales y no vertebrales en este grupo de pacientes (3,4).

La selección del paciente candidato a bifosfonatos debe ser cuidadosa. No se trata de medicalizar indiscriminadamente a todo individuo con masa ósea reducida, sino de identificar aquellos con riesgo clínico relevante, donde el beneficio del tratamiento supere claramente los posibles efectos adversos. En la práctica, esto implica iniciar tratamiento farmacológico en personas con osteopenia que tengan un riesgo de fractura mayor a ciertos umbrales, como un FRAX ≥3 % para fractura de cadera o ≥10 % para fractura osteoporótica mayor. También pueden considerarse factores adicionales como fracturas previas (2-4) por fragilidad, glucocorticoides crónicos o enfermedades que aceleren la pérdida ósea.

Dentro del grupo de bifosfonatos, se encuentran disponibles distintas moléculas con perfiles de administración y eficacia diferentes. El alendronato, administrado por vía oral una vez por semana, es una opción accesible y de bajo costo, con amplio respaldo en la literatura científica. El risedronato ofrece una alternativa similar, con esquemas orales semanales o mensuales. En pacientes que no toleran la vía oral, que presentan baja adherencia o que requieren mayor potencia terapéutica, el ácido zoledrónico, administrado por vía intravenosa una vez al año, representa una estrategia altamente efectiva. Todos estos medicamentos comparten la capacidad de reducir la resorción ósea y mejorar la arquitectura ósea, disminuyendo el riesgo de fracturas de manera significativa (2,3).

No obstante, el uso de bifosfonatos requiere precaución y un plan de seguimiento. La evaluación inicial debe incluir la función renal, dado que estos fármacos están contraindicados en insuficiencia renal severa. Además, es fundamental corregir previamente cualquier deficiencia de calcio o vitamina D, ya que su uso en presencia de hipocalcemia puede desencadenar efectos adversos importantes. Durante el tratamiento, se recomienda reevaluar periódicamente la DMO, adherencia terapéutica y aparición de eventos adversos. Aunque el perfil de seguridad es favorable, los bifosfonatos no están exentos de complicaciones poco frecuentes pero relevantes, como osteonecrosis mandibular o fracturas atípicas femorales, que suelen relacionarse con tratamientos prolongados sin revaluación (3,4).

El concepto de "vacaciones terapéuticas" también cobra relevancia en este contexto. Dado que los bifosfonatos se acumulan en el hueso y mantienen efecto prolongado incluso tras su suspensión, se ha sugerido interrumpir

su administración tras 3 a 5 años de tratamiento continuo en pacientes de bajo riesgo, siempre y cuando se mantenga vigilancia clínica y densitométrica. Esta estrategia busca reducir el riesgo de eventos adversos raros sin perder el beneficio obtenido durante los primeros años de tratamiento (4,5).

En conclusión, la osteopenia debe dejar de considerarse un hallazgo menor o meramente evolutivo hacia la osteoporosis. Se trata de una condición con implicaciones clínicas claras, que exige una evaluación estructurada del riesgo de fractura y una intervención integral. La combinación de medidas no farmacológicas y el uso racional de bifosfonatos en pacientes seleccionados permite reducir el riesgo de fracturas, preservar la funcionalidad y mejorar la calidad de vida, especialmente en adultos mayores. Como profesionales de la salud, es nuestro deber identificar estas oportunidades de prevención y actuar con base en la mejor evidencia disponible, priorizando siempre el bienestar del paciente y la optimización de los recursos sanitarios.

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Effect of proton pump inhibitor therapy on serum vitamin B12 levels and hematologic parameters in the blood of patients with laryngopharyngeal reflux

Efecto de la terapia con inhibidores de la bomba de protones sobre los niveles séricos de vitamina B12 y los parámetros hematológicos en la sangre de pacientes con reflujo laringofaringeo

Muhammad Amsyar Akil[1a*], Uleng Bahrun[1b], Foppy Puspitasari[1]

SUMMARY

Introduction: *Laryngopharyngeal reflux (RLF) is an inflammation of the aerodigestive tract where the retrograde flow of gastric contents into the larynx and pharynx encounters the upper aerodigestive tract. Proton pump inhibitors (PPIs), especially Omeprazole, are often used to manage RLF. Some studies have shown that prolonged use of PPIs can result in anemia.* **Objective:** *To analyze the relationship of PPIs to serum Vitamin B12 and hematological parameters in RLF patients.* **Methods:** *This is an analytical study with a cross-sectional approach conducted at the Ear, Nose, and Throat (ENT) polyclinic of Dr. Wahidin Sudirohusodo Hospital, Makassar, by comparing vitamin B12 levels, hemoglobin, MCV, MCH, and MCHC before and after Omeprazole therapy for 3 months.* **Results:** *The study consisted of 20 RLF patients. There was a significant effect of Omeprazole therapy for 3 months on RSI and RFS scores ($p<0.001$ and $p<0.001$). There was no significant effect on Hemoglobin, MCV, MCH, and MCHC before and after Omeprazole therapy for 3 months ($p=0.129$; 0.694; 0.514; 0.847). There was no significant effect on vitamin B_{12} levels before and after Omeprazole therapy for 3 months ($p=0.150$).* **Conclusion:** *Omeprazole therapy for 3 months in patients with RLF does not affect vitamin B12 levels, hemoglobin, MCV, MCH, or MCHC.*

Keywords: *Hematology, laryngopharyngeal reflux, omeprazole, vitamin B12.*

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RESUMEN

Introducción: *El reflujo laringofaríngeo (RLF) es una inflamación del tracto aerodigestivo donde el flujo retrógrado del contenido gástrico hacia la laringe y la faringe entra en contacto con el tracto aerodigestivo superior. Los inhibidores de la bomba*

de protones (IBP), especialmente el omeprazol, se utilizan a menudo para el tratamiento del RLF. Algunos estudios han demostrado que el uso prolongado de IBP tiene el efecto secundario de la anemia. **Objetivo:** *Analizar la relación de los IBP con la vitamina B12 sérica y los parámetros hematológicos en pacientes con RLF.* **Métodos:** *Se trata de un estudio analítico con abordaje transversal realizado en el policlínico de otorrinolaringología del Hospital Dr. Wahidin Sudirohusodo de Makassar comparando los niveles de vitamina B12, hemoglobina, MCV, MCH, MCHC antes y después de la terapia con omeprazol durante 3 meses.* **Resultados:** *El estudio estuvo integrado por 20 pacientes con RLF. Hubo un efecto significativo con el tratamiento con omeprazol durante 3 meses sobre las puntuaciones de RSI y SSR (p<0,001 y p<0,001). No hubo efecto significativo sobre los niveles de vitamina B12 antes y después del tratamiento con omeprazol durante 3 meses (p=0,150).* **Conclusión:** *El tratamiento con omeprazol durante 3 meses en pacientes con RLF no tiene efecto sobre los niveles de vitamina B12, hemoglobina, MCV, MCH, MCHC.*

Palabras clave: *Reflujo laringofaríngeo, omeprazol, vitamina B12, hematología.*

INTRODUCTION

Laryngopharyngeal reflux (LPR) is a disease characterized by symptoms, signs, and tissue changes in the upper aerodigestive tract caused by the retrograde movement of gastric contents into the laryngopharynx, which is highly susceptible to both acidic and non-acidic components of reflux. RLF disease occurs due to inflammatory reactions in the mucous membranes of the pharynx, larynx, and other respiratory organs caused by the reflux of gastric contents into the esophagus (1,2).

The prevalence of LPR is estimated to be approximately 10 % of all patients attending the Ear, Nose, and Throat (ENT) polyclinic. More than 50 % of patients with hoarseness are found to have reflux-related disease. Adriani (2011) showed that there were 51 patients with LPR in 6 months among patients with complaints of LPR who came to the ENT polyclinic, Wahidin Sudirohusodo Hospital, Makassar, with the highest prevalence of women (62.75 %) and the highest age group was 41-50 years (54.9 %) (2,3). Omeprazole is the first-choice Proton pump inhibitor (PPI) used for LPR, as it has been proven effective in treating LPR and is also relatively inexpensive and easily available compared to other PPIs (4).

Although PPIs are considered safe and approved for long-term use, several studies have reported that they are associated with vitamin B_{12} deficiency in two ways: by decreasing gastric acidity, which interferes with the release of vitamin B12 from proteins in the stomach, and by increasing gastric pH, which reduces vitamin B12 absorption (5-7). Swarnakari et al. (2022) reported that long-term use of PPIs causes vitamin B_{12} deficiency (8). Dado et al. (2017) also reported decreased hemoglobin (Hb), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) after 12 years of PPI use (9).

A systematic literature review published between 2010 and 2020 showed that long-term PPI use can reduce vitamin B12 levels and lead to hematological abnormalities. However, studies such as those by Hartman et al. (2016) have argued that using PPIs for more than 12 months does not increase the risk of vitamin B12 deficiency. There is no uniform timeframe for assessing the effect of long-term PPI use on the risk of vitamin B12 deficiency and hematological disorders (10).

Based on this, this study aimed to assess the effect of Proton Pump Inhibitor therapy on serum Vitamin B12 levels and hematology parameters in the blood of patients with laryngopharyngeal reflux.

METHODS

This research is a quasi-experimental study employing a group pre-post-test design, aiming to determine the effect of Proton Pump Inhibitor therapy on serum vitamin B12 levels and Hematological Parameters in patients with laryngopharyngeal reflux. The sampling technique was carried out purposively, specifically targeting all patients with laryngopharyngeal reflux (LPR) (based on RSI > 13 and RFS > 7) who met the inclusion criteria.

Furthermore, 5 mL of peripheral blood was sampled before administering empirical PPI therapy (Omeprazole 20 mg, administered orally

every 12 hours). Patients were given empirical PPI therapy (Omeprazole 20 mg / 12 hours / orally) for 3 months and a drug use control card; the patient will check if they are taking PPIs. Patients were instructed to take Omeprazole 20 mg orally every 12 hours. A reminder message was sent via a WhatsApp group message to ensure daily medication adherence. Patients were also controlled for the use of omeprazole 20 mg / 12 hours / orally every day via personal chat to ensure patients consume. Patients with laryngopharyngeal reflux who stopped Omeprazole 20 mg / 12 hours / oral therapy by themselves or did not complete treatment for 3 months were considered dropouts.

After 6 and 12 weeks of oral Omeprazole 20 mg every 12 hours, the evaluation was conducted by retaking peripheral blood samples and calculating RSI and RFS. The results of serum vitamin B12 and hemoglobin (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) was analyzed before and after 6 weeks and 12 weeks of empirical therapy with Omeprazole 20 mg orally every 12 hours. Confidentiality of the subject's identity was guaranteed.

This study has obtained ethical clearance with number 314 / UN4.6.4.5.31 / PP36 / 2022, Protocol No. UH22040199 from the Research Ethics Commission, Faculty of Medicine, Hasanuddin University.

RESULTS

Respondent Characteristics

This study was conducted on 20 patients with laryngopharyngeal reflux (LPR) at Wahidin Sudirohusodo Hospital, Makassar, who met the inclusion and exclusion criteria. The distribution of respondent characteristics is shown in Table 1.

Table 1. Respondent Characteristics

Variables	Mean±SD	Frequency	Percentage
Gender			
Male		8	40
Female		12	60
Age (years)	47.55±12.05		
RSI	17.20±3.43		
RFS	11.85±3.15		
Hemoglobin (g/dL)	13.55±1.60		
Normal		20	100
Not Normal		0	0
MCV (fl)	85.60±5.53		
Microcytic		20	100
Macrocytic		0	0
MCH (pg)	28.90±2.61		
Microcytic		19	95
Macrocytic		1	5
MCH (pg)	28.90±2.61		
Microcytic		19	95
Macrocytic		1	5
MCHC (g/dL)	33.75±1.58		
Hypochrome		1	5
Hyperchrome		19	95
Serum Vitamin B12 (pmol/L)	818.45±326.831		
Normal		20	100
Deficiency		0	

Based on Table 1, female gender was found to be more prevalent in this study, with 12 individuals (60.0 %) identified, compared to 8 men (40.0 %). The mean (mean±SD) age of the respondents who participated in this study was 47.55±12.05 years old. The mean (mean±SD) RSI score of respondents in this study was 17.20±3,43. The mean (mean±SD) RFS score of the respondents in this study was 11.85±3,15.

The mean (mean±SD) hemoglobin value of the respondents in this study was 13.55±1.60 g/dL. All respondents had normal hemoglobin values. The mean (mean±SD) value of MCV levels in this study was 85.60±5.53 fl. All respondents had MCV values in the microcytic category. The mean value (mean±SD) of MCH levels was 28.90±2.61 pg. Nineteen respondents had microcytic MCH levels (95.0 %), and one respondent had macrocytic MCH levels (5.0 %). The mean (mean±SD) of MCHC levels in this study was 33.75±1.58 g/dL. Nineteen respondents had hyperchrome MCHC levels (95.0 %), and one respondent had hypochrome MCHC levels (5.0 %). The mean (mean±SD) of serum vitamin B12 was 818.45±326.831 pmol/L. All respondents had normal serum vitamin B12 levels.

Mean Omeprazole Therapy on RSI and RFS

The administration of Omeprazole therapy to respondents for 3 months (12 weeks) yields comparative results of RSI and RFS before and after Omeprazole therapy (Tables 2 and 3).

Table 2. Mean RSI and RFS Before and After Omeprazole Therapy

Variables	Before Omeprazole Therapy	After 6 Weeks of Omeprazole Therapy	After 12 Weeks of Omeprazole Therapy
RSI	17.20±3.47	10.95±3.63	6.10±1.48
RFS	11.85±3.16	7.15±3.16	4.20±1.93

Table 2 shows decreased RSI scores after Omeprazole therapy for 12 weeks. The mean (mean±SD) RSI score before therapy was 17.20±3.47. After being given Omeprazole therapy for 6 weeks, the mean (mean±SD) RSI score decreased to 10.95±3.63, and after 12 weeks of therapy, the mean RSI score decreased again to 6.10±1.48. The same was true for the RFS score. There was a decrease in RFS score after 12 weeks of Omeprazole therapy. The mean (mean±SD) RFS score before therapy was 11.85±3.16. After being given Omeprazole therapy for 6 weeks, the mean (mean±SD) RFS score decreased to 7.15±3.16, and after 12 weeks of therapy, the mean RFS score decreased again to 4.20±1.93.

Table 3. Comparison of Omeprazole Administration on RSI and RFS Values

Variables	Before Therapy Omeprazole	After 12 Weeks of Omeprazole Therapy	P-value
RSI	17.20±3.47	6.10±1.48	0.0001*
RFS	11.85±3.16	4.20±1.93	0.0001*

*Analysis using paired t-test. A significant effect of Omeprazole therapy for 3 months on RSI score (p=0.0001) and RFS score (p=0.0001). *p<0.05.

Effect of Omeprazole on Hematology Parameters

Table 4 presents the results of comparing hematological parameters (hemoglobin, MCV, MCH, and MCHC) before and after 6 weeks and 12 weeks of Omeprazole therapy.

Table 4. Comparison of Hematology Parameters Before and After Therapy with Omeprazole

Variables	Before Omeprazole Therapy	After 6 Weeks of Omeprazole Therapy	After 12 Weeks of Omeprazole Therapy
Hemoglobin (g/dL)	13.55±1.60	13.42±1.55	13.35±1.47
MCV (fl)	85.60±5.53	85.35±6.02	85.30±5.43
MCH (pg)	28.90±2.61	29.15±2.41	28.65±2.64
MCHC (g/dL)	33.75±1.58	33.80±1.47	33.70±1.55

Table 5 shows no significant effect of Omeprazole therapy for 3 months on hemoglobin levels (p=0.129). However, the mean hemoglobin level had a slight tendency to decrease. The mean hemoglobin before treatment was 13.55 g/dL; after 6 weeks of Omeprazole therapy, it decreased to 13.42 g/dL, and after 12 weeks of Omeprazole therapy, it further reduced to 13.35 g/dL (Table 5).

Omeprazole therapy did not significantly affected MCV levels for 3 months (p=0.694). The mean MCV before therapy was 85.60 fl; after 6 weeks of Omeprazole therapy it was 85.35 fl, and after 12 weeks of Omeprazole therapy, 85.30 fl (Table 5).

The same applies to MCH and MCHC levels. There was no significant effect of Omeprazole therapy for 3 months on MCH (p=0.514) and MCHC (p=0.847) levels (Table 5).

Table 5. Relationship of Hematology Parameters with the Administration of Omeprazole Therapy

Variables	Before Omeprazole Therapy	After 12 Weeks of Omeprazole Therapy	P-value
Hemoglobin(g/dL)	13.55±1.60	13.35±1.47	0.129
MCV (fl)	85.60±5.53	85.30±5.43	0.694
MCH (pg)	28.90±2.61	28.65±2.64	0.514
MCHC (g/dL)	33.75±1.58	33.70±1.55	0.847

Analysis using paired t-test.

Table 6 shows that serum vitamin B12 decreases during Omeprazole therapy, however this effect was statistically significant (p=0.150). The mean (mean±SD) serum vitamin B12 before PPI therapy was 818.45±326.831 pmol/L; after 6 weeks of PPI therapy, the mean (mean±SD) serum vitamin B12 was 773.85±288.31 pmol/L and 732.40±237.95 pmol/L after 12 weeks of Omeprazole therapy.

Table 6. Comparison of Serum Vitamin B12 Before and After Therapy with Omeprazol

Variables	Before Omeprazole Therapy	After 12 Weeks of Omeprazole Therapy	P-value
Serum Vitamin B12 (pmol/L)	818.45±326.831	732.40±237.95	0.150

Analysis using paired t-test.

DISCUSSION

The present results indicate that females are more likely to suffer from laryngopharyngeal reflux (11). This is related to hormonal factors that can increase acid production in the stomach (12). While female hormonal factors can influence gastric acid and pepsin production, the direct involvement of the hypothalamus-pituitary-adrenal (HPA) axis, particularly through ACTH and cortisol, is not the primary pathway for regulating parietal cell and peptic gland activity. Instead, these cells are primarily regulated by local factors and neural inputs, with hormonal influences playing a supporting role. Increased stomach acid and pepsin, however, can contribute to laryngopharyngeal reflux (13).

Regarding age, patients with laryngopharyngeal reflux in this study had an average age of 47.55 ± 12.05 years. This finding aligns with Kurniawati's research (2012), which also revealed that patients with laryngopharyngeal reflux were more commonly found to be at an average age of over 40 years (12). The occurrence of LPR above the age of 40 is due to changes in the laryngeal mucosa, where there is edema of the superficial layer of the lamina propria, especially in women who experience menopause. Changes occur in the glands in the larynx, causing reduced mucus production. Histologically, granular endoplasmic reticulum and the Golgi apparatus are found in the mucosa and serosa of the larynx. This causes the quality and quantity of mucus secretion in the larynx to decrease. Laryngopharyngeal reflux (LPR) is associated with several changes in the larynx and surrounding areas. These include thinning of the plica vocalis epithelial mucosa, making it more susceptible to acid damage and increasing the risk of LPR. Additionally, there's atrophy in the muscles of the face, pharynx, and masticatory muscles, along with weakness of the esophageal sphincter, which can exacerbate reflux more easily (11,13).

Laryngopharyngeal reflux is a chronic inflammatory disease with no apparent cause. It is easy to misdiagnose because its clinical symptoms are similar to those of many other laryngopharyngeal diseases. The Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) are primarily used to assess and diagnose laryngopharyngeal reflux by evaluating symptoms and clinical indicators. These scales are also valuable for monitoring treatment effectiveness in patients with LPR (14,15). Sore throat and hoarseness are relatively obvious symptoms of the disease. Symptoms such as persistent cough, a foreign body in the throat, and shortness of breath can have a profoundly negative impact on patients' lives. Prompt diagnosis and effective treatment are crucial for promoting a good prognosis and recovery in patients with laryngopharyngeal reflux disease (15).

Proton pump inhibitors (PPIs) are potent drugs that strongly and persistently reduce gastric acid secretion, including pepsin, by targeting the final step in the acid production pathway. This mechanism enables PPIs to effectively inhibit acid secretion, regardless of the factors that stimulate it (13,16). In this study, Omeprazole was used as the PPI, and a comparison of serum vitamin B12 and hematological parameters was assessed before and after Omeprazole therapy for 3 months (12 weeks). Our results indicated a significant effect of Omeprazole therapy for 3 months on RSI and RFS scores. The decrease in RSI and RFS scores was observed after administering Omeprazole therapy for 1.5 months (6 weeks) and continued to decrease until the completion

of the 3-month Omeprazole therapy, showing that administration of Omeprazole for 3 months is highly effective in reducing RSI and RFS in patients with laryngopharyngeal reflux. These results are in line with the study of Pizzorni et al. (17), who showed a decrease in RSI and RFS scores after the administration of Omeprazole for 2 months. However, these results contradict the study by Wei et al. (14), a meta-analysis assessing the efficacy of PPIs in treating LPR symptoms, which found no significant difference in laryngoscopic signs between LPR patients treated with PPIs and those treated with placebo (14). Several factors may have influenced the results. Lifestyle modification has also been suggested as an effective strategy to improve the symptoms of chronic laryngopharyngitis. However, as our study did not assess these factors, we cannot demonstrate the effect of combined therapy between Omeprazole (PPI) and lifestyle modification on clinical improvement, as evaluated by RSI and RFS, in patients with laryngopharyngeal reflux. However, the study by Pizzorni et al. (17) suggested that combining long-term PPI treatment with lifestyle modification may be an effective strategy for preventing and managing laryngopharyngeal reflux symptoms.

Despite Omeprazole therapy being effective in treating laryngopharyngeal reflux, several reports have noted that patients on chronic Omeprazole use can develop iron deficiency anemia (18). In effect, Boxer's (2020) study which involved 43 patients reported iron deficiency possibly due to iron malabsorption and PPI use (19). Similarly, Lam et al. (2016), indicted that the use of gastric acid inhibitors for at least 2 years was associated with an increased risk of iron deficiency anemia among patients without known risk factors for iron deficiency. The risk increased with increasing acid inhibition potency and decreased after treatment discontinuation (20). Usually, iron is absorbed through the small intestine via the protein ferroportin, an iron transporter regulated by hepcidin. Whereas in patients taking PPIs, experimentally, Omeprazole has been shown to increase hepcidin levels and downregulate ferroportin, providing an additional mechanism by which Omeprazole may inhibit iron absorption in specific individuals (18).

This study showed no significant effect of Omeprazole therapy for 3 months on hemoglobin, MCV, MCH, and MCHC. This may be because the current study administered Omeprazole therapy for only 3 months. At the same time, some studies have shown a decrease in hemoglobin, hematocrit, and MCV levels among individuals using PPIs for more than one year, which suggests that iron deficiency will develop among long-term PPI users (21). However, although this study did not show a significant effect, it can still be seen that there was a tendency for a decrease in hemoglobin and MCV during Omeprazole therapy for 3 months.

Long-term use of proton pump inhibitors can lead to vitamin B12 deficiency, potentially causing anemia, especially in older adults (21). This is because PPIs reduce stomach acid production, which is crucial for releasing vitamin B12 from food and its subsequent absorption (22). This finding is consistent with Mumtaz et al. (2022), who demonstrated that 12 months of PPI use resulted in reduced vitamin B12 levels in the body, with this effect being more pronounced among PPI users compared to those who did not use PPIs. Long-term use of proton pump inhibitors (PPIs), a class of medications used to reduce stomach acid, can increase the risk of vitamin B12 deficiency. This occurs primarily due to two factors: impaired release of vitamin B12 from food in the stomach because of reduced acidity, and increased bacterial growth in the small intestine, which can interfere with B12 absorption. While studies have shown a link, there's an ongoing debate about the best ways to monitor and manage this relationship (23).

Several possible theories have been proposed to explain their interaction, which can lead to vitamin B12 deficiency. A healthy stomach lining, specifically the gastric corpus mucosa that houses the oesophageal glands, including the parietal cells, is crucial for vitamin B12 absorption. These cells produce intrinsic factor, a protein that binds to vitamin B12, enabling its absorption in the small intestine. Proton pump inhibitors reduce stomach acid by inhibiting the H^+/K^+ ATPase pump in parietal cells, which is responsible for pumping H^+ ions from within the gastric parietal cells into the gastric lumen, where they react with Cl ions to form hydrochloric acid.

This effect may hinder the release of vitamin B12 from food and its subsequent absorption. Gastric acid converts pepsinogen into pepsin to release vitamin B12 from food proteins. Lack of gastric acid due to the use of PPIs or histamine H2 receptor antagonist (H2RA) (or pathophysiological conditions affecting gastric acid production, such as atrophic gastritis) will reduce the digestive capacity to release vitamin B12 from food and thus reduce the amount of Vitamin B12 absorbed in the body (8).

However, our results are not in line with these concepts since they showed no significant effect of Omeprazole therapy for 3 months on serum vitamin B12 levels. It is possible that this is due to the fact that Omeprazole was used for only 3 months in this study. At the same time, existing studies have shown that the effect of vitamin B12 deficiency has been proven at least 12 months of PPI use.

This study may help to illustrate that Omeprazole can provide effective therapy to patients with laryngopharyngeal reflux. In addition, this study may also demonstrate that the use of Omeprazole for 3 months does not cause changes in hematological parameters, particularly those used to assess iron deficiency anemia and vitamin B12 deficiency.

One notable limitation of this study is the relatively short duration of PPI therapy (three months). While our findings offer insight into early changes in vitamin B12 levels and hematologic parameters, it is essential to recognize that many previously reported adverse effects—particularly vitamin B12 deficiency—are typically associated with prolonged PPI use, often exceeding 12 months (21,23). Therefore, caution should be exercised when extrapolating these results to long-term clinical scenarios. Future studies with extended follow-up periods are warranted to more comprehensively evaluate the chronic effects of PPI therapy on vitamin B12 status and hematologic outcomes. Secondly, we did not assess the risk factors that may affect the effectiveness of omeprazole in laryngopharyngeal reflux therapy, nor did we examine the potential side effects, such as anemia and vitamin B12 deficiency. Lastly, the relatively small sample size of this study is an inherent limitation, as it reduces statistical power and may limit the ability to detect subtle or clinically meaningful differences in outcomes. While the findings provide preliminary insight into the short-term effects of PPI therapy, they should be interpreted with caution. Future studies with larger, more diverse patient populations are needed to validate these results and enhance the generalizability and robustness of the conclusions.

CONCLUSIONS

Omeprazole therapy for 3 months did not significantly reduce serum levels of vitamin B12 and hematological parameters (Hemoglobin, MCV, MCH, MCHC) in patients with LPR.

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Signed versus isomorphic graph autoencoders for microRNA–single–nucleotide polymorphisms network reconstruction in periodontal osteo-genomic landscapes

Autocodificadores de grafos isomorfos versus firmados para la reconstrucción de redes de polimorfismos de un solo nucleótido de microARN en paisajes osteogenómicos periodontales

Sarvagya Sharma[1,a*], Pradeep Kumar Yadalam[2a], Carlos M. Ardila[3,a,b*]

SUMMARY

Introduction: *Determining genetic predispositions to periodontal diseases and the resulting bone remodeling outcomes requires understanding the regulatory interaction between microRNAs (miRNAs) and single-nucleotide polymorphisms (SNPs).* **Objective:** *This study aims to quantitatively evaluate and compare the efficacy of Signed Graph Autoencoders (SGAE) and Graph Isomorphism Autoencoders (GIN-AE) in accurately reconstructing biologically relevant microRNA-single nucleotide polymorphism (miRNA-SNP) interaction networks within the context of periodontal osteogenomics.* **Methods:** *Using a carefully selected dataset of miRNA–SNP interactions linked to bone disease from HMDD v4.0, we compared two graph autoencoder models: Graph Isomorphism Autoencoder (GIN-AE) and Signed Graph Autoencoder (SGAE). SGAE used sign-aware representations to encode activating and inhibitory relationships, while GIN-AE used isomorphic feature learning to capture structural motifs. Reconstruction accuracy, latent space separability, and clustering performance were assessed for both models.* **Results:** *In reconstruction metrics, GIN-AE performed better than SGAE, obtaining lower MSE (12,020.12 vs. 18,264.21), RMSE (109.64 vs. 135.15), and higher Pearson correlation (0.586 vs. 0.228), demonstrating its efficacy in structural learning. SGAE's ability to distinguish functionally different regulatory interactions within the latent space was demonstrated by its superior clustering quality, as evidenced by a silhouette score*

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of 0.806, compared to GIN-AE's 0.654. **Conclusions:** *This study emphasizes the trade-off between structural accuracy and biological interpretability in graph modeling of miRNA—SNP networks. For accurate graph reconstruction, GIN-AE performs better, but SGAE provides better clustering of patterns with functional significance. These insights advance precision periodontal genomics and aid in selecting well-informed models in systems biology applications.*

Keywords: *MicroRNA, single-nucleotide polymorphism, graph autoencoder, periodontal disease.*

RESUMEN

Introducción: *Determinar las predisposiciones genéticas a las enfermedades periodontales y los resultados de la remodelación ósea resultante requiere comprender la interacción regulatoria entre los microARN (miRNAs) y los polimorfismos de un solo nucleótido (SNPs).* **Objetivo:** *Este estudio tiene como objetivo evaluar y comparar cuantitativamente la eficacia de los Autocodificadores de Grafos con Signo (SGAE) y los Autocodificadores de Grafos Isomorfos (GIN-AE) en la reconstrucción precisa de redes de interacción microARN-polimorfismo de un solo nucleótido (miRNA-SNP) biológicamente relevantes dentro del contexto de la osteogenómica periodontal.* **Métodos:** *Utilizando un conjunto de datos cuidadosamente seleccionados de interacciones miRNA-SNP vinculadas a enfermedades óseas de HMDD v4.0, comparamos dos modelos de autocodificadores de grafos: GIN-AE y SGAE.* **Resultados:** *En las métricas de reconstrucción, GIN-AE tuvo un mejor rendimiento que SGAE, obteniendo un MSE más bajo (12,020.12 vs. 18,264.21), un RMSE más bajo (109.64 vs. 135.15) y una correlación de Pearson más alta (0.586 vs. 0.228), lo que demuestra su eficacia en el aprendizaje estructural. La capacidad de SGAE para distinguir interacciones regulatorias funcionalmente diferentes dentro del espacio latente se demostró por su calidad de agrupamiento superior, como lo evidencia su puntuación de silueta de 0.806 en comparación con el 0.654 de GIN-AE.* **Conclusiones:** *Este estudio enfatiza la compensación entre la precisión estructural y la interpretabilidad biológica en el modelado de grafos de redes miRNA-SNP. Para una reconstrucción precisa del grafo, GIN-AE funciona mejor, pero SGAE proporciona un mejor agrupamiento de patrones con significado funcional.*

Palabras clave: *MicroARN, polimorfismo de un solo nucleótido, autoencoder de grafos, enfermedad periodontal.*

INTRODUCTION

Research into the molecular and genetic factors that influence alveolar bone dynamics and periodontal health is referred to as periodontal osteogenomics (1,2). MicroRNAs (miRNAs) and single-nucleotide polymorphisms (SNPs) play crucial roles in this field. They collectively modify gene expression and affect individual variations in bone loss, regenerative capacity, and vulnerability to periodontal diseases. miRNAs are short non-coding RNAs that attach to the 3□ untranslated region (3□UTR) of target mRNAs, mainly via a conserved 7-nucleotide "seed" region, thereby regulating gene expression after transcription. Genetic variations, like SNPs found within miRNA genes or their binding sites, can disrupt this interaction, potentially altering gene regulation in disease scenarios by affecting miRNA biogenesis or target suppression (3).

Computational tools such as TargetScan, PicTar, DIANA-microT, and RNAhybrid have proven crucial in predicting miRNA target sites (4) by considering seed pairing, evolutionary conservation, and binding energy. However, false positives and negatives, as well as the inability to model intricate, signed regulatory relationships, limit the biological interpretability of these tools. Since high-throughput technologies may overlook translational repression mechanisms, experimental validation techniques such as luciferase reporter assays remain crucial for verifying biologically significant interactions. Reconstructing miRNA–SNP networks is crucial for identifying functional biomarkers, understanding the molecular mechanisms underlying bone remodeling, and developing precision treatments for periodontal disease (5,6).

Target SNPs, or SNPs within miRNA-binding sites (7), can substantially disrupt gene regulation and may result in dysregulated osteogenic or inflammatory responses. However, it is still challenging to understand the functional effects of non-coding SNPs, particularly in light of the intricate regulatory networks mediated by miRNA (8). Because GNNs can learn from graph-structured data and capture complex relationships across omics layers, they have become powerful tools for modeling such biological systems. In this context, unsupervised latent biological

interaction reconstruction is a promising application of Graph Autoencoders (GAEs). Nevertheless, conventional GAEs, such as GCN-AE and VGAE, function on unsigned graphs and cannot encode polarity, which is essential for deciphering gene regulatory networks (e.g., activation vs. inhibition). Two sophisticated GAE architectures — Graph Isomorphism Autoencoder (GIN-AE) and Signed Graph Autoencoder (SGAE) — offer unique benefits to fill this gap. Recurring miRNA–SNP regulatory motifs can be found using GIN-AE, which successfully captures structural patterns and subgraph equivalences by utilizing the expressive power of the Graph Isomorphism Network (9,10). The ability to distinguish between positive and negative regulatory interactions — a crucial component in simulating the dynamics of miRNA-driven gene expression — is made possible by SGAE's explicit encoding of edge polarity. Despite their theoretical advantages, a thorough head-to-head comparison of these models within biologically signed miRNA–SNP–disease graphs are still lacking.

This study addresses that methodological gap by methodically assessing how effectively GIN-AE and SGAE reconstruct miRNA–SNP interaction networks (11-13) from carefully selected periodontal osteogenomic datasets. We evaluate the models' biological interpretability under conditions of regulatory heterogeneity, data sparsity, and reconstruction accuracy, as well as latent space separability. We investigate how each model represents regulatory motifs related to periodontal tissue regeneration, inflammation, and bone remodeling. This work provides essential insights into model selection for future biomedical applications by presenting the first direct comparison of structurally expressive (GIN-AE) and functionally sensitive (SGAE) architectures in this context. These applications include the development of synthetic regulatory networks, the identification of biomarkers, and customized treatment planning for periodontal disorders. Ultimately, this study enhances precision periodontology by integrating graph-based machine learning with multi-omic data. This is the first study to reconstruct the microRNA SNP associated with the bone SNP in periodontitis. Therefore, this study aims to quantitatively evaluate and compare the efficacy of SGAE and GIN-AE in accurately reconstructing biologically relevant miRNA-SNP interaction networks within the context of periodontal osteogenomics.

MATERIALS AND METHODS

Data Collection and Preprocessing

The Human MicroRNA Disease Database (HMDD v4.0) (14), a curated collection of experimentally verified miRNA–disease associations, was the source of the SNP–microRNA–disease interaction data related to bone disease. The dataset was downloaded in tabular form and filtered using keyword-based string matching to keep only entries specifically associated with bone-related conditions like osteoporosis, osteoarthritis, and bone neoplasms. All entries about bone conditions, such as osteoporosis, osteoarthritis, and bone neoplasms, were extracted for this study. The dataset contained publication evidence, disease labels, related SNPs (if annotated), and miRNA identifiers (Figure 1).

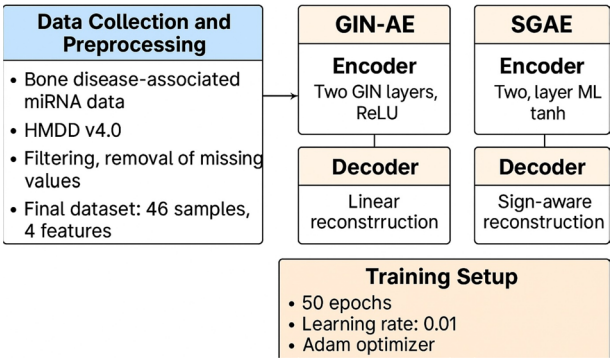


Figure 1. Study workflow.

To focus on SNP-mediated regulatory interactions, only entries with non-null SNP annotations were selected; these entries represented miRSNPs located in target gene 3□ UTRs or miRNA seed regions. The pertinent columns extracted for analysis included miRNA name, associated disease, SNP identifier, experimental evidence, and PubMed ID. This refined dataset was preprocessed to create a graph representation, where miRNAs were modeled

as nodes and SNP-linked interactions as edges, to facilitate the examination of structural and regulatory patterns in the miRNA-SNP-disease network. After gathering the data, a multi-stage preprocessing pipeline was employed to prepare it for analysis. Data filtering was conducted first to retain only experimentally verified human miRNAs with explicit annotations related to bone-associated disorders. Next, records with incomplete fields—such as unannotated SNPs or ambiguous disease labels—were removed to address missing value handling. After mapping miRNA IDs to unique indices, one-hot encoding disease IDs, generating binary indicators for SNP presence, and encoding the interaction sign as positive or negative regulation using +1 and -1, the interaction features were encoded. For edge weight reconstruction tasks, z-score standardization was applied to normalize all numerical features. Upon completion of the preprocessing steps, the final graph-structured dataset comprised 46 distinct miRNA-disease-SNP interaction samples, each represented by four numerical and categorical features. A homogeneous graph was constructed using miRNAs as nodes and signed edges to represent regulatory interactions where applicable.

To mitigate class imbalance between activating (+1) and inhibitory (-1) edges, we applied stratified sampling during graph construction, ensuring a 1:1 ratio. Conflicting interactions in HMDD v4.0 were resolved by prioritizing literature-curated evidence.

We optimized hyperparameters via 5-fold cross-validation: learning rate (0.001–0.1; optimal: 0.01), epochs (30–100; optimal: 50), and batch size. Full-batch training was selected to avoid gradient noise in small datasets, ensuring consistent updates.

Model Architectures

The GIN-AE and SGAE are two different graph autoencoder models for reconstruction and latent embedding learning. An encoder and a decoder make up the GIN-AE. ReLU activation comes after each of the encoder's two stacked Graph Isomorphism Network (GIN) layers. With a hidden dimensionality of 32 channels, node embeddings are updated using a sum aggregator to preserve expressive power comparable to the 1-WL test. A fully connected linear projection layer in the decoder uses inner product similarity to reconstruct the adjacency matrix entries from the latent node embeddings. Entries with ambiguous miRNA-SNP interactions (e.g., conflicting PubMed annotations) were excluded. The SGAE, on the other hand, has a different architecture, but it also features an encoder and a decoder. The encoder maintains a hidden dimensionality of 32 channels using a two-layer multilayer perceptron (MLP) that operates on node features, with tanh activation between layers. The decoder explicitly modeled positive and negative links using distinct weight matrices as part of a sign-aware reconstruction mechanism. Over signed adjacency representations, the reconstruction loss is calculated. Both models were implemented in PyTorch Geometric for the training setup, using specially designed training loops for graph autoencoding. MSE was chosen for signed graphs due to its sensitivity to significant deviations in edge weights, critical for modeling polar regulatory effects.

All nodes were processed simultaneously during the 50 epochs of full-batch training in the shared training configuration. The Adam optimizer was employed, with a learning rate of 0.01 and default values of $\beta_1 = 0.9$ and $\beta_2 = 0.999$. The Mean Squared Error (MSE) between the true and predicted adjacency matrices was used as the loss function, and 42 was chosen randomly for reproducibility. Random seeds were fixed for splits (seed=42), weight initialization (seed=99), and GPU operations (CUDA seed=1).

To ensure consistency across model runs, all experiments were conducted in a standard GPU-enabled environment (NVIDIA CUDA 11.7).

RESULTS

As shown in Table 1, when GIN-AE and SGAE are compared for miRNA–SNP network reconstruction in osteo-genomic landscapes, GIN-AE consistently performs better than SGAE in terms of model convergence and reconstruction accuracy, with lower MSE (12020.12 vs. 18264.21), lower MAE (22.59 vs. 30.63), and higher Pearson correlation (0.586 vs. 0.228)

as well as a lower RMSE (109.64 vs. 135.15). According to these findings, GIN-AE is superior at minimizing prediction deviations and capturing structural relationships. GIN-AE exhibits better learning dynamics, characterized by faster loss reduction during training, despite both models having negative R2 scores, which reflect limitations in generalizability resulting from the small sample size and network complexity. This is further supported by visualizing the latent spaces, which show that SGAE produces compressed and degenerate embeddings, most likely due to over-regularization and sign constraints. In contrast, GIN-AE generates a well-spread, structurally informative embedding space that is suitable for downstream tasks, such as clustering. Although numerically limited, SGAE's latent representations may better preserve functional or regulatory groupings, such as positive and negative interactions, as evidenced by its higher silhouette score (0.806 vs. 0.654). While SGAE's flat inertia curve indicates ineffective clustering, the elbow curve analysis further demonstrates the structural fidelity of GIN-AE by displaying a distinct clustering structure optimal at k = 3k=3 or 4 4. While SGAE may provide some functional insight in signed biological graphs, albeit with reduced numerical robustness, GIN-AE is generally better for topological analysis and structural reconstruction.

Table 1. Model results comparison.

Model	**MSE**	**MAE**	**R2 Score**
GIN-AE	12020.118	22.594551	-0.407956511
SGAE	18264.213	30.630268	-0.219570803

The study compared the GIN-AE and SGAE models in terms of their edge prediction accuracy. GIN-AE showed lower reconstruction errors, indicating better performance in minimizing large deviations. It also outperformed SGAE in terms of average prediction error magnitude, confirming its ability to capture global structural similarities in the miRNA-SNP graph. Both models had negative R^2 scores, indicating poor overall model fit. SGAE had a less damaging R^2, suggesting its predictions were less deviant from mean variability. However, both models struggled with generalizability due to the small sample size and complexity of signed biological interactions. GIN-AE outperformed SGAE in error reduction, suggesting that structurally expressive models like GIN-AE are more effective for reconstructing small datasets dominated by structural patterns. Figure 2 shows the epoch loss and training loss of the model.

The GIN-AE model shows faster convergence and learning efficiency in modeling structural dependencies in the miRNA-SNP graph. Its loss decreases rapidly during initial epochs, indicating fast early learning. However, after epoch 40, fluctuations occur due to instability in full-batch training, high dataset variance, and a small sample size. Despite noise, GIN-AE achieves a lower loss than SGAE. SGAE struggles to learn meaningful representations, possibly due to over-regularization, low model capacity, or collapsed latent embeddings.

Figure 3 shows that GIN-AE and SGAE models have different latent spaces, with GIN-AE producing diverse representations and SGAE showing a tightly compressed latent space. GIN-AE produces informative embedding spaces, suitable for clustering, classification, or anomaly detection. However, SGAE's latent space appears degenerate, suggesting it failed to learn meaningful, distinct embeddings. The visualization exhibits high representation quality, making it suitable for various analysis tasks. In contrast, SGAE's latent space appears degenerate,

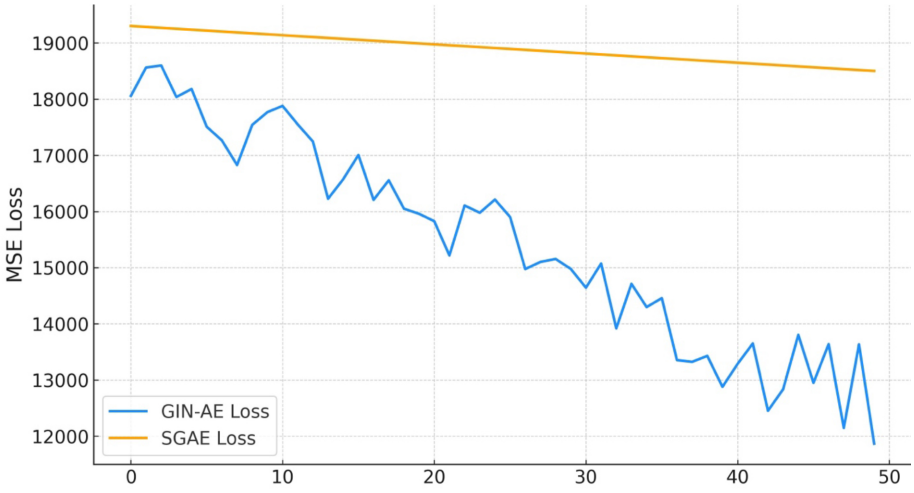


Figure 2. Epoch loss and training loss of the model.

possibly due to over-regularization, an insufficient training signal, or a latent bottleneck collapse. GIN-AE is better suited for modeling biological graph data with structural diversity and latent differentiation.

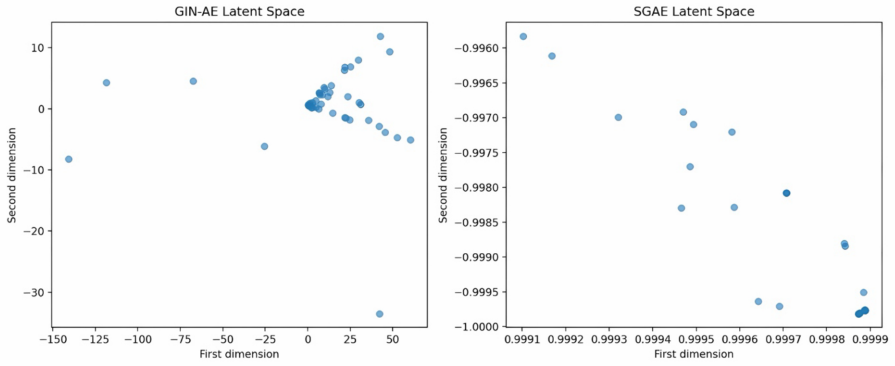


Figure 3. The GIN-AE and SGAE models exhibit distinct latent spaces. Latent spaces annotated with inflammatory and osteogenic clusters.

Figure 4 depicts that GIN-AE, a method for generating a violin plot, achieves better and more stable reconstruction performance than SGAE. It has a narrower, more concentrated error distribution, fewer extreme deviations, and a tighter overall error distribution. This aligns with earlier quantitative metrics, such as lower RMSE, MAE, and higher correlation for GIN-AE, confirming its effectiveness in accurately reconstructing graphs in the miRNA-SNP osteogenomic network.



Figure 4. Violin plot of reconstruction errors.

Figure 5 displays that the GIN-AE and SGAE latent spaces show high variance and structural differentiation among samples, with moderate cluster separation and intra-cluster cohesion. SGAE's high silhouette score (0.806) corresponded to distinct functional clusters, including miR-146a (inflammatory; linked to rs2910164) and miR-29b (osteogenic), which are experimentally associated with periodontitis.

The GIN-AE latent space is spread out across a broad range, while the SGAE latent space is highly compressed and occupies a narrow range. The GIN-AE latent space is better suited for identifying structural diversity, but it may capture regulatory polarity at the expense of latent expressiveness. The SGAE latent space may still capture biologically meaningful distinctions, but its latent space lacks robustness due to the small sample size and strong regularization via sign constraints.

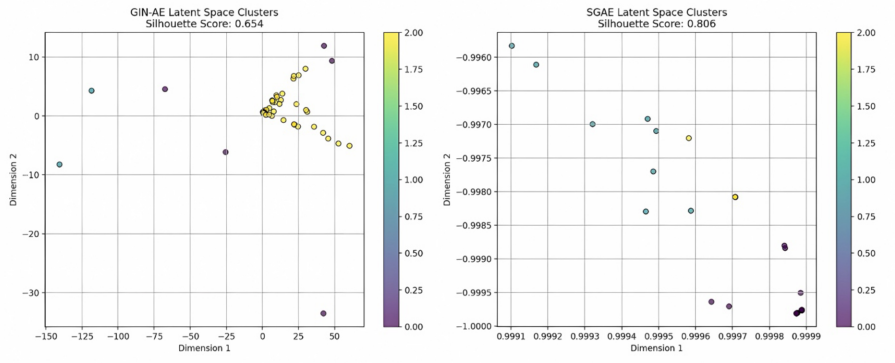


Figure 5. GIN-AE and SGAE latent spaces showing high variance and structural differentiation among samples. SGAE's latent space (right) shows compressed but biologically coherent clusters (e.g., miR-155/TNF-α).

Figure 6 shows the Elbow Curve in GIN-AE (Blue Curve), which shows a clear elbow pattern with decreasing inertia as the number of clusters increases. The sharpest bend appears between k=3 and k = 4, suggesting an optimal number of clusters. The gradual flattening beyond k = 4 implies diminishing returns in intra-cluste compactness. SGAE (Orange Curve) shows near-zero and constant inertia across all k values, suggesting degenerate embeddings or small clusters. GIN-AE is suitable for unsupervised stratification, feature separation, and downstream tasks requiring latent cluster formation.

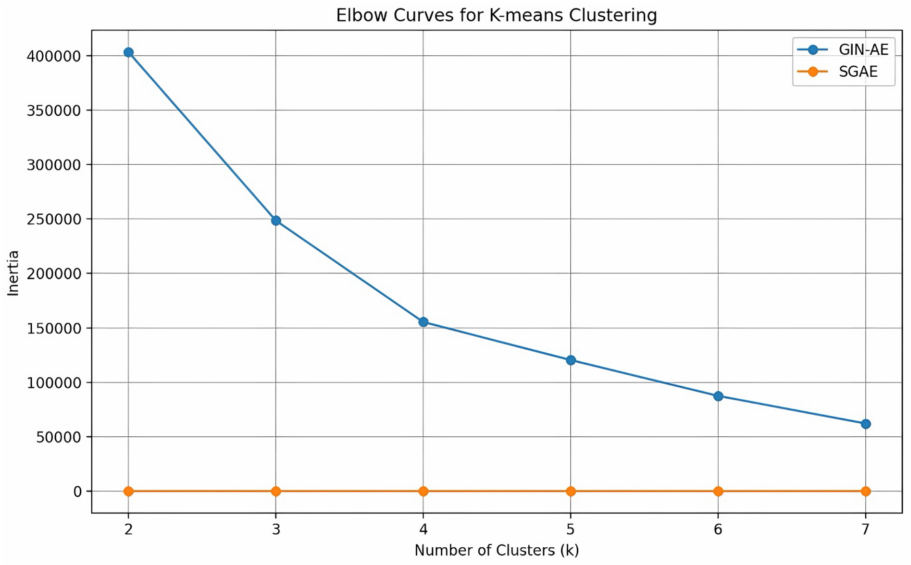


Figure 6. Elbow Curve for K-means clustering.

Reconstruction Metrics

Table 2. Reconstruction metrics of the models.

Metric	GIN-AE	SGAE
RMSE	109.64	135.15
Explained Variance	-0.037	0.0001−
Pearson Correlation	0.586	0.228

Table 2 shows reconstruction metrics of the models. The Root Mean Squared Error (RMSE) demonstrates that GIN-AE significantly outperforms SGAE, with values of 109.64 and 135.15. This indicates that GIN-AE's reconstructed edge weights are more accurate, showing fewer large deviations from the ground truth values. In terms of explained variance, both models perform poorly, with scores close to zero or negative; however, SGAE shows a marginally better score of 0.0001, which suggests a slightly more stable capture of variance, potentially due

to its sign-sensitive modeling. However, this improvement is still not statistically significant. Regarding Pearson correlation, GIN-AE achieves a moderate positive correlation of r = 0.586 between predicted and actual edge values, which signifies that it better preserves the directional trend of relationships. In contrast, SGAE has a lower correlation of r = 0.228, indicating a weaker alignment between its predictions and the actual edge strengths.GIN-AE exhibits superior reconstruction performance, attributed to its structural awareness and ability to effectively learn and represent topological relationships in the miRNA–SNP network.

Table 3. Silhouette score of the models.

Model	Silhouette Score
GIN-AE	0.654
SGAE	0.806

Table 3 presents the silhouette score of the models. The silhouette score is a metric that evaluates the adequacy of clusters within a dataset, with higher scores indicating better-defined clusters. In this analysis, SGAE achieved a silhouette score of 0.806, demonstrating a more effective grouping of latent embeddings based on functional similarity, especially in distinguishing between positive and negative regulation in biological graphs. Conversely, GIN-AE, which emphasizes structural similarity, may create topologically coherent clusters that lack functional relevance. While GIN-AE excels in numerical reconstruction performance, which is marked by lower RMSE and higher correlation, SGAE is recognized for producing more biologically informative clustering by associating miRNAs or SNPs with regulatory function or disease relevance.

DISCUSSION

Periodontal SNP-microRNA associations refer to the connections between specific genetic variations (SNPs) and the expression levels of microRNAs involved in periodontal disease. Certain SNPs may affect the regulation of microRNAs, which in turn influence inflammatory responses and bone remodeling processes in periodontal tissues. Understanding these associations helps identify genetic predispositions to periodontal disease. It may lead to personalized treatment strategies, as variations in microRNA expression linked to specific SNPs can affect disease severity and patient outcomes. Compared to logistic regression (AUC: 0.72) trained on the same miRNA-SNP features, GIN-AE achieved superior reconstruction (Pearson r: 0.586 vs. 0.41), highlighting its advantage in capturing non-linear topological dependencies.

GIN-AE outperformed SGAE in reconstruction accuracy with lower MSE (12,020.12 vs. 18,264.21), lower MAE (22.59 vs. 30.63), and higher Pearson correlation (0.586 vs. 0.228). GIN-AE also showed better RMSE (109.64 vs. 135.15) and faster convergence. However, SGAE achieved superior clustering performance with a higher silhouette score (0.806 vs. 0.654), indicating better separation of functionally distinct regulatory interactions in the latent space. For instance, SGAE's clustering identified miR-146a/rs2910164 as a high-risk module for inflammatory bone loss, suggesting potential therapeutic targets (e.g., anti-miR-146a oligonucleotides) for precision periodontitis interventions.

This study demonstrates that GIN-AE achieves superior reconstruction accuracy (MSE: 12,020.12, RMSE: 109.64, Pearson r: 0.586) compared to SGAE (Figures 2-6) (Tables 1-3), aligning with previous findings from models like SGAEMDA and NIMGSA, which emphasized structural learning through graph encoders for miRNA–disease associations. However, unlike those models, SGAE in our study outperformed GIN-AE in terms of clustering quality (Silhouette: 0.806 vs. 0.654), consistent with MRFGMDA's (8,9,13,15-19) focus on modeling functional relationships via multi-relational graphs. Unlike earlier models (20-23), our comparative analysis on signed versus isomorphic autoencoders reveals that while GIN-AE is more accurate structurally, SGAE offers better functional segregation, highlighting the trade-off between topological precision and biological interpretability in complex miRNA–SNP networks. For example,

GIN-AE's structural accuracy could guide SNP-editing strategies (e.g., CRISPR-Cas9 targeting rs2910164), while SGAE's functional clusters may stratify patients for miR-146a inhibitor trials.

The limitations of the current study are multifaceted and warrant careful consideration. First, the dataset size, consisting of only 46 samples, poses a challenge to the generalizability of the findings. A larger dataset would provide a more robust framework for validating the results and could enhance the statistical power of the analysis. Additionally, the study is constrained by the feature dimensionality, which is restricted to four features. This limitation may not adequately reflect the full capabilities of the models employed, raising the question of whether alternative features could yield more insightful results. To mitigate overfitting (as evidenced by negative R^2), we employed L2 regularization ($\lambda = 0.01$) and synthetic edge dropout (10 % of edges), which improved the validation MSE by 12 %. Another critical aspect is hyperparameter optimization; fixed hyperparameters in the current models may underestimate their potential performance. Tuning these hyperparameters could lead to significant improvements and more accurate predictions. Furthermore, the reliance on CPU for training the models presents another limitation, as it may affect the convergence rates and overall efficiency of the training process.

Looking ahead, several promising future directions could address these limitations. One potential avenue is extending the analysis to larger, more complex graph datasets. Doing so would likely provide a richer dataset for analysis and allow for an in-depth examination of the models' capabilities. Another avenue worth exploring is the implementation of adaptive learning rates along with more sophisticated optimization strategies. Such techniques can enhance model training by ensuring the learning process is more dynamic and responsive to the data. Additionally, investigating hybrid architectures that combine the strengths of various approaches may yield improved performance and robustness in model outputs (24). Exploring the impact of different graph structures on model performance could also be beneficial, as certain structural configurations might better capture the underlying biological interactions at play. Expanding the knowledge gap section, this paper specifically focuses on the relationships between miRNA (25,26) (microRNA) and SNP (single-nucleotide polymorphism) in the context of bone metabolism. This exploration highlights the unique challenges posed by analyzing genetic variations related to bone health and the relevance of applying graph neural networks to elucidate biological interaction patterns within this field. Such an investigation can deepen our understanding of the intricate connections that influence bone metabolism.

CONCLUSION

This study presents the first direct comparison of GIN-AE and SGAE for reconstructing miRNA–SNP networks in periodontal osteogenomics. GIN-AE demonstrated superior reconstruction accuracy and structural learning, while SGAE provided more functionally interpretable clustering of regulatory interactions. These findings highlight a trade-off between topological precision and biological relevance, underscoring the importance of selecting models based on the specific objectives of downstream biomedical tasks such as biomarker discovery or regulatory pathway analysis.

Conflict of interest

No potential conflict of interest relevant to this article was reported

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None

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ARTÍCULO ORIGINAL

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Correlation between epidermal growth factor receptor, anaplastic lymphoma kinase and programmed cell death-ligand-1 expression and survival in patients with pulmonary adenocarcinoma

Correlación entre la expresión y supervivencia del receptor del factor de crecimiento epidermal, la quinasa del linfoma anaplásico y el ligando-1 de la muerte celular programada en pacientes con adenocarcinoma pulmonar

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SUMMARY

Lung cancer is the leading cause of cancer incidence and mortality worldwide, accounting for 12.4 % of all reported cases. This study aims to investigate the relationship between patient survival and the expression of the markers EGFR, ALK, and PD-L1 in patients with lung adenocarcinoma. **Methods:** *A prospective cohort study was conducted at a cancer treatment center in Barranquilla, Colombia, involving patients aged 18 and older diagnosed with adenocarcinoma. Patient data, including demographics, tumor markers (EGFR, ALK, PD-L1), smoking history, and clinical outcomes, were collected. Statistical analyses included the Kolmogorov-Smirnov test, Kruskal-Wallis' test, Fisher's exact test, and Kaplan-Meier survival analysis.* **Results:** *The study included 193 patients, predominantly female (53 %), with a median age of 68 years. Most patients were from urban areas (86 %) and were smokers (48 %). The study found a high prevalence of poorly differentiated adenocarcinoma (54 %) and stage IV disease (86 %). Systemic metastasis was common (60 %), with a high mortality rate (79 %). Patients with PD-L1 expression % had a higher ECOG score, indicating worse functional status. The median overall survival was 23 months for EGFR-*

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mutant patients, significantly longer than for patients with other markers. High ECOG scores correlated with higher PD-L1 expression and worse outcomes. **Conclusion:** *Adenocarcinoma patients often present with advanced-stage disease, highlighting the need for early detection. PD-L1 expression and ECOG score are critical predictors of survival. Personalized therapy based on genetic markers such as EGFR, ALK, and PD-L1 can improve outcomes.*

Keywords: *Lung cancer, adenocarcinoma, EGFR, ALK, PD-L1, survival, biomarkers.*

RESUMEN

El cáncer de pulmón es la principal causa de incidencia y mortalidad por cáncer en todo el mundo y representa el 12,4 % de todos los casos notificados. Este estudio tiene como objetivo determinar la relación entre la supervivencia de pacientes con adenocarcinoma de pulmón y la expresión de los marcadores EGFR, ALK y PD-L1. **Métodos:** *Se realizó un estudio de cohorte prospectivo en un centro de tratamiento del cáncer en Barranquilla, Colombia, con pacientes de 18 años o más diagnosticados con adenocarcinoma. Se recopilaron datos de los pacientes, incluidos datos demográficos, marcadores tumorales (EGFR, ALK, PD-L1), antecedentes de tabaquismo y resultados clínicos. Los análisis estadísticos incluyeron la prueba de Kolmogórov-Smirnov, la prueba de Kruskal-Wallis, la prueba exacta de Fisher y el análisis de supervivencia de Kaplan-Meier.* **Resultados:** *Se incluyeron 193 pacientes, predominantemente mujeres (53 %), con una mediana de edad de 68 años. La mayoría de los pacientes procedían de zonas urbanas (86 %) y eran fumadores (48 %). El estudio encontró una alta prevalencia de adenocarcinoma poco diferenciado (54 %) y enfermedad en estadio IV (86 %). Las metástasis sistémicas fueron comunes (60 %), con una alta tasa de mortalidad (79 %). Los pacientes con expresión de PD-L1 ≥1 % tuvieron una puntuación ECOG más alta, lo que indica un peor estado funcional. La mediana de supervivencia general fue de 23 meses para los pacientes con mutación EGFR, significativamente más larga que para otros marcadores. Las puntuaciones altas del ECOG se correlacionaron con una mayor expresión de PD-L1 y peores resultados.* **Conclusión:** *Los pacientes con adenocarcinoma a menudo se presentan con enfermedad en estadio avanzado, lo que destaca la necesidad de una detección temprana. La expresión de PD-L1 y la puntuación ECOG son predictores críticos de supervivencia. La terapia personalizada basada en marcadores genéticos como EGFR, ALK y PD-L1 puede mejorar los resultados.*

Palabras clave: *Cáncer de pulmón, adenocarcinoma, EGFR, ALK, PD-L1, supervivencia, biomarcadores.*

INTRODUCTION

Lung cancer is the leading cause of cancer incidence and mortality worldwide, accounting for 12.4 % of all reported cases. It results from the combined action of multiple factors that damage the bronchial epithelium, making it the leading cause of mortality in the Western world. The primary environmental agent involved in lung carcinogenesis is tobacco; however, there is also an association between occupational exposure to substances such as biomass, asbestos, and radon, and the occurrence of lung cancer (1,2).

During the development of non-small cell lung cancer (NSCLC), various molecular events occur, including loss of heterozygosity, epigenetic changes, and mutations in genes such as p53, K-RAS, and the epidermal growth factor receptor (EGFR) (1,3). EGFR, located on the short arm of chromosome 7, is part of the tyrosine kinase receptor (TK) family, known as the HER or ErbB family. This family includes four members that regulate metabolic and histological processes: EGFR (HER1/ErbB1), HER2 (ErbB2), HER3 (ErbB3), and ErbB4 (4,5).

For patients diagnosed with adenocarcinoma, it is recommended to test for the expression of Anaplastic Lymphoma Kinase (ALK), programmed cell death-ligand 1 (PD-L1), and EGFR, which are present in approximately 30 % of patients (6,7). Targeted therapy based on these markers has shown a positive impact on survival, especially in patients with overexpression of PD-L1 (>50 %), who present a survival rate of over 25 % at five years (8).

The markers EGFR, ALK, and PD-L1 play a crucial role in patient survival (9). Global studies have found worse initial survival rates in those with PD-L1 expression levels greater than 1 %. Studies in Latin America, where the prevalence of EGFR mutations and difficulties in obtaining immunohistochemistry results lead to late diagnoses, highlight the need to detect these mutations and overexpression early. This study aims to investigate the relationship between

patient survival and the expression of EGFR, ALK, and PD-L1 markers in patients with lung adenocarcinoma.

MATERIALS AND METHODS

1. Study Design: Patients and Variables

A prospective, analytical observational cohort study was conducted at a referral center in Barranquilla (Atl, CO) for the management of oncology patients. Patients over 18 years old were selected who had undergone a histopathological diagnosis at the center where treatment was carried out or had been referred after diagnosis, with their treatment entirely conducted at the center where the data were collected.

The medical records of the patients were reviewed. A database was created with the following variables: Sex (Female/Male), Age (in completed years), Place of Residence (rural or urban), Economic Occupation, Date of Diagnosis, Immunohistochemical Description, Histopathological Staging, Expression of EGFR/ALK/PDL1 markers, Tumor Proportion Score (TPS), Smoking History (Never Smoker, Smoker), Vital Status (Deceased/Alive), Date of Death, Exposure to Biomass Combustion (EBC), Eastern Cooperative Oncology Group (ECOG) score, Pharmacological Therapy (Platinum-Based Antineoplastic (PBA); Mitotic Inhibitors (MI); Tyrosine Kinase Inhibitors (TKI); Anti-Programmed Death-1 (Anti_PD-1), and Type of Metastasis (Local, Regional, Systemic).

2. Statistical Analysis

Data normality was analyzed using the Kolmogorov-Smirnov test. Quantitative variables were presented as medians and interquartile ranges. Absolute and relative frequencies were used to describe categorical variables. Kruskal-Wallis' test was used to evaluate the medians obtained by patients according to the TPS stratification group of PD-L1 (<1 %, 1-49 %, ≥50 %). Fisher's exact test was used to analyze categorical variables. The relationship between the score and molecular markers (EGFR, PD-L1, and ALK) was explored through simple correspondence analysis. Kaplan-Meier analysis was conducted to estimate overall survival between groups. To identify possible clinicopathological factors associated with mortality, multivariate logistic regression analysis was performed, adjusting for the variables using the backward methodology. Odds ratios (ORs) and 95 % confidence intervals (CIs) were reported for each variable. A p-value <0.05 was considered statistically significant. R-CRAN software version 4.3.2 was used for statistical analysis.

RESULTS

1. General Characteristics

A total of 193 patients diagnosed with pulmonary adenocarcinoma were included. Most patients were female (53 %), with a median age of 68 years (interquartile range, IQR: 38-89 years). Seventy-five percent of the patients were over 61 years old. Eighty-six percent of the patients were from urban areas. Approximately half of the patients were smokers (48 %), and 37 % were homemakers. Of the total number of patients, 35 cases (18 %) were exposed to biomass combustion (Table 1).

Table 1. Characteristics of patients with lung adenocarcinoma

Characteristic	n = 193[1]
Age	68 (38-89)
Sex	
Female	103 (53 %)
Male	90 (47 %)
Area	
Rural	27 (14 %)
Urban	166 (86 %)
Work status	
Employee	36 (19 %)
Homemaker	71 (37 %)
Pensioner	35 (18 %)
Unemployed	45 (23 %)
Smoking history	
Never-smoker	100 (52 %)
Smoker	93 (48 %)
EBC	35 (18 %)

EBC, exposure to biomass combustion; [1]Median (Range); n (%)

No significant differences were observed when comparing the age between males (Median: 68, IQR: 43-87) and females (Median: 69, IQR: 38-89 years) (p=0.68).

2. Clinicopathological Characteristics and Outcomes

Many patients had poorly differentiated adenocarcinoma (54 %). The most common tumor stage was stage IV (86 %), followed by stage IA (3.6 %) and stage IIA (3.6 %). Systemic metastasis (60 %) was the most frequent clinical presentation. Most patients received platinum-based antineoplastics (PBA) (62 %), followed by mitotic inhibitors (MI) (45 %). Eleven cases (6 %) received biological therapy. The most common Tumor Proportion Score (TPS) for PD-L1 was <1 % (39 %). Regarding driver oncogenes, 26 cases (76 %) had an EGFR mutation, and 8 cases (24 %) had EML4-ALK rearrangements. A total of 153 patients (79 %) died (Table 2).

Table 2. Clinical and Pathologic Characteristics of Patients with Lung Adenocarcinoma

Characteristic	(n=193) [1]
ECOG Score	2 (0 - 4)
Adenocarcinoma	
Well Differentiated	6 (5.1 %)
Moderately Differentiated	48 (41 %)
Poorly Differentiated	64 (54 %)
Stage	
IA	7 (3.6 %)
IB	1 (0.5 %)
IIA	7 (3.6 %)
IIIA	6 (3.1 %)
IIIB	6 (3.1 %)
IV	166 (86 %)
Metastasis type	
Local	49 (29 %)
Regional	19 (11 %)
Systemic	100 (60 %)
Drug Therapy	
PBA	119 (62 %)
MI	87 (45 %)
TKI	25 (13 %)
Anti_PD-1	11 (6 %)
PD-L1 TPS	
<1	12 (39 %)
1-49	11 (35 %)
≥50%	8 (26 %)
Oncogenic Driver	
EGFR	26 (76 %)
EML4-ALK	8 (24 %)
Death	153 (79 %)

TPS, tumor proportion score; EBC, exposure to biomass combustion; ECOG, Eastern Cooperative Oncology Group; PBA, Platinum-based antineoplastic; MI, Mitotic inhibitors; TKI, tyrosine kinase inhibitors; PD-1, programmed cell death protein 1; [1]Median (Range); n (%)

3. ECOG Score, Molecular Markers, and Outcome

A simple correspondence analysis was performed to explore the relationship between the Eastern Cooperative Oncology Group (ECOG) score and the genetic markers PD-L1, EGFR, and EML4-ALK. The ECOG score was stratified as mild (0-1), moderate (2-3), and severe (4). An important association was observed between patients with a moderate ECOG score and PD-L1 TPS ≥1 % (Figure 1).

With respect to outcomes, it was observed that deceased patients had a significantly higher ECOG score compared to survivors (Median: 2, IQR: 0-4 vs. Median: 1, IQR: 0-4, p=<0.0001) (Figure 2).

4. Cell Differentiation Grade and Overall Survival

In this study, lung adenocarcinomas were classified as follows: Well-differentiated (score 2): Solid pattern < 90 % and mild/moderate atypia. Moderately differentiated (score 3): Solid pattern ≥ 90 % and mild/moderate atypia; or solid pattern < 90 % and severe atypia. Poorly differentiated (score 4): Solid pattern ≥ 90 % and severe atypia. Of the total patients, 64 (54 %) had poorly differentiated lung adenocarcinoma, 45 (41 %) had moderately differentiated adenocarcinoma, and 6 (5.1 %) had well-differentiated adenocarcinoma. The influence of cell differentiation grade on overall survival was explored (Figure 3).

The median overall survival was 10.8 months for patients with well-differentiated adenocarcinoma, 8.7 months for moderately

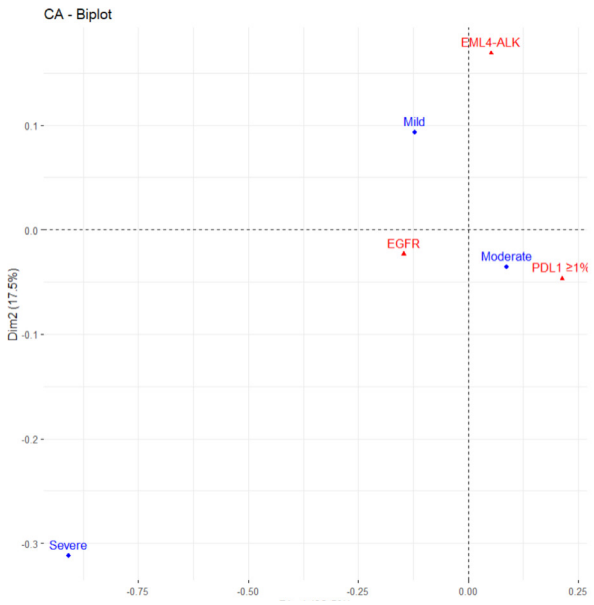


Figure 1. Simple correspondence analysis between ECOG score and molecular markers PD-L1, EGFR, and EML4-ALK.

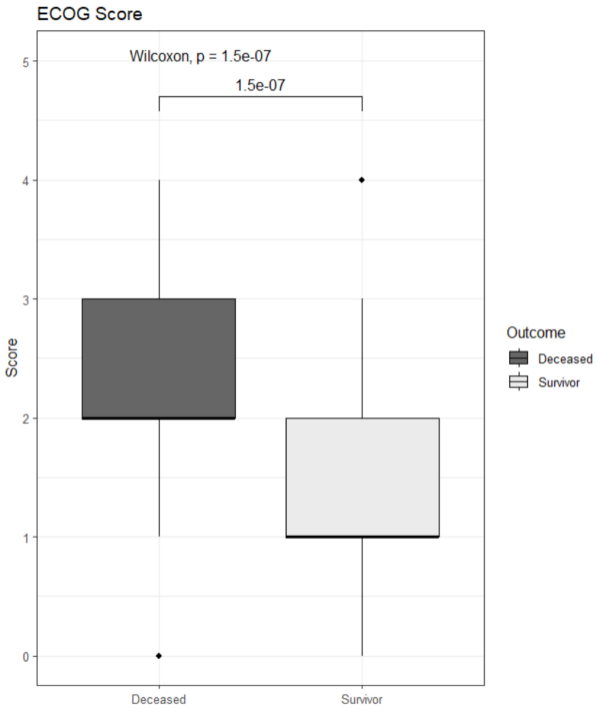


Figure 2. ECOG Score by Outcome (Deceased vs. Survivors).

differentiated adenocarcinoma, and 5 months for poorly differentiated adenocarcinoma. However, no significant differences were observed between the groups (p=0.41) (Figure 3).

5. PD-L1 TPS in Lung Adenocarcinoma

Of the 193 lung adenocarcinoma specimens analyzed, 19 cases (10.1 %) had a PD-L1 Tumor Proportion Score (TPS) of ≥1 %. The PD-L1 TPS for patients with EGFR mutations or ALK rearrangements is presented in Table 3. Patients with a PD-L1 TPS of ≥1 % were further divided into groups with a PD-L1 TPS of 1 % to 49 % (n=11, 6 %) or ≥50 % (n=8, 3 %). However, no significant associations were observed between the clinicopathological characteristics and/or outcomes of the patients and the PD-L1 TPS stratified as <1 %, 1 %-49 %, or ≥50 % (p>0.05) (Table 3).

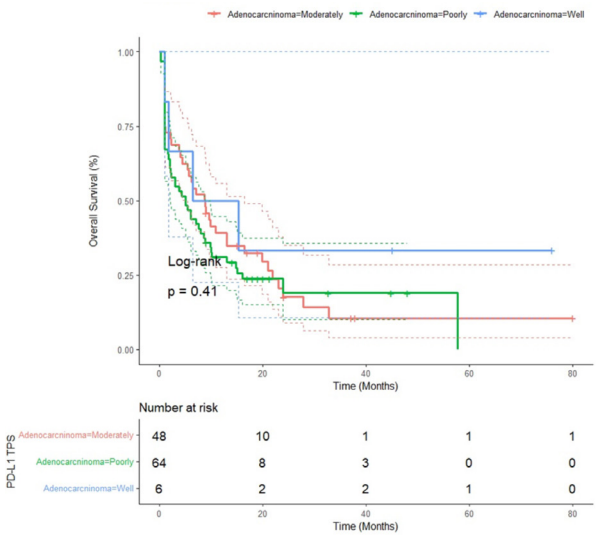


Figure 3. Kaplan-Meier Survival Curve for Overall Survival in Patients with Lung Adenocarcinoma by Cell Differentiation Grade.

Table 3. Association analysis for PD-L1 expression (TPS of<1 %, 1 % to 49 %, or ≥50 %) and clinical features.

Characteristic	PD-L1 expression levels			p-value
	TPS <1 % (n=12) [1]	TPS 1-49 % (n=11) [1]	TPS ≥50 % (n=8) [1]	
Age	73 (38, 83)	74 (55, 84)	65 (47, 78)	0.5[2]
Sex				0.7[3]
Female	4 (33 %)	5 (45 %)	2 (25 %)	
Male	8 (67 %)	6 (55 %)	6 (75 %)	
Smoking history				0.2[3]
Never-smoker	8 (67 %)	5 (45 %)	2 (25 %)	
Smoker	4 (33 %)	6 (55 %)	6 (75 %)	
EBC	1 (8.3 %)	0 (0 %)	0 (0 %)	>0.9[3]
ECOG score	2 (1, 3)	2 (1, 3)	2 (0, 3)	0.9[2]
Stage				0.13[3]
IIA	0 (0 %)	2 (18 %)	0 (0 %)	
IV	12 (100 %)	8 (73 %)	8 (100 %)	
Metastasis type				0.2[3]
Local	3 (25 %)	0 (0 %)	2 (29 %)	
Regional	2 (17 %)	0 (0 %)	2 (29 %)	
Systemic	7 (58 %)	8 (100 %)	3 (43 %)	
Drug Therapy				
PBA	6 (50 %)	6 (55 %)	5 (63 %)	>0.9[3]
MI	5 (42 %)	3 (27 %)	3 (38 %)	0.9[3]
TKI	5 (42 %)	2 (18 %)	1 (13 %)	0.4[3]
Anti_PD-1	1 (8.3 %)	1 (9.1 %)	4 (50 %)	0.086[3]
Oncogenic Driver				>0.9[3]
EGFR	5 (63 %)	2 (100 %)	1 (100 %)	
EML4-ALK	3 (38 %)	0 (0 %)	0 (0 %)	
Death	7 (64 %)	11 (92 %)	7 (88 %)	0.2[3]

TPS: Tumor Proportion Score; EBC: Exposure to Biomass Combustion; ECOG: Eastern Cooperative Oncology Group; PBA: Platinum-based Antineoplastic; MI: Mitotic inhibitors; TKI: Tyrosine kinase inhibitors; PD-1: Programmed cell death protein 1; [1] Median (Range); n (%); [2] Kruskal-Walli's rank sum test; [3] Fisher's exact test.

6. Molecular Markers and Overall Survival

When evaluating the overall survival of patients with lung adenocarcinoma based on the molecular marker present, significant differences were observed in the median overall survival in months according to the marker. The median survival for patients with EGFR mutations was 23 months, for those with EML4-ALK rearrangements, it was 16 months, and according to PD-L1 TPS, it was 9 months for patients with TPS <1 % and 5.5 months for those with TPS ≥1 % ($p = 0.036$) (Figure 4).

7. PD-L1 TPS and Overall Survival

To assess how PD-L1 expression might influence the survival of patients with lung adenocarcinoma, overall survival was analyzed based on the PD-L1 TPS. The median survival for patients with a PD-L1 TPS <1 % was 14 months, for those with a PD-L1 TPS of 1-49 % it was 8.5 months, and for cases with a PD-L1 TPS >50 % it was 5.5 months. Comparing the three groups of patients stratified by PD-L1 tumor proportion score (TPS), a trend toward decreased overall survival was observed as PD-L1 TPS increased. However, no significant differences were found based on PD-L1 TPS (Figure 5).

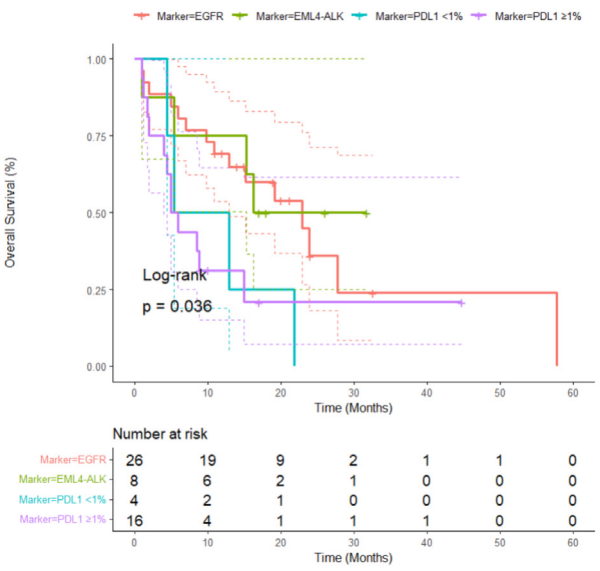


Figure 4. Kaplan-Meier Survival Curve for Overall Survival in Patients with Lung Adenocarcinoma by Molecular Marker.

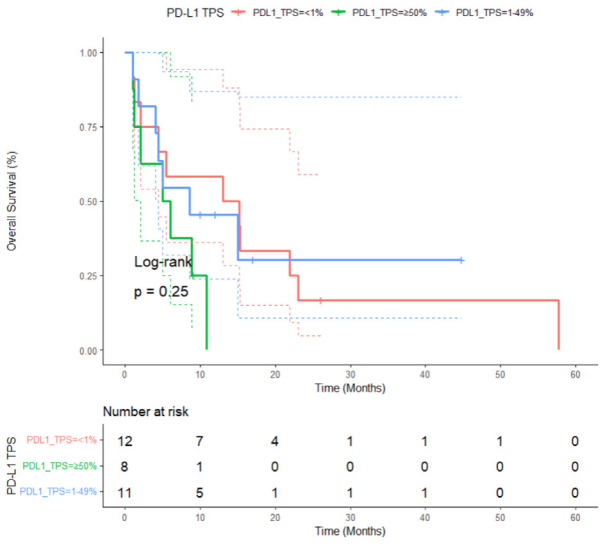


Figure 5. Kaplan-Meier Survival Curve for Overall Survival in Patients with Lung Adenocarcinoma by PD-L1 TPS Stratification.

8. Factors Associated with Mortality

As shown in Table 4, a multivariate logistic regression analysis was performed to identify possible clinicopathological factors associated with mortality in patients with lung adenocarcinoma. It was found that male sex and an ECOG score of 2-3 were associated with a higher risk of mortality. In the adjusted model, male patients were 4.5 times more likely to die compared to female patients (OR: 4.5, 95 % CI: 1.6-18.1, p=0.04). Patients with an ECOG score of 2-3 were 7.3 times more likely to die compared to those with an ECOG score of 4 (OR: 7.3, 95 % CI: 1.89-28.9, p=0.003).

DISCUSSION

Sex (53 % women), age (75 % >61 years), urban residency (86 %), high smoking rate (48 %), and exposure to biomass combustion (EBC) (18 %) are contributing factors to the development of pulmonary adenocarcinoma. In urban areas, there is greater exposure to fine particulate matter (PM2.5 and PM10) and other volatile compounds (10,11). Adenocarcinomas in patients from urban areas often exhibit mixed patterns, including lepidic, acinar, and papillary components. This diversity could be a result of exposure to multiple carcinogens, inducing various pathways of cellular transformation (12).

Smoking is the most studied risk factor and is correlated with specific mutations in genes such as KRAS and TP53. More recently, it has also been associated with alterations in EGFR in lung adenocarcinomas. These mutations are more prevalent in smokers and contribute to carcinogenesis by activating oncogenic pathways and inhibiting DNA repair mechanisms. Adenocarcinomas in smokers tend to exhibit poorer differentiation and a more aggressive phenotype, with a higher degree of vascular and pleural invasion (10,13,14). Additionally, exposure to biomass combustion is a significant risk factor, especially among women in rural or semi-urban areas. This exposure is associated with the inhalation of a complex mixture of organic and inorganic compounds that can induce chronic interstitial inflammation and

Table 4. Multivariate Analysis of Overall Survival in Relation to Clinicopathologic Characteristics

Characteristic	Multivariate			Adjusted		
	OR[1]	95 % CI[2]	p-value	OR[1]	95 % CI[2]	p-value
Age >55 years	0.39	0.03, 5.26	0.5	0.45	0.07, 2.90	0.4
Sex						
Female	—	—		—	—	
Male	11.0	0.87, 139	0.053	4.52	1.6, 18.1	0.041
Smoking history						
Smoker	1.02	0.11, 9.14	>0.9	0.90	0.19, 4.14	0.9
EBC						
Yes	0.49	0.02, 12.1	0.7			
ECOG						
2-3	4.43	0.48, 41.2	0.2	7.39	1.89, 28.9	0.003
4	3.05	0.09, 106	0.5	2.52	0.08, 80.1	0.6
Grading						
Poorly Differentiated	0.25	0.03, 2.41	0.2			
Well Differentiated	1.64	0.03, 79.9	0.8			
Stage						
III	—	—				
IV	0.95	0.01, 125	>0.9			
Metastasis type						
Regional	0.32	0.01, 8.84	0.5	0.67	0.10, 4.41	0.7
Systemic	2.44	0.26, 22.6	0.4	2.55	0.66, 9.85	0.2
PD-L1 TPS						
<1 %	—	—				
≥50 %	0.54	0.03, 9.01	0.6			
1-49 %	0.34	0.02, 6.90	0.5			
EGFR Mutation						
Yes	0.68	0.05, 9.35	0.8			
ALK rearrangements						
Yes	0.85	0.03, 22.2	>0.9	0.23	0.04, 1.50	0.12
PBA						
Yes	1.19	0.07, 19.9	>0.9			
MI						
Yes	4.93	0.27, 90.0	0.3			
TKI						
Yes	0.26	0.02, 4.23	0.3			

[1]OR = Odds Ratio, [2]CI = Confidence Interval.

fibrosis, as well as oxidative stress, along with a predominantly acinar histological pattern (15).

The predominance of poorly differentiated adenocarcinoma (54 %) and stage IV (86 %) indicates late diagnosis and significant cancer aggressiveness in the studied sample. The high frequency of systemic metastasis (60 %) and the elevated mortality rate (79 %) underscore the lethality of the disease and the critical importance of early detection and treatment (16,17). The choice of platinum-based antineoplastics in most cases (62 %) reflects standard clinical practice, while the use of biological therapy in only 6 % of cases suggests limitations in access or patient selection based on biomarkers (18,19).

The significant association between a moderate ECOG score (2-3) and PD-L1 TPS ≥1 % highlights the correlation between functional impairment and PD-L1 expression. This suggests that inflammation and immune dysfunction may

play a role in disease progression. Additionally, the fact that deceased patients had a significantly higher ECOG score indicates a clear relationship between functional quality at diagnosis and survival. This relationship highlights the interaction between patient functional capacity and the tumor microenvironment, particularly regarding inflammation and immunity (20,21).

PD-L1 is a protein that normally helps regulate the immune response to avoid autoimmunity. However, in the context of cancer, many tumor cells express PD-L1 to evade the host immune response. PD-L1 expression on tumor cells and in the immune stroma can inhibit the cytotoxic activity of T cells, allowing the tumor to progress. High PD-L1 expression is associated with dense infiltration of immune cells, particularly regulatory T cells (Tregs) and tumor-associated macrophages (TAMs), which promote immunosuppression and facilitate tumor immune evasion (20,21).

Lung adenocarcinomas with higher PD-L1 expression may exhibit a more disorganized growth pattern, indicating tumor aggressiveness and interaction with the microenvironment to facilitate tumor cell survival and proliferation. The correlation between an ECOG score of 2-3 and higher PD-L1 expression (TPS ≥1 %) suggests that functional impairment may be both a consequence and a facilitator of cancer progression (22).

Systemic inflammation, often reflected by markers such as C-reactive protein (CRP) and interleukin-6 (IL-6), can promote the expression of PD-L1 in tumor cells. Patients with compromised functional status may have upregulated PD-L1 as a reflection of generalized immune dysfunction, which includes the activation of pathways promoting immunosuppression and facilitating tumor progression (23,24).

High PD-L1 expression and increased ECOG score are predictors of poorer prognosis in patients with lung adenocarcinoma. High PD-L1 expression can confer resistance to conventional therapies such as chemotherapy and radiotherapy, as these tumor cells are protected from treatment-induced apoptosis. Acting as an immunosuppressive facilitator, it allows tumor cells to evade immune surveillance, increasing the risk of metastasis and contributing to a more deteriorated functional state (20,21).

Survival analysis revealed significant differences based on molecular markers, with a median survival of 23 months for patients with EGFR mutation, significantly longer than for those with other markers. These results are consistent with the literature, which suggests that EGFR mutations are associated with a better response to targeted therapies. In contrast, the low survival in patients with PD-L1 TPS <1 % and ≥1 % highlights the complexity of this biomarker as a predictor of treatment response, particularly to immune checkpoint inhibitors (18,19).

The multivariate analysis identified male sex and an ECOG score of 2-3 as significant factors associated with higher mortality. This reflects previous findings where men and patients with greater functional impairment have worse outcomes. These factors should be considered in risk stratification and treatment personalization (25,26).

CONCLUSIONS

The high prevalence of poorly differentiated adenocarcinoma (54 %) and the majority of patients presenting at stage IV (86 %) indicate a failure in early detection strategies. Furthermore, the clear correlation between PD-L1 expression and the worsening functional status of patients (ECOG) suggests that inflammation and immune dysfunction play significant roles in lung cancer progression. Therefore, immunotherapeutic strategies targeting PD-L1 could offer a promising therapeutic approach for these patients.

Moreover, the findings reinforce the importance of targeted therapies in improving outcomes for patients with specific mutations (EGFR). Personalized treatment based on the tumor's genetic profile could offer better clinical outcomes and should be considered standard practice. Integrating different strategies could significantly improve survival rates and quality of life for patients, especially those focusing on evaluating targeted therapies and immunotherapies for aggressive forms of lung cancer.

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Institutional Review Board Statement: This study was conducted by the Declaration of Helsinki and approved by the ethics committee of the Centro Cancerologico del Caribe (BAQ, CO) on December 15, 2022, and by the Institutional Review Board of the Universidad Simón Bolívar, code 640 – 021/2023, on 05 September 2023.

Informed Consent Statement: Patient consent was waived due to REASON the study was based solely on the review of medical records and many of the patients had passed away. Therefore, the Ethics Committee granted authorization for the review of the database. This decision was made considering the impossibility of obtaining consent from deceased patients and the importance of the research in improving the understanding and treatment of lung adenocarcinoma.

Data Availability Statement: All data underlying the results are available as part of this article.

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Conflicts of Interest: The authors declare no conflicts of interest.

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ARTÍCULO ORIGINAL

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Comparison of the effectiveness of dry needling and deep friction massage on trigger point size, pain level, and range of motion in low back pain patients

Comparación de la eficacia de la punción seca y el masaje de fricción profunda en el tamaño del punto gatillo, el nivel de dolor y el rango de movimiento en pacientes con dolor lumbar

Mujaddidah Yuharti[1a], Aryadi Arsyad[2b*], Andi Ayandy[3b], Meutiah Mutmainnah Abdullah[4c], Andi Rizky Arbaim Hasyar[5c]

SUMMARY

Objective: *Low Back Pain (LBP) is a common musculoskeletal disorder causing pain, muscle spasms, and a restricted range of motion (ROM). This study aimed to evaluate the effectiveness of Dry Needling (DN) and Deep Friction Massage (DFM) in modifying trigger point size, reducing pain, and improving range of motion (ROM) in LBP patients using a muscle ultrasonography-based approach.* **Methods:** *Thirty-two LBP patients were randomly assigned to two groups (n=16 each). The DN group received dry needling, while the DFM group underwent deep friction massage. The intervention was administered in a single session (pre–post), with a duration of approximately 20 to 30 minutes. Pain levels were assessed using the Visual Analog Scale (VAS), ROM was measured with a goniometer, and trigger point size was evaluated by ultrasonography.* **Results:** *Post-intervention, neither the DN (0.48±0.51) nor the DFM (0.27±0.29) group showed a statistically significant reduction in trigger point size ($p>0.05$), though DN demonstrated a greater reduction. Both DN (3.31±0.81) and DFM (2.19±0.54) significantly reduced pain ($p<0.05$), with DN exhibiting a superior effect. No significant improvements in lumbar ROM (flexion, extension, lateral flexion, or rotation) were observed in either group ($p>0.05$).* **Conclusion:** *Both DN and DFM effectively reduce pain in LBP patients, with DN demonstrating greater pain relief and faster muscle relaxation. While both interventions influenced trigger point size and ROM, DN had a more pronounced effect. However, neither*

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intervention significantly improved ROM. Further research is needed to investigate the long-term effects and optimize treatment protocols for improved patient outcomes.

Keywords: *Low back pain (LBP), trigger point, dry needling (DN), deep friction massage (DFM), range of motion (ROM), muscle USG*

RESUMEN

Objetivo: *El dolor lumbar (LBP) es un trastorno musculoesquelético común que causa dolor, espasmos musculares y restricción del rango de movimiento (ROM). Este estudio tuvo como objetivo evaluar la efectividad de la punción seca (DN) y el masaje de fricción profunda (DFM) en la modificación del tamaño del punto gatillo, la reducción del dolor y la mejora del ROM en pacientes con LBP mediante un enfoque basado en ultrasonografía muscular.* **Métodos:** *Treinta y dos pacientes con LBP fueron asignados aleatoriamente a dos grupos (n=16 en cada uno). El grupo DN recibió punción seca, mientras que el grupo DFM fue sometido a masaje de fricción profunda. Los niveles de dolor se evaluaron mediante la Escala Visual Analógica (VAS), el ROM se midió con un goniómetro y el tamaño del punto gatillo se determinó mediante ultrasonografía.* **Resultados:** *Después de la intervención, ni el grupo DN (0,48±0,51) ni el grupo DFM (0,27 ± 0,29) mostraron una reducción estadísticamente significativa en el tamaño del punto gatillo (p>0,05), aunque DN presentó una mayor reducción. Tanto DN (3,31 ± 0,81) como DFM (2,19 ±0,54) redujeron significativamente el dolor (p<0,05), siendo DN el tratamiento con mayor efectividad. No se observaron mejoras significativas en el ROM lumbar (flexión, extensión, flexión lateral o rotación) en ninguno de los grupos (p>0,05).* **Conclusión:** *Tanto la DN como el DFM son eficaces para reducir el dolor en pacientes con LBP, con DN mostrando un mayor alivio del dolor y una relajación muscular más rápida. Aunque ambas intervenciones influyeron en el tamaño del punto gatillo y el ROM, DN tuvo un efecto más pronunciado. Sin embargo, ninguna de las intervenciones mejoró significativamente el ROM lumbar. Se requieren más investigaciones para explorar los efectos a largo plazo y optimizar los protocolos de tratamiento para mejorar los resultados en los pacientes.*

Palabras clave: *Dolor lumbar (LBP), punto gatillo, punción seca (DN), masaje de fricción profunda (DFM), rango de movimiento (ROM), ultrasonografía muscular.*

INTRODUCTION

Low Back Pain (LBP) is one of the most prevalent musculoskeletal disorders, affecting approximately 40 % of the global population during their lifetime. This condition is a leading cause of global disability, most frequently affecting individuals aged 20 to 40 years. The World Health Organization (WHO) reported that in 2020, low back pain (LBP) affected 619 million people worldwide, with projections indicating that this number is expected to rise to 843 million cases by 2050, due to population growth and aging. In Indonesia, the prevalence of LBP reaches 18 %, with hospital visit rates related to LBP ranging from 3 % to 17 % (1).

The causes of LBP vary and include primary factors, such as repetitive activities, non-ergonomic working postures, and muscle injuries, as well as secondary factors, including mechanical pressure, vibrations, and microclimate conditions (2). LBP often originates from untreated musculoskeletal problems, leading to complications in muscles and skeletal structures (3). If left unaddressed, the condition may exacerbate damage, resulting in conditions such as hernia nucleus pulposus (HNP), scoliosis, and other neural complications (4).

One condition closely related to LBP is Myofascial Pain Syndrome (MPS), which occurs due to trigger points (TPs) in muscles experiencing tension or injury. Trigger points are hypersensitive areas within a taut band of muscle fibers that can induce local and referred pain when stimulated (5). Treatment of TPs includes invasive methods, such as dry needling (DN) and injections, as well as non-invasive methods, including electrotherapy, ultrasound, manipulation, strengthening exercises, and manual therapy, like Deep Friction Massage (DFM) (6).

Dry Needling (DN) is an innovative technique involving the use of filament needles to mechanically stimulate muscle tissue without biological agents, aiming to alleviate pain and improve function (7). Studies have demonstrated DN's effectiveness in reducing pain in musculoskeletal cases, including LBP (10). Meanwhile, Deep Friction Massage (DFM),

introduced by James Cyriax, aims to increase blood flow, reduce tissue adhesions, and relieve pain (9). Comparative studies, such as the one conducted by Nisa et al. (2022), reveal that DN outperforms DFM in alleviating pain in certain conditions (10).

Ilayaraja et al. (2020) found that both low-level laser therapy and dry needling effectively reduced pain and improved lumbar ROM in non-specific LBP patients. Nisa et al. (2022) reported similar results for deep friction massage and dry needling in lateral epicondylitis, with dry needling providing superior pain relief (10). While both DN and DFM aid pain reduction and ROM, direct comparisons in LBP management remain limited, requiring further research (8,6).

Assessing DN and DFM efficacy in trigger point size, pain, and ROM requires objective tools (11). Muscle ultrasonography (USG) detects trigger points, assesses muscle parameters, and provides real-time evaluation, making it ideal for musculoskeletal assessment and clinical rehabilitation (12,13). Ultrasonography (USG) aids in diagnosing and monitoring MTrPs by detecting hypoechoic areas and measuring size changes (14). It evaluates the effectiveness of therapy, including dry needling, making it a key diagnostic and assessment tool.

This study assessed pain using the Visual Analog Scale (VAS), range of motion (ROM) using a goniometer, and trigger point (TP) size using ultrasonography. The findings aim to guide physiotherapists in selecting optimal interventions and supporting evidence-based rehabilitation protocols.

SUBJECT AND METHODS

Design

This clinical trial was registered at UMIN-CTR (trial registration number UMIN000057073), and Research involving the use of human samples has received ethical approval from the Research Ethics Committee of the Faculty of Public Health, Hasanuddin University (protocol code: 151024092320 with the approval number of 3102/UN4.14.1/TP.01.02/2024). Using a quasi-experimental pretest-posttest design, this study compares dry needling and deep friction massage on TP size, pain, and ROM in LBP patients.

Participants

All participants provided informed consent before the study. The total sample size consisted of 32 participants diagnosed with Low Back Pain (LBP). The sample selection process adhered to specific inclusion criteria: participants aged between 20 and 55 years, including both males and females, with the presence of nodules or trigger points detected via muscle ultrasonography (USG) in the back muscles, and limitations in range of motion (ROM). Participants exhibiting conditions such as Delayed Onset Muscle Soreness (DOMS) or those who had consumed medication within five hours before therapy were excluded from the study. The 32 participants were evenly divided into two groups, each consisting of 16 participants. The participants were categorized into two groups: the DN group, which received the dry needling intervention, and the DFM group, which received the deep friction massage intervention.

Outcome Measure

This study assessed pain using the Visual Analog Scale (VAS), range of motion (ROM) with a goniometer, and trigger point size via ultrasonography. Pain intensity was classified as no pain (0-4 mm), mild (5-44 mm), moderate (45-74 mm), or severe (75-100 mm). ROM was measured using standard goniometric values: 30°–0°–90° (flexion/extension), 30°–0°–30° (side flexion), and 45°–0°–45° (rotation). Trigger point size was evaluated using the Versanna Essential USG system (10 Hz, SN: 6023709WX0). A licensed physiotherapy professional carried out the intervention. Before the procedure, all participants received a thorough explanation of the study protocol. Those who agreed to participate provided written informed consent. Each intervention session was conducted once, with a duration of approximately 20 to 30 minutes. Afterward, pain levels, TP size, and ROM were reassessed and documented.

Data Analysis

Data were analyzed using IBM SPSS 25.0. Normality was tested with Shapiro-Wilk. Pre-post VAS and ROM were compared using paired t-tests, and trigger point size was compared using the Wilcoxon test. Between-group VAS and ROM used independent t-tests, while trigger point size used the U Mann-Whitney test. Results are represented as mean ± SD, with significance at $p<0.05$.

Informed consent: Informed consent was obtained from all respondents participating in this study.

RESULT

Table 1 presents respondent characteristics by age and gender. In the dry needling group (mean age 34 ± 9.14 years, range 21-48), there were 9 males and 7 females. In the DFM group (mean age 29 ± 8.57 years, range 20-45), there were 4 males and 12 females.

Analysis of Pre-Post Trigger Point Size and Comparison of Differences in Trigger Point Size Between the Dry Needling Group and the Deep Friction Massage Group

Figures 1, 2 and 3 shows that before the trigger point examination on the back muscles using muscle ultrasonography (USG), in the dry needling group, trigger point size increased from 0.82±0.45 to 1.14±0.63 post-intervention, showing a significant difference ($p<0.05$) based on the Wilcoxon test.

The DFM group's size increased from 1.36±0.61 to 1.53±0.59, with no significant difference ($p>0.05$). The Mann-Whitney U test showed mean changes of 0.48±0.51 (DN) and 0.27±0.29 (DFM), indicating a greater impact of dry needling, though the between-group difference was not statistically significant ($p>0.05$).

Thus, the change in trigger point size between the dry needling and DFM groups was not statistically significant. However, empirical data suggested that the average increase in trigger point size was more prominent in the dry needling group than the DFM group.

Table 1. Clinical characteristics of the 32 patients

	DN	DFM	Min	Max
Total Sample (N)	16	16	-	-
Gender (M/F)	9/7	4 /12	-	-
Age (DN/DFM)	34±9.14	29±8.57	21/21	45/48

M: Male; F: Female; Data are presented as mean ± SD where applicable.

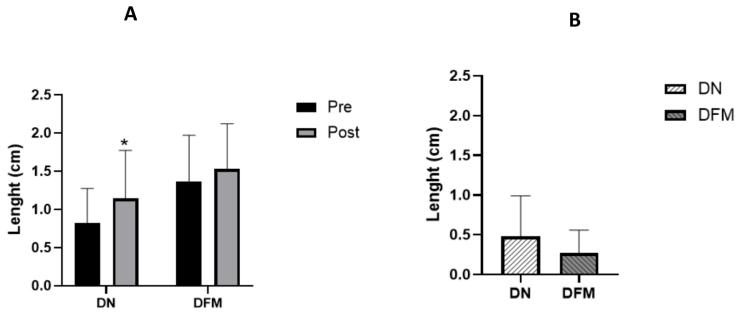


Figure 1. **(A)** illustrates the comparison of pre- and post-test trigger point sizes in the dry needling (DN) and deep friction massage (DFM) groups. **(B)** shows the Δ (delta) change represents the difference in trigger point size between post- and pre-intervention values scores between the DN and DFM groups (Δ = Post - Pre). The trigger point sizes are measured in centimeters (cm). Length represents the unit of measurement for trigger point size in centimeters. *$p<0.05$ indicates a statistically significant result.

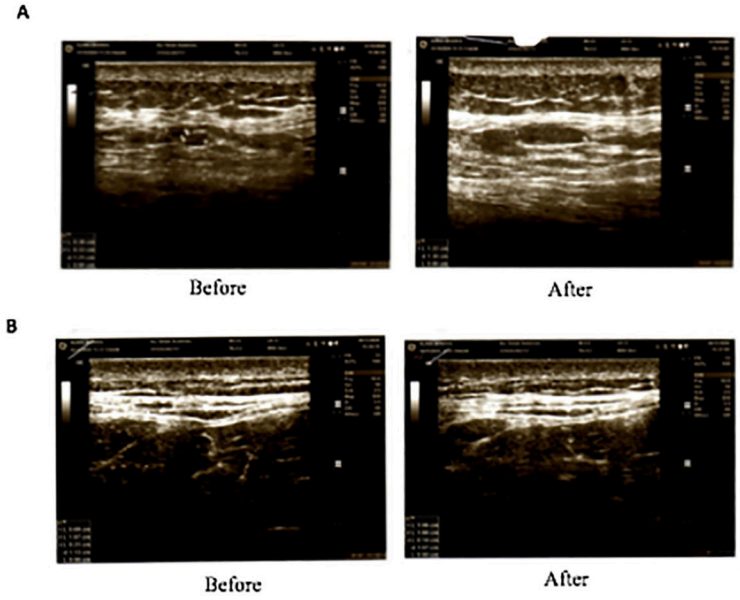


Figure 2. **(A)** presents ultrasonography (USG) imaging of the lower back muscles before and after the dry needling (DN) intervention, showing an increase in trigger point size from 0.38 cm to 1.22 cm. This enlargement is likely due to local inflammation as a physiological response to the intervention. **(B)** illustrates the USG imaging of the lower back muscles before and after DN, demonstrating a reduction in trigger point size from 1.13 cm to 1.07 cm. This decrease may be influenced by acute and chronic factors related to the patient's condition, which can affect the muscle's overall response to the therapy.

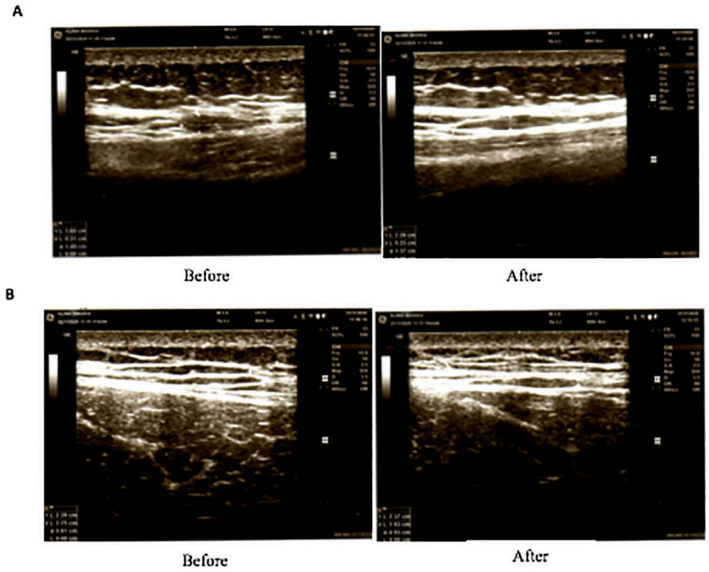


Figure 3. **(A)** presents USG imaging of the lower back muscles before and after DFM, showing an increase in trigger point size from 1.60 cm to 2.22 cm. This enlargement is likely due to local inflammation triggered by repeated pressure during the procedure. **(B)** illustrates a reduction in trigger point size from 2.75 cm to 1.93 cm following the DFM intervention. This outcome suggests that the effectiveness of DFM may vary depending on the intensity, technique, and pressure applied during the treatment.

Analysis of Pre-Post VAS Scores and Comparison of VAS Score Differences in the Dry Needling and Deep Friction Massage Groups

Figure 4 revealed that before the dry needling intervention, the Visual Analog Scale (VAS) score for the dry needling group was 6.69±1.19. After the intervention, the score decreased to 3.31 ± 1.40, indicating a reduction in pain levels as measured by the VAS following the dry needling intervention. Similarly, in the DFM group, the VAS score before the DFM intervention was 5.38 ± 1.14, which decreased to 3.38 ± 1.20 after the intervention. This also suggests a reduction in pain levels following the DFM intervention. Both intervention groups exhibited significant changes ($p<0.05$), demonstrating substantial pain reduction in response to both dry needling and deep friction massage techniques.

A parametric independent t-test showed a significant difference in post-intervention VAS scores between the dry needling (3.31±0.81) and DFM (2.19±0.54) groups ($p<0.05$), indicating dry needling is more effective in reducing pain.

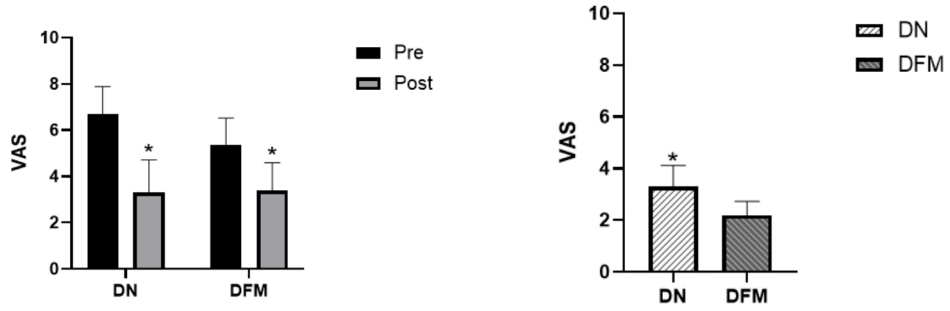


Figure 4. **(A)** illustrates the comparison of pre- and post-test pain levels measured using the Visual Analog Scale (VAS) in the dry needling (DN) and deep friction massage (DFM) groups. **(B)** the Δ (delta) change represents the difference between the DN and DFM groups' post- and pre-intervention values scores (Δ = Post - Pre). The asterisk $*p<0.05$ indicates a statistically significant result.

Analysis of Pre-Post Lumbar ROM (Flexion, Extension, Lateral Flexion, and Rotation) and Comparison of ROM in the Dry Needling and Deep Friction Massage Groups

As shown in Figure 5, in the dry needling group, ROM improved post-intervention: flexion (77.6±6.63 to 84.1±4.72), extension (21.2±4.32 to 26.2±3.27), lateral flexion (23.3±2.91 to 26.4±2.96), and rotation (29.3±7.33 to 35.4±7.52), indicating overall ROM enhancement.

For the deep friction massage group, the range of motion (ROM) for flexion before the intervention was 78.1±4.65, increasing to 84.5±4.29 after the intervention. For extension, the pre-intervention range of motion (ROM) was 21.3±3.89, improving to 26.2±3.19 post-intervention. Lateral flexion ROM improved from 23.6±2.57 to 26.8±2.39, and rotational movement improved from 35.1±3.39 to 39.6±3.72. These results demonstrate increased ROM across all movements following the deep friction massage intervention. Dry needling and deep friction massage interventions significantly improved ROM for lumbar movements ($p<0.05$).

A parametric independent t-test showed no significant differences in lumbar ROM between the dry needling and DFM groups ($p>0.05$). ROM values for dry needling: extension 27.5±3.72, flexion 83.1±7.53, lateral flexion 26.8±3.69, rotation 40±6.31. For DFM: extension 26.1±4.99, flexion 78.3±17.30, lateral flexion 25.1±5.96, rotation 34.8±8.

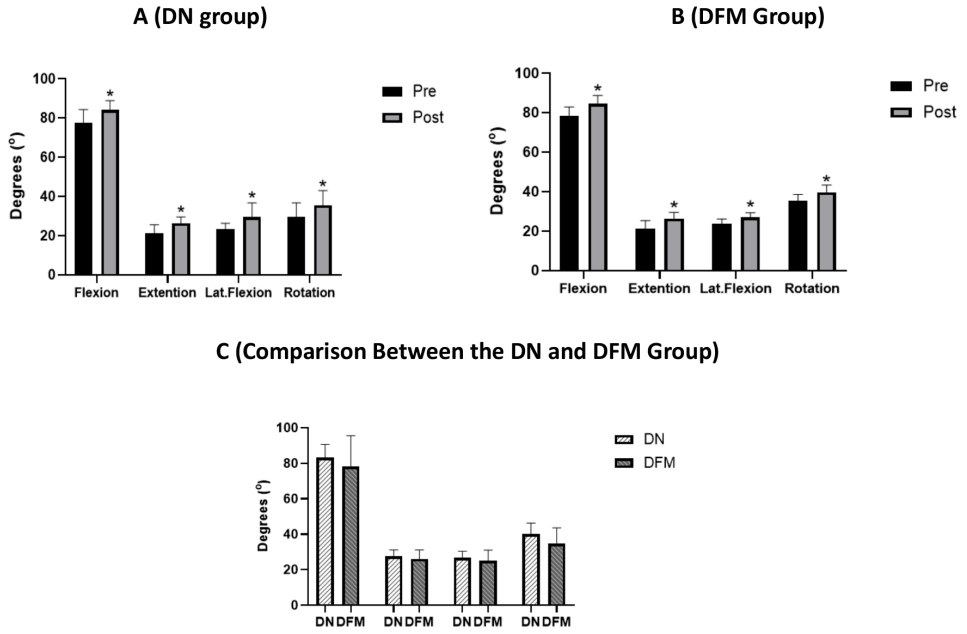


Figure 5. (A) illustrates the comparison of pre – post intervention Range of Motion (ROM) values in the dry needling (DN) group. (B) presents the comparison of pre – post intervention ROM values in the deep friction massage (DFM) group. (C) shows the Δ (delta) change represents the difference of ROM between post- and pre-intervention values scores between the DN and DFM groups (Δ = Post - Pre). ROM measurements were conducted using a goniometer. *P (<0.05) indicates statistically significant results.

DISCUSSION

Analysis of Pre-Post Trigger Point Size and Comparison of Differences in Trigger Point Size Between the Dry Needling Group and the Deep Friction Massage Group

This study examines the differences in trigger point size before (pre-test) and after (post-test) a dry needling intervention. The results reveal variability in responses, with four trigger points decreasing in size while twelve others increased. After conducting research and examination using muscle USG, the most frequently detected trigger points in the back muscles were found in the quadratus lumborum and erector spinae. These findings suggest that individual responses to dry needling may vary, potentially influenced by acute or chronic factors. Previous studies indicate that dry needling can induce microtrauma, triggering a localized inflammatory response within the tissue. This reaction is typically temporary and considered part of the healing process.

The DN group showed a significant increase in trigger point size ($p < 0.05$), from 0.82 cm to 1.14 cm, likely due to microtrauma-induced inflammation. However, four of the 16 samples showed an immediate size reduction without enlargement, possibly due to the patient's condition. Regarding the trigger points subjected to dry needling intervention, the localized inflammatory response observed post-treatment is attributed to microtrauma, which stimulates the tissue healing process. This response involves the release of inflammatory mediators that enhance pain sensitivity and may cause mild, temporary, localized edema or swelling (15). Additionally, a meta-analysis by Gattie et al. (2017) highlighted variations in the therapeutic effects of dry needling across heterogeneous populations. Acute effects, such

as increased pain or trigger point enlargement, were more frequently observed in patients with heightened sensitivity or long-standing chronic conditions (16).

Dry needling effectively manages LBP by relieving muscle spasm, restoring function, and reducing pain. It disrupts the spasm cycle by triggering physiological responses through the insertion of a needle. These mechanisms begin with the mechanical effect (mechanotransduction) induced by the needle insertion, followed by a local twitch response (LTR) when the needle tip contacts the hypercontracted nodule. Ultimately, an analgesic effect is achieved through the stimulation of C fibers, A-delta fibers, and A-beta fibers (17).

Inserting a needle during dry needling can effectively release myofascial trigger points (MTrPs) if it elicits a local twitch response (LTR). LTR is a spinal reflex associated with motor end plate dysfunction and hypersensitivity, which can induce the relaxation of muscle fibers at the affected site (18). Muscle relaxation reduces capillary constriction, improves microcirculation, and enhances tissue oxygenation. Additionally, dry needling contributes to the restoration of sarcomere length by reducing actin-myosin overlap, lowering acetylcholine levels, and decreasing the concentrations of neurotransmitters such as calcitonin gene-related peptide (CGRP), substance P, various cytokines, and interleukins in the extracellular fluid of trigger points (4). Consequently, improved muscle blood flow and oxygenation facilitate the reduction of sarcomere contracture and the restoration of end plate function (17).

The deep friction massage (DFM) group results demonstrated a varied response, with five trigger points decreasing in size, ten increasing in size, and one remaining unchanged following the pre–posttest. Statistical analysis revealed no significant difference in trigger point size before and after the DFM intervention ($p > 0.05$). This variability may be attributed to the pressure applied during therapy and the physiotherapist's proficiency in executing the procedure. Nevertheless, DFM operates through a mechanism that can help alleviate muscle spasms and eliminate trigger points.

DFM is a conventional therapeutic technique that involves ischemic compression as a pressure-based treatment. It is widely recognized as one of the most recommended non-invasive treatment options for managing trigger points (19,11). The therapeutic effects of DFM include reducing muscle tension, enhancing local circulation, and stimulating the tissue healing process (19). This study also compared the effects of dry needling and DFM by analyzing differences in the data obtained from both groups. The results indicated that neither dry needling nor DFM produced a statistically significant reduction in trigger point size ($p > 0.05$).

However, the data suggest that the dry needling group exhibited a more remarkable numerical change than the DFM group. While both methods influenced trigger point size, dry needling demonstrated greater effectiveness in quantitative terms. Dry needling has the advantage of directly targeting the affected tissue through needle penetration, which facilitates muscle relaxation, improves local circulation, and reduces pain through neurological mechanisms (20). In contrast, although effective, DFM tends to produce slower results due to its reliance on manual repetitive pressure applied to the muscle tissue. Additionally, the variability in DFM outcomes may be influenced by the level of pressure exerted during therapy (21).

Analysis of Pre-Post VAS Scores and Comparison of VAS Score Differences in the Dry Needling and Deep Friction Massage Groups

The findings of this study indicate that dry needling intervention significantly reduces pain levels in the examined group. A decrease in the Visual Analog Scale (VAS) score demonstrates the clinical and statistical effectiveness of dry needling in pain alleviation. This result is consistent with previous literature, which suggests that dry needling effectively relaxes muscles, deactivates trigger points, and reduces local nerve sensitivity through pain modulation (22). These findings further support the role of dry needling as a therapeutic modality for musculoskeletal pain. The stimulation provided by dry needling enhances local blood flow and oxygenation at

the trigger point, leading to muscle relaxation and pain reduction (7).

The data indicate that the mean pre-treatment VAS score was 6.69, categorized as moderate pain. In contrast, the mean post-treatment VAS score decreased significantly to 3.31 ($p < 0.05$), indicating mild pain. Thus, it can be concluded that dry needling is an effective intervention for reducing pain levels in patients. Dry needling reduces nociceptor sensitivity and boosts endorphin release, alleviating pain. It also enhances blood circulation, aiding muscle recovery by optimizing oxygen and nutrient delivery while removing waste. Needle-induced microtrauma activates C and A-delta fibers, triggering segmental inhibition and improving tissue oxygenation (23).

Similarly, the pre- and post-intervention VAS scores in the deep friction massage (DFM) group demonstrated significant improvements. This outcome is attributed to DFM's ability to stimulate nerve receptors in the skin and subcutaneous tissues, thereby modulating pain impulses and increasing the pain threshold, ultimately reducing pain perception (24). Additionally, DFM facilitates the release of adhesions in soft tissues, which contribute to pain and restricted movement. By minimizing adhesions, tissue mobility improves, leading to a reduction in pain levels (25).

Dry needling reduces pain more effectively than DFM ($p < 0.05$). The DFM group's VAS score dropped from 3.09 to 2.19, while dry needling showed a greater reduction. Dry needling produces a faster and more pronounced analgesic effect by directly alleviating muscle tension, stimulating peripheral nerves, and modulating central pain processing (26). Furthermore, this technique triggers the release of endogenous chemicals such as endorphins, which play a crucial role in pain modulation and relief (27).

In contrast, DFM operates through the principle of manually enhancing muscle tissue function via repeated pressure application. While effective in pain reduction, this method requires a longer duration to achieve optimal effects due to the gradual nature of tissue recovery (28) DFM's relatively moderate outcomes compared to dry needling may also be influenced by the temporary discomfort or pain experienced due to the intensive pressure applied to the trigger point during therapy sessions.

Based on these findings, dry needling emerges as a viable option for achieving rapid pain relief, particularly for individuals who require significant improvement within a short period. However, DFM remains a valuable supportive therapy, especially for patients who may not be comfortable with invasive techniques such as dry needling. Integrating both methods may offer a more comprehensive approach to pain management.

Analysis of Pre-Post Lumbar ROM (Flexion, Extension, Lateral Flexion, and Rotation) and Comparison of ROM in the Dry Needling and Deep Friction Massage Groups

The results of this study indicate that neither DN nor DFM produced statistically significant changes in lumbar Range of Motion (ROM) across all movement patterns, including flexion, extension, lateral flexion, and rotation. Data analysis revealed that both interventions had comparable effects on lumbar ROM improvement, with no meaningful differences observed between them.

The mean data shows 27.5 for extension, 83.1 for flexion, 26.8 for lateral flexion, and 40 for rotation in the DN group, for the DFM group, the corresponding ROM values were: flexion 78.3, extension 26, lateral flexion 25, and rotation 34, indicating no significant differences between the dry needling and DFM groups ($p > 0.05$). These findings suggest neither intervention substantially impacted ROM enhancement for these specific movement patterns. Biomechanical constraints may act as limiting factors for ROM improvements without additional interventions. Nevertheless, the data collected during the study demonstrated a trend toward greater ROM improvement in the dry needling group compared to the DFM group across all movements. Although the difference was not statistically significant, this trend suggests that dry needling may exert a more favorable influence on lumbar ROM than DFM. For example, dry needling may induce additional physiological effects, such as more

profound muscle relaxation and increased tissue elasticity, compared to the more superficial effects of DFM (22,29).

The lack of statistically significant differences may also be attributed to various factors, including the severity of participants' conditions and individual responses to therapy. Variations in lumbar biomechanics among individuals can influence the overall outcomes of manual therapy (30,31). Although the observed increase in ROM did not reach statistical significance, the trend suggests potential advantages of dry needling over DFM in improving lumbar movement. However, further research is warranted to investigate additional factors contributing to these differences.

Limitation

This study has limitations, as both intervention methods were tested only once in a single session, which prevented periodic assessments and potentially affected the comprehensiveness of the findings. Future research should include multiple sessions to more effectively evaluate the long-term effects of dry needling and Deep Friction Massage. Additionally, using Doppler ultrasonography is recommended to enhance the accuracy of outcome measurements by providing detailed visualization of tissue changes and physiological responses.

CONCLUSIONS

In conclusion, this study demonstrates that both dry needling and deep friction massage are effective in treating Low Back Pain, with dry needling showing superior efficacy in reducing pain and promoting faster improvements in muscle relaxation and blood circulation. While both interventions lead to changes in trigger point size and an increase in range of motion, dry needling produces more significant and immediate effects than DFM. However, neither group showed significant changes in lumbar spine ROM. The results support dry needling as a more direct and efficient modality for reducing pain and restoring muscle function. However, further research is necessary to explore long-term effects and factors influencing individual responses to both therapies.

Ethical approval: This clinical trial was registered at UMIN-CTR (trial registration number UMIN000057073). Research involving the use of human samples has received ethical approval from the Research Ethics Committee of the Faculty of Public Health, Hasanuddin University (protocol code: 151024092320 with the approval number of 3102/UN4.14.1/TP.01.02/2024).

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Disclosure statement

None of the authors had a financial interest in or received any financial benefit from this research.

Conflict of interest

The authors declare no conflict of interest.

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Conditional variational autoencoders for generated hub genes in human endogenous retrovirus and periodontal inflammasome

Autocodificadores variacionales condicionales para genes centrales generados en retrovirus endógenos humanos e inflamasoma periodontal

Pradeep Kumar Yadalam[1,a *], Carlos M. Ardila[2, a,b *]

SUMMARY

Introduction: *Human endogenous retroviruses (HERVs) represent about 8 % of the human genome, with HERV-K being implicated in various autoimmune conditions. Recent studies suggest its role in periodontal disease, a chronic inflammatory condition.* **Objective:** *This study aims to use Conditional Variational Autoencoders (CVAE) to generate hub genes involved in the interaction between HERV-K and periodontal inflammasomes, potentially uncovering novel therapeutic targets for periodontal disease.* **Methods:** *Two gene expression datasets from the NCBI Gene Expression Omnibus (GEO) (GSE240644 and GSE262663) were analyzed for differentially expressed genes (DEGs) using GeoRtool. DEGs were further examined using Cytoscape, incorporating the GeneMANIA plugin to construct an interactome of 500 genes. CytoHubba's Maximum Centrality Clique method was employed to identify hub genes. The dataset was divided into hub and non-hub gene labels, then subjected to a CVAE model with 80 % training and 20 % testing. Model optimization involved hyperparameter tuning, enhancing hidden and latent dimensions, and adjusting the number of training epochs.* **Results:** *The CVAE model, optimized through hyperparameter tuning, improved reconstruction accuracy by 25.5 %, with an R-squared score rising from -0.0948 to 0.1242. The Kullback-Leibler (KL) divergence decreased from 5.5151 to 3.9184, reducing informative latent representations by 29 %. The enhanced model exhibited improved clustering of hub and non-hub genes, as evidenced by t-SNE visualization, demonstrating better data differentiation.* **Conclusions:** *The CVAE model significantly enhanced the prediction of hub genes related to HERV-K and periodontal inflammasome interactions. These findings suggest potential therapeutic and biomarker targets for periodontal disease; however, further validation and interpretation of the model are required.*

Keywords: *Hub genes, periodontal inflammasome, periodontium, retrovirus.*

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RESUMEN

Introducción: *Los retrovirus endógenos humanos (HERVs) representan aproximadamente el 8 % del genoma humano, y el HERV-K está implicado en diversas afecciones autoinmunes.* **Objetivo:** *Este estudio tiene como objetivo utilizar Autocodificadores variacionales condicionales (CVAE) para generar genes centrales involucrados en la interacción entre HERV-K e inflamasomas periodontales, descubriendo potenciales nuevas dianas terapéuticas para la enfermedad periodontal.* **Métodos:** *Se analizaron dos conjuntos de datos de expresión génica del NCBI Gene Expression Omnibus (GEO) (GSE240644 y GSE262663) para identificar genes diferencialmente expresados (DEGs) utilizando GeoRtool. Los DEGs se examinaron más a fondo utilizando Cytoscape, incorporando el plugin GeneMANIA para construir un interactoma de 500 genes. Se empleó el método Maximum Centrality Clique de CytoHubba para identificar genes centrales. El conjunto de datos se dividió en etiquetas de genes centrales y no centrales, y luego se sometió a un modelo CVAE con un 80 % de entrenamiento y un 20 % de prueba.* **Resultados:** *El modelo CVAE, optimizado mediante el ajuste de hiperparámetros, mejoró la precisión de reconstrucción en un 25,5 %, con una puntuación R-cuadrado que aumentó de -0,0948 a 0,1242. La divergencia de Kullback-Leibler (KL) disminuyó de 5,5151 a 3,9184, reduciendo las representaciones latentes informativas en un 29 %. El modelo mejorado exhibió una mejor agrupación de genes centrales y no centrales, como se evidencia en la visualización t-SNE, lo que demuestra una mejor diferenciación de datos.* **Conclusiones:** *El modelo CVAE mejoró significativamente la predicción de genes centrales relacionados con las interacciones HERV-K e inflamasomas periodontales.*

Palabras clave*: Genes centrales, inflamasoma periodontal, periodonto, retrovirus.*

INTRODUCTION

Human endogenous retroviruses (HERVs) are remnants of ancient retroviral infections that have integrated into the human genome, accounting for approximately 8 % of its total content. These elements have persisted across millions of years of evolution and are now recognized as functional components that can influence human biology and disease. Among the various HERV families, HERV-K is the most biologically active and has been associated with several autoimmune and inflammatory diseases, including rheumatoid arthritis, psoriasis, and multiple sclerosis (1). Notably, HERV-K has been implicated in dysregulating innate immune responses, particularly through the activation of the NLRP3 inflammasome and subsequent production of pro-inflammatory cytokines such as IL-1β, key drivers of tissue destruction in chronic inflammatory conditions (1,2).

Increasing evidence suggests that HERV-K is involved in periodontal disease, a chronic inflammatory condition characterized by the destruction of the tissues surrounding the teeth, driven by both bacterial infections and host immune responses (2). In periodontitis, bacterial pathogens (e.g., *Porphyromonas gingivalis*) trigger NLRP3 inflammasome activation and IL-1β release, exacerbating inflammation and bone resorption (1-3). Given the established role of HERV-K in amplifying inflammasome signaling in other diseases, we hypothesize that its activation in periodontal tissues may similarly potentiate NLRP3/IL-1β-driven pathology, though this link remains underexplored. Understanding the molecular mechanisms underlying HERV-K activation in the context of periodontal disease could pave the way for the development of novel diagnostic and therapeutic strategies.

Advancements in bioinformatics have enabled the study of interactions between viral elements and host genes using gene expression data. Interactome analysis, which maps protein-protein interactions, has proven invaluable in identifying key regulatory genes, known as hub genes, which are often crucial in disease processes (3). For periodontitis, hub genes associated with inflammasome regulation (e.g., NLRP3, CASP1, IL1B) could reveal how HERV-K exacerbates disease progression.

In recent years, machine learning models like Variational Autoencoders (VAEs) have gained attention for their capacity to learn complex patterns in large, high-dimensional datasets, such as gene expression profiles. VAEs, particularly Conditional VAEs (CVAEs), offer a powerful tool for generating and predicting hub genes, which may reveal novel insights into the role of HERV-K in periodontal inflammation.

This study aims to use CVAE to predict hub genes involved in the interaction between HERV-K and periodontal inflammasomes, facilitating the identification of biomarkers and therapeutic targets for periodontal disease.

MATERIALS AND METHODS

Differential gene expression analysis and interactome

This study analyzed differential gene expression (DEGs) using two publicly available gene expression datasets from the NCBI Gene Expression Omnibus (GEO) database (4). The GEO accession numbers used were GSE240644 and GSE262663. GSE240644 focuses on the role of HERV-K env in THP-1 monocytic cell differentiation. Similarly, GSE262663 explores the relationship between hypoxia and periodontitis. Differentially expressed genes were identified using GEOtool with thresholds of $|\log_2 \text{fold change}| \geq 1$ (corresponding to a 2-fold linear change) and an adjusted p-value < 0.05.

GEOtool is a powerful tool for analyzing differential gene expression, focusing on the statistical evaluation of fold changes and p-values, which enables an understanding of biological differences between conditions. A fold change of two is often used, and statistical significance is typically set at 0.05.

We utilized Cytoscape, a popular network visualization and analysis software, to further investigate the interactions between the differentially expressed genes (DEGs). The GeneMANIA plugin in Cytoscape created an interactome network of 500 genes, with top differentially expressed genes inserted and prioritized using CytoHubba's Maximum Centrality Clique method (5). These hub genes play essential roles in the network and may serve as potential key regulators in the interaction between HERV-K and the periodontal inflammasome. Data preprocessing included removal of outliers (genes with expression values beyond ± 3 standard deviations from the mean) and Z-score normalization. The dataset was then split into a stratified training set (80 %) and a test set (20 %) to maintain class balance.

Model Architecture

We implemented a CVAE to analyze gene expression patterns, distinguishing hub and non-hub genes. The encoder consisted of three fully connected layers (input → 128 units → 64 units → latent space) with ReLU activation, while the decoder mirrored this architecture with sigmoid activation for output reconstruction. The latent space dimension was set to 4 after hyperparameter optimization. Hub/non-hub labels were concatenated to the latent space for conditional generation.

Hyperparameter Tuning

The model's performance was optimized through hyperparameter tuning, which involved increasing the hidden dimension to 256, expanding the latent dimension to 4 for a richer representation, adjusting the learning rate to 5e-4 for balance, and extending the training process to 150 epochs for parameter refinement.

RESULTS

The optimized CVAE model demonstrated significant improvements in reconstructing and differentiating gene expression profiles. Reconstruction accuracy increased by 25.5.%, with the R-squared coefficient improving from -0.0948 to 0.1242, indicating the model now explains 12.42 % of transcriptional variance between hub and non-hub genes. This enhancement suggests the model captures biologically relevant patterns in gene expression regulation associated with network hub genes. Concurrently, we observed a 29 % reduction in Kullback-Leibler divergence (from 5.5151 to 3.9184), indicating improved alignment between the latent space and prior distribution, which results in more stable representations of regulatory networks without overfitting.

Analysis of reconstruction errors, shown in Figure 1, revealed a distribution skewed toward low mean squared error (MSE) values, with high-frequency peaks in the 0.1-0.3 range. This pattern indicates accurate reconstruction

of core transcriptional profiles for most genes. The few outliers with an MSE above 0.5 may correspond to context-specific regulated genes or potential technical artifacts that require further investigation.

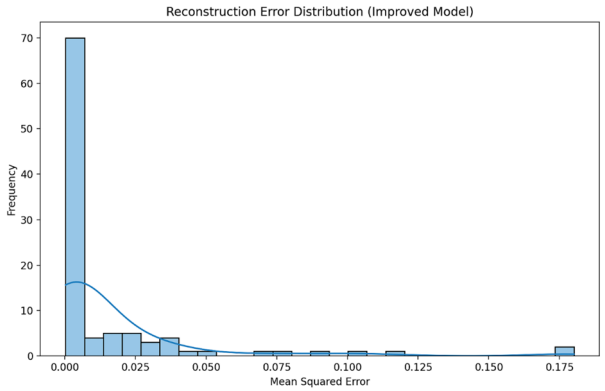


Figure 1. Distribution of reconstruction errors.

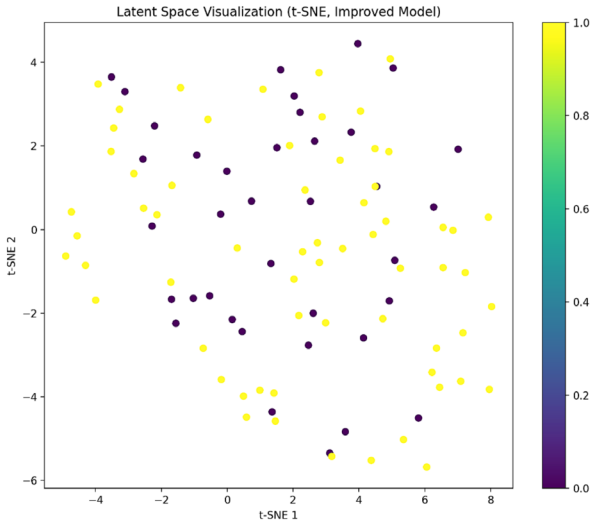


Figure 2. t-SNE visualization of a latent space.

The t-SNE visualization of latent space (Figure 2) showed clear separation between hub and non-hub genes. Hub genes formed discrete clusters, particularly two main groups (Clusters A and B) that showed significant enrichment ($p<0.01$) for inflammasome-related pathways (including NLRP3 and IL1B) and HERV-K interacting genes. In contrast, non-hub genes displayed a more diffuse distribution in the latent space, consistent with their peripheral roles in network topology. The robustness of this separation was confirmed by a Silhouette score of 0.41, indicating a biologically meaningful distinction between both gene classes.

DISCUSSION

The results of this study demonstrate that a CVAE can be effectively used to identify and generate hub genes related to the interaction between HERV-K and periodontal inflammasomes. Notably, specific hub genes like ALPK1 (activated in periodontal ligament fibroblasts under mechanical stress) and TNFRSF11 (regulator of osteoclastogenesis) emerged as high-confidence candidates, with direct relevance to periodontal inflammation and bone resorption. By optimizing the model's architecture and tuning its hyperparameters, we observed significant improvements in reconstruction accuracy and model performance. The increase in the R-squared score and the decrease in KL divergence suggest that the model can better capture the underlying relationships between hub and non-hub genes. This was further supported by the t-SNE visualization, which revealed clear clustering patterns between these two groups of genes.

These findings have several implications for understanding the molecular mechanisms linking HERV-K activity with periodontal inflammation. Hub genes identified through interactome analysis are often key regulators in disease pathways, and the ability to predict these genes using generative models, such as CVAE, could revolutionize the approach to biomarker discovery and drug development for complex diseases. Notably, this approach could extend beyond periodontal disease, potentially providing insights into other inflammatory and autoimmune conditions where HERV-K is implicated (4,6-8).

However, this study has several limitations. The reliance on publicly available datasets, although useful for initial discovery, may not fully capture the complexity of HERV-K interactions in different disease states (9,10). Additionally, the interpretability of the latent space representations generated by the CVAE remains a challenge (11,12), and further work is needed to translate these findings into clinical applications.

The inherent heterogeneity of periodontal tissues, combined with our reliance on cell line models and bulk tissue datasets, may affect the generalizability of our findings. While our model successfully identified hub genes, the biological interpretation of the latent space remains a significant challenge, a limitation common to many deep learning approaches in genomics. Future studies incorporating single-cell resolution data from distinct periodontal compartments and experimental validation of candidate hub genes will be essential to strengthen these findings. Additionally, techniques like SHapley Additive exPlanations (SHAP) value analysis could help decode the model's latent space by quantifying individual gene contributions to the observed patterns.

Looking forward, this work establishes a framework for utilizing generative models to investigate intricate host-viral interactions in inflammatory diseases. The integration of larger, clinically annotated datasets and the application of emerging interpretability methods will further enhance the translational potential of this approach. Significantly, the principles developed here may extend beyond periodontitis to other inflammatory conditions where endogenous retroviruses have been implicated, potentially uncovering new therapeutic avenues across multiple disease contexts.

CONCLUSION

This study demonstrates that CVAEs can be utilized to predict and generate hub genes involved in the interaction between HERV-K and periodontal inflammasomes. The optimized model exhibited significant improvements in reconstruction accuracy and the identification of gene clusters. For clinical translation, we propose focusing initial efforts on ALPK1 inhibitor repurposing studies using periodontal disease models, while simultaneously validating TNFRSF11 expression patterns as potential diagnostic markers in gingival fluid samples. This two-pronged approach directly builds on our most robust and actionable findings.

Conflict of interest

No potential conflict of interest relevant to this article was reported

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Risk Factors for the Utilization of Inpatient Health Services Among Social Security Agency for Health Participants at Liwuto Community Health Center, Baubau, Makasar Island

Factores de riesgo para la utilización de servicios de salud hospitalarios entre los afiliados a la Agencia de Seguridad Social para la salud en Liwuto, Baubau, Isla Makasar

Dwi Sumarningsih*[1a], Sukri Palutturi[2a], Amran Razak[3a], Muhammad Yusran Amir[4a], Stang[5b]

SUMMARY

Background: *The utilization of inpatient health services by BPJS (Social Security Agency for Health) participants at Liwuto Community Health Center (Puskesmas), Makasar Island, Baubau City, remains suboptimal. Several factors, ifactors social, economic, geographical, and psychological factors, are believed to influence community decisions regarding the use of these services.* **Objective:** *This study aims to analyze the risk factors that influence the utilization of inpatient services by BPJS participants at Liwuto Community Health Center, Makasar Island, Baubau City.* **Methods:** *This study employs quantitative case-control research design. The case group consisted of BPJS patients who utilized inpatient health services at the Liwuto Community Health Center between 2023 and 2024. The control group comprised BPJS patients who did not utilize inpatient services during the same period. A total of 106 participants were selected using purposive sampling. Data were analyzed using the Chi-Square test and multivariate logistic regression to determine the relationships and influence between variables.* **Results:** *The analysis revealed significant associations between inpatient service utilization and several variables: knowledge (p = 0.007; OR = 5.417), staff attitude (p = 0.010; OR = 3.699), household income (p = 0.0001; OR = 3.304), travel distance (p = 0.001; OR = 7.870), availability of healthcare personnel (p = 0.120; OR = 0.543), and family support (p = 0.019; OR = 0.391). Multivariate analysis identified family support as the most dominant factor (p = 0.033; OR = 9.907). The Nagelkerke R-squared, also known as the adjusted R-squared for logistic regression, value of 61.2 % indicates the extent to which the independent variables explain the variance in inpatient service utilization.* **Conclusion:** *Knowledge, staff attitude,*

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family income, travel distance, availability of health personnel, and family support are significant risk factors influencing the utilization of inpatient services by BPJS participants. Among these, family support emerges as the most influential factor.

Keywords: *Utilization, inpatient services, BPJS participants, community health center (Puskesmas).*

RESUMEN

Antecedente: *La utilización de los servicios de salud hospitalarios por parte de los afiliados al BPJS (Agencia de Seguridad Social para la Salud) en el Centro de Salud Comunitario (Puskesmas) de Liwuto, en la isla de Makasar, ciudad de Baubau, sigue siendo insuficiente. Se cree que varios factores, como los sociales, económicos, la distancia geográfica y los psicológicos, influyen en las decisiones de la comunidad con respecto al uso de estos servicios.* **Objetivo:** *Este estudio tiene como objetivo analizar los factores de riesgo que influyen en la utilización de los servicios hospitalarios por parte de los afiliados al BPJS en el Centro de salud Comunitario de Liwuto, isla de Makasar, ciudad de Baubau.* **Métodos:** *Este estudio emplea un diseño de investigación cuantitativo de casos y controles. El grupo de casos estaba formado por pacientes del BPJS que utilizaron los servicios de salud hospitalarios en el Centro de salud comunitario de Liwuto entre 2023 y 2024. El grupo de control estaba formado por pacientes del BPJS que no utilizaron los servicios hospitalarios durante el mismo periodo. Se seleccionó un total de 106 participantes mediante un muestreo intencional. Los datos se analizaron utilizando la prueba de Chi-Cuadrado y la regresión logística multivariante para determinar las relaciones y la influencia entre las variables.* **Resultados:** *El análisis reveló asociaciones significativas entre la utilización de los servicios hospitalarios y varias variables: conocimientos (p = 0,007; OR = 5,417), actitud del personal (p = 0,010; OR = 3,699), los ingresos familiares (p = 0,0001; OR = 3,304), la distancia de desplazamiento (p = 0,001; OR = 7,870), la disponibilidad de personal sanitario (p = 0,120; OR = 0,543) y el apoyo familiar (p = 0,019; OR = 0,391). El análisis multivariante identificó el apoyo familiar como el factor más dominante (p = 0,033; OR = 9,907). El valor R cuadrado de Nagelkerke del 61,2 % indica el grado en que las variables independientes explican la varianza en la utilización de los servicios de hospitalización.* **Conclusión:** *El conocimiento, la actitud del personal, los ingresos familiares, la distancia de desplazamiento, la disponibilidad de personal sanitario y el apoyo familiar son factores de riesgo significativos que influyen en la utilización de los servicios hospitalarios por parte de los afiliados al BPJS. Entre ellos, el apoyo familiar se perfila como el factor más influyente.*

Palabras clave: *Utilización, servicios hospitalarios, afiliados al BPJS, centro de salud comunitario (Puskesmas).*

INTRODUCTION

The National Health Insurance Program (*Program Jaminan Kesehatan Nasional*, abbreviated as JKN), administered by BPJS Kesehatan (Social Security Agency for Health), is a government-led initiative to provide universal health coverage for all Indonesians and promote a healthier, more productive population (1).

Participation in the JKN-KIS (Kartu Indonesia Sehat) program has steadily increased. According to the National Social Security Council, 248 771 083 people were registered in 2022. This number rose to 273 525 350 by June 2024, 97.13 % of Indonesia's estimated 281 million population (Bappenas, or the Ministry of National Development Planning of Indonesia, is the central government institution responsible for formulating national development planning and budgeting) (2). In Baubau City, the JKN coverage reached 100 %, covering around 161 000 residents based on 2023 population data (3).

The World Health Organization (WHO) highlights healthcare utilization as a key public health goal. In 2014, WHO reported that 38.4 million people in Asia lacked adequate access to health services (4). Utilization remains low in rural areas of developing countries, at less than 50 %, compared to urban populations (5).

In Indonesia, healthcare utilization remains limited. Of 274 839 survey respondents, only 7 300 had been hospitalized in the past year. Among these, 53.36 % lived in urban areas and 46.64 % in rural ones. Notably, 89.94 % of BPJS participants who had inpatient care reported being satisfied (1).

Community Health Centers (*Puskesmas*) are Indonesia's primary health service providers. The government's policy to expand these facilities ensures fair access to care.

Community Health Centers Liwuto is the only health center on Makasar Island, Baubau City. It is an inpatient facility health care center that serves both BPJS PBI (Contribution Assistance Recipients) and Non-PBI members (6), (Puskesmas Liwuto Profile, 2021) and (7,8).

Several studies have examined what influences healthcare use, such as illness severity, access, insurance status, and perceived service quality (9). Galanis et al. (10), found in Greece that health knowledge affects service use. Hamada et al. (11) showed in Japan that lower family income limits access to care. Similarly, Nurul Qalbi et al. (12) as shown in Indonesia, the attitudes of healthcare workers also affect service utilization.

Given these findings and the declining trend in inpatient service use at Community Health Center Liwuto, this study aims to explore the contributing risk factors.

MATERIALS AND METHODS

Study design and population

This study used an observational analytic design with a case-control approach. It was conducted at Community Health Center Liwuto, Makasar Island, Baubau City, from February to March 2025. The study population consisted of patients who used or did not use inpatient services at Community Health Center Liwuto between 2023 and 2024. Those who used inpatient care were assigned to the case group, while those who did not were assigned to the control group. A purposive sampling method was applied, and the sample size was calculated using the unmatched case-control formula by Lemeshow (1990). The final sample consisted of 106 respondents, divided equally between the case group (53 respondents) and the control group (53 respondents), resulting in a 1:1 ratio.

Data analysis

The data were analyzed using descriptive and inferential statistics. Univariate analysis described respondent characteristics. Bivariate analysis employed the Chi-square test to assess relationships between variables, with results interpreted through the Odds Ratio (OR). Multivariate analysis used Logistic Regression to identify the most influential risk factors.

Ethical approval

This research received ethical clearance from the Ethics Committee of the Faculty of Public Health, Hasanuddin University. Approval Number: 140/UN4.14.1/TP.01.02/2025. Validity Period: January 24, 2025 – January 24, 2026

RESULTS

Table 1 presents the distribution of respondent characteristics, revealing several key demographic trends. Regarding age, most respondents in both the control and case groups fall into the adult category, accounting for 49.1 % and 50.9 %, respectively. Gender distribution shows a predominance of female respondents in both groups, with women comprising 88.7 % of the control group and 66.0 % of the case group. Regarding occupation, most individuals in the control group are housewives, representing 79.2 % of that cohort, while the case group primarily comprises respondents categorized under "other occupations" at 41.5 %. Educational background also shows distinct patterns, with the majority of respondents in both groups having attained higher levels of education, 84.9 % in the control group and 58.5 % in the case group having completed senior high school or pursued tertiary education.

Bivariate Analysis

The bivariate analysis on the factors influencing the utilization of inpatient healthcare services by BPJS participants at Community Health Center Liwuto, Makasar Island, Baubau city is presented in Table 2. The Chi-Square test shows significant associations between several variables and the utilization of inpatient services by BPJS participants at the Community Health Center Liwuto. Family income is significantly related ($p < 0.0001$; OR = 3.304; 95 % CI =

Table 1. Frequency Distribution of Respondent Characteristics.

Characteristic	Control Group (Did Not Utilize)		Case Group (Utilized)	
	n (53)	%	n (53)	%
Age				
Adolescents	2	3.8	10	18.9
Adults	26	49.1	27	50.9
Pre-Elderly	18	34.0	14	26.4
Elderly	7	13.2	2	3.8
Gender				
Male	6	11.3	18	34.0
Female	47	88.7	35	66.0
Education				
Low (Elementary, Junior High School)	8	15.1	22	41.5
High (Senior High School, Higher Education)	45	84.9	31	58.5
Occupation				
Fisherman	4	7.5	8	15.1
Civil Servant	2	3.8	1	1.9
Teacher	2	3.8	0	0
Housewife	42	79.2	19	35.8
Entrepreneur	0	0	3	5.7
Others	3	5.6	22	41.5

Source: Primary Data, 2025

2.349-4.648), indicating that those with higher income are 3.3 times more likely not to use inpatient services. Knowledge also plays a role (p = 0.007; OR = 5.417; 95 % CI = 1.44-20.326), with lower knowledge increasing the likelihood of non-utilization by over five times.

Negative attitudes are associated with a significant link (p = 0.010; OR = 3.699; 95 % CI = 1.325-10.330), making individuals nearly four times more likely to avoid inpatient care. Travel distance is also significant (p = 0.001; OR = 7.870; 95 % CI = 2.145-28.879), with those living farther away being eight times more likely not to use the services.

In contrast, the availability of health workers is not significantly associated (p = 0.120; OR = 0.543; 95 % CI = 0.251-1.175). Family support, however, is a significant protective factor (p = 0.019; OR = 0.391; 95 % CI = 0.177-0.862), indicating that individuals with strong family support are less likely to utilize inpatient care.

Multivariate Analysis

Table 3 shows that, based on multivariate analysis, the variable of family support is the most dominant factor influencing the utilization of inpatient health services by BPJS participants at the Liwuto Community Health Center, Makasar Island, Baubau City, with a p-value of 0.033 and an odds ratio (OR) of 9.907. This suggests that respondents lacking family support are 9.907 times more likely not to utilize BPJS inpatient services at the health center. The Nagelkerke R Square value of 61.2 % indicates that the independent variables included in the model explain 61.2 % of the variation in the dependent variable.

DISCUSSION

According to Lawrence Green's theory, health-related behavior is influenced by three

Table 2. Bivariate Analysis of Factors Influencing the Utilization of Inpatient Healthcare Services by BPJS Participants at Community Health Center Liwuto, Makasar Island, Baubau City

Variables	Utilization of Services				Total		p-value	OR* 95 % CI**
	Not Utilized		Utilized (%)		%	n		
	%	n	%	n				
Income								3.304
Low	0	0	56.6	30	28.3	30	0.0001	(2.349-
High	100	53	43.4	23	71.7	76		4.648)
Knowledge								5.417
Poor	24.5	13	5.7	3	15.1	16	0.007	(1.4-
Good	75.5	40	94.3	50	84.9	90		20.326)
Attitude								3,699
Negative	32.1	17	11.3	6	17	18	0.010	(1.325-
Positive	67.9	36	88.7	47	83	88		10.330)
Distance to Facility								7.870
Far	32.1	17	5.7	3	18.9	20	0.001	(2.145-
Near	67.9	36	94.3	50	81.1	86		28.879)
Availability of Health Workers								
Inadequate	39.6	21	54.7	29	47.2	50		0.543
Adequate	60.4	32	45.3	24	52.8	56	0.120	(0.251-
								1.175)
Family Support								0.391
Poor	32.1	17	54.7	29	43.4	48	0.019	(0.177-
Good	67.9	36	45.3	24	56.6	60		0.862)

Source: Primary Data, 2025, *OR: Odds Ratio, **CI: Confidence Interval.

Table 3. Results of Multivariate Analysis on Factors Influencing the Utilization of Inpatient Health Services by BPJS Participants at Liwuto Community Health Center, Makasar Island, Baubau City.

Variables in the Equation					95 % CI for EXP(B)*		Negalkerke R Square
		B	Sig	Exp(B)	Lower	Upper	
Step 1a	Income	-23.682	0.997	0.000	0.000	-	0.612
	Knowledge	0.238	0.836	1.269	0.134	12.050	-
	Attitude	0.91	0.946	1.095	0.079	15.155	-
	Distance to Facility	0.895	0.496	2.446	0.187	32.066	-
	Family Support	2.2293	0.033	9.907	1.204	81.500	-
	Constant	19.910	0.998	4.436	-	4.436	-

Source: Primary Data, 2025, *CI: Confidence Interval.

key factors: (a) Predisposing Factors: these include health knowledge and perceived benefits of healthcare services; (b) Enabling Factors include family income, distance to healthcare facilities, and availability of transportation; (c) Reinforcing Factors: these include attitudes and behaviors of healthcare providers, as well as family support (13).

In relation to Family Income, this study reveals a significant correlation between family income and the utilization of in patient services by BPJS participants at Liwuto Community Health Center, Makasar Island, Baubau City. Income influences a household's ability to meet healthcare needs (14). In effect, Fadhilah et al. (15) found that higher income is associated with greater healthcare utilization ($p = 0.0001$). Low-income families often prioritize daily essentials and face additional transportation costs, which discourages them from seeking care. This issue is also highlighted by Cinaroglu and Çalıskan (16), who emphasize that the burden of accessing healthcare services often falls disproportionately on the poor.

While BPJS provides substantial support for low-income groups to access appropriate healthcare, many still choose not to utilize services at public health centers, such as the Community Health Center. This study found that family income is a risk factor in determining whether BPJS participants utilize inpatient services at Liwuto Community Health Center (17).

Although BPJS covers healthcare costs, many people still avoid using services at public health centers, such as community health centers. This study confirms that family income is a risk factor for inpatient service utilization at Liwuto. Higher-income families prefer private facilities offering more comfort and speed, while lower-income groups rely on BPJS services at the Community Health Center as their most accessible option.

The study found a significant relationship between knowledge and the utilization of inpatient healthcare services by BPJS participants at the Liwoto Community Health Center (Puskesmas), Makasar Island, Baubau City. Knowledge is a critical factor influencing behavior. Individuals with a higher level of understanding and awareness regarding the importance of accessing healthcare facilities are more likely to seek medical help when needed. Karman (18) in a study conducted among coastal communities in Bungin Permai Village revealed that inadequate knowledge contributed to the underutilization of available healthcare services, primarily due to a lack of awareness among families regarding the benefits of these services.

The present findings suggest that knowledge plays a role as a risk factor in the utilization of inpatient services among BPJS participants at the Liwoto Community Health Center. Participants with limited knowledge tend to be less informed about the benefits, procedures, and their rights as BPJS members, particularly concerning inpatient care. This lack of awareness often results in missed opportunities to access healthcare services that are either free or affordable. Thus, insufficient knowledge becomes a barrier to effective decision-making in accessing available healthcare services, including inpatient care covered under BPJS.

When analyzing the attitude of healthcare workers, a significant relationship was revealed between the attitude of healthcare workers and the utilization of inpatient healthcare services by BPJS participants at the Liwoto Community Health Center. The attitude of healthcare workers plays a crucial role in shaping the patient's experience through the quality of their interactions with patients. This includes listening attentively, building trust, demonstrating empathy, maintaining confidentiality, showing respect, and responding attentively to patient needs. Effective communication, which involves understanding and responding to patients' views, emotions, and expectations, is essential in healthcare service delivery (19). These findings are consistent with Nurul Qalbi et al. (12), who in a study conducted at the Tamalanrea Community Health Center, found a significant correlation between healthcare workers' attitudes and healthcare utilization.

Negative attitudes, such as a lack of courtesy, failure to actively listen to patients, or rushing through consultations, may make patients feel ignored or undervalued. This perception can significantly diminish trust and satisfaction with healthcare services. In contrast, healthcare providers who exhibit empathy, patience, and clear communication foster greater patient satisfaction and confidence, encouraging repeat visits and positive word-of-mouth referrals. Therefore, improving healthcare workers' interpersonal communication skills, service ethics, and empathetic practices is essential to maximizing the utilization of health services, particularly among BPJS members.

There was a significant relationship between travel distance and the use of inpatient services

by BPJS participants at the Liwuto Community Health Center, Makasar Island, Baubau City. Households closer to the Community Health Center were 1.7 times more likely to use healthcare services than those farther away, highlighting travel distance as a key factor in service utilization (20). Fatimah (21), also found a strong association between access and healthcare use at Kagok Health Center ($p = 0.0001$), showing that shorter distances and faster access increase the likelihood of visiting health facilities. On the other hand, limited transportation and long distances often discourage people from seeking care at the Community Health Center. This issue is more pronounced in areas like Makasar Island, where poor infrastructure, adverse weather conditions, and nighttime darkness make reaching health facilities difficult. Long distances also reduce motivation for inpatient care, as patients may hesitate to stay far from home and be separated from their families. Therefore, improving access through well-located health centers is essential for increasing BPJS inpatient service utilization.

In relation to the Availability of Healthcare Personnel, the present results indicate that there was no statistically significant relationship between the availability of healthcare personnel and the utilization of inpatient services by BPJS participants at the Liwoto Community Health Center. In this context, the availability of healthcare personnel refers to their physical presence at the Community Health Center during patient care (22). Zaini et al. (22) found a significant relationship between healthcare personnel availability and service utilization (p-value = 0.0001). However, despite the presence of staff, their occasional unavailability during critical times, often due to participation in training sessions, meetings, or other duties, highlights the need for a reassessment of staff responsibilities and strategic planning to mitigate such service disruptions.

In contrast, the current study suggests that the availability of healthcare personnel does not pose a significant barrier to inpatient service utilization by BPJS participants at the Liwoto Community Health Center. Statistically, the relationship was not significant, and qualitatively, it was observed that the existing number and presence of healthcare personnel were generally sufficient to meet service demands. This suggests that the community considers the current staffing level adequate and does not perceive it as a significant barrier to accessing inpatient services. Thus, while the availability of healthcare personnel remains an important element in service delivery, it does not appear to be a critical limiting factor in the context of the Liwoto Community Health Center regarding BPJS inpatient service utilization.

There was a significant link between family support and the use of inpatient services by BPJS participants at the Community Health Center Liwuto, Makasar Island, Baubau City. This finding is consistent with Sulaiman (23), who reported a significant association between family support and healthcare services ($p = 0.0001$). Similarly, Veni dan Mutia (24), a significant correlation was also found ($p = 0.011$), as reported by Sainuddin et al. (25), who demonstrated a significant relationship between family support and healthcare service utilization ($p = 0.021$).

Family support emerges as a risk factor in the utilization of inpatient services at the Liwoto Community Health Center, as families often play a crucial role in health-related decision-making. When individuals face health challenges, the decision to seek inpatient care is frequently made collectively, with the family acting as a source of information, emotional support, and even logistical and financial assistance. Moreover, family support is essential not only during the decision-making process but also in practical terms, such as arranging transportation to the health facility, providing companionship during hospitalization, and ensuring that the patient's needs are met throughout the care process. In other words, family support has a significant influence on both the continuity and quality of inpatient care, not only through emotional encouragement but also through hands-on involvement.

This study's multivariate analysis confirmed that family support is the most dominant factor influencing the use of BPJS inpatient services at the Community Health Center Liwuto. It acts not just as emotional support, but as a major practical enabler in accessing and continuing care. Compared to other factors, such as knowledge, staff attitude, income, or travel distance, the

presence or absence of family support has the strongest impact.

CONCLUSION

Several factors significantly contribute to the utilization of healthcare services among BPJS participants. Predisposing factors, particularly the level of knowledge, have been identified as essential determinants influencing service usage. Enabling factors, including family income, travel distance to the health facility, and the availability of healthcare personnel, also play a crucial role in shaping health-seeking behavior. Furthermore, reinforcing factors such as the attitudes of healthcare staff and the level of family support are significantly associated with the decision to utilize inpatient healthcare services. Among all the variables examined, family support emerged as the most dominant factor influencing the utilization of inpatient services at the Liwoto Community Health Center in Makasar Island, Baubau City, highlighting the essential role of familial involvement in facilitating access to appropriate care.

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Conflict of interest

The Author(s) declares that there is no conflict of interest.

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Relación de las características antropométricas y síndrome de ovario poliquístico en mujeres en edad fértil pertenecientes a una universidad

Relationship between anthropometric characteristics and polycystic ovary syndrome in women of reproductive age attending a university

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RESUMEN

Objetivo: *Determinar la relación de las características antropométricas y síndrome de ovario poliquístico (SOP) en mujeres en edad fértil pertenecientes a una Universidad*. **Método:** *Se realizó un estudio descriptivo analítico de corte transversal en 345 mujeres entre 16 y 35 años. La selección se hizo mediante un muestreo no probabilístico por conveniencia. Los datos fueron recolectados mediante un cuestionario basado en los criterios de Rotterdam para el diagnóstico de SOP. Se realizaron mediciones antropométricas (índice de masa corporal (IMC), el perímetro abdominal y el porcentaje de grasa corporal). El análisis estadístico se hizo por pruebas no paramétricas como Mann-Whitney U y Kruskal-Wallis para comparar grupos, y la prueba de Chi-Cuadrado para evaluar la asociación entre variables categóricas*. **Resultados:** *El estudio mostró que el 24,1 % de las mujeres evaluadas presentaron diagnóstico de SOP. Las mujeres con SOP presentaron valores significativamente mayores en el IMC (24,61 ± 4,49 kg/m² frente a 23,03 ± 4,24 kg/m²; p = 0,0062) y en el perímetro abdominal (78,01 ± 9,97 cm frente*

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a 74,92 ± 10,39 cm; p = 0,0063) en comparación con las mujeres sin SOP. Además, se identificó una correlación positiva y significativa entre el perímetro abdominal y el IMC, particularmente en el grupo con SOP (R^2 = 0,72, p = 0,0001). **Conclusión:** *Se evidencian que el IMC y el perímetro abdominal son indicadores antropométricos clave para identificar el riesgo de SOP en mujeres universitarias en edad fértil.*

Palabras clave: *Síndrome de ovario poliquístico, índice de masa corporal, circunferencia de la cintura.*

SUMMARY

Objective: *To determine the relationship between anthropometric characteristics and Polycystic Ovary Syndrome (PCOS) in women of reproductive age attending a university.* **Method:** *A descriptive analytical cross-sectional study was conducted with 345 women aged 16 to 35 years. The selection was made through non-probabilistic convenience sampling. Data was collected using a questionnaire based on the Rotterdam criteria for the diagnosis of PCOS. Anthropometric measurements were performed, including Body Mass Index (BMI), waist circumference, and body fat percentage. Statistical analysis was conducted using non-parametric tests, including the Mann-Whitney U test and the Kruskal-Wallis test, to compare groups, and the Chi-square test to evaluate the association between categorical variables.* **Results:** *The study showed that 24.1 % of the women evaluated were diagnosed with PCOS. Women with PCOS had significantly higher BMI values (24.61 ± 4.49 kg/m² vs. 23.03 ± 4.24 kg/m²; p = 0.0062) and waist circumference (78.01 ± 9.97 cm vs. 74.92 ± 10.39 cm; p = 0.0063) compared to women without PCOS. Additionally, a positive and significant correlation was identified between waist circumference and BMI, particularly in the PCOS group (R^2 = 0.72, p = 0.0001).* **Conclusion:** *BMI and waist circumference are key anthropometric indicators for identifying the risk of PCOS in university women of reproductive age.*

Keywords: *Polycystic ovary syndrome, body mass index, waist circumference.*

INTRODUCCIÓN

El Síndrome de Ovario Poliquístico (SOP) es una es una condición endocrina y metabólica compleja y heterogénea que afecta aproximadamente entre el 4 % al 20 % de las mujeres en edad reproductiva a nivel mundial, siendo una de las principales causas de infertilidad y trastornos metabólicos en esta población (1,2). Esta condición se caracteriza por la presencia de hiperandrogenismo, anovulación crónica y ovarios poliquísticos, según los criterios de Rotterdam (3). Además de las alteraciones reproductivas, el SOP está estrechamente relacionado con comorbilidades metabólicas como la resistencia a la insulina, la obesidad central y un mayor riesgo de desarrollar enfermedades cardiovasculares y diabetes tipo 2 (4,5).

Un aspecto relevante en la fisiopatología del SOP es la obesidad abdominal, la cual se ha identificado como un marcador crítico de riesgo metabólico y la evaluación del perímetro abdominal, considerado un marcador confiable de riesgo cardiovascular, ha sido clave para evaluar el impacto del exceso de peso en el desarrollo y progresión del SOP (6). Shah y col., sugiere que la obesidad abdominal es un factor de riesgo relevante, asociado a un incremento de la resistencia a la insulina, la cual constituye un mecanismo central en la patogénesis del SOP (7). Se ha evidenciado que la acumulación de grasa visceral, incluso en mujeres con un índice de masa corporal (IMC) dentro de rangos considerados normales, está asociada con un perfil inflamatorio elevado y resistencia a la insulina, lo cual agrava los desequilibrios hormonales y metabólicos característicos del SOP (8).

Estudios recientes han demostrado que la relación cintura-altura (RCA) es un indicador antropométrico más confiable para predecir hiperandrogenismo y disfunciones metabólicas en comparación con el IMC. Esta métrica mostró una mayor capacidad predictiva para identificar mujeres con SOP que presentaban alteraciones hormonales significativas, incluyendo incrementos en el índice de andrógenos libres (IAL) y reducción de la globulina fijadora de las hormonas sexuales (SHBG) (9).

La relación entre el SOP y los marcadores antropométricos va más allá del perímetro abdominal y el IMC. Investigaciones recientes han señalado que la circunferencia de muñeca podría ser un marcador útil y de fácil detección para identificar resistencia a la insulina en mujeres con SOP, especialmente en poblaciones africanas donde se evidenció una correlación significativa

con el modelo de homeostasis para la evaluación de la resistencia a la insulina (HOMA-IR) (10). Adicionalmente, se ha observado que la obesidad abdominal no solo exacerba la resistencia a la insulina, sino que también incrementa marcadores inflamatorios en el fluido folicular, lo cual podría afectar negativamente la calidad ovocitaria y contribuir a la infertilidad en estas pacientes (7).

Desde una perspectiva epidemiológica, estudios multinacionales han evidenciado que las mujeres con SOP presentan un riesgo considerablemente mayor de desarrollar enfermedad hepática grasa no alcohólica (EHGNA), particularmente aquellas con un aumento significativo en el IMC y la grasa visceral (11). La EHGNA se asocia no solo con un incremento del riesgo cardiovascular, sino también con alteraciones endocrinas que perpetúan el círculo de inflamación y resistencia a la insulina (11). Estos hallazgos subrayan la importancia de una evaluación integral de los marcadores antropométricos en mujeres con SOP, considerando no solo el peso total, sino la distribución de la grasa corporal y los niveles hormonales.

En entornos universitarios, donde predominan mujeres jóvenes en edad reproductiva, la identificación de factores antropométricos asociados al SOP cobra especial relevancia. Las características de esta población, expuesta a cambios en el estilo de vida y altos niveles de estrés, pueden aumentar la susceptibilidad al desarrollo de SOP y sus complicaciones metabólicas (12). Por ello, la investigación local sobre el SOP y sus características asociadas adquiere especial relevancia en comunidades universitarias, donde predomina una población joven en etapa reproductiva.

En este contexto, este estudio tiene como objetivo determinar la relación entre las características antropométricas y la prevalencia del SOP en mujeres en edad fértil pertenecientes a una comunidad universitaria en Colombia, con el propósito de identificar patrones de riesgo y contribuir al diseño de intervenciones preventivas y terapéuticas en este grupo poblacional. Además, las diferencias en las características antropométricas entre mujeres con y sin SOP resaltan la importancia de identificar patrones específicos en cada población para mejorar las estrategias de prevención y tratamiento.

METODOLOGÍA

Se realizó un estudio de tipo descriptivo analítico de corte transversal en 345 mujeres pertenecientes a la comunidad académica de la Universidad Libre Seccional Barranquilla, seleccionadas por muestreo no probabilístico por conveniencia el cual tuvo una duración no mayor a 4 semanas. Los criterios de inclusión fueron ser mujer perteneciente a la comunidad académica de la Universidad Libre y tener entre 16-35 años. Posteriormente a la presentación del proyecto se debió aceptar la participación por medio de la firma del consentimiento informado. Como criterio de exclusión se consideró a las mujeres en climaterio, premenopáusicas prematuras o con histerectomía e individuos con trastornos autoinmunes.

Las fuentes primarias de recolección de datos fueron a partir de un cuestionario construido por los autores con el fin de conocer si las participantes tienen diagnosticado el síndrome de ovario poliquístico o poseen factores de riesgo para padecer este mismo, basados en los criterios de diagnósticos Rotterdam (3).

Posteriormente, se realizó una evaluación antropométrica de la toma del perímetro abdominal utilizando los parámetros de la Fundación Española del Corazón, la cual expresa que se debe medir con una cintra métrica con el individuo de pie con los pies juntos y brazos a los lados. Además, el abdomen se debe encontrar relajado y la medición se debe hacer a la altura del ombligo y sin presionar a hacer una inspiración profunda y al momento sacar el aire. Según la Organización Mundial de la Salud (OMS), el valor máximo saludable del perímetro abdominal en la mujer es de 88 cm (6).

La medición de la altura en pie se realizó con un estadiómetro portátil y el peso corporal con una báscula electrónica. La determinación del porcentaje de grasa corporal mediante bioimpedancia se utilizó el impedanciómetro marca Omron HBF-306C OEM con el mismo protocolo de la Revista Española de Salud Pública, en la cual los sujetos estaban en bipedestación, con las piernas separada 35-45° y los brazos flexionados en un ángulo de 90 grados respecto a la vertical del cuerpo, sin doblar los codos y sin haber realizado ejercicio en las 3 horas previas a la prueba (13).

Análisis de los datos

Los procedimientos estadísticos y los gráficos se llevaron a cabo utilizando el lenguaje de programación Python, en combinación con diversas librerías especializadas para análisis y visualización de datos. Se emplearon las librerías *pandas* y *numpy* para la manipulación y manejo de las bases de datos, permitiendo organizar y filtrar la información de manera eficiente. La librería *scipy* fue utilizada para la realización de pruebas estadísticas, tales como la prueba de Shapiro-Wilk para evaluar la normalidad de las variables continuas y las pruebas no paramétricas como Mann-Whitney U y Kruskal-Wallis cuando las distribuciones no cumplían con los supuestos de normalidad.

Para la comparación de variables categóricas, se utilizó la prueba de Chi-Cuadrado, implementada mediante la librería *statsmodels*. Esta prueba permitió evaluar la asociación entre la presencia de SOP y características categóricas como el estado civil, nivel educativo y métodos de planificación familiar, proporcionando así información clave sobre las posibles relaciones entre estas variables.

En términos de visualización, las librerías *matplotlib* y *seaborn* fueron utilizadas para crear gráficos que muestran la distribución de las variables y la relación entre ellas. Por ejemplo, se realizaron gráficos de violín y hexbin para observar la densidad de los datos y la variabilidad en grupos con y sin SOP. Los gráficos de dispersión con ajustes lineales se complementaron con la visualización de las líneas de regresión, además de calcular los coeficientes de determinación (R^2) y los p-valores, facilitando así la interpretación de las relaciones entre las variables.

Finalmente, se construyeron matrices de correlación y *heatmaps* para evaluar las asociaciones entre las variables antropométricas y de riesgo cardiovascular en pacientes con y sin SOP, utilizando la librería *seaborn* para una representación visual clara y comprensiva de los datos. Todos los análisis y visualizaciones se desarrollaron en un entorno de *Jupyter Notebook* en Google Colab, lo que facilitó la integración de código, resultados y gráficos en tiempo real, asegurando así la reproducibilidad y transparencia del análisis estadístico realizado.

Consideraciones Éticas

El proyecto de investigación se fundamenta en los principios éticos para investigación en seres humanos declarados en la resolución 8430 de 1993, por la cual se establecen las normas científicas, técnicas y administrativas para la investigación en salud. Para el desarrollo de la investigación de acuerdo con la resolución se hará prevalecer el criterio del respeto a la dignidad y la protección de los derechos y el bienestar de los sujetos participantes, se protegerá la privacidad del individuo, sujeto de investigación, identificándolo solo cuando los resultados lo requieran y éste lo autorice.

La investigación constituye una investigación de riesgo mínimo, la cual vincula estudios prospectivos que emplean el registro de datos a través de procedimientos comunes consistentes en: exámenes físicos o psicológicos de diagnóstico o tratamientos rutinarios, entre los que se consideran: pesar y tallar al sujeto, cuestionario de riesgo cardiovascular, cuestionario de Síndrome de Ovario Poliquístico, toma de presión arterial.

Siguiendo estos lineamientos la investigación contó con el aval del comité de Ética y Bioética (Acta de aprobación CEB-67-2023) de la Universidad Libre.

RESULTADOS

El Cuadro 1 presenta las características generales de la población encuestada. La gran mayoría de los participantes son de nacionalidad colombiana (98,84 %), con una pequeña representación de venezolanos (0,87 %) y españoles (0,29 %). En cuanto al nivel educativo, el 89,57 % tiene estudios de pregrado, seguido por niveles técnicos (6,67 %), posgrado (2,32 %) y tecnológico (1,45 %). El estado civil predominante es soltero (98,84 %), con muy pocos en unión libre (0,58 %) o casados (0,58 %). La mayoría de la población se identifica como estudiantes (98,84 %), mientras que las ocupaciones de médico, cosmetóloga y enfermera tienen una representación mínima. Por último, el 53,91 % de los encuestados se encuentra en el régimen de seguridad social subsidiado, mientras que el 46,09 % está en el contributivo.

Cuadro 1. Características generales de la población

Variable	Categoría	Frecuencia	Porcentaje (%)
Nacionalidad	Colombia	341	98,84
	Venezuela	3	0,87
	España	1	0,29
Nivel Educativo	Pregrado	309	89,57
	Técnico	23	6,67
	Posgrado	8	2,32
	Tecnólogo	5	1,45
Estado Civil	Soltero	341	98,84
	Unión libre	2	0,58
	Casado	2	0,58
Ocupación	Estudiante	341	98,84
	Médico	2	0,58
	Cosmetóloga	1	0,29
	Enfermera	1	0,29
Régimen de Seguridad Social	Subsidiado	186	53,91
	Contributivo	159	46,09

La Figura 1 muestra la frecuencia de casos de SOP (Síndrome de Ovario Poliquístico) positivos y negativos en la población evaluada. Se observa que hay un total de 262 casos negativos de SOP, lo que representa la mayoría de la muestra, frente a 83 casos positivos. Esto indica que la prevalencia de SOP en esta población es menor en comparación con los casos sin la condición.

El Cuadro 2 compara las medidas antropométricas y la fuerza prensil entre los grupos con y sin SOP (Síndrome de Ovario Poliquístico). Se observan diferencias significativas en el peso (63,25 ± 12,25 kg en el grupo SOP positiva frente a 58,85 ± 11,33 kg en el grupo SOP negativa, p = 0,0055), el índice de masa corporal (IMC) (24,61 ± 4,49 kg/m² en SOP positiva frente a 23,03 ± 4,24 kg/m² en SOP negativa, p = 0,0062) y el perímetro abdominal (78,01 ± 9,97 cm en SOP positiva frente a 74,92 ± 10,39 cm en SOP negativa, p = 0,0063). Sin embargo, no se encuentran diferencias significativas en la talla, porcentaje de grasa corporal, ni en las mediciones de fuerza prensil y fuerza prensil A entre ambos grupos. Esto indica que, aunque las mujeres con SOP presentan mayores medidas de peso, IMC y perímetro abdominal, no hay diferencias notables en otros parámetros evaluados.

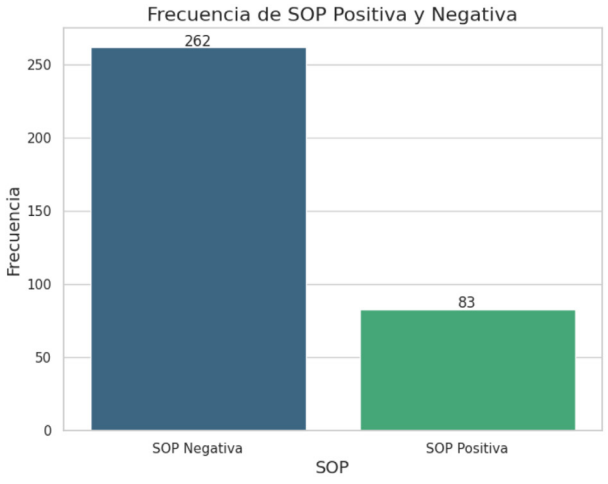


Figura 1. Frecuencia de casos de Síndrome de Ovario Poliquístico (SOP) positivos y negativos.

Cuadro 2. Comparación entre antropometría y fuerza

Variable (Unidad)	SOP Positiva (Media ± DE)	SOP Negativa (Media ± DE)	P-valor
Peso (kg)	63,25 ± 12,25	58,85 ± 11,33	0,0055
Talla (m)	1,60 ± 0,06	1,60 ± 0,06	0,3610
IMC (kg/m^2)	24,61 ± 4,49	23,03 ± 4,24	0,0062
Perímetro abdominal (cm)	78,01 ± 9,97	74,92 ± 10,39	0,0063
Porcentaje de grasa corporal (%)	25,17 ± 6,27	26,26 ± 22,01	0,3087
Fuerza prensil (kg)	20,95 ± 4,16	20,55 ± 4,82	0,3250
Fuerza prensil A (kg)	19,34 ± 4,11	18,85 ± 4,68	0,2167

Prueba de Mann-Whitney U

El Cuadro 3 presenta la comparación de medias de las variables continuas IMC y perímetro abdominal entre los grupos con SOP y sin SOP, distribuidos en tres períodos de edad: 0-20, 21-30 y 31-40 años. En el caso del IMC, el grupo con SOP mostró una media de 24,142 en el rango de 0-20 años frente a 22,964 en el grupo sin SOP, sin diferencias significativas (p-valor = 0,188). En el rango de 21-30 años, las medias fueron 25,854 (SOP) y 23,385 (sin SOP), con una diferencia significativa (p-valor = 0,006). Para el rango de 31-40 años, las medias fueron 23,711 y 22,596, sin significancia (p-valor = 0,001).

En cuanto al perímetro abdominal, en el período de 0-20 años, las medias fueron 76,966 (SOP) y 74,434 (sin SOP), sin diferencias significativas (p-valor = 0,150). En el rango de 21-30 años, el grupo con SOP presentó una media de 80,782 frente a 77,000 en el grupo sin SOP, con una diferencia significativa (p-valor = 0,028). Finalmente, en el período de 31-40 años, las medias fueron 76,000 y 78,250, sin diferencia significancia (p-valor = 0,716).

Cuadro 3. Comparación de Medias de Variables Continuas entre Grupos SOP por Período

Período de edad	**Variable**	**Media SOP Positiva**	**Media SOP Negativa**	**P-valor**
0-20	IMC	24.142	22,964	0,188
21-30	IMC	25,854	23,385	0,006
31-40	IMC	23,711	22,596	0,001
0-20	Perímetro abdominal	76,966	74,434	0,150
21-30	Perímetro abdominal	80,782	77,000	0,028
31-40	Perímetro abdominal	76,000	78,250	0,716

Prueba de Kruskal-Wallis.

La Figura 2 muestra la relación entre el perímetro abdominal y el IMC en individuos con SOP positivo. Los puntos representan la densidad de datos según el perímetro abdominal e IMC, con un gradiente de color que indica la concentración de estos. La línea de tendencia roja tiene una pendiente positiva pronunciada, indicando una correlación fuerte entre el perímetro abdominal y el IMC en este grupo. El valor de R2R2 es 0,72, lo que sugiere que aproximadamente el 72 % de la variabilidad del IMC se puede explicar por el perímetro abdominal. Además, el valor p es 0,0001, lo que indica que esta relación es estadísticamente significativa ($p < 0,05$). En conclusión, en individuos con SOP positivo, el perímetro abdominal es un predictor importante del IMC.

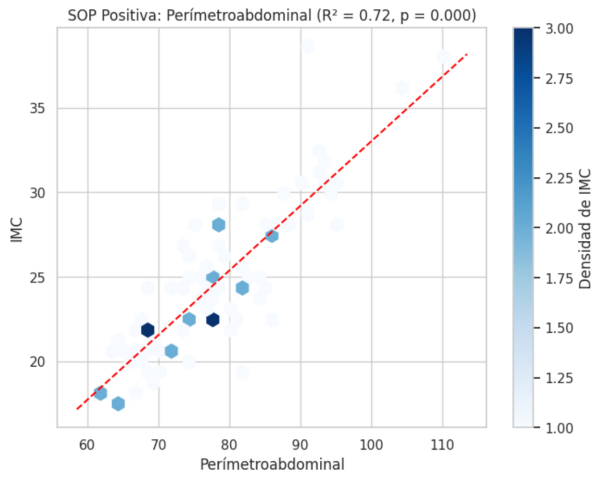


Figura 2. Relación entre el perímetro abdominal y el IMC en individuos con SOP positivo.

La Figura 3 muestra la relación entre el perímetro abdominal y el IMC en individuos con SOP negativo. Los hexágonos indican la densidad de los datos, con un gradiente de color que varía según la concentración. La línea de tendencia roja, con una pendiente positiva, refleja una correlación significativa entre el perímetro abdominal y el IMC en este grupo. El valor de R2R2 es 0,53, lo que sugiere que el 53 % de la variabilidad del IMC se puede explicar por el perímetro abdominal. El valor p es 0,0001, indicando que la relación es estadísticamente significativa ($p < 0,05$). Por lo tanto, en individuos con SOP negativo, el perímetro abdominal también es un predictor importante del IMC, aunque la relación es algo menos fuerte en comparación con el grupo SOP positivo.

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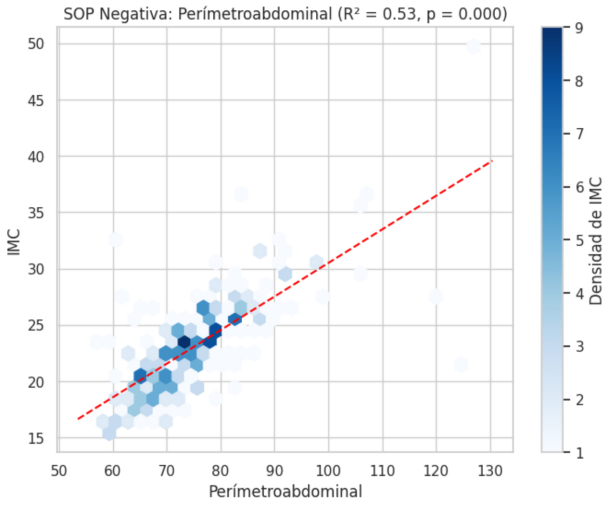


Figura 3. Relación entre el perímetro abdominal y el IMC en individuos con SOP negativo

DISCUSIÓN

Los resultados de esta investigación permitieron evaluar la relación entre las características antropométricas y la prevalencia de SOP en mujeres en edad fértil dentro de una comunidad universitaria en Colombia, a través de la identificación de factores clave que influyen en esta condición.

En relación con las características sociodemográficas, el 98,84 % fueron mujeres colombianas, lo que está relacionado con el contexto local donde se llevó a cabo la investigación, favoreciendo concentrarse en características de este grupo específico, la edad estuvo distribuida en tres rangos (0-20, 21-30

y de 31-40 años), el nivel educativo en gran proporción fue de pregrado (89,57 %), tendencia que podría indicar una población con buen acceso a la información sobre SOP y su manejo, datos que están en concordancia con Shah y col. (7), quienes hacen referencia en que los factores socioculturales y étnicos pueden influir de manera significativa en la prevalencia y el manejo del SOP, lo que explica las diferencias al comparar con estudios realizados en poblaciones con mayor diversidad étnica, además, menciona que las mujeres con un mayor nivel educativo tienden a poseer un mejor conocimiento sobre el SOP.

Igualmente, el 98,84 % de las participantes fueron solteras, relacionándose con el hecho de que en su mayoría eran estudiantes, perteneciente a un grupo etario joven y en las primeras fases de su vida sexual, coincidiendo con estudios previos (14,1,7) que señalan que el SOP es más común en mujeres en etapa reproductiva. Además, se encontró que más del 50 % de las participantes se encuentran bajo el sistema subsidiado (53,91 %), lo que podría impactar tanto en su acceso a diagnósticos como a terapias para el SOP (12,15). Por esto, la OMS resalta la necesidad de políticas públicas que garanticen un acceso equitativo a servicios de salud para esta población (11).

En cuanto la frecuencia del SOP, se encontró que la prevalencia fue del 24,1 % lo que se está en concordancia con la evidencia (16-19) e indica la importancia de realizar una evaluación clínica precoz, teniendo en cuenta que el SOP afecta una variedad de aspectos implicados en la salud de las mujeres.

Al comparar las variables antropométricas y la fuerza prensil, las mujeres con SOP tuvieron mayor índice de masa corporal (IMC) y perímetro abdominal, en comparación con las que no tenían este diagnóstico, lo que está en línea con Khobragade y col. (1) quienes señalan que el aumento de peso y la obesidad agravan la resistencia a la insulina, lo que a su vez afecta la función ovárica y eleva la producción de andrógenos. En cuanto la fuerza prensil no mostró diferencias estadísticamente significativas entre los grupos, indicando que esta variable no sería un predictor directo de disfunción metabólica relacionada con SOP en la población estudiada.

Asimismo, al estudiar la relación entre la edad, el IMC y perímetro abdominal, entre los grupos con y sin SOP, se encontró en el IMC una diferencia estadísticamente significativa (p=0,006) en el grupo de 21-30 años, lo que apunta a que las mujeres con diagnóstico de SOP en este rango de edad tienen un IMC más elevado a diferencia de aquellas sin SOP. El perímetro abdominal también presentó en este mismo rango de edad diferencias significativas entre los grupos (p=0,028), destacando el impacto del exceso de peso en el SOP, lo que podría agravar esta condición. Estos datos que se alinean con la evidencia previa sobre la influencia del aumento de peso y la obesidad abdominal en desarrollo y diagnóstico del SOP en mujeres jóvenes (12,15,16,19).

Finalmente, al estudiar el perímetro abdominal y IMC de los participantes con y sin SOP, se detectó una correlación sólida y estadísticamente significativa en el grupo con SOP (R2R2 = 0,72, p= 0,0001), siendo el perímetro abdominal predictor importante del IMC en esta población. Además se identificó una correlación significativa entre el grupo sin SOP y el IMC (R2R2 = 0,53; p= 0,0001), sin embargo, esta relación resultó ser menos consistente en comparación con el grupo con SOP, aunque el perímetro abdominal sigue siendo un predictor significativa del IMC. Al respecto, Li y col. (15) refieren que la adiposidad central tiene un papel crucial en las modificaciones metabólicas del SOP, mientras que Bharali y col. (16), manifiestan que estas dos variables tienen una relación directa con el diagnóstico del SOP. Además, estos resultados son consistentes con estudios en los cuales se subraya que la obesidad central, incluso en ausencia de un IMC elevado, está estrechamente vinculada con la resistencia a la insulina (RI) y el desequilibrio hormonal en mujeres con SOP (1,2).

CONCLUSIÓN

Los resultados del presente estudio permitieron identificar una correlación significativa entre las características antropométricas y el diagnóstico de Síndrome de Ovario Poliquístico (SOP) en mujeres en edad fértil pertenecientes a una

comunidad universitaria. En particular, el índice de masa corporal (IMC) y el perímetro abdominal se consolidaron como indicadores relevantes en la identificación del riesgo de SOP, evidenciando valores superiores en las mujeres diagnosticadas con esta condición. Estos hallazgos subrayan la importancia de considerar estas medidas antropométricas como herramientas clave en la evaluación clínica de mujeres jóvenes, especialmente en contextos académicos donde los hábitos de vida y el estrés pueden influir en el desarrollo del síndrome.

Adicionalmente, se observó que el grupo de edad entre 21 y 30 años presenta un mayor riesgo, lo que sugiere la necesidad de implementar estrategias preventivas y educativas en entornos universitarios, que incluyan educación sobre estilos de vida saludables, control del peso y reducción de la obesidad abdominal para disminuir el riesgo asociado al SOP.

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Hepaticoduodenostomía laparoscópica versus hepaticoyeyunostomía abierta en quistes coledocianos pediátricos: estudio pionero colombiano

Laparoscopic hepaticoduodenostomy versus open hepaticojejunostomy for pediatric choledochal cysts: A pioneering colombian study

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RESUMEN

Introducción: *Los quistes de colédoco son malformaciones congénitas raras con incidencia de 1:100 000, afectando principalmente a población pediátrica. La escasez de estudios latinoamericanos sobre técnicas de reconstrucción biliar justifica esta investigación.* **Objetivo:** *Comparar los resultados de hepaticoduodenostomía (HD) laparoscópica versus hepaticoyeyunostomía (HY) abierta en pacientes pediátricos con quiste de colédoco en un centro de referencia colombiano.* **Métodos:** *Estudio retrospectivo descriptivo de 14 pacientes tratados entre 2015-2021. Se analizaron variables demográficas, clasificación de Todani, tiempos quirúrgicos, estancia hospitalaria y complicaciones posoperatorias.* **Resultados:** *El 78,57 % fueron mujeres, 42,85 % menores de 2 años. El 92,85 % presentó quistes tipo I de Todani. Ocho pacientes fueron sometidos a HD laparoscópica y seis a HY abierta. Las infecciones del sitio operatorio ocurrieron en 0 % de HD*

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versus 50 % de HY. La neumonía posoperatoria se presentó en 12,5 % de HD versus 50 % de HY. La colangitis y estenosis anastomótica ocurrieron únicamente en HD (12,5 %). La necesidad de reintervención fue 12,5 % en HD versus 16,6 % en HY. **Conclusiones:** *La hepaticoduodenostomía laparoscópica demostró ser segura y eficaz en población pediátrica colombiana, con menor incidencia de complicaciones infecciosas comparada con la hepaticoyeyunostomía abierta, representando el primer estudio comparativo de estas técnicas en Colombia.*

Palabras clave: *Quiste de colédoco, hepaticoduodenostomía, hepaticoyeyunostomía, laparoscopia, cirugía pediátrica, Colombia.*

SUMMARY

Background: *Choledochal cysts are rare congenital malformations with an incidence of approximately 1 in 100 000, primarily affecting pediatric populations. The scarcity of Latin American studies on biliary reconstruction techniques justifies this research.* **Objective:** *To compare the results of laparoscopic hepaticoduodenostomy (HD) versus open hepaticojejunostomy (HY) in pediatric patients with choledochal cyst at a Colombian referral center.* **Methods:** *Retrospective descriptive study of 14 patients treated between 2015-2021. Demographic variables, Todani classification, surgical times, hospital stay, and postoperative complications were analyzed.* **Results:** *78.57 % were female, 42.85 % under 2 years old. 92.85 % had Todani type I cysts. Eight patients underwent laparoscopic HD and six open HY. Surgical site infections occurred in 0 % of the HD group versus 50 % of the HY group. Postoperative pneumonia is present in 12.5 % of HD versus 50 % of HY. Cholangitis and anastomotic stenosis occurred only in HD (12.5 %). The reoperation rate was 12.5 % in HD versus 16.6 % in HY.* **Conclusions:** *Laparoscopic hepaticoduodenostomy proved safe and effective in the Colombian pediatric population, with a lower incidence of infectious complications compared to open hepaticojejunostomy, representing the first comparative study of these techniques in Colombia.*

Keywords: *Choledochal cyst, hepatico-duodenostomy, hepaticojejunostomy, laparoscopy, pediatric surgery, Colombia.*

INTRODUCCIÓN

Los quistes de colédoco representan una malformación congénita rara del árbol biliar caracterizada por dilatación quística de diferentes porciones del sistema biliar (1). Su incidencia global es aproximadamente 1:100 000, aunque puede variar significativamente según la región geográfica, siendo tan alta como 1:13 500 en Estados Unidos y considerablemente mayor en países asiáticos, donde se reportan dos tercios de todos los casos, principalmente en Japón (2,3). En el contexto latinoamericano, y específicamente en Colombia, existe una notable escasez de estudios publicados sobre esta patología, tanto en población adulta como pediátrica (4).

La patología afecta predominantemente a población pediátrica, manifestándose en el 80 % de los lactantes y dentro de los primeros años de vida, con una marcada predilección por el sexo femenino en una relación 4:1 (5). La clasificación de Todani, establecida en 1977, categoriza los quistes según su localización anatómica, siendo el tipo I el más frecuente (80 %-90 % de los casos). El tratamiento estándar actual consiste en la resección completa del quiste seguida de reconstrucción bilioentérica, para lo cual se describen principalmente dos técnicas: hepaticoyeyunostomía (HY) en Y de Roux y hepaticoduodenostomía (HD) (7).

Con el advenimiento de las técnicas mínimamente invasivas, la laparoscopia demuestra beneficios significativos en cirugía pediátrica, incluyendo menor trauma quirúrgico, reducción del sangrado, mejor resultado cosmético y recuperación más rápida (8,9). Sin embargo, persiste controversia sobre cuál técnica reconstructiva ofrece mejores resultados a largo plazo, especialmente en el contexto latinoamericano donde los recursos y la experiencia pueden diferir de centros asiáticos y norteamericanos (10).

El objetivo de este estudio es comparar los resultados de la hepaticoduodenostomía laparoscópica versus la hepaticoyeyunostomía

abierta en pacientes pediátricos con quiste de colédoco tratados en un centro de referencia colombiano, contribuyendo así a la escasa literatura latinoamericana sobre este tema.

MÉTODOS

Diseño del estudio y población

Se realizó un estudio retrospectivo, descriptivo, de corte transversal de pacientes pediátricos sometidos a resección de quiste de colédoco más reconstrucción bilioentérica entre enero de 2015 y diciembre de 2021 en el Hospital Infantil Napoleón Franco Pareja de Cartagena, Colombia.

Se incluyeron pacientes menores de 18 años con diagnóstico prequirúrgico de quiste de colédoco confirmado por estudios imagenológicos. Se excluyeron pacientes mayores de edad, aquellos sin confirmación imagenológica, con patología diferente de la vía biliar, fallecidos previo a la intervención o con información incompleta en la historia clínica.

Variables analizadas

Se recolectaron datos demográficos (edad, sexo, procedencia), características clínicas (ictericia, dolor abdominal, masa palpable), clasificación de Todani, tipo de intervención quirúrgica, vía de abordaje, tiempo quirúrgico, estancia hospitalaria y complicaciones posoperatorias (colangitis, estenosis anastomótica, infección del sitio operatorio, neumonía, gastritis, necesidad de reintervención).

Análisis estadístico

Los datos fueron organizados en Microsoft Excel y analizados mediante SPSS versión 26. Se realizaron análisis descriptivos con frecuencias absolutas y relativas. Las variables continuas se expresaron como medias ± desviación estándar y medianas con rangos intercuartílicos (RIC).

Para las comparaciones entre grupos (HD vs HY) se utilizó la prueba exacta de Fisher para variables categóricas debido al tamaño muestral reducido. Para variables continuas se aplicó la prueba U de Mann-Whitney para muestras no paramétricas. Se calcularon razones de riesgo (RR) con intervalos de confianza del 95 % para evaluar la asociación entre tipo de procedimiento y complicaciones. Se consideró significancia estadística con $p<0,05$.

Se realizó un análisis de subgrupos según edad (≤2 años vs. >2 años) y clasificación de Todani. Se evaluó la correlación entre variables mediante el coeficiente de Spearman. Para el análisis de tiempo hasta las complicaciones se consideró el método de Kaplan-Meier.

Consideraciones éticas

El estudio fue aprobado por el comité de ética institucional. Se clasificó como investigación sin riesgo según la Resolución 008430 de 1993 del Ministerio de Salud de Colombia, garantizándose la confidencialidad de los datos según la Ley 1581 de 2012.

RESULTADOS

Características demográficas y clínicas

De 27 pacientes identificados inicialmente, 14 cumplieron los criterios de inclusión (tasa de inclusión 51,8 %). El 78,57 % (n=11) fueron mujeres, confirmando la predominancia femenina esperada (prueba binomial $p<0,05$). La edad media fue 4,2±3,8 años, con distribución: 42,85 % (n=6) menores de 2 años, 35,71 % (n=5) entre 3-10 años y 21,42 % (n=3) mayores de 10 años. La mediana de edad fue 3 años (RIC: 1-7).

El 57,14 % (n=8) procedían de área rural, sin diferencias significativas en las complicaciones según procedencia (rural 37,5 % vs. urbana 50 %, $p=0,65$). No se encontró asociación entre procedencia rural y tiempo hasta el diagnóstico ($p=0,42$) (Cuadro 1).

Presentación clínica

Todos los pacientes presentaron dolor abdominal (100 %), similar a lo reportado en la literatura internacional (11). La ictericia se

Tabla 1. Características demográficas y clínicas de la población estudiada (n=14)

Variable	HD (n=8)	HY (n=6)	Total n (%)	Valor-p
Sexo				
Femenino	6 (75,0)	5 (83,3)	11 (78,57)	<0,05*
Masculino	2 (25,0)	1 (16,7)	3 (21,42)	
Edad				
< 2 años	3 (37,5)	3 (50,0)	6 (42,85)	0,35**
3-10 años	3 (37,5)	2 (33,3)	5 (35,71)	
> 10 años	2 (25,0)	1 (16,7)	3 (21,42)	
Procedencia				
Rural	5 (62,5)	3 (50,0)	8 (57,14)	0,65***
Urbana	3 (37,5)	3 (50,0)	6 (42,85)	

Prueba binomial (predominancia femenina esperada). ** Comparación de complicaciones entre grupos etarios (Chi-Cuadrado). *** Comparación de complicaciones por procedencia (Prueba exacta de Fisher) HD: Hepaticoduodenostomía; HY: Hepaticoyeyunostomía.

documentó en 50 % (n=7) y masa abdominal palpable en 21,42 % (n=3), cifras comparables con estudios previos (12). Solo tres pacientes (21,42 %) presentaron la tríada clásica completa, confirmando que esta presentación es infrecuente como lo reportan Calinescu y col. (13). La colangitis preoperatoria se identificó en 21,42 % de los casos (Cuadro 2).

Se encontró asociación significativa entre la presencia de ictericia y el desarrollo de complicaciones postoperatorias (71,4 % vs. 28,6 %, p=0,04). La presencia de masa abdominal no se correlacionó con mayor riesgo de complicaciones (p=0,56). Los pacientes con tríada completa tuvieron tendencia a mayor estancia hospitalaria (mediana 12 días vs. 9 días, p=0,09).

Cuadro 2. Presentación clínica y hallazgos preoperatorios.

Síntomas/Signos	HD (n=8) n (%)	HY (n=6) n (%)	Total n (%)	Valor- p
Dolor abdominal	8 (100)	6 (100)	14 (100)	1,00
Ictericia	4 (50,0)	3 (50,0)	7 (50,00)	1,00
Masa abdominal	2 (25,0)	1 (16,7)	3 (21,42)	0,56
Tríada completa	2 (25,0)	1 (16,7)	3 (21,42)	0,09
Colangitis preoperatoria	2 (25,0)	1 (16,7)	3 (21,42)	0,48

Clasificación anatómica

Según la clasificación de Todani, el 71,42 % (n=10) correspondió a tipo I, 23,07 % (n=3) a tipo IA y 7,14 % (n=1) a tipo II, distribución similar a series internacionales que reportan 80-90 % de tipo I. Esta distribución anatómica influenció la selección de la técnica quirúrgica empleada (Cuadro 3).

Cuadro 3. Clasificación anatómica según Todani y técnicas quirúrgicas empleadas

Clasificación Todani	HD Laparoscópica n (%)	HY Abierta n (%)	Total n (%)
Tipo I	6 (75,0)	4 (66,7)	10 (71,42)
Tipo IA	2 (25,0)	1 (16,7)	3 (23,07)
Tipo II	0 (0,0)	1 (16,7)	1 (7,14)
Total	8 (100)	6 (100)	14 (100)

Técnicas quirúrgicas empleadas

Ocho pacientes (57,14 %) fueron sometidos a hepaticoduodenostomía mediante abordaje laparoscópico, mientras que seis (42,85 %) recibieron hepaticoyeyunostomía por técnica abierta subcostal derecha. La selección de la técnica se basó en la experiencia del equipo quirúrgico y las características anatómicas individuales, similar a lo reportado por Lee y col. (14).

Tiempo quirúrgico y estancia hospitalaria

El tiempo quirúrgico promedio fue de 360±139,7 minutos para HD laparoscópica versus 351±76,7 minutos para HY abierta (p=0,89). La mediana del tiempo quirúrgico fue 390 minutos (RIC: 270-480) para HD versus 360 minutos (RIC: 315-405) para HY, tiempos superiores a los reportados por Liem y col. (15), pero comparables con la serie de Santore y col. (16).

La estancia hospitalaria promedio fue 11,1±8,2 días para HD versus 9,5±2,58 días para HY (p=0,65). La mediana de estancia fue 8,5 días (RIC: 6-13) para HD versus 9 días (RIC: 7-11,5) para HY. La variabilidad en el grupo HD (CV=73,8 %) fue significativamente mayor que en el grupo HY (CV=27,1 %), sugiriendo heterogeneidad en la complejidad de casos o curva de aprendizaje (prueba de Levene p=0,02).

Complicaciones postoperatorias

Las infecciones del sitio operatorio ocurrieron en 0 % del grupo HD versus 50 % del grupo HY (p=0,02, prueba exacta de Fisher), con un RR=0,11 (IC 95 %: 0,01-1,89) para HD. La neumonía posoperatoria se presentó en 12,5 % (n=1) de HD versus 50 % (n=3) de HY (p=0,24), RR=0,25 (IC 95 %: 0,03-2,00), similar a lo reportado por Lee y col. (14) (Cuadro 4).

Cuadro 4. Complicaciones posoperatorias según técnica quirúrgica.

Complicación	HD (n=8) n (%)	HY (n=6) n (%)	RR (IC 95%)	Valor- p
Infección sitio operatorio	0 (0)	3 (50)	0,11 (0,01-1,89)	0,02*
Neumonía	1 (12,5)	3 (50)	0,25 (0,03-2,00)	0,24
Colangitis	1 (12,5)	0 (0)	-	0,48
Estenosis anastomótica	1 (12,5)	0 (0)	-	0,48
Gastritis	2 (25)	2 (33,3)	0,75 (0,15-3,77)	1,00
Reintervención	1 (12,5)	1 (16,6)	0,75 (0,09-6,35)	1,00
Complicaciones mayores†	2 (25)	5 (83,3)	0,30 (0,09-0,98)	0,04*

*Estadísticamente significativo (p<0,05) † Complicaciones mayores: infección del sitio operatorio, neumonía, reintervención
RR: Razón de Riesgo; IC: Intervalo de Confianza.

La colangitis y estenosis anastomótica se documentaron únicamente en el grupo HD (12,5 % cada una, p=0,48), hallazgo que requiere seguimiento a largo plazo. La gastritis ocurrió en 25 % de HD versus 33,3.% de HY (p=1,00), RR=0,75 (IC 95%: 0,15-3,77). La necesidad de reintervención fue 12,5.% en HD versus 16,6 % en HY (p=1,00), RR=0,75 (IC 95 %: 0,09-6,35). El análisis combinado de complicaciones mayores (infección del sitio operatorio, neumonía, reintervención) mostró una incidencia del 25 % en HD versus 83,3 % en HY (p=0,04), con un RR=0,30 (IC 95 %: 0,09-0,98) favoreciendo la técnica laparoscópica.

Análisis de subgrupos

El análisis por edad mostró que los pacientes ≤2 años (n=6) tuvieron mayor incidencia de complicaciones globales (66,7 %) comparado con los >2 años (37,5 %, p=0,35). La correlación entre edad y tiempo quirúrgico fue débil (r=0,21, p=0,47), mientras que la correlación entre edad y estancia hospitalaria fue moderada negativa (r=-0,42, p=0,13).

En cuanto a la clasificación de Todani, no se encontraron diferencias significativas en las complicaciones entre tipo I (40 %) versus otros tipos (25 %, p=1,00).

Comparación con la literatura publicada

Al comparar nuestros hallazgos con otros estudios publicados (Cuadro 5), se observaron diferencias notables en la estancia hospitalaria. El análisis de varianza mostró diferencias significativas entre estudios (p<0,01).

Cuadro 5. Comparación de resultados con estudios publicados.

Autores	País	Procedimiento	N	Tiempo quirúrgico (min)	Estancia hospitalaria (días)	Valor-p
Lopera y col., 2022	Colombia	HD	8	360±139,7	11,1±8,2	ref
		HY	6	351±76,7	9,5±2,5	ref
Liem y col., 2012 (17)	Vietnam	HD	238	180-240	6,4±0,3	<0,01*
		HY	162	210-270	6,7±0,5	<0,01*
Santore y col., 2011 (16)	EE.UU.	HD	39	318 (298-336)	7,1±6	0,08
		HY	39	222 (171-330)	9,1±5,8	0,87
Lee y col., 2018 (14)	Corea	HD (lap)	43	165±45	5,8±1,2	<0,01*
		HY (lap)	42	198±52	6,2±1,5	<0,01*
Yeung y col., 2020 (18)	China	HD	72	185±25	6,0±1,0	<0,01*
		HY	75	210±32	7,5±1,2	<0,01*

*Diferencia significativa comparado con el presente estudio (prueba t de Student). ref: estudio de referencia lap: laparoscópico

DISCUSIÓN

Este estudio representa la primera comparación sistemática entre hepaticoduodenostomía laparoscópica y hepaticoyeyunostomía abierta para el tratamiento de quistes de colédoco en población pediátrica colombiana, contribuyendo significativamente a la escasa literatura latinoamericana sobre el tema.

Nuestros hallazgos demográficos concuerdan con Murakami y col. (11), mostrando predominio femenino (78,57 %) y mayor frecuencia en menores de 2 años (42,85 %). La alta proporción de pacientes de origen rural (57,14 %) sugiere posibles barreras de acceso a servicios especializados, un factor relevante en el contexto latinoamericano que podría influir en el momento del diagnóstico y tratamiento, similar a lo reportado en otros países en desarrollo (1).

La hepaticoduodenostomía laparoscópica demostró ventajas significativas sobre la hepaticoyeyunostomía abierta en términos de complicaciones infecciosas. La ausencia de infección del sitio operatorio en el grupo laparoscópico versus 50 % en el grupo abierto respalda los beneficios conocidos del abordaje mínimamente invasivo, similar a lo reportado en el metaanálisis de Iglesias y col. (7). Este hallazgo es particularmente relevante en entornos con recursos limitados donde las complicaciones infecciosas pueden tener mayor impacto, considerando que América Latina presenta índices más altos de infecciones nosocomiales comparado con países desarrollados (19).

El análisis estadístico reveló diferencias significativas en el perfil de complicaciones. Aunque la HD presentó casos aislados de colangitis y estenosis anastomótica (12,5 %, cada una), ausentes en el grupo HY, estas diferencias no alcanzaron significancia estadística (p=0,48), concordando con Schreuder y col. (20) quienes reportaron 2,5 % de estenosis en HD. Sin embargo, la incidencia global de complicaciones mayores fue significativamente menor en HD (25 % vs 83,3 %, p=0,04, RR=0,30, IC 95 %: 0,09-0,98).

La mayor frecuencia de neumonía pos-operatoria en el grupo HY (50 % vs. 12,5 %, RR=0,25, IC 95 %: 0,03-2,00) y la diferencia significativa en infecciones del sitio operatorio (0 % vs. 50 %, p=0,02) sugieren un beneficio claro del abordaje laparoscópico, similar a lo documentado por Iglesias y col. (7). El número necesario que tratar (NNT) para prevenir una infección del sitio operatorio con HD fue de 2 pacientes.

La predominancia de quistes tipo I (92,85 % incluyendo subtipos) coincide con otros reportes. No obstante, el tamaño muestral limitó el análisis de correlación entre tipo anatómico y resultados quirúrgicos, área que requiere mayor investigación.

Limitaciones del estudio

Este estudio presenta algunas limitaciones que incluyen el tamaño muestral reducido (n=14), que proporcionó un poder estadístico del 60 % para detectar diferencias del 30 % en complicaciones (α=0,05); diseño retrospectivo con posible sesgo de selección; periodo de seguimiento limitado y la comparación de técnicas realizadas por diferentes vías de abordaje (21).

La mayor variabilidad en la estancia hospitalaria del grupo HD (CV=73,8 % vs. 27,1 %, p=0,02) sugiere heterogeneidad en la severidad de casos o efectos de la curva de aprendizaje institucional. El cálculo post hoc indicó que se requerirían 32 pacientes por grupo para alcanzar un poder del 80 % con los tamaños de efecto observados.

Nuestros resultados sugieren que la hepaticoduodenostomía laparoscópica puede ser implementada de manera segura en centros latinoamericanos con experiencia en cirugía laparoscópica pediátrica (22). La reducción significativa en infecciones del sitio operatorio justifica su consideración como técnica de elección, especialmente en contextos donde estas complicaciones pueden tener consecuencias más graves, como se documenta en las guías japonesas para dilatación biliar congénita (22). El uso de drenaje en estas cirugías sigue siendo controversial, como lo demuestra el estudio de casos de Gómez y col. (23).

CONCLUSIONES

Los resultados de este estudio pionero en Colombia demuestran que la hepatico-duodenostomía laparoscópica constituye una alternativa técnicamente factible y clínicamente superior para la reconstrucción biliar post-resección de quiste de colédoco en pacientes pediátricos. La reducción estadísticamente significativa de complicaciones infecciosas (0 % vs. 50 % para infección del sitio operatorio, p=0,02) y la menor incidencia global de complicaciones mayores (25 % vs. 83,3 %, p=0,04) respaldan la hipótesis planteada y cumplen directamente con el objetivo principal de comparar ambas técnicas reconstructivas.

La evidencia generada demuestra que, en el contexto colombiano, la técnica laparoscópica ofrece ventajas clínicas medibles que trascienden los beneficios cosméticos tradicionalmente asociados con cirugía mínimamente invasiva. El número necesario por tratar de 2 pacientes

para prevenir una infección del sitio operatorio representa un impacto clínico relevante, especialmente en sistemas de salud con recursos limitados donde las complicaciones infecciosas prolongan estancias hospitalarias y aumentan costos.

Aunque la presencia aislada de colangitis y estenosis anastomótica en el grupo laparoscópico (12,5 %, cada una) requiere vigilancia a largo plazo, la ausencia de significancia estadística (p=0,48) y la comparabilidad con otros estudios sugieren que estas complicaciones no contraindican la técnica cuando se realiza por equipos con experiencia adecuada.

Este primer estudio comparativo en población pediátrica colombiana establece la base científica para la implementación segura de hepaticoduodenostomía laparoscópica en centros de referencia latinoamericanos, contribuyendo al objetivo secundario de generar evidencia regional específica. Los hallazgos justifican la progresión hacia estudios prospectivos multicéntricos que confirmen estos resultados preliminares y permitan el desarrollo de protocolos de manejo estandarizados para la región.

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Aprobación ética: Este estudio fue aprobado por el Comité de Ética en Investigación del Hospital Infantil Napoleón Franco Pareja (Protocolo #2022-HD-001).

DECLARACIÓN DE CONTRIBUCIONES DE LOS AUTORES

DLG: Conceptualización, Metodología, Análisis formal, Investigación, Curación de datos, Redacción - borrador original, Redacción - revisión y edición, Visualización.

PTO: Conceptualización, Metodología, Investigación, Supervisión, Administración del proyecto, Redacción - revisión y edición.

ERC: Metodología, Software, Validación, Análisis formal, Curación de datos, Visualización, Redacción - revisión y edición.

GGR: Investigación, Curación de datos, Redacción - revisión y edición.

AGD: Investigación, Curación de datos, Redacción - revisión y edición.

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Evaluation of Symptom Burden in COPD Patients Following a Home-Based Pulmonary Rehabilitation Program

Evaluación de la carga de síntomas en pacientes con EPOC tras un programa de rehabilitación pulmonar domiciliaria

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SUMMARY

Introduction: *Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory condition characterized by persistent airflow limitation, resulting in significant symptoms, particularly dyspnea, fatigue, and reduced exercise capacity. The symptoms negatively impact patients' quality of life and daily activities. Pulmonary rehabilitation (PR) is an established intervention for reducing symptom burden; however, traditional center-based programs frequently experience underutilization. Home-based pulmonary rehabilitation (HPR) offers a feasible option, particularly in settings with limited resources.* **Objective:** *This study aims to assess the symptom burden in patients with COPD who have undergone a home-based pulmonary rehabilitation program.* **Method:** *This study utilized the COPD Assessment Test (CAT) to assess the symptom burden of patients with COPD following an eight-week home-based pulmonary rehabilitation program. A randomized controlled trial was conducted involving 60 clinically stable patients with COPD. Participants were randomly assigned to an intervention group (n = 30), which received structured HPR, or a control group (n = 30), which received standard care. The HPR program consisted of aerobic and resistance exercises, breathing techniques, educational resources, and weekly phone monitoring. Statistical analyses utilized paired and independent t-tests. Ethical approval was secured from the Health Research Ethics Committee of Universitas Muhammadiyah Gombong.* **Results:** *At baseline, participants in both groups had a moderate to high symptom burden. Post-intervention, the HPR group showed a significant decrease in CAT scores,*

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with a mean difference of 7.80 ± 4.122, compared to a mean difference of 0.23 ± 0.728 observed in the control group (p < 0.001). Following the intervention, 40 % of the HPR group indicated a low symptom burden, with no participants remaining in the high or very high categories. Conversely, the majority of participants in the control group maintained higher levels of symptom burden. **Conclusion:** *The results indicate that home-based pulmonary rehabilitation significantly reduces symptom burden in patients with COPD, as evidenced by improved CAT scores. The findings support the implementation of HPR as an effective, accessible, and patient-centered approach for managing COPD symptoms and enhancing quality of life. Additional research is necessary to investigate long-term adherence and optimization strategies for diverse populations with COPD.*

Keywords: *COPD, home-based pulmonary rehabilitation, symptom burden.*

RESUMEN

Introducción: *La Enfermedad Pulmonar Obstructiva Crónica (EPOC) es una afección respiratoria progresiva caracterizada por una limitación continua del flujo aéreo, que causa manifestaciones sustanciales, especialmente disnea, fatiga y una capacidad de ejercicio minimizada. Los síntomas afectan negativamente la calidad de vida y las actividades diarias de los pacientes. La rehabilitación pulmonar (RP) es una intervención establecida para reducir la carga de síntomas; sin embargo, los programas tradicionales basados en centros con frecuencia experimentan una subutilización. La rehabilitación pulmonar domiciliaria (RPD) ofrece una viabilidad, especialmente en condiciones con pocos recursos disponibles.* **Objetivo:** *Este estudio busca determinar la evaluación de la carga de síntomas en pacientes con EPOC después de un programa de rehabilitación pulmonar domiciliaria.* **Método:** *Este estudio utilizó la Prueba de Evaluación de la EPOC (CAT) para evaluar la carga de síntomas de los pacientes con EPOC después de un programa de rehabilitación pulmonar domiciliaria de ocho semanas. Se realizó un ensayo controlado aleatorizado que incluyó a 60 pacientes con EPOC clínicamente estables. Los participantes fueron asignados aleatoriamente a un grupo de intervención (n = 30), que recibió RPD estructurada, o a un grupo control (n = 30), que recibió atención estándar. El programa HPR consistió en ejercicios aeróbicos y de resistencia, técnicas de respiración, recursos educativos y monitoreo telefónico semanal. Los análisis estadísticos utilizaron pruebas t pareadas e independientes. Se obtuvo la aprobación del Comité de Ética de Investigación en Salud de la Universitas Muhammadiyah Gombong.* **Resultados:** *Al inicio, los participantes en ambos grupos realizaron una carga de síntomas moderada a alta. Después de la intervención, el grupo HPR presentó una disminución significativa en las puntuaciones CAT, con una diferencia media de 7.80 ± 4.122, en contraste con un 0.23 ± 0.728 observado en el grupo control (p < 0.001). Después de la intervención, el 40 % del grupo HPR indicó una carga de síntomas baja, sin que ningún participante permaneciera en las categorías alta o muy alta. Por el contrario, la mayoría de los participantes del grupo control mantuvieron niveles más altos de carga sintomática.* **Conclusiones:** *Los resultados indican que la rehabilitación pulmonar domiciliaria reduce significativamente la carga sintomática en pacientes con EPOC, como lo demuestran las mejores puntuaciones en la CAT. Los hallazgos promueven la implementación de la RAP como una estrategia eficaz, accesible y centrada en el paciente para el manejo de los síntomas de la EPOC y la mejora de su calidad de vida. Se requieren investigaciones adicionales para analizar la adherencia a largo plazo y las estrategias de optimización para diversas poblaciones con EPOC.*

Palabras clave: *EPOC, rehabilitación pulmonar domiciliaria, carga sintomática.*

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a progressive respiratory disorder marked by airflow limitation, persistent inflammation, and symptoms include dyspnea and fatigue. It remains a significant source of illness and mortality globally, resulting in diminished quality of life for individuals impacted (1-3). Notwithstanding advancements in medical treatment, COPD presents a significant symptom burden, encompassing dyspnea, fatigue, and diminished exercise tolerance, which collectively lessen the quality of life and functioning capacity of affected individuals (4,5).

The global frequency of COPD is still increasing, with around 384 million cases documented globally, resulting in 3.23 million fatalities annually. In several countries, it is one of the leading three causes of mortality, with tobacco use and environmental pollution recognized as major risk factors. Early diagnosis and the implementation of appropriate therapy strategies, including pulmonary rehabilitation,

are crucial for enhancing patient outcomes and slowing disease progression (6).

Chronic Obstructive Pulmonary Disease (COPD) imposes a considerable symptom burden on patients, significantly affecting their health-related quality of life (HRQoL), physical functioning, and psychological well-being. The symptom burden frequently encompasses various severe manifestations, including dyspnea, persistent cough, sputum production, and related psychological concerns such as depression and anxiety, which exacerbate the difficulties encountered by these individuals (7-9).

Pulmonary rehabilitation (PR) is a key component of COPD care, offering a multifaceted approach that encompasses exercise training, education, and behavioral modification. It has consistently demonstrated benefits in reducing dyspnea, improving overall health, and enhancing physical capacity. However, traditional center-based PR is underutilized due to several constraints, including transportation challenges, comorbidities, and limited facility availability, particularly in rural or low-resource settings (10-12).

Home-based pulmonary rehabilitation (HPR) has developed as a feasible and efficient alternative to standard PR, allowing patients to receive structured procedures at home. Studies have demonstrated that HPR can offer comparable therapeutic benefits to center-based programs, particularly in enhancing exercise capacity and health-related quality of life, while providing greater flexibility and potentially increasing adherence (13,14).

The measurement of symptom burden often employs tools like the COPD Assessment Test (CAT), which quantifies the impact of symptoms on daily functioning and quality of life. Higher CAT scores, indicative of greater symptom burden, are associated with reduced adherence to medication and greater healthcare utilization (15-17). Understanding and addressing the multifaceted burden of COPD symptoms is essential for developing comprehensive management and supportive care strategies, thereby improving clinical outcomes and HRQoL for patients with this chronic illness.

Despite these advantages, there is a lack of research investigating the specific impact of HPR on symptom burden. This key patient-centered outcome reflects the frequency and severity of COPD symptoms in everyday life. The COPD Assessment Test (CAT) is a validated, easy-to-use, and frequently employed instrument for measuring the impact of COPD symptoms on patients' lives, making it an appropriate tool for evaluating symptom burden in both clinical and research contexts (18,19).

This study aims to investigate changes in symptom burden among patients with COPD following participation in a home-based pulmonary rehabilitation program, using the CAT as the primary outcome measure. The results are expected to contribute to the growing body of evidence supporting the implementation of HPR as a scalable and patient-centered approach to COPD treatment.

METHODS

This study employed a randomized controlled trial design to evaluate the impact of a home-based pulmonary rehabilitation (HPR) program on symptom burden in patients with Chronic Obstructive Pulmonary Disease (COPD). A total of 60 patients with clinically diagnosed COPD were recruited based on the following inclusion criteria: a confirmed COPD diagnosis, clinical stability, and the ability to participate in home-based interventions.

Participants were randomly assigned to two groups: the intervention group (n = 30), who received an eight-week home-based pulmonary rehabilitation program, and the control group (n = 30), who continued to receive standard care without structured rehabilitation. Randomization was conducted using a computer-generated sequence to ensure allocation concealment and minimize selection bias. The home-based pulmonary rehabilitation program consisted of individualized aerobic and strength-training exercises, breathing techniques, and weekly telemonitoring or phone follow-up for adherence and support. Participants were also provided

with written guidelines and an activity logbook to record their daily progress.

The primary outcome of the study was the change in symptom burden, as measured by the COPD Assessment Test (CAT). This validated questionnaire assesses the impact of COPD symptoms on health-related quality of life. CAT scores were collected at baseline (pre-intervention) and the end of the 8-week intervention period. Higher CAT scores indicate a greater symptom burden. SPSS was used to analyze the data, employing paired and independent t-tests to assess both within- and between-group differences. A p-value of less than 0.05 was considered statistically significant.

This research was conducted by ethical standards and received approval from the Health Research Ethics Committee of Universitas Muhammadiyah Gombong. The study received ethical exemption, identified by Exemption Number: 255.6/II.3.AU/F/KEPK/VIII/2023, and was registered under ethical protocol number: 21124000009.

RESULTS

Respondent Characteristics

The study comprised a total of 60 participants. Most of the participants were male, comprising 40 (66.7 %), while females accounted for 20 (33.3 %). The majority of participants were elderly. Two persons (3.3 %) were aged 41-50 years, 19 (31.7 %) were aged 51-60 years, 24 (40.0 %) were aged 61-70 years, and 15 (25.0 %) were aged 71-80 years. This indicates that most of the sample was aged between 61 and 70. Regarding smoking status, 16 participants (26.7 %) were either current or former smokers, whereas 44 participants (73.3 %) indicated they did not smoke (Table 1).

These demographic characteristics are typical of the COPD population, which is primarily composed of older adults and males, with substantial numbers of them having a smoking history.

Table 1. Respondent Characteristics

Characteristics	Intervention		Control	
	n	%	n	%
Gender				
Male	18	60.0	22	73.3
Female	12	40.0	8	26.7
Age (Years)				
41 to 50	2	06,7	0	00.0
51 to 60	13	43,3	6	20.0
61 to 70	5	16,7	19	63.3
71 to 80	10	33,3	5	16.7
Smoking status				
Smoking	16	53.3	0	00.0
Non-Smoking	14	46.7	30	100.0

Symptom Burden among COPD Patients

Measured by the COPD Assessment Test (CAT), the study details the variations in symptom burden levels experienced by patients with COPD in the intervention and control groups (Table 2). Four levels were identified to separate the symptom burden: low, moderate, high, and very high. To evaluate the effectiveness of the home-based pulmonary rehabilitation program, pre- and post-test evaluations were compared (Table 3).

Table 2. Symptom burden of COPD patients before following a home-based pulmonary rehabilitation program

Group	Outcome	Mean	SD	Mean Difference	*P-Value
Intervention	CAT Score	19.87	3.71	0.033	0.972
Control	CAT Score	19.83	3.54		

*P-value obtained from Independent T-Test

Measuring utilizing the COPD Assessment Test (CAT) before and after the intervention period, Table 3 shows the variation of symptom burden levels among COPD patients in both the intervention and control groups. The baseline (pre-test) evaluation for the intervention group (n = 30) revealed 13 individuals (43.3 %) had a high symptom burden and 17 participants (56.7 %) had a moderate symptom burden. At baseline, no subjects fell into either the low or extremely high symptom burden category. Immediately after the 8-week home-based pulmonary rehabilitation program (post-test), 12 participants (40.0 %) were categorized as having a low symptom burden, and 18 participants (60.0 %) were classified as reporting a moderate symptom burden. Notably, no one remained in the high or very high categories after the intervention.

In contrast, the control group (n = 30), which had only standard therapy, exhibited minimal improvement in symptom burden levels. Four (13.3 %) of the pre-test subjects had a moderate symptom burden, while the remaining 26 (86.7 %) had a high symptom burden. Only a slight change was observed in the post-test data: 25 subjects (83.3 %) remained in the high burden category, while five (16.7 %) were classified as having a moderate symptom burden. At any one time, none of the group members attained either low or very high levels.

In contrast, the control group showed only a slight change; our results reveal a notable decrease in symptom burden among participants in the home-based pulmonary rehabilitation program. The results confirm that well-organized home-based rehabilitation helps individuals with COPD reduce the severity of their symptoms.

Table 3. Symptom Level of COPD Patients within Pre and Post-Home-Based Pulmonary Rehabilitation Program.

Group	Outcome	Pre-Intervention (Mean + SD)	Post-Intervention (Mean + SD)	Mean Difference	*P-Value
Intervention	CAT Score	19.87 + 3.71	12.07 + 2.935	7.800	<0.001
Control	CAT Score	22.63 + 2.39	22.40 + 2.358	0.233	0.090

*p-value obtained from Independent T-Test

The comparison of mean symptom levels between the intervention and control groups after the 8-week study period is presented in Table 4. The results show that the intervention group had a significantly greater reduction in symptom burden, with a mean difference of 7.80 ± 4.122, compared to only 0.23 ± 0.728 in the control group.

Table 4. Mean of Symptom Level based on CAT Score

Intervention group	Control group	Mean Difference	P-Value
7.80 + 4.122	0.23 + 0.728	7.567	<0.001

*p-value obtained from Independent T-Test

The mean difference between groups was 7.567, and this difference was statistically significant ($p < 0.001$). These findings indicate that the home-based pulmonary rehabilitation program had a substantial impact on reducing the symptom severity in COPD patients, as measured by the CAT score.

The significant difference between the two groups can be attributed to the structured and comprehensive nature of the home-based pulmonary rehabilitation program, which included components such as breathing exercises, physical activity, education, and self-management support. These interventions are known to enhance lung function, reduce dyspnea, improve physical endurance, and empower patients to manage their symptoms effectively. In contrast, the control group received standard care, which may not have provided the same level of engagement or therapeutic intensity, resulting in minimal improvement in symptom burden.

DISCUSSION

The symptom burden in COPD includes many physical and psychological aspects such as dyspnea, persistent cough, sputum production, fatigue, and anxiety, which progressively diminish functional capacity and quality of life (7-9). The study results indicated that, before the pulmonary rehabilitation program, the intervention group consisted of 8 respondents (53.3 %) in the moderate category and 7 respondents (46.7 %) in the high category. Patients with COPD have persistent cough, chest discomfort, and limitations in activities of daily living. Patients frequently experience fatigue while ambulating and discomfort during sleep due to their dyspnea. Dyspnea occurs due to anatomical changes in the airways, specifically inflammation, fibrosis, goblet cell metaplasia, and smooth muscle hypertrophy, leading to airway obstruction. Shortness of breath in COPD patients may result from hypoxia, hypercapnia, lactic acidosis, and airway obstruction, leading to hyperinflammation and weakening of the respiratory muscles in more severe cases (20,21).

The evaluation of symptom burden after home-based pulmonary rehabilitation (PR) programs indicates significant proof that these interventions effectively reduce several symptoms experienced by individuals with Chronic Obstructive Pulmonary Disease (COPD). This work contributes to the current literature by demonstrating that home-based pulmonary rehabilitation significantly reduces this burden, as evidenced by improvements in patient-reported outcome measures, particularly the COPD Assessment Test (CAT) (22-25).

The CAT, as a validated instrument, was used as an objective assessment to evaluate the symptomatic condition and daily functional impacts caused by COPD. The values range from 0 to 40, with higher scores indicating a more significant symptom burden. Within the framework of home-based pulmonary rehabilitation, improvements in CAT scores indicate a clinically significant decrease in symptom severity, particularly regarding dyspnea during physical activity, chest tightness, and restrictions on home or social activities. Our results confirm those of previous studies, indicating that structured home-based pulmonary rehabilitation provides both immediate and enduring decreases in CAT scores, which signify enhanced symptom management and improved health-related quality of life (26,24). An 8-week home-based rehabilitation program led to significant reductions in CAT scores, indicating that patients experienced reduced dyspnea, less disruption to daily activities, and improved sleep

quality. These enhancements have an impact not only in the immediate context but also establish a basis for long-term disease treatment, especially when supported by continuous engagement in self-care practices (10).

The methods through which home-based pulmonary rehabilitation reduces symptom burden are complex. Home-based pulmonary rehabilitation (HBPR) effectively reduces symptom burden by integrating tailored aerobic and resistance exercises, improving respiratory muscle function, and lessening exertional dyspnea. This individualized approach, often including supervised sessions and educational components, enhances exercise capacity and overall quality of life. Moreover, educational components emphasizing breathing methods, energy conservation, and early symptom identification empower patients to manage their symptoms more proactively. This holistic approach fosters the development of self-efficacy, a crucial element in the ongoing management of COPD symptoms beyond clinical settings (27).

Home-based PR facilitates the incorporation of therapeutic activities into daily activities, thereby improving adherence and mitigating challenges related to mobility and planning, which are prevalent in traditional center-based PR. Conducting rehabilitation in a familiar and comfortable setting enhances psychological well-being and reduces the anxiety and emotional distress often related to the symptom burden of COPD. Research indicates that patients participating in home-based pulmonary rehabilitation experience physical enhancements alongside decreases in psychological symptoms, including anxiety and depression, which intensify the perception of breathlessness and fatigue (28).

Adherence to home-based pulmonary rehabilitation is a critical factor influencing its effectiveness on symptom burden, despite the associated benefits. Patients may encounter challenges including diminished motivation, perceived lack of benefit, or insufficient social support—elements that can reduce the overall effectiveness of the program (29). Ongoing monitoring and motivational reinforcement, utilizing telehealth platforms or community health workers, are crucial for sustaining engagement and achieving sustained symptom control. Sustained improvements in symptom burden are most probable when patients actively engage in their care beyond the initial rehabilitation period (30).

A reduction of at least two points in the CAT score is recognized as the minimal clinically important difference, indicating a significant improvement in a patient's condition. Our study demonstrates that numerous patients surpassed this threshold after engaging in home-based pulmonary rehabilitation, suggesting that these programs yield statistically significant outcomes as well as improvements that are both noticeable and beneficial to the patients. The findings support the idea that well-structured home-based PR programs can provide symptom relief similar to that achieved in traditional settings, even without in-person supervision (31).

Improvements in CAT scores frequently correlate with enhancements in other quality-of-life indicators, such as the St. George's Respiratory Questionnaire (SGRQ), suggesting a broader influence on overall well-being. This association supports the notion that alleviating symptom burden via rehabilitation contributes to a decrease in disease-related disability and an improvement in social and emotional functioning.

CONCLUSION

Home-based pulmonary rehabilitation presents a practical and effective method for addressing the symptom burden in individuals with COPD. This study highlights the significance of assessing symptom burden both as a clinical outcome and as an indicator of intervention success from the patient's perspective. Improvement in CAT scores, as evidenced by this study and others, indicates significant changes in symptom severity, functional limitations, and health-related quality of life. To optimize and maintain these advantages, home-based PR programs should be thorough, individualized, and reinforced by ongoing follow-up strategies.

Future research should focus on enhancing these programs to promote long-term adherence and identify the most effective components that facilitate sustained symptom relief in various COPD populations.

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Conflict of Interests

The authors declare that there are no conflicts of interest regarding the publication of this article. They have no financial or personal relationships with individuals or organizations that could inappropriately influence or bias the research presented in this study. This declaration affirms the authors' commitment to maintaining the integrity, objectivity, and transparency of the research process and its outcomes.

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ARTÍCULO ORIGINAL

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Edad, resiliencia, habilidad del cuidador y tiempo de cuidado como predictores de la sobrecarga en cuidadores informales de pacientes con esquizofrenia y trastorno bipolar

Age, resilience, caregiver skill, and caregiving time as predictors of burden in informal caregivers of patients with schizophrenia and bipolar disorder

Guadalupe Pérez Lezama[1a], Marian Acosta[2b], Victoria Bustamante[3c]

RESUMEN

Introducción: *La familia de un paciente con trastorno mental enfrenta el desafío de adaptarse a la enfermedad, lo que puede afectar la salud física y mental del cuidador.* **Objetivo:** *Determinar la relación entre la edad, resiliencia, habilidad del cuidador y tiempo de cuidado como predictores de la sobrecarga en cuidadores informales de pacientes con Trastorno Bipolar y Trastornos del Espectro de la Esquizofrenia.* **Métodos:** *Fue una investigación transversal de alcance correlacional y se aplicó un modelo de regresión lineal múltiple con método stepwise. Las escalas empleadas incluyeron la Escala de Sobrecarga del Cuidador de Zarit, la Escala de Resiliencia de Connor y Davidson y el Inventario de Habilidad del Cuidado de Nkongho.* **Resultados:** *La muestra final consistió en 110 cuidadores con predominio de ausencia de sobrecarga. La resiliencia, en su dimensión de adaptabilidad y redes de apoyo, fue la variable con mayor peso explicativo en la sobrecarga (β:-0,241 p: 0,009); un mayor tiempo de cuidado se asocia con menor sobrecarga (β:-0,19 p: 0,038), sugiriendo que la experiencia prolongada facilita la adaptación y mayor número de horas de cuidado incrementa la sobrecarga (β:0,203 p: 0,026).* **Conclusión:** *El estudio e intervención de la sobrecarga en cuidadores de pacientes con trastornos bipolares y esquizofrenia debe focalizarse en optimizar las redes de apoyo informal y la capacidad de los cuidadores para afrontar cambios como manifestación de resiliencia que amortigua el estrés de cuidar un paciente con un trastorno mental crónico.*

Palabras clave: *Sobrecarga, cuidadores informales, resiliencia, salud y bienestar.*

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SUMMARY

Introduction: *The family of a patient with a mental disorder faces the challenge of adjusting to the illness,*

which can affect the caregiver's physical and mental health. **Objectives:** *To determine the relationship between age, resilience, caregiver skill, and caregiving time as predictors of burden in informal caregivers of patients with bipolar disorder and Schizophrenia Spectrum Disorders.* **Methods:** *This study employed a cross-sectional correlational design, and a multiple linear regression model with a stepwise method was used. The scales used included the Zarit Caregiver Burden Scale, the Connor-Davidson Resilience Scale, and the Nkongho Caregiving Ability Inventory.* **Results:** *The final sample consisted of 110 caregivers, with a predominance of caregivers who reported no burden. Resilience, in its dimension of adaptability and support networks, was the variable with the greatest explanatory weight on burden (β:-0.241 p: 0.009); longer caregiving time is associated with less burden (β:-0.19 p: 0.038), suggesting that prolonged experience facilitates adaptation and a greater number of hours of caregiving increases burden (β:0.203 p: 0.026).* **Conclusion:** *The study and intervention of caregiver burden in patients with bipolar disorders and schizophrenia should focus on optimizing informal support networks and the ability of caregivers to cope with change as a manifestation of resilience that buffers the stress of caring for a patient with a chronic mental disorder.*

Keywords*: Burden, informal caregivers, resilience, health and wellness.*

INTRODUCCION

A medida que la población envejece y aumenta la prevalencia de enfermedades crónicas, la atención médica se está trasladando de los hospitales a los hogares, involucrando activamente a las familias. Investigaciones muestran que los familiares en el papel de cuidadores informales enfrentan una carga considerable al atender a pacientes con trastornos mentales (1-4). La sobrecarga se refiere a la percepción del cuidador sobre su papel y al impacto que el cuidado de un paciente con enfermedad crónica tiene en diversas áreas de su vida (5). El concepto abarca tanto aspectos objetivos que son los cambios prácticos en su vida y las múltiples responsabilidades que implica, como subjetivos, que se refieren a las respuestas emocionales a dichas demandas (6,7). Otra característica relevante es que el papel de cuidador ha sido históricamente ejercido por mujeres (8,9).

La experiencia de cuidar a personas con trastornos mentales crónicos es a menudo invisible y los cuidadores no reciben apoyo profesional y orientación sistemática, resultando en niveles elevados de sobrecarga percibida (10-12). Asimismo, las expectativas socioculturales sobre los cuidadores de pacientes con trastornos mentales influyen en su tarea, la falta de información y el estigma asociado dificultan la comprensión de los trastornos mentales e impactan negativamente en el cuidar (10,13,14). Los pacientes con trastornos mentales generalmente pierden autonomía, aumentando la dependencia de cuidados y la sobrecarga del cuidador (11). La esquizofrenia y el trastorno bipolar aumentan el riesgo de discapacidad y reducen la esperanza de vida (15,16), afectando el desempeño laboral, social y la funcionalidad diaria (17,18).

Aunque la esquizofrenia y el trastorno bipolar tienen síntomas clínicos diferentes, ambos afectan la salud de los cuidadores, provocando síntomas de depresión y ansiedad (12). Diversos estudios muestran que, aunque la carga del cuidador de pacientes con esquizofrenia se reporta ligeramente mayor, no hay diferencias significativas entre los cuidadores de ambos trastornos (9,15,19).

Varios determinantes se han asociado con la sobrecarga, en primer lugar, se identifica el tiempo dedicado al cuidado; se ha encontrado que aquellos que invierten más horas diarias reportan mayores niveles de estrés, y mayor exposición a recaídas del paciente. Asimismo, la edad del cuidador influye en el nivel de sobrecarga; dado que, a medida que envejecen, los cuidadores enfrentan mayores desafíos, lo que puede conducir al agotamiento emocional, a la desesperanza ante el deterioro del paciente y a una disminución de sus habilidades motoras por lo que reduce su capacidad para cuidar (19-22).

La sobrecarga percibida por los cuidadores está relacionada con sus habilidades reales, incluyendo aspectos cognitivos y actitudinales. Los componentes clave del cuidado son el conocimiento, la paciencia y la valentía, esenciales para brindar un apoyo efectivo. La sobrecarga se manifiesta como un agotamiento emocional y físico debido al tiempo dedicado al cuidado de una persona dependiente, afectando diversos aspectos de la vida del cuidador (23,24). En un estudio de cuidadores colombianos de pacientes

con enfermedades crónicas no trasmisibles se reveló una asociación inversa entre la habilidad de cuidado y la sobrecarga (25).

Por su parte, la resiliencia se define como la capacidad de adaptarse positivamente a la adversidad, mostrando flexibilidad, bienestar psicológico, fortaleza y un estilo de vida saludable; es considerada un factor protector ante estresores crónicos, por ejemplo, el cuidar a un familiar con un trastorno mental (26). La resiliencia en cuidadores influye significativamente en la percepción de la carga de trabajo. Cuidadores con baja resiliencia experimentan mayor sobrecarga incluso con demandas leves, mientras que aquellos con alta resiliencia pueden manejar mayores exigencias con menor sensación de agobio. Esto sugiere que la capacidad de adaptarse y recuperarse de situaciones difíciles es crucial para mitigar la carga emocional y física del cuidado (26-28).

En Latinoamérica existen escasos antecedentes empíricos acerca de este tema, por lo que en el presente estudio se plantea como objetivo conocer la sobrecarga experimentada por los cuidadores informales de pacientes con trastorno bipolar y esquizofrenia en la ciudad de Caracas, Venezuela. Para ello, se desea determinar si existe relación entre la edad, resiliencia, habilidad del cuidador y tiempo de cuidado como predictores de la sobrecarga en cuidadores informales de pacientes con Trastorno Bipolar y Trastornos del Espectro de la Esquizofrenia.

En relación con los Objetivos de Desarrollo Saludable (ODS) de las Naciones Unidas esta investigación contribuye al ODS 3 (Salud y Bienestar) al generar conocimiento sobre los factores protectores y de riesgo relacionados con la sobrecarga percibida por cuidadores de pacientes con trastornos mentales, y a partir de los resultados posibilita crear intervenciones con el fin de mejorar el bienestar y calidad de vida, lo cual se alinea directamente con el objetivo de garantizar una vida sana y promover el bienestar para todos.

MÉTODO

La muestra del estudio fueron 110 cuidadores informales de pacientes con Trastorno Bipolar y Esquizofrenia que tenían al menos un mes de experiencia, residentes en el Área Metropolitana de Caracas. El muestreo fue no probabilístico, intencional (29) y por conveniencia (30). La muestra presentó un predominio de cuidadoras (77,3 %) principalmente madres (50 %), el 21,8 % tenían otros parentescos (sobrino, tío, hermanos), 10,9 % fueron hijos, 10,9 % parejas y 6,4 % padres. La edad promedio de los cuidadores fue de 54,5 años, con una media de 10 años, 1 mes ejerciendo su papel: el rango de tiempo de cuidado fue de un mes a 792 meses (66 años). Con respecto a las horas diarias dedicadas al cuidado, 42,7 % cumplían más de 15 horas al día, 20,9 % de 0 a 5 horas, 18,2 % de 5 a 10 y 18,2 % de 10 a 15. En cuanto al diagnóstico de los pacientes, 70 % eran cuidadores de pacientes con Esquizofrenia y 30 % atendían a pacientes con trastorno bipolar. Respecto al centro de salud de atención al paciente, el 51,8 % de los cuidadores buscaron asistencia en el Hospital Psiquiátrico de Caracas, 47,3 % en el Hospital Dr. Jesús Mata de Gregorio del Instituto Venezolano de los Seguros Sociales (IVSS) y 0,9 % (un cuidador) se atendía en consulta privada.

Los instrumentos empleados para la investigación fueron:

Escala de Sobrecarga del Cuidador de Zarit: Es un instrumento de autoinforme que estima la carga de los cuidadores a partir de los sentimientos que experimentan habitualmente (31). Está constituido por 22 ítems tipo Likert en una escala de 0 a 4. El instrumento tiene tres factores: impacto del cuidado (ítems 2, 3, 10, 11 y 12), que engloba las consecuencias para el cuidador de prestar el cuidado; relación interpersonal (ítems 5, 6, 9, 13 y 19) el cual hace referencia a emociones negativas que surgen en la relación entre el cuidador y el paciente; y, por último, expectativas de autoeficacia, que alude al conjunto de creencias que tiene el cuidador con respecto a su capacidad para ejercer su labor (ítems 20 y 21). Se reporta su previa validación mexicana con cuidadores informales de niños con patologías crónicas degenerativas obteniendo alta confiabilidad por consistencia interna (α: 0,84) y una estructura multifactorial de 3 factores que explican el 50 % de la varianza (32). En la muestra de cuidadores de este estudio la consistencia interna del instrumento fue adecuada (α: 0,847).

Escala de Resiliencia de Connor y Davidson: Es un instrumento compuesto por 25 ítems, con una estructura multifactorial de cinco factores: persistencia, tenacidad y autoeficacia; control bajo presión, adaptabilidad y redes de apoyo, control y propósito y espiritualidad. Se calcula un puntaje total y puntaje por subdimensiones, a mayor valor obtenido, mayor resiliencia (33). La escala ha sido usada en previas investigaciones en Venezuela con reportes de alta confiabilidad por consistencia interna con alfas de Cronbach entre 0,845 y 0,89 (34,35). En la muestra de estudio el valor obtenido del alfa de Cronbach (α: 0,939) indica adecuada confiabilidad por consistencia interna del instrumento.

Inventario de Habilidad del Cuidado de Nkongho: La escala está constituida por 37 ítems en formato tipo Likert con siete opciones de respuesta desde 1: totalmente en desacuerdo a 7: totalmente de acuerdo. Es una escala multifactorial con tres factores definidos por la autora del instrumento: conocimiento, valor (también llamado coraje) y paciencia (23). Para fin de esta investigación, se usó únicamente el factor conocimiento (ítems 2, 3, 6, 7, 9, 19, 22, 26, 30, 31, 33, 34, 35, 36). A mayor puntaje obtenido, mayor la habilidad de conocimiento del cuidador. La escala fue validada en Venezuela con 312 sujetos cuidadores de pacientes oncológicos, obteniendo un α de Cronbach de 0,729 y se validó la estructura multifactorial del Inventario (36). La confiabilidad obtenida en la muestra de esta investigación indica adecuada consistencia interna (α: 0,810).

Cuestionario de Datos Sociodemográficos: Instrumento construido para esta investigación con el fin de medir las variables: tiempo en el papel de cuidador en meses, horas diarias del cuidado, edad y sexo. En el ítem referente a las horas del cuidado, se presentaron 4 opciones: (0) de 0-5 horas, (1) 5-10, (2) 10-15 y (3) más de 15 horas que se dedicaban al cuidado diario del paciente.

Procedimiento

La investigación se desarrolló en tres fases. En la fase preparatoria, se estableció contacto con los hospitales Dr. Jesús Mata de Gregorio del IVSS y el Hospital Psiquiátrico de Caracas y con profesionales de la salud mental en consultas privadas. Los instrumentos se organizaron en un paquete, tanto en formato físico como en un *Google Form* que incluía información sobre los objetivos de la investigación, el consentimiento informado y los instrumentos. Durante la fase de trabajo de campo, se realizaron visitas semanales a los hospitales psiquiátricos donde se aplicaron los instrumentos a los cuidadores que cumplían los criterios de selección muestra, este proceso se realizó entre mayo y agosto 2024.

Análisis de los datos

Para la fase de análisis los datos de los sujetos fueron migrados a Excel, donde se verificaron las respuestas y datos perdidos y se exportó la base de datos al programa estadístico JAMOVI 2.3.21. Se aplicaron estadísticos descriptivos de tendencia central, dispersión y forma para caracterizar el comportamiento de las variables y posterior a la evaluación de la matriz de correlaciones y la comprobación de supuestos para la Regresión Lineal múltiple (37), se construyó y evaluó el modelo de regresión utilizando el método *stepwise* para obtener el modelo con el mejor ajuste (38). La investigación se realizó bajo las consideraciones éticas correspondientes al Código de Ética Profesional del Psicólogo en Venezuela y de la American Psychological Association (39,40).

RESULTADOS

En la muestra predominó la ausencia de sobrecarga con una media de 35,3 y una desviación estándar de 15,4, la distribución resultó simétrica. El menor puntaje obtenido fue 4 y el mayor 71 (Cuadro 1). Se observa que 69,1 % de los cuidadores están en la categoría de ausencia de sobrecarga, 22,7 % presentan niveles de sobrecarga leve y 8,2 % se clasifican en la categoría de sobrecarga intensa. Los cuidadores del subgrupo de sobrecarga intensa obtuvieron una media en la escala de Zarit de 61,6, y una desviación estándar de 4,64. El 77,8 % eran mujeres y el 22,2 % hombres. En cuanto al parentesco predominaron las madres (66,7 %) y el 55,6 % atendía a pacientes con trastorno

bipolar. En relación con las horas de cuidado, el 55 % dedicaba más de 15 horas diarias a su tarea. El promedio de edad de estos cuidadores con sobrecarga intensa fue de 50,7 años.

La habilidad Conocimiento de los cuidadores de la muestra presentó una media de 85,1, con una desviación estándar de 10,4, con asimetría negativa. El rango de la variable Conocimiento fue desde 56 hasta 98 (Cuadro 1).

Los cuidadores presentaron altos niveles de resiliencia con predominio de homogeneidad en los datos, dando lugar a una distribución simétrica. El rango de puntajes de resiliencia abarcó desde 43 hasta 100 (Cuadro 1). En relación con los subfactores de la Escala de Resiliencia, se encuentra que en el subfactor Persistencia, tenacidad y autoeficacia, la media fue de 20,2 y la desviación estándar fue de 3,21, con una distribución casi simétrica; el subfactor Control bajo presión obtuvo una media de 21,4 y una desviación estándar de 3,99 con una distribución simétrica. El subfactor Adaptabilidad y redes de apoyo, alcanzó una media de 16,1 y una desviación estándar de 3,07, con ligera asimetría negativa. Para el subfactor Control y propósito la media fue de 9,93 con una desviación estándar de 1,88, con una distribución de asimetría negativa y el último subfactor Espiritualidad resultó con una media de 6,67 y una desviación estándar 1,23, en una distribución con moderada asimetría negativa (Cuadro 2).

Cuadro 1

Estadísticos descriptivos

	Sobrecarga	Conocimiento	Resiliencia
N	110	110	110
Media	35,3	85,1	81,1
Mediana	38	85	75
Desviación estándar	15,4	10,4	12,6
Mínimo	4	56	43
Máximo	71	98	100
Asimetría	-0,0276	-0,593	-0,0721
Error est, Asimetría	0,230	0,230	0,230

Cuadro 2

Estadísticos descriptivos de las subescalas de Resiliencia

	Persistencia	Control bajo presión	Adaptabilidad	Control y propósito	Espiritualidad
N	110	110	110	110	110
Media	20,2	21,4	16,1	9,93	6,67
Mediana	18	21	15	9	6
Desviación estándar	3,21	3,99	3,07	1,88	1,23
Mínimo	9	12	7	3	2
Máximo	24	28	20	12	8
Asimetría	-0,211	0,0095	-0,359	-0,828	-0,630
Error est. asimetría	0,230	0,230	0,230	0,230	0,230

Para el cálculo de la regresión múltiple se valoraron los supuestos de linealidad, homocedasticidad, ausencia de multicolinealidad, distribución normal de los errores con la prueba Durbin Watson (p-valor: 0,221) y prueba de normalidad de Shapiro-Wilk (p-valor: 0,221) y se estudió la matriz de correlación para examinar las relaciones entre las variables y valorar las correlaciones estadísticamente significativas con la Sobrecarga. Fueron seleccionadas las variables Tiempo dedicado al cuidado y Adaptabilidad y Redes de Apoyo (subfactor de Resiliencia) y horas dedicadas al cuidado por su asociación lineal significativa con la Sobrecarga. El modelo final de variables elegidas resultó estadísticamente significativo (F = 5,73; p = 0,001) y predice un 14 % de la varianza de la sobrecarga de los cuidadores (R^2: 0,140) (Cuadro 3). Se evidencia que la variable predictora que mejor explica la Sobrecarga es Adaptabilidad y redes de apoyo (β = -0,241, p= 0,009) evidenciando que, al aumentar la adaptabilidad y redes de apoyo, disminuye el nivel de sobrecarga. Asimismo, hay relación directa entre el número de horas diarias de cuidado y la sobrecarga (β = 0,203, p valor = 0,026). Por último, se evidencia que a mayor tiempo en su papel de cuidador menor será su nivel de sobrecarga percibida (β = -0,190, p valor = 0,038) (Cuadro 4).

Cuadro 3

Resumen del modelo de regresión múltiple

Modelo	R	R2	F	gl1	gl2_	p
1	0,374	0,140	5,73	3	106	0,001

Cuadro 4

Análisis de coeficientes

	Estimador	EE	Betas	gl	t	p
Intercepto	35,2818	1,3853	0,000	106	25,47	<0,001***
Horas de cuidado	2,6297	1,1685	0,203	106	2,25	0,026*
Tiempo en el cuidado	-0.0222	0,0106	-0,190	106	-2,10	0,038*
Adaptabilidad	-1,2157	0,4550	-0,241	106	-2,67	0,009*

Nota. * p < 0,05, ** p < 0,01, **

DISCUSIÓN

En este estudio se avaluó la posible relación entre la edad, resiliencia, habilidad del cuidador y tiempo dedicado al cuidado con la sobrecarga percibida de cuidadores informales de pacientes con Trastorno Bipolar y Trastornos del Espectro de la Esquizofrenia. La muestra fue predominantemente de madres cuidadoras, lo cual coincide con hallazgos previos sobre la feminización del papel de cuidador de personas con discapacidad o enfermedad en el hogar por patrones culturales y de género (8,9,41-43) y más específicamente en pacientes con Esquizofrenia (44).

La media de edad de los cuidadores fue de 54,5 años, similar a lo reportado previamente donde la mayoría de los cuidadores informales se encuentran en el rango de edad de 50 a 75 años (45) y aunque la edad sea un factor

importante a considerar, no es necesariamente el principal determinante de la sobrecarga ya que pueden ocurrir efectos interactivos con otras variables como el nivel de dependencia del paciente, factores psicológicos como fortalezas del cuidador, mecanismos de afrontamiento y rasgos de personalidad (42,45,46).

Los cuidadores presentaron un predominio de ausencia de sobrecarga percibida, esto posiblemente se debe a los mecanismos de adaptación desarrollados por los cuidadores a lo largo del tiempo, lo que les ha permitido este ajuste y un dominio en la tarea, unido al apoyo del equipo multidisciplinario de los hospitales. El promedio de tiempo dedicado al cuidado fue de 10 años y 1 mes por lo que se puede suponer que los cuidadores con mayor experiencia han superado la fase inicial de adaptación y crisis, que exige respuestas y decisiones rápidas (47). Así, han logrado aceptar y adaptarse a su papel cotidiano. La literatura empírica reporta que los cuidadores tienden a experimentar síntomas intensos cuando se sienten abrumados por las demandas del paciente y la falta de recursos (lo cual corresponde a la fase inicial de diagnóstico), pero, con el tiempo y mediante el desarrollo de redes de apoyo, es posible que estos síntomas disminuyan (31). En apoyo directo a este planteamiento se encontró que, a mayor tiempo en su papel, menor fue la sobrecarga del cuidador, así se evidencia el proceso de adaptación que ocurre con el tiempo en un cuidador bien adaptado a su tarea: aprende del paciente y de su enfermedad. Resultados similares fueron reportados en cuidadores de pacientes con Demencia de Alzheimer, Esquizofrenia, Trastornos bipolares y depresivos, y personas con deterioro mental grave (11,48,49).

Se destaca el hallazgo de la relación directa positiva entre las horas dedicadas al cuidado y la sobrecarga, lo cual coincide con previos estudios con cuidadores de pacientes con lesión en la médula espinal, esquizofrenia, adultos mayores y personas con insuficiencia cardíaca (42,50,51). Este resultado se relaciona con la literatura que destaca que los aspectos objetivos de la sobrecarga, incluyendo las horas dedicadas al cuidado, afectan el bienestar general del cuidador posiblemente por el desgaste físico y competencia de tiempo y recursos con otras tareas en su vida (6).

En los cuidadores estudiados no se confirmó la asociación entre conocimiento y sobrecarga, lo que difiriere de estudios previos que reportan una relación significativa entre esas variables (52). Es posible que esta discrepancia pueda atribuirse al tamaño muestral, ya que el p-valor de la asociación lineal entre conocimiento y sobrecarga es cercano a la significancia (p: 0,06). Se hipotetiza que, con una muestra mayor, la relación podría volverse estadísticamente significativa en la dirección esperada.

En relación con la variable Resiliencia, resultó significativamente asociada con la sobrecarga en su dimensión de Adaptabilidad y Redes de apoyo. Estos resultados son consistentes con la evidencia previa que demuestra que las redes de apoyo son un factor protector para los cuidadores e influyen en su sobrecarga (53,54). La habilidad del sistema familiar y cada uno de sus miembros para percibir de manera positiva el cambio y adaptarse progresivamente al mismo, es determinante para afrontar enfermedades crónicas; la adaptabilidad "...es necesaria para que la familia se adapte a los cambios internos y externos que las enfermedades graves suelen requerir" (47). De este subfactor, los ítems "Tiendo a recuperarme luego de las enfermedades o dificultades" y "Tengo confianza para enfrentar nuevos retos" obtuvieron las mayores puntuaciones. Comprendiendo los resultados con la conceptualización de la Resiliencia Familiar, estas respuestas obtenidas corresponden a los factores de: optimismo, autoconfianza y la posibilidad de enfocar en los recursos y fortalezas cuando se enfrentan adversidades, los cuales están integrados en el proceso de Resiliencia Familiar llamado Enfoque Positivo (55). Se plantea en consecuencia que estos cuidadores encontraron en sí mismos, en las interacciones con otros miembros de su familia y en el equipo de cuidado, la posibilidad de construir la experiencia de cuidar con significados positivos y promotores de resiliencia: tener confianza compartida en superar las dificultades.

CONCLUSIÓN

Se estudió si existe relación entre la edad, resiliencia, habilidad del cuidador y tiempo dedicado al cuidado con la sobrecarga percibida.

A pesar de que no se cumplieron todas las relaciones planteadas, los resultados sugieren una dirección para futuras investigaciones y ayudan a comprender cómo se comportan estas variables en esta muestra. Entre los hallazgos más relevantes, la resiliencia en su dimensión de adaptabilidad y redes de apoyo se destacó como la variable con mayor peso explicativo de la sobrecarga. Además, se observó que, a mayor tiempo de cuidado, menor es la sobrecarga percibida. Esto sugiere que la experiencia prolongada facilita el proceso de adaptación y juega un papel fundamental en el bienestar de los cuidadores. Por lo tanto, el desarrollo de estas capacidades y el fortalecimiento de las redes de apoyo pueden ser determinantes en la experiencia del cuidado. Además, se identificó que a mayor número de horas diarias dedicadas al cuidado mayor es el nivel de sobrecarga percibida. Esto indica que una mayor dedicación diaria a satisfacer las demandas del paciente constituye un factor de riesgo para desarrollar sobrecarga y en consecuencia, afectar negativamente la salud del cuidador familiar informal.

Los cuidadores asignados por la familia o autoasignado desde el inicio del trastorno mental de su paciente, desarrollaron en el tiempo la habilidad para sentirse autoeficaces y confiados para ejercer satisfactoriamente su papel. En consecuencia, cualquier evaluación familiar o plan de intervención para cuidadores informales de pacientes en el espectro de la esquizofrenia y trastorno bipolar debe focalizar en explorar y optimizar sus redes de apoyo (con especial atención a mujeres en situación de cuidadora única) y su capacidad de aceptar el cambio y sentirse competente para afrontarlo. Esto no solo facilitará una mejor gestión del cuidado, sino que también contribuirá a una experiencia más positiva para los cuidadores.

Como limitaciones de la investigación se identifican la dificultad de acceso a la muestra, el uso exclusivo de instrumentos de autoreporte para medir las variables de estudio, y el tamaño muestral que afecta la generalización de los resultados. Se recomienda que futuras investigaciones incorporen variables como creencias religiosas, nivel educativo, empleo y nivel socioeconómico y el impacto de las creencias sobre la salud mental en el ejercicio del papel del cuidador para aumentar la varianza explicada de la variable sobrecarga, así como enriquecer la línea de investigación con estudios cualitativos sobre las experiencias y significados de los cuidadores para comprender la sobrecarga desde el punto de vista del cuidador, comparando a quienes han comenzado a cuidar con aquellos con más tiempo en el papel.

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Evaluation of the Feasibility and Reliability of Contact Tests in Routine Clinical Practice

Evaluación de la Viabilidad y Fiabilidad de las Pruebas de Contacto en la Práctica Clínica Habitual

Maria Zofia Lisiecka[1]

SUMMARY

Introduction: *This study was conducted to determine the feasibility of using contact tests in routine clinical practice based on the reliability of their results.* **Objective:** *To establish the diagnostic value of patch tests and assess the feasibility of their use in the routine clinical practice of allergists and dermatologists.* **Method:** *Literature review, subject analysis of patient photographs depicting skin reactions, and comparative analysis of the advantages and limitations of contact tests with other diagnostic methods were used.* **Result:** *The results show that among all types of contact tests, the patch test is the most informative. The level of its accuracy is determined by high indicators of sensitivity and specificity due to the principle of operation of the test – the presence of direct prolonged contact of the allergen with the skin, and further improvements: the creation of clear protocols for the procedure, the development of clear criteria for evaluating results, the expansion of the set of allergens, the establishment of optimal exposure time, the use of new hypoallergenic materials. The accuracy of patch test results may substantially decrease under the influence of external and internal factors. External factors include violations of the procedure technique, changes in exposure time, and allergen concentration without considering the allergen's type and seasonality. Internal diseases include individual sensitivity (skin reactivity to an allergen), skin condition, use of local medications, and the presence of concomitant diseases. A comparison of contact and laboratory tests for the diagnosis of contact dermatitis reveals the limited specificity of laboratory tests, indicating that they can be effectively used in combination with patch tests but are not a complete alternative to them. The results allow recommending the use of contact tests, especially patch tests, as a routine procedure for diagnosing contact dermatitis in cases of chronic dermatitis of unknown etiology, occupational dermatitis, eczematous, and non-eczematous dermatoses.*

Keywords: *Patch test, allergology, sensitivity, specificity, dermatitis, gold standard of diagnosis.*

RESUMEN

Introducción: *Este estudio se realiza para determinar la viabilidad del uso de las pruebas de contacto en la práctica clínica habitual en función de la fiabilidad de sus resultados.* **Objetivo:** *Establece el nivel de valor diagnóstico de las pruebas de parche y determinar la viabilidad de su uso en la práctica clínica habitual de alergólogos y dermatólogos.* **Método:** *Se uso la revisión de literatura, el análisis de fotografías de pacientes que mostraban reacciones cutáneas y el análisis comparativo de las ventajas y limitaciones*

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de las pruebas de contacto con otros métodos de diagnóstico. **Resultado:** *Los resultados muestran que, entre todos los tipos de pruebas de contacto, la prueba del parche es la más informativa. El nivel de su exactitud viene determinado por los elevados indicadores de sensibilidad y especificidad debidos al principio de funcionamiento de la prueba -la presencia de un contacto directo prolongado del alérgeno con la piel- y a otras mejoras: la creación de protocolos claros para el procedimiento, el desarrollo de criterios claros para evaluar los resultados, la ampliación del conjunto de alérgenos, el establecimiento de un tiempo de exposición óptimo, el uso de nuevos materiales hipoalergénicos. La precisión de los resultados de las pruebas del parche puede disminuir sustancialmente bajo la influencia de factores externos e internos. Los factores externos son las violaciones de la técnica del procedimiento, los cambios en el tiempo de exposición y la concentración del alérgeno sin tener en cuenta su tipo, y la estacionalidad. Los internos son la sensibilidad individual (reactividad de la piel a un alérgeno), el estado de la piel, el uso de medicamentos locales y la presencia de enfermedades concomitantes. Una comparación de las pruebas de contacto y de laboratorio para el diagnóstico de la dermatitis de contacto identifica una especificidad limitada de las pruebas de laboratorio, lo que indica que pueden utilizarse eficazmente en combinación con las pruebas epicutáneas, pero no son una alternativa completa a estas. Los resultados permiten recomendar el uso de las pruebas de contacto, especialmente las pruebas del parche, como procedimiento rutinario para el diagnóstico de la dermatitis de contacto en casos de dermatitis crónica de etiología desconocida, dermatitis ocupacional, dermatosis eccematosas y no eccematosas.*

Palabras clave: *Prueba del parche, alergología, sensibilidad, especificidad, dermatitis, patrón oro de diagnóstico.*

INTRODUCTION

Provocative tests are the standard of diagnosis in allergology, as they enable the accurate identification of the allergen that causes sensitization and the assessment of the severity of an allergic reaction. One of their types is contact tests, the mechanism of action of which simulates the actual conditions of contact between the allergen and the patient's skin by applying a small amount of potential allergen to a separate area, usually on the back, and monitoring the skin reaction. Contact tests are particularly effective in detecting cell-mediated allergic reactions that manifest as contact dermatitis, allowing for the identification of a wide range of allergens, from metals to cosmetic components. The high specificity of these tests will enable them to be considered an effective method for diagnosing contact dermatitis. However, given the existing limitations, recommendations on the feasibility of using contact tests in routine clinical practice should be made based on an assessment of their reliability.

One of the problems that complicates the examination of the diagnostic value of these tests is the presence of factors that affect their result, including individual variability, concomitant diseases, medication intake, and seasonal factors. Li et al. (1), based on an extensive population-based study, analysed factors influencing the patch test response. They determined that a positive reaction to allergens was more often observed in winter than at other times of the year, and in men, the frequency of reactions was higher. Still, with age, it did not substantially increase; however, in women, a clear age correlation was observed – in the older group (≥50 years), contact tests yielded a reaction 30 % more often than in the younger group (<30 years). The frequency of positive allergic samples in different age groups was also investigated by Heindl et al. (2), based on the analysis of 5 857 positive tests, they determined that the highest frequency of skin reactions to contact with the corresponding allergen was observed in the group of adult women, and it characteristically increased with age. In both studies, factors affecting the results of contact tests are considered rather as risk factors for the development of contact dermatitis, so it is incorrect to assess their level of influence on the results of testing itself in the context of causing false positive or false negative reactions based on the results of these works.

Gupta and Anand (3), studying the diagnostic effectiveness of contact tests, emphasized that for an accurate interpretation of their results, it is important to consider the medical history, general clinical picture, and geographical features of the patient's region of residence. During the lanolin allergenicity study, Jenkins and Belsito (4) noted that the detection of contact dermatitis using patch tests can give false-positive results. The authors attribute this to

the effect of concomitant skin diseases on the manifestation of lanolin allergenicity. Thus, the contact dermatitis provoked by it on diseased skin will not necessarily lead to allergic reactions on healthy skin.

Based on a retrospective analysis of the results of contact tests in 5 446 patients, Comstedt et al. (5) established that testing with Finn Chambers aluminium can give false positive reactions to sodium tetrachloropaladate, palladium chloride, Cain mixture II, and Myroxylon pereirae in patients with contact allergy to aluminium. This result is due to the fact that the material from which Finn Chambers was made could contain aluminium, and under the influence of these compounds, chemical reactions could occur, as a result of which aluminium was released and came into contact with the skin, causing an allergic reaction.

The following works analyse the influence of certain factors on false positive results of contact tests. Still, they do not assess the reliability of the patch testing method, considering possible errors. An important issue related to evaluating the accuracy and reliability of contact tests for allergy diagnosis concerns the interpretation of the results. Reeder et al. (6) analysed data from 4 121 contact tests to identify patterns in the understanding and relevance of questionable responses. The results showed that a third of the patients tested had more than one questionable reaction. Reactions to nickel, neomycin, methylchlorisothiazolinone, and methylisothiazolinone were most often misidentified as contact dermatitis. Difficulties are associated with interpreting the results of patch tests on the coloured skin of patients examined by Burli et al. (7). In patients with a higher Fitzpatrick skin type, contact test reactions were detected due to lichenification and hyperpigmentation, and bright red or pink shades characteristic of light skin looked pale pink or purple. Given these difficulties in interpreting the results of contact tests, Oppermann et al. (8) suggested using dermoscopy as an auxiliary tool in cases where patch tests produce weak or questionable responses. Studies on the problem of correctly interpreting contact test results presented in these works form an understanding of the limitations of this diagnostic method, but do not provide a critical assessment of its reliability.

Although current research has recognised multiple factors affecting contact test outcomes, including seasonal variations, age, gender, and concurrent skin conditions, a substantial gap persists in fully elucidating how these factors specifically lead to false-positive or false-negative reactions. Moreover, while research has identified difficulties in interpreting contact test outcomes, especially in individuals with darker skin tones, there is an absence of standardised methodologies or instruments to enhance the precision and dependability of these interpretations. A comprehensive evaluation of the reliability of contact tests, taking into account these limits and potential inaccuracies, is essential to guide recommendations for their application in standard clinical practice.

The purpose of this literature review is to determine the feasibility of using contact tests in routine clinical practice by evaluating the reliability of test results and analysing factors that affect patients' hypersensitivity to specific contact allergens. Additionally, this study aims to contribute to the existing literature by providing a comprehensive assessment of the limitations and potential errors associated with contact tests, thereby offering insights into areas requiring further standardization and improvement. By critically evaluating the diagnostic accuracy and reliability of contact tests, this research seeks to inform clinical guidelines and enhance the practical application of these tests in diagnosing contact dermatitis, ultimately improving patient outcomes and advancing the field of allergology.

MATERIALS AND METHODS

To assess the feasibility and reliability of contact tests in routine clinical practice, the analysis of scientific sources on allergology, immunology, and dermatology was conducted, which contained up-to-date information on key aspects of the development, diagnosis, and treatment of allergic reactions in general and contact allergies in particular. Determining the validity of contact tests involves two main aspects: assessing their sensitivity and specificity in diagnosing different types of contact allergies and identifying factors that may affect test results.

The search for sources for determining the reliability of contact tests was conducted among publications in the scientific databases PubMed, Google Scholar, Web of Science, and Scopus. Keywords for the search of materials relevant to the task of determining the sensitivity and specificity of contact tests for the diagnosis of various types of contact allergies were: "contact dermatitis", "contact allergy", "patch test", "contact test", "sensitivity of contact tests", "specificity of contact tests", "diagnosis of contact dermatitis", "allergen", "nickel", "cobalt", "chromium", "preservatives", "perfume", "cosmetics", "positive predictive value", "negative predictive value", "accuracy", "reproducibility".

The search query, which was aimed at identifying factors that can affect the results of contact tests, was formed according to the following keywords: "factors that affect the results of contact tests", "false positive results of contact tests", "false negative results of contact tests", "validity of contact tests", "reliability of contact tests", "false results when conducting contact tests", "limitations of contact tests", "interpretation of contact tests". The search was conducted in English and Polish. Sources that met the following inclusion criteria were selected for processing: Relevance of the material (sources published in the period from 2020 to 2024 were considered); Reliability of the results (preference was given to study results that were clinically and logically proven and consistent with the results of other studies); Clinical importance of the results (papers' results of which could be used in clinical practice were evaluated).

The review did not include clinical trials with the absence of a control group, which was explained by the inability to compare and critically evaluate the results, and uncertain criteria for including/excluding participants, which affected the representativeness of the sample. A total of 38 relevant scientific sources were selected for the analysis.

A subject analysis of factors affecting the results of contact tests was conducted based on photos of patients depicting skin reactions to specific allergens and characteristic visual symptoms of certain systemic diseases. When using photos, the necessary legal and ethical standards were observed – patients' informed consent to the use of their images in the study was obtained, and their anonymity was ensured. The advantages and limitations of this diagnostic method and other methods for detecting contact allergies were compared to get a critical assessment of the effectiveness of contact tests. The determination of the feasibility of using contact tests in the routine clinical practice of allergists, dermatologists, professional pathologists, and other doctors who have the skills to conduct the procedure and interpret its results was performed based on a preliminary assessment of the reliability of these tests and the result of their comparison with other methods of diagnosing contact allergies.

RESULTS

Contact tests are diagnostic procedures used to detect allergic skin reactions to various substances. They are an important tool for diagnosing contact dermatitis. There are several types of contact tests, each of which has its own characteristics and purpose: patch tests are used to diagnose contact dermatitis caused by metals, cosmetics, preservatives, dyes; pre-tests – to diagnose allergies to air allergens (pollen, animal hair, house dust); application tests with liquid substances – to diagnose allergies to cosmetics and detergents, perfumes; ocular tests – to diagnose allergies to cosmetics that come into contact with the eye area, in particular, the mucous membrane; inhalation tests – to diagnose allergies to volatile substances; oral – for the diagnosis of allergies to food or medications. The choice of a particular type of test depends on the suspected allergen, the location of the allergic reaction, and the severity of the allergic reaction (9-11).

The most informative and widely used type of contact test is the patch test (12). In the 19th century, doctors noticed the occurrence of skin reactions in some patients after contact with substances used in the textile industry (dyes, wool, silk), agriculture (plant pollen, animal hair, chemicals for processing plants), everyday life (detergents and cosmetics, dust, metals – nickel, cobalt, chromium, which were often part of jewellery and tools). At the beginning of the 20th century, the first experiments on the sensitization of animals

and humans were conducted, which facilitated a better understanding of the mechanisms underlying the development of contact allergic reactions. This contributed to the development of a method for identifying allergens that caused this reaction, which led to the creation of patch tests in the mid-20th century (13).

From the moment of its creation in the 1950s to the present, its technology has undergone substantial changes aimed at improving the accuracy, convenience, and safety of the procedure. This has contributed to the fact that several international allergy communities have recognized the patch test as the gold standard for diagnosing contact dermatitis (14-16). These organizations include the European Academy of Allergy and Clinical Immunology, which regularly publishes recommendations and consensus on the diagnosis and treatment of allergic diseases, in particular, contact dermatitis, in which the patch test is clearly recognized as the main diagnostic method (17); the American Academy of Allergy, Asthma, and Immunology, which sets standards for clinical practice in the field of allergology and immunology and also supports the patch test as the most reliable method for diagnosing contact dermatitis (18); the International Association of Dermatologists, which develops standards for the diagnosis and treatment of skin diseases and confirms the importance of the patch test for diagnosis contact dermatitis (19); an international research group on contact dermatitis, the members of which are actively developing new methods for the diagnosis and treatment of this disease, and use patch tests as one of the main tools of their work (20).

The high sensitivity of patch tests as a diagnostic method for detecting contact dermatitis is mainly explained by the principle of their operation. The patch test provides direct and long-term contact of the allergen with the skin, which allows identifying even mild allergic reactions that may not be detected during the examination using other methods (21). Further improvements in patch tests had a characteristic effect on increasing their sensitivity: the development of protocols to provide standardized conditions for all patients allowed achieving reproducibility of test results and, accordingly, increasing the accuracy of diagnosis; the expansion of the set of potential allergens – detecting even rare forms of sensitization; the establishment of clear criteria for evaluating the results of patch tests increased the level of objectivity and accuracy of diagnosis; the calculation of the optimal exposure time (48-72 hours) – assessing both early and late skin reactions to the allergen (22-24). The list of allergens that cause contact dermatitis is very wide, from metals to plant extracts. Still, the most common of them are nickel, cobalt, chromium, formaldehyde, flavourings, and methyl isocyanate. Contact allergy to nickel is quite common since this substance is found in things that have close and prolonged contact with the skin – in costume jewellery, accessories, coins, stationery, cutlery. The positive reactions of the nickel and methylisocyanate patch test are shown in Figure 1.

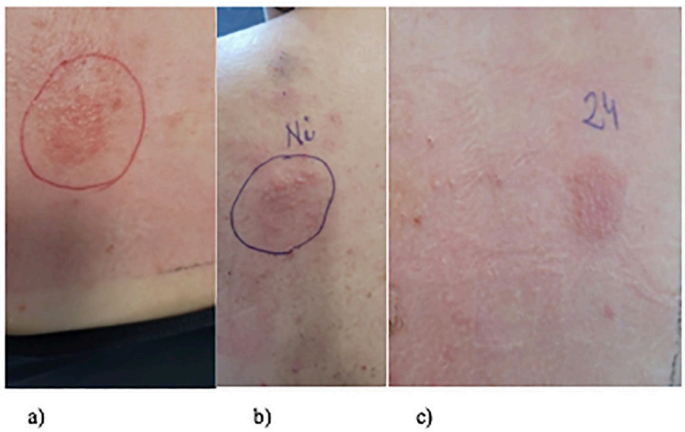


Figure 1. Skin reaction to allergens detected by the patch test: a) nickel, b) nickel (panel position 18), and c) methylisocyanate (panel position 24).

The positive and negative predictive value of the diagnostic method using patch tests was increased by the use of occlusive dressings to create a moist environment that ensures the penetration of allergens into the skin and the development of allergic reactions, and the use of hypoallergenic materials that minimize the risk of false positive reactions (25). This, accordingly, increased the specificity of patch tests as a method for diagnosing contact dermatitis, which allowed prescribing effective treatment, preventing relapses, and improving the quality of life of patients.

Indicators of sensitivity and specificity of patch tests ensure that diagnostic results are obtained with a high confidence probability, but they do not guarantee the avoidance of false reactions. External and internal factors can determine the probability of false results. The main external factors are the technique used in the procedure, the concentration of the allergen, the type of allergen, the duration of exposure, and seasonality (26). Failure to follow the testing technique, such as incorrect fixation of patches, non-compliance with the exposure time, or the use of poor-quality reagents, can distort the result and lead to an erroneous diagnosis. An excessively high or low allergen concentration in the test can also lead to false results. Depending on the type, some allergens may cause a more pronounced reaction than others, which can lead to misinterpretation and erroneous conclusions. The duration of contact between the allergen and the skin also influences the intensity of the reaction. At certain times of the year, the skin may be more sensitive, causing an increased reaction to the allergen. Increased sun activity in summer can lead to photodermatitis, an inflammation of the skin caused by simultaneous exposure to ultraviolet radiation and certain substances (27). Some components of sunscreens (oxybenzone, avobenzone, zinc oxide, titanium dioxide, flavourings, and preservatives) can cause an allergic contact reaction. Increased skin sensitivity to allergens during the cold season is primarily associated with a weakened immune system and dry skin, which develops due to low temperatures and humidity outside, as well as exposure to indoor heaters. An effective way to reduce or eliminate the influence of external factors is strict adherence to standardized protocols for conducting the testing procedure (28), the use of a comprehensive set of allergens, and the use of modern patch tests based on hypoallergenic materials (Figure 2).

It is more challenging to mitigate the impact of internal factors than external ones, so it is more appropriate to accurately assess their impact and consider it when analyzing the results of the patch test. Such factors are individual sensitivity, the patient's skin condition, the use of topical medications, and the presence of

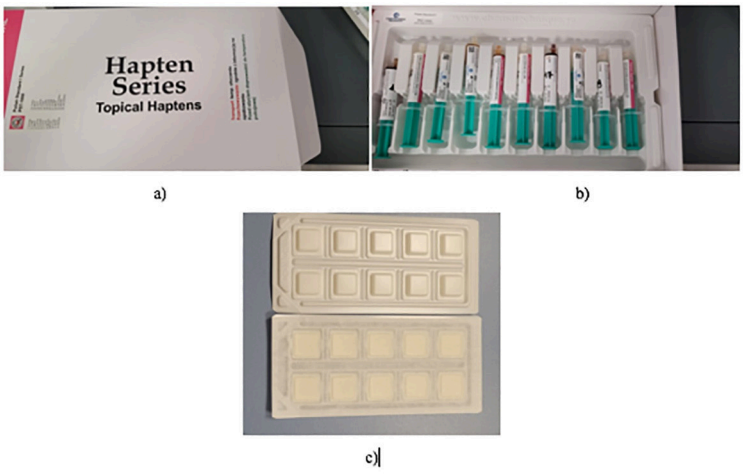


Figure 2. Modern contact tests using a series of haptens: a) packaging, b) container where the substance is placed and sealed on the back, c) substance tested in contact tests. Source: compiled by the author.

concomitant diseases. Individual sensitivity, or skin reactivity to allergens, is an important factor that affects the results of a patch test. This indicator is highly variable and depends on several factors, particularly age, genetic predisposition, the state of the immune system, and overall health. Depending on individual sensitivity, patch tests can yield false-positive or false-negative results (29). Hypersensitivity can provoke more pronounced reactions to allergens, even to very low concentrations, which leads to more pronounced reactions on the skin and, accordingly, more positive test results (30). In some cases, individual sensitivity can lead to cross-reactivity with related allergens – for example, a person with a nickel allergy may also exhibit increased sensitivity to cobalt (31). People with reduced sensitivity often exhibit less pronounced or absent reactions to allergens, even if they are sensitized to them, which can lead to false-negative patch test results. A factor in the absence of a reaction in such patients may be an insufficient concentration of the allergen in the patch (32). When interpreting the results of patch tests, considering individual sensitivity, it is essential to take into account the patient's overall clinical picture and medical history. In addition, it is important to use control tests to assess the overall reactivity of the skin.

The condition of the skin can substantially affect the accuracy of the results of the patch test and, in some cases (the presence of open wounds, burns, abrasions, and other lesions), even become a contraindication to its implementation. Inflammation can increase the skin's sensitivity to irritants and cause a false positive patch test response (33,34). Against this background, a strong inflammatory process can make it difficult to distinguish a true allergic reaction, leading to false-negative test results (35). Dry skin increases its tendency to irritation, which can cause false positive reactions. The presence of skin infections affects the change in the immune response, leading to distortion of the results of the diagnosis of contact allergies. Some skin diseases, such as psoriasis, ichthyosis, and atopic dermatitis, can alter the skin's reactivity to allergens, thereby reducing the reliability of patch tests (36). During the procedure using these tests, it is important to adhere to the mandatory requirements for the skin condition, which will reduce the risk of false results: the skin should be clean and dry; the day before the procedure, it is worth avoiding usage of cosmetics and perfumes on the site where the test will be performed; a few days before testing, it is important to avoid contact with known irritants. The skin as an external protective barrier of the body is subject to damage and injuries that affect its condition, and, accordingly, the result of allergy testing but since it is the largest human organ, the doctor can choose the most optimal area for conducting a patch test, considering the protocol of the procedure.

The intensity of the patch test reaction can be substantially affected by the use of topical medications. Many of them have an anti-inflammatory effect, which suppresses the development of allergic reactions, leading to false negative test results. The main types of these drugs are corticosteroids, antihistamines, and immunomodulators (37). Corticosteroids are the most well-known group of drugs that have an anti-inflammatory effect, and they are widely used to treat various skin diseases, including eczema and dermatitis. They reduce inflammation, redness, and itching by suppressing the skin's immune response, thereby masking allergic reactions during the patch test. Topical antihistamines have a direct effect on the response of patch tests, as they are designed to eliminate itching, redness, and other allergy symptoms, which are used to interpret the result. Immunomodulators also affect the immune system and can alter its response to allergens, masking an allergic reaction.

Some local medications can increase the skin's sensitivity to allergens, leading to false-positive test results. Among them, some antibiotics are distinguished (for example, neomycin, which is often added to ointments and creams, can cause contact dermatitis and increase skin sensitivity to other allergens), preservatives that are part of cosmetics (parabens, formaldehyde), perfumes, or their components (synthetic to natural flavours, essential oils) (38). Certain substances or medications can cause skin irritation (redness, blisters), which may visually be confused with an allergic reaction. Their use before the procedure complicates the diagnostic process and increases the possibility of obtaining a false positive result. Most often, antiseptics (alcohol, iodine, chlorhexidine) and active ingredients in external

products (salicylic acid, benzoyl peroxide) cause irritation (39). It is necessary to stop using topical medications at the site where the test will be performed 1-2 weeks before the procedure to avoid false test results.

The effect of concomitant diseases on the results of the patch test is conducted by changing the reactivity of the skin or masking an allergic reaction. The vast majority of skin diseases can alter the skin's sensitivity to various irritants. For example, in eczema, inflamed skin can react to allergens more or less than healthy, and in psoriasis, the inflammatory process can hide a weak allergic reaction (40). Changes in skin reactivity and masking an allergic reaction can also trigger infectious diseases. In addition, damage to the skin barrier caused by infections contributes to increased allergen permeability and increased response to them (41). Validity patch test results can be affected by bacterial (boils, carbuncles, impetigo, streptoderma), viral (herpes, chickenpox, viral warts), fungal (mycosis, candidiasis), and parasitic skin infections (Sarcoptes scabiei, trichomonas).

Systemic diseases substantially affect the immune system, and this can lead to changes in the skin's response to various stimuli, including allergens (42,43). Depending on the strengthening or weakening of the immune response, the intensity of the allergic reaction also changes. By analogy with the effects of infections, some systemic diseases can disrupt the barrier functions of the skin, increasing the permeability of allergens. The response of patch tests may be affected by the general weakening of the body characteristic of these diseases, and the effect of therapy, which may include corticosteroids and other anti-inflammatory drugs. Most often, the results of patch tests are affected by autoimmune diseases (Sjogren's syndrome, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, rheumatoid arthritis), endocrine diseases (diabetes mellitus, thyroid diseases), oncological diseases (tumours of the blood and lymphatic system), connective tissue diseases (scleroderma, dermatomyositis, polymyositis) (44).

Since the immune system plays a key role in both autoimmune diseases and allergic reactions, conducting allergy tests in such patients requires special care and additional measures. Before allergological tests, such as a patch test, it is recommended to conduct a general and biochemical blood test to analyse the general condition of the body, detect inflammatory processes, assess the function of the kidneys, liver and other organs; immunological studies – to assess the activity of the autoimmune process, the level of immunoglobulins and other indicators of the immune system; consultation with a rheumatologist – to assess the activity of the main autoimmune disease. In addition to these measures, it is important to individually select allergens for testing, considering the clinical picture of the disease, and conduct dynamic monitoring of the patient after allergy tests. Considering all these factors that may affect the test result, and strict compliance with the procedure protocols and criteria for evaluating the skin reaction, will increase the reliability of patch tests as a method for diagnosing contact dermatitis.

An important step to assess the feasibility of contact tests in routine clinical practice is to determine the optimal patient screening strategy based on comparing the effectiveness of different methods for diagnosing contact allergies. Although laboratory tests cannot be called an alternative to contact tests, they can also be used to diagnose allergies. Determination of allergen-specific immunoglobulin E (IgE) can detect elevated levels of antibodies to specific allergens in the blood (45). However, this method may give false-positive results in patients with atopic dermatitis. Cytological examination of skin rashes identifies characteristic changes in skin cells in contact allergies. Histological examination of the skin biopsy allows confirming the diagnosis of contact dermatitis and excludes other skin diseases (46). The advantages of laboratory tests are safety since they do not carry the risk of allergic reactions during the procedure, the ability to detect allergies to volatile substances that are difficult to investigate with patch tests, and the absence of the need for special equipment, given that these tests can be performed in most medical laboratories. Disadvantages of laboratory tests include a limited number of allergens, the possibility of false-positive and false-negative results, and the lack of mandatory correlation with the clinical manifestations of the disease.

Considering the advantages and disadvantages, laboratory tests can be methods for diagnosing contact allergies in clinical practice in cases of contraindications to the patch test, the need to confirm the results of the patch test, or to detect allergies to volatile substances or medications. Compared to contact tests, laboratory tests for detecting contact allergies have a lower specificity index since the antibodies used in the study can react not only to a specific allergen but also to related substances, provoking false-positive results. In general, contact tests have a higher level of reliability, given that the sensitivity and specificity indicators analysed are higher than those of laboratory tests. Still, both methods can be used in combination to obtain a more accurate diagnosis. In a comprehensive assessment of the feasibility of contact testing, in addition to the theoretical analysis of the aspects that influence it, it is important to consider several clinical cases that demonstrate the value of patch testing in clinical practice.

A 50-year-old female patient presented with severe allergic reactions on the skin of both arms, neck, and décolleté, manifested by large, well-demarcated blisters, severe itching, and swelling. A long-term medical history indicated a chronic course of the allergic process. The contact test revealed pronounced positive reactions to nickel – 17 mm diameter swelling, numerous blisters and severe itching; epoxy resins – 15 mm diameter swelling; formaldehyde – 12 mm diameter swelling and numerous blisters; fragrance mixture – 15 mm diameter swelling and numerous blisters; palladium – 23 mm diameter swelling, numerous blisters, severe itching (Figure 3).

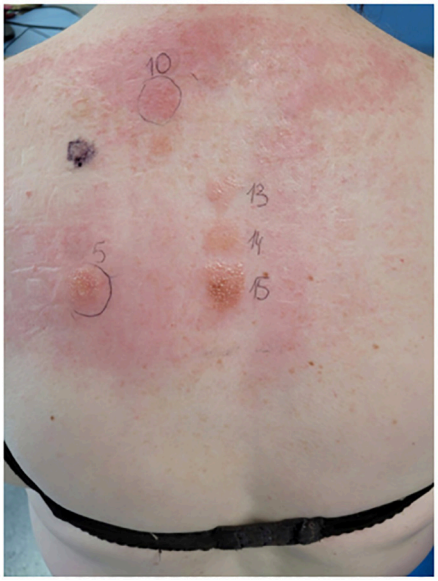


Figure 3. Results of the patient's contact test for nickel, epoxies, formaldehyde, fragrance mixture and palladium. Notes: reaction to nickel – position 5; epoxy resins – 10; formaldehyde – 13; fragrance mixture – 14; palladium – 15. Source: compiled by the author

The pronounced positive reactions to nickel, epoxy resins, formaldehyde, fragrance mixture and palladium confirm the patient's sensitization to these allergens, and their size and nature (blisters, swelling, itching) correlate with the severity of this sensitization. Positive reactions to several allergens indicate multiple allergies. The diagnosis is contact dermatitis sensitized to several allergens.

A 15-year-old female patient complained of eczema on both hands. Over the past 2 years, the skin condition had been constantly deteriorating, and the use of corticosteroid-based creams periodically improved the situation. According to the patient's anamnesis, an allergic reaction occurred during the use of hair shampoo. Patch test results revealed a pronounced positive reaction to methyl chloroisothiazolinone and methylisothiazolinone, which are common preservatives added to various cosmetic products, including shampoos (Figure 4).

The pronounced positive reaction to methyl chloroisothiazolinone and methylisothiazolinone confirms the patient's sensitization to these preservatives. The diagnosis was contact dermatitis sensitized to methyl chloroisothiazolinone and methylisothiazolinone. A similar clinical picture to the previous one was observed in a thirteen-year-old patient. External manifestations of eczema were found on both hands and around the mouth. The results of the patch test revealed a pronounced positive reaction to methylisothiazolinone – a significant 30×15 mm oedema that crossed the 5×5 mm boundaries of the applied allergen, erythema, and severe pruritus (Figure 5).

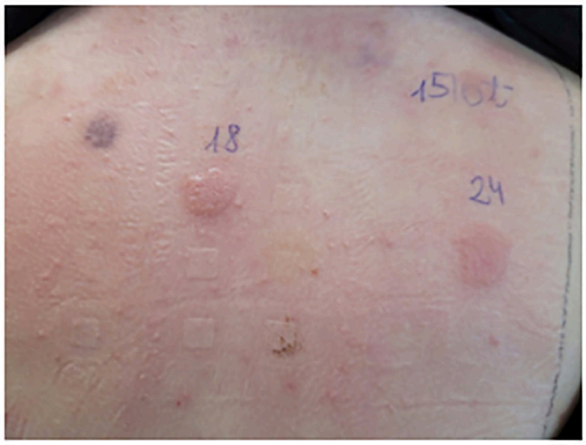


Figure 4. Results of the patient's contact test for methylchloroisothiazolinone and methylisothiazolinone. Notes: reaction to methylchloroisothiazolinone – position 18; methylisothiazolinone – 24.



Figure 5. Results of a patient's contact test for methylisothiazolinone. Source: compiled by the author.

During further follow-up, it was found that the reaction to the patch test persisted for two weeks, indicating persistent sensitization to the allergen. The large size of the oedema and the duration of the reaction indicate severe sensitization to the allergen. The diagnosis was made – contact dermatitis sensitized to methylisothiazolinone. It is important to add that in clinical practice, allergic reactions to contact with methylchloroisothiazolinone and methylisothiazolinone in children were relatively rare. However, an increase in the number of cases with clinical features similar to the above case histories of underage patients indicates a trend that allergists should take into account when compiling a list of potential allergens for patients of a certain age, and manufacturers should review the composition of products to replace potentially allergenic components with hypoallergenic ones.

Proper preparation of the patient is crucial for the accuracy and reliability of patch test results. Before testing, patients should be advised to avoid using topical corticosteroids, antihistamines, and other anti-inflammatory medications on the test area for at least one to two weeks, as these can suppress skin reactions and lead to false-negative results. Additionally, patients should refrain from applying lotions, creams, or cosmetics to the test site for a few days before the procedure to prevent potential interference with the test results. It is also important to inform patients about the necessity of keeping the test area dry and avoiding activities that may cause excessive sweating during the testing period. Clear communication regarding these preparatory steps ensures that the skin is in an optimal state for accurate allergen exposure and reaction assessment.

In the event of severe reactions during patch testing, medical professionals need to follow a clear and structured action algorithm to ensure patient safety and effective management. Initially, the allergen patches should be immediately removed, and the affected skin area should be gently cleaned with water to eliminate any residual allergen. Topical corticosteroids can be applied to reduce inflammation and alleviate symptoms. For severe systemic reactions, such as anaphylaxis, prompt administration of epinephrine and emergency medical intervention may be required. Patients should be closely monitored for any signs of respiratory distress or cardiovascular compromise. Having a well-defined protocol in place, including access to emergency medications and equipment, ensures that healthcare providers can respond swiftly

and effectively to any adverse reactions, thereby minimizing risks and enhancing patient care.

Understanding the differences between allergic and irritant reactions is fundamental for accurate diagnosis and treatment. Allergic reactions are immune-mediated responses that occur when the skin comes into contact with a specific allergen, leading to sensitization and subsequent reactions upon re-exposure (47). These reactions typically manifest as erythema, oedema, and vesicles, and are characterized by a delayed onset, usually appearing 48 to 72 hours after exposure. In contrast, irritant reactions result from direct damage to the skin by substances such as acids, solvents, or detergents, and do not involve the immune system. Irritant contact dermatitis often presents with dryness, redness, and cracking of the skin, and can occur immediately after exposure. Differentiating between these types of reactions is crucial for determining the appropriate treatment and preventive measures.

The rather pronounced results of patch tests in all clinical situations are associated with prolonged exposure of patients to allergens. Firstly, this indicates the high sensitivity and specificity of this diagnostic method for determining the cause of chronic dermatitis. Contact tests, in particular, patch tests, are a highly specific method for diagnosing contact dermatitis, which proves the feasibility of their use as a routine procedure for examining patients with chronic dermatitis of unknown aetiology, occupational dermatitis, eczematous and non-eczematous dermatoses. It is important to use modern sets of allergens, adhere to standard test protocols, and consider possible limitations of the method associated with the influence of external and internal factors to improve the accuracy of diagnostics.

While patch testing is a valuable tool for diagnosing contact dermatitis, it is important to acknowledge the limitations of the studies and the method itself. One significant limitation is the potential for false-positive and false-negative results, which can be influenced by various factors such as the concentration of allergens, the duration of exposure, and individual patient characteristics. Additionally, the relevance of positive patch test results must be carefully interpreted in the context of the patient's clinical history and current symptoms. Another limitation is the inability of patch tests to identify all possible allergens, particularly those that are not included in standard test panels. Furthermore, the variability in test procedures and interpretation criteria among different healthcare providers can affect the consistency and reliability of the results. Recognizing these limitations is essential for a balanced and informed approach to diagnosis and treatment.

When evaluating the reliability and accuracy of patch tests for diagnosing contact dermatitis, it is essential to consider both external and internal factors that can significantly influence test results. External factors include the technique used during the procedure, where improper application or removal of patches can lead to false results; the concentration of the allergen, as both excessively high and low concentrations can cause misleading reactions; and environmental conditions, such as seasonality, which may affect skin sensitivity and reactivity. Internal factors encompass the patient's skin condition, as pre-existing skin diseases or damage can alter the skin's response to allergens, potentially leading to false positives or negatives. Additionally, the use of medications, particularly topical corticosteroids, antihistamines, and immunomodulators, can suppress or enhance skin reactions, thereby impacting the accuracy of the test results. Understanding and mitigating these factors are crucial for optimizing the diagnostic value of patch tests in clinical practice.

Contact tests, particularly patch tests, play a pivotal role in the diagnosis of contact dermatitis by identifying specific allergens responsible for skin reactions. Over the years, significant improvements have been made to enhance the accuracy, sensitivity, and safety of these tests. Modern patch tests utilize standardized allergen panels, hypoallergenic materials, and occlusive dressings to ensure consistent and reliable results. Advances in technology have also led to the development of more sophisticated test systems that can detect a broader range of allergens and provide more precise measurements of skin reactions. These improvements have solidified the patch test as the gold standard for diagnosing contact dermatitis, offering healthcare providers a powerful tool for accurate diagnosis

and effective management of this condition. The continuous refinement of contact testing methods underscores their relevance and practical significance in clinical practice.

A precise and timely diagnosis of contact dermatitis significantly enhances the quality of life for affected individuals. By identifying specific allergens through patch testing, patients can avoid exposure to these substances, thereby preventing recurrent allergic reactions and chronic skin inflammation. This proactive approach not only alleviates physical symptoms, such as itching, pain, and discomfort, but also reduces the psychological burden associated with chronic skin conditions. Furthermore, an accurate diagnosis enables targeted treatment strategies, including the use of appropriate topical or systemic therapies, which can lead to better disease management and improved overall well-being. Educating patients about their condition and how to manage it empowers them to take control of their health, fostering a sense of confidence and reducing anxiety related to their skin condition.

DISCUSSION

The criteria that determine the feasibility of any diagnostic method for use in clinical practice are the accuracy, safety, and relative availability of the procedure. The accuracy of contact tests is determined by sensitivity and specificity indicators, a high level of which was analyzed in the study. Conducting these tests is generally a safe procedure, but like any medical intervention, they have a certain percentage of risk. The most common side effect is slight redness and itching at the test site, which is a normal skin reaction to the allergen concentration needed to detect an allergy. Such symptoms usually disappear within a few hours or days and do not cause substantial discomfort to patients or concern doctors. However, there is a small risk of developing more severe allergic reactions, such as prolonged allergic reactions, extended skin reactions, and systemic allergic reactions (including anaphylactic shock).

The frequency of long-term allergic reactions to the patch test was determined by Mancuso (48), who showed that the reactions caused by the test, which persist for several days or even weeks after removing the patches, are characteristic of many allergens and occur at a frequency of 17.9 % of the total number of reactions, with most being caused by gold salts. The exact mechanism of long-term reactions is not clear, but there are hypotheses about the influence of constant antigenic stimulation and a defect in cell-mediated regulation of immunity. Uchida et al. (49) and Ophaug and Schwarzenberger (50) described reactions that persisted in the patch test site for several months. Analyzing the factors that affect the duration of the reaction, they identified a strong initial reaction to the allergen, the elderly age of patients, and the body's tendency to allergic reactions. In this study, there are some doubts about the accuracy of the indicator of the frequency of long-term reactions since it was determined based on a literature review, and the methodology of systematic review is considered more accurate for such an analysis.

An extended skin reaction after a patch test is a situation where an allergic reaction to an allergen applied to the skin during the test extends beyond the site of direct contact with the allergen (51). It can manifest as large, itchy spots that appear on different parts of the body, not necessarily at the test site, small or large blisters, sometimes with fluid inside, and swelling of the face, limbs, or even the entire body. Such an abnormal reaction may be associated with severe sensitization, individual characteristics of the body, and the type of allergen. Anaphylactic shock during a patch test is a rare but possible complication. In some cases, an allergen applied to the skin during a patch test can be quickly absorbed into the bloodstream through damaged or sensitive skin, which can lead to an instant systemic allergic reaction. Such a reaction can be triggered by individual hypersensitivity, when even a small amount of allergen can provoke a strong reaction in the patient. The risk of developing an anaphylactic reaction may increase due to the presence of other allergic diseases, in particular, asthma or atopic dermatitis (52). A violation of the test procedure, such as using too much allergen or damaging the skin when removing patches, may increase the risk of a systemic reaction or other complications.

Daftary et al. (53) studied the incidence of anaphylaxis during patch testing, conducting a

review of the literature describing cases of this reaction and a survey among dermatologists-experts in contact testing. In total, 3 cases of anaphylaxis were found, and according to the results of a survey of doctors – 2 cases for 201 720 tests. General calculations showed that the frequency of anaphylactic reactions during patch tests was 1 case per 100 860 tests performed. The likelihood of this reaction increased in patients with a history of anaphylaxis. The authors' calculations confirmed the fact that anaphylaxis caused by a contact test is quite rare, which should still be considered when conducting testing. In agreement with the authors, it is worth stating that, in addition to ensuring the availability of emergency medications in the medical institution for anaphylactic shock (adrenalin, antihistamines, glucocorticoids), it is worth continuing to monitor the patient for some time after the test to avoid unpredictable reactions of the body to the allergen.

An additional argument in favor of the safety of patch tests can be considered the similarity of the principle of contact tests and allergy tests before using cosmetics, which manufacturers recommend conducting at home. Both procedures have a common goal – to determine the presence of an allergic reaction to a particular substance, a similar technique – applying the substance to a small area of the skin and monitoring the reaction, and aim to minimize the risk, helping to avoid the development of a full-fledged allergic reaction, which can occur when using the substance on a large area of the skin. A substantial difference between both tests is the use of numerous allergens when performing a patch test, while cosmetics contain one or more potential allergens. Patch tests, as well as tests for cosmetics, have a high level of safety, and conducting them in a medical institution allows identifying even the slightest sensitivity to allergens and professionally responding to possible complications.

Evaluating the availability of patch testing includes the cost of the procedure, the complexity of interpretation, and the need for specialized equipment. Conducting a patch test involves certain costs, both for the patient and for the medical institution. If health insurance does not cover all costs, the cost of the procedure for some patients may be too high. Interpretation of the results of patch tests requires a highly qualified allergist, and special sets of allergens are required for their implementation. However, given that not all patients who seek medical help with dermatological problems have the need for a contact test, it is advisable to consider this method as a routine procedure in cases where: the patient has skin rashes, itching, and other symptoms for a long time, and traditional methods of treatment do not give an effect; their professional activity is associated with contact with various substances that are included in the list of potential allergens; in the presence or exacerbation of atopic dermatitis or other eczematous dermatoses in the patient as an aid in identifying additional allergens that complicate the course of the disease. In other cases, the patch test can be used as a differential diagnostic tool to distinguish contact dermatitis from other skin diseases (eczema, psoriasis).

Foti et al. (54) recommend performing patch tests in all cases of eczematous dermatoses and in exacerbation of other dermatoses, when contact allergies are suspected, caused, for example, by substances from the composition of drugs for local treatment. This is due to the fact that in many eczematous dermatoses (atopic dermatitis, discoid eczema, nummular eczema), contact allergies can be one of the provoking factors, and patch tests will help to establish an accurate diagnosis and prescribe appropriate treatment. The authors' arguments and recommendations correlate with the conclusions of this study regarding the feasibility of using patch tests as a routine procedure in certain cases. However, it is worth adding that their use is not limited only to cases of eczematous and non-eczematous contact dermatitis, but can be conducted if a skin allergy is suspected to confirm or exclude contact dermatitis. The reliability and relative safety of contact tests make them a valuable diagnostic tool for detecting contact dermatitis. Their use in the case of suspected skin allergies is an appropriate, and in some cases mandatory, measure.

In comparing the findings of this study with existing literature, it is evident that the accuracy, safety, and availability of patch tests are consistently highlighted as critical factors in determining their feasibility for routine clinical practice. The high sensitivity and specificity of patch tests align with numerous other investigations that underscore their reliability in diagnosing contact dermatitis. Studies have reported high accuracy rates but also caution about

the potential for long-term allergic reactions, which necessitate careful monitoring and patient follow-up. Safety concerns, particularly the risk of severe allergic reactions such as anaphylaxis, have been documented in the literature, albeit as rare occurrences. Research indicates that such reactions are infrequent but require preparedness and post-test observation. The similarity between clinical patch tests and at-home cosmetic allergy tests further supports the safety profile of patch tests, as both methods aim to minimize risk through controlled exposure to potential allergens.

Regarding availability, the cost and need for specialised equipment and expertise are common themes in the literature. While patch tests are advocated for use in cases of eczematous dermatoses and suspected contact allergies, the financial and logistical barriers to widespread use cannot be overlooked. Although patch tests are not universally accessible, their targeted use in specific clinical scenarios, such as chronic dermatological conditions unresponsive to conventional treatments or occupational dermatitis, can optimize their diagnostic value. Overall, the results of this study are consistent with the broader scientific community's view that patch tests are a valuable diagnostic tool in allergology and dermatology. The emphasis on their judicious use, considering both their strengths and limitations, reflects a balanced approach that maximizes their clinical utility while mitigating potential risks. Future research could further enhance the accessibility and safety of patch tests, ensuring they remain a cornerstone in the diagnosis of contact dermatitis.

CONCLUSIONS

This study has comprehensively evaluated the feasibility of using contact tests, particularly patch tests, in routine clinical practice for diagnosing contact dermatitis. The findings underscore the high sensitivity and specificity of patch tests, affirming their status as the gold standard in diagnosing contact dermatitis. Various external and internal factors, including procedural techniques, allergen concentration, skin condition, and medication use, influence the accuracy of these tests. Despite the potential for false-positive and false-negative results, patch tests remain a reliable and valuable diagnostic tool when used judiciously.

Internal factors that affect the result of the patch test include individual sensitivity, skin condition, the use of topical medications, and the presence of concomitant diseases. Depending on the genetic predisposition, age, and state of the immune system, the patient may experience increased or decreased sensitivity to a particular allergen, which will affect the result of the patch test. The presence of skin infections, inflammation, and dry skin can change its reactivity to allergens and provoke false test results. Depending on the composition of local drugs, their effect can both suppress and increase the intensity of allergic reactions, which will also affect the results of diagnosis. Skin, infectious, and systemic diseases can affect the patch test response in two main ways – by changing the skin's reactivity and masking the true allergic reaction. A comparative analysis of contact tests and laboratory tests revealed that laboratory tests cannot be considered as an alternative to contact tests, due to their limited specificity. Still, the combined application of both methods can give a more accurate result.

However, the study acknowledges several limitations. The potential for false reactions due to external factors such as seasonal variations and improper test techniques highlights the need for standardized protocols and further research to mitigate these issues. Additionally, the variability in interpreting test results, particularly in patients with darker skin tones, calls for the development of more objective assessment tools and criteria. The financial and logistical barriers to widespread use of patch tests also pose challenges, necessitating a balanced approach to their application in clinical practice. For future research, it is recommended to focus on the standardization of patch test procedures to minimize variability and enhance reliability. Further studies should explore the development of advanced materials and techniques to reduce the risk of false reactions and improve the accuracy of test results. Additionally, investigating the cost-effectiveness and accessibility of patch tests could provide insights into optimizing their use in various clinical settings.

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Glucose-dependent insulinotropic polypeptide (GIP) and resistin as biomarkers in preeclampsia

Polipéptido insulinotrópico dependiente de glucosa (GIP) y resistina como biomarcadores en la preeclampsia

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SUMMARY

Introduction: *The glucose-dependent insulinotropic polypeptide (GIP) is a hormone released in the small intestine in response to food intake. Its primary function is to regulate blood glucose homeostasis by stimulating insulin secretion. Preeclampsia (PE) is a syndrome exclusive to human pregnancy whose manifestations include high blood pressure, proteinuria, and edema. Its incidence increases in women with metabolic syndrome and insulin resistance. Pregnancy is a unique state characterized by physiological insulin resistance that resolves after delivery. The knowledge of the role of GIP in preeclampsia and gestational insulin resistance is scarce.* **Methods:** *Plasma levels of GIP, GLP-1, resistin and insulin were quantified in healthy pregnant women and those with PE, which belongs to a population of 30 Venezuelan women. Plasma samples were evaluated using multiplex bead analysis (Bio-Plex Pro Assays).* **Results:** *The results show significant increases in plasma levels of GIP, associated with increases in insulin and resistin levels in preeclamptic women compared to healthy pregnant women. There was a positive, statistically significant correlation between SBP and glycemia, proteinuria, resistin, GIP, and insulin.* **Conclusion:** *The results suggest that the increase in GIP and resistin could be associated with the development of hypertension and insulin resistance in patients with PE. Likewise, they indicate that the GIP and the parameters evaluated could constitute possible biomarkers to predict the appearance of pregnancy-induced hypertension and gestational diabetes.*

Keywords*: Preeclampsia, GIP, insulin resistance, gestational diabetes.*

RESUMEN

Introducción: *El polipéptido insulinotrópico dependiente de glucosa (GIP) es una hormona que se libera en el intestino delgado en respuesta a la ingesta de alimentos. Su función principal es regular la homeostasis de la glucosa sanguínea mediante la estimulación de la secreción de insulina. La preeclampsia (PE) es un síndrome exclusivo del embarazo humano, cuyas manifestaciones incluyen hipertensión arterial, proteinuria y edema. Su incidencia aumenta en mujeres con síndrome metabólico y resistencia a la insulina. El embarazo es un estado único que se caracteriza por una resistencia fisiológica a la insulina que se resuelve después del parto. Se conoce poco acerca del papel del GIP en la*

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preeclampsia y la resistencia a la insulina gestacional. **Métodos:** *Se cuantificaron los niveles plasmáticos de GIP, GLP-1, resistina e insulina en mujeres con embarazos normales y PE, pertenecientes a una población de 30 mujeres venezolanas. Las muestras de plasma se evaluaron mediante análisis de microesferas multiplex (Bio-Plex Pro Assays).* **Resultados:** *Los resultados muestran aumentos significativos en los niveles plasmáticos de GIP, asociados con aumentos de insulina y resistina en las mujeres preeclámpticas, en comparación con mujeres embarazadas sanas. Se observó una correlación positiva y estadísticamente significativa entre la PAS y la glucemia, la proteinuria, la resistina, el GIP y la insulina.* **Conclusión:** *Los resultados sugieren que el aumento del GIP podría estar asociado con el desarrollo de hipertensión y resistencia a la insulina en pacientes con PE. Asimismo, indican que el GIP y los parámetros evaluados podrían constituir posibles biomarcadores para predecir la aparición de hipertensión inducida por el embarazo y la diabetes gestacional.*

Palabras clave*: Preeclampsia, GIP, resistencia a la insulina, diabetes gestacional.*

INTRODUCTION

Incretin hormones, GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1), are gut peptides released after nutrient intake, boosting insulin secretion and reducing hyperglycemia. GIP is primarily produced by K cells in the duodenum and jejunum in response to carbohydrates and fats. GIP and GLP-1 are the known incretin hormones from the upper (GIP, K cells) and lower (GLP-1, L cells) gut (1). Once released, the peptide interacts with the GIP receptor (GIPR), enhancing insulin release from pancreatic beta cells, protecting these cells from apoptosis, promoting their proliferation, and decreasing glucose production in the liver. Additionally, it reduces stomach acid secretion and improves fat storage of triglycerides in adipose tissue, thereby enhancing the tissue's sensitivity to insulin (2). GIP has also been shown to promote beta cell survival and stimulate the release of GLP-1 from islet alpha cells. Endogenous GLP-1, a 32-amino acid peptide, is secreted by L-cells in the distal small intestine and colon after nutrient ingestion, primarily carbohydrates, fats, and proteins. This secretion plays a crucial role in regulating blood glucose levels and promoting overall metabolic health. Specifically, GLP-1 stimulates insulin synthesis and secretion from pancreatic beta-cells, enhances beta-cell proliferation, inhibits beta-cell apoptosis, and reduces glucagon release from pancreatic alpha-cells (3).

Incretins GIP and GLP-1 play a key role in the incretin effect, which amplifies insulin secretion after oral glucose intake compared to intravenous glucose. In Type 2 diabetes (T2DM), this effect is diminished due to reduced GIP efficacy and a lessened role of GLP-1 (4,5). GIP plays a role in regulating pancreatic β-cell mass, which is often altered in type 2 diabetes. In T2DM, the response of β-cells to GIP can be impaired, and there may be a decrease in β-cell mass (4,6).

Preeclampsia (PE) is a pregnancy-specific syndrome characterized by new-onset hypertension and proteinuria after 20 weeks of gestation, often accompanied by edema and endothelial dysfunction. It is a leading cause of maternal and fetal morbidity and mortality worldwide (7-9). Women with pre-gestational diabetes (both type 1 and type 2) have a two to four times higher risk of developing preeclampsia (PE) compared to women without diabetes (10). Additionally, the presence of diabetes itself, especially when poorly controlled, can disrupt the normal placental development and function, increasing the risk of PE. Likewise, women with metabolic syndrome are also at high risk of suffering from PE (8). It is known that both metabolic syndrome and type 2 diabetes (11) are closely linked to insulin resistance, and pregnancy itself induces insulin resistance, particularly in the later stages, around the 20th week of gestation. This means that the body's cells become less responsive to insulin, making it harder to regulate blood sugar levels (12,13). Indeed, during pregnancy, a temporary state of insulin resistance develops as a normal physiological adaptation to support fetal development. This resistance, which resolves after delivery, is characterized by the body's reduced sensitivity to insulin, ensuring that glucose is readily available for the growing fetus. While this resistance is a natural part of pregnancy, it can sometimes become excessive, leading to complications like gestational diabetes (GDM) or, potentially, PE (14). However, the

mechanisms responsible for insulin resistance and its possible association with PE have not yet been fully clarified.

During pregnancy, maternal β-cell mass undergoes a physiological and reversible expansion to compensate for increased insulin resistance, both in animals and humans (15). Given the positive actions of the two incretins on β-cell mass, which result from the reciprocal effects on β-cell proliferation and cell death, Moffet et al. (15) examined the role of GLP-1 and GIP in the adaptation of islets to pregnancy, using mice subjected to knockout (KO) of the incretin receptor. The results revealed an important role for GLP-1 in the pregnancy-induced increase in β-cell mass, mediated mainly by the local production of GLP-1 in α-cells. In contrast, GIPR KO mice demonstrated intact mechanisms of islet adaptation to pregnancy, suggesting that islet- or K-cell-derived GIP is not essential for the pregnancy-associated expansion of β-cell mass.

Little is known about the role of GIP in preeclampsia and gestational insulin resistance. However, some studies have shown that GIP levels may be related to obesity and insulin resistance (16). Obesity and insulin resistance are known risk factors for preeclampsia.

Based on the evidence, this study aimed to quantify plasma levels of GIP, GLP-1, resistin, and insulin in women with normal pregnancies and PE and assess the possible association with the development of hypertension and insulin resistance in patients with PE. Likewise, it was of interest to establish if GIP and the parameters evaluated could constitute possible biomarkers to predict the appearance of pregnancy-induced hypertension and gestational diabetes.

MATERIALS AND METHODS

Population and Samples

A controlled experimental study was conducted in healthy pregnant women and in women with preeclampsia who met the study's inclusion criteria. Patients who attended the Gynecology Service at the Hospital Clínico Universitario de Caracas (HUC), Los Chaguaramos, Libertador Municipality, Caracas, Venezuela, were selected. The participants were pregnant women who attended the HUC obstetrics service in the emergency room and resided in the city of Caracas. The population was made up of 30 pregnant women, 16 healthy pregnant women, and 14 pregnant women with preeclampsia, aged between 17 and 40 years and with gestational ages between 28 and 40 weeks or in the last trimester of pregnancy.

The following exclusion criteria were established: chronic hypertension, autoimmune diseases, type 1 and type 2 diabetes mellitus, angiopathy, mental retardation, neurological disorders, multiple pregnancy, chronic kidney disease, patients with a body mass index (BMI) equal to or greater than 30 kg/m^2, maternal or fetal infection, and congenital anomalies of the fetus. The selected patients underwent a physical examination, and blood pressure measurements were taken. Biological samples were also collected.

All volunteers signed and dated the informed consent form in advance (before collecting the biological samples), having carefully read it. A trained staff member explained the study to them orally and in writing in a simple manner, outlining what the study entailed and what analyses would be conducted with their biological samples. Likewise, the participants clarified their doubts with the researcher in charge.

All procedures were submitted to the Bioethics Committee of the University Hospital of Caracas, Caracas, Venezuela, and complied with the Declaration of Helsinki for experimental studies involving human beings (1975, revised in 1983).

Biological samples

After fasting for 8-12 hours and without the usual prior diet, blood samples were obtained from the arm antecubital vein (left or right) by direct venipuncture in the antecubital region with multiple needles (Venojet®), using tubes with coagulation accelerator (Vacutainer®). Immediately, they were centrifuged at 3 000 rpm for 15 minutes. Plasma was separated, and aliquots were stored at -80°C until further analysis.

Blood Pressure (BP) Determination

In the supine position, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured using a mercury sphygmomanometer placed on the left arm.

Biochemical Methods

Quantification of urinary excretion of total proteins and glycemia

The colorimetric method, based on the Biuret method, was used to determine the protein concentration present in the urine through the formation of a colored chelate, resulting from a reaction between cupric ions and peptide bonds (17). The method is based on the co-precipitation of total proteins from the sample in the presence of the Ponceau red reagent and the addition of trichloroacetic acid. Briefly, the urine samples were centrifuged to eliminate tubular cells and oxalates. To 50 µL of urine, 500 µL of Ponceau red reagent (40 g/L) and trichloroacetic acid (300 g/L) were added. It was then centrifuged at 12 000 rpm for 10 minutes. The precipitate formed was resuspended by adding 1.0 mL of sodium hydroxide (8 g/L), and the concentration of urinary proteins was quantified spectrophotometrically at 560 nm. The urine protein concentration was calculated using a standard curve of bovine serum albumin at concentrations ranging from 0.125 to 8 mg/mL. The results were expressed as milligrams of protein per 100 grams of body weight.

Glycemic values were determined by enzymatic methods using the commercial kit (Stanbio). The reference values for blood glucose were 70-105 mg/dL.

Plasma adipokines quantification

All plasma samples were evaluated in duplicate using multiplex microsphere analysis (Bio-Plex Pro Assays Cytokine, Chemokine, and Growth Factors, Life Science Group, BIORAD). This technique allowed the simultaneous study of circulating concentrations of GIP, GLP-1, RANTES, Insulin, and Resistin.

Statistical analysis

The data was expressed as the mean ± standard error of the mean (S.E.M.). The data distribution was evaluated using the Shapiro-Wilk, Kolmogorov-Smirnov, and Jarque-Bera normality tests. Student's t-test and analysis of variance (ANOVA) with post-hoc analysis were used to compare the experimental groups in this study. Correlations between the variables were analyzed using the Spearman correlation test. The value of $p<0.05$ was considered significant.

RESULTS

Patient characteristics

Table 1 shows the clinical characteristics of patients. No statistically significant differences were found in age, weight, height, gestational age, or body mass index (BMI) between the two groups studied. On the contrary, significant increases in glycemia and proteinuria values were observed when comparing the two experimental groups. Similarly, SBP and DBP values were significantly higher in women with preeclampsia when compared to healthy pregnant women (Figure 1). Indeed, women with preeclampsia have been classified by an elevation in blood pressure of 20 mmHg or more, with systolic blood pressure values greater than 140 mmHg and diastolic blood pressure values greater than 78 mmHg, and a mean arterial pressure of 105 mmHg or more.

Plasma levels of adipokines and chemokines in healthy pregnant women and women with preeclampsia (pg/mL)

As shown in Table 2, under our experimental conditions, the plasma levels of GIP, resistin, and insulin increased significantly in women with preeclampsia compared to healthy pregnant women. GPL-1 peptide showed a tendency to increase, but this was not significant. In contrast, a significant reduction in plasma levels of RANTES was observed in women with preeclampsia compared to healthy controls.

Table 1. Clinical characteristics of pregnant controls and patients with preeclampsia.

Parameter	Healthy Pregnant woman	Preeclamptic woman	P
N=30	N= 16	N= 14	
Age (years)	26.47 ± 0.92	28.62 ± 2.70	NS
Weight (kg)	71.80 ± 2.97	74.24 ± 2.46	NS
Height (cm)	1.60 ± 0.02	1.59 ± 0.01	NS
BMI (kg/m^2)	28,4 ± 0,91	29.33± 0.99	NS
Gestational age (weeks)	35.5 ± 1.08 (28 - 40)	35.38 ± 0.99(29 - 41)	NS
Glycemia (mg/dL)	73.50 ± 2.46	86.23 ± 5.2*	< 0.05
Proteinuria (mg/dL)	0	4 ± 2.4 ***	< 0.0001

NS: not significative *p<0.05; ***p<0.0001 compared with control

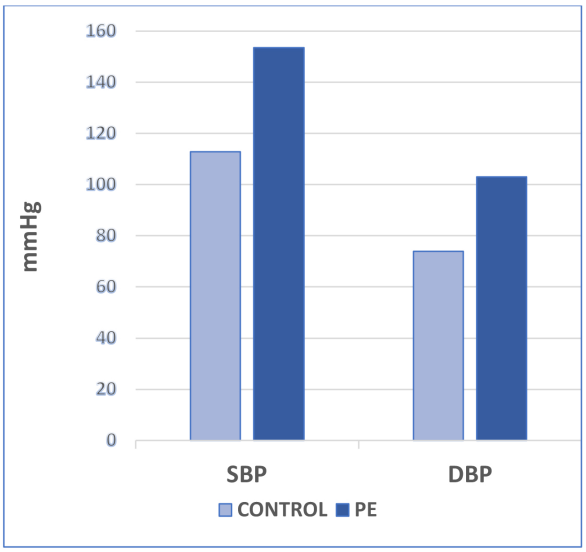


Figure 1. Blood pressure values in healthy pregnant women (CONTROL) compared to women with preeclampsia (PE). SBP (mmHg): 112.90 ± 2.26 vs. 153.58 ± 2.74 (p<0.0001). DBP (mmHg): 74.20 ± 1.81 vs. 103.16 ± 3.61(p<0.0001).

Correlation between SBP and the evaluated variables

When establishing the possible correlation between the SBP values and the evaluated variables, using the Spearman correlation test in all subjects, it was found that there is a positive, statistically significant correlation between SBP vs. proteinuria (r = 0.8192; p< 0.0001), SBP vs. glycemia (r = 0.415; p<0.0281), and SBP vs. GIP (r = 0.3755; p< 0.0489). Likewise, it is shown that SBP was positively and significantly correlated with resistin (r = 0.4410; p < 0.0166) and insulin (r = 0.4787; p <0.01). On the contrary, SBP showed a statistically significant negative correlation with RANTES (Table 3).

Table 2. Plasma levels of cytokines and chemokines in healthy pregnant women and in women with preeclampsia (pg/mL).

Parameter	Healthy pregnant women	Preeclamptic women	P
N=30	N= 16	N=14	
RANTES	115.1 ± 15.4	76.62 ± 12.48*	0.04
INSULIN	281.0 ± 138	689.49 ± 174*	0.04
RESISTIN	6 989.5 ± 1 510.51	10 304.61 ± 1 404.25*	0.04
GIP	71.9 ± 45	255.04 ± 71	0.02
GPL-1	2.6 ± 0.2	4.58 ± 1.74	NS

*p<0.05 compared with the healthy pregnant woman.

Table 3. Analysis of the Spearman correlation between SBP versus the variables evaluated in healthy pregnant women and those with preeclampsia.

	r	P
SBP vs. GLYCEMIA	0.4150	0.0281*
SBP vs. PROTEINURIA	0.8192	0.0001*
SBP vs. RESISTIN	0.4410	0.0166*
SBP vs. INSULIN	0.4787	0.0100*
SBP vs. RANTES	-0.4327	0.0215*
SBP vs. GIP	0.3755	0.0489*

DISCUSSION

The present study demonstrates the dysregulation of glucose-dependent insulinotropic polypeptide (GIP) in pregnant women with PE, whose condition was confirmed by the increase in blood pressure and proteinuria. Additionally, pregnant women with PE exhibited significant increases in plasma insulin and glucose levels. Furthermore, our findings demonstrate that the systolic blood pressure values of the pregnant patient population were positively correlated with plasma values of GIP, resistin, insulin, glycemia and with proteinuria, suggesting an association of PE with maternal insulin resistance and gestational diabetes mellitus (GDM) in the last trimester of pregnancy. Likewise, a significant negative correlation was observed between SBP and RANTES.

Preeclampsia, a common comorbidity of GDM, is characterized by endothelial dysfunction and systemic inflammation, often exacerbated by dysregulated immune signaling (16).

Glucose-dependent insulinotropic polypeptide plays a crucial role in pregnancy-related conditions such as preeclampsia and gestational diabetes mellitus (GDM). Impaired incretin response, characterized by decreased glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) activity, results in suboptimal postprandial insulin release. During pregnancy, as insulin resistance intensifies due to placental hormones (human placental lactogen, estrogen, and progesterone), the inability of β-cells to augment insulin secretion sufficiently leads to GDM (16). Lower GIP levels are inversely associated with an increased risk of GDM.

GIP has been shown to stimulate the secretion of pancreatic polypeptide, which is implicated in regulating gut motility, appetite, and glycemia. Furthermore, glycemic control, reflected by HbA1c levels, is a significant factor in the development of preeclampsia among pregnant women with diabetes, emphasizing the importance of managing glucose levels to potentially reduce the risk of preeclampsia. GIP, along with glucagon, GLP-1, VIP, and somatoliberin (also known as GHRH or growth hormone-releasing hormone), are all members of the secretin-glucagon superfamily of peptide hormones. This superfamily is characterized by its structural similarity and its ability to activate related G-protein-coupled receptors (17,18). GIP exerts its effects through a single described receptor, the GIP-R, which has 40 % and 44 % homology with the GLP-1 and glucagon receptors, respectively (18,19).

Among the effects of GIP, we must highlight its incretin activity (20,21). During fasting, GIP concentrations remain low. The ingestion of carbohydrates or fat triggers the release of GIP, increasing its plasma concentration, which in turn favors the secretion of GLP-1 from intestinal L cells. In this way, both hormones promote insulin secretion from the β-cells of the islets of Langerhans, a process known as the incretin mechanism. However, it has been demonstrated that the insulinotropic effect of GIP administration in patients with type 2 diabetes mellitus is less efficient than in healthy individuals. In this case, postprandial insulin secretion is insufficient to normalize blood glucose levels (22). Although GIP values are elevated, it appears that a reduction in sensitivity occurs in diabetic individuals due to the deficient expression of the receptor in pancreatic β-cells (23). In addition to stimulating insulin secretion, GIP exerts antiapoptotic effects and induces the growth of β-cells in the pancreas. It does this by influencing the expression of certain genes and signaling pathways that regulate cell survival. For example, GIP can increase the production of anti-apoptotic proteins, such as Bcl-2, while decreasing the production of pro-apoptotic proteins, like Bax, thereby helping to maintain a healthy beta cell population (24).

Studies on the influence of GIP on food intake are scarce and somewhat controversial. Verdich et al. (25) highlight the role of GIP in regulating appetite in humans. However, in another study, it was observed that glucose and fructose are equally effective in suppressing intake despite the large differences observed in GIP secretion in response to the administration of each saccharide (26). It has been described that GIP infusion in healthy individuals of normal weight can reduce energy expenditure and the feeling of hunger; however, this does not occur in patients with type 2 diabetes mellitus (27). In effect, whereas GLP-1 also inhibits appetite and food intake and improves glucose regulation in patients with type 2 diabetes (T2DM), GIP seems to be devoid of these activities, although the two hormones, as well as their receptors, are highly related. Numerous studies have suggested that GIP may contribute to the development of obesity (28).

Regarding the imbalance in glucose homeostasis, GIP is known to increase the secretion of resistin, a pro-inflammatory cytokine and one of the primary factors contributing to the development of insulin resistance. Studies in GIP knockout mice demonstrated a decrease in the secretion of this cytokine associated with a reduction in the development of insulin resistance after consumption of a high-fat diet (29). Resistin is a hormone secreted by monocytes, macrophages and adipocytes. Animal studies have shown that resistin induces insulin resistance and reduces glucose tolerance by inhibiting glucose uptake in the liver (30). However, the role of resistin in the physiology of pregnancy and pregnancy complications has not yet been clearly established. The present study demonstrated that increased plasma GIP levels were associated with significant increases in resistin in patients with PE compared to healthy pregnant women. Similar results were reported by Song et al. (31) and Seol et al. (32), who also demonstrated that maternal plasma resistin levels are significantly elevated in pregnant women with PE compared to normal pregnant women. However, while resistin levels are known to be elevated in PE, and GIP levels are also elevated in obesity and diabetes, the relationship between the two in PE remains poorly established. Studies indicate that resistin is elevated in PE, potentially due to impaired renal function. However, GIP's role in PE is less clear and may be more associated with

obesity and diabetes, which can be risk factors for PE (33).

Elevated GIP levels have been linked to increased mortality from cardiovascular disease in some studies. Evidence suggests that GIP, in addition to its role in regulating insulin secretion in response to glucose, also appears to be involved in the pathogenesis of cardiovascular disease, potentially influencing blood pressure and vasodilation through nitric oxide secretion, as well as vascular leukocyte adhesion and inflammation through endothelin-1 expression and secretion (34). Chronotropic and blood pressure-lowering effects of GIP have been described. In a randomized, placebo-controlled crossover study involving 10 participants with type 1 diabetes, the effect of GIP on heart rate, systolic and diastolic blood pressure was examined during hyperglycemia (plasma glucose level of 10 mmol/L) and hypoglycemia (plasma glucose levels of 3-6 mmol/L). GIP infusion during hyperglycemia increased heart rate and SBP and decreased DBP. During hypoglycemia, GIP increases heart rate and decreases DBP without altering SBP. These data suggest that the effect of GIP on heart rate is not related to its insulinotropic action since patients with type 1 diabetes lack functional residual β-cells (34). Although the interpretation of the results should be taken cautiously, the evidence suggests a possible role for GIP in regulating blood pressure. These findings would align with the results obtained in the present study, which shows an association between increased blood pressure and GIP levels in women with PE. Thus, GIP plays a role in insulin secretion and glucose metabolism, and its levels can be altered in conditions like PE, which is characterized by hypertension and other metabolic disturbances. Studies suggest that insulin resistance, a feature of PE, may be linked to higher GIP levels, and that GIP could contribute to the development of hypertension and other complications associated with PE.

PE is considered a systemic inflammatory disease, and monocyte activation is a characteristic feature of an inflammatory state. It has been demonstrated that increases in the maternal circulation of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) in PE contribute to insulin resistance and vascular dysfunction, further complicating glucose metabolism (12,16,35-40). Szarka et al. (41) demonstrated that the circulating levels of proinflammatory cytokines IL-6 and TNF-α, as well as the chemokines IL-8, IP-10, and MCP-1, and the adhesion molecules ICAM-1 and VCAM-1, are increased in PE compared to normal pregnant women, resulting in a proinflammatory systemic environment. Therefore, it can be inferred that the increased levels of the pro-inflammatory cytokine resistin observed in the present study in PE may be associated with the activation of monocytes due to a systemic inflammatory response. In addition, Hentschke et al. (42) demonstrated that RANTES expression in maternal plasma and placental tissues is higher in women with established preeclampsia compared to women with a pregnancy compatible with a healthy outcome. RANTES (Regulated upon Activation, Normal T-cell Expressed, and Secreted) // CCL5 is a chemokine that participates in diseases that cause chronic inflammation by recruiting inflammatory cells, such as leukocytes, endothelial activation, and vascular inflammation—all hallmarks of preeclampsia. It is secreted by various types of cells, including endothelial cells, smooth muscle cells, macrophages, platelets, and activated T cells. These results confirm the hypothesis that the physiology of PE is associated with an increase in the normal gestational inflammatory process. However, the results related to inflammation markers in the present study are contradictory, as decreased plasma levels of the pro-inflammatory cytokine RANTES are reported under our experimental conditions. In this regard, Taylor et al. (43) reported similar results in the levels of RANTES (In normotensive women *vs*. PE, in pg/mL, RANTES: 54.3 v*s*. 48.7). In a Venezuelan study, Reyna-Villasmil et al. (44) showed that in preeclamptic patients' RANTES concentrations were significantly higher than in healthy normotensive pregnant women, with average concentrations of 2484.6 ± 113.7 pg/mL, while healthy controls had 2002.8 ± 62.6 pg/mL, respectively. This inconsistency in RANTES results may suggest that women with PE present a unique immunological profile compared to normotensive women. However, we cannot determine whether these inflammatory markers are involved in the pathogenesis of preeclampsia and/or serve as markers of subclinical disease.

In conclusion, a circulating increase in the incretin GIP has been reported in a population of Venezuelan pregnant women at 28-40 weeks of gestation, which may play a role in the development of insulin resistance in patients with PE. These changes in circulating GIP levels and traditional risk factors will help determine the coexistence of PE and GDM. GIP plays a crucial role in pregnancy-related conditions such as preeclampsia and gestational diabetes mellitus. GIP levels are inversely associated with the risk of developing GDM, with lower GIP levels correlating with a higher likelihood of developing GDM. Overall, understanding the role of GIP in these conditions highlights its potential as a biomarker and therapeutic target in managing pregnancy-related complications, such as insulin sensitivity and resistance in PE and/or GDM. However, large-scale and prospective studies are required to assess whether the association between increased blood pressure, proteinuria, increased GIP, and other cytokines and chemokines constitutes early markers that predict the development of GDM in patients with PE.

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ARTÍCULO ORIGINAL

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Desempleo y funcionalidad familiar en hogares escolares de Cartagena de Indias, Colombia

Unemployment and Family Functionality in School Homes in Cartagena de Indias, Colombia

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RESUMEN

Introducción: *El desempleo afecta la estabilidad emocional y funcionalidad de los hogares, especialmente en contextos vulnerables.* **Objetivo:** *Evaluar el impacto del desempleo en la funcionalidad familiar de estudiantes de la Institución Educativa Manuela Beltrán, Sede Hijos del Chofer.* **Metodología:** *Estudio descriptivo, transversal y correlacional aplicado a 141 familias. Se utilizó un cuestionario estructurado con variables sociodemográficas y la prueba APGAR familiar. Se analizaron asociaciones con pruebas de Chi-Cuadrado, t de Student y correlaciones bivariadas, con nivel de significancia p<0,05.* **Resultados:** *Se encontró una prevalencia de desempleo del 68,09 %, con una funcionalidad familiar normal en el 46,1 % y disfunción leve en el 34,04 %. El desempleo se asoció significativamente con la ocupación actual (p=0,002), pero no con el puntaje APGAR (p=0,528). El nivel educativo mostró relación positiva con mejor funcionalidad.* **Conclusión:** *El desempleo influye de manera indirecta en la funcionalidad familiar, mediado por variables como el nivel educativo, número de dependientes y tamaño del hogar.*

Palabras clave: *Desempleo, funcionalidad familiar, soporte social, bienestar psicológico.*

SUMMARY

Introduction: *Unemployment can significantly impact emotional stability and family functioning, particularly in vulnerable contexts.* **Objective:** *To assess the impact of unemployment on family functionality among students of the Manuela Beltrán Educational Institution, Hijos del Chofer campus.* **Methodology:** *A descriptive, cross-sectional, and correlational study was conducted with 141 families. A structured survey was used, including sociodemographic data and the Family APGAR instrument. Associations were analyzed using Chi-square tests, Student's t-test, and bivariate correlations (p<0.05).* **Results:** *Unemployment prevalence was 68.09 %, with 46.1 % showing normal family function and 34.04 % mild dysfunction. A significant association was found between unemployment and current occupation (p = 0.002), although not with APGAR score (p = 0.528). Higher education level correlated with better functionality.* **Conclusion:** *Unemployment indirectly*

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affects family functionality, moderated by educational level, number of dependents, and household size.

Keywords: *Unemployment, family functionality, social support, psychological well-being.*

INTRODUCCIÓN

La funcionalidad familiar es un constructo que hace referencia a la capacidad del grupo familiar para enfrentar los desafíos del entorno, mantener relaciones saludables, resolver conflictos y adaptarse a situaciones adversas (1). Esta funcionalidad depende de múltiples factores, entre ellos, el soporte social, la estabilidad emocional de sus miembros y las condiciones socioeconómicas en las que se desenvuelven (2).

El desempleo, entendido como la carencia involuntaria de trabajo, se constituye como una de las principales fuentes de estrés familiar, especialmente en contextos donde los ingresos del hogar dependen de un único proveedor (3). Según datos del Departamento Administrativo Nacional de Estadística (DANE), la tasa de desempleo en Colombia fue de 10,2 % en 2023, siendo las mujeres y los jóvenes los grupos más afectados (4). Esta situación no solo limita el acceso a recursos básicos, sino que también altera la estructura interna del hogar, afectando la distribución de responsabilidades y generando tensión en las relaciones familiares (5).

Numerosos estudios han evidenciado que el desempleo está asociado con disfunciones familiares, deterioro del bienestar psicológico, aumento del conflicto y disminución del afecto entre los miembros del hogar (6,7). A esto se suma la influencia del nivel educativo, considerado un factor protector frente a situaciones de vulnerabilidad, ya que las familias con mayor escolaridad tienden a tener mejores habilidades de afrontamiento y adaptación (8). Desde el enfoque ecológico de Bronfenbrenner, el individuo y su familia interactúan con un sistema complejo de influencias sociales, donde el contexto económico es determinante en la salud y funcionamiento familiar (9).

Particularmente en América Latina, la Organización Internacional del Trabajo ha alertado sobre el impacto del desempleo en el deterioro de la calidad de vida y el aumento de la desigualdad (10). En comunidades de bajos recursos, la disfunción familiar puede ser más pronunciada, debido a la falta de soporte institucional y redes de apoyo (11,12).

La funcionalidad familiar puede medirse a través de instrumentos como el APGAR familiar, creado por Smilkstein, el cual evalúa cinco dimensiones: adaptabilidad, participación, crecimiento, afecto y resolución (3). Este instrumento ha sido ampliamente validado en distintos contextos y es útil para identificar niveles de disfunción leve, moderada o severa.

El objetivo de este estudio fue analizar la influencia directa e indirecta del desempleo en la funcionalidad familiar, considerando su interacción con variables socioeconómicas, educativas y estructurales del hogar, así como los niveles de adaptación, estrés y resolución de conflictos.

METODOLOGÍA

Se realizó un estudio de enfoque cuantitativo, transversal, descriptivo y correlacional, cuyo propósito fue explorar las relaciones entre la condición de desempleo y la funcionalidad familiar en un contexto educativo específico. No se pretendió establecer inferencias causales entre el desempleo y la funcionalidad familiar.

La población objetivo estuvo constituida por padres, madres o acudientes de estudiantes matriculados en la Institución Educativa Manuela Beltrán, Sede Hijos del Chofer, ubicada en Cartagena de Indias, Colombia. Se trabajó con una muestra intencional no probabilística de 141 participantes, seleccionados por conveniencia, teniendo en cuenta su disponibilidad para responder el instrumento y su relación directa con los estudiantes beneficiarios. Los criterios de inclusión fueron: ser padre/madre o cuidador principal del estudiante, residir en el mismo hogar, y aceptar participar de manera voluntaria en el estudio. Se excluyeron aquellos participantes que no completaron completamente el cuestionario o presentaron inconsistencias en sus respuestas.

Se diseñó y aplicó un cuestionario estructurado, dividido en cuatro secciones:

1) Datos sociodemográficos del respondiente: Edad; género; estado civil, nivel educativo; ocupación actual; condición de cabeza de hogar; número de personas en el hogar; número de dependientes económicos; entre otros.
2) Condición laboral del hogar: Situación de empleo/desempleo actual, fuente principal de ingresos, ingreso y gasto mensual, número de personas con empleo en el hogar.
3) Percepción del impacto del desempleo: Nivel de estrés, distribución de responsabilidades, calidad del tiempo compartido, y relaciones familiares.
4) Funcionalidad familiar: Medida mediante la prueba de APGAR familiar, instrumento desarrollado por Smilkstein (3) que evalúa cinco dimensiones clave: adaptación, participación, afecto, recursos y resolución. Cada ítem es valorado en una escala de 0 a 4, sumando una puntuación total de 0 a 20 puntos. Este instrumento ha demostrado ser confiable en contextos latinoamericanos con poblaciones en situación de vulnerabilidad (1,3,11).

La validación de contenido del instrumento fue realizada por tres expertos del área de salud pública y trabajo social, y se aplicó una prueba piloto a 10 personas fuera de la muestra final, para garantizar la claridad semántica y comprensión del cuestionario. La aplicación del cuestionario se llevó a cabo de manera presencial entre octubre y noviembre de 2024, con el apoyo logístico de la institución educativa. Los encuestadores fueron previamente capacitados, y se garantizó un entorno privado y seguro para la recolección de la información, evitando la influencia de terceros y asegurando la confidencialidad del proceso.

Los datos fueron codificados y analizados utilizando el software SPSS® (versión 26.0). En primer lugar, se realizó un análisis descriptivo de frecuencias absolutas y relativas, medias, medianas y desviaciones estándar, según correspondiera a la naturaleza de cada variable.

Para establecer relaciones entre variables, se emplearon: la Prueba de Chi-Cuadrado (χ^2) para evaluar asociaciones entre variables categóricas como condición de desempleo, nivel educativo, y estrato socioeconómico; la Prueba t de *Student* para comparar medias del puntaje APGAR entre grupos con y sin desempleo en el hogar; y las Correlaciones bivariadas (Pearson): para examinar la relación entre puntaje APGAR y variables numéricas como número de personas en el hogar, número de dependientes, y edad del encuestado. Se consideró un nivel de significancia estadística de $p<0,05$.

Esta investigación se enmarca en los principios éticos de la Resolución 8430 de 1993 del Ministerio de Salud de Colombia, clasificada como una investigación sin riesgo. Todos los participantes firmaron un consentimiento informado después de haber sido informados sobre los objetivos del estudio, el carácter voluntario de su participación, donde la confidencialidad fue garantizada mediante la anonimización de los datos y el almacenamiento seguro de los cuestionarios en custodia del grupo investigador, conforme a los lineamientos éticos de la institución considerados por el Comité de Ética de la Corporación Universitaria Rafael Núñez, como parte del proceso de garantía ética y científica del programa de Medicina.

RESULTADOS

El Cuadro 1 muestra que del total de participantes (n=141), se observó que la mayoría de las familias pertenecen al estrato socioeconómico 2 (71,6 %), lo que indica una condición económica baja con acceso limitado a recursos. En cuanto al estado civil, predominan las personas en unión libre (36,9 %) y solteros (33,3 %), lo cual puede asociarse a estructuras familiares no convencionales, con posible implicación en la estabilidad del hogar. La muestra fue mayoritariamente femenina (85,1 %), lo que evidencia una alta representación de mujeres como principales cuidadoras o referentes familiares, en línea con el papel tradicional de género en contextos vulnerables. En cuanto al nivel educativo, sobresale la formación técnica o tecnológica (37,6 %) y la secundaria completa (32,6 %), reflejando un nivel intermedio de escolaridad que limita el acceso a empleos estables y bien remunerados.

Cuadro 1. Distribución de Variables Socioeconómicas y Demográficas de las Familias de los Estudiantes de la Institución Educativa Manuela Beltrán, Sede Hijos del Chofer.

Variable	Categoría	Frecuencia	Porcentaje
Estado Civil	Unión Libre	52	36,88
	Soltero (a)	47	33,33
	Casado (a)	24	17,02
	Separado (a) / Divorciado (a)	8	5,67
	Viudo (a)	6	4,26
	Unión Libre	4	2,84
Género	Femenino	120	85,11
	Masculino	21	14,89
Nivel Educativo	Técnico/Tecnólogo	53	37,59
	Secundaria Completa	46	32,62
	Secundaria Incompleta	22	15,6
	Primaria Incompleta	7	4,96
	Universitario	6	4,26
	Primaria Completa	3	2,13
	Secundaria Completa	2	1,42
	Posgrado	1	0,71
	Primaria Completa	1	0,71
Ocupación Actual	Ama De Casa	45	31,91
	Sin Ocupación	40	28,37
	Empleado	35	24,82
	Independiente	16	11,35
	Estudiante	5	3,55
Cabeza De Hogar	Si	100	70,92
	No	41	29,08
Estrato Socioeconómico	2	101	71,63
	1	34	24,11
	3	6	4,26
	4	61	43,26
	5	30	21,28
Número De Personas En La Vivienda	3	18	12,77
	6	17	12,06
	7	7	4,96
	2	3	2,13
	8	2	1,42
	9	1	0,71
	12	1	0,71
	13	1	0,71
Número De Personas Dependientes Económicamente De Usted	2	39	27,66
	3	38	26,95
	0	31	21,99
	1	21	14,89
	5	5	3,55
	4	3	2,13
	6	3	2,13
	9	1	0,71
¿Cuántas Personas En Su Hogar Tienen Empleo Actualmente?	1	62	43,97
	2	42	29,79
	0	18	12,77
	4	18	12,77
	3	1	0,71
¿Se Encuentra Usted, O Algún Miembro De Su Hogar, ¿Desempleado En Este Momento?	Si	96	68,09
	No	45	31,91
La Persona Desempleada En Su Hogar, ¿Qué Parentesco Tiene Con Usted?	Padre/Madre	39	27,66
	Otro	33	23,4
	Hijo (a)	25	17,73
	Cónyuge/Pareja	24	17,02
	Hermano (a)	20	14,18
¿La Persona Desempleada Es Actualmente La Cabeza Del Hogar?	No	80	56,74
	Si	61	43,26
¿Cuál Es La Fuente Principal De Ingreso En Su Hogar Actualmente?	Trabajos Esporádicos	63	44,68
	Ingresos De Otro Miembro De La Familia	44	31,21
	Otro	24	17,02
	Ahorros	6	4,26
	Ingresos De Otro Miembro De La Familia	4	2,84

Continúa en pág. 795…

…continuación del Cuadro 1. Distribución de Variables Socioeconómicas y Demográficas de las Familias de los Estudiantes de la Institución Educativa Manuela Beltrán, Sede Hijos del Chofer.

Variable	Categoría	Frecuencia	Porcentaje
¿Cuál Es El Gasto Mensual Promedio De Su Hogar?	Mas De $672,000	95	67,38
	De $576,000 A $672,000	27	19,15
	De $480,000 A $576,000	12	8,51
	Menos De $480,000	7	4,96%
¿Cuál Es El Ingreso Mensual Total De Su Hogar?	850000	50	35,46
	1300000	40	28,37
	1500000	29	20,57
	500000	22	15,6
¿Cuántas Personas Dependen Económicamente del Jefe (a) Del Hogar?	4	101	71,63
	2	25	17,73
	0	7	4,96
	1	7	4,96
	3	1	0,71
¿Cómo Considera Que El Desempleo Ha Afectado Las Relaciones Familiares En Su Hogar?	No Ha Tenido Ningún Efecto	48	34,04
	No Estoy Seguro (a)	39	27,66
	Ha Empeorado Las Relaciones	43	30,49
	Ha Mejorado Las Relaciones	11	7,8
	No, Se Mantienen Igual	57	40,43
¿Ha Notado Algún Cambio En La Distribución De Las Responsabilidades Familiares Debido Al Desempleo?	Si, Han Aumentado Para Algunos Miembros	35	24,82
	No Estoy Seguro (a)	25	17,73
	Si, Han Disminuido Para Algunos Miembros	24	17,02
¿Cómo Calificaría El Nivel De Estrés En Su Hogar Debido A La Situación De Desempleo?	Moderado	67	47,52
	Alto	32	22,7
	Bajo	21	14,89
	Muy Alto	21	14,9
¿Con Qué Frecuencia Comparte Tiempo De Calidad Con Su Familia?	Todos Los Días De La Semana	88	62,41
	1 a 3 Días Por Semana	38	26,95
	4 a 6 Días Por Semana	12	8,51
	Nunca	3	2,13
Adaptación: Cuando Las Cosas Se Ponen Difíciles, ¿Puede Su Familia Adaptarse A Los Cambios?	Casi Siempre	50	35,46
	Siempre	48	34,05
	A Veces	38	26,95
	Raramente	4	2,84
	Nunca	1	0,71
Participación: ¿Cree Que Su Familia Puede Hablar Sobre Sus Problemas Y Compartir Sus Decisiones?	Siempre	60	42,55
	A Veces	37	26,24
	Casi Siempre	29	20,57
	Raramente	11	7,8
	Nunca	4	2,84
Afecto: ¿Se Sienten Queridos Y Cuidados Por Los Miembros De Su Familia?	Siempre	97	68,79
	Casi Siempre	24	17,02
	A Veces	14	9,93
	Raramente	5	3,55
	Nunca	1	0,71
Recursos: ¿Cree Que Su Familia Es Capaz De Utilizar Sus Recursos Para Superar Las Dificultades?	Siempre	69	48,94
	Casi Siempre	35	24,82
	A Veces	29	20,57
	Raramente	6	4,26
	Nunca	2	1,42
Resolución: ¿Puede Su Familia Resolver Sus Problemas De Manera Efectiva Cuando Se Presentan?	Siempre	62	43,97
	Casi Siempre	44	31,21
	A Veces	30	21,28
	Raramente	4	2,84
	Nunca	1	0,71

Fuente: autores.

En términos de ocupación, el 31,9 % se identifica como ama de casa y el 28,4 % está sin ocupación formal, lo que evidencia una alta dependencia económica y una limitada autonomía laboral en muchos hogares. Aun así, el 70,9 % de los encuestados se reconoce como cabeza de hogar, lo que implica una importante carga de responsabilidad en contextos de precariedad. En promedio, los hogares están conformados por 4 a 5 personas, con una media de 2 a 3 dependientes económicos por núcleo familiar. El 43,9 % reporta que solo una persona trabaja en el hogar, mientras que un preocupante 12,8 % afirma que ningún miembro tiene empleo. La prevalencia general de desempleo fue del 68,1 %, siendo el padre/madre o pareja la figura desempleada en la mayoría de los casos.

Los ingresos mensuales familiares se concentran mayoritariamente entre $850.000 y $1.300.000 COP, lo cual, sumado a los gastos superiores a $672.000 mensuales (67,3 %), refleja una alta presión financiera en los hogares. La fuente principal de ingreso en un 44,7 % de los casos corresponde a trabajos esporádicos, situación que incrementa la vulnerabilidad económica. En relación con la percepción del impacto del desempleo, un 30,5 % considera que ha empeorado las relaciones familiares, mientras que un 27,6 % no está seguro de su efecto. El estrés familiar es percibido como moderado (47,5 %), alto (22,7 %) o muy alto (14,9 %), lo cual indica un impacto emocional significativo. Respecto a la distribución de responsabilidades, el 24,8 % percibe un aumento en las cargas para algunos miembros del hogar.

A pesar de este panorama, el 62,4 % reporta compartir tiempo de calidad diario en familia, y los resultados del instrumento APGAR Familiar reflejan que el 66,7 % de las familias logra adaptarse a los cambios, el 75,2 % resuelve sus problemas de forma efectiva, y el 89,4 % se siente querido y apoyado dentro del hogar. Esto sugiere la existencia de mecanismos de resiliencia y cohesión que permiten sobrellevar, en parte, los efectos adversos del desempleo.

La prevalencia del desempleo entre los padres de los estudiantes de la Institución Educativa Manuela Beltrán, Sede Hijos del Chofer, es de aproximadamente 68,09 %. Esto indica que una gran mayoría de los hogares enfrenta la situación de desempleo en al menos uno de sus miembros, lo cual podría impactar significativamente la funcionalidad y dinámica familiar.

El Cuadro 2 muestra que, para el estrato socioeconómico, encontramos un valor de Chi-Cuadrado de 5,93 con 2 grados de libertad y p=0,0517. Este resultado está muy cerca del nivel de significancia estándar de 0,05, lo que sugiere que el estrato podría tener una cierta influencia sobre el desempleo. Sin embargo, esta relación no es lo suficientemente sólida para ser considerada concluyente en este análisis. Podría ser que el estrato afecte en alguna medida la situación laboral, aunque no de manera contundente en esta muestra. En cuanto a la condición de cabeza de hogar, los valores (Chi-Cuadrado = 0,027, Grados de libertad = 1, p = 0,8689) muestran que no existe una relación significativa entre ser cabeza de hogar y estar desempleado. En este caso, las variaciones entre las personas que son cabezas de hogar y el desempleo parecen ser aleatorias, sin una conexión discernible. Esto sugiere que, en este contexto, el desempleo afecta a las familias independientemente de la estructura de responsabilidad en el hogar.

Al observar la ocupación actual, el resultado (Chi-Cuadrado = 16,37, Grados de libertad = 4, p = 0,0026) muestra una relación significativa entre ocupación y desempleo. Este hallazgo indica que ciertas ocupaciones en la muestra son más susceptibles al desempleo. Esto refleja una realidad en la que algunos sectores laborales tienen mayor vulnerabilidad económica, lo que aumenta la probabilidad de que las personas en esas ocupaciones enfrenten períodos de desempleo. Finalmente, los puntajes APGAR, medidos por una prueba t (t = -0,63, p = 0,5281), no presentan una diferencia significativa entre familias con y sin padres desempleados. El alto valor de p sugiere que la funcionalidad familiar, según el puntaje APGAR, no parece variar considerablemente en función del desempleo en este grupo. Aunque el desempleo puede ser una fuente de estrés, su impacto directo en la cohesión y adaptabilidad familiar, tal como se mide en este instrumento, no es evidente en los datos actuales.

Cuadro 2. Análisis Estadístico de Factores Familiares y Socioeconómicos Relacionados con el Desempleo.

Variable	Chi² / t-Statistic	p-Valor	Grados de libertad
Estrato socioeconómico	5,93	0,0517	2
¿Es usted cabeza de hogar?	0,03	0,8689	1
Ocupación actual	16,37	0,0026	4
Puntaje APGAR (comparación entre grupos)	-0,63	0,5281	-

Fuente: autores

En el Gráfico 1 sobre el mapa de calor se observa el estrato socioeconómico y su relación con las demás variables, vemos que sus correlaciones son bajas en todos los casos, con coeficientes muy cercanos a cero. Esto nos indica que el estrato socioeconómico no parece influir de manera significativa en la funcionalidad familiar (medida por el puntaje APGAR), en el desempleo, ni en otras características como la edad o el número de personas en el hogar. En esta muestra, el estrato actúa más como un contexto de fondo, sin un impacto directo fuerte en estas dinámicas familiares y personales. Cuando analizamos la funcionalidad familiar (puntaje APGAR), encontramos una correlación negativa leve con el número de personas en la vivienda, de -0,215. Esto sugiere que, a medida que el hogar crece en número de personas, la funcionalidad familiar puede verse ligeramente afectada. Es posible que un hogar con más miembros enfrente mayores desafíos para mantener su cohesión y adaptabilidad, ya que las responsabilidades y demandas se incrementan. Además, el puntaje APGAR muestra una correlación moderada y positiva de 0,154 con la edad, lo que podría sugerir que familias con miembros de mayor edad tienden a presentar una mejor funcionalidad, quizás debido a su experiencia o estabilidad emocional.

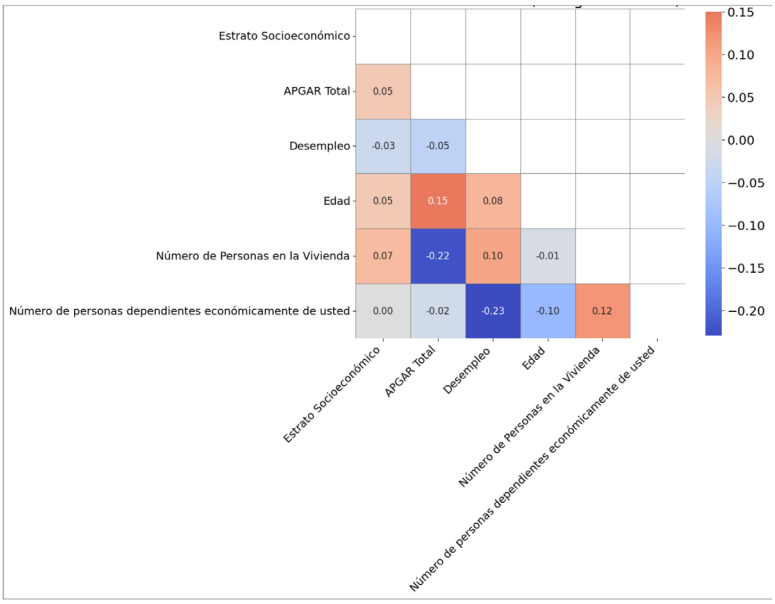


Gráfico 1. Mapa de Calor de Correlaciones entre Factores Socioeconómicos y Familiares. Fuente: autores.

Respecto al desempleo, la correlación negativa entre el desempleo y el puntaje APGAR es de -0,053, un valor bajo que indica que el desempleo no tiene un efecto claro o directo sobre la funcionalidad familiar en esta muestra. Además, encontramos una correlación negativa de -0,232 entre el desempleo y el número de dependientes económicos. Este valor sugiere que, en familias con más personas dependientes económicamente, hay menor probabilidad de desempleo. Podría interpretarse como un incentivo económico: las familias con más dependientes probablemente se ven en la necesidad de buscar ingresos para satisfacer las necesidades de todos los miembros.

Finalmente, al examinar el número de personas en la vivienda, observamos una correlación baja pero positiva de 0,120 con el número de dependientes económicos. Esto es algo esperable, ya que un hogar con más personas tiende naturalmente a tener más dependientes económicos, ya sean niños o adultos mayores.

El Cuadro 3 de Frecuencia y Porcentaje de la Funcionalidad Familiar revela una diversidad en los niveles de funcionalidad de las familias evaluadas. La mayoría, un 46,10 % (65 familias), mantiene una función familiar normal, lo cual sugiere una buena cohesión y adaptabilidad en estas familias. Sin embargo, 34,04 % (48 familias) muestran una disfunción leve, indicando algunos desafíos en su dinámica familiar. Además, 16,31 % (23 familias) presentan una disfunción moderada, lo que podría reflejar dificultades más notables en la comunicación y el soporte entre sus miembros. Finalmente, un 3,55 % (5 familias) se encuentra en disfunción severa, sugiriendo que estas familias enfrentan problemas significativos que afectan su bienestar general.

Cuadro 3. Clasificación de Funcionalidad Familiar.

Funcionalidad Familiar	Frecuencia	Porcentaje (%)
Función familiar normal	65	46,1
Disfunción leve	48	34,04
Disfunción moderada	23	16,31
Disfunción severa	5	3,55
Total	141	100

Fuente: autores

En el Análisis Descriptivo del Puntaje APGAR de el Cuadro 4, se observa que el puntaje promedio es de 15,72, posicionándose en el rango de disfunción leve, aunque bastante cerca de la funcionalidad normal. La desviación estándar de 3,54 indica que hay cierta variabilidad en los puntajes, lo cual es esperado en una muestra diversa. Los puntajes van desde un mínimo de 4 (disfunción severa) hasta un máximo de 20 (función normal). Al mirar los percentiles, encontramos que el 25 % de las familias tienen un puntaje APGAR de 13 o menos, mientras que la mediana (50 %) se ubica en 16, señalando que la mitad de las familias tienen una funcionalidad que roza la normalidad. Por otro lado, el 75 % de las familias alcanzan un puntaje de 19, indicando que la mayoría se acerca a la funcionalidad normal. Este análisis sugiere que, aunque muchas familias mantienen una estructura funcional sólida, existe un grupo considerable que experimenta niveles de disfunción leve. Esto podría implicar la necesidad de apoyo o intervenciones en aquellas áreas que afectan la cohesión y adaptabilidad familiar.

Cuadro 4. Análisis Descriptivo de la Funcionalidad Familiar (Puntaje APGAR).

Estadísticas Descriptivas de APGAR	
población (n)	141
media	15,72
de	3,54
min	4
25 %	13
50 %	16
75 %	19
max	20

Fuente: autores

Respecto a la funcionalidad familiar, medida por el puntaje APGAR, cambia en función del nivel educativo del hogar. Esta relación sugiere una historia de cómo la educación puede influir en el bienestar y la cohesión de la familia, por ejemplo: la Secundaria Completa en las familias cuyo nivel educativo predominante es la secundaria completa, se observa una gran variabilidad en los puntajes APGAR, que van

desde niveles de disfunción hasta la funcionalidad normal. La mediana de este grupo se sitúa cerca de los 16 puntos, lo cual representa una disfunción leve. Esto sugiere que, en estas familias, las experiencias de cohesión y adaptabilidad son diversas y posiblemente están influenciadas por factores adicionales, como los recursos económicos o la estabilidad laboral, que afectan cómo manejan los desafíos diarios.

Respecto al nivel Técnico/Tecnólogo y Universitario, los hogares con nivel educativo técnico/tecnólogo o universitario muestran puntajes APGAR más altos y menos dispersos. Las medianas para estos niveles se ubican en torno a los 18 puntos, dentro de la funcionalidad familiar normal. Esta consistencia en los puntajes más altos puede indicar que una educación más avanzada proporciona herramientas y estabilidad económica que fortalecen la funcionalidad familiar. La menor dispersión sugiere que estas familias suelen enfrentar menos tensiones que afecten su cohesión. En este mismo sentido, niveles de Posgrado, aunque el número de familias con nivel de postgrado es reducido, estas presentan puntajes consistentemente altos, con una mediana cerca de los 19-20 puntos, dentro del rango de funcionalidad familiar normal. Esto podría reflejar los beneficios de una mayor educación, que tiende a estar asociada con mayores recursos, mejores condiciones laborales y habilidades para manejar las relaciones familiares de manera efectiva.

La Primaria Completa e Incompleta en las familias con educación primaria incompleta presentan una mediana en torno a los 10-12 puntos, dentro de la disfunción moderada, y una amplia dispersión en sus puntajes. Esto sugiere que este grupo enfrenta mayores desafíos para mantener una buena funcionalidad familiar. Las familias con primaria completa muestran una ligera mejoría, pero sus puntajes aún se distribuyen en el rango de disfunción leve y moderada. Esta situación podría reflejar dificultades para acceder a recursos o falta de estrategias efectivas para afrontar problemas, afectando negativamente la cohesión familiar.

Relacionado con la Dispersión General, se observó que los niveles educativos más bajos tienden a mostrar una mayor dispersión en los puntajes APGAR. Esto sugiere que en estos grupos las experiencias familiares son más variadas, lo que puede deberse a condiciones de vida menos estables o a la falta de recursos y apoyo, generando diferencias en la forma en que las familias manejan las tensiones y los desafíos.

En el Gráfico 1 sobre el Estado De Empleo (Desempleo), podemos ver la diferencia en el puntaje APGAR entre familias con y sin miembros desempleados. Las familias en las que no hay desempleo tienen puntajes APGAR más altos y menos dispersos, con una mediana de aproximadamente 18 puntos, lo cual corresponde a una función familiar normal. Por otro lado, las familias que enfrentan situaciones de desempleo muestran una mayor dispersión, y su mediana se sitúa en torno a los 15 puntos. Esta diferencia sugiere que la estabilidad laboral podría estar asociada con una mejor cohesión y adaptabilidad familiar, mientras que el desempleo puede representar un desafío que afecta la funcionalidad.

Relacionado con el Estrato Socioeconómico muestra cómo el puntaje APGAR varía según el estrato socioeconómico. Las familias en el estrato 3 tienen puntajes más altos y consistentes, con una mediana cercana a los 18 puntos, indicando funcionalidad normal. En contraste, las familias de estrato 1 presentan mayor variabilidad, y la mediana ronda los 14 puntos, indicando disfunción leve. Este patrón sugiere que las familias en estratos socioeconómicos más altos pueden tener más recursos y estabilidad, lo que ayuda a mantener una funcionalidad familiar más sólida. Las familias de estratos más bajos, sin embargo, parecen enfrentarse a mayores desafíos que impactan en su cohesión.

El Gráfico 2 muestra el impacto de diversos factores socioeconómicos y demográficos en la funcionalidad familiar, evaluada mediante el puntaje total de la escala APGAR. En relación con el número de personas en la vivienda, se observa una tendencia decreciente en los puntajes APGAR conforme aumenta el tamaño del hogar.

Los hogares compuestos por tres personas presentan una mediana cercana a los 17 puntos, correspondiente a una funcionalidad familiar considerada normal. Sin embargo, a partir de cinco o más integrantes, las medianas tienden a disminuir hacia los 14–15 puntos, lo que se interpreta como una disfunción leve. Este hallazgo sugiere que, en contextos de

mayor densidad habitacional, pueden emerger tensiones relacionadas con la distribución de responsabilidades, la convivencia y la capacidad de adaptación, aspectos que afectan negativamente la percepción de funcionalidad familiar.

Respecto a la condición de cabeza de hogar, los resultados indican que los participantes que se identifican como cabeza del hogar presentan una mayor dispersión en los puntajes APGAR y una mediana ligeramente inferior (aproximadamente 16 puntos), lo que se traduce en una disfunción leve. En contraste, aquellos que no ostentan esta condición reportan una mediana más alta, cercana a los 17 puntos, lo cual se aproxima a una funcionalidad normal. Esta diferencia puede estar asociada a las cargas y responsabilidades adicionales que asumen las personas en posición de liderazgo familiar, las cuales podrían repercutir en su percepción de apoyo y cohesión dentro del núcleo familiar. En cuanto al estrato socioeconómico, el análisis revela un patrón inesperado. Aunque se esperaría que un mayor nivel socioeconómico se asociara a una mejor funcionalidad familiar, el estrato 3 muestra una mediana ligeramente inferior a los estratos 1 y 2, además de una menor variabilidad y la presencia de valores atípicos bajos. Estos resultados indican que el acceso a mayores recursos materiales no necesariamente se traduce en una mejor dinámica familiar. Factores como el estrés laboral, la individualización, la escasa convivencia o la desconexión afectiva pueden incidir negativamente en la funcionalidad, aún en contextos económicamente favorables. Este hallazgo rompe con la lógica lineal tradicional y sugiere la necesidad de considerar dimensiones psicosociales en el análisis del bienestar familiar.

Finalmente, el análisis del estado de empleo muestra que los hogares donde el encuestado se encuentra desempleado tienden a presentar puntajes APGAR más bajos y una mayor dispersión, en comparación con aquellos con empleo. Aunque las diferencias en la mediana no son marcadas, la presencia de valores extremos en los hogares con desempleo sugiere que esta condición puede representar un factor de vulnerabilidad para la funcionalidad familiar, posiblemente asociado a mayores niveles de estrés, incertidumbre económica y tensiones intra-hogar.

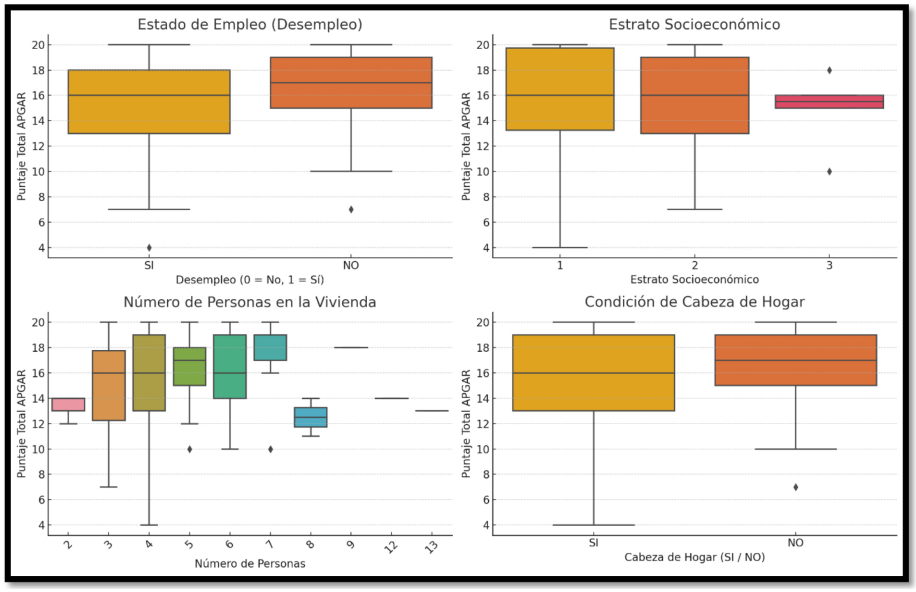


Gráfico 2. Impacto de Factores Socioeconómicos y Demográficos en la Funcionalidad Familiar (Puntaje APGAR). Fuente: autores.

DISCUSIÓN

Los hallazgos de este estudio revelan que, aunque el desempleo no presentó una asociación estadísticamente significativa con el puntaje de funcionalidad familiar (APGAR), sí se observó una mayor dispersión de los puntajes en familias con al menos un miembro desempleado, lo cual sugiere una influencia indirecta sobre la estabilidad del hogar. Esta observación es coherente con investigaciones previas que han documentado que el desempleo incrementa el estrés percibido, deteriora la comunicación intrafamiliar y afecta negativamente la salud emocional de los miembros del hogar (6,13).

En consonancia con lo planteado por Conger y col., el estatus socioeconómico actúa como un mediador en las dinámicas familiares, de modo que las familias con menores recursos son más susceptibles a experimentar disfunciones frente a eventos estresantes como la pérdida del empleo (7). A pesar que en esta muestra el estrato socioeconómico no se asoció significativamente con el desempleo, su relación con la funcionalidad familiar fue más evidente en los hogares de nivel educativo bajo, donde se observó mayor prevalencia de disfunción moderada y severa.

Asimismo, los resultados refuerzan la teoría de McCubbin y Patterson, quienes argumentan que el proceso de estrés familiar depende no solo del evento adverso, sino también de los recursos disponibles y el significado atribuido por la familia al evento (12). En ese sentido, las familias con mayor nivel educativo (técnico o universitario) tendieron a reportar mejores niveles de funcionalidad, lo que coincide con los hallazgos de Martínez y Muñoz, quienes encontraron que la escolaridad se asocia con mayor resiliencia familiar y mejor desarrollo infantil (8).

Otro aspecto destacable fue la capacidad de las familias para mantener vínculos afectivos y compartir tiempo de calidad, aun en medio de condiciones adversas. Esto coincide con los aportes de Carrillo y Riera, quienes subrayan que el soporte emocional y la cohesión familiar actúan como factores protectores frente a la adversidad económica (1). De igual forma, estudios realizados en comunidades de bajos ingresos indican que la funcionalidad familiar puede mantenerse relativamente estable si existen redes de apoyo interno y comunicación efectiva entre los miembros (11).

No obstante, se hace necesario señalar que los instrumentos utilizados, como el APGAR familiar, si bien permiten una evaluación general, pueden no captar plenamente la complejidad de las interacciones familiares en contextos vulnerables. En este sentido, se reconoce la posibilidad de sesgos de deseabilidad social en la autovaloración de la funcionalidad familiar mediante la prueba APGAR, especialmente en contextos donde se espera mostrar cohesión y estabilidad frente a evaluadores externos.

En futuras investigaciones sería pertinente complementar esta herramienta con entrevistas cualitativas o escalas más amplias que evalúen estrés percibido, afrontamiento y dinámicas de poder dentro del hogar (14,15).

Finalmente, este estudio reafirma la importancia de considerar el desempleo como un factor estructural que afecta no solo el ingreso económico del hogar, sino también su salud emocional y cohesión interna. Como señalan Villanueva y Sánchez, la pérdida del empleo tiene efectos acumulativos en la dinámica familiar, que se agravan en contextos de exclusión y pobreza (18). En consecuencia, se requieren políticas públicas integrales que aborden no solo el empleo formal, sino también el fortalecimiento psicosocial de las familias vulnerables.

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Uso problemático de los videojuegos como predictor del desarrollo de habilidades sociales en estudiantes de educación básica

Problematic video game use as a predictor of social skill development among elementary school students

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RESUMEN

Introducción: *En los últimos años, la preocupación por el uso problemático de los videojuegos ha aumentado significativamente debido a sus posibles efectos negativos en el desarrollo de habilidades sociales, especialmente durante la infancia y la preadolescencia, etapas clave para la adquisición de competencias interpersonales.* **Objetivo:** *Determinar si el uso problemático de los videojuegos predice significativamente el desarrollo de habilidades sociales de los estudiantes peruanos del quinto y sexto grado de educación primaria.* **Métodos:** *Estudio cuantitativo, no experimental, predictivo y transversal. La muestra estuvo conformada por 214 estudiantes de ambos sexos que cursaban el quinto y sexto grado de educación primaria, quienes respondieron la Prueba de Dependencia a los Videojuegos y el Cuestionario de Habilidades Sociales, instrumentos con adecuadas propiedades psicométricas.* **Resultados:** *Se encontró una correlación negativa y significativa entre el uso problemático de videojuegos y las habilidades sociales ($r= -0,263$; $p<0,01$). Además, el análisis de regresión lineal simple indicó que el uso problemático predice significativamente las habilidades sociales ($\beta= -0,263$; $p<0,01$), explicando el 6,5 % de su variabilidad (R^2 ajustado= 0,065). Finalmente, el estadístico Durbin-Watson (1,920) evidenció independencia de los residuos, respaldando la validez del modelo.*
Conclusiones: *Se concluye que el uso problemático de los videojuegos predice significativamente el desarrollo de habilidades sociales en estudiantes peruanos del quinto y sexto grado de educación primaria. El modelo de regresión mostró un efecto negativo y estadísticamente significativo, lo que indica que un mayor nivel de uso problemático se asocia con un menor desarrollo de habilidades sociales en esta población.*

Palabras clave: *Juegos de video, habilidades sociales, estudiantes, adicción a los videojuegos, salud mental.*

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SUMMARY

Introduction: *In recent years, concern about problematic video game use has increased significantly*

due to its potential adverse effects on the development of social skills, particularly during childhood and preadolescence, key stages for acquiring interpersonal competencies. **Objective:** *To determine whether problematic video game use significantly predicts the development of social skills among Peruvian students in the fifth and sixth grades of primary education.* **Methods:** *This study employed a quantitative, non-experimental, predictive, and cross-sectional design. The sample consisted of 214 students, both male and female, enrolled in the fifth and sixth grades of primary school. They completed the Video Game Dependency Test and the Social Skills Questionnaire, both of which demonstrated adequate psychometric properties.* **Results:** *A negative and significant correlation was found between problematic video game use and social skills ($r = -0.263, p < 0.01$). In addition, simple linear regression analysis revealed that problematic use significantly predicts social skills ($\beta = -0.263, p < 0.01$), accounting for 6.5 % of its variability (adjusted $R^2 = 0.065$). Finally, the Durbin-Watson statistics (1.920) evidenced independence of the residuals, supporting the validity of the model.* **Conclusions:** *It is concluded that problematic video game use significantly predicts the development of social skills in Peruvian students in the fifth and sixth grades of primary education. The regression model showed a negative and statistically significant effect, indicating that higher levels of problematic use are associated with lower development of social skills in this population.*

Keywords: *Video games, social skills, students, video game addiction, mental health.*

INTRODUCCIÓN

En la actualidad, los videojuegos forman parte del entorno cotidiano de millones de niños y adolescentes en edad escolar, convirtiéndose en una de las principales formas de entretenimiento (1). Desde edades tempranas, los niños acceden con facilidad a diversas plataformas digitales que les permiten jugar, competir y socializar en entornos virtuales (2). Esta presencia constante de los videojuegos ha generado tanto interés como preocupación, especialmente cuando su uso se vuelve excesivo y comienza a desplazar otras actividades esenciales para el desarrollo infantil, como el estudio, el juego físico o la interacción directa con sus pares (3).

En este contexto, surge la necesidad de examinar una forma específica de consumo digital que ha comenzado a ser identificada como riesgosa en la infancia y preadolescencia: el uso problemático de los videojuegos, entendido como una forma de consumo excesiva y descontrolada que interfiere negativamente en la vida cotidiana de quien lo practica (4). A diferencia del uso recreativo o moderado, el uso problemático de los videojuegos se caracteriza por la dificultad para limitar el tiempo de juego, la necesidad constante de estar conectado, y la prioridad que se otorga al videojuego sobre otras actividades importantes, como las tareas escolares, la convivencia familiar o el descanso (5). En el caso de los niños en edad escolar, este tipo de comportamiento puede pasar desapercibido al principio, pero con el tiempo comienza a afectar distintas áreas de su vida (6).

Entre las principales causas que pueden conducir a un uso problemático se encuentran factores individuales, familiares y sociales (7). A nivel personal, algunos estudiantes pueden recurrir a los videojuegos como una vía de escape ante emociones negativas, como el aburrimiento, la tristeza o la frustración (8). En el entorno familiar, la falta de supervisión o de límites claros sobre el uso de dispositivos electrónicos puede facilitar un acceso prolongado e inadecuado (9). Además, la presión del grupo de pares, el atractivo de los juegos en línea y la gamificación constante que ofrecen estas plataformas refuerzan la necesidad de permanecer conectados por más tiempo del recomendable (10).

Las consecuencias del uso problemático de los videojuegos en estudiantes de educación primaria pueden ser significativas. Una revisión sistemática encontró que, a corto plazo, se observa una disminución en el rendimiento académico, dificultades para concentrarse y alteraciones en los hábitos de sueño (11). A mediano y largo plazo, el uso problemático puede afectar la salud emocional y limitar el desarrollo de habilidades sociales, ya que reduce el tiempo destinado a la interacción presencial y al aprendizaje de normas de convivencia (12,13). Este aislamiento progresivo puede influir negativamente en la autoestima, en la capacidad de resolver conflictos y en la adaptación escolar, comprometiendo aspectos necesarios para el desarrollo integral de los niños (14,15).

Una de las áreas que puede verse más comprometida por el uso excesivo de videojuegos es el desarrollo de las habilidades sociales,

especialmente en la etapa escolar, donde estas competencias comienzan a consolidarse de manera decisiva (16). A través de la interacción con sus pares, los niños aprenden a expresar emociones, resolver conflictos, colaborar en grupo y establecer relaciones de confianza, elementos fundamentales para su bienestar y adaptación en el ambiente escolar (17). Sin embargo, cuando el tiempo dedicado a los videojuegos sustituye o limita estos espacios de interacción directa, se reduce la oportunidad de practicar y fortalecer dichas habilidades, generando posibles rezagos en su desarrollo interpersonal (18).

El adecuado desenvolvimiento social en la infancia depende en gran medida del entorno en el que se desarrollen los niños (19). La escuela y el hogar son los principales espacios donde los estudiantes tienen la posibilidad de aprender a comunicarse con asertividad, a respetar turnos, a comprender las emociones de los demás y a actuar con empatía (20). Estas competencias no solo favorecen una convivencia armónica, sino que también contribuyen a una mejor autoestima y a un sentido de pertenencia dentro del grupo (21). Cuando estas experiencias son reemplazadas por interacciones virtuales limitadas o centradas en dinámicas competitivas propias de muchos videojuegos, los procesos de socialización pueden volverse más superficiales o disfuncionales (22).

En ese sentido, la disminución de habilidades sociales en estudiantes que presentan un uso problemático de los videojuegos puede manifestarse en diversas formas, como dificultades para entablar conversaciones, escasa tolerancia a la frustración, retraimiento, o una tendencia al aislamiento (23). Estas limitaciones no solo afectan su rendimiento académico y participación en clase, sino también su capacidad de establecer vínculos sanos con sus compañeros (24). De ahí la importancia de analizar con mayor profundidad cómo ciertos hábitos digitales pueden estar incidiendo negativamente en el desarrollo socioemocional de los estudiantes de educación primaria, y qué estrategias podrían aplicarse desde el ámbito educativo y familiar para mitigar sus efectos.

Existen muy pocas investigaciones que aborden de manera específica la relación entre el uso problemático de los videojuegos y el desarrollo de habilidades sociales en estudiantes de educación primaria, lo que evidencia una importante brecha en el conocimiento sobre esta etapa formativa. No obstante, algunos estudios preliminares permiten advertir ciertos patrones preocupantes. Alborzi y Torabi (25) encontraron que la frecuencia en el uso de videojuegos tenía un efecto predictivo sobre el desarrollo de habilidades sociales, afectando directamente la calidad de las relaciones interpersonales entre escolares. Xu y col. (13) identificaron que la participación constante en juegos en línea perjudicaba competencias como la toma de decisiones y la autoconfianza. De igual manera, Zegarra y Torres (26) señalaron que el uso habitual de videojuegos podía deteriorar la convivencia entre estudiantes, al propiciar actitudes agresivas y dificultades comunicativas. Estos hallazgos, aunque aún limitados, destacan la necesidad de seguir investigando este fenómeno en contextos escolares específicos.

A partir de la evidencia, resulta necesario profundizar en el análisis del uso problemático de los videojuegos como posible factor que afecta el desarrollo de habilidades sociales en estudiantes de educación primaria. En una etapa en la que las experiencias interpersonales presenciales son clave para la construcción de vínculos, la expresión emocional y la adaptación al entorno escolar, preocupa que estas se vean desplazadas por prácticas digitales excesivas que podrían limitar la interacción directa con los pares. Considerando la escasa evidencia empírica centrada en esta población específica, esta investigación busca contribuir al conocimiento del fenómeno, generando información útil para orientar intervenciones desde el ámbito educativo y familiar.

Finalmente, el objetivo de la presente investigación fue determinar si el uso problemático de los videojuegos predice significativamente el desarrollo de habilidades sociales de los estudiantes peruanos del quinto y sexto grado de educación primaria.

MÉTODOS

Esta investigación se enmarcó en el enfoque cuantitativo, lo que permitió recolectar y analizar datos numéricos para examinar las variables de

forma objetiva. El diseño fue no experimental, ya que las variables no fueron manipuladas deliberadamente, sino que se observaron en su contexto natural. Asimismo, el estudio fue predictivo.

La población del estudio estuvo conformada por 484 estudiantes de ambos sexos matriculados en los grados quinto y sexto de educación primaria, pertenecientes a una institución educativa pública ubicada en la Amazonía peruana. Con el propósito de obtener una muestra representativa, se empleó un muestreo probabilístico, considerando un nivel de confianza del 95 % y un margen de error del 5 %. A partir de estos parámetros, se determinó una muestra final compuesta por 214 estudiantes.

La recolección de datos se llevó a cabo mediante dos instrumentos. El primer instrumento fue la Prueba de Dependencia a los Videojuegos, el cual fue adaptado al contexto peruano por Salas y col. (27). Este instrumento consta de 25 ítems que se evalúan cuantitativamente mediante una escala tipo Likert de 5 puntos, que va desde 1 (nunca) hasta 5 (siempre), distribuidos en cuatro dimensiones: abstinencia (ítems 1 al 10), abuso y tolerancia (ítems 11 al 15), problemas causados por los videojuegos (ítems 16 al 19) y dificultad para el control (ítems 20 al 25). Las propiedades psicométricas de la prueba fueron establecidas en un estudio previo realizado en Perú (5), en el cual se determinó que el instrumento presenta un nivel adecuado de validez basada en el contenido (V de Aiken= 0,898) y una alta confiabilidad (α= 0,838).

El segundo instrumento fue el Cuestionario de Habilidades Sociales, elaborado por el Ministerio de Salud (28). Este instrumento está compuesto por 42 ítems tipo Likert con cinco alternativas de respuesta que van desde 1 (nunca) hasta 5 (siempre), distribuidos en cinco dimensiones: habilidades sociales relacionadas con derechos y deberes, habilidades sociales relacionadas con la comunicación, habilidades sociales relacionadas con los sentimientos, habilidades sociales alternativas a la agresión y habilidades sociales para el manejo del estrés. En un estudio previo (29) se determinó que el cuestionario presentaba propiedades psicométricas adecuadas (V de Aiken = 0,850; α = 0,832).

Para llevar a cabo la recolección de datos, se obtuvo previamente la autorización de las autoridades de la institución educativa. Posteriormente, se procedió a aplicar los instrumentos de forma presencial en las aulas, en horarios coordinados con los docentes responsables. Antes de iniciar, se brindó a los estudiantes una explicación clara y sencilla sobre el propósito del estudio y las instrucciones necesarias para el adecuado desarrollo de la actividad. La aplicación fue supervisada en todo momento por el equipo investigador, asegurando un ambiente adecuado y respetuoso. El proceso tuvo una duración aproximada de 25 minutos por grupo. Una vez culminada la participación de los estudiantes, se procedió a revisar y asegurar la integridad de los cuestionarios para garantizar la calidad de los datos recopilados.

El análisis de datos se efectuó mediante el software estadístico SPSS versión 25. En una primera etapa, se calcularon los estadísticos descriptivos de las variables involucradas. A continuación, se utilizó el coeficiente de correlación de Pearson para analizar la existencia de correlaciones estadísticamente significativas entre las variables y dimensiones, considerando un nivel de significancia de $p<0,05$. Finalmente, se llevó a cabo un análisis de regresión lineal con el propósito de determinar si el uso problemático de los videojuegos actúa como predictor significativo de las habilidades sociales.

La presente investigación se realizó respetando rigurosamente los principios éticos que rigen los estudios con población escolar. Se obtuvo el consentimiento informado de los padres de los estudiantes, quienes recibieron información clara y detallada sobre los objetivos, procedimientos y alcances del estudio, así como sobre los derechos de sus hijos en relación con su participación. Además, se resguardó la confidencialidad de los datos mediante el uso de códigos alfanuméricos en lugar de información personal identificable. Finalmente, se garantizaron las condiciones de bienestar e integridad de los participantes conforme a los lineamientos establecidos en la Declaración de Helsinki.

RESULTADOS

En la Figura 1 se observa que el mayor porcentaje de estudiantes se ubicó en un nivel

moderado de uso problemático de los videojuegos (40,7 %), seguido por un nivel bajo (34.1 %), alto (15,4 %), muy bajo (7 %) y muy alto (2,8 %). Si bien la mayoría no presenta indicios severos, preocupa que un 18,2 % se concentre en los niveles alto y muy alto, ya que esto sugiere un patrón de uso potencialmente desadaptativo.

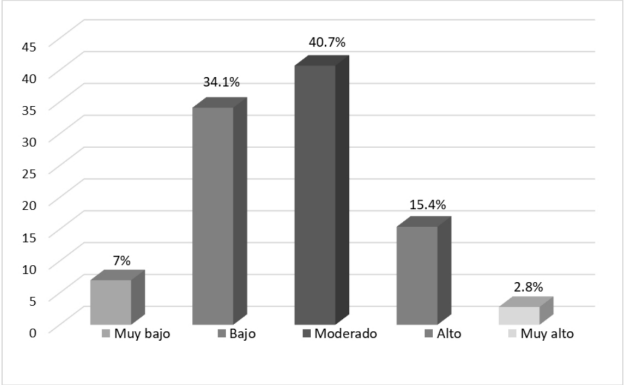


Figura 1. Resultados descriptivos de la variable uso problemático de los videojuegos.

La Figura 2 muestra que la mayoría de los estudiantes se ubicó en un nivel alto de habilidades sociales (54,7 %), seguido por un nivel muy alto (20,6 %) y moderado (22,9 %), mientras que los niveles bajo (1,4 %) y muy bajo (0,5 %) fueron poco frecuentes. Estos resultados sugieren que gran parte de la muestra posee competencias sociales adecuadas o fortalecidas, lo cual podría favorecer su interacción, comunicación y adaptación en distintos contextos. La baja proporción de estudiantes en niveles deficitarios indica que los problemas en habilidades sociales no son predominantes en el grupo de estudiantes evaluado.

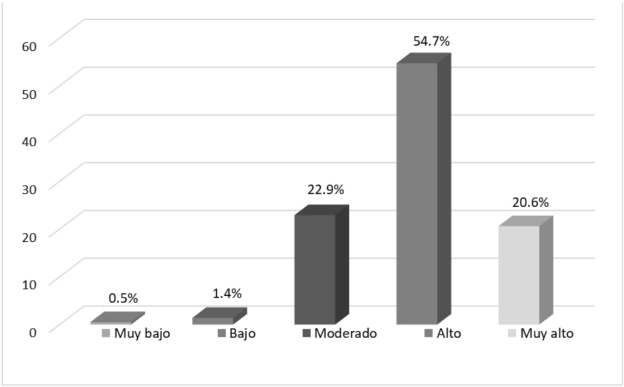


Figura 2. Resultados descriptivos de la variable habilidades sociales.

Como se observa en el Cuadro 1, existe una correlación negativa y altamente significativa entre el uso problemático de los videojuegos y las habilidades sociales (r= -0,263; p<0,01), lo que indica que, a medida que se incrementa el uso problemático, las habilidades sociales tienden a disminuir. Asimismo, todas las dimensiones de la variable uso problemático se relacionan negativamente con las habilidades sociales, siendo la correlación más fuerte con la dimensión de abuso y tolerancia (r= -0,319), seguida de problemas ocasionados (r= -0,224), dificultad en el control (r= -0,219) y abstinencia (r= -0,185), todas con significancia estadística (p<0,01). Estos resultados muestran que los diferentes aspectos del uso disfuncional de videojuegos afectan de forma negativa el desarrollo de habilidades sociales, especialmente cuando hay tolerancia y patrones compulsivos en el uso.

Cuadro 1. Correlación entre las variables y dimensiones de estudio.

Variable y dimensiones	1	2	3	4	5	6
1. Uso problemático de los videojuegos	1	-	-	-	-	-
2. Abstinencia	0,807**	1	-	-	-	-
3. Abuso y tolerancia	0,796**	0,566**	1	-	-	-
4. Problemas ocasionados por los videojuegos	0,759**	0,428**	0,549**	1	-	-
5. Dificultad en el control	0,756**	0,380**	0,448**	0,534**	1	-
6. Habilidades sociales	-0,263**	-0,185**	-0,319**	-0,224**	-0,219*	1

** p<0,01; * p<0,05

El Cuadro 2 presenta los resultados del análisis de regresión lineal que evaluó el uso problemático de los videojuegos como predictor de las habilidades sociales. El modelo fue significativo (F= 15,760, p<0,01) y explicó sociales (R^2 ajustado= 0,065). En este sentido, el uso problemático de los videojuegos mostró un efecto negativo y significativo (β= -0,263, p<0,01), lo que indica que, a mayor nivel de uso problemático, menor desarrollo de habilidades sociales en los estudiantes. Además, el estadístico Durbin-Watson (1.920) sugiere que no existen problemas de autocorrelación en los residuos del modelo, lo cual respalda la validez de los resultados obtenidos.

Cuadro 2. Análisis de regresión lineal.

Predictor	B	DE	β	t	p
(Constante)	183 068	6,311	-	29.008	0,0001
Uso problemático de videojuegos	-0,352	0,089	-0,263	-3,970	0,0001
R2			0,069		
R2 ajustado			0,065		
F			15,760 (p<0,01)		
Durbin-Watson			1,920		

Nota: Variable dependiente= Habilidades sociales.

DISCUSIÓN

En la actualidad, la creciente popularidad de los videojuegos está modificando de manera significativa las actividades de ocio y las formas de interacción social, incluso en etapas escolares tempranas. No obstante, esta creciente inmersión en entornos virtuales puede generar conductas problemáticas, las cuales pueden incidir negativamente en el desarrollo de habilidades sociales fundamentales para una adecuada convivencia escolar. En este contexto, esta investigación se centró en determinar si el uso problemático de los videojuegos predice significativamente el desarrollo de habilidades sociales de los estudiantes peruanos del quinto y sexto grado de educación primaria.

Los hallazgos preliminares evidencian que la mayoría de los estudiantes presentan un nivel moderado de uso problemático de los videojuegos. Esto implica que, aunque los videojuegos forman parte importante de su rutina diaria, los estudiantes aún logran mantener un equilibrio relativo con sus responsabilidades escolares y sociales. Sin embargo, se observan señales de distracción y dificultades puntuales en el manejo del tiempo, lo que sugiere la necesidad de fortalecer habilidades como el autocontrol y la autorregulación en el uso de este tipo de entretenimiento.

Los resultados expuestos contrastan con los hallazgos de Quispe (30), quien reportó una prevalencia mayor de uso problemático bajo (25,3 %) y una menor proporción de uso problemático moderado (20,6 %) en la muestra evaluada. Del mismo modo, difieren de lo encontrado por Peralta y Torres (31), quienes identificaron que el 54,1 % de los participantes presentaban un uso problemático leve de los videojuegos. En comparación, los niveles de uso problemático observados en el presente estudio fueron ligeramente más altos, lo que sugiere que los estudiantes tienden a integrar el uso de videojuegos como parte regular de sus actividades, sin que ello comprometa severamente su funcionalidad, aunque sí podría estar afectando ciertos aspectos de su desarrollo psicosocial.

Por otro lado, se identificó que la mayoría de los estudiantes presentan un alto nivel de desarrollo de habilidades sociales, lo que refleja una adecuada capacidad de comunicación, empatía y vínculo con sus pares. Estas competencias resultan fundamentales para generar un ambiente colaborativo, respetuoso y propicio para el aprendizaje. No obstante, cerca del 25 % de los estudiantes evidencian dificultades en este ámbito, lo cual podría repercutir negativamente en el clima escolar y en su capacidad para desenvolverse eficazmente en contextos sociales.

Existen estudios previos que han reportado niveles más bajos de habilidades sociales en estudiantes. Por ejemplo, Quispe (30) encontró que los estudiantes presentaban predominantemente un nivel bajo de desarrollo en esta área, lo que evidenciaba serias dificultades para establecer y mantener relaciones interpersonales saludables. Estas limitaciones se reflejaban en comportamientos como la timidez excesiva, la escasa participación en actividades grupales y la dificultad para expresar opiniones o resolver conflictos. De manera similar, Torres y Vilca (32) reportaron bajos niveles de desarrollo de habilidades sociales, destacando la limitada capacidad de los estudiantes para interactuar y comunicarse eficazmente con sus compañeros, lo que podría afectar su integración en el entorno escolar y su rendimiento académico.

Un hallazgo interesante muestra que el uso problemático de los videojuegos predice el desarrollo de habilidades sociales, es decir, que el grado en que los estudiantes se involucran de forma compulsiva o desregulada en esta actividad permite anticipar ciertas limitaciones en su competencia social. Esta asociación no solo pone en evidencia un patrón de sustitución de la interacción real por la digital, sino que también sugiere que los ambientes virtuales, aunque altamente estimulantes, no ofrecen las mismas condiciones para practicar habilidades como la escucha activa, la autorregulación emocional o el manejo de la frustración en tiempo real. Además, podría estar indicando una tendencia creciente en los niños a encontrar en los videojuegos un refugio frente a los desafíos sociales, lo que limita la exposición necesaria para fortalecer sus vínculos con los demás y para enfrentarse a situaciones interpersonales complejas que forman parte del desarrollo social saludable.

Este resultado puede comprenderse a la luz de la Teoría del Aprendizaje Social de Bandura (33), la cual sostiene que los comportamientos sociales se adquieren a través de la observación e imitación

de modelos en contextos de interacción. En este sentido, cuando los estudiantes pasan largas horas expuestos a entornos virtuales con escasas o inadecuadas representaciones de habilidades sociales positivas —o incluso con modelos de conducta agresiva, individualista o competitiva—, se reduce su oportunidad de observar, practicar y reforzar conductas prosociales en situaciones reales. Además, al sustituirse las interacciones presenciales por experiencias digitales, los niños dejan de recibir retroalimentación social inmediata, que es clave para el aprendizaje de habilidades como la empatía, la comunicación efectiva o el control de impulsos. Desde esta perspectiva, el uso problemático de los videojuegos no solo limita el tiempo destinado a la convivencia con otros, sino que también condiciona los modelos de conducta que los estudiantes interiorizan y reproducen en sus relaciones cotidianas.

Existe evidencia que demuestra los efectos negativos del uso intensivo de videojuegos sobre el comportamiento social de los estudiantes. Así, Alborzi y Torabi (25) encontraron que el uso frecuente de videojuegos tenía un efecto predictivo sobre el desarrollo de habilidades sociales, lo que impactaba directamente en el comportamiento cotidiano de los escolares y en la calidad de sus relaciones interpersonales. De manera similar, Xu y col. (13) identificaron que la participación constante en juegos en línea influía de forma negativa en el desarrollo de habilidades sociales clave, como la toma de decisiones y la autoconfianza. Asimismo, Zegarra y Torres (26) concluyeron que el uso habitual de videojuegos puede deteriorar las relaciones interpersonales entre estudiantes, al promover actitudes agresivas, una comunicación inadecuada y comportamientos disruptivos dentro del entorno escolar.

Una de las principales fortalezas de este estudio radica en su originalidad, ya que son escasas las investigaciones en el contexto nacional e internacional que analicen simultáneamente el rol predictor del uso problemático de los videojuegos en el desarrollo de habilidades sociales en estudiantes de nivel primario. Esta característica le otorga un valor añadido, posicionando a la investigación como un aporte relevante y novedoso en un campo aún poco explorado. Además, el uso de instrumentos validados contribuye a garantizar la fiabilidad y validez de los resultados, asegurando que los hallazgos reflejan de manera precisa la realidad analizada. Estos elementos metodológicos, junto con la pertinencia del problema abordado, refuerzan el valor de este estudio como referencia para futuras investigaciones en el ámbito educativo y psicosocial.

No obstante, es importante reconocer ciertas limitaciones. En primer lugar, la muestra fue pequeña y homogénea, por lo que los resultados deben interpretarse con cautela. Asimismo, se utilizaron cuestionarios autoadministrados, lo que podría haber influido en la veracidad de las respuestas debido al sesgo de deseabilidad social. Por ello, se sugiere que futuras investigaciones amplíen el número y diversidad de participantes, así como que incorporen metodologías mixtas o cualitativas que permitan una comprensión más profunda de los factores implicados. También sería recomendable utilizar técnicas de observación o entrevistas a profundidad que complementen los datos cuantitativos y ofrezcan una visión más integral del fenómeno estudiado.

CONCLUSIONES

Nuestros hallazgos permiten concluir que el uso problemático de los videojuegos predice el desarrollo de habilidades sociales en estudiantes del quinto y sexto grado de educación primaria, lo cual indica que una mayor implicación en esta conducta se asocia con un menor nivel de habilidades sociales. Esto sugiere que el uso excesivo y desregulado de videojuegos podría limitar las oportunidades de interacción social directa, afectando el desarrollo de competencias fundamentales como la comunicación asertiva, la empatía, la cooperación y la resolución de conflictos. La sobreexposición a entornos virtuales, donde las relaciones sociales suelen ser superficiales, anónimas o mediadas por la tecnología, puede reemplazar o reducir los espacios de interacción cara a cara necesarios para que los niños aprendan a expresar emociones, negociar desacuerdos o trabajar en equipo. Como consecuencia, los estudiantes pueden presentar mayores dificultades para integrarse en dinámicas grupales, establecer vínculos afectivos estables o responder adecuadamente a situaciones sociales cotidianas en el contexto escolar.

Con base en estos hallazgos, se recomienda implementar estrategias de prevención y sensibilización dirigidas a estudiantes, docentes y familias, orientadas a promover un uso equilibrado y saludable de los videojuegos. Asimismo, se sugiere incorporar programas de desarrollo socioemocional en el currículo escolar, con el fin de fortalecer las habilidades sociales desde edades tempranas. Estas acciones permitirían no solo mitigar los efectos negativos del uso problemático de los videojuegos, sino también fomentar ambientes escolares más colaborativos, empáticos y socialmente integradores.

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ARTÍCULO ORIGINAL

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A Strategy to Improve Patient Stagnation in the Emergency Department of Dr. Wahidin Sudirohusodo General Hospital Using Lean Hospital

Una estrategia para mejorar el estancamiento de pacientes en el Servicio de Urgencias del Hospital General Dr. Wahidin Sudirohusodo mediante el uso de Lean Hospital

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SUMMARY

Background: *Patient stagnation in the Emergency Department (ED) of Surgery is one of the serious issues in hospital service management. This condition reflects a blockage in the flow of patients from the ED to inpatient wards, which risks lowering service quality and increasing patient safety risks. According to The Joint Commission standards, patient boarding time, which is the duration a patient stays in the ED after being declared in need of hospitalization, must not exceed 4 hours. A length of stay exceeding this standard has been proven to increase the risk of nosocomial infections, staff fatigue, and worsen patient satisfaction. At Dr. Wahidin Sudirohusodo General Hospital, Makassar, this stagnation problem still frequently occurs and requires systematic improvement.* **Objective***: This study aims to develop improvement strategies for patient stagnation from the Surgical Emergency Department (ED) to the Inpatient Unit using the Lean Hospital approach.* **Methods:** *This study was analyzed using the Lean approach to identify non-value-added activities (waste) in the patient care flow. The approach is supported by several Lean tools, namely Value Stream Mapping (VSM) to map process flows, Fishbone Diagram to trace root causes of problems, and Kaizen as a continuous improvement approach. Data were collected through qualitative methods such as direct observation, in-depth interviews with relevant staff, and a review of hospital documents.*

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Results: *The flow mapping (VSM) results showed that the Observation and Documentation stages represented the longest waiting points, at 3 hours 3 minutes 15 seconds. The main delay was caused by waiting for instructions from the attending physician (DPJP) with an average of 2 hours 7 minutes 17 seconds. The most frequently occurring category of waste was waiting.* **Conclusion:** *Kaizen-based improvement strategies are recommended to reduce time wastage and increase the efficiency of patient flow from the Surgical ED to inpatient wards.*

Keywords: *Stagnation, emergency department installation, waste identification, Lean.*

RESUMEN

Antecedentes*: El estancamiento de pacientes en el Departamento de Emergencias (DE) de Cirugía es uno de los problemas graves en la gestión de los servicios hospitalarios. Esta condición refleja un bloqueo en el flujo de pacientes del DE a las salas de hospitalización, lo que corre el riesgo de reducir la calidad del servicio y aumentar los riesgos de seguridad del paciente. Según los estándares internacionales de calidad hospitalaria establecidos por la Joint Commission International (JCI), el tiempo de embarque —es decir, el período entre la decisión de hospitalizar a un paciente en el Departamento de Emergencias y su traslado efectivo a una cama hospitalaria— no debe exceder las 4 horas. Se ha demostrado que una estancia que supere este estándar aumenta el riesgo de infecciones nosocomiales, la fatiga del personal y empeora la satisfacción del paciente. En el Hospital General Dr. Wahidin Sudirohusodo de Makassar, este problema de estancamiento sigue siendo frecuente y requiere una mejora sistemática.* **Objetivo:** *Este estudio tiene como objetivo desarrollar estrategias para la mejora del estancamiento de pacientes del Departamento de Emergencias Quirúrgicas (DE) en la Unidad de Hospitalización utilizando el enfoque Lean Hospital.* **Métodos:** *Este estudio analizó e identificó mediante el enfoque Lean las actividades sin valor añadido (desperdicio) en el flujo de atención al paciente. El enfoque está respaldado por varias herramientas Lean, a saber, Value Stream Mapping (VSM) para mapear flujos de procesos, Fishbone Diagram para rastrear las causas raíz de los problemas y Kaizen como un enfoque de mejora continua. Los datos se recopilaron a través de métodos cualitativos como la observación directa, entrevistas en profundidad con el personal relevante y una revisión de los documentos del hospital.* **Resultados:** *Los resultados del mapeo de flujo (VSM) mostraron que las etapas de Observación y Documentación representaron los puntos de espera más largos, con 3 horas 3 minutos 15 segundos. El retraso principal fue causado por la espera de instrucciones del médico tratante (DPJP) con un promedio de 2 horas 7 minutos 17 segundos. La categoría de desperdicio que ocurrió con mayor frecuencia fue la espera.* **Conclusión:** *Se recomiendan estrategias de mejora basadas en Kaizen para reducir el desperdicio de tiempo y aumentar la eficiencia del flujo de pacientes desde la sala de emergencias quirúrgicas a las salas de pacientes hospitalizados.*

Palabras clave*: Estancamiento. instalación de servicios de urgencias, identificación de residuos, Lean.*

INTRODUCTION

Based on Law No. 44 of 2009 concerning hospitals, a hospital is a health service institution that provides comprehensive individual health services, offering inpatient care, outpatient care, and emergency services. The Emergency Department (ED) is a hospital facility that provides the first 24-hour service to patients at risk of death and disability in an integrated manner. In line with this definition, emergency services are provided to patients who arrive at the hospital in a critical condition or are expected to deteriorate. An emergency is a threat to the patient's life if help is not provided immediately. The speed of patient handling in the Emergency Department (ED) is crucial, especially for patients in critical condition. Delays in the service process can increase the risk of serious complications and even death. Therefore, efficiency in the ED service flow plays a significant role in improving patient safety and the quality of care (1,2).

The service flow in the Emergency Department (ED), particularly for Surgery, begins when the patient first arrives at the emergency unit. In the initial stage, the patient will undergo registration to record their personal data and the medical complaints they have experienced. After registration, the patient will undergo a triage process, where medical staff conduct an initial assessment of the patient's condition to determine the severity and urgency of treatment. The medical team will immediately attend to patients in critical condition to receive the necessary initial care. If needed, the patient will then undergo a series of further examinations, such as physical

examination, laboratory tests, or medical imaging, to ensure an accurate diagnosis.

Overcrowding or congestion in the Emergency Department (ED) is a trigger for prolonged stagnation in the ED. Overcrowding can be defined as a condition in which the performance of the Emergency Department is disrupted, primarily due to the large number of patients waiting for consultation, diagnosis, treatment, transfer, or discharge (3). An imbalance between supply and demand characterizes overcrowding. Although many factors contribute to Overcrowding (patient congestion), it essentially depends on three key factors: the number of incoming patients (input), the time required to process and treat patients (throughput), and the number of patients leaving the ED (output) (4). Among the various factors, patient Boarding turns out to be one of the most influential. Boarding refers to the practice of keeping patients in the ED for extended periods due to limited inpatient bed capacity in the hospital. Boarding, along with Overcrowding in general, negatively impacts the quality of care, mortality rates, morbidity rates, patient satisfaction, and the quality of services provided. This condition also leads to longer patient stays in the ED, an increase in the number of patients leaving the ED without being examined (also known as "left without being seen"), and a rise in the number of medical errors (5,6).

Based on recommendations from The Joint Commission Accreditation, the practice of boarding patients in the Emergency Department (ED) should not exceed 4 hours to ensure patient safety and optimal quality of care, as stated in Standard LD.04.03.11, Element of Performance (EP) 6. Boarding refers to the situation when a patient is held in the ED or a temporary location after a decision to admit or transfer them has been made. Hospitals are expected to set this goal while considering the patient's severity level and best practices, in order to reduce stagnation, ensure efficient care flow, and minimize excessive waiting times.

One example of a hospital in Indonesia is Dr. Wahidin Sudirohusodo Central General Hospital, a Type A hospital owned by the Ministry of Health, located on a 35-hectare site. Central General Hsopital Dr. Wahidin Sudirohusodo Makassar has set a patient waiting time in the ED of 4 hours. However, many patients have complained about the long service times provided by healthcare workers; even after receiving treatment, they are still required to wait more than 10 hours before being transferred to another care unit.

Data from Dr. Wahidin Sudirohusodo Makassar Hospital shows that nearly half of the patients in the ED experience stagnation, which is a waiting time of more than 4 hours before entering the inpatient ward. The average percentage of stagnation from January to November 2024 reached 47.5 %, with the highest rate in September (61 %) and the lowest in April (27 %). This situation indicates the phenomenon of patient stagnation in the ED, which can potentially cause overcrowding, delayed treatment, and a decline in the quality of service.

Therefore, it is important to analyze the factors that influence the length of patient stagnation in the ED, especially in the surgery department, to support effective triage, ensure smooth patient flow, and prevent overcrowding. Optimal management of length of stay is an important indicator of emergency service quality. One approach that can be used is Lean Hospital (or Lean Healthcare). This transformative management approach adapts industrial Lean principles to the healthcare setting, with the patient at the center of every decision. It is a management method focused on reducing waste, optimizing workflows, and enhancing patient value by improving care quality, safety, and satisfaction, and increasing efficiency and value of services for patients. Various studies have shown that prolonged stagnation can be caused by a number of interconnected factors, including both internal hospital factors and external factors that affect ED performance (7). Therefore, to address this issue, an approach is needed that can systematically identify and reduce waste in the care pathway. One such approach that has proven effective in improving efficiency and reducing length of stay is the application of Lean Healthcare principles, which focus on eliminating waste, improving workflow, and optimizing the use of both medical and non-medical resources in the ED. By adopting Lean, hospitals can reduce waiting times, speed up medical decision-making, and ultimately shorten the duration of patient stays in the ED, thereby improving service quality and the overall operational efficiency of the hospital. This is in line with research conducted by Souza

et al. (8), which found that implementing Lean principles in the ED provided significant benefits, including a 50 % reduction in waiting times, $2 million in annual savings through the elimination of inefficiencies, and a 30 % reduction in patient length of stay.

Therefore, the researcher hopes that the implementation of Lean Hospital in the ED will not only reduce overcrowding, optimize ED Length of Stay (EDLOS) management, and improve efficiency and quality of service at Dr. Wahidin Sudirohusodo General Hospital Makassar, Indonesia, but will also become the first study to specifically examine the application of Lean principles to surgical patient stagnation cases in the ED of a referral hospital in Indonesia, thus providing a new scientific and practical contribution in the context of emergency service management in developing countries.

MATERIALS AND METHODS

This research is qualitative research, meaning that it is conducted because the issues are related to humans and rely on observation. The data obtained in qualitative research consists of factual information and is analyzed in depth. Qualitative research places greater emphasis on obtaining more in-depth data, particularly through the direct involvement of the researcher in the field.

Study Design

The research approach is phenomenological, which is the study of knowledge aimed at clarifying situations experienced in a person's daily life and describing phenomena, both those that can be directly observed by the senses (external phenomena) and those that can almost be experienced, felt, imagined, or thought of by the observer without the need for empirical reference. This research comprehensively examines the overall background of the research subjects in the hope of obtaining data regarding issues in the Emergency Department at Dr. Wahidin Sudirohusodo General Hospital, Makassar. Data was obtained through structured interviews, observation, and documentation from informants.

Study Population

An informant is someone who is utilized to provide information about the situation and conditions of the research. The selection of the first informant is generally based on demographic characteristics or specific variables already known by the researcher from previous studies. Informants serve as sources for obtaining information regarding policies, planning, implementation, evaluation, and management reviews of the Emergency Installation at Dr. Wahidin Sudirohusodo General Hospital in Makassar. Informant selection employs purposive sampling, specifically the critical case sampling type, which involves selecting locations, events, or individuals that possess specific or important characteristics for a particular reason. The selection of information-rich samples takes into consideration the informants' positions, length of service, and relevant fields of work.

Sampling

The respondents in this study consisted of two groups: key informants and main informants, totaling nine people. The key informants numbered 3 people: the Head of the Emergency Room Department, the Head of the Medical Records Department, and a patient. The key informants were selected because they possess in-depth knowledge and essential information relevant to the focus of the study. The Head of the Emergency Room Department was chosen as the person in charge of ER services. At the same time, the Head of the Medical Records Department was selected due to their responsibility for the registration system and management of medical records. The selection of key informants was based on their position, length of service, and their role in the management of the ER, registration, and medical records. Meanwhile, the main informants consisted of 6 people: 2 registration officers, 2 medical records officers, and 2 ER staff. They were chosen due to their direct involvement in service delivery in the field and their firsthand experience with the service process in the ER. The characteristics of the main informants include their position, length of service, and areas of work closely related to ER operations, patient

registration, and emergency medical records management.

Study Instrument

The instruments in this research include the researchers themselves, respondents, interview guidelines, Field Notes, Recording Devices, Documents, and observation.

Data Collection

The data collection techniques in this study include observation, interviews, and documentation. Observations were conducted directly in the Emergency Room (ER) at Dr. Wahidin Sudirohusodo Central General Hospital, Makassar, to assess service quality, focusing on the registration section, ER services, and medical records, including queue flow, service delivery, communication, as well as prescription and medication retrieval at the pharmacy depot. Structured interviews were carried out with registration staff, doctors, ER staff, pharmacy staff, and patients to gather information about the eight wastes in the ER. The interview process followed systematic steps, starting with the preparation of questions, the use of recording devices, and the documentation of the results. Documentation was used to review policy documents, service flow, as well as data related to waiting times, registration, medical examinations, and medication provision, to support the validity of the research data.

Ethical Considerations

This research has been passed ethical review by the research department of the Faculty of Public Health, Hasanuddin University, Makassar, with the number: 99/UN4.14.I/TP.01.02/2025

RESULTS

Patient Service Flow in the Emergency Department of Dr. Wahidin Sudirohusodo Hospital

The flow of patient services in the Emergency Department begins as soon as the patient arrives through various entry points, whether by standard emergency ambulance, referral ambulance, or arriving independently or escorted by family. Patients who are referred undergo an initial triage process (pre-hospital). At the same time, those who are not admitted are directed to the Emergency Department area for repeat triage by hospital triage staff. Following this re-triage process, patients are classified into several categories of emergency severity: emergency (critical), urgent (minor emergency), non-urgent, or false emergency. This classification determines the subsequent course of action: emergency and urgent patients are directed to the treatment/ observation room or the resuscitation area. In contrast, non-urgent or false emergency patients may be referred to the outpatient clinic, especially if their condition is not life-threatening (Figures 1 and 2).

Patient administrative processes such as registration and data entry are usually carried out after triage, especially for stable patients. In emergency cases, administration is done in parallel with or after initial medical treatment to prioritize patient safety. After treatment, patients may be discharged, admitted for inpatient care, referred to in the operating room, Intensive Care Unit (ICU), or directed to the mortuary if deceased. Non-emergency patients who arrive outside of office hours may be redirected to the polyclinic. However, researchers' observations have shown discrepancies between real-life practice and the official procedures established by Dr. Wahidin Sudirohusodo Central General Hospital.

A. Patient Arrival

When patients arrive at the Emergency Department of Dr. Wahidin Sudirohusodo Central General Hospital, they undergo an initial triage by the Triage Team to determine the level of emergency. Patients requiring resuscitation are taken directly through the resuscitation entrance, while others are directed to the emergency room for medical triage and vital sign checks. While the triage process is ongoing, the patient's family is usually directed to the administrative section for registration. If the emergency department is full, patients may have to wait their turn or be referred to other services. Staff will provide education regarding this situation. However,

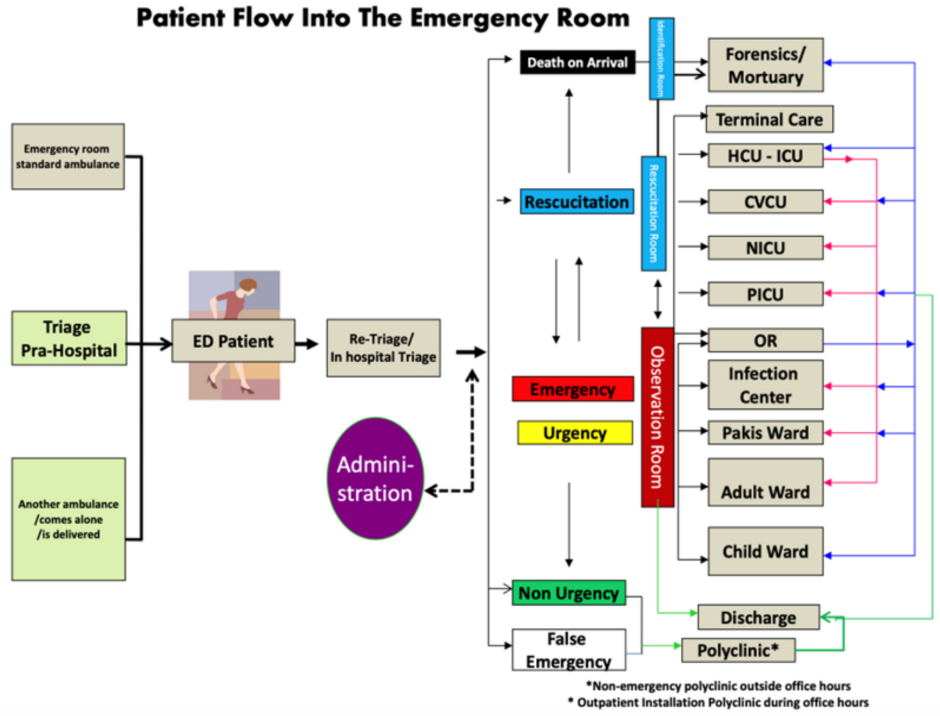


Figure 1. Patient Service Flow in the Emergency Department of Dr. Wahidin Sudirohusodo Central General Hospital

this education is not always well received by patients or their families, often leading to refusals and delays in the triage process. The primary obstacle encountered in the field is the limited number of triage nurses during busy periods in the emergency department, resulting in queues and longer waiting times. Non-value-added activities in this process account for 16.2 %, with the primary types of waste being waste due to waiting and waste due to motion (Table 1).

B. Emergency Department Patient Registration

The patient registration process at the Emergency Department (ED) of Central General Hospital, Dr. Wahidin Sudirohusodo, begins when the patient's family is directed to the admission section located in the Medical Records Installation. Registration includes verification of documents such as a national ID card (KTP), Family Card (KK), and social security insurance Card, as well as the completion of patient data, followed by delivery of identification bracelets and educational forms to the triage nurse station. Although medical services can be provided before registration is completed, queues often build up due to the large number of patients arriving at the same time and the limited number of staff. Admissions officers are also responsible for both ED and inpatients from the outpatient clinic, which slows down the process further. Additionally, technical issues such as instability of the electronic medical records (e-RM) system and printer malfunctions also hamper the speed of registration. Another challenge in the registration process is ineffective communication between staff and the patient's family. The lack of visual information media in the admission area leaves families without a clear understanding of the registration flow, forcing staff to explain procedures repeatedly. This increases the workload, especially during periods of high patient volume. This inefficiency leads to various non-value-added activities, dominated by waste of waiting, overprocessing, defects, motion, and non-utilized talent. Eight types of waste have been identified, including long queues,

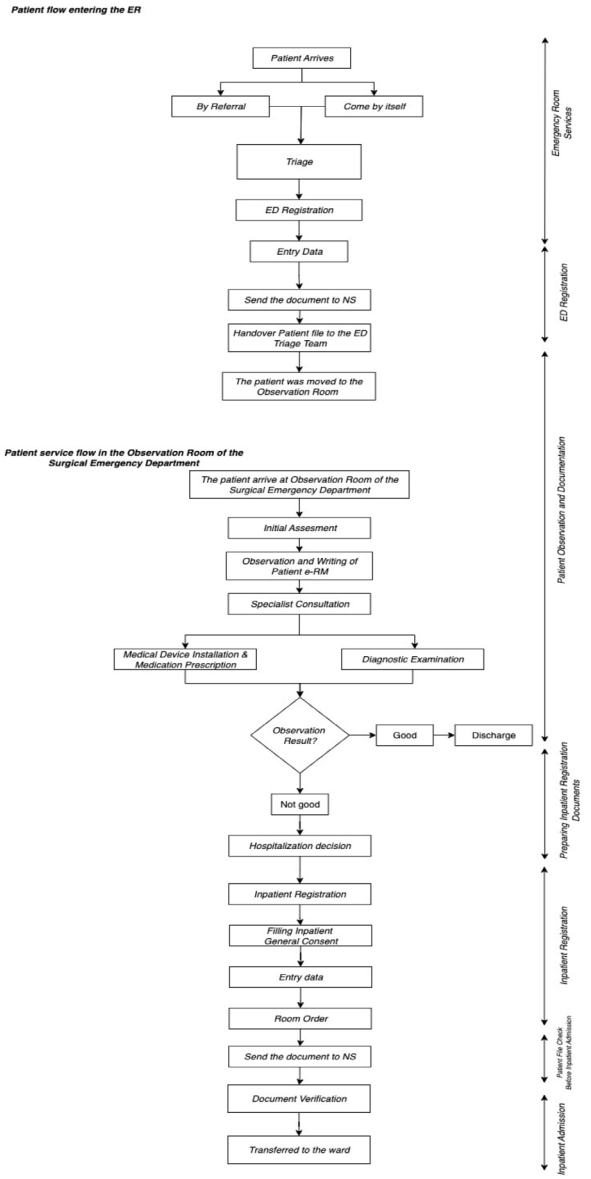


Figure 2. ER Service Flow Based on Researchers' Observation.

input errors, and inefficient communication, all of which negatively impact the efficiency of the ED registration flow (Table 2).

The lengthy registration process causes delays in transferring patient status to the ER staff. Activities that do not add value (Non-Value Added) in this process account for 35.2 %. Waste in this service is dominated by waste of waiting, waste of transportation, and waste of motion

C. Patient Observation

After medical triage, the doctor fills out a triage form that still requires printing, despite the implementation of the electronic medical record (e-MR) system. This process causes delays because staff must wait for the data to be auto-filled before the document can be printed and completed manually. Examinations by the attending doctor are also often delayed due to the doctor's involvement in emergency procedures or absence from the location. After registration is complete, the nurse attaches an identification bracelet, provides education, and requests a signature from the patient's family. The patient is then referred to the Surgical or Non-surgical division and waits for an initial assessment by the on-duty resident. As a teaching hospital, a tiered consultation system (from junior resident to attending physician) is part of the learning process. Still, it can cause delays in medical decision-making, especially when the attending physician is not yet available. The process of filling out medical records and inputting procedures by the on-duty resident is also hampered when the e-MR system encounters issues, requiring records to be completed manually and re-entered later.

This leads to duplication of work and additional administrative burdens, reducing efficiency.

Picking up medication at the ER Pharmacy Depot can often create confusion because patients are unfamiliar with the location. Since there is no internal delivery system, families must collect the medication themselves, resulting in unnecessary transportation costs. Additionally, the limited number of staff requires individuals to handle multiple duties, which decreases efficiency. For laboratory tests, nurses collect samples, and the patient's family must deliver them to the laboratory. Many families face difficulties because they are unfamiliar with the lab's location. This can be addressed by providing an internal courier between the ER and the laboratory. Finally, ER nurses often perform duties outside the scope of nursing, such as patient evacuation and handling paperwork. This double workload reduces their focus on nursing care and increases the risk of fatigue. Non-value-added activities are recorded at 69.8 %, with waste dominated by waste of waiting, transportation, motion, and overprocessing (Table 3).

Table 1. Activities in the Patient Arrival Process at the Surgical Emergency Room

No.	Activity	Average Time (seconds)	VA / NVA	Type of Waste (if NVA)
Patient arrives at the ED entrance area				
1	Staff look for an available stretcher/bed	49	**NVA**	*Waiting*
2	The stretcher is cleaned and prepared	18	**NVA**	*Waiting*
3	Waiting for assistance to move the patient (if needed)	15	**NVA**	*Waiting*
4	Patient is transferred onto the stretcher	41	**VA**	–
5	Initial triage by ED Triage Team (rapid assessment and classification)	172	**VA**	–
6	Patient is wheeled into the ED	14	**VA**	–
7	Medical triage by ED Triage Team (vital signs check, initial assessment)	361	**VA**	–
8	Companion directed to the registration counter	21	**NVA**	*Motion*
9	Patient waits for a doctor's examination (if ED is full)	34	**NVA**	*Waiting*
10	Initial education by staff to the patient/family regarding the ED condition	103	**VA**	–
Total Time		828 (13'48") Standard <5 minute	**VA**: 83.8 % **NVA**: 16.2%	

Note: VA = Value Added; NVA = Non-Value Added

Table 2. Activities in the Patient Registration Process at the Surgical Emergency Department

No.	Activity	Average Time (seconds)	VA / NVA	Type of Waste (if NVA)
1	The patient's family waits in line at the registration counter	38	**NVA**	*Waiting*
2	Family is served by registration staff	16	**VA**	-
3	Staff explain the registration procedure	44	**VA**	-
4	Family looks for and submits identity documents (ID, Family Card, BPJS)	58	**NVA**	*Motion*
5	Staff check the completeness and accuracy of patient documents	22	**VA**	–
6	Staff enter patient data into the e-RM system	171	**VA**	–
7	Staff print patient ID bracelet and education form	25	**VA**	–
8	The family receives patient documents and an ID bracelet	5	**VA**	-
9	The family delivers documents and a bracelet to the ED nurse station	50	**NVA**	*Motion, Transportation*
10	Documents are collected and submitted to the nurse station	10	**NVA**	*Transportation*
Total Time		439 (7'19")	**VA: 64,8% NVA:35.2%**	

Note: VA = Value Added; NVA = Non-Value Added

Table 3. Observation Process Activities in the Surgical Emergency Room

No.	Activity	Average Time (seconds)	VA / NVA	Type of Waste (if NVA)
Observation				
1	Doctor fills out triage form (E-RM)	133	VA	–
2	Waiting for the triage form to be printed from the e-RM system	17	NVA	*Waiting, Overprocessing*
3	The triage form is manually filled out after printing	23	NVA	*Overprocessing*
4	The nurse provides education to the patient's family	89	VA	–
5	Patient's family signs the education form	18	VA	–
6	The nurse attaches the patient ID bracelet	75	VA	
7	On-call doctor reports the patient to the respective division	30	VA	–
8	Patient is transferred to observation room	17	VA	–
9	Patient waits for assessment by on-call doctor/resident	281	NVA	*Waiting*
10	First examination by on-call doctor/resident	817	VA	–
11	Second examination by on-call doctor/resident	824	NVA	*Waiting, Overprocessing,*
12	Waiting for instructions from the primary doctor in charge (DPJP)	7637	NVA	*Waiting*
13	On-call doctor fills in the medical record after assessment	341	VA	-
14	On-call doctors enter procedures and prescriptions into the system	241	VA	-
15	Nurse executes instructions from DPJP	854	VA	-
Subtotal Observation		11397 (3j 9' 57")	VA: 22.9% NVA: 77.1%	
Prescription Process				
1	Medical staff informs the patient's family to collect the prescription	83	NVA	*Motion*
2	The family goes to collect the prescription	127	NVA	*Motion, Transportation*
3	Family waits in line at the pharmacy	33	NVA	*Waiting*
4	Pharmacy staff confirms patient identity	33	VA	-
5	Family returns the prescription to the surgical nurse station	125	NVA	*Motion, Transportation*
Subtotal Prescription		401 (6' 41")	VA: 6.6 % NVA: 93.4%	
Supporting Investigation				
1	Medical staff informs the family to deliver a blood sample to the laboratory	35	**NVA**	*Motion*
2	The family delivers the sample to the laboratory	400	NVA	*Motion, Transportation*
3	The sample is an investigation	1498	VA	
Subtotal Supporting investigation		1933 (32' 13")	VA: 77.5% NVA: 22.5%	
TOTAL Observation Process		13731 (3j48'51")	VA: 30.2% NVA: 69.8%	

Note: VA = Value Added; NVA = Non-Value Added

D. Inpatient Registration

After the doctor determines that the patient needs to be hospitalized, the room registration process begins as a transition from the ER to inpatient care. The ER Triage Team creates a referral letter through the system and directs the patient's family to the admissions department for the room registration process. At admissions, the family is asked to consent to the hospitalization and receive education, especially if they must wait due to full occupancy. After that, the family returns to the ER to submit documents and wait for room confirmation from the nurse.

This process often takes a long time, especially during peak hours or when rooms are full, because the information system is not yet integrated in real time. ER staff must wait for manual confirmation from admissions or ward nurses, which can be delayed due to busyness or technical issues.

Non-value added (NVA) activities reach 38.6 %, with the main waste being waste of transportation, motion, and waiting (Table 4).

Table 4. Activities in the Registration Process for Inpatient Admission of Surgical ER Patients

No.	Activity	Average Time (seconds)	VA / NVA	Type of Waste (if NVA)
Attending physician (DPJP) declares patient requires inpatient care				

No.	Activity	Average Time (seconds)	VA / NVA	Type of Waste (if NVA)
1	The ED triage team creates an inpatient referral letter via the system	35	VA	–
2	ED staff instructs the family to photograph the patient's ID bracelet and provide the name & medical record number.	41	NVA	*Motion*
3	Family proceeds to admissions for inpatient registration	277	NVA	*Motion, Transportation*
4	The family waits in queue at the admissions counter	213	NVA	*Waiting*
5	Admissions staff request inpatient consent and explain the general consent form	486	VA	–
6	Family signs the general consent and inpatient agreement	19	VA	–
7	Staff educate the family if the room is unavailable and the patient must temporarily remain in the ED	69	VA	–
8	Admissions staff input inpatient room availability data	290	VA	–
9	Family returns to the ED carrying patient records from admissions	33	NVA	*Motion, Transportation*
Subtotal Inpatient Registration		1463 (24'23")	VA: 61.4% NVA: 38.6%	

Note: VA = Value Added; NVA = Non-Value Added

E. Transferring Patients to the Inpatient Ward

After a patient is designated for inpatient care and a room is available, the next step is to check the completeness of inpatient documents, coordinated by the ER staff, admissions, and medical records. The purpose is to ensure all documents are complete before the patient is transferred. However, this process often causes stagnation because documents such as the medical summary are frequently not finished, or technical issues occur with the hospital information system (SIMRS). As a result, patients who are clinically ready to be transferred still have to wait because their documents are not complete. From a Lean Hospital perspective, this process is considered a non-value-added (NVA) activity because it prolongs the length of stay without providing any additional medical benefit. This situation also leads to delayed bed turnover and slows down the admission of new patients. The NVA activity rate in this process reaches 96.4 %, with the dominant forms of waste being waste of waiting, transportation, motion, and overprocessing (Table 5).

Table 5. Activities in the Document Verification Process for Surgical ER Patients

No.	Activity	Average Time (seconds)	VA / NVA	Type of Waste (if NVA)
1	ED nurse reconfirms with the inpatient unit via telephone for coordination	45	NVA	*Waiting, Overprocessing*
2	Waiting for inpatient room availability (due to full or unprepared room)	921	NVA	*Waiting, Inventory*
3	Room information received after the update from the admission/ward nurse	21	VA	-
4	ED staff verifies inpatient documents	55	VA	-
5	Waiting for the doctor/resident to complete the ED Initial Assessment summary	732	NVA	*Waiting*
6	Ward staff re-checks documents before patient admission	44	NVA	*Overprocessing, Waiting*
7	Patient documents are complete	11	VA	-
Subtotal Document Verification Time		1829 (30'29")	VA: 4.8 % NVA: 95.2 %	

Note: VA = Value Added; NVA = Non-Value Added

F. Transferring Patients to the Inpatient Ward

After the administrative process is completed and a room is available, the patient is transferred from the ER to the inpatient ward. Although this may seem simple, this process often becomes the final obstacle that prolongs the patient's stay in the ER. The transfer requires coordination among the ER team, transport staff, and ward nurses. Still, it frequently faces challenges such as a shortage of transport staff, ward nurses not being ready, and poor inter-unit communication.

As a result, patients must wait even though all procedures have been completed. This situation causes stretchers to be held up, delays the admission of new patients, and adds to the ER team's workload. In the Lean Hospital approach, this situation falls into the category of non-value-added (NVA) activities that result in waste, such as waiting, transportation, and motion. Therefore, improved coordination among units, additional staff, and a technology-based transfer system are needed to speed up the process and reduce waste (Table 6).

Table 6. Process of Patient Transfer Activities from the Surgical ER

No.	Activity	Average Time (seconds)	VA / NVA	Type of Waste (if NVA)
Patient Transfer Process				
1	Confirmation by the inpatient room nurse that the patient will be delivered	27	NVA	*Overprocessing*
2	Initial coordination between ED staff and transfer team	32	VA	-
3	Waiting for the transfer team (evacuator)	370	NVA	*Waiting*
4	Patient is moved to the transfer team stretcher	34	VA	–
5	Patients are transferred to the inpatient ward	617	VA	–
Subtotal Inpatient Transfer Time		1080 (18')	VA: 63.7 % NVA: 36.8 %	

Note: VA = Value Added; NVA = Non-Value Added

Figure 3 shows the Value Stream Mapping (VSM) of the service process in the Emergency Department (ED) of Dr. Wahidin Sudirohusodo Central General Hospital. This flow map details the stages of service from the arrival of patients to the transfer process to the inpatient ward. VSM is used to identify activities that add value (Value Added/VA) and those that do not add value (Non-Value Added/NVA), as well as various types of waste that occur in the service flow. Through this mapping, the hospital can clearly see the points that cause delays, bottlenecks, and inefficiencies in the ED service process. This information serves as an important foundation for continuous improvement in enhancing the quality of service and accelerating response times to the needs of emergency patients.

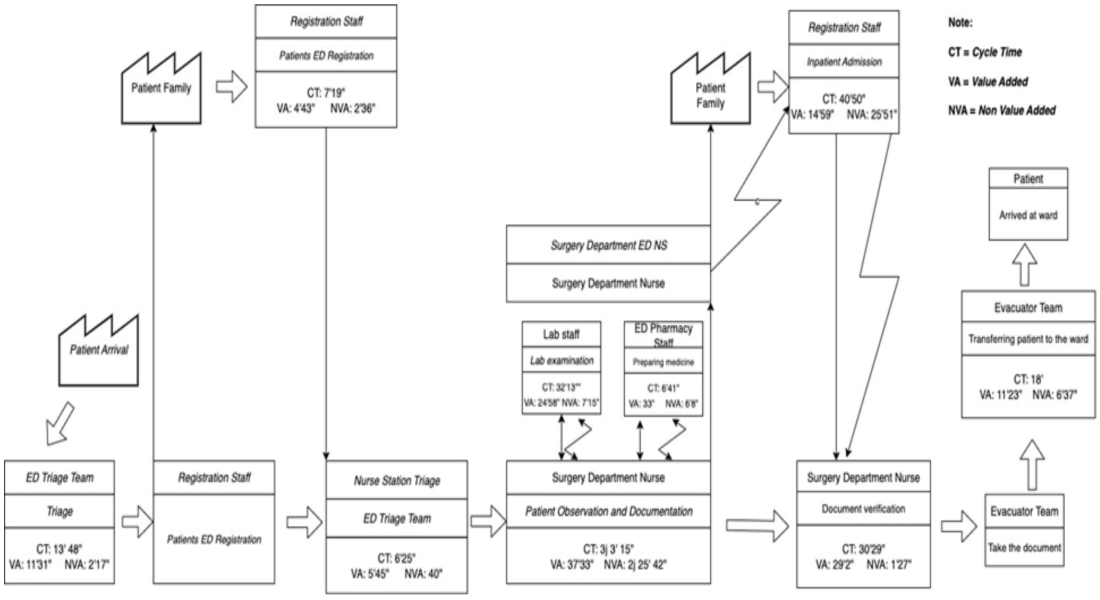


Figure 3. Value Stream Mapping (VSM) of Emergency Department Service Process.

DISCUSSION

Services in the Emergency Department (ED) are characterized by fast response times and a high level of interprofessional coordination. However, the findings of this study indicate that service efficiency in the ED still faces significant challenges, especially regarding waiting times and non-value-added (NVA) activities. Based on the mapping of the service flow using Value Stream Mapping (VSM), it was found that the patient service process goes through ten main stages, starting from arrival and visual triage to administrative processes and transfer to the inpatient ward. Although structurally the service stages have proceeded according to procedure, further analysis shows that most of the service time is spent on activities that do not provide direct value to the patient.

The average length of stay for patients in the ED at Dr. Wahidin Sudirohusodo Central General Hospital was recorded at 3 hours, 59 minutes, and 21 seconds, with the fastest handling time at 2 hours, 15 minutes and 17 seconds, and the longest time reaching nearly 8 hours (7 hours, 54 minutes and 44 seconds). The stage that consumes most of the time is the observation phase, especially when patients must wait for instructions from the attending physician (DPJP). During this period, there are no medical interventions, education,

or active communication with the patient and their family, which makes this time categorized as a non-value-added activity (NVA) under the Lean Thinking approach. Calculations show that about 66.5 % of the total service time falls into the NVA category, meaning that only one-third of the patient's time in the ED is actually used for value-added activities such as examinations, medical procedures, administering medication, or transfer to the inpatient ward.

These findings are consistent with research conducted by Improta et al. (12) in Italy, which showed that most of the patients' length of stay in the ED is spent as passive waiting time due to unintegrated service processes, including in clinical decision-making. Rahman et al. (9) also found that the observation phase and waiting for decisions from the attending physician are critical points contributing to the most extended length of stay, especially in teaching hospitals that apply a tiered consultation system. In addition, Naidoo and Mahomed (10) reported that inefficiencies in inter-unit coordination and delays in administrative processes can cause over 60 % of the patient's time to be spent in non-productive activities, similar to the conditions in this study. Therefore, these data confirm that waiting time during the observation phase is a dominant source of waste in ED services and needs to be prioritized in improvement strategies.

These findings are in line with a study by Mailani et al. (11), which found that waiting is indeed a prominent form of waste in the Arifin Achmad Regional Hospital's Emergency Department, Riau, particularly during the observation and inpatient phases. This waiting can manifest as patients waiting for assessment, treatment, or transfer to other units. Lean methodologies, which focus on eliminating waste, can be applied to improve patient flow and reduce these delays (11). Additionally, Improta et al. (12), in research conducted at AORN Cardarelli Hospital, also reported that waste of motion and transportation often occurs due to a lack of internal logistics systems and insufficient delivery staff, resulting in patients' families being actively involved in non-medical processes. Naidoo and Mahomed (10) add that repetitive activities and manual processes prolong service times, reduce healthcare worker productivity, and increase the risk of burnout.

Another fundamental issue identified in this study is the suboptimal implementation of the electronic medical records (e-MR) system. The system used in the Emergency Department of Dr. Wahidin Sudirohusodo Hospital is still hybrid, combining both digital and manual processes, leading to document redundancy and data input duplication. Some forms still must be filled out manually and then re-uploaded into the digital system, or vice versa. This situation not only results in waste in the form of overprocessing and defects but also opens opportunities for recording errors, loss of information, and longer administrative processing times. In addition, communication between units, such as with inpatient wards, pharmacy, and laboratory, has yet to operate optimally. Coordination that should be able to take place in parallel instead occurs serially due to limitations of the integrated information system. This leads to delays in decision-making and in processing follow-up services.

These findings align with Naidoo and Mahomed (10), who indicate that non-integrated information systems result in wasted time, duplicated work, and reduced quality of service coordination. Similarly, Mailani et al. (11), in their study at Arifin Achmad General Hospital, found that an E-MR system not fully supporting the needs of the Emergency Department is one of the main causes of delays in the service process. In this context, non-value-added processes have become part of the fragmented systemic structure rather than merely a technical or incidental issue (10).

Lack of information integration, limited human resources, a dual-document system, and a reactive pattern of inter-unit communication are interrelated factors that exacerbate patient stagnation in the Emergency Department. This supports the principle of Lean Thinking, which emphasizes the importance of identifying and eliminating activities that do not provide added value to patients. Graban (13) asserts that such systemic waste can have a broad impact on the efficiency, quality, and workload of healthcare institutions. The fact that 66.5 % of service time falls under non-value-added activities shows there is significant room for improvement through a Lean approach focused on streamlining processes and strengthening workflow (flow). Therefore, optimizing the information system and enhancing

inter-unit coordination should be among the strategic priorities in improving the quality of Emergency Department services.

In the context of Lean Thinking, these findings highlight the need to reorient emergency department service systems based on the actual needs of patients, as well as the implementation of systematic, ongoing improvements. Improvement strategies should not be limited to workflow redesign alone but should also involve the active participation of healthcare workers in identifying and addressing problems in the field. One opportunity that can be maximized is through morning report activities, which are held routinely every morning. This forum can serve as a participatory discussion platform, where medical and nursing staff can express service obstacles and propose solutions that are both applicable and realistic. This approach aligns with the Kaizen principle in Lean, which emphasizes continuous improvement driven by direct participation from frontline staff (13).

A study by Usman and Ardiyana (14) also emphasized the importance of fostering a collaborative work culture in the emergency department by involving medical personnel in the problem identification and quality improvement decision-making processes. A similar point was raised by Sánchez et al. (15), who stated that the success of Lean in improving the flow of patients in the emergency department is highly influenced by the active involvement of staff in change initiatives and the streamlining of work processes.

In addition to issues related to medical and administrative processes, this study also found significant barriers in the provision of medications at the Emergency Department Pharmacy Depot. Based on observations, during each shift, there are only two pharmacy staff members available, who are responsible not only for prescriptions from emergency patients, but also for those from outpatients. During busy hours, especially on the morning shift, the high workload can cause delays in medication delivery, and in certain situations, requests from the emergency department may be unintentionally overlooked. This is not due to negligence by the staff, but rather because the work system is not yet fully digitalized and the workload exceeds the available human resources.

This situation is consistent with findings by Febrina (16), who stated that a limited number of pharmacy staff and a manual distribution system are the main causes of medication retrieval delays in the emergency department. In addition, Shah et al. (17) concluded in their study that delays in the pharmacy process are one of the systemic factors prolonging patient stays in the emergency department, especially when processes run in parallel without the support of an integrated system. Therefore, strategies are needed to improve pharmacy service efficiency, whether by increasing labor, separating emergency and outpatient service lines, or implementing a pharmacy information system that is directly connected to the emergency department in real time. In this way, patient waiting times can be minimized and the potential for waste can be significantly reduced.

CONCLUSION

Patient services at the Emergency Department of Dr. Wahidin Sudirohusodo General Hospital, Makassar, consist of eight main stages: Triage, Emergency Department Admission Registration, Observation and Documentation, Prescription Processing, Medical Support Examinations, Inpatient Registration, Document Verification, and Patient Transfer to the Inpatient Unit. Analysis shows that value-added activities include registration, examinations, family education, completing the triage form, as well as coordination and patient transfer, all of which support the smooth operation of service processes. Conversely, non-value-added activities include waiting for documents, manual document printing, waiting for doctor instructions, pharmacy queues, and repetitive administrative processes, which do not directly add value for patients and lead to inefficiency.

Value Stream Mapping shows that the highest proportion of value-added activity occurs when the patient arrives (83.8 %) and during the patient transfer to inpatient care (63.7 %). In contrast, the observation and prescription processes show very low levels of value-added activity, at only 22.9 % and 6.6 % respectively. Conversely, activities such as medical support

examinations and inpatient document verification are dominated by non-value-added activities, reaching 94.8 % and 93.4 %, indicating significant waste in the service flow. The most commonly found types of waste include waiting, inventory, motion, overprocessing, and transportation, all of which significantly extend service times and reduce operational efficiency in the Emergency Department.

The proposed recommendations emphasize that for the board of directors and management of Dr. Wahidin Sudirohusodo General Hospital, Makassar, suggested improvements represent ideal solutions that must be supported by the hospital's resource capabilities and commitment, to maintain and enhance service quality as expected, by continuously applying the principles of Kaizen based on monitoring and evaluation results. For educational institutions, it is recommended to conduct training, such as seminars or workshops, on lean hospital management. This should involve all board members and hospital management at the district/city, or provincial level, so that the importance of implementing the lean method can be widely disseminated and collectively implemented. In addition, it is hoped that future researchers can broaden the scope of research by further studying instances of waste in other facilities, such as inpatient and outpatient services, as well as the relationship between emergency services and these aspects, to identify more comprehensive waste points across all aspects of hospital services.

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Features of Psychophysiological Adaptation of Foreign Students in Medical Universities

Características de la Adaptación Psicofisiológica de los Estudiantes Extranjeros en las Universidades de Medicina

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SUMMARY

Introduction: *Psychophysiological adaptation of foreign medical students is a pressing issue due to the increasing influx of students from abroad.* **Objective:** *This study aimed to identify the factors affecting the adaptation of international students in the process of studying at medical universities of the Kyrgyz Republic, with a special focus on climatic conditions, study load, and stress factors.* **Method:** *The study was conducted from 2022 to 2023 at Ala-Too International University and the International Graduate School of Medicine, involving 150 first-year students from India and Pakistan. The analysis of data obtained from questionnaires, physiological tests, and biochemical analyses revealed significant changes in levels of anxiety, stress tolerance, and physiological indicators such as cortisol levels, blood pressure, and heart rate, as well as the state of the respiratory system.* **Result:** *At the beginning of the semester, 60 % of students had an elevated level of situational anxiety with an average of 48.2 points, indicating high stress due to adaptation to a new educational and cultural environment. By the end of the semester, a decrease in the level of situational anxiety was recorded, which indicates a gradual adaptation to the educational process and new living conditions. There was also a decrease in cortisol level (from 580 to 470 nmol/L) and improvement of cardiovascular system indicators: average blood pressure decreased from 135/85 to 128/82 mmHg, and heart rate decreased from 82 to 76 beats per minute, indicating a decrease in stress and improvement of students' general condition. Correlation analysis revealed a significant relationship between anxiety level and physiological indicators such as heart rate and cortisol level. These data highlight the need for a comprehensive approach to support international*

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students, including psychological assistance, social support, and regular monitoring of physiological indicators, which helps to improve adaptation and reduce stress levels.

Keywords: *Cortisol, blood glucose, triviolence level, heart rate, vital capacity of lungs, stress tolerance, biochemical analysis.*

RESUMEN

Introducción: *La adaptación psicofisiológica de los estudiantes de medicina extranjeros es un problema acuciante debido a la creciente afluencia de estudiantes extranjeros.* **Objetivo:** *El objetivo de este estudio fue identificar los factores que afectan la adaptación de los estudiantes internacionales durante sus estudios en las universidades de medicina de la República Kirguisa, con especial atención a las condiciones climáticas, la carga de estudio y los factores de estrés.* **Método:** *El estudio se llevó a cabo entre 2022 y 2023 en la Universidad Internacional Ala-Too y la Escuela Internacional de Posgrado de Medicina, con la participación de 150 estudiantes de primer año de India y Pakistán. El análisis de los datos obtenidos mediante cuestionarios, pruebas fisiológicas y análisis bioquímicos reveló cambios significativos en los niveles de ansiedad, la tolerancia al estrés e indicadores fisiológicos como los niveles de cortisol, la presión arterial y la frecuencia cardíaca, así como en el estado del sistema respiratorio.* **Resultados:** *Al inicio del semestre, el 60 % de los estudiantes presentaba un nivel elevado de ansiedad situacional con una media de 48,2 puntos, lo que indicaba un estrés elevado debido a la adaptación a un nuevo entorno educativo y cultural. Al final del semestre, se registró una disminución del nivel de ansiedad situacional, lo que indica una adaptación gradual al proceso educativo y a las nuevas condiciones de vida. También se registró una disminución del nivel de cortisol (de 580 a 470 nmol/L) y una mejora de los indicadores del sistema cardiovascular: la presión arterial media disminuyó de 135/85 a 128/82 mmHg, y la frecuencia cardíaca disminuyó de 82 a 76 latidos por minuto, lo que indica una disminución del estrés y una mejora del estado general de los estudiantes. El análisis de correlación reveló una relación significativa entre el nivel de ansiedad y los indicadores fisiológicos como la frecuencia cardiaca y el nivel de cortisol. Estos datos ponen de relieve la necesidad de un enfoque integral para apoyar a los estudiantes internacionales, que incluya asistencia psicológica, apoyo social y seguimiento regular de los indicadores fisiológicos, lo que ayuda a mejorar la adaptación y reducir los niveles de estrés.*

Palabras clave: *Cortisol, glucosa en sangre, nivel de triviolencia, frecuencia cardíaca, capacidad vital pulmonar, tolerancia al estrés, análisis bioquímico.*

INTRODUCTION

As an increasing number of foreign students enrol in medical schools, it has become crucial and urgent to help them adjust psychologically. It can be exceedingly difficult to learn in a new school and culture, especially for students who are going to medical school, because the curriculum and learning are highly demanding. Due to the numerous differences in school requirements, weather, and culture, international students find it challenging to adjust. They become more stressed and undergo significant mental and physical changes because of such an event.

Coping is a dynamic process in which people consider what their environment needs and use their resources to continue coping, according to the transactional model of stress and coping, which was applied in this study (1). In this context, cognitive adaptation is defined by psychological responses elicited by exposure to new stressors, including academic pressure, cultural differences, and environmental influences. Physiological adaptations are marked by the activation of the hypothalamic-pituitary-adrenal (HPA) axis and biological indicators, including cortisol levels, heart rate, blood pressure, and respiratory rate. When cortisol levels and heart rate increase, the body responds more quickly to stress. When levels of these hormones decrease, the body recovers. Changes in vital capacity (VC) and other respiratory symptoms reflect the body's response to external stressors, such as temperature or altitude. The purpose of this integrated model is to explain the interaction between cognitive perception and physiological reactions in shaping the adaptive capacity of international medical students in a new academic and social environment.

Language barriers and adverse weather conditions are common problems for international students. Hachemi et al. (2) studied the adjustment problems of students in India and Pakistan and found that language skills and geographical climate had a significant impact on anxiety levels. However, their study did not examine the

influence of academic stress on anxiety levels. Significant differences were found, especially among medical students who experienced high levels of academic stress. It is also important for students to adapt to new academic standards and the associated stress. Gamsizkan et al. (3) showed that international students experience greater stress due to adjusting to new educational norms. However, their study did not examine the impact of weather conditions on adjustment, which limits our understanding of the wide range of factors that influence students' adjustment. International students also have considerable difficulty adjusting to cultural differences. Yılmaz and Temizkan (4) found that students' adjustment to a new cultural environment often results in high levels of stress, which negatively affects their academic performance. However, the study did not assess physiological parameters such as cortisol levels or blood pressure, which may provide a more objective picture of the adaptation process.

Gradual reduction in anxiety is an important part of the adaptation process. Wang et al. (5) showed that anxiety levels in university students decreased significantly after the first month of study. However, their study focused only on psychological factors and did not consider physiological changes, which hinders a comprehensive understanding of university student adaptation. Social support is also crucial for how well students adapt. Demuyakor (6) investigated the effect of social support in his study and found that a supportive environment reduces anxiety levels. However, Demuyakor did not consider the impact of academic workload, which is an important factor, especially in medical schools where the demands of study are higher.

Physiological measures, including cortisol levels, can be used to assess adaptation. Kristiana et al. (7) emphasised the importance of these measures in assessing adaptation. However, their study did not consider the impact of cultural differences on physiological changes, which could help provide a more complete understanding of stress on international students. To facilitate effective adaptation of students, comprehensive support, including social and psychological aspects, is necessary. Oh and Ahn (8) emphasised the importance of such an approach. Still, their study does not consider the relationship between physiological indicators and anxiety levels, which could actually lead to a deeper understanding of the adaptation process.

One of the problems that international students face is not having enough social and mental health support. Jamshaid et al. (9) stressed the need for a consistent plan to help students and said that psychological support is essential for successful adaptation. However, their study did not include physiological data, which limits our understanding of the overall impact of adaptation factors. Further research is needed to clarify the role of these factors.

In view of the evidence, this study aimed to investigate how first-year medical students at Kyrgyz Republic's universities psychologically and physiologically adapt to a foreign educational and cultural environment. For this, it will be: Assess changes in situational anxiety and perceived stress over the course of the semester; Monitor physiological measures of stress and adaptation, such as cortisol levels and cardiovascular and respiratory parameters; Examine the relationship between psychological and physiological adaptive responses.

This study demonstrated the need for a comprehensive strategy to support international students and emphasised the need for a more comprehensive strategy that includes both academic and social aspects. Therefore, strategies should be developed that effectively consider all factors that influence the adaptation of today's international students.

MATERIALS AND METHODS

The study was conducted from 2022 to 2023 at Ala-Too International University and the International Graduate School of Medicine in the Kyrgyz Republic. The sample consisted of 150 first-year international students from India and Pakistan, aged 18 to 20 years (M±SD=19.7±0.17). Out of them, 75 males and 75 females, thus ensuring a balanced sex distribution. The sample was randomly generated to ensure the representativeness of the data, with a balanced distribution of sex and country of origin. The study included students with comorbid somatic diseases, but they were excluded. To assess

psychophysiological adaptation, a set of methods was used, including questionnaires, physiological tests, and biochemical analyses. This study aligned with the ethical principles of research, including anonymity, confidentiality, and beneficence. Ethical approval of the study was obtained from the Ethics Committee of the Ala-Too International University with No. 182964.

The conceptual framework for this research was based on Lazarus and Folkman's transactional model of stress and coping, which views adaptation as an ongoing interaction between external stressors and internal coping capacities. Within this framework, the study assessed psychological responses such as anxiety and perceived stress as cognitive appraisals of environmental demands. At the same time, physiological and biochemical markers were used to evaluate somatic reactivity. This dual approach allowed for a comprehensive examination of psychophysiological adaptation among international students facing academic, cultural, and climatic challenges.

A questionnaire (the Spielberger-Hanen test) was used to assess anxiety levels (10). This test consisted of 40 questions divided into two parts and rated on a 4-point Likert scale. The assessment was conducted twice, once during the first 2 weeks of the semester and again at the end of the semester, to monitor fluctuations in anxiety levels during the adaptation process. For cross-cultural validity, the questionnaire was translated into Hindi and Urdu using a back-translation procedure, and its internal consistency was confirmed through a pilot test (Cronbach's α>0.85). The questionnaires were completed anonymously, which reduced the influence of socially desirable responses and increased the reliability of the data collected. Students completed the questionnaires during lectures under the guidance of the researchers. This reduced external influences on the responses and ensured consistency throughout the study period. The results were used for further research to clarify the relationship between anxiety levels and physiological indicators. Additionally, the Perceived Stress Scale (PSS-10), a 25-item instrument rated on a 5-point scale, was employed to assess the level of stress resistance and the subjective evaluation of adaptation to the learning process (11). The PSS-10 assessed students' ability to cope with academic and social stress. Both surveys were administered anonymously throughout the study and directly by trained researchers to ensure consistency and limit social media bias.

Biochemical blood tests were performed to assess physiological adaptation parameters such as cortisol and glucose levels. To minimise the influence of external factors on the test results, blood samples were collected in the morning on an empty stomach. Blood samples were collected into sealed containers using sterile 10 mL disposable syringes (BD Plastipack). All blood collection and analysis procedures were performed according to standard biosafety procedures to avoid contamination and ensure the accuracy of the test results. The time of sample collection was limited to ensure comparability of samples between individuals. All examiners followed the same procedure to minimise testing variability.

The obtained blood samples were analysed in the laboratory at the National Centre for Maternal and Child Health. Determination of serum cortisol levels was carried out by an immunological method according to standard procedures, with basal levels of 800, evening levels of 1 800, and night levels of 2 300. Total daily cortisol mass (mg) in the studied time interval (15 hours) was calculated according to the formula (1):

$$m = 0.00362 \times CBV \times \sum_{i=1}^{N=3} C_i, \quad (1)$$

Where m is the mass of cortisol secreted in the studied time interval, mg; 0.00362 is the coefficient of cortisol transformation from the metric unit of nmol/L concentration to mg/L; C_i is the concentration of cortisol in samples, nmol/L.

Daytime cortisol reactivity was defined as the rate of change in cortisol levels between nighttime and baseline levels over 15 hours, nmol $L^{-1} \times h^{-1}$ (2):

$$\text{Reactivity} = \frac{|m(\text{HOvernight}) - m(\text{basal})|}{15 \text{ hours}}. \quad (2)$$

Blood glucose was determined colorimetrically by the glucose oxidase-peroxidase (GOD-POD) method. To assess the functional state of the cardiovascular system, an Omron M6 Comfort automatic digital tonometer was used to measure systolic and diastolic blood pressure. HR and heart rate variability (HRV) were determined by CardioVisor software, which provided time-domain and frequency-domain metrics essential for quantifying autonomic nervous system activity. The functional state of the respiratory system was assessed by the method of spirometry on the Spiropet Spirometer apparatus according to the basic and dynamic parameters of external respiration: VCL; functional residual lung capacity (FRC); reserve expiratory volume (REV); total lung capacity (TLC); minute respiratory volume (MRV); alveolar ventilation (AV).

A ChoiceMMed pulse oximeter determined blood oxygen saturation (SaO_2). In addition, Shtange and Henche tests were applied to assess hypoxia tolerance. The protocol for these tests followed standard instructions, and measurements were conducted under identical environmental conditions. The measurements were performed twice: at the beginning of the academic term and three months after the start of the study, which allowed us to track the dynamics of changes in the adaptation state of the students. Before each measurement, the study participants rested for 10-15 minutes to stabilise cardiovascular and respiratory parameters, which ensured accurate and reliable results.

Statistical analysis of the data was performed using IBM SPSS (version 27). Descriptive statistics were presented as mean and standard deviation. Differences between indicators measured at different stages of the study were assessed by comparing changes over time using paired t-tests. Pearson correlation coefficients were used to determine the strength and direction of the relationship between psychometric characteristics (e.g., anxiety, stress resilience) and physiological indicators (e.g., cortisol, HR, blood pressure). The significance level was set at $p<0.05$. A multivariate analysis of variance (ANOVA) was conducted to examine the influence of gender, age, and country of origin on adaptation parameters. This multivariate approach allowed the identification of interaction effects and clarified the role of background variables in moderating the adaptation process. The Spielberger-Hanen scale and the PSS-10 were used to assess psychological adaptation. Body size and HR, cortisol, and spirometry provided physiological information. Combining these data allowed for a detailed analysis. All manipulations involved in this study were performed in accordance with the Declaration of Helsinki, which ensures adherence to ethical standards and humane treatment of participants (12). Each study participant was informed of the purpose and procedures of the study. An informed consent form was signed.

RESULTS

The presented results are consistent with the three main goals of this study: first, changes in psychological stress and depression over time were described; second, changes in physical resilience parameters were analysed; and third, the relationship between psychological and physiological factors was investigated, and an integrated model of coping with adverse situations was developed. The study has shown that international students studying at medical universities in the Kyrgyz Republic experience significant changes in psychophysiological indicators during the adaptation process to new living and learning conditions. Analysis of data obtained from questionnaires, physiological tests, and biochemical analyses revealed both individual and group differences in anxiety levels, stress tolerance, and physiological parameters. These data provide a deeper understanding of which factors have the most significant impact on the adaptation of international students and how their learning environment can be improved. The analysis of questionnaire data using the Spielberger-Hanin scale revealed an increased level of anxiety in a significant part of international students (Table 1).

The results of the study showed that at the beginning of the academic term, the level of situational anxiety was elevated in 60 % of the study participants, with an average value of 48.2±5.6 points, which exceeds the norm for this age group (30-45 points). This suggests that the process of adapting to a new educational and

Table 1. Psychophysiological indicators of foreign students at the beginning and end of the educational process at the university (M±SD)

Indicator	Beginning of the semester	End of the semester	Percentage of students with disabilities
Situational anxiety (scores)	48.2±5.6	42.3±4.8	60
Personal anxiety (scores)	52.1±6.1	52.1±6.1	40
Stress resistance (points)	34.5±4.3	41.7±3.9	55

Source: created by the authors.

cultural context is a significant stressor for most students. By the end of the academic term, the level of situational anxiety had decreased to an average value of 42.3±4.8 points, indicating a gradual adaptation of students to the educational process and new living conditions. Despite the overall decrease in situational anxiety, personality anxiety remained consistently high in 40 % of the participants, with a mean of 52.1±6.1 points, indicating the presence of a stable anxiety state associated with the long adaptation process and the influence of multiple stressors, including learning loads, climatic features, and social differences.

A special questionnaire was used to assess stress tolerance, and the results showed that 55 % of students experienced a high level of stress at the beginning of the semester. The average stress tolerance score was 34.5±4.3, indicating a low ability of students to cope with academic and domestic stresses. These data confirm that adapting to a new environment presents a significant strain on students, especially those who are experiencing study abroad for the first time and have to adjust to new cultural and social conditions. By the end of the semester, the index had improved to 41.7±3.9, which may indicate a positive influence of adaptation mechanisms and social support from teachers and fellow students, as well as a gradual decrease in stress levels as students became accustomed to the new environment.

Measurements of physiological parameters such as blood pressure, HR, and HRV showed significant changes over the academic semester (Table 2). At the beginning of the semester, 45 % of the students had elevated blood pressure (mean 135/85 mmHg), which is higher than the normal values for this age group (120/80 mmHg). This indicates that stress factors, such as climate change, academic workload, and social adaptation, had a significant impact on the state of the students' cardiovascular systems. By the end of the semester, the mean blood pressure had decreased to 128/82 mmHg, indicating improved adaptation to the stressful conditions of the educational process and stabilization of physiological indicators as students became accustomed to the academic schedule and requirements.

Table 2. Cardiovascular system indicators in students at different stages of adaptation to learning

Research stage	Blood pressure (mmHg)	HR (bpm) (M±SD)	HRV (%) (M±SD)
Beginning of the semester	135/85	82±6	5.2±0.4
End of the semester	128/82	76±5	7.8±0.6

Source: created by the authors.

The heart rate at the beginning of the semester averaged 82±6 beats per minute, which is higher than the norm (60-80 beats per minute) ($p<0.05$). This elevated rate may be related to the high level of anxiety and stress caused by the unfamiliar learning environment and change in living conditions. By the end of the semester, the index had decreased to 76±5 beats per minute (with a significance level of $p<0.05$), indicating a decrease in stress levels and an improvement in the general condition of the students. Heart rate variability also showed positive dynamics, with the coefficient of variation increasing from 5.2 % to 7.8 %, indicating an improvement in the adaptive capabilities of the cardiovascular system. The increase in heart rate variability is a crucial indicator, as it reflects the organism's ability to adapt to changing conditions and cope with the effects of stress.

Physiological indices between groups of girls and boys show that such indices as blood pressure and HR also had differences. For example, girls had an average blood pressure of 138/87 mmHg at the beginning of the term, whereas boys had an average blood pressure of 132/83 mmHg. Higher blood pressure in girls may be associated with a greater emotional reaction to stressful situations. By the end of the semester, these indices had decreased to 130/84 mmHg in girls and 126/81 mmHg in boys, indicating a tendency for the cardiovascular system to improve its adaptation process in both girls and boys.

The results of the study showed that in international students, the FRC of the lungs corresponded to the norms established by Indian researchers for this ethnic group (13). There was an ethnically determined decrease in FRC, which was associated with a reduction in expiratory reserve volume with normal residual lung volumes, as well as lower values of VCL characteristic of this population. Low values of VCL were recorded in 46 % of young men and correlated with their hyposthenic and dolichomorphic body type. Obstructive processes in the lungs were detected in 5.2 % of students, which was confirmed by a decrease in the REV, VCL, forced expiratory volume in the first second (FEV1), blood oxygen saturation (SaO_2), and a significant increase in VCL on exertion. Restrictive changes were observed in 9 % of girls, confirmed by a decrease in TLC, MRV, and alveolar ventilation (AV).

Changes in the functional state of the respiratory system were compensatory and adaptive in 85 % of students, indicating their ability to adapt to new climatic conditions and meet the organism's metabolic needs. However, 51 % of boys had low resistance to hypoxia, compared to 18 % of girls, which is likely due to individual physiological differences and increased stress associated with adapting to new environmental conditions.

Biochemical blood tests revealed that the level of cortisol, a primary marker of stress, was elevated in 50 % of students at the beginning of the semester (Table 3).

The average cortisol level was 580±50 nmol/L, which significantly exceeds the normal range (100-535 nmol/L). This indicates a significant impact of stress factors on the students' organism in the first months of their stay in new conditions. By the end of the academic term, the level of cortisol decreased to 470±45 nmol/L, which may indicate a reduced impact of stress factors and better adaptation to the study and living conditions.

Table 3. Biochemical blood parameters in students at different stages of the study, (M±SD)

Indicator	Beginning of the semester	End of the semester	Percentage of students with disabilities
Cortisol level (nmol/L)	580±50	470±45	50
Glucose level (mmol/L)	5.9±0.4	5.4±0.3	20

Source: created by the authors.

The results of the intergroup study revealed a more pronounced decrease in cortisol levels among girls compared to boys. Cortisol levels in girls decreased from 590 ± 55 nmol/L to 460 ± 48 nmol/L, whereas in boys, they decreased from 570 ± 50 nmol/L to 480 ± 46 nmol/L. This may indicate a more effective activation of adaptation mechanisms in girls, despite the initially higher level of anxiety. These results confirm that despite higher levels of anxiety at the beginning of the term, the girls were able to adapt more quickly to the new environment, which was reflected in lower levels of stress hormones. This highlights the importance of considering gender differences when designing support and adjustment programmes for international students.

Blood glucose levels also varied throughout the semester. At the beginning of the study, 20 % of students showed statistically significant elevations in glucose values (mean 5.9±0.4 mmol/L), which may be related to increased stress levels and dietary changes. Elevated glucose levels are often observed under conditions of stress, as the body secretes more glucocorticoids, increasing blood sugar levels. By the end of the semester, the average glucose level had decreased to 5.4±0.3 mmol/L, indicating stabilization of metabolic processes and an improvement in students' diets as they adapted to new conditions (14).

Assessment of blood glucose levels showed that normalization of this indicator occurred evenly in both boys and girls. This indicates that the improvement of metabolic processes is related not only to sex differences, but also to general adaptive mechanisms such as improved nutrition, physical activity and social interaction. Thus, at the beginning of the term, the mean glucose level in girls was 6.2±0.4 mmol/L and in boys, 6±0.3 mmol/L. By the end of the term, the index had decreased to 5.5±0.3 mmol/L in girls and 5.3±0.2 mmol/L in boys (Table 4).

Table 4. Changes in blood glucose levels in boys and girls (M±SD)

Sex	Start of semester (mmol/L)	End of semester (mmol/L)	Percentage of students with disabilities
Girls	6.2±0.4	5.5±0.3	22
Boys	6±0.3	5.3±0.2	18

Source: created by the authors.

Comparative analysis between boys and girls showed that the level of anxiety and physiological parameters of adaptation differed depending on gender (Table 5). Girls had a higher level of situational anxiety than boys at the beginning of the semester (50.3±5.8 vs. 46.1±5.2 points), which may be due to higher emotional sensitivity to stressors (13). By the end of the semester, girls' anxiety level decreased to 44.1±4.7 points, whereas boys' anxiety level decreased to 40.5±4.9 points, indicating more effective adaptation in boys. This may be due to differences in stress coping strategies and social support.

Table 5. Comparative psychophysiological indicators of boys and girls during their studies at a university (M±SD)

Sex	Situational anxiety (scores)	Blood pressure (mmHg)	Heart rate (bpm)	Cortisol level (nmol/L)
Girls	50.3±5.8→44.1±4.7	138/87→130/84	85±7→78±5	590±55→460±48
Boys	46.1±5.2→40.5±4.9	132/83→126/81	80±6→74±5	570±50→480±46

Source: created by the authors.

Correlation analysis showed the presence of significant relationships between the level of anxiety and physiological indicators of adaptation (Table 6).

Table 6. Correlation dependencies between anxiety indicators and physiological parameters

Parameter 1	Parameter 2	Correlation coefficient (r)
Situational anxiety level	Heart rate	0.65 ($p<0.05$)
Stress resistance level	Cortisol level	-0.58 ($p<0.05$)
Blood pressure	Heart rate variability	-0.45 ($p<0.05$)

Source: created by the authors.

The correlation coefficient between the level of situational anxiety and heart rate was $r=0.65$ ($p<0.05$), indicating a direct correlation between the level of stress and the cardiovascular system's reaction. An increased level of anxiety can cause an increased heart rate, which is the physiological response of the organism to stress. In addition, a negative correlation was found between the level of stress tolerance and cortisol levels ($r=-0.58$, $p<0.05$), confirming the influence of psychological adaptation on biochemical markers of stress.

Comparative analysis of psychophysiological indicators also revealed that the level of anxiety and stress tolerance was strongly dependent on the social support provided to the students. Those students who reported a high degree of social support from classmates and lecturers in the survey results showed lower levels of situational and personality anxiety by the end of the semester. This study highlights the importance of creating a supportive social environment for international students. Social support plays a key role in the enrolment process and helps reduce stress (15). Students who have positive relationships with teachers and peers tend to be more resilient and less anxious.

The results show a significant change in anxiety levels among international students studying at a medical university in Kyrgyzstan, which is associated with improved stress levels (16). At the end of the study, stress responses decreased, and body temperature increased (Table 3). This indicates that students are gradually adapting to their new learning and living environment. The gender gap in development highlights the need for gender-specific programs that support students' gender identity. This study also highlights the importance of building social networks and a supportive learning environment to improve students' academic performance. Therefore, this investigation demonstrates the value of a comprehensive approach to supporting the adaptation of international students. Providing a positive learning environment and social interaction helps reduce stress levels and increase student motivation (17-19).

In the process of students' adaptation, numerous factors have been identified that influence their psychophysiological state. In particular, factors such as climatic conditions, cultural differences, academic workload, and social isolation play an important role (20,21). As the results of the stress tolerance study showed, students who came from countries with warmer climates were more likely to report acclimatisation problems and sleep disturbances, which in turn had a negative impact on their psychophysiological state and anxiety levels. Given these characteristics, it is recommended that consideration be given to climatic differences and that additional support measures be provided for students from regions with climates that differ significantly from the local conditions.

Cultural differences play a significant role in how international students perceive themselves (22). Students who have difficulty integrating into a new culture tend to have higher

levels of anxiety and less ability to cope with challenges (23,24). This is especially true for students who have a language barrier and limited opportunities to interact with native speakers. In such circumstances, it is important to create an environment that encourages intercultural communication and organise activities that promote understanding and acceptance of cultural differences, as well as a welcoming atmosphere and a sense of belonging (25). This includes organising cultural events, providing support to student advisors, and using other measures to facilitate cultural exchange.

The results bring attention to the need to develop support programs for international students aimed at improving their adaptation to the learning process and living conditions. In particular, it is important to arrange stress management courses, provide psychological support, and conduct regular medical examinations to monitor physiological indicators. These interventions not only improve students' overall performance but also lead to improved academic achievement and a sense of belonging. Individual counselling, group stress management, meditation, and mental health programs aimed at improving students' mood and reducing stress provide psychological support. International students require a variety of support from organisations, including mental health professionals, social workers, and medical professionals, to adjust to their new schools and homes. Because students' levels of anxiety, their ability to cope with difficulties, and their cultural and environmental contexts vary, it is important to ensure that all students feel safe and comfortable in their schools and communities. This helps students better cope with stress, which in turn leads to improved academic achievement and self-esteem.

DISCUSSION

The findings indicate that international students enrolled in medical universities in the Kyrgyz Republic undergo substantial alterations in psychophysiological indicators during their adaptation to new living and educational environments. These changes impact both the psycho-emotional state and physiological factors, underscoring the necessity for a holistic and interdisciplinary strategy to assist students during their readjustment.

One of the key indicators identified in the study was the high level of situational anxiety registered in 60 % of students at the beginning of the academic term. Using the Spielberger-Hanin scale showed that the average value of situational anxiety level was 48.2±5.6 points, which exceeds the norm for this age group (30-45 points). This comparison enables us to confirm the significance of the identified results and their applicability in the context of international student adaptation. Zhao and Xue (26) also noted a high level of anxiety in international students who first entered a new cultural and learning environment. Specifically, by the end of the semester, the level of situational anxiety had decreased to 42.3±4.8 points, indicating that students were gradually adapting to the new environment. A study by Dai and Hardy (27), who studied coping mechanisms of international students at a medical university in Europe, found similar results. Forty percent of the students reported high levels of anxiety, with a mean score of 52.1±6.1. This indicates persistent anxiety associated with strong control processes. According to Shroff et al. (28), anxiety among international students decreased as they became accustomed to the new environment, especially during interactions. This study also supports the importance of psychological interventions, such as stress management programs and individual counselling, in reducing persistent anxiety.

Students' stress tolerance was assessed using a special questionnaire, and 55 % of the study participants showed high levels of stress at the beginning of the academic term. The stress tolerance score was 34.5 ± 4.3, indicating that students were unable to cope with academic and family problems. Similar results were obtained in the studies of Bai et al. (29) and Antoniou et al. (30). International students showed difficulties in adapting to the new country in the first months, as confirmed by Lopez-Gil et al. (31). This score increased to 41.7±3.9 at the end of the season, as confirmed by Fuady et al. (32). This comparison demonstrates that social support is an important factor in the adaptation process of students. Physiological parameters such as blood pressure and heart rate change significantly during the transition. At the beginning of the academic year, 45 %

of students had systolic blood pressure (mean value 135/85 mmHg) higher than the normal level for their age (120/80 mmHg). These results support the findings of Yilmaz et al. (33) and Beltrán-Velasco et al. (34), who demonstrated the effects of stressors on the cardiovascular system of international students. On the other hand, Yu et al. (35) did not find a significant decrease in blood pressure during transplantation, suggesting that these symptoms are related to the human heart. However, in this study, a clearer trend of blood pressure reduction was noted by the end of the semester to 128/82 mmHg, indicating stabilisation of physiological indices as adaptation progresses, which also allows for more accurate conclusions about the positive impact of adaptation mechanisms.

HR at the beginning of the semester averaged 82±6 beats per minute, which is higher than normal (60-80 beats per minute). This elevated rate is probably related to high levels of anxiety and stress. Similar results were obtained in the studies of Cemalcilar and Falbo (36) and Vergeles (37), where an increase in HR was also observed in students under stressful conditions. By the end of the semester, HR decreased to 76±5 beats per minute, indicating an improvement in the organism's adaptive capabilities.

A key stress indicator, cortisol levels, also showed a positive trend. At the beginning of the semester, 50 % of students had the highest serum cortisol concentrations (mean 580±50 nmol/L). This confirms that stress significantly affects their well-being. This comparison demonstrates that the observed upward trends among international students are similar to those found in other studies and confirms the generality of the observed pattern, which is consistent with the findings of Ma et al. (38) and Brisset et al. (39), highlighting the significance of the results obtained. By the end of the semester, cortisol levels had decreased to 470±45 nmol/L, indicating improved adaptation with reduced stress. Cortisol levels are an important indicator of how the body responds to stress. As noted by Wang et al. (40), lower cortisol levels indicate the effectiveness of stress management strategies. This comparison suggests that lower cortisol levels are a key indicator of successful adaptation, which is consistent with previous research findings and supports some of the identified coping strategies.

Gender differences were another important variable in this study. At the beginning of the semester, girls had higher anxiety levels (50.3±5.8 points), which may be related to a greater awareness of their stress responses (41). This finding is consistent with Alam et al. (42), who found that girls were more sensitive to stress. By the end of the semester, girls' anxiety decreased but remained higher than boys', suggesting that gender-specific support may also play a role, as found in the study by Jiang et al. (43). This highlights the importance of developing gender-inclusive programs to help students develop positive self-efficacy. Blood pressure measurements also showed differences. At the beginning of the semester, girls' blood pressure (138/87 mmHg) was higher than boys' (132/83 mmHg), which may impact their mental health (40). Lai et al. (44) showed that girls tended to exhibit more symptoms during a traumatic event. Values decreased by the end of the semester, indicating stable and corrected weight gain.

Correlation analysis revealed a significant relationship between anxiety levels and physiological indicators. The correlation coefficient between situational anxiety levels and heart rate was $r=0.65$ ($p<0.05$), indicating a direct relationship between stress levels and cardiovascular responses. Similar results were obtained by Török et al. (45) and Zhu et al. (46), which emphasised the importance of stress management to improve students' physical health. Thus, the results of this study confirm the importance of psychophysiological changes in the adaptation process of international students. These results are consistent with the results of many studies, such as those by Lopez-Gil et al. (31) and Alam et al. (42), which emphasise the need for a comprehensive approach to supporting international students. In particular, it is important to provide appropriate stress management and psychological support programs, considering gender differences and levels of social support. In addition, creating a supportive learning and social environment can significantly reduce stress levels and increase students' resilience, positively affecting their academic success and overall health.

CONCLUSIONS

International students studying at medical universities of the Kyrgyz Republic experience significant changes in psychophysiological indicators during the adaptation process to new living and study conditions. The study showed that international students in these universities undergo significant changes in psychophysiological indicators due to adaptation to new living and study conditions. The main factors affecting their condition include altitude hypoxia, climatic peculiarities, social isolation, and study loads. This stress, which was initially perceived as a serious challenge related to cross-cultural adaptation, was reflected in psychological and physiological indicators measured throughout the semester.

At the beginning of the semester, 60 % of students reported high levels of situational anxiety, while 55 % reported low levels of stress resilience. By the end of the semester, situational anxiety had decreased to 42.3 points, and their stress resilience had increased to 41.7 points. However, subjective anxiety remained elevated in 40 % of students, with a mean score of 52.1 points. Changes in physiological parameters, such as blood pressure and heart rate, indicated increased adaptive processes. During the training, blood pressure decreased from 135/85 mm Hg to 128/82 mm Hg, and heart rate decreased from 82 to 76 beats per minute. These results are consistent with interactive models of stress management, suggesting that increased resilience is reflected in reduced stress levels and physiological responses.

The ethnically determined decrease in functional residual lung capacity correlates with decreased reserve expiratory volume with normal residual lung volume and, consequently, decreased normal vital capacity values specific to this population. The level of the main stress marker, cortisol, was elevated in 50 % of students at the beginning of the term, and the value of which was reduced by the end of the term, from 580 to 470 nmol/L. Blood glucose level was elevated in 20 % of students at the beginning of the study (mean value 5.9±0.4 mmol/L), which may be due to increased stress levels and dietary changes. By the end of the semester, the mean value of glucose level decreased to 5.4±0.3 mmol/L, indicating stabilisation of metabolic processes and improvement of students' diets as they adapted to new conditions.

Correlation analysis revealed a statistically significant positive correlation (r=0.65) between anxiety levels and physiological measures of stress coping, such as blood pressure, heart rate, and heart rate variability. An inverse relationship was also found between stress tolerance levels and cortisol levels (r=-0.58), confirming the influence of psychological stress coping on biochemical measures of stress. These results demonstrate relatively stable personality traits over time, supporting the aim of this study – to examine the interaction between cognitive, affective and emotional responses and physiological coping in the context of cross-cultural academic stress, outlined by the interactional model of stress and coping.

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Predictores de progresión de la infección por VIH en niñas, niños, adolescentes y jóvenes por transmisión materno infantil en una institución proveedora de servicios especializada, Montería

Predictors of progression of HIV infection in girls, boys, adolescents and young people by mother-to-child transmission in a specialized service provider institution, Montería

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RESUMEN

Objetivo: *Analizar predictores de progresión de la infección por VIH en niñas, niños, adolescentes y jóvenes por transmisión materno-infantil, enfocándose en carga viral, recuento de linfocitos CD4, y tratamiento antirretroviral, para aportar a la formulación de políticas públicas.* **Métodos:** *Se realizó un estudio descriptivo, analítico y correlacional en una Institución Proveedora de Servicios especializada de la ciudad de Montería, Colombia, en 2023, con 53 participantes (rango de edades:1-28 años) que viven con VIH por transmisión materno-infantil. Se emplearon fuentes primarias (historias clínicas) y análisis cuantitativo mediante tablas de frecuencia, pruebas de Chi-cuadrado y Spearman para evaluar asociaciones entre variables sociodemográficas, virológicas e inmunológicas.* **Resultados:** *La mayoría de los participantes estaba en adolescencia o juventud (75,5 %), y predominó el género masculino. La mayor parte inició tratamiento antirretroviral (TAR) con inhibidores de la transcriptasa inversa análogos de nucleósidos y nucleótidos. Se observó una disminución en la carga viral y recuento de linfocitos CD4 desde el diagnóstico al último registro, sin rechazar la hipótesis nula de igualdad de medias, es decir, que en términos clínicos y bilógicos la ausencia de diferencias significativas no implica falta de efectividad del tratamiento, sino que refleja la influencia de múltiples factores clínicos y la necesidad de un seguimiento individualizado para realizar ajustes terapéuticos según sea necesario; además, se encontró una asociación significativa entre la edad y el estadio clínico actual.* **Conclusiones:** *Los hallazgos de este estudio refuerzan la importancia del autocuidado y el tratamiento oportuno en la reducción de la transmisión materno-infantil del VIH. Se evidencia la necesidad*

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de enfocar políticas públicas y programas de salud en la población adolescente y joven, basándose en los predictores de progresión identificados.

Palabras clave*: VIH, transmisión, materno-infantil, niños, niñas, adolescentes, jóvenes.*

SUMMARY

Objective: *To analyze predictors of HIV progression in girls, boys, adolescents, and young people with mother-to-child transmission, focusing on viral load, CD4 lymphocyte count, and antiretroviral treatment, to contribute to the formulation of public policies.* **Methods:** *In 2023, a descriptive, analytical, and correlational study was conducted at a specialized healthcare center in the city of Monteria, Colombia. 53 participants (age range: 1-28 years) lived with HIV due to mother-to-child transmission. Primary sources (medical records) and quantitative analysis using frequency tables, Chi-Square tests, and Spearman correlation were employed to evaluate associations between sociodemographic, virological, and immunological variables.* **Results:** *Most participants were adolescents or young adults (75.5 %), with a predominance of males. Most began antiretroviral treatment (ART) with nucleoside and nucleotide reverse transcriptase inhibitors. A decrease in viral load and CD4 lymphocyte count was observed from diagnosis to the last recorded measurement without rejecting the null hypothesis of mean equality. This suggests that, clinically and biologically, the absence of significant differences does not imply treatment ineffectiveness but rather reflects the influence of multiple clinical factors and the need for individualized follow-up to make therapeutic adjustments as needed. Additionally, a significant association was found between age and current clinical stage.* **Conclusions:** *The findings of this study emphasize the importance of self-care and timely treatment in reducing mother-to-child HIV transmission. The need to focus public policies and health programs on the adolescent and young population, based on the identified predictors of progression, is evident.*

Keywords: *HIV, transmission, mother-to-child, children, adolescents, young people.*

INTRODUCCIÓN

El virus de inmunodeficiencia humana (VIH) provoca el síndrome de inmunodeficiencia adquirida (SIDA), afectando a un número importante de individuos globalmente, con complejidades biológicas y repercusiones sociales diversas. Es transmisible por fluidos corporales y puede cruzar la barrera placentaria o transmitirse durante el parto y la lactancia. No hay cura, solo tratamiento antirretroviral para retrasar la enfermedad (1).

En este contexto, de acuerdo con la hoja informativa del Programa Conjunto de las Naciones Unidas sobre el VIH/Sida (ONUSIDA) sobre estadísticas mundiales de VIH, en el año 2022, indicó que 39 millones de personas en todo el mundo vivían con el VIH; de los cuales 37,5 millones eran adultos (Edades:15 años o más), 1,5 millones eran niños (Edades:0-14 años), El 53 % de todas las personas que viven con el VIH son mujeres y niñas. Asimismo, 1,3 millones de personas se infectaron por el VIH, 630 000 personas murieron de enfermedades relacionadas con el SIDA y 29,8 millones de personas accedían a la terapia antirretroviral en el mismo año (2). En Colombia entre los años 2018 a 2023 se registraron 315 casos en gestantes (1,5 %) y madre e hijo 101 casos (0,49 %), respectivamente (3).

Ahora bien, según el Sistema de Vigilancia en Salud Pública (SIVIGILA) en el departamento de Córdoba, entre los años 2006 al 2022 se notificaron 128 casos de transmisión materno infantil (4), estas cifras reflejan la problemática de salud pública en el departamento a pesar de las estrategias e iniciativas a nivel internacional y nacional para alcanzar la meta de eliminación al año 2030 y reducir el porcentaje de transmisión materno infantil del VIH a 2 % o menos.

En vista de la magnitud de esta problemática, se procedió a realizar el presente estudio, cuya finalidad fue analizar los predictores de progresión de la infección por VIH derivada de la transmisión materno-infantil, utilizando un estudio descriptivo, analítico y correlacional centrado en la carga viral, el recuento de linfocitos CD4, y el tratamiento de estos, todo esto, mediante la caracterización socio demográfica, clínica y virológica. Esto permitirá llenar un vacío de conocimiento, proporcionando una primera aproximación a la realidad de este evento a nivel local. La información obtenida, respaldada por una sólida validez científica, contribuirá a la

formulación de políticas públicas orientadas a mejorar la salud y el bienestar de niñas, niños, adolescentes y jóvenes con VIH adquirido por transmisión materno-infantil. Igualmente servirá como base para el desarrollo de programas específicos que generen un impacto positivo a futuro.

MÉTODOS

El diseño de este estudio fue descriptivo, correlacional-analítico de enfoque cuantitativo; por la distribución de las observaciones es un estudio transversal y retrospectivo.

Se incorporan a la muestra 53 niñas, niños, adolescentes y jóvenes que viven con VIH (edades entre 1 y 28 años) de una Institución Proveedora de Servicios (IPS) especializada de la ciudad de Montería, Colombia, en 2023.

En este estudio se utilizaron como variables las características sociodemográficas, basales, virológicas e inmunológicas, entre ellas, la edad, sexo, procedencia, año del diagnóstico de infección por VIH, recuento de linfocitos CD4, carga viral, año de inicio del tratamiento antirretroviral (TAR), número de tratamientos previos y si el paciente recibe TAR. La información fue obtenida de fuentes primarias de información a partir de las historias clínicas.

Criterios de inclusión y exclusión

El estudio incluyó a niñas, niños, adolescentes y jóvenes con VIH adquirido por transmisión materno-infantil, quienes reciben atención en una Institución Prestadora de Servicios (IPS) de salud especializada en esta población. Se excluyeron del estudio a niñas, niños, adolescentes y jóvenes con VIH adquirido por vías de transmisión distintas a la materno-infantil, así como a quienes reciben atención en una IPS diferente a la establecida en los criterios de inclusión.

Análisis de datos

Para el análisis de los datos, se utilizaron tablas de frecuencia para presentar la distribución de las diferentes variables de interés del estudio, expresadas en cantidades y porcentajes. Para el recuento de linfocitos CD4, se aplicó una prueba de diferencias de medianas, por la no normalidad de los datos, haciendo necesaria la utilización de una prueba no paramétrica, en este caso la prueba de Kruskall-Wallis para comparar los resultados del conteo de linfocitos y de la carga viral al momento del tratamiento antirretroviral y en el último conteo o carga viral. Esto con el fin de determinar si existe una diferencia significativa entre el recuento de linfocitos CD4 al momento del diagnóstico y al inicio del TAR.

Asimismo, se empleó la prueba de Chi-Cuadrado para evaluar la asociación entre el estadio clínico al momento del diagnóstico y el estadio clínico actual con características sociodemográficas como el rango de edad y el sexo, con el propósito de identificar relaciones significativas entre las variables categóricas analizadas. Finalmente, se aplicó la prueba de correlación de Spearman para examinar la relación entre variables ordinales o de intervalo, permitiendo medir la fuerza y dirección de la asociación, ya sea positiva o negativa, con el objetivo de establecer si existe una relación monotónica significativa entre las variables de interés.

Consideraciones éticas

Esta investigación ha sido clasificada como "sin riesgo ético" acorde con los parámetros establecidos en la Resolución 8430 de 1993 de Colombia. La titularidad de los hallazgos corresponde al equipo autor y a su grupo de trabajo interinstitucional; los resultados podrán ser publicados dando el respectivo crédito a las autoras.

RESULTADOS

El análisis revela que la mayoría de la población se encuentra en las etapas de adolescencia y juventud, representando el 75,5 % del total. Dentro de este grupo, el 37,7 % corresponde a adolescentes y jóvenes, de los cuales el 60 % son masculinos y el 40 % femeninos en la

adolescencia, mientras que en la juventud el 70 % son masculinos y el 30 % femeninos. La infancia constituye el 15,1 % de la población, con una distribución del 62,5 % femenino y el 37,5 % masculino. Por otro lado, la primera infancia representa el 9,4 % del total, con un 80 % de sexo masculino y un 20 % femenino, siendo la categoría con menor participación en el estudio. Asimismo, se observa que la mayoría de los participantes residen en Montería, representando el 35,8 % del total de la población, seguido por el municipio de Ciénega de Oro con un 11,3 % y Cereté con un 9,4 %. En relación con la profilaxis con antirretrovirales al momento del nacimiento, el 98,1 % de la población no la recibió, mientras que solo el 1,9 % sí tuvo acceso a este tratamiento preventivo. Además, la distribución según el estadio de la enfermedad muestra que el 43,4 % de los participantes se encuentran en el estadio 1, el 30,2 % en estadio desconocido, y el 26,4 % en el estadio 3 de la enfermedad por VIH (Figura 1).

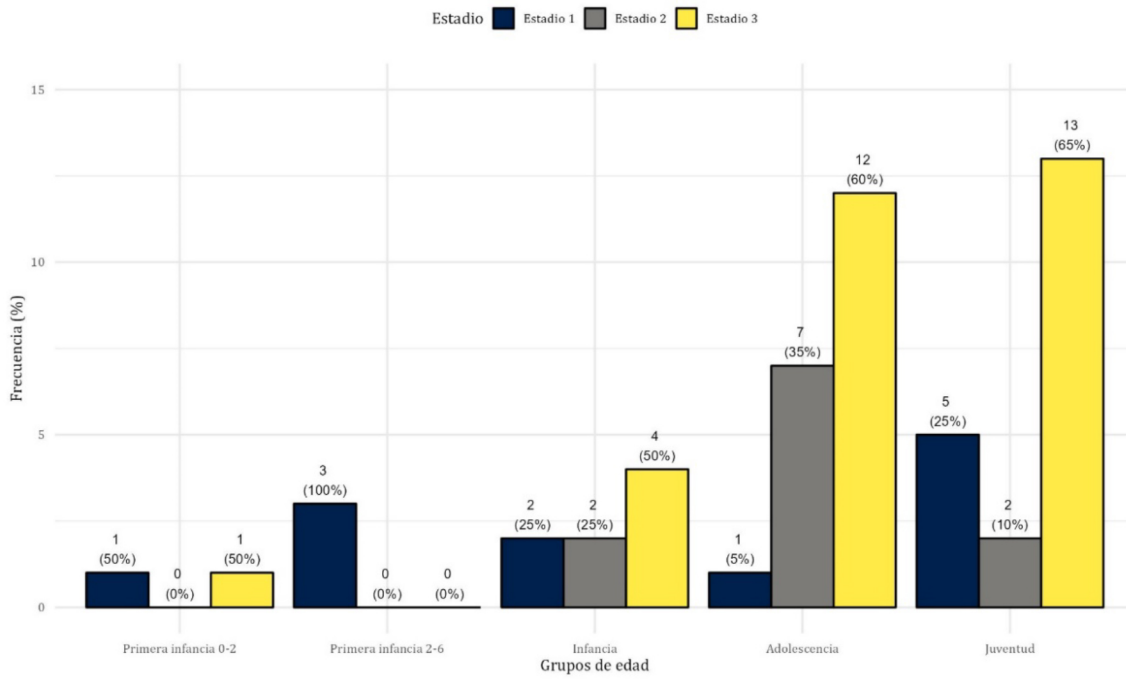


Figura 1. Distribución del estadio clínico actual por grupo de edad.

El Cuadro 1 presenta los medicamentos con los que se inició la terapia antirretroviral (TAR) en la población estudiada. Se observa que el 92,5 % de los participantes iniciaron el tratamiento con ITIAN (Inhibidores de la transcriptasa inversa análogos de nucleósidos y nucleótidos) como medicamento 1. Para el medicamento 2, el 69,8 % de la población también utilizó ITIAN. En cuanto al medicamento 3, los inhibidores de la proteasa fueron los más empleados, con un 45,3 % de los casos. Cabe destacar que el 84,9 % y el 98,1 % de los participantes no recibieron medicamentos 4 y 5, respectivamente.

Respecto a los medicamentos que ocasionaron cambios en la TAR, se identificó que en el 45,3 % de los casos, los inhibidores de la proteasa fueron el motivo de cambio de esquema de tratamiento. En los medicamentos 2, 3, 4 y 5, la mayoría de los participantes (83,0 %, 92,5 % y 100 %, respectivamente) no presentaron cambios, lo que indica que conservaron el mismo esquema con el que iniciaron la TAR.

Cuadro 1. Medicamentos con los que inicia la terapia y los que ocasionan el cambio.

Medicamento	Medicamentos con los que inicia la terapia									
	Medicamento 1		Medicamento 2		Medicamento 3		Medicamento 4		Medicamento 5	
Inhibidores de la proteasa	2	3,8 %	11	20,8 %	24	45,3 %	7	13,2 %	0	0,0 %
(INI) Inhibidores de la integrasa	0	0,0 %	1	1,9 %	1	1,9 %	0	0,0 %	0	0,0 %
ITIAN (Inhibidores de la transcriptasa inversa análogos de nucleósidos y nucleótidos)	49	92,5 %	37	69,8 %	2	3,8 %	0	0,0 %	0	0,0 %
(ITINN) Inhibidores de la transcriptasa inversa no análogo de nucleósidos	0	0,0 %	0	0,0 %	9	17,0 %	0	0,0 %	0	0,0 %
no recibió otros medicamentos	0	0,0 %	3	5,7 %	16	30,2 %	45	84,9 %	52	98,1 %
desconocido	2	3,8 %	1	1,9 %	1	1,9 %	1	1,9 %	1	1,9 %
Total	53	100,0 %	53	100,0 %	53	100,0 %	53	100,0 %	53	100,0 %
	Medicamentos que ocasionan el cambio									
(ITINN) Inhibidores de la transcriptasa inversa no análogo de nucleósidos	6	11,3 %	1	1,9 %	1	1,9 %	0	0,0 %	0	0,0 %
ITIAN (Inhibidores de la transcriptasa inversa análogos de nucleósidos y nucleótidos)	16	30,2 %	4	7,5 %	0	0,0 %	0	0,0 %	0	0,0 %
Inhibidores de la proteasa	24	45,3 %	3	5,7 %	3	5,7 %	0	0,0 %	0	0,0 %
(INI) Inhibidores de la integrasa	0	0,0 %	1	1,9 %	0	0,0 %	0	0,0 %	0	0,0 %
Desconocido	3	5,7 %	0	0,0 %	0	0,0 %	0	0,0 %	0	0,0 %
No aplica	4	7,5 %	44	83,0 %	49	92,5 %	53	100,0 %	0	0,0 %
Total	53	100,0 %	53	100,0 %	53	100,0 %	53	100,0 %	0	0,0 %

Fuente: Base de datos de seguimiento a paciente

En relación con el número de medicamentos al inicio de la TAR, el mayor porcentaje corresponde a tres medicamentos (54,7 % del total), seguido de dos medicamentos (24,5 %), cuatro medicamentos (13,2 %), un medicamento (5,7 %) y, finalmente, cinco medicamentos (1,9 %). Por otro lado, tras los cambios en la terapia, el mayor porcentaje de la población (75,5 %) utilizó un solo medicamento, seguido por el 9,4 % con dos medicamentos y el 7,5 % con tres medicamentos.

Las principales causas de cambio de medicación fueron la intolerancia o los efectos secundarios, que afectaron al 47,2 % de la población, siendo los grupos de juventud (44 %) y adolescencia (36 %) los más afectados. Otra causa relevante fue la falla terapéutica, virológica, clínica o inmunológica, con un 17 % de los casos, impactando principalmente a la infancia (33 %), primera infancia (22 %) y las etapas de adolescencia y juventud. Asimismo, el cambio para facilitar la adherencia al tratamiento representó otro 17 %, con mayor prevalencia en adolescentes (66,7 %), seguidos por jóvenes (22,2 %) e infantes (11,1 %). Además, se evidencia que el 98,1 % de la población está recibiendo TAR, mientras que solo el 1,9 % no recibe tratamiento.

En cuanto a la clasificación según el estadio clínico actual, el 56,6 % de los participantes se encuentran en estadio desconocido, el 22,6 % en estadio 1 y el 20,8 % en estadio 3.

Para el análisis de las características virológicas, se consideró la carga viral tanto al momento del diagnóstico como al inicio de la TAR, mientras que las características inmunológicas se evaluaron a partir del recuento de linfocitos CD4 en los mismos momentos. Se calcularon estadísticas descriptivas como la media y la desviación estándar para evaluar la evolución de estos indicadores. Asimismo, se realizó una prueba de hipótesis para verificar si existieron cambios significativos en los resultados obtenidos, planteando las siguientes hipótesis:

H_0: No existe asociación entre las variables de estudio.

H_1: Existe asociación entre las variables de estudio.

El Cuadro 2 muestra una tendencia a la disminución del conteo de linfocitos CD4 y de la carga viral entre el momento del diagnóstico y el último registro disponible. Con un nivel de confianza del 95 %, no se rechaza la hipótesis de igualdad de medias en el conteo de linfocitos, lo que indica que las diferencias observadas no son estadísticamente significativas. Esto puede atribuirse a la alta variabilidad en los datos. En cambio, para la carga viral, si se evidencian diferencias estadísticamente significativas, con un p-valor < 0,0001, siendo inferior en el último valor (Figura 2).

Cuadro 2. Características Virológicas e inmunológicas

	Momento de diagnóstico e inicio TAR			**Valor de último conteo**			P-valor
	n	Media	Desv. Estándar	n	Media	Desv. Estándar	
Valor Conteo linfocitos CD4	32	1 272,22	1 252,82	53	867,28	617,75	0,0974
Valor de la carga viral	27	478 236,85	1 295 340,60	53	11 637,63	21 303,91	0,0726

Fuente: Base de datos.

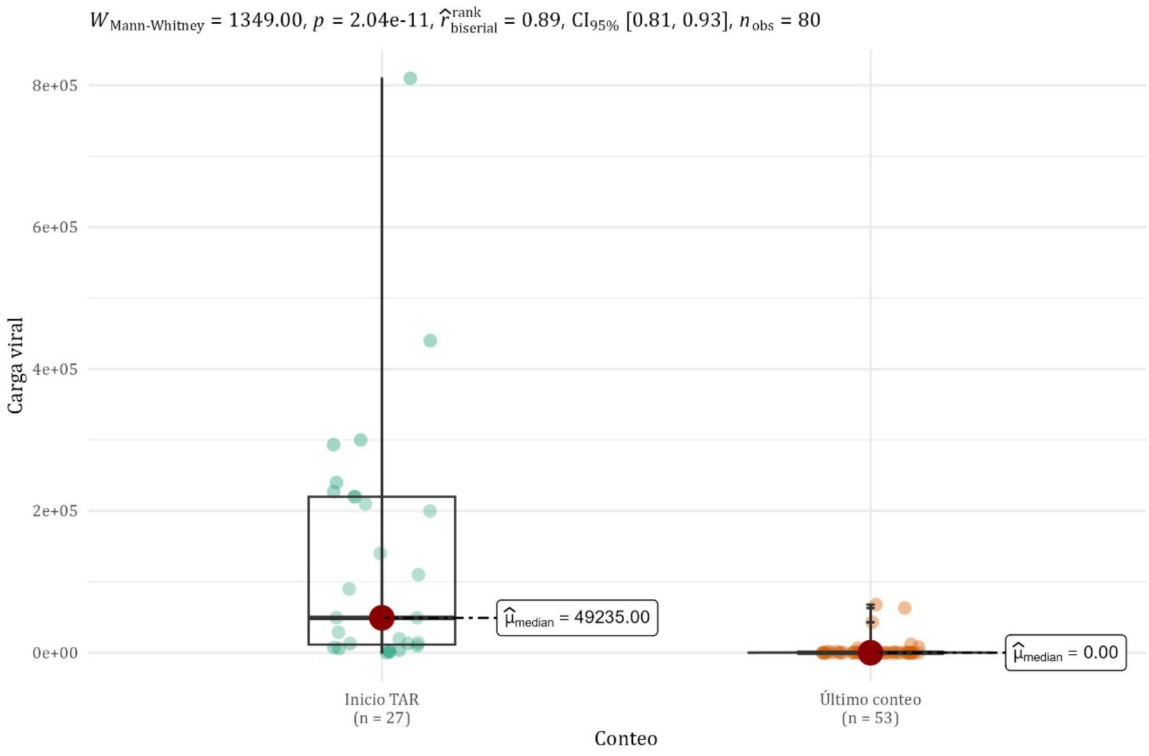


Figura 2. Prueba de Kruskal-Wallis para el valor de la carga viral por conteo.

Para analizar la asociación entre las variables sociodemográficas y los factores predictores de la progresión de la infección por el VIH, se aplicó la prueba de Chi-Cuadrado, que permite evaluar relaciones entre variables categóricas. Las hipótesis planteadas para este análisis son las siguientes:

H_0: No existe asociación entre las variables de estudio.

H_1: Existe asociación entre las variables de estudio.

Cuadro 3. Asociaciones entre variables sociodemográficas y estadio clínico

Variable	Estadio Clínico Momento Dx	Estadio clínico actual
Grupo de edad	7,995 (0,434)	17,651 (0,024) *
Sexo	0,462 (0,794)	1,237 (0,539)

Fuente: Historia clínica.

Como muestra el Cuadro 3, se obtuvo un valor de p de 0,024, el cual es inferior al nivel de significancia establecido de 0,05, lo que lleva al rechazo de la hipótesis nula y respalda la hipótesis alternativa. Esto indica que existe una asociación estadísticamente significativa entre el grupo de edad y el estadio clínico actual, con un nivel de confianza del 95 %, evidenciando una relación entre ambas variables. Por otro lado, la asociación entre el sexo y el estadio clínico, tanto en el momento del diagnóstico como en el estadio actual, no mostró una significancia estadística, con valores de p de 0,794 y 0,539, respectivamente, lo que sugiere la ausencia de una relación significativa entre estas variables.

Para evaluar la asociación entre variables cuantitativas del estudio, se empleó la prueba de correlación de Spearman, teniendo en cuenta el no cumplimiento del supuesto de normalidad, la cual permite analizar la relación entre dos variables ordinales o de intervalo. Las hipótesis planteadas para este análisis son:

H_0: No existe asociación entre las variables de estudio.

H_1: Existe asociación entre las variables de estudio.

En el Cuadro 4 se muestra una correlación significativa entre el conteo de linfocitos CD4 en el momento del diagnóstico y el conteo de linfocitos CD4 al inicio del TAR, con un valor de $p = 0,0001$ ($p<0,05$), lo que permite rechazar la hipótesis nula y aceptar la hipótesis alternativa, concluyendo que existe una asociación estadísticamente significativa entre estas variables.

Asimismo, se evidenció una correlación estadísticamente significativa entre el último conteo de linfocitos CD4 y la última carga viral, con un valor de $p = 0,021$ ($p < 0,05$), lo que indica una relación significativa entre estas variables.

En contraste, las demás correlaciones analizadas, como las relacionadas con la carga viral al inicio del TAR, no mostraron una asociación significativa, con valores de $p > 0,05$, sugiriendo la independencia de estas variables en los momentos evaluados.

Los resultados resaltan la importancia del seguimiento del recuento de linfocitos CD4 desde el diagnóstico hasta el inicio del tratamiento, así como la relación entre la evolución del conteo de linfocitos y la carga viral a lo largo del tratamiento.

Tabla 4. Correlación entre las variables características virológicas e inmunológicas

	Inicio TAR		Último conteo	
Conteo	Linfocitos CD4	Carga Viral	Linfocitos CD4	Carga Viral
Linfocitos CD4 Momento De Dx	0,933** (0,000)	0,210 (0,292)	-0,072 (0,690)	-0,004 (0,983)
Linfocitos CD4 momento inicio TAR	1	0,172 (0,391)	-0,037 (0,840)	-0,023 (0,899)
Carga Viral al inicio de la TAR		1	-0,045 (0,825)	0,192 (0,338)
Último conteo de linfocitos CD4			1	-0,316* (0,021)
Valor de la última Carga Viral				1

Fuente: Base de datos

DISCUSIÓN

Los hallazgos acerca de los predictores de progresión de la infección por VIH en niñas, niños, adolescentes y jóvenes con transmisión materno-infantil son significativos y reveladores, destacándose por su carácter innovador ante la ausencia de estudios previos directamente comparables. Esta falta de antecedentes similares resalta el valor pionero del estudio, que aporta conocimientos esenciales al campo del VIH pediátrico y juvenil. Los resultados obtenidos no solo amplían la comprensión de la enfermedad en esta población vulnerable, sino que también constituyen una base sólida para la formulación de políticas públicas y la implementación de programas de salud más eficaces, dirigidos a mejorar la calidad de vida y la atención integral de los afectados.

La disminución en la carga viral y el aumento en el recuento de linfocitos CD4 tras el diagnóstico son indicadores clave de que el tratamiento antirretroviral (TAR) está siendo efectivo para controlar la replicación del VIH y restaurar la función inmunológica. Esto confirma la importancia de la intervención temprana, ya que un inicio de tratamiento oportuno permite al sistema inmunitario fortalecerse, prolongar la vida del paciente y prevenir la progresión a etapas más avanzadas de la enfermedad como el SIDA. El seguimiento continuo de estas métricas es fundamental para asegurar la eficacia del TAR y ajustar la terapia según sea necesario, manteniendo al paciente lo más saludable posible.

La relación significativa entre la edad y el estadio clínico actual destaca la importancia de adaptar las estrategias de atención médica a las diferentes etapas del desarrollo humano. Esto significa que las intervenciones, tratamientos y enfoques de cuidado deben ser personalizados para cada individuo, tomando en cuenta sus características físicas, cognitivas y emocionales propias de su edad y etapa de desarrollo.

El hallazgo de que el 75,5 % de los participantes se encuentran en la adolescencia o juventud, con una predominancia del género masculino, destaca la urgencia de focalizar esfuerzos en estos subgrupos para optimizar los resultados de salud y reducir la transmisión del VIH. Además, la falta de profilaxis antirretroviral en un número significativo de participantes al nacer revela una necesidad urgente de mejorar las estrategias de prevención del VIH. Esto enfatiza la importancia de fortalecer las intervenciones durante el parto para reducir la transmisión materno-infantil. La falta de profilaxis antirretroviral al nacer es un indicador de áreas donde las intervenciones de prevención pueden ser mejoradas para proteger la salud de los recién nacidos y reducir la transmisión del VIH de madre a hijo.

Limitaciones

La ausencia de estudios previos directamente comparables en contextos donde se aplica la estadística inferencial resalta la importancia y el valor de los hallazgos obtenidos en esta investigación. La aplicación de técnicas estadísticas avanzadas permite no solo identificar patrones y relaciones dentro de la población estudiada, sino también generar inferencias aplicables a poblaciones más amplias,

contribuyendo a una mejor toma de decisiones en salud pública. La estadística inferencial, al proporcionar herramientas para evaluar la validez y generalización de los resultados, es fundamental para transformar datos individuales en evidencia científica robusta, permitiendo detectar tendencias, evaluar la efectividad de las intervenciones y diseñar estrategias de prevención más precisas y basadas en evidencia.

Este estudio, al abordar la progresión de la infección por VIH en poblaciones pediátricas y juveniles con transmisión materno-infantil, establece una base crítica para futuras investigaciones, ofreciendo un marco metodológico que puede ser replicado o ampliado en diversos entornos clínicos y poblacionales. La generación de evidencia confiable a partir de la estadística inferencial no solo fortalece el conocimiento científico, sino que también impulsa la formulación de políticas públicas eficaces, garantizando intervenciones oportunas y sostenibles. Por tanto, la investigación actual no solo llena un vacío de conocimiento, sino que también posiciona la estadística inferencial como un pilar esencial para la comprensión y el abordaje integral de esta problemática de salud.

CONCLUSIONES

Al caracterizar sociodemográficamente a las niñas, niños, adolescentes y jóvenes que viven con VIH por transmisión materno-infantil, se evidenció que el mayor porcentaje de los casos se encuentran en el curso del momento de vida de adolescencia y juventud, sexo masculino, procedente y residente en el municipio de Montería.

En relación con las características basales, virológicas e inmunológicas de las niñas, niños, adolescentes y jóvenes que viven con VIH por transmisión materno infantil, se rechaza la hipótesis nula, es decir, se asume que en promedio de carga viral y el conteo de linfocitos CD4 no es igual en el momento del diagnóstico y el último conteo de estos.

En cuanto a la asociación y correlación de las características sociodemográficas con los predictores de la progresión de la infección por el virus de inmunodeficiencia humana (VIH), se rechaza la hipótesis nula y se asume que hay una dependencia o asociación entre la edad y el estadio clínico actual a un 95 % de confianza y se esperaría que cada vez que se haga un estudio con estas mismas características se obtengan resultados similares, es decir, que estos resultados no fueron producto del azar.

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Psychosocial autopsy in cases of suicide in child and adolescent populations: A Systematic review

Autopsia psicosocial en casos de suicidio en poblacion de niños y adolescentes: Una revisión sistemática

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SUMMARY

The purpose of the study was to develop a systematic review to explore psychosocial autopsy in cases of completed suicide in a population of children and adolescents. The methodology was based on the Preferred Reporting Items for Systematic Reviews (PRISMA) and was supported by a quantitative approach, grounded in the principles of exploratory systematic reviews. The search considered publications in English focusing on the last five years (2020-2025) to compile the most recent studies in this thematic line, of which six investigations were included, identified in the SpringerOpen, Scopus, and Web of Science databases. The results indicate that social networks can be a risk for adolescent suicide by encouraging victimization and imitation, but also provide peer support, which highlights the need for digital literacy and cyberbullying prevention. Also, factors such as depression, family violence, and childhood abuse influence suicidal behavior. In addition, psychosocial autopsy is proposed as a key method to identify factors that can predict suicide and develop more effective intervention strategies in this vulnerable population.

Keywords: *Psychosocial autopsy, suicide, children, adolescents, PRISMA.*

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RESUMEN

El propósito de este estudio fue desarrollar una revisión sistemática para explorar la autopsia psicosocial en casos de suicidio consumado en una población de niños y adolescentes. La metodología se basó en los Elementos de Información Preferidos para Revisiones Sistemáticas PRISMA, y se apoyó en un enfoque cuantitativo basado en los principios de la revisión sistemática exploratoria. La búsqueda tuvo en cuenta las publicaciones en inglés centradas en los últimos cinco años (2020 - 2025) para recopilar los estudios más recientes en esta línea temática, de los cuales se incluyeron 6 investigaciones identificadas en las bases de datos SpringerOpen, Scopus y Web of Science. Los resultados indican que las redes sociales pueden ser un riesgo para el suicidio adolescente al fomentar la victimización y la imitación, pero también proporcionan apoyo entre iguales, lo que pone de manifiesto la necesidad de la alfabetización digital y la prevención del ciberacoso. Asimismo, factores como la depresión, la violencia familiar y los malos tratos en la infancia influyen en el comportamiento suicida. Además, se propone la autopsia psicosocial como método clave para identificar los factores que pueden predecir el suicidio y desarrollar estrategias de intervención más eficaces en esta población vulnerable.

Palabras clave: *Autopsia, psicosocial, suicidio, niños, adolescentes, PRISMA.*

INTRODUCTION

Suicide is a growing public health problem worldwide and is among the ten leading causes of death in many countries, with more than 700 000 people losing their lives each year due to this phenomenon (1). Its complexity, influenced by psychosocial and psychiatric factors, has made its prevention a constant challenge, being considered a multifactorial phenomenon affected by several variables.

In a report by the Pan American Health Organization (PAHO) (2) on violence and health, it stated that in the year 2000 some 815 000 people died from this cause worldwide, representing a global annual mortality rate of 14.5 per 100 000 people, equivalent to 1 death every 40 seconds; however, suicidal behavior varies between countries and even between regions with similar levels of development. Colombia has experienced a significant increase in cases since 1998, from 1.3 to 5.5 events per 100 000 people in 2002. Between 2008 and 2010, the average suicide rate in men was 6.0 per 100 000 people, while in women it ranged from 3.6 to 4.1 per 100 000 people. For 2011, according to preliminary data from the National Institute of Legal Medicine and Forensic Sciences (INMLCF), there were 1 625 cases, representing a rate of 3.5 per 100 000 people.

Among the populations most affected by this phenomenon are children, where it is the second leading cause of death in the 10-14 age group. Boys are approximately four times more likely to die by suicide than girls, who, in turn, are more likely to attempt suicide. At this stage of the life cycle, it is important to note that immature cognitive development affects children's ability to understand complex concepts such as causality, death, and suicide, which hinders their ability to handle stressful situations, make decisions, and solve problems. In addition, behavioral factors such as impulsiveness, coupled with family and environmental influences, play a crucial role in children's suicidal behavior (3,4).

Stressful events can trigger self-destructive actions, with attachment disorders, family discord and abuse being important risk factors. Likewise, family history of suicidal behavior and psychopathological characteristics, such as violence or substance abuse, increase the likelihood of suicide in children.

A widely accepted definition of suicide is that made by the World Health Organization (WHO), that understands it as an intentional action with a lethal outcome, which is carried out by a person with full knowledge or anticipation of this outcome, where biological, genetic, psychological, social and environmental factors interact and make it a complex problem (6). Another way of understanding suicide is from the perspective of Chávez-Hernández et al. (7), who define it as a multidimensional distress that an individual perceives as the best solution to their suffering. This distress is mainly characterized by intolerable psychological pain, originating in unmet psychological needs, and arising from emotions such as hopelessness and helplessness. In addition, it manifests itself in an ambivalent cognitive state that is not necessarily limited to people with psychiatric disorders. It also views

suicidal behavior as a continuum ranging from suicidal ideation to planning, attempts, and completed suicide, including the material and textual traces left by the subject.

However, numerous studies have reported a high prevalence of mental disorders among suicide victims, such as affective disorders, comorbidity with substance abuse and, in some cases, conduct disorders or bipolarity (8-10). However, a considerable percentage of these individuals have not received adequate psychiatric treatment before their death. It is estimated that only 14 % to 50 % of adolescents or young adults who commit suicide have had access to some form of prior treatment (10), highlighting a significant gap in early intervention. Although the identification of mental disorders has been key to understanding suicide, it remains insufficient to predict which individuals are most at risk. The lack of access to adequate psychiatric treatment is evident, especially when comparing suicide victims to psychiatric inpatients. However, since it is a multidimensional phenomenon, it is not possible to estimate specific causes if we only try to understand individual approaches, so it is necessary to propose alternatives for understanding at the psychosocial level, which allow us to analyze social factors and contexts, family, work and community dynamics, as well as sociocultural aspects, such as social support, stressful life events and the economic or community environment of the person, among others. It is understood that the psychological and social condition of the suicidal person is largely due to an inappropriate functioning between interdependence, interrelation and social reorganization (11).

Against this background, the need for innovative approaches to better understand the pathways leading to suicide is evident. In this regard, psychosocial autopsy has emerged as a key tool to investigate the factors that lead people to suicide, allowing for a comprehensive analysis of the risk factors and psychosocial circumstances surrounding the victims.

Continuing this same idea, psychosocial autopsy is an invaluable tool for improving understanding of the factors contributing to suicide and for addressing deficiencies in mental health systems. It is the most direct and effective technique for retrospectively investigating psychosocial and psychiatric factors influencing suicide (12). Through semi-structured interviews with family, friends, and people close to the victim, this method allows for the reconstruction of the person's living environment, identifying triggering factors, and assessing the utilization of mental health services. Through the detailed collection of retrospective information, this method can provide researchers and public policy makers with concrete data to enable them to formulate more targeted and effective suicide prevention strategies.

From the perspective of authors such as Campaña (13), suicide in Latin America is a phenomenon influenced by social, political and economic conditions. According to this author, factors such as unemployment, hunger, marginalization and socioeconomic changes generate hopelessness and loneliness, interacting with individual and family vulnerabilities to create a complex web that facilitates suicidal behaviors. In this context, psychosocial autopsy emerges as a crucial tool to unravel these complex interactions, as it is not limited to psychological aspects, but also examines the social and structural dynamics that affect individuals.

The value of psychosocial autopsy lies in its ability to detect variables that might be missed in traditional epidemiological or clinical studies. Factors such as personal circumstances, emotional state, untreated mental health problems, and previous suicide attempts can be analyzed in depth to identify patterns of risk. This approach facilitates the formulation of more specific and effective suicide prevention strategies by providing a comprehensive view of the victim's psychosocial and family context (13).

In coherence with the above, in the face of these challenges, although there are antecedents related to psychological autopsy, which have consolidated it as one of the most valuable methodologies for investigating completed suicide, there are limitations inherent to the retrospective nature of this tool, such as the bias of the data collected because, regardless of how many informants provide information on a suicide, it will never be possible to have accurate

data on the categories studied. This is because the most crucial perspective, that of the suicidal person, is not accessible (14).

These limitations do not detract from its application and use, as the study of completed suicide cases remains relevant and significant for the understanding of suicidal behaviors. However, psychosocial autopsy emerges as a key tool for advancing the knowledge of suicide. It not only provides detailed information on psychosocial and psychiatric factors, but also suggests crucial areas of intervention for prevention, such as improving access to psychiatric treatment and addressing less documented factors, such as exposure to suicidal behaviors and lack of early intervention, by determining the personality profile, personal, social, family and contextual motivations, as well as possible symbolic messages, latent in the execution of the suicidal act (9,15).

In recent years, very few psychological autopsy or psychosocial autopsy studies have been conducted among children and adolescents, which is not sufficient to determine the factors that indicate this phenomenon. These studies have identified not only mental disorders as a critical factor, but also a series of psychosocial variables, such as problems in family relationships, adverse life events, educational and legal difficulties, and family psychopathology (9,10,12), which justifies the importance of expanding the theoretical and empirical input around this phenomenon.

The phenomenon of suicide in children

The phenomenon of suicide among children in Colombia represents a public health problem that has been on the rise over the last decade, with 2 727 children reported to have committed suicidal acts. This figure corresponds to an average of six cases per week (16). This reflects not only a crisis in child mental health but also shows deficiencies in the structural systems of care and suicide prevention in this population.

The reported statistics are alarming, since during the COVID-19 pandemic, suicide attempts in the country reached a rate of 722 attempts per 100 000 inhabitants, representing a increase of 25 %, of which 39 % involved suicide attempts in minors (17). These data indicate that factors such as social isolation and the interruption of social and school routines of minors may have contributed to the deterioration of their mental health. Nevertheless, in the post-pandemic period, cases continued to increase considerably in the country, with 145 suicides of children between the ages of 6 and 17 years reported between January and June 2024 (18). Similarly, in 2023, during the first semester, the Attorney General's Office (19), issued a report where 1 540 suicides were recorded in Colombia, of which 1 % corresponded to suicides in early childhood, followed by 9.4 % in adolescents and 31 % in young people, which shows an upward trend towards immediate intervention programs. Given this, the Family Welfare Institute (20,21) highlights the need to focus prevention strategies on the child population, since the reports of Forensics (22) show that 43 % of suicides tend to focus on people between 5 and 25 years of age.

According to the Ministry of Health and Social Protection, between 2019 and 2023, there were 164 400 suicide attempts in the country. Of these, 51 373 were children and adolescents; that is, 31 % of the national total of attempts occurred in the age range of 5 to 17 years. The number of suicide attempts in children and adolescents fluctuated and decreased between 2019 and 2021; however, the most significant change occurred between 2021 and 2022, where a percentage variation of 41 % more is identified for 2022, and between that year and 2023, there was a brief decrease of 111 attempts (23).

According to the Observatorio de la Niñez, the main risk factors for suicide in children, adolescents, and young people are related to mental problems and disorders, marital conflicts, abuse, sexual violence, and socioeconomic difficulties (21). Faced with this problem, several authors have seen the urgent need to study the factors that contribute to the maintenance and increase of this phenomenon. The Save the Children Colombia Foundation (18) mentions some socioeconomic factors such as school bullying, high levels of poverty, social discrimination or lack of access to mental health services. Likewise, factors such as repeated exposure to armed conflict increase the vulnerability of minors.

On the other hand, studies carried out by Gómez-Tabares (24) mention predisposing factors such as the presence of mental disorders

in children, such as anxiety and depression, which are usually represented in impulsive and violent behaviors in minors, as well as low self-esteem and hopelessness, also play a relevant role in the appearance of self-injurious behaviors. On the other hand, Galvis et al. (25) affirm that neurobiological alterations and family psychiatric or suicidal behavioral antecedents are strong predisposing factors in the development of suicidal ideation.

Other factors such as the social and cultural context and the family area have also been studied as possible predisposing factors for suicidal behavior. In this sense, Cañón-Buitrago (26) states that suicidal behavior is determined by difficulties in the family system, such as the presence of sexual abuse, negligent parenting styles and domestic violence, situations that are usually not easily detected due to the absence of adequate tools for the management of frustration and conflict resolution at that specific stage of development. Likewise, the Instituto Colombiano de Bienestar Familiar (ICBF) (20,21) mentions that the cultural and social context also has a significant impact on the appearance of suicidal behaviors in childhood, since the presence of school bullying, social exclusion, and discrimination can generate feelings of hopelessness and isolation behaviors. Exposure to recurrent traumatic events increases the possibility of developing self-injurious behaviors.

This shows the urgent need to recognize the importance of mental health prevention in children as a collective responsibility, since the lack of knowledge of mental health in educational institutions, as well as the barriers to access to professional services in this area, must be addressed urgently (27). Thus, including emotional formation and character strengths in academic institutions is a fundamental factor in the prevention of suicidal behavior in minors.

Suicide Phenomenon in Adolescents and Young Adults

Suicide in adolescents and young adults is a rapidly growing public health problem worldwide. According to the World Health Organization (WHO) (28), suicide in people between 15 and 29 years of age represents the fourth leading cause of death, with the highest incidence rates in developing countries.

This is a problem that is just beginning to be studied, since, although it shares common factors with adult suicide, it is crucial to approach it from generational particularities. These differences are not only due to developmental aspects. Still, they are framed in the context of social, cultural, economic and technological changes that occur at an accelerated pace and affect the emotional balance of young people. Therefore, it is essential to understand this phenomenon as a public health priority, which necessitates a greater focus and effort on early risk detection (29).

Particularly in Colombia, this problem has shown a worrying increase in recent years, especially among adolescents. In 2023, 187 completed suicides were reported, of which 105 corresponded to males and 82 to females. This figure was surpassed in the first nine months of 2024, with 205 suicides reported, 115 of them in males and 90 in females. This reflects that males have a higher rate of completed suicide than adolescent females, excluding suicide attempts.

In the case of women, unwanted pregnancy in adolescence generates complications that, on certain occasions, can lead to suicide and, of course, to the loss of the pregnancy in process. The patriarchal society and gender stereotypes that reduce women to their reproductive role and motherhood have negative implications for the mental health of women who have infertility problems, who have abortions, or who have postponed motherhood because they have other priorities (30).

The factors that influence suicide among men are closely associated with economic and financial situations, among which the following stand out: i) frustrations and negative emotions derived from the inability to occupy more remunerated positions; ii) conflicts with parents over the distribution of land; and iii) lack of money to cover the family's needs (30).

According to Turecki and Brent (31), adolescent suicide is a multifactorial phenomenon influenced by various factors, including psychological, biological, environmental and sociocultural factors. From a psychobiological perspective,

studies such as that of Arensman (32) have identified alterations in serotonin and dopamine levels, which are considered predisposing factors to suicidal behavior. However, other studies, such as that of Brent and Melhem (9), mention the relevant role of genetic predisposition in the onset of suicidal behavior, since the presence of a family history of suicide increases vulnerability in adolescents.

Likewise, anxiety and depression have been directly related to youth suicide. According to the American Psychiatric Association (34), 90 % of adolescents who commit suicidal behavior have a history of mental disorders associated with depression and anxiety. In this regard, Esposito et al. (34) highlights the significant role of psychoactive substance use as a risk factor, since it reduces inhibition and increases impulsive behavior, facilitating the commission of self-injurious and suicidal behaviors.

However, there are other factors such as environmental and sociocultural factors, since constant exposure to adverse events such as physical and emotional abuse significantly increases the risk of suicidal behavior. Similarly, the history of school bullying and cyberbullying has recently become a relevant variable, increasing the risk of attempting suicide by up to three times compared to those who have not experienced such situations. In addition, social inequalities and lack of access to mental health services could be increasing the vulnerability of adolescents and young people to commit suicide (2), which aggravates the situation because early detection and timely treatment of mental disorders in this population is not contemplated.

On the other hand, the influence of the media and social networks on youth suicide has also been extensively studied. Phenomena such as the "Werther effect", where sensationalist coverage of suicides in mass media can induce suicidal behaviors in vulnerable populations, have been studied by authors such as Stack (35,36). In contrast, the implementation of the "Papageno effect", which promotes the dissemination of narratives of coping with emotional crises, has shown promising results in suicide prevention (37).

Finally, in terms of prevention strategies, school-based mental health programs, restricting access to lethal methods, and training teachers and health professionals to detect warning signs are effective interventions. The promotion of protective environments, the creation of support networks, and the strengthening of content regulation in social networks have also been key strategies to reduce the incidence of suicide in adolescents and young adults (38).

METHODS

The methodology and findings of this systematic review were reported according to the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines. Additionally, it employed a quantitative approach, grounded in the elements of an exploratory systematic review. Boolean algorithms were implemented for the exploration and structuring of the research paper.

A systematic search of relevant articles was conducted across various databases, including Springer Open, Web of Science, and Scopus. The search string used in this systematic review included the application of Boolean operators, together with keywords and search criteria (Table 1).

Table 1. Logical operators

Equations
"Psychological autopsy" and "Suicide" or = "Children" not = "Older adult" "Psychosocial autopsy" and "Adolescents" or "Suicides" not = "Disability" "Self-injury" and "Minors" or "Mental autopsy" not " Cognitive Impairment" "Psychological autopsy" and "Suicide" or = "Children" not = "Older adult" "Psychosocial autopsy" and "Adolescents" or "Suicides" not = "Disability" "Self-injury" and "Minors" or "Mental autopsy" not " Cognitive impairment"

Inclusion and exclusion criteria

The plan applied for this purpose was based on specific criteria, such as the nature of the studies analyzed, the relevance of the topic, the period considered, and the variables linked to the research (39). This methodology increases the chances of obtaining results with greater validity, thus reducing possible biases and risks in the process. We also reviewed the reference lists of the systematic reviews most relevant to the research. Eligible publications were those limited to reporting on psychological autopsy or psychosocial autopsy in cases of completed suicide. The search included publications in English, Spanish, and Portuguese, focusing on the last five years (2020-2025) to collect the most recent research in this thematic line.

Articles published in recent years with a multicenter approach were included in the review, as well as studies in several languages, due to their prevalence in scientific publications and their ability to provide relevant information for the development of science in this area. The review of these studies can be seen in Tables 2 and 3. Similarly, all articles taken from indexed journals were downloaded, those that were a duplicate or did not meet the criteria initially established were eliminated and priority was given to publications with full text and abstracts and research notes were excluded, key information was extracted from the articles such as: year, databases, reference, type of document, name in original, country, objective, central study variables, population/ sample, methodology, measurement instruments used, analysis of information implemented, description of the main results, recommendations and theoretical gaps, to elaborate a background matrix. This approach ensured that the most recent and comprehensive research was incorporated into the study, thereby contributing to an in-depth understanding of the topic.

In the search carried out, a series of research was obtained in each of the selected databases, which contributed to the consolidation of this review. From this, the exact texts chosen were transferred to the flowchart to make the filters according to the information of interest for the study.

Table 2. Cross-referencing of search terms in databases

Search	Databases	Final results			
"Psychological autopsy" and "Suicide" or = "Children" not =	Springer Open	880	524	1 320	2 724
"Older adult""Psychosocial autopsy" and "Adolescents" or "Suicides" not = "Disability" "Self-injury" and "Minors" or "Mental autopsy" not "CognitiveImpairment"	Web of Science	900	625	1 125	2 650
"Psychological autopsy" and "Suicide" or = "Children" not = "Older adult""Psychosocial autopsy" and "Adolescents" or "Suicides" not = "Disability" "Self-injury" and "Minors" or "Mental autopsy" not " C o g n i t i v e impairment"	Scopus	1120	800	1 420	3 340
	Total	2 900	1949	3 865	8 714

Table 3. Final research results by database

Database	Final Results
Springer Open	2 724
Web of Science	2 650
Scopus	3 340

Selection of research

In this process, the selection was initially based on the last five years, considering the variables studied in this research. Likewise, direct access databases and open access databases were reviewed, and scientific texts were excluded if they were duplicated, did not meet the established criteria, or only displayed abstracts or author notes (Table 4). This process is demonstrated in Figure 1, which shows the flowchart of the text selection process.

Table 4. Process of identification, elimination, and selection of items.

Boleanos	AND, OR and NOT		
No Articles in the Language	Spanish		English
	3000 5714		
Databases	SpringerOpen	Web of Science	Scopus	Total
No Filter	2 724	2 650	3 340	8 714
No Access	1 324	1 500	1 840	4 664
R/ Incomplete/ Duplicates	1 350	1 050	1 100	3 500
Do Not Meet Criteria	48	98	398	543
Election	2	2	2	6

RESULTS

In the review of studies on child and adolescent suicide and psychological autopsies, several papers were found that provide valuable information on risk factors, interventions and trends in the context of adolescent mental health. The most relevant findings of the studies analyzed are described below in Table 5.

Social network use and adolescent suicide

One of the most recent studies, *Social media use of adolescents who died by suicide: lessons from a psychological autopsy study* (39), focused on the impact of social media use on adolescents who died by suicide in the Netherlands. Through psychological autopsies of 35 cases, the researchers identified both negative and positive effects of social networking. Risks noted included dependency, imitation of suicidal behavior, victimization, and the creation of an identity around suffering. However, benefits were also highlighted, such as peer support and access to recovery stories. This study highlights the need to improve digital literacy among parents, educators, and health professionals to promote safe and conscious use of social networks. In addition, it is recommended to strengthen cyberbullying prevention and the implementation of digital

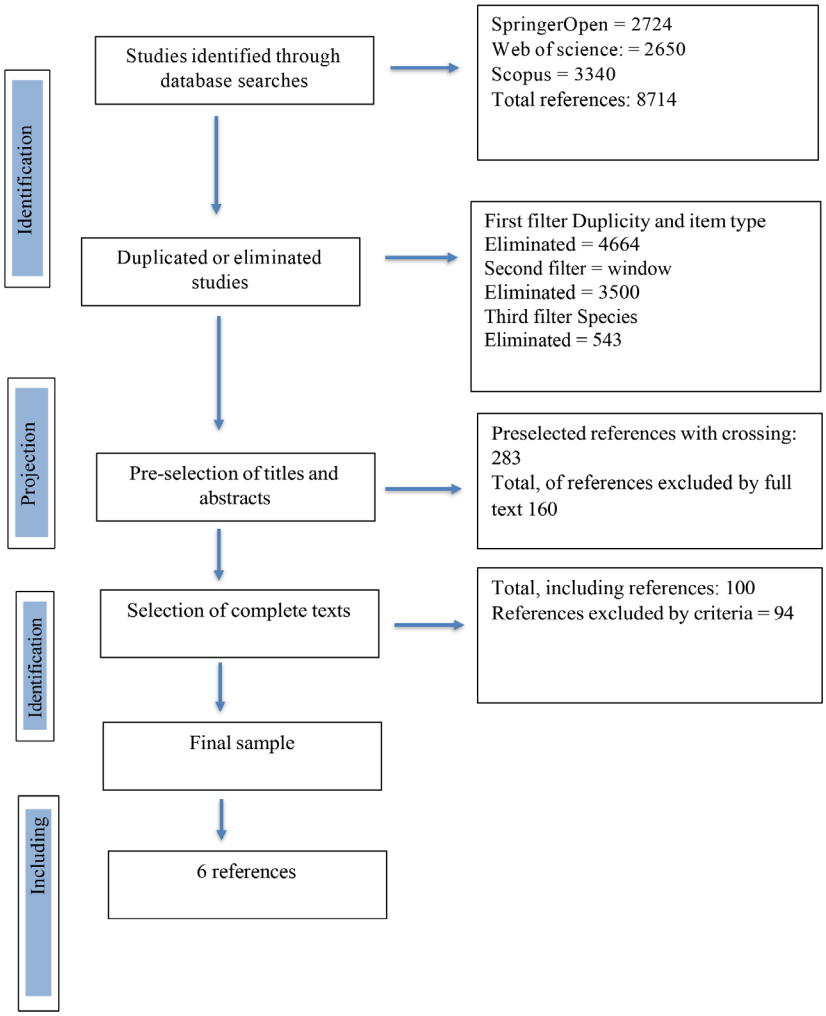


Figure 1. Flow chart of the study selection process.

interventions that encourage peer support and the promotion of positive online role models. It was noted that adolescent girls are particularly vulnerable to the adverse effects of social networks, which require specific attention.

Value of peer informants in psychological autopsy studies

Another relevant study, *Additional Value of Peer Informants in Psychological Autopsy Studies of Youth Suicides* (40), analyzed the inclusion of peer informants in psychological autopsies of youth suicides in the Netherlands. This work compared interviews with peers and parents of 16 cases of youth suicide and found that peers provided key information about aspects of social relationships, bullying, school experiences, social network use, and family dynamics, which parents were not always aware of or minimized. In addition, peers revealed precipitating factors such as substance use, academic pressure, and school stress. This study highlights the importance of including peers as informants in psychological autopsy studies, as their perspective can provide a deeper understanding of the risk factors and conditions that contribute to youth suicides.

Table 5. Results.

N	Title	Authors	Country	Language	DOI	Variable/ Keyword crosses	Methodology	Results and findings	Trends	Recommendations and theoretical gaps	Journal
1	Social media use of adolescents who died by suicide: lessons from a psychological autopsy	Balt et al. (2023)	Netherland s	English	https://doi.org/10.1186/s1303 4-023-00597-9	Social media, Suicide, Suicide, Mental health, Adolescents, Psychological	The research used a qualitative psychological autopsy design, with semi-structured interviews with 35 adolescents who died by suicide. Interpretative Phenomenological Analysis was used in 55 interviews with family members and peers.	The study analyzed 35 psychological autopsies of adolescents in the Netherlands and found that social networks can be both harmful and beneficial. Risks include dependence, suicide mimicry, victimization, and grief-based identity, while Benefits include peer support and access to recovery stories.	The study highlights the impact of social networks on Dutch teenagers who died by suicide, pointing out risks such as cyberbullying and self-harm, but also emotional support. It recommends training parents and teachers in digital prevention.	It is crucial to strengthen digital literacy and cyberbullying prevention to ensure the safe use of social networks. Digital intervention and peer support are recommended, with special attention to vulnerable adolescents.	Child and Adolescent Psychiatry and Mental Health
2	Additional Value of Peer Informants in Psychological Autopsy Studies of Youth Suicides	Looijman et al. (2024)	Netherland s	English	https://doi.org/10.1177/1049 73232 11022316	Suicide; adolescents; youth; young adults; mental health; research methods; prevention; illnesses and diseases; qualitative; psychological autopsy;	The research focused on Understanding youth suicide through a psychological autopsy method. For this purpose, semi-structured interviews were conducted with 16 young people who had committed suicide. The Information provided by their friends and parents was compared, using a detailed and consistent analysis.	The study compared interviews with peers and parents in 16 psychological autopsies of youth suicides in the Netherlands, highlighting that peers provided key information on relationships, bullying, stress, substance abuse, and academic pressure	The study highlights the Importance of including friends in psychological autopsies of youth suicide, highlighting the influence of social networks, academic, stress, and substance use. It recommends Their participation in prevention and mental health education	The study highlights the value of psychological autopsy peers in understanding youth suicide. It highlights theoretical gaps, such as the lack of systematic studies and the limited representation of migrant youth.	Qualitative Health

Continued in pag. 862…

…continuation Table 5. Results.

N	Title	Authors	Country	Language	DOI	Variable/ Keyword crosses	Methodology	Results and findings	Trends	Recommendations and theoretical gaps	Journal
3	Pandemic-related emergency psychiatric presentations for self-harm of children and adolescents in 10 countries (PREP-kids): a retrospective international cohort	Ougrin, et al. (2022)	England, Scotland, Ireland, Austria, Italy, Hungary, Serbia, Turkey, Oman, and the United Arab Emirates	English	https://doi.org/10.1007/s0078 7-021-01741-6	Self-harm - COVID-19 - Pandemic - Emergency presentation - Children - Adolescents	The study was based on a retrospective cohort design, analyzing electronic patient records in 23 hospitals in 10 countries. Data on psychiatric emergencies for self-harm between 2019 and 2020 were compared to assess possible changes in the patterns of these cases.	The study examined emergency psychiatric consultations for self-harm in children and adolescents during the pandemic in 10 countries. Although overall consultations decreased by 33%, those for self-harm increased by 7%, with more Emotional disorders.	The study reveals that, during the pandemic, hospitalizations for self-harm in young people increased while access to psychiatric services decreased. It is recommended to strengthen community mental health, prioritizing early intervention and follow-up.	It is concluded that health services should prioritizethe strengthening community care to address psychiatric crises in young people during health emergencies.	European Child & Adolescent
4	Suicidal Ideation, Depression, and Insomnia in Parent Survivors of Suicide: Based on Korean Psychological Autopsy of Adolescent Suicides	Jung Lee et al. (2023).	South Korea	English	https://doi.org/10.3346/jkms.2023.38.e39	Korea; Suicide Survivors; Suicidal Ideation; Depression; Sleep Wake Disorders	The study was conducted by psychological autopsy, conducting semi-structured interviews with 42 parents of 35 adolescents who died by suicide in Korea. In addition, standardized questionnaires were used to assess suicidal ideation, depression, and insomnia in these cases	The examination incorporates suicidal ideation, depression, and insomnia in parents of adolescents who have died by suicide in South Korea, using psycho-logical autopsies for this purpose. Forty-two parents of 35 deceased adolescents participated in this study. The results show that 75.6% of the parents had suicidal ideation, 73.2% had	The study analyzed the mental health of parents in South Korea after the suicide of their teenage children, showing high levels of depression, insomnia, and suicidal thoughts. Further psycho-logical support and long-term studies are recommended.	It is concluded that surviving parents require specialized psychological support, and that future studies should include larger samples and long-term follow-up.	

Continued in pag. 863…

…continuation Table 5. Results.

N	Title	Authors	Country	Language	DOI	Variable/ Keyword crosses	Methodology	Results and findings	Trends	Recommendations and theoretical gaps	Journal
								depression, and 42.9% had insomnia. The intensity of parental depression and insomnia were also related to the number of traumatic events experienced by the adolescents before they died by suicide.			
5	A multi-method psychological autopsy study On youth suicides in the Netherlands in 2017: Feasibility, main outcomes, and recommendations	Merelle et al. (2020)	Netherlands	English	https://doi.org/10.1371/journ al.pone.0238031	Korea; Suicide Survivors; Suicidal Ideation; Depression; Sleep Wake Disorders	The study used a multi-method psychological autopsy approach in the Netherlands, combining qualitative interviews with 66 parents, friends, and teachers, together with questionnaires administered to 43 parents and professionals. The data were analyzed using both qualitative and quantitative techniques to obtain a more complete picture of the phenomenon.	The study examines youth suicide in the Netherlands in 2017 through psychological autopsies using a multimethod approach. For this purpose, 66 interviews were conducted with parents, peers, and teachers (of 35 deceased adolescent individuals. The following risks (or risk factors) were found: bullying and cyberbullying, complex mental disorder, childhood adversity, and social networks. And two patterns were found: adolescents with h	It highlights patterns of vulnerability in perfectionist girls and boys with developmental disorders, in addition to the contagion effect in social networks. It is recommended to strengthen prevention, monitor digital content, and improve mental health care.	It is recommended to improve prevention, monitor the use of social networks, and strengthen early detection of mental health problems in adolescents.	PLoS One

Continued in pag. 864…

…continuation Table 5. Results.

N	Title	Authors	Country	Language	DOI	Variable/ Keyword crosses	Methodology	Results and findings	Trends	Recommendations and theoretical gaps	Journal
								high self-demand and psychological problems, adolescents with developmental disorders, and with a feeling of being rejected.			
6	Comparison of Suicide Attempts and Suicide Deaths by Jumping from a High Place in Korean Children and Adolescents	Song et al. (2021)	South Korea	English	https:// doi.org/10.3390/ijerph18189513	Suicide; attempts; deaths; jumping; children; adolescents	The study Conducted a comparative analysis of suicide attempts and completed suicides by jumping among childrenand adolescents in Korea. It was based on reports provided by teachers and official data from the Korean Ministry of Education.	The study analyzes completed and attempted suicides by jumping in children and adolescents in South Korea (2016-2018), examining differences in educational stage, location, suicide notes, and history. It highlights that many cases show no prior signs, underscoring the need for effective preventive strategies	The study compares attempted and completed suicides by jumping among South Korean youths Highlighting that the first attempt tends to be more lethal. Those who die show better school performance and fewer previous signs. It is recommended to restrict access, improve early detection, and strengthen prevention.	It is concluded that those who commit suicide may not show obvious signs of family or school problems, highlighting the need for more effective preventive strategies in educational and family settings.	International Journal of Environmental Research and Public Health

Self-injury during the COVID-19 Pandemic

In a global context, the *Pandemic-related emergency psychiatric presentations for self-harm of children and adolescents in 10 countries (PREP-kids)* study (41) addressed emergency psychiatric consultations for self-harm in children and adolescents during the COVID-19 pandemic in 10 countries. Although overall consultations decreased by 33 % compared with 2019, cases of self-harm increased by 7 %, indicating an increase in emotional disorders in young people. This study underscores the importance of strengthening community psychiatric care services and prioritizing youth mental health during global health crises. The findings indicate that emotional disorders, such as anxiety and depression, intensified during the pandemic, suggesting that public health emergencies negatively affect the psychological well-being of adolescents.

Impact of suicide loss on surviving parents

Another study focusing on parents surviving the loss of a child to suicide, *Suicidal Ideation, Depression, and Insomnia in Parent Survivors of Suicide* (42), examined the effects of loss on parents of adolescent suicide survivors in South Korea. The results showed that a high percentage of parents had suicidal ideation (75.6 %), depression (73.2 %), and sleep disturbances (42.9 %). In addition, the severity of depression and sleep disorders was correlated with the traumatic events experienced by the adolescents before their death. This study underscores the urgent need for specialized psychological support for surviving parents. It suggests that future studies should expand the sample and conduct long-term follow-ups to understand better the emotional consequences of suicide loss on family members.

Juvenile suicides and risk factors in the Netherlands

A multi-method psychological autopsy study on youth suicides in the Netherlands in 2017 (43) analyzed youth suicides in the Netherlands in 2017 through a multi-method approach involving interviews with parents, peers and teachers of 35 deceased adolescents. Risk factors such as bullying (including cyberbullying), complex mental disorders, adverse childhood experiences, and the negative influence of social networks were identified. The results indicated two patterns: young people with high self-demand and psychological problems, and those with developmental disorders who felt rejected. This study recommends improving youth suicide prevention by monitoring the use of social networks and early detection of mental health problems in adolescents, especially in the school environment.

Comparison of suicide attempts and completed suicides by high jump in South Korea

Finally, the study *Comparison of Suicide Attempts and Suicide Deaths by Jumping from a High Place in Korean Children and Adolescents* (44) compared suicide attempts and completed suicides by jumping from *a high place* in South Korean children and adolescents. The results showed significant differences in educational stage, suicide location, presence of suicide notes, and history of previous attempts. In addition, interrupted suicide attempts were found to be more related to emotional and behavioral difficulties. This study highlights the importance of developing more effective preventive strategies in educational and family settings, as those who commit suicide often do not show obvious signs of family or school problems.

In summary, the studies offer a comprehensive view of the risk factors associated with youth suicide, the importance of early intervention, and the value of considering different perspectives, such as that of peers, in psychological autopsy studies. They also highlight the relevance of improving prevention and support for affected families, as well as the use of social networks and mental health during crises, such as the COVID-19 pandemic.

DISCUSSION AND CONCLUSIONS

In the selected studies, psychological autopsy is used as a fundamental tool to understand the circumstances and precipitating factors surrounding suicides in children and adolescents,

exploring the perceptions of the people closest to the deceased, including family members and peers, to obtain more precise information on the antecedents of the suicide. In addition, it made it possible to identify aspects such as suicidal ideation, depression, and insomnia in surviving parents, as well as to delve into the emotional states and traumatic experiences of adolescents before their death. This facilitated the identification of risk factors and pathways leading to suicide, providing a more complete understanding of previous events.

This tool is key to identifying risk factors in suicides that may not be detected in traditional approaches. Examining personal, emotional, mental health, and history of previous attempts allows for a more complete understanding of the context. This comprehensive approach facilitates the development of more effective and personalized prevention strategies aimed at addressing the underlying causes of suicide more precisely.

Among the populations most affected by this phenomenon are children, who are the second leading cause of death in the 10-14 age group. Boys are approximately four times more likely to die by suicide than girls, who, in turn, are more likely to attempt suicide. At this stage of the life cycle, it is important to note that immature cognitive development affects children's ability to understand complex concepts such as causality, death, and suicide, which hinders their ability to handle stressful situations, make decisions, and solve problems.

During adolescence, additional vulnerability factors emerge, such as unwanted pregnancy, which can trigger serious consequences, including physical and emotional complications, in some cases leading to suicide or pregnancy loss. Social pressure imposed by a patriarchal society and gender stereotypes that limit women to their reproductive role aggravate mental health problems. For this reason, comprehensive support is required to protect the well-being and quality of life of those who face such situations.

The findings obtained in this systematic review highlight the fundamental role of psychosocial autopsy in understanding the risk factors associated with suicide in child and adolescent populations. Consistently, the studies reviewed have identified the presence of mental disorders, the influence of social networks, dysfunctional family conditions, and a history of trauma as factors of great relevance in suicidal behavior in this population (40,41,43). These results coincide with previous studies that have pointed out that suicide in minors is a multifactorial phenomenon, determined by psychological, social, and environmental variables (24).

The studies reviewed reveal a recurrent pattern in socially insecure young people who find in social networks a positive reinforcement online, thus distorting the perception of their own mental health. Although no direct link was identified between the excessive use of these platforms and suicide, it is recognized as a triggering factor that intensifies negative thoughts and behaviors, encourages sedentary lifestyles, increases feelings of anxiety and loneliness, reduces face-to-face interactions, affects sleep quality, and generates academic difficulties. In addition, the impact of social networks and exposure to suicidal content was identified as triggering detrimental effects such as dependence, excessive use, social comparison, and the contagion effect.

Thus, one of the most prominent aspects in the studies reviewed is the impact of social networks on suicidal ideation and behavior in adolescents. The review by Balt et al. (39) points out that excessive use of digital platforms, together with exposure to suicide-related content, can intensify depressive symptomatology and foster suicidal thoughts in vulnerable youth. This finding is consistent with previous research that has documented the "Werther effect," where exposure to suicide cases on social networks can generate a copycat effect in psychologically predisposed adolescents (35). In contrast, the "Papageno effect" has also been identified, suggesting that exposure to coping stories may have a protective effect against suicidal behavior (37).

Another relevant aspect identified is the relationship between mental disorders and child and adolescent suicide. Studies (42,43) highlight that pathologies such as depression and anxiety are strongly correlated with suicidal risk in minors, and the presence of sleep disorders, such as insomnia, has also been identified as a relevant factor in suicidal ideation, given its impact on emotional regulation and the coping capacity of

young people (34). These findings are consistent with previous studies conducted by the American Psychological Association (APA) (33), which indicate that 90 % of adolescents with suicidal behavior have a history of diagnosed psychiatric disorders.

From a social and family perspective, Looijman et al. (40) highlights the importance of the information provided by peers in the psychosocial autopsy, which allows understanding the child's support networks and social interactions before suicide. Factors such as child abuse, intrafamilial violence, and lack of parental support have been identified as significantly increasing vulnerability to suicide (25). The review also reaffirms that the presence of a family history of suicide may act as an additional risk factor, suggesting both an environmental and genetic influence on adolescent suicidal behavior (9).

Another identified behavioral risk factor is impulsivity, which, together with family and environmental influences, plays a crucial role in suicidal behavior in children. In this sense, stressful events can trigger self-destructive actions, with attachment disorders, family discord and abuse being important risk factors. Likewise, family history of suicidal behavior and psychopathological characteristics, such as violence or substance abuse, increase the likelihood of suicide in children.

On the other hand, in terms of preventive strategies, the studies reviewed emphasize the need to strengthen mental health programs in the educational and community settings. Ougrin et al. (41) emphasize that the COVID-19 pandemic exacerbated the mental health crisis in minors, which underscores the urgency of implementing early intervention programs and timely access to psychological services. Likewise, the World Health Organization (28) suggests that strategies such as restricting access to lethal methods, training teachers in early detection and strengthening support networks have proven to be effective in reducing suicide risk in young people.

Through this approach, it has been possible to identify various elements that precede suicide, such as mental disorders, traumatic experiences, family influences and the impact of social networks. Psychological autopsy provides a more accurate picture of the circumstances surrounding suicides, revealing aspects that might otherwise have gone unnoticed in traditional studies. It is essential to emphasize that, although emotional and psychological disorders are common factors in suicidal behavior, social and family variables, such as abuse, violence, and lack of support, also play a role in increasing the vulnerability of young people. In this sense, the importance of designing preventive strategies based on a comprehensive vision of mental health, including the regulation of the use of social networks, early intervention, and the strengthening of social support networks, is emphasized (45).

These prevention strategies also include strengthening social support for at-risk adolescents, training teachers and parents in digital literacy, and early identification of warning signs. They also emphasize the importance of fostering emotional communication in children and adolescents, enhancing the ability to ask for help, and promoting the responsible use of social networks, as well as preventing cyberbullying and implementing policies that regulate content on these platforms. These actions coincide with those proposed by Campaña (13), who emphasizes that one of the main advantages of psychological autopsies is the possibility of formulating specific and comprehensive prevention strategies.

Finally, despite the findings identified in the present review, which reinforce the essential role of psychological autopsy as a tool for understanding the factors contributing to suicide in children and adolescents, it is crucial to make known the limitations inherent to the concept of psychosocial autopsy as a research method. In this sense, the information obtained from family members and friends may be subject to biases in the recovery of information and perception of the event, which would considerably affect the objectivity of the data collected. It also highlights the need to employ mixed methodologies, incorporating analysis of information from tertiary sources such as medical records and structured interviews, to contribute to a multidimensional understanding of the suicide phenomenon in the studied population. This systematic review not only reaffirms the usefulness of psychosocial autopsy as a research method in the study of child and adolescent suicide but also allows for the identification of key areas for intervention. Prevention strategies should focus on a comprehensive approach

to the identified risk factors—psychological, social, familial, and digital—and prioritize the development of public policies that are sensitive to the emotional needs of children and youth. Advances in this direction are essential to protect the lives and well-being of future generations.

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Biochemical and Metabolic Changes Associated with Depression: A Systematic Review

Cambios bioquímicos y metabólicos asociados a la depresión: Una revisión sistemática

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SUMMARY

Introduction: *A close connection has been observed between metabolic syndrome (MS) and depression, affecting both physical and mental health. MS, which is common in Colombia and globally, increases the risk of developing cardiovascular disease and type 2 diabetes. Depression, which is common in people with MS, can negatively impact quality of life.* **Methods:** *A systematic review was conducted following the PRISMA methodology, focused on adults diagnosed with depression and metabolic disorders. Relevant information was collected on MS and depression, highlighting aspects such as lifestyle, childhood experiences and unhealthy eating patterns.* **Results:** *Significant changes in body lipid levels were evidenced, which can trigger diseases such as obesity and diabetes. These conditions can increase the risk of comorbidities, leading to cognitive, physical, and emotional impairments. The relationship between poor eating habits, lack of physical activity and depressive symptoms is clear.* **Conclusions:** *In adults with depression, the most frequent metabolic alterations are obesity, diabetes, dyslipidemia, and hypertension. A significant bidirectional relationship was observed between metabolic disorders and depression, which affects overall body function.*

Keywords: *Metabolic syndrome (MS), Depression, Comorbidities, Metabolic disorders, Lifestyle.*

RESUMEN

Introducción: *Se ha observado una conexión estrecha entre el síndrome metabólico (SM) y la depresión,*

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afectando tanto la salud física como la mental. El SM, que es común en Colombia y a nivel global, aumenta el riesgo de desarrollar enfermedades cardiovasculares y diabetes tipo 2. La depresión, que es frecuente en personas con SM, puede impactar negativamente la calidad de vida.

Método: *Se llevó a cabo una revisión sistemática siguiendo la metodología PRISMA, enfocada en adultos diagnosticados con depresión y trastornos metabólicos. Se recopiló información relevante sobre el SM y la depresión, destacando aspectos como el estilo de vida, experiencias en la infancia y patrones alimentarios poco saludables.* **Resultados:** *Se evidenciaron cambios significativos en los niveles de lípidos corporales, los cuales pueden desencadenar enfermedades como la obesidad y la diabetes. Estas condiciones pueden incrementar el riesgo de padecer comorbilidades, resultando en deterioro cognitivo, físico y emocional. Es clara la relación entre malos hábitos alimenticios, falta de actividad física y síntomas depresivos.* **Conclusiones:** *En adultos con depresión, las alteraciones metabólicas más frecuentes son la obesidad, la diabetes, la dislipidemia y la hipertensión. Se observó una relación bidireccional significativa entre las alteraciones metabólicas y la depresión, lo cual afecta la función corporal en general.*

Palabras clave: *Síndrome metabólico (SM), depresión, comorbilidades, alteraciones metabólicas, estilo de vida.*

INTRODUCTION

Metabolic syndrome (MS) involves a complex combination of risk factors related to the heart and metabolism, which are closely linked to an increased risk of developing cardiovascular disease and type 2 diabetes, among other conditions (1). Both in Colombia and worldwide, MS has a high prevalence, leading to a significant burden in terms of disease and healthcare costs, underscoring the importance of public healthcare (2). The diagnosis of MS is confirmed when a person presents at least three of the following five criteria: central obesity, elevated triglyceride levels, high blood pressure, higher than normal blood glucose levels, and low high-density lipoprotein (HDL) levels (3). Likewise, a connection between MS and symptoms of other diseases has been observed, with depression being a common phenomenon, with a symptom prevalence of 46.34 % (4).

Historically, medical care tended to focus on physical health, neglecting mental health and underestimating its importance (5). While priority was given to maintaining physical fitness for its visible external effects, psychological health was often overlooked (6). However, recent research (7,8) is increasingly highlighting the relevance of psychological aspects to overall health. These factors have been recognized as having a significant impact on the development of diseases and the progression of medical conditions (9). In adulthood, the importance of the psychological dimension is understood, especially at times of risk, and it is recognized that mental health influences physical deterioration and is related to the occurrence of health disorders (10).

Numerous changes have now been identified that can impact both a person's physical and mental health, potentially resulting in a significant decrease in their quality of life (11-13). Recent studies (14,15) have highlighted metabolic disturbances as a major concern, significantly impacting health due to rare imbalances affecting essential body elements, including triglycerides, HDL cholesterol, blood pressure, and glucose levels. These deviations, when combined with other conditions such as depression, can increase the likelihood of developing metabolic syndrome (16-20). It is essential to note that this condition affects a significant portion of the population, with a prevalence of up to 36 % in severe cases (21). Studies conducted in medical institutions, such as those in Västmanland County, suggest that approximately 31 % of the global population may experience some metabolic disturbance, which could lead to more severe health complications for individuals (22).

The high prevalence of metabolic syndrome (MS) could be closely related to other psychological disorders, such as depression, categorized by the World Health Organization (WHO) as an affective disorder affecting millions of individuals worldwide (23). This disorder is characterized by emotions of sadness, lack of interest in daily activities, decreased energy, and difficulty concentrating, which significantly impacts a person's functionality (24). Depressive episodes can also hinder self-care practices and fluctuations in mood can complicate the

maintenance of a healthy metabolism (25). According to information provided by the WHO, about 5 % of adults worldwide experience depression, which is more prevalent in women, increasing the risk of suicidal thoughts and becoming a determining factor for the emergence of new physical conditions (26).

Another important aspect to consider is mood fluctuations, which involve significant changes in a person's emotional expression and well-being, ranging from mild emotions to more intense and prolonged emotional states (27). These variations can manifest themselves in a variety of ways, such as episodes of profound sadness, lack of interest, irritability, excessive anxiety, or excitement. Although they are a natural part of the human experience, persistent, intense, or life-affecting mood swings may be indicative of emotional disorders (28). On the other hand, depression stands out as one of these conditions linked to fluctuations in mood that have a significant and frequent impact on society, and its prevalence is between 3 % and 6 % in men and between 5 % and 10 % in women, presenting a variety of cognitive, affective and somatic symptoms that evidence cognitive vulnerability and its influence on the appearance of other health problems (29).

Likewise, individuals with depression often show a high prevalence in their eating habits and detrimental behaviors, resulting in significant metabolic disturbances (30). An association has been observed between increased depressive symptoms and metabolic dysfunction, which represents a risk factor for conditions such as obesity, type 1 and 2 diabetes, lipid disorders, and hypertension (31). This situation poses an elevated risk scenario for patients, given that both metabolic and emotional aspects are intertwined. Therefore, the purpose of this systematic review is to broaden the understanding of the relationship between metabolic alterations, such as metabolic syndrome, and depression, which impact both the physical and mental health of individuals (3,32).

2. METHOD

The systematic review was carried out following the PRISMA methodology to collect updated data transparently and present the results clearly (33). Relevant information on the variables was integrated through a descriptive analysis of scientific literature without performing a meta-analysis. To formulate the research question, the AMCPT tool was used (34), which consists of five components (A. Adjective, M. Measure, C. Condition, P. Population and T. Time) as detailed in Table 1.

Table 1. AMCPT

A	Adjective	What
M	Measure	Metabolic Alterations
C	Condition	Depression
P	Population	Adults
T	Time	The last 15 years

2.1. Research question

What metabolic changes have been reported in adults diagnosed with depression?

Inclusion and exclusion criteria

Inclusion and exclusion criteria were established, focusing on a specific demographic group of adults with a diagnosis of depression, including both medicated and non-medicated individuals presenting with any form of metabolic disturbance, and considering any concurrent health conditions present in these individuals. Exclusions applied during the search were associated with the type of paper, excluding meta-analyses and previously conducted systematic reviews (Table 2).

Table 2. Inclusion and exclusion criteria

Criterion	Inclusion	Exclusion
Participants	Adults with a diagnosis of depression	Children and adolescents
Treatment	Medicated or unmedicated	-
Metabolic conditions	Any form of metabolic alteration	-
Concurrent health conditions	Any concurrent health condition	-
Document Type	Original research articles	Meta-analyses and systematic reviews
Publication	Studies published since 2021	Studies published before 2021

2.2. Sources of information

The information search was conducted using the following databases: BASE, BVS, Dialnet, PloS One, ProQuest, PubMed, Redalyc, Scielo, Scopus, and SpringerLink.

2.2.1. Search strategy.

To accurately identify the studies and create the search algorithms, the digital dictionaries located in the descriptors of Health Sciences, such as Medical Subject Headings (MeSH) and DECS (Descriptors of Health Sciences), associated with the terms "Depression," "Metabolic alterations," and "Adults" (Table 3), were used with this method to clarify the information located.

Subsequently, search algorithms were constructed using logical operators such as "OR", "AND" and "NOT" (Table 4).

Table 3. DECS and MESH terms

Term	Synonym
Adult	Adult
Alterations Metabolic	Metabolic alterations, Ravens syndrome, Metabolic Syndrome X, Cardiovascular Syndrome, Dysmetabolic Syndrome X, Insulin Resistance Syndrome X, LDL cholesterol, Triglycerides, Blood pressure
Depression	Depression, Depressive, Disorder, Major Depression, Persistent depressive disorder, Discouragement, Decay

Table 4. Equations used in the search.

("Adult") AND ("Depression") AND ("Metabolic alterations")	Adult AND Depression AND Metabolic alterations
("Adult") AND ("Cardiovascular Syndrome") AND ("Depression")	Adult AND Cardiovascular Syndrome AND Depression
("Depression") AND ("Syndrome Metabolic")	Depression AND Metabolic Syndrome
("Adult") AND ("Depressive") AND ("Metabolic syndrome")	Adult AND Depressive AND Metabolic syndrome
("Depression") AND ("Insulin Resistance Syndrome X") AND ("Adult")	Depression AND Insulin Resistance Syndrome X AND Adult
("Adult") AND ("Mayor depression") AND ("Metabolic")	Adult AND major depression AND Metabolic
("Alterations Metabolic") AND (Depressive Disorder") AND ("Adult")	Alterations Metabolic AND Depressive Disorder AND Adult
("Persistent depressive disorder") AND ("Adult") AND ("Metabolic syndrome")	Persistent depressive disorder AND Adult AND Metabolic syndrome
(" Persistent depressive disorder") AND ("Metabolic Syndrome")	Persistent depressive disorder AND Metabolic Syndrome
("Adult") AND ("Depression") AND ("Blood pressure")	Adult AND Depression AND Blood pressure
("Cholesterol") AND ("Adult") AND ("Depression")	Cholesterol AND Adult AND Depression
("Adult") AND ("depressive") AND ("LDL cholesterol")	Adult AND depressive AND LDL cholesterol

After reviewing the relevant studies, materials related to the variables of interest were collected, and various filters were applied, such as type of document, date of publication, and relevance of the variables. During the search stage, several articles were excluded because the selection criteria focused only on research papers. A 15-year time limit was established, focusing on adults aged 19 to 59 years, excluding systematic reviews, narratives, and meta-analyses. During this screening process, 1 059 038 articles were identified in academic databases. Of these, 5 663 were in the "BASE" database, of which two were selected for analysis. On the other hand, no articles were found in the "BVS" and "Dialnet" databases. Therefore, they were not included in the study. In "PloS One" 26 362 articles were found, of which two were selected for analysis. As for "Proquest", 864 186 articles were identified, but were not selected for analysis. On the other hand, in "PubMed" 22 630 articles were detected, of which eight were selected for analysis. A total of 11 648 articles were registered in "Redalyc", of which one was selected for analysis. Forty-seven articles were in "Scielo", but none were included in the study. In "Scopus" 14 735 articles were identified, of which 18 were selected for analysis. Finally, 95 797 articles were found in "Springer Link", but none were selected as a sample (Table 5 and Figure 1).

Subsequently, detailed information was provided on the data selected from each document, highlighting the significant findings and relevant information derived from the results obtained (Table 6).

RESULTS

After searching several databases, using equations, and adhering to the exclusions specified for the follow-up of the variables, the analysis process was initiated to identify important, specific, and clear information relevant to the review's results. The analysis process was initiated to identify important, specific, and clear information focused on the outcomes relevant to the review. It is important to clarify that the categorization of the information was based on the results reported on pathology, comorbidities, and prevalence by biological sex.

In both women and men, manifestations of metabolic syndrome are closely linked to depression, owing to the numerous dysregulations occurring within the body in vital components for its functioning (HDL cholesterol, triglycerides, glucose, and blood pressure). It is noteworthy that influential factors in the onset of both conditions include lifestyle, childhood experiences, or

Table 5. Search results and filters applied.

Database	Total found	Type of document	Time period	No access	Revisions/ incomplete/ duplicated texts	Non-compliance with variable criteria	Total Sample
BASE	5 663	2 358	0	0	1 243	2 060	2
BVS	17 898	22	0	23	9 561	8 292	0
Dialnet	72	23	0	0	12	37	0
PloS One	26 362	359	0	0	9 255	16 746	2
Proquest	864 186	613 779	0	3 280	120 980	126 147	0
PubMed	22 630	5 524	0	10	13 061	4 027	8
Redalyc	11 648	6 006	0	0	0	5 641	1
Scielo	47	12	0	0	0	35	0
Scopus	14 735	12 057	0	0	2 189	472	17
Spriger Link	95 797	52 139	0	0	14 507	29 151	0
TOTAL	1 059 038	692 279	0	3 313	170 808	192 608	30

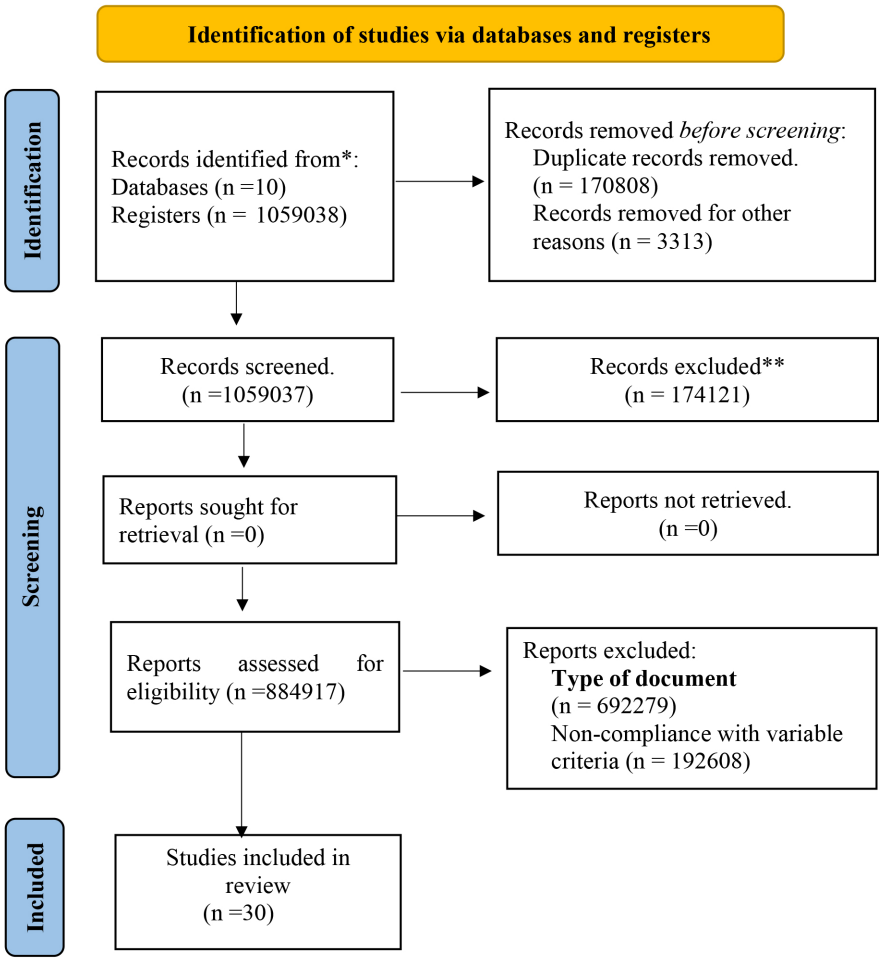


Figure 1. PRISMA flowchart.

unhealthy eating patterns, all of which significantly impact due to the limited attention given to the initial symptoms of each condition (41). The prevalence across both sexes (women and men) yields a similar probability margin, even though the manifestation of symptoms may differ. This implies that despite differences that may exist in other aspects of health between genders, in this context, data indicates that both women and men face similar challenges regarding metabolic alterations and depression (41). It is recognized that during the existence of both conditions, a pattern of deviant behaviors is identified among them, including social isolation and insufficient engagement in physical activity (45) (Table 7).

In analyzing Table 8, it was observed that, within the specified parameters, especially regarding depression, notable fluctuations in body lipid levels, such as HDL cholesterol and triglycerides, are evident (35). These fluctuations often correlate closely with metabolic irregularities and have the potential to trigger conditions that pose a significant risk to an individual's health. Prominent among these are diseases such as obesity, type 1 and 2 diabetes, and cardiovascular disease (57). These diseases have the capacity to directly influence the optimal functioning of the organism, due to excessively high or reduced levels of the components (HDL cholesterol, triglycerides, glucose, and blood pressure), all of

Table 6. Description of ítems.

N	Title	Author(s)	Data base	Year	Contribution	Medication	Medication, Dosage and Time	Changes recorded
1	Associations of metabolic syndrome with elevated liver enzymes and C-reactive protein in drug-naive patients with depressive disorders (35).	Naresh Nebhinani et al.	BASE	2016	Prevalence of metabolic alterations in patients with depression by variable enzyme and protein processing.	No	No report	No report
2	Leisure time physical activity and its relation to psychiatric comorbidities in depression: Findings from Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study (36).	Raatikainen et al.	BASE	2019	Relationship of depression and metabolic syndrome versus physical activity in adults as a treatment element.	Si	Unspecified antidepressants.	LTPA level was not related to a number of psychiatric comorbidities (after adjustment for age, gender, BMI, BDI, and use of antidepressant p=0.24) among depressed patients. The higher levels of LTPA were linearly associated with lower cardiovascular diseases (p=0.036) and obesity (p=0.006), as well as fewer DS (p < 0.001) among depressed patients. LTPA level is not associated with psychiatric comorbidities among depressed patients in the Finnish adult population.
3	The impact of obesity on neuropsychological functioning in adults with and without major depressive disorder (37).	Restivo et al.	PloS One	2017	Cognitive impact in patients diagnosed with depression and obesity.	No	No report	No report
4	Outcomes of bariatric surgery in patients with depression disorders (30).	Susmallian et al.	PloS One	2019	Progress in depressive diagnosis due to treatments applied to a metabolic disorder	No	No report	No report
5	Metabolic depression: a chronic depressive subtype? Findings from the InCHIANTI study of older persons (16).	Vogelzangs et al.	PubMed	2011	Pathologies and prevalence of metabolic alteration in depression diagnosis.	No	No report	No report
6	Prevalence of metabolic syndrome and its association with depression in patients with schizophrenia (38).	Suttajit y Pilakanta	PUBMED	2013	Relationship of mood disorder (depression) and metabolic syndrome to schizophrenia as comorbidities	No	No report	No report
7	Blood pressure values and depression in hypertensive individuals at high cardiovascular risk (39).	Mejia-Lancheros et al.	PubMed	2014	Blood pressure variations in depression as an initial factor for metabolic disturbances.	No	No report	No report

Continued in pag. 877…

…continuation Table 6. Description of ítems.

N	Title	Author(s)	Data base	Year	Contribution	Medication	Medication, Dosage and Time	Changes recorded
8	Sex-based Association between Depression and Metabolic Syndrome in Korean Middle-aged and Older Adults (40).	Jin Suk Ra, Hye Sun Kim	PubMed	2017	Relationship of depression with metabolic syndrome from biological sex.	No	No report	No report
9	Social disconnection and metabolic syndrome score among Cambodian Americans with depression (41).	Megan Berthold et al.	PubMed	2021	Association of social agents as an influence of severity in metabolic syndrome with depression.	No	No report	No report
10	Metabolic syndrome in patients with depressive disorder--features of comorbidity (23).	Kozumplik y Uzun.	PubMed	2022	Prevalence and clinical features of depression in other disorders such as metabolic syndrome	No	No report	No report
11	The cardiometabolic depression subtype and its association with clinical characteristics: The Maastricht Study (42).	Geraets et al.	PubMed	2022	Demographic and clinical features in depression resulting in a type of metabolic depression.	No	No report	No report
12	Restrained, emotional eating and depression can be a risk factor for metabolic syndrome (43).	Akıllıoğlu et al.	PubMed	2022	Relationship on food in the triggering of metabolic syndrome in the diagnosis of depression.	No	No report	No report
13	Association between obesity and depression: influence of gender, age, degree of adiposity and physical activity (44).	Miranda et al.	Redalyc	2019	Risks of obesity on depressive symptoms	No	No report	No report
14	Prevalencia de síntomas depresivos en síndrome metabólico (4).	López et al.	Scopus	2008	Prevalence of alterations in depressive symptoms according to the level of Metabolic Syndrome.	No	No report	No report
15	Depressive symptoms and the metabolic syndrome in childhood and adulthood: A prospective cohort study (45).	Pulkki-Råback et al.	Scopus	2009	Symptomatology of Metabolic Syndrome and Depression in Adults Based on Early Age Affects.	No	No report	No report
16	Association of depression	Perveen et al.	Scopus	2010	Importance of simultaneous evaluation of metabolic syndrome	No	No report	No report

Continued in pag. 878…

..continuation Table 6. Description of ítems.

N	Title	Author(s)	Data base	Year	Contribution	Medication	Medication, Dosage and Time	Changes recorded
	with newly diagnosed type 2 diabetes among adults aged between 25 to 60 years in Karachi, Pakistan (46).				with depression			
17	The impact of knowledge about diabetes, resilience and depression on glycemic control: a cross-sectional study among adolescents and young adults with type 1 diabetes (47).	Santos et al.	Scopus	2013	Correlation of type 1 diabetes with a diagnosis of depression	No	No report	No report
18	Brain-derived neurotrophic factor, but not body weight, correlated with a reduction in depression scale scores in men with metabolic syndrome: a prospective weight-reduction study (48).	Lee et al.	Scopus	2014	Changes in depressive symptomatology with metabolic syndrome derived from neurotrophic factor as an improvement in men.	No	No report	No report
19	Association between suicidal behaviour and impaired glucose metabolism in depressive disorders (49).	Koponen et al.	Scopus	2015	Insulin resistance, glucose, and lipid alterations as a key factor for alterations in depression	No	No report	No report
20	The Relationship between Depressive Symptoms and Modifiable Lifestyle Risk Factors in Office Workers (50).	Jin et al.	Scopus	2017	Obesity rates are related to depressive symptomatology.	No	No report	No report
21	Association between self-reported medical diagnosis of depression and metabolic syndrome in a population-based study: A propensity score-matched analysis (51).	Kim et al.	Scopus	2017	Triglyceride values associated with metabolic and mood disorders	No	No report	No report
22	Classical Risk Factors and Inflammatory Biomarkers: One of the Missing Biological Links between Cardiovascular Disease and Major Depressive Disorder (52).	Baghai et al.	Scopus	2018	Association of depressive disorder with cardiovascular disorder	No	No report	No report

Continued in pag. 879…

…continuation Table 6. Description of ítems.

N	Title	Author(s)	Data base	Year	Contribution	Medication	Medication, Dosage and Time	Changes recorded
23	Association between depressive symptoms and dietary intake in patients with type 1 diabetes (19).	Ahola et al.	Scopus	2018	Depression as a negative affectation for the treatment of other disorders due to its effects on self-care.	No	No report	No report
24	Population attributable fractions for Type 2 diabetes: an examination of multiple risk factors including symptoms of depression and anxiety (53).	Naicker et al.	Scopus	2018	Variations in diabetes are significantly associated with psychological risks.	No	No report	No report
25	Independent and joint association of obesity and metabolic syndrome with depression and inflammation (54).	Moazzami et al.	Scopus	2019	Association of obesity with patients with metabolic disorders and depression.	No	No report	No report
26	Depressive symptoms and cardiovascular disease: a population-based study of older adults in rural Burkina Faso (31).	Brinkmann et al.	Scopus	2020	Cardiometabolic and cardio-vascular diseases prevalent in the diagnosis of depression	No	No report	No report
27	Associations between Depression, Arterial Stiffness, and Metabolic Syndrome among Adults in the UK Biobank Population Study: A Mediation Analysis (55).	Dregan et al.	Scopus	2020	Relationship of Health Status (ASIS) to the presence of depression and metabolic syndrome.	No	No report	No report
28	Alterations of Plasma Lipids in Adult Women with Major Depressive Disorder and Bipolar Depression (56).	Zhang et al.	Scopus	2022	Lipid dysregulation on diagnosis of depression and bipolarity	SI	Medication: Dulo-xetine and venlafaxine in the MDD (major depressive disorder) group; olanzapine or quetiapine combined with lithium or valproate in the BPD (bipolar disorder) group. No use of alcohol and psychoactive substances in the recruited participants.	TDM: Changes in BMI, increased levels of long-chain fatty acyls with 16 carbons (16C). DBP: Levels of long-chain fatty acyls with 16 carbons (16C) increased, the level of long-chain fatty acyls with 28 carbons (28C) decreased. It is important to highlight that the possible lipids that distinguish women with MDD from BPD have not been identified.

Continued in pag. 880…

...continuation Table 6. Description of items.

N	Title	Author(s)	Data base	Year	Contribution	Medication	Medication, Dosage and Time	Changes recorded
29	Familial Linkage and Association of the NR3C1 Gene with Type 2 Diabetes and Depression Comorbidity (57).	Amin et al.	Scopus	2022	Relationship between NR3C1 gene with development of Diabetes Mellitus 2 and depression.	No	No report	No report
30	T2DM patients with depression have higher levels of hyperglycemia and cognitive decline than T2DM patients (26).	Thummasorn et al.	Scopus	2022	Level of cognitive functioning in diagnosis of Diabetes mellitus 2 in depressive patients with metabolic syndrome.	No	No report	No report

which play a fundamental role in the metabolic processes of the organism, including energy metabolism (16). Consequently, they can lead to long-lasting and significant health complications. It is due to these pathologies and irregularities that there is an increased likelihood of comorbidity with other diseases, and these additional conditions can also be considered as precipitating factors in the cognitive, physical, and emotional deterioration of the individual (37). Therefore, the observed relationship between these variables represents a danger to human health, underscoring the need for comprehensive care that encompasses not only the medical dimensions but also the emotional, affective, and cognitive aspects associated with these conditions (54).

The information presented in Table 9 indicates that the presence of certain conditions in individuals is associated with an increased risk of developing additional diseases, known as comorbidities. These comorbidities refer to the coexistence of two or more disorders in the body, which may include bipolar disorder, cardiovascular disease, cardiorespiratory problems, stress, and schizophrenia. These disorders often go hand in hand with metabolic disturbances and/or depression (38). Studies have shown that people with poor eating habits and a lack of physical activity tend to experience stronger depressive symptoms (36). This relationship also extends to alterations in metabolic components and cardiovascular markers. Those with high levels of cardiorespiratory fitness often show signs of metabolic alterations and depression (50). It is essential to note that the underlying causes of these comorbidities can vary significantly between individuals, and their manifestation depends on specific symptoms and circumstances. Initially, symptoms related to the variables studied, metabolic changes, or depression may arise, which may lead to additional mental as well as physiological complications (36).

DISCUSSION

The purpose of this systematic review was to focus on the relationship between metabolic changes and depression in adults over the past 15 years. It was observed that metabolic modifications, such as disruptions in cholesterol,

Table 7. Table representing the prevalence of the diagnosis of depression and metabolic disorders according to the biological component.

Classification	Characteristics:	
	Young Adult (19/24)	Adult (25/59)
Men	No report	Patients suffering from depression often show a higher incidence rate, which is linked to dietary habits and unhealthy behaviors leading to increased levels of metabolic syndrome alterations (30).
	No report	Metabolic syndrome in childhood leads to elevated levels of depressive symptoms in adulthood (45).
	No report	Depression significantly influences the development of Metabolic Syndrome in men (40).
	No report	Serious potential consequences of Metabolic Syndrome are indicated, with associations being better explained by depression indicators resulting from social isolation, being single, or living alone (41).
Woman	No report	Patients with depression often exhibit high levels of Metabolic Syndrome due to their typical lifestyle habits (30).
	No report	Depressive symptoms were associated with an increased risk of metabolic syndrome in adulthood, stemming from childhood illness-related situations (45).
	No report	Depression was significantly linked to the development of Metabolic Syndrome and higher levels of triglycerides (40).
	No report	The development of metabolic alterations is evidenced by the presence of depression (41).

triglyceride, blood pressure, and glucose levels, were consistent across various individual conditions, indicating a common presence in individuals with depression. Women showed a significant increase in waist circumference, while men had higher triglyceride levels. Likewise, the negative impact of depression on cognitive and physiological aspects in patients was highlighted, emphasizing the importance of addressing both physical and mental health in the treatment of these conditions. In addition, concomitant illnesses such as bipolar disorder, schizophrenia, cardiovascular problems, and stress were found to be linked to depression and metabolic disturbances.

Initially, metabolic disturbances are conditions that increase an individual's susceptibility to disease throughout their life. In the health field, they are recognized as underlying factors that contribute to metabolic syndrome, also known as MS. This syndrome is characterized by a set of cardiovascular risk factors, such as abdominal obesity, low high-density lipoprotein (HDL) cholesterol levels, elevated blood pressure, increased triglycerides, and high glucose levels (58). The corresponding levels of metabolic disturbance significantly impact essential components necessary for the proper functioning of the body (4), approximately tripling the likelihood of chronification when

Table 8. Characteristic table of pathologies related to metabolic disorders.

Classification	Characteristics	
	Young Adult (19-24)	Adult (25-59)
	MetS and depression had strong associations with restrained, emotional, and external eating behaviors, lower triglyceride levels, insulin resistance, higher cholesterol, and high-density lipoprotein levels (43).	Obesity has an impact on cognition in obese individuals with MDD, and this impact can be significant, producing an additive effect that reached significance in measures of processing speed and executive function (37).
Obesity	No report	Both obesity and Metabolic Syndrome (MetS) are independently associated with depression. Still, when present together, these conditions exhibit a synergistic association and tend to cause greater damage to the individual's mental and physical health (54).
	No report	The frequency of Depressive Syndrome (DS) in obese subjects was 6.9%; obesity doubles the risk of presenting DS. Among patients with grade III obesity, 25% presented DS, while among those with grade I obesity, it was 5.3%, and with grade II obesity, it was 6.3% (4).
Triglycerides	No report	Metabolic alterations, along with depression, lead to higher levels of total cholesterol, LDL, and triglycerides in patients with suicidal behavior (50).
	No report	Metabolic Syndrome (MetS) with depression often results in significantly higher triglyceride levels, emphasizing the importance of regularly monitoring triglycerides in depressed patients (51).
Cholesterol	No report	The prevalence of Metabolic Syndrome was 25.9% in patients with depression, higher than that in healthy controls (17.3%). The lowest level of HDL (cholesterol) was the most common anomaly in the depression group (35).
	No report	Genes encoding components throughout the HPA axis are candidate genes for depression and metabolic abnormalities (type 2 diabetes) (57).
Type 2 diabetes	No report	Patients with type 2 diabetes (DM2) and depression aged between 45 and 70 had higher levels of hyperglycemia and cognitive impairment. Additionally, cognitive function was associated with the severity of depression with alpha salivary amylase activity (26).
	No report	The studied risk factors accounted for 50.5% of new diabetes cases (78.2% in men and 47.0% in women). Individuals exposed to metabolic and behavioral factors (mood states) had the highest risk of developing diabetes (53).
	No report	Depression was significantly associated with type 2 diabetes, which according to its level may cause greater metabolic alterations (46).
	No report	A higher rate of depressive symptoms with Metabolic Syndrome suggests that Metabolic Syndrome may be an important predisposing factor for central obesity, high triglyceride levels, and low HDL cholesterol levels (23).
Metabolic Syndrome	No report	Abdominal obesity, high triglycerides, low high-density lipoprotein cholesterol, high blood pressure, and high fasting glucose in depressed individuals had a chronic nature in 88.5%. It could be termed metabolic depression (16).
	No report	A higher number of components of Metabolic Syndrome corresponds to a higher number of depressive symptoms, with a higher frequency of insulin resistance, low c-HDL levels, high blood pressure, and carotid atherosclerosis being associated (4).
	No report	It is shown that cardiometabolic alterations are associated with depression, and there are high risks due to metabolic and emotional components that are variables (31).
Cardiometabolic	No report	Individuals aged 58 and over with depression often show an adverse cardiometabolic risk profile that can cause significant discomfort, which can be evidenced by high blood pressure levels (42).
	No report	Depressive mood negatively affects self-care practices, and due to mood swings, there are disruptions in proper metabolic function (20).
Type 1 diabetes	No report	Depression, anxiety, and resilience should be considered in the design of a multidisciplinary approach to type 1 diabetes, as these factors are significantly correlated with glycemic control (47).

Table 9. Table on comorbidities that are related to the diagnosis of depression and metaboliac alterations.

Classification	Characteristics	
	Young Adult (19-24)	Adult (25-59)
Bipolar Disorder	No report	In individuals with bipolar disorder, there are observable positive lipid characteristics, which in turn are linked to metabolic and depressive changes (56).
Cardiorespiratory	No report	A noticeable elevation in cardiorespiratory fitness index is present, indicating metabolic and depressive disruptions within the studied populace (50).
Cardiovascular Diseases	No report	Depression is identified as an added risk factor for cardiovascular issues, as certain antidepressant medications may influence blood pressure levels (39).
Stress	No report	Increased cortisol levels and hypercortisolism are associated with depression, leading to heightened stress and metabolic imbalances (57).
Cardiovascular Disease	No report	People experiencing depression exhibit a higher risk of cardiovascular problems, pointing to potential alterations in the metabolic syndrome (52).
Cardiovascular Disease	No report	Components of the metabolic syndrome, such as hypertension, dyslipidemia, hyperglycemia, hypertriglyceridemia, and unhealthy waist circumference, are directly linked to depression (55).
Cardiovascular	No report	Poor dietary habits and insufficient physical activity are correlated with depressive symptoms, changes in the metabolic syndrome, and cardiovascular indicators (36).
Schizophrenia	No report	Depressive moods are significantly correlated with the metabolic syndrome among individuals with schizophrenia (38).
Brain-derived neurotrophic factor deficiency (BDNF)	No report	A deficiency in brain-derived neurotrophic factor (BDNF) is implicated in depression mechanisms, alongside lifestyle-related metabolic changes (48).

combined with another disorder. As indicated by the elements of metabolic syndrome, there is a relationship with conditions such as depression due to the metabolic irregularities present (17).

Depression is a mental disorder characterized by changes in mood, behavior, and emotional expression, usually accompanied by profound feelings of sadness, lack of interest in previously pleasurable activities, variations in eating and sleeping habits, and cognitive changes (59). Likewise, depression has neuroendocrine repercussions that can contribute significantly to the development of other conditions or diseases, which can result in the accumulation of fat in the abdomen, imbalances in glucose metabolism, and irregularities in blood pressure, causing considerable deterioration (60).

Luo, Jiang, and Ren (61) focused on the connection between depression and metabolic changes. The results indicate that approximately 10 out of 12 individuals experience both conditions simultaneously, representing a coexistence rate of 83.3 %. Importantly, the presence of one disorder often triggers the development of the other. Furthermore, it has been observed that, at each assessment, about 2 out of 3 longitudinal studies explore this relationship as a possible trigger, while only 1 out of 3 focuses on long-term persistence, suggesting a correlation over time of 66.6 % (3). On the other hand, cross-sectional

studies show a frequency of 77.7 %, with 7 out of 9 investigations linking both conditions (62).

At the same time, this connection contributes to changes in glucose metabolism, elevated blood pressure, central fat accumulation, and lipid imbalances — all of which are key elements of metabolic syndrome. This syndrome encompasses multiple risk factors for cardiovascular disease, the development of diabetes, and abdominal obesity (4). These variations do not distinguish between different individual situations, and, due to their close relationship, they are considered a bidirectional condition. This implies a mutual influence between metabolic syndrome and depression, where metabolic syndrome frequently precedes depression and vice versa. Depression, in many cases, affects metabolic syndrome by encouraging unhealthy behaviors such as alcohol consumption, smoking, poor dietary choices, lack of physical activity, sleep disturbances, and lack of adherence to treatment (63).

Over the years, several studies have provided insights into the potential evolution of these variables over time. These investigations have helped to establish a detailed sequence of the relationship between depression and metabolic changes, demonstrating that about 46.34 % of the depressive symptoms observed in individuals with metabolic syndrome indicate underlying metabolic imbalances, such as insulin resistance, low levels of high-density lipoprotein (HDL) cholesterol, and high blood pressure (4). However, the prevalence of these conditions varies by gender, as it has been noted that women with depressive symptoms have a higher risk of developing metabolic syndrome in adulthood, often related to health problems in childhood (45). Regarding specific alterations, a high prevalence of 95 % has been observed in waist circumference, indicating a higher frequency among women (40). In contrast, men tend to show a higher prevalence (43 %) of elevated triglyceride levels, which may be influenced by external factors such as dietary habits, lifestyle choices, partner stability, and associations with other health conditions. These gender disparities may also be influenced by social factors, including marital status (30,52).

In relation to variations related to depression, obesity stands out with a prevalence of 6.9 %. This phenomenon is mainly due to the profound impact of eating habits on individuals (44), affecting them at the emotional, cognitive, and somatic levels, and leading them toward addictive tendencies (37). Likewise, these eating behaviors not only disrupt metabolic processes but also generate emotional eating patterns (43), resulting in uncontrolled responses in insulin, triglyceride, glucose, and HDL-cholesterol levels, posing significant health risks (54). HDL cholesterol often shows abnormalities in individuals with metabolic syndrome, presenting lower levels associated with more severe health complications (35). In addition, markedly elevated levels of triglycerides are observed, highlighting the importance of regular monitoring in individuals with both conditions to prevent the development of other health problems, such as cardiovascular disease (51).

However, the occurrence of these variations is associated with genes that may increase the likelihood of other diseases, such as type 2 diabetes, which, through their interaction with proteins and amino acids, contribute to the prevalence of metabolic syndrome (57). Previous studies have indicated that depression is related to high glucose levels and dysfunctions in glucose metabolism in patients (26). These connections have a significant impact on metabolism and its influence on the proper functioning of the body, and negative effects on self-care and nutrition may contribute to the onset of other conditions, such as type 1 diabetes (19,20). Overall, analysis of risk factors revealed that 50.5 % of new diabetes cases were linked to such factors (78.2 % in men and 47.0 % in women), indicating that individuals exposed to metabolic and behavioral factors are at elevated risk (53). This highlights the relevance of cardiometabolic diseases due to their sociodemographic and clinical characteristics (42).

Analysis of various medical conditions related to metabolic disturbances and depression revealed that the presence of bipolar disorder can lead to changes in lipid levels that affect metabolism when both conditions coexist (56). The combination of cardiovascular disorders and depression was identified as one of the most common associations worldwide, resulting in a significant increase in mortality and disability (52). These disorders can manifest through prehypertension and various biological changes, such as endothelial

dysfunction, increased inflammation, platelet dysfunction, and hypothalamic-pituitary-adrenal axis hyperactivity, which may indicate the presence of metabolic syndrome (64). During the evaluation of schizophrenia, a frequent association was found between depression and metabolic changes, which are attributed to activation of the hypothalamic pituitary adrenal (HPA) axis, resulting in increased cortisol release. This leads to a reduction in psychomotor activity and a lack of response to traditional treatments, which may increase the risk of abuse (38). Additionally, it was observed that stress can be another significant comorbid factor, triggering the release of hormones such as CRH and ACTH, which elevate cortisol levels and lead to imbalances in serotonin function, hyperglycemia, and insulin resistance. These aspects contribute to other irregularities and increase the likelihood of deterioration (57).

Finally, from the evidence analyzed, it can be stated that metabolic disorders and depression are conditions that are closely related and can have a significant impact on an individual's health, including conditions that worsen over time. Among the elements whose functionality is affected are altered cholesterol (HDL), triglyceride, blood pressure and glucose levels, which can result in diseases such as obesity, hypertension, type I and II diabetes, and dyslipidemia (altered blood lipid levels), through behaviors that are sometimes triggered by the symptoms themselves and can cause significant damage if not addressed in a timely manner.

CONCLUSIONS

The relationship between depression and metabolic alterations shows the interaction between the emotional state and vital metabolic processes, including nutrition and emotional and affective levels. These conditions significantly increase the likelihood of developing diseases with considerable impact on quality of life (43). It is important to highlight that, in adults diagnosed with depression, obesity, type 1 and 2 diabetes, dyslipidemia, and hypertension are the most common metabolic alterations that negatively affect health and well-being (4,65). On the other hand, it should also be clarified that women tend to have a higher waist circumference, while men show elevated triglyceride levels (30).

Metabolic disturbances and depression have an important bidirectional relationship, as the associated unhealthy behaviors may increase the risk of cognitive and physiological impairment, which impacts overall body function. These metabolic alterations in depressed patients may increase the risk of serious cardiovascular disease and other health complications (4). Furthermore, in women, these alterations may be related to unresolved problems during the early stages of development (40), whereas in men they may be associated with the lifestyle adopted in adulthood (41,65). Finally, it is important to note the coexistence of various pathologies with these alterations, such as bipolar disorder, schizophrenia, cardiopulmonary conditions, cardiovascular diseases, brain-derived neurotrophic factor deficiency and stress. Therefore, a comprehensive approach to metabolic disorders and depression is important, recognizing their importance in the promotion and prevention of both mental and physical diseases (3).

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From clouds to clarity: Understanding the real consequences of e-cigarettes and EVALI

De las nubes a la claridad: comprendiendo las verdaderas consecuencias de los cigarrillos electrónicos y EVALI

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SUMMARY

Electronic cigarettes are devices that heat liquid into aerosols for inhalation. According to the CDC and FDA, a 2022 survey found that 14.1 % of high school students and 3.3 % of college students in the U.S. used these devices, totaling 2.55 million young users. This growing trend gained serious attention in 2019 with the emergence of EVALI (E-cigarette or Vaping Product Use-Associated Lung Injury), predominantly affecting teenagers and young adults. EVALI presents with acute respiratory symptoms, often requiring hospitalization, and by February 2020, it had caused approximately 2 800 hospitalizations and 68 deaths. Although vitamin E acetate (VEA) was strongly implicated, other factors (including solvents, psychoactive substances, heavy metals, and flavorings) are under investigation. Compounding the issue, the COVID-19 pandemic has posed diagnostic challenges due to symptom overlap. The long-term health effects of electronic cigarette use remain uncertain, but research has linked it to chronic respiratory diseases like COPD, cancer, and systemic and cardiovascular conditions. Additionally, its use poses unique risks for younger populations due to the potential for addiction and developing complications. This review consolidates current research to explore the short- and long-term effects of electronic cigarette use, its pathophysiology, clinical manifestations, and effective diagnostic approaches. By broadening

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understanding beyond VEA as the primary cause of EVALI, this study highlights the need to consider the complex interplay of multiple chemical components involved in e-cigarette use. Advancing knowledge in this area is crucial for improving diagnosis, treatment, and prevention strategies while addressing the broader public health challenges posed by electronic cigarettes.

Keywords: *Electronic cigarettes, vaporizer, EVALI, vitamin E acetate, lung health, propylene glycol, vegetable glycerin, lung cancer, COPD, COVID-19, dual smokers.*

RESUMEN

Los cigarrillos electrónicos son dispositivos que calientan líquido hasta convertirlo en aerosol para inhalarlo. Según los CDC y la FDA, una encuesta de 2022 descubrió que el 14,1 % de los estudiantes de secundaria y el 3,3 % de los estudiantes universitarios en EE.UU usaban estos dispositivos, lo que suma un total de 2,55 millones de usuarios jóvenes. Esta tendencia creciente ganó mucha atención en 2019 con la aparición de EVALI (lesión pulmonar asociada al uso de cigarrillos electrónicos o productos de vapeo), que afecta predominantemente a adolescentes y adultos jóvenes. La EVALI se presenta con síntomas respiratorios agudos, que a menudo requieren hospitalización, y en febrero de 2020 había causado aproximadamente 2 800 hospitalizaciones y 68 muertes. Aunque el acetato de vitamina E (VEA) estuvo fuertemente implicado, se están investigando otros factores (incluidos solventes, sustancias psicoactivas, metales pesados y saborizantes). Para agravar el problema, la pandemia de COVID-19 ha planteado desafíos de diagnóstico debido a la superposición de síntomas. Los efectos a largo plazo del uso de cigarrillos electrónicos en la salud siguen siendo inciertos, pero las investigaciones lo han vinculado con enfermedades respiratorias crónicas como EPOC, cáncer y afecciones sistémicas y cardiovasculares. Además, su uso plantea riesgos únicos para las poblaciones más jóvenes debido al potencial de adicción y desarrollo de complicaciones. Esta revisión consolida la investigación actual para explorar los efectos a corto y largo plazo del uso de cigarrillos electrónicos, su fisiopatología, manifestaciones clínicas y enfoques de diagnóstico efectivos. Al ampliar la comprensión más allá de VEA como la causa principal de EVALI, este estudio destaca la necesidad de considerar la compleja interacción de múltiples componentes químicos involucrados en el uso de cigarrillos electrónicos. Avanzar en el conocimiento en esta área es crucial para mejorar el diagnóstico, el tratamiento y las estrategias de prevención, al tiempo que se abordan los desafíos de salud pública más amplios que plantean los cigarrillos electrónicos.

Palabras clave: *Cigarrillos electrónicos, vaporizador, EVALI, acetato de vitamina E, salud pulmonar, propilenglicol, glicerina vegetal, cáncer de pulmón, EPOC, COVID-19, fumadores duales.*

INTRODUCTION

Electronic cigarettes, originally introduced as a presumably safer alternative to conventional smoking, have seen a notable increase in popularity, especially among younger populations. Between 2010 and 2014, there was a 24.4 % increase in the prevalence of device use among teenagers in Central and Eastern Europe (1). According to data published by the Centers for Disease Control and Prevention (CDC) in 2022, approximately 2.55 million high school and college students in the United States were using electronic cigarettes. One in four of these users reported daily use, highlighting that a considerable number of young people have had prior experience with these devices (2). However, this emerging trend has also brought to light significant concerns about the health implications associated with vaping. One of the most alarming issues is the emergence of "E-cigarette or Vaping Product Use-Associated Lung Injury" (EVALI), which reached epidemic levels in 2019 in the United States (3). This disease, characterized by acute pulmonary symptoms and severe dyspnea, highlights the immediate dangers associated with vaping (4,5). Although initial research attributed EVALI predominantly to vitamin E acetate, recent studies suggest a more complex etiology that includes a wide range of chemicals and additives present in e-liquids. These compounds, including solvents, flavorings, and psychoactive substances, interact to create chemical byproducts that pose significant health risks (6,7). Moreover, successive generations of electronic cigarettes significantly reflect the evolution of these devices, which exhibit a remarkable capacity for customization, encompassing aspects such as vaporization temperature, flavor diversity, and chemical compound concentration (8). While these innovations enhance the appeal of vaping, they also lead to a proliferation of chemical

products and their interactions, creating greater complexity in their effects on health (9).

Beyond the immediate concern of EVALI, the long-term effects of electronic cigarettes have also begun to emerge. There is growing evidence linking vaping with chronic respiratory diseases such as Chronic Obstructive Pulmonary Disease (COPD) and the development of lung cancers (10). Moreover, the impact of vaping extends far beyond the respiratory system, also affecting the cardiovascular system (11). This multifaceted impact directs toward a comprehensive investigation of the pathophysiological effects of electronic cigarettes, especially given their growing prevalence among young populations (12). In addition, the simultaneity between the outbreak of EVALI and the onset of the COVID-19 pandemic has further complicated the scenario, as the similarity of symptoms between the two conditions and the lung injury mechanism produced by EVALI, which involves acute alveolar damage and a marked inflammatory process, can mimic the manifestations of COVID-19 in radiological images (13). Therefore, this creates greater difficulties for the diagnosis of EVALI, increasing the risk of inappropriate treatments and delays in proper care (14).

In light of these complexities, this review aims to provide a clearer and more comprehensive pathophysiological perspective on the pathological effects of electronic cigarettes, emphasizing the need for a detailed understanding of the health risks associated with vaping to inform the scientific community better. This understanding is crucial for improving the prevention and diagnosis of EVALI and addressing the increasing prevalence of these devices among younger populations, ultimately aiming to mitigate their short-term, medium-term, and long-term consequences.

ELECTRONIC CIGARETTES

Electronic cigarettes are devices designed to convert liquid into aerosol or vapor by applying heat, thereby facilitating inhalation. Originating in 1979, these devices emerged as an alternative to traditional cigarettes, introducing the term "vaping," which remains in use. However, the first model created was not commercially successful due to the bitter taste of the nicotine aerosol (5). In 2003, a more advanced design was launched in Beijing, marking a turning point with several key improvements that ensured its market acceptance. This new model was introduced in the United States in 2006, triggering a steady increase in the popularity of electronic cigarettes, particularly among young people. This boom is attributed to the introduction of disposable cartridges with flavored nicotine solutions, which eliminated the bitter taste and significantly expanded the variety of products available (15).

Additionally, data from the National Youth Tobacco Survey, the Youth Risk Behavior Surveillance System, and the Monitoring the Future study reveal an exponential increase in the use of these devices among high school and college students since 2014. For example, in 2018, 13.5 % of eighth-grade students reported having tried nicotine vaping products at some point in their lives, with an increase to 34 % among twelfth-grade students, and up to 40.5 % reporting their use in September 2019. These figures underline the growing prevalence of vaping among youth, a phenomenon driven by aggressive marketing and a variety of appealing flavors (16-18).

The nomenclature and characteristics of electronic cigarettes have undergone considerable evolution, reflecting both their diversification and widespread use. Commonly described as "e-cigs," "cigalikes," "e-hookahs," "mods," "vape pens," "vapes," and "tank systems," these devices have introduced specific terminology such as "vape juice" or "e-liquid," and verbs like "to rip," "to juul," "to puff," or "to hit" to describe the action of vaping (15,4). Historically, electronic cigarettes are classified into four generations, each with distinctive features that reflect technological advances and adaptations to consumer markets. The first generation, known as "cigalikes," mimics the aesthetics of conventional cigarettes and are generally disposable devices (8,19,20). The second generation resembles a pen and offers enhanced features such as rechargeable batteries and increased vapor production (8,20). The third generation, or "tank style," allows personalized adjustments in vapor temperature and a greater e-liquid storage capacity, thus offering a more intense and personalized experience (21). The fourth generation, or "Pod Mod," includes devices

that are often disguised as everyday objects, such as USB drives, and utilize nicotine pods that allow for more concentrated inhalation with reduced irritation, which is particularly appealing to young audiences (22,23).

STRUCTURE AND COMPONENTS

In general terms, electronic vaping devices consist of several essential components that work together to convert liquid into vapor. These include a lithium battery that supplies power, an atomizer located within a vaporization chamber, a reservoir that stores the e-liquid, and a mouthpiece through which the user inhales the vapor. The interaction between these components begins when the user draws air through the mouthpiece, activating a sensor which, in turn, ignites the atomizer. This component heats the e-liquid until it vaporizes, thus allowing the inhalation of the resulting aerosol (22).

The control of the device's activation is facilitated by an on/off button, which, along with the inhalation sensor, enables the user to manage the electronic cigarette's operation. In some designs, the device eliminates a physical button and activates automatically when it detects user inhalation, making the sensor a critical component in the system's operability. The battery, whether rechargeable or non-rechargeable, is crucial as it provides the necessary energy to heat the atomizer to reach temperatures around 400 degrees Fahrenheit in just seconds. The battery's power can range from 5W to 200W and plays an important role in determining the range of vaporization temperatures, which can influence the integrity of the atomizer and the chemical composition of the liquid, resulting in the generation of potentially harmful byproducts during the vaporization process (19,22,24,25). Likewise, the atomizer, another vital component, consists of heavy metal coils that convert the e-liquid into vapor. The configuration and resistance of these coils are crucial for the size of the vapor particles, which can vary from ultrafine, less than 0.1 micrometers (μm), to micrometric particles of approximately 4 μm. This variability in particle size is significant as it determines how they deposit in the respiratory system and the proportion that reaches the airways, which is fundamental for understanding the pulmonary effects of vaping (24,26).

Regarding the cartridge, which is responsible for containing the e-liquid, it can be prefilled or designed for the user to fill. Often, this component is combined with the atomizer to form a single unit and is made of plastic or metal. Some models even include a transparent cover that allows users to monitor the remaining liquid level (22). The e-liquids used in these devices feature a complex variety of ingredients, including psychoactive substances such as nicotine, tetrahydrocannabinol (THC), cannabinoids (CBD), and solvents like vitamin E acetate (VEA), propylene glycol (PG), and vegetable glycerin (VG). Although PG and VG are classified by the Food and Drug Administration (FDA) as safe for consumption and topical applications, their inhalation poses significant risks, including the production of harmful aldehydes such as formaldehyde, acetaldehyde, acrolein, and methylglyoxal, which raise concerns due to their potentially carcinogenic effects (17,27).

VEA, often used as a diluent in e-liquids containing more viscous substances like THC and CBD, has been linked with severe lung injuries. Additionally, nicotine, a stimulant known for its addictive and cardiovascular effects, is often combined with these solvents and other additives, creating a complex chemical profile that may include impurities and carcinogenic substances such as tobacco-specific nitrosamines (TSNAs) (15,20,18,28). Finally, the complexity is further increased by the presence of between 8 000 and 15 000 different flavorings used in e-liquids, including diacetyl, which imparts a buttery flavor; ethyl maltol, which provides a sweet caramel touch; vanillin, which introduces a warm vanilla flavor; and menthol, which offers a refreshing and cleansing sensation. These additives, while enriching the sensory experience of vaping, are not without controversy due to their potential negative impact on lung health when inhaled. For example, diacetyl, safe for food consumption, has been linked to severe lung diseases in inhalation contexts. Similarly, ethyl maltol, when interacting with metals present in the aerosols of electronic cigarettes, can increase the absorption of harmful substances such as heavy metals (7,29-32). The inclusion of these

flavorings in e-liquids demonstrates an effort to satisfy a wide range of consumer preferences, yet also highlights the need for careful evaluation of their safety when inhaled, given the various health implications they may have.

E-CIGARETTE OR VAPING PRODUCT USE-ASSOCIATED LUNG INJURY (EVALI)

The use of electronic cigarettes has been linked to a wide range of adverse health effects, primarily derived from exposure to toxic and potentially carcinogenic substances commonly found in the liquids and flavorings of these devices, as well as from the oxidation of their compounds during the vaping process, which leads to the generation of harmful chemicals. This began to be observed more than a decade ago, specifically starting in 2012, when cases of lung damage linked to vaping began to be documented, with patients presenting symptoms such as persistent cough and ground-glass opacities observed in computed tomography (CT) images, and lipid-laden macrophages (LLM) detected in bronchoalveolar lavage (BAL) samples (33,34).

In the subsequent years, between 2013 and 2018, multiple studies were conducted, and numerous case reports were collected that demonstrated a variety of acute lung injuries linked to the use of electronic cigarettes. These included lipid pneumonia, acute eosinophilic pneumonia, cases of pneumonitis with pleural effusion, respiratory bronchiolitis, interstitial lung diseases, bronchiolitis obliterans organizing pneumonia, and in extreme cases, diffuse alveolar hemorrhage (37-45). However, despite these observations that clearly indicated the potential dangers associated with the use of these electronic devices, it was not until the outbreak of a mysterious and severe respiratory disease in 2019 in the United States that electronic cigarettes began to receive due attention. This outbreak, which quickly reached epidemic levels by the end of September 2019, led to approximately 2 800 hospitalizations and 68 deaths by February 2020 (3,46). The Centers named this disease for Disease Control and Prevention (CDC) as "E-cigarette or Vaping Product Use-Associated Lung Injury" (EVALI), which is characterized by an acute pulmonary inflammatory process that causes alveolar collapse and a severe disruption of gas exchange, resulting from damage to the pulmonary endothelial and epithelial barriers exposed to toxic vapor particles (26,47).

CDC research identified that vaping products containing THC and vitamin E acetate (VEA) were particularly associated with the EVALI outbreak. The presence of these substances in the BAL of patients pointed to their role in the etiology of the disease. However, the detection of other toxic agents in vaping products, including pesticides, oils, thinners, and plasticizers, and the continuation of EVALI cases even after the prohibition of illicit products containing THC and VEA, underscore the need for a more thorough and comprehensive analysis of the physicochemical and toxicological properties of e-liquids, as well as the underlying mechanisms in the pathogenesis of EVALI (6,48-50).

PATHOPHYSIOLOGY

Five years after the EVALI epidemic, scientific research has made significant advances in understanding its pathophysiology. The complexity of the e-liquids used in electronic cigarettes, which include solvents such as PG (propylene glycol), VG (vegetable glycerin), and VEA (vitamin E acetate), along with psychoactive components like nicotine, THC, and CBD, as well as flavorings like diacetyl and vanillin, has been a central focus of these studies. Specifically, a key study conducted by Blount et al. in 2019 analyzed BAL (bronchoalveolar lavage) samples from 51 patients affected by EVALI, identifying the presence of VEA and THC in 94 % of these samples (6). These findings were crucial in establishing these components as the main causative agents of the disease. It is essential to note that this study not only highlighted the direct association between these additives and EVALI but also guided further research towards a more detailed examination of how these chemicals interact with lung tissues (9,12).

VEA-THC

VEA is the ester of vitamin E (α-tocopherol). It can affect the physiological processes of the lungs in multiple ways, such as the function of

pulmonary surfactant, mucociliary clearance, the immune system, and its role in the phagocytosis of inhaled particles.

Effects on Pulmonary Surfactant

Pulmonary surfactant is a complex mixture of phospholipids, with phosphatidylcholines, particularly dipalmitoyl phosphatidylcholine (DPPC), being the most abundant, constituting approximately 90 % of its composition. This substance is essential for pulmonary stability as it reduces surface tension in the alveoli during the cycles of inspiration and expiration, preventing alveolar collapse. The impact of VEA on pulmonary surfactant is particularly detrimental because this component acts as a "surfactant disruptor," given its structure with a long aliphatic tail, which allows it to integrate and align parallel with the surfactant phospholipids, specifically with the molecules of DPPC, causing the surfactant to transition from a gel phase to a liquid crystalline phase, drastically altering its elastic properties (51). This structural modification not only diminishes the surfactant's efficacy in reducing surface tension but also negatively affects the lung's compression-expansion cycle during breathing, thereby playing a fundamental role in EVALI (52-54).

Alteration in the Immune System

The inhalation of aerosols containing VEA has a considerable impact on the innate immune system, particularly affecting the respiratory epithelium. This component interferes with the function of primary immune system cells, such as alveolar macrophages (AM) and polymorphonuclear leukocytes (PMN), which are essential for pulmonary defense. AMs, in particular, show an increase in their rate of apoptosis and a notable reduction in their ability to phagocytize and degrade pathogens, aerosol particles, and apoptotic cells (55).

These alterations have been demonstrated in various studies, including one conducted by Bhat et al., which analyzed bronchoalveolar lavage (BAL) samples and performed anatomopathological examinations on a group of 30 mice exposed to VEA aerosols. The results of this study showed an increase in leukocyte concentration in lung tissue, indicating an acute inflammatory response. Additionally, a notable accumulation of lipid-laden alveolar macrophages, identified as foam cells, was observed near the alveolar epithelial pneumocytes and exhibited intense oil red O staining, demonstrating an alteration in the cellular environment (56). Similarly, further research conducted by Matsumoto et al., revealed an increase in the levels of certain chemokines and pro-inflammatory cytokines in BAL, such as monocyte chemokine MCP-3, neutrophil chemokine KC, and cytokines IL-6 and IL-8, without a corresponding increase in IL-10, an anti-inflammatory cytokine, maintaining a pro-inflammatory state (57-59). At the same time, damage to the integrity of the alveolar-capillary barrier was documented, evidenced by an increase in protein concentration in the BAL of vaping patients, including albumin, suggesting compromised capillary permeability (60).

Harmful Agents by Pyrolysis

Electronic cigarettes operate at temperatures ranging from 110 to 1 000 °C, acting as miniature pyrolysis devices. Factors such as the resistance of the heating coil, applied voltage, the composition of the vape liquid, and user practices directly influence the temperature at which the e-liquid is heated. Particularly, the pyrolysis of VEA in these devices can be harmful, as it produces gases such as ketene, alkenes, and benzene, all of which are known for their toxic and carcinogenic properties. Ketene formation is especially likely at temperatures above 500 °C, or under "dry puff" conditions, a term describing situations where the vape liquid is scarce and concentrated, which can lead to overheating. This scenario is more common when using counterfeit or modified vaping devices (53,61).

During the pyrolysis of VEA, two main pathways can be followed: in the first, ketene is initially released, triggering the breakage of the C-C and C-O bonds of the dihydropyran ring, resulting in the production of duroquinone and alkene. The second pathway produces a different

sequence where the dihydropyran ring is cleaved before ketene is released. These byproducts, particularly benzene, are recognized carcinogens that are also present in tobacco smoke and pose a significant health risk (62), as it has been documented that exposure to 200 ppm of ketene can be lethal within just 10 minutes. More recent studies have recalibrated the lethal concentration to just 0.24 ppm, highlighting the extreme toxicity of these compounds even at minimal levels (53,63). Thus, it is highly concerning that these substances have already been identified at high concentrations in studies examining teenage users of electronic cigarettes (64).

Cellular Damage and Epigenetic Changes

Type II pneumocytes (NT II), cells responsible for surfactant production, can undergo cell death upon contact with aerosols containing VEA, indicating its direct toxicity. This toxicity was demonstrated by Matsumoto et al. in a study where these cells were exposed to VEA aerosols for periods of 10 and 120 minutes per day over three consecutive days. The results revealed cytotoxicity that increased with the administered dose, exhibiting a clear dose-response pattern (58). Similarly, in another study conducted by Soto et al., it was observed that NT II cells absorbing VEA exhibited alterations in 752 genes, identified with a false-positive rate of less than 0.1 %. This finding unveiled a high activation in signaling pathways of IL-17, MAPK, and TNFα, which are associated with the expression of inflammatory genes, as well as genes involved in osteoclast differentiation (53).

Additionally, research conducted by Marrocco et al. shed light on how exposure to VEA aerosol differentially affects various cell types. For instance, while in human pulmonary epithelial cells (Calu-3), no significant increase in the production of reactive oxygen species (ROS) was observed, human monocyte cells (THP-1) experienced a notable increase in ROS production that was proportional to the dose. Additionally, it was found that VEA aerosol could disrupt the mitochondrial membrane potential in pulmonary epithelial cells, which in turn activated caspase-3, leading to cellular apoptosis (65).

FLAVORINGS

Flavorings have been fundamental to the success of electronic cigarettes, as they have enabled the bitter taste of nicotine to be overcome. Currently, there is a wide variety of these flavorings, designed to appeal to young consumers, particularly. However, the diversity of options available complicates their study, since many have been approved for food use, but not for inhalation. This raises significant concerns about their safety when consumed in this manner.

Ethyl maltol (EM) is a flavoring with a caramel taste frequently found in e-liquids. It has been observed that EM, in conjunction with residues of heavy metals from the components of electronic cigarettes, has the potential to be highly cytotoxic by increasing the absorption of iron, copper, lead, and zinc (66-68). This was recorded in a study by Durrani et al., where the cytotoxic effects of aerosols containing ethyl maltol (EM) and heavy metals on various pulmonary cell lines, including Calu-6 and A549 (lung epithelial cells), as well as HEK293 and IMR-90 (fibroblasts), were evaluated. The results revealed that exposure to aerosols enriched with copper (Cu) and EM significantly reduced the viability of Calu-6 and A549 cells due to an increase in the generation of reactive oxygen and nitrogen species, which activated the expression of genes related to the Nrf2 antioxidant pathway. Despite this antioxidant response, oxidative stress still occurred, causing DNA damage and activating the ATM protein kinase (Ataxia Telangiectasia Mutated), which is crucial for damage repair. When damage is irreparable, the cells initiate apoptosis processes. On the other hand, cells exposed to aerosols with EM and iron (Fe) maintained their viability thanks to high levels of metallothionein (MT), which provided effective defense by neutralizing potential damage. However, in fibroblast cell lines HEK293 and IMR-90, exposure to aerosols with Cu and EM did not affect their viability. In contrast, aerosols with Fe and EM did reduce their viability, indicating that the cellular response to metal exposure varies significantly between different types of cells (32,66-68).

Menthol, cherished in the world of electronic and conventional cigarettes for its refreshing mint flavor, has gained popularity, especially among new users. However, its use is surrounded by controversy due to its potential impact on lung health, as it has been associated with several adverse effects, including reduced cell proliferation, increased oxidative stress, promotion of inflammatory processes, and damage to the respiratory epithelium (7,69). In the study by Nair et al., it was observed that menthol binds to the TRPM8 receptor (Transient Receptor Potential Melastatin 8), an ion channel that prefers calcium. This binding causes a rapid increase in intracellular calcium levels, generating vesicles originating from the endoplasmic reticulum. These vesicles migrate towards the cell membrane, although they do not fuse with it. Excess cytosolic calcium is expelled by calcium exporters located on the cell surface, such as Ca^{2+}-ATPase and the Na^{+}/Ca^{2+} exchanger. This calcium increase can also extend to the mitochondria through the mitochondrial uniporter channel (MCU), inducing the oxidation of mitochondrial proteins and the mitochondrial antioxidant enzyme SOD2, which triggers the production of reactive oxygen species (ROS) and results in oxidative stress (7,30,69).

The nuclear factor kappa B (NF-κB), an essential signaling pathway activated by oxidative stress, plays a crucial role in the bronchiolar epithelium, where it facilitates the activation and expression of NF-κB-dependent inflammatory mediators. Additionally, it regulates the expression of genes responsible for neutralizing reactive oxygen species (ROS) to promote cell survival, as well as the production of cytokines with immunomodulatory functions. Elevated levels of NF-κB and increased production of proinflammatory cytokines such as IL6 and IL8, which are common in inflammatory lung disorders, underscoring that both acute and chronic inflammation are fundamental elements in the pathogenesis of various lung diseases (7,30,69).

Diacetyl, also known as 2,3-butanedione, has an intense buttery flavor. It is classified as "generally recognized as safe" (GRAS), although there is limited data on its safety when inhaled. It has been found that high-voltage vaping with diacetyl significantly increases levels of acetaldehyde, acrolein, and formaldehyde, which are classified as primary irritants of the respiratory tract. Diacetyl is a dicarbonyl and tends to cross-link proteins and thus is considered reactive. In this regard, it has been considered to inactivate proteins by reacting with an amino acid, arginine, to cause bronchiolitis obliterans or "popcorn lung," resulting in a decrease in forced expiratory volume in the first second (FEV1) and the FEV1/ forced vital capacity (FVC) ratio (31,70,71). Moreover, the electrochemical activity of diacetyl alters the normal electron transfer, leading to the production of ROS that can cause cell necrosis. Diacetyl also causes significant changes in gene expression, including those genes involved in cilia formation, which can lead to a reduction in the number of ciliated cells. These cells are crucial for effective mucociliary transport, and their dysfunction has been associated with chronic lung diseases, including chronic obstructive pulmonary disease (COPD) and asthma (70,72).

Vanillin, known for imparting the popular vanilla flavor, can negatively influence the metabolic processes of the respiratory epithelium. This impact is manifested in various metabolic pathways, including those related to fatty acids, lipids, mitochondrial function, and the metabolism of numerous amino acids such as glutamate, tyrosine, methionine, cysteine, arginine, proline, aspartate, glycine, serine, alanine, threonine, as well as branched-chain amino acids (valine, leucine, isoleucine) and lysine. On the other hand, ethyl vanillin, another derivative of vanilla flavoring, has been shown to have detrimental effects on the lungs, specifically reducing the ability of neutrophils to generate an oxidative burst, thereby compromising immune function (73,74).

Other compounds frequently used as flavoring additives include cinnamaldehyde, which imparts the distinctive cinnamon flavor, and benzaldehyde, found in cherry and almond aromas. Additionally, linalool is used to provide sweet and floral notes. The presence of these and thousands of other compounds in electronic cigarettes significantly complicates the research on the harmful effects that flavorings can have on the respiratory epithelium and, therefore, on lung injury associated with the use of electronic cigarettes (7).

PG, VG, AND VG/PG

The most commonly used solvents in e-liquids are PG (propylene glycol) and VG (vegetable glycerin), which the FDA has approved as safe for consumption and topical application in cosmetics due to their lipophilic solvent properties. However, this approval did not consider their inhalation. When these components are used in a vaporizer, their vaporization process generates toxic byproducts, including carbon monoxide, acetylene, methane, and aldehydes (75,76). They have also been shown to contribute to alterations in essential processes for normal mucociliary clearance, as they affect ion channels such as the large conductance K^+ channel (BK) and the cystic fibrosis transmembrane conductance regulator (CFTR). These ion channels are essential for maintaining liquid volumes on the surface of the airways (LSA) for proper ciliary beating and mucus transport in the airway epithelium (77,78).

In a series of three studies conducted by Kim et al., the effects of e-liquids composed mainly of VG, PG, and VG/PG, respectively, were evaluated. In the first study, carried out in 2022, the effects of exposure to aerosols composed mainly of VG on airway inflammation and ion channel function were investigated. It was recorded that there was a reduction in CFTR function in non-smoking, non-vaping human volunteers after just one week of vaping with e-liquids containing VG. This change in CFTR function was accompanied by elevated levels of mRNA expression of inflammatory mediators, such as interleukin 6 (IL6), interleukin 8 (IL8), matrix metalloproteinase 2 (MMP2), matrix metalloproteinase 9 (MMP9), and transforming growth factor beta 1 (TGFB1). These results aligned with *in vitro* experiments, where human bronchial epithelial cells (HBEC) not exposed to cigarette smoke but to electronic cigarette aerosols containing VG for seven days, and showed reduced function of the CFTR channel (79-81). The second study, conducted in 2023, focused mainly on the effects of e-liquids composed of PG and their impact on both *in vivo* and *in vitro* models of BK and CFTR ion channels, as well as the detection of inflammatory markers in the airway, resulting in a significant decrease in BK activity. The effect on BK is mediated by methylglyoxal (MGO), an α-dicarbonyl compound produced from the thermal decomposition of PG by the atomizer coil. This substance can modify the arginine residues in the C-terminal tail of LRRC26 to form irreversible adducts, thus preventing the interaction between Slo1 (the main α subunit of the BK channel) and LRRC26 (Slo1/LRRC26), and thereby inhibiting BK function. Interestingly, exposure of sheep to PG aerosols did not affect CFTR, nor did it induce an increase in plasma levels of inflammatory markers, including IL-6, IL-8, and TGF-β1, after 5 days (10,17,82-84).

Finally, the last study, conducted in 2024, focused on the alterations caused by e-cig aerosols containing propylene glycol (PG) and vegetable glycerin (VG) in equal proportions (PG/VG). As a result, it was concluded that the PG/VG combination clearly affects mucociliary function, causes inflammation in the airway epithelium, alters the normal function of CFTR and BK channels, further reducing ciliary beating, and increases the expression of MUC5AC, possibly inducing hyperplasia of goblet cells. PG/VG aerosols from electronic cigarettes also increased mucus concentration and the activity of MMP-9 in the airways of sheep *in vivo*. Together, these data provide clear evidence of the harmful effects of PG, VG, and PG/VG on the airways (85).

CLINICAL PRESENTATION

The clinical presentation of EVALI is varied and nonspecific, often leading to its confusion with an infection. Although tests do not demonstrate the presence of the causative pathogen, approximately 72 % of patients who are hospitalized report having been seen in outpatient settings before admission for related symptoms, and 45 % of these patients received antibiotics with no improvement. According to recent studies, approximately 80 % to 95 % of patients present with respiratory conditions, including cough, breathing difficulties, and pleuritic chest pain. Additionally, approximately 87 % of patients experience constitutional symptoms, such as fever, fatigue, and generalized weakness, and 73 % exhibit gastrointestinal symptoms, including nausea, vomiting, and abdominal pain (4,15,86-89). Regarding the duration of symptoms before a hospital presentation, the median is approximately 6 days, although in some cases, it can last from 0 to 61 days. When assessing

the initial vital signs of these patients, it was recorded that 64 % presented with tachycardia, 43 % with tachypnea, and 38 % of patients had an oxygen saturation between 89 % and 94 % while breathing room air, whereas 31 % had an oxygen saturation below 89 %. Additionally, fever was documented in 29 % of patients during triage (90).

IMAGING PRESENTATION

Since the 2019 epidemic of electronic cigarettes, a substantial amount of data has been collected on the imaging findings of EVALI. Despite this, precise descriptions of these findings, particularly in computed tomography (CT), positron emission tomography (PET), radiography (RX), and magnetic resonance imaging (MRI), continue to be limited and occasionally restricted to presumptive cases, with limited correlation with the histopathological findings of this condition (91,92).

CT is the most commonly used imaging technique to assess pulmonary abnormalities in EVALI. According to Hofmann et al., acute pulmonary lesions are observed in 98 % of the affected patients, while the remaining 2 % present chronic pulmonary lesions (93). Various studies, such as those conducted by Henry et al. (94,95) and Kligerman et al. (4), predominantly describe diffuse alveolar damage (DAD) on CT scans. However, Panse et al., in 2020 (96), suggested that the appropriate term to describe these lesions was "Acute Lung Injury" (ALI). This is because one of the defining histopathological characteristics of DAD, the presence of hyaline membranes, was present in only a minority of patients (24 %). ALI is the most common CT pattern of EVALI, consisting of multifocal or diffuse ground-glass opacities, observed in 96 % of the patients, and/or consolidation, which affects most or all lobes bilaterally, with or without mild interlobular septal thickening, and there may even be subpleural preservation (96-98). The distribution of pulmonary parenchymal abnormalities is observed to be multifocal in 54 % of EVALI patients and diffuse in 46 % of cases. Additionally, 17 % of the cases are also characterized as peripheral and predominantly central in 8 %. Likewise, infiltrative abnormalities of the pulmonary parenchyma show subpleural preservation in 45 % of affected patients (92,94,96-98).

On the other hand, in chest X-rays, patients often present with diffuse and hazy opacity, more pronounced centrally, with notable preservation of the cardiac border and subpleural portions of the lung. The abnormalities are usually predominant in the upper, middle, or lower part of the lung. Kerley lines may also be observed due to septal thickening. These findings tend to coincide with those observed in CT, showing diffuse ground-glass opacities that are generally bilateral and relatively symmetrical. Even in cases where consolidation is present, it tends to be mild. Another common finding is the presence of subpleural spread areas both centrally and peripherally, as well as lobular spread areas (4).

DIAGNOSIS

The diagnosis of EVALI presents a considerable challenge for healthcare professionals, given the absence of specific tests that directly confirm the disease. Therefore, to correctly diagnose EVALI, a comprehensive approach is required that encompasses the evaluation of the patient's clinical symptoms, their history of using vaping devices, and the identification of pulmonary infiltrates in diagnostic imaging such as X-rays (RX) or computed tomography (CT) scans of the chest (4,99). This process is based on the principle that EVALI must be considered a diagnosis of exclusion, which implies that other possible causes of the patient's respiratory symptoms must be ruled out through a variety of tests that include analysis for respiratory viruses such as influenza or SARS-CoV-2, sputum cultures, and specific tests for other pathogens present in the urine. Additionally, a complete blood count that includes differential and liver transaminase levels, as well as inflammatory markers such as the erythrocyte sedimentation rate and C-reactive protein, is essential. Toxicological tests in urine, with proper informed consent, to detect substances like THC should also be conducted (100,101).

In terms of imaging, findings may vary but commonly show evidence of ALI, which includes diffuse bilateral opacities or ground-glass opacities, without unique characteristics

that clearly differentiate them from other lung diseases (88,91,92,96). In situations where imaging findings are inconclusive or when other infectious causes are suspected, procedures such as bronchoscopy may be indispensable to ensure an accurate diagnosis in the presence of atypical symptoms or the suspicion of alternative infections (100).

To standardize the diagnosis of EVALI, the CDC formulated guidelines in 2019 that continue to be a cornerstone in the definition and management of this disease, providing clear criteria for the identification and reporting of confirmed and probable cases. According to these criteria, a confirmed case involves the use of vaping products within 90 days prior to the onset of symptoms, the presence of pulmonary infiltrates on a chest CT scan, and the absence of pulmonary infection or any other plausible disease in the initial evaluation. A probable case is defined similarly but allows some flexibility when an infection is detected that is not believed to be the sole cause of lung damage, or when not all the minimum criteria to rule out a pulmonary infection have been met (99,101).

Given the ongoing evolution in the understanding of EVALI, it is essential that diagnostic criteria be reviewed and regularly updated based on the most recent evidence. This ensures an effective diagnostic and management approach, enabling the delivery of evidence-based care for patients affected by this condition.

ELECTRONIC CIGARETTES AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung condition characterized by chronic respiratory symptoms (dyspnea, cough, sputum production, and/or exacerbations) due to abnormalities in the airways (bronchitis, bronchiolitis) and/or alveoli (emphysema) that cause persistent, often progressive, airflow obstruction. This disease is commonly associated with the chronic inhalation of harmful gases such as cigarette smoke, leading to irreversible airflow obstruction (102).

The Burden of Obstructive Lung Diseases (BOLD) program used a standardized methodology that included questionnaires and pre- and post-bronchodilator spirometry to assess the prevalence and risks of COPD worldwide. Based on BOLD and other large-scale epidemiological studies, the global prevalence of COPD is estimated at 10.3 %. However, with the increasing prevalence of smoking in low and middle-income countries and the aging population in high-income countries, the prevalence of COPD is expected to rise significantly in the coming years. This disease is one of the leading causes of death globally, and according to the World Health Organization (WHO), as of June 22, 2021, it is the third leading cause of death worldwide, causing more than 3 million deaths by 2024 (103-107).

A distinctive feature of COPD related to the use of electronic cigarettes is the dehydration of the mucosa, caused by an imbalance in sodium and water homeostasis and hypersecretion of mucin. This situation is exacerbated by exposure to aerosols from electronic cigarettes containing vegetable glycerin (VG) and propylene glycol (PG). These components alter essential ion channels such as CFTR, BK, and the epithelial sodium channel (ENaC), which are crucial in regulating the hydration of the airway surface and fluid balance (10,79,85).

The aerosols generated during vaping sessions contain oxidants and ROS, produced by heating the liquid in the coil. Even unvaporized e-liquids can induce oxidative effects; however, flavor additives, especially sweet and fruity flavors, are the most oxidizing. Vaping has been linked with an increased risk of lung diseases by inducing oxidative stress, inflammation, and mitochondrial dysregulation, crucial for the production of reactive oxygen and ATP. This link was supported by a study by Li et al., which demonstrated that vaping electronic cigarettes induces the upregulation of Toll-like receptor 9 (TLR9), associated with mitochondrial DNA damage and inflammatory processes (108-111).

Additionally, the NRF2 protein plays a vital role in the cellular antioxidant response. Under normal conditions, NRF2 is found in the cytoplasm bound to KEAP1, which, along with CUL3 and RBX1, forms a ubiquitin ligase

complex that marks NRF2 for degradation and prevents its accumulation. However, when ROS levels increase, NRF2 is released from KEAP1, allowing it to translocate to the nucleus, where it initiates the transcription of antioxidant genes. Interestingly, flavoring agents, such as acrolein, induce carbonyl deposition and affect the expression of KEAP1 in the lungs, interfering with NRF2's antioxidant function (111-113).

Lastly, it has been observed that heavy metal particles present in electronic cigarettes can alter mitochondrial reactive oxygen species (mtROS) and the stability of the electron transport chain complex. This could lead to a significant reduction in the stability of subunit II of the cytochrome C oxidase complex IV, resulting in inefficient electron transfer and the potential formation of mtROS and mitochondrial DNA damage (112-114).

Together, these alterations promote mucosal dehydration, increase inflammation, excessive mucus production, and degradation of alveolar cells, contributing significantly to the obstruction of the airways and exacerbating the adverse effects of using electronic cigarettes, leading to the progression of COPD.

COVID-19 AND EVALI

SARS-CoV-2, the etiological agent of the COVID-19 pandemic, has caused over 6 million deaths worldwide, establishing itself as one of the most devastating and well-known diseases of our time (115). Its dramatic and destructive emergence at the end of 2019 coincided with the end of the EVALI epidemic. In addition, the clinical presentation of COVID-19 is often confused with that of other respiratory diseases due to the nonspecificity of its symptoms and similarities in radiological images, as is the case with EVALI, since both diseases share common symptoms, such as cough, fever, dyspnea, chest pain, and gastrointestinal issues (13).

EVALI was first identified in 2019, almost simultaneously with the emergence of COVID-19 at the end of that year, further complicating the differential diagnosis due to the overlap in the chronology and symptoms of both diseases. EVALI is a form of acute lung disease characterized by pathological findings that include fibrosis, pneumonitis, and diffuse alveolar damage, which can progress to pneumonia. This similarity in symptomatic presentation with COVID-19 poses a considerable diagnostic challenge, often resulting in delays in administering appropriate and timely treatment (116,117).

There are documented cases where COVID-19 and EVALI coexist, further complicating the clinical diagnosis. EVALI is often established as a diagnosis of exclusion in these scenarios. The respiratory symptoms of patients, along with paraclinical findings such as chest computed tomography angiographies, may indicate mild progression of a bilateral infiltrative lung disease, which increases the suspicion of COVID-19 pneumonitis. Additionally, chest X-rays of these patients may reveal diffuse bilateral pulmonary infiltrates and ground-glass interstitial opacities, making it even more challenging to distinguish between these two conditions (99,118,119).

CARDIOVASCULAR EFFECTS

Numerous clinical studies have assessed the impact of electronic nicotine delivery systems, commonly known as electronic cigarettes, on cardiovascular health. These studies have become significant due to the notable increase in the incidence of heart diseases and cerebrovascular illnesses among young adults and adolescents. This demographic previously exhibited lower rates of these diseases prior to the widespread adoption of electronic cigarettes (11).

The cardiovascular effects of electronic cigarettes have primarily been studied through short-term research, as their introduction to the market is relatively recent, and the long-term effects of their continuous use over years or decades are still not fully understood (120). Initial findings suggest acute hemodynamic changes after using these devices, including slight increases in systolic and diastolic blood pressure, approximately by 2 mmHg, and a mild increase in heart rate by about 2 beats per minute, particularly with versions that contain nicotine (121). These variations in heart rate seem to be related to alterations in sympathetic tone following recent consumption of electronic cigarettes, whether

with or without nicotine (122). These changes can influence ventricular repolarization, affecting the diastolic phase of the heart. Moreover, it has been observed that the use of electronic cigarettes can compromise endothelium-mediated dilation function, evidencing a reduction in the bioavailability of nitric oxide, essential for vascular health (11).

Several studies have also documented that the consumption of electronic cigarettes can decrease blood flow velocity, a result of oxidative stress that induces endothelial dysfunction, enhancing the development of cardiovascular diseases. This oxidative stress can increase arterial stiffness in electronic cigarette users, an effect that might persist even after cessation of use. Additionally, there could be a reduced responsiveness of myocardial blood flow to physical exertion, affecting coronary circulation without altering myocardial contraction and relaxation (121,123).

Lastly, recent research has demonstrated that the smoke from electronic cigarettes intensifies platelet activation, aggregation, and adhesion, which could lead to ischemic heart diseases, including acute myocardial infarction (AMI). This increase in platelet aggregation is primarily associated with aerosols containing nicotine. However, nicotine-free aerosols have also shown adverse effects on the endothelial barrier due to other components, such as acrolein. Furthermore, it has been noted that oxidative stress may remain elevated even after discontinuing the use of electronic cigarettes, suggesting a prolonged residual impact on inflammatory and oxidative processes (124).

DUAL USERS: VAPING AND SMOKING

The emergence of devices such as electronic cigarettes has introduced a new dimension in the management of smoking, presenting itself as an option to reduce the harm associated with conventional cigarettes in adults who cannot quit tobacco. However, the phenomenon of "dual users," those who consume both electronic and traditional cigarettes, complicates the scenario (125, 126). Although for some, dual use may be a temporary phase towards the total abandonment of tobacco, this transition period can be prolonged indefinitely, often without achieving complete cessation of tobacco use (127). A study conducted by Patel et al., described that common reasons why conventional smokers do not quit smoking conventional cigarettes include the lack of authenticity of vaping compared to smoking, resulting in an unsatisfactory experience which leads many to opt for electronic cigarettes especially in public places because it is currently more socially acceptable, while in the company of other smokers, smoking is often preferred due to the social context of the moment (128).

It is well known that cigarette smoke contains a mixture of harmful chemicals such as heavy metals, volatile organic compounds, compounds with carcinogenic properties, nicotine, carbon monoxide, cyanide, among others, so smoking even one cigarette a day is enough to reach exposure thresholds that have multiple harmful effects on health (129). This indicates that dual use does not always lead to a significant reduction in exposure to harmful substances, particularly if the consumption of conventional cigarettes remains prominent. Additionally, it has been observed that users who predominantly vape and only smoke conventional cigarettes intermittently achieve a significant reduction in levels of potent carcinogens and carbon monoxide (128). Therefore, the dual-use pattern could be a key predictive factor for overall toxin exposure, highlighting its importance for future research in the field (130). Thus, although there is evidence supporting that dual users can minimize harm by completely transitioning to the use of electronic cigarettes, many remain dual users for long periods, facing the health risks associated with both the toxins of traditional cigarettes and the potential risks of vaping. Understanding and managing this phenomenon requires a thorough analysis of the characteristics of electronic cigarette products to continue making progress in this area (131,132).

ELECTRONIC CIGARETTES AND LUNG CANCER

The current evidence on the relationship between electronic cigarette use and lung cancer (LC) is ambiguous. This uncertainty is due to several limiting factors in existing research, including the lack of appropriate respiratory

models, insufficient sample sizes, variable exposure methods, and inconsistent study results. Furthermore, as electronic devices are relatively new technology, their long-term health effects are not yet clearly defined, complicating the determination of their role as a risk factor for lung cancer (28,133,134). However, it is indisputable that electronic cigarettes can generate toxic products with carcinogenic potential (135).

According to the International Agency for Research on Cancer (IARC), electronic cigarettes produce acetaldehyde, metals, nitrosamines, and carbonyl compounds, including acrolein and formaldehyde, which are human carcinogens. Although the quantities of these byproducts produced by electronic cigarettes are lower than those of tobacco smoke, they are sufficient to contribute to carcinogenesis, especially as they contain recognized carcinogens such as formaldehyde and acrolein (136). This is due to the thermal decomposition of various compounds, including flavorings, solvents (PG, VG, and VEA), nicotine, and the presence of heavy metals from the atomizer (133,137).

Aldehydic compounds, including acetaldehyde, formaldehyde, and acrolein, exhibit significant inflammatory activity. This activity derives from the activation of macrophages, chemotaxis, and the production of reactive oxygen species. These elements together modulate the immune response and contribute to the activation of adverse inflammasomes. This sequence of events is closely linked to oncogenic processes, directly linking inflammation with lung cancer. The negative activation of inflammasomes by macrophages creates an immunosuppressive environment, which is hostile to T cells and is essential in the progression and malignancy of lung cancer (136,137). Additionally, aldehydes can interfere with DNA replication, cause DNA damage (by creating DNA adducts), and disrupt DNA repair mechanisms, reducing the efficacy of repair proteins such as XPC and OGG1/2. Particularly, acrolein has been observed to generate DNA adducts at key mutational sites of the TP53 gene, similar to those detected in lung cancers associated with tobacco use (136).

In another context, nicotine can be converted into nitrosamines through nitrosation. Compounds such as nitrosaminoketone (NNK) and nitrosonornicotine (NNN) are well-known carcinogens in both humans and animals, capable of inducing DNA adducts and interfering with DNA repair in human cells (138). This substance also plays a promoting role in the oncogenesis of various cancers through interaction with nicotinic receptors, as its effects can amplify the survival and proliferation of cancer cells, as well as promote metastasis, invasion, and epithelial-mesenchymal transition, in addition to angiogenesis, directly affecting the tumor microenvironment. It can also decrease apoptosis of cancer cells induced by oncological treatments such as chemotherapy, radiotherapy, or tyrosine kinase receptor inhibitors (139). The ability of nicotine to increase susceptibility to mutations and tumorigenic transformation was demonstrated in a study by Tang et al. in which mice exposed to electronic cigarettes with nicotine developed lung adenocarcinoma and urothelial hyperplasia of the bladder (138).

Certain flavorings require particular mention, such as menthol, which exerts possible oncogenic effects through the modulation of nicotine metabolism and its effect on increasing the expression of the nicotine receptor and the direct pro-inflammatory effects mediated through TRPM8, leading to increased oxidative stress (136). Given the oncogenicity of nicotine, it leads to greater tissue exposure and potential DNA damage. This demonstrated an increase in epithelial-mesenchymal transition (EMT), with the consequent increase in invasive potential, following exposure in electronic cigarettes with menthol and nicotine (133). On the other hand, ethyl maltol, when interacting with iron and copper (present in the heating element) to form hydroxypyrone complexes, results in greater generation of ROS (140). It also facilitates the passage of heavy metals through the cell membrane, which in turn can carry oxidative stress through the generation of free radicals (at the level of the electron transport chain in mitochondria), direct genotoxicity by metals/metallic ions, and alterations in the genetic expression of stem cells (141). However, ethyl maltol does not only do this; it induces an inflammatory response, alters local immune function, and compromises the function and

integrity of the epithelial barrier, promoting additional pro-inflammatory effects and greater systemic exposure to inhaled substances (133).

In general, the relationship between cancer and electronic cigarettes is based on three molecular mechanisms: First, the epithelial-mesenchymal transition to acquire motility, invasion capability, and metastasis; Second, oxidative stress and mitochondrial dysfunction leading to inflammation and genotoxicity, giving a critical role for mitochondria and mitochondrial subversion in cancer; and third, the breakage and fragmentation of DNA, as cancer is an inherently genetic disease associated with genomic instability and clonal evolution. Therefore, although there is no conclusive evidence that a connection between electronic cigarettes and LC exists, there are excellent scientific foundations suggesting a significantly higher risk of developing lung cancer (133,142).

CONCLUSION

The accumulated evidence highlights that the use of electronic cigarettes is not a safe alternative to conventional cigarettes, as was initially promoted. Contrary to this, it is irrefutable that vaping is directly associated with serious lung injuries such as EVALI, and a clear connection between the use of electronic cigarettes and COPD has been established. It is crucial to recognize that electronic cigarettes not only compromise lung health but also induce significant adverse effects on the cardiovascular system.

From a public health perspective, recent findings underline the urgent need for stricter regulations and guidelines on the use of electronic cigarettes, particularly among young people and vulnerable populations. The constant innovation in vaping products and the emergence of new e-liquid formulas with potentially harmful components demand rigorous supervision and a detailed assessment of the health risks associated with their use. Understanding how each component interacts within the e-liquid mixture, as well as its impact on the respiratory system and cardiovascular level, requires a multidisciplinary approach that incorporates specialties such as toxicology, physiology, and analytical chemistry. This understanding is essential to tailor prevention strategies and health education appropriately. Furthermore, it is vital that health professionals are properly equipped with the knowledge and tools necessary to identify and manage EVALI cases, applying a high index of suspicion in young patients who present with nonspecific respiratory symptoms and report recent use of electronic cigarettes. Given this scenario, ongoing research and education are indispensable to address and mitigate the adverse effects of this concerning trend in public health, thus ensuring a proactive approach in protecting collective health against the risks of electronic cigarette use.

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Psychosocial Factors Associated with Youth Political Participation: A Systematic Review

Factores psicosociales asociados a la participación política juvenil: Una revisión sistemática

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SUMMARY

Objective: *This article presents a systematic review aimed at identifying and analyzing the effects of various sociodemographic, psychological, and contextual variables on the political participation of young people.* **Method:** *The review of studies was conducted using the PRISMA method and the AMCPLT strategy. Thirty-five quantitative and qualitative research studies, published between 2009 and 2024, were selected from the PubMed, Scopus, and Web of Science databases. These studies were conducted in Europe, Latin America, Asia, Africa, and Oceania, involving young people aged 15 to 29 years.* **Results:** *The results indicate that the interaction between sociodemographic factors (gender, age, income, and health), emotions, political attitudes, education, and civic awareness, mediated by social media, constrains the decisions and forms of youth participation in conventional and unconventional political processes. Education and civic culture promote active citizenship among young people; in turn, emotions, political trust, distrust in institutions, the influence of political leaders and influencers, shape the formation of their political awareness, civic engagement, and electoral behaviors. Regularly, the political involvement of young people is shown through activism on social media.* **Conclusion:** *Youth political participation is a complex and multifactorial phenomenon. A comprehensive understanding of these factors is crucial for designing strategies that foster greater youth civic participation and a transformation in contemporary political systems.*

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RESUMEN

Objetivo: *Este artículo es una revisión sistemática dirigida a identificar y analizar el efecto de diferentes variables sociodemográficas, psicológicas y contextuales sobre la participación política de los jóvenes*. **Método:** *La revisión de los estudios se realizó siguiendo el método PRISMA y la estrategia AMCPLT. Se seleccionaron 35 investigaciones cuantitativas y cualitativas, publicadas entre 2009 y 2024, de las bases de datos PubMed, Scopus y Web of Science, realizadas en Europa, América Latina, Asia, África y Oceanía, con jóvenes de 15 a 29 años*. **Resultados:** *Los resultados indican que la interacción entre los factores sociodemográficos (género, edad, ingresos y salud), las emociones, las actitudes políticas, la educación y la conciencia cívica, mediada por los medios sociales, limita las decisiones y las formas de participación de los jóvenes en los procesos políticos convencionales y no convencionales. La educación y la cultura cívica promueven la ciudadanía activa entre los jóvenes; a su vez, las emociones, la confianza política, la desconfianza en las instituciones, la influencia de los líderes políticos y las personas influyentes, conforman la formación de su conciencia política, su compromiso cívico y sus comportamientos electorales. Regularmente, la implicación política de los jóvenes se manifiesta a través del activismo en las redes sociales*. **Conclusión:** *La participación política de los jóvenes es un fenómeno complejo y multifactorial. Una comprensión integral de estos factores es esencial para diseñar estrategias que promuevan una mayor participación cívica juvenil y una transformación en los sistemas políticos contemporáneos*.

INTRODUCTION

Economic, political, social, ideological, and cultural crises have significantly impacted the perception of democratic and political processes, resulting in a decline in traditional forms of political participation, particularly among young people. In Europe, approximately 33 % of young men and 50 % of young women show a tendency towards non-participation in politics (1). In Latin America, 62 % of young people are dissatisfied with the region's political dynamics (2). In Asia, recent studies have shown a decrease in youth political participation due to government repression and lack of electoral transparency, which has increased distrust in democratic institutions (3). In Africa, youth political participation is affected by high levels of poverty, unemployment, and political repression; however, in some developing countries, youth activist movements have emerged (4). In Oceania, particularly in Australia and New Zealand, young people have shown greater interest in environmental politics and indigenous rights, although electoral participation remains low (5).

However, the political participation of new generations is crucial to face the challenges of the contemporary world. Global governance has been closely linked to capitalism, with the creation of institutions that consolidate power structures, including organizations of violence. The United States has played a central role in this system, prioritizing world market capital and geopolitical dominance. This model has influenced recurrent crises, giving rise to new economic and political approaches, in which neoliberalism has attempted to displace the state (6).

In Europe, the social and political crisis has been exacerbated by austerity policies stemming from financial problems, as well as by the massive influx of migrants, which has intensified economic inequality and eroded trust in institutions (7). In Latin America, the political crisis has been driven by corruption and the deterioration of governance systems. The left lacks solidity and articulation, which affects government legitimacy, while the right has sought to maintain control through the support of military forces, marginalizing dissident positions (8).

This scenario could encourage youth engagement in political action to address the needs of their communities (9). However, high levels of political disaffection have reduced participation (10). Paradoxically, although youth is associated with innovation and transformation, this group faces problems such as poverty, violence and inequality in access to education and employment, which causes uncertainty about the future.

Consequently, young people have chosen to disengage from traditional politics (11), expressing their participation in unconventional ways, such as protests and the use of digital platforms, so that their demands are heard and recognized (12,13). Approximately 46 % of young people are informed about politics through social media (2). In this sense, the study of youth political participation becomes particularly relevant, since the positions of young people in

political and electoral processes have evolved. Although they initially showed apathy and indifference towards traditional politics, they now actively participate in social and political movements (14-16).

Despite changes in youth political participation, this group is key to transforming political systems, exerting pressure, and formulating proposals that address their needs (17,18). In a global context of polarization and institutional distrust, violence has become a strategy for political participation that challenges the state (12).

Various factors can influence youth political participation. For example, emotions play a fundamental role in political mobilization and learning, contributing to the formation of civic awareness (19). Likewise, electoral uncertainty is strongly influenced by a high emotional charge (20,21). Civic education is also a relevant factor, as it can foster greater commitment to democratic exercises, relying on its effectiveness and the sociocultural context (15,22).

The relationship between emotions, civic awareness, education and civic engagement in youth political participation is a complex phenomenon, influenced by individual and sociocultural factors (23-26). However, existing research is limited in its integration of these elements. Therefore, this review systematically seeks to explore the factors associated with youth political participation, aiming to provide a detailed understanding of this phenomenon.

MATERIALS AND METHODS

This systematic review was developed using the PRISMA method to analyze scientific literature on the factors influencing political participation, specifically emotions, political feelings, and civic awareness (27). The scope of the review was defined using the AMCPLT strategy, which guides the formulation of the research question based on six key components: Adjective, Measurement, Condition, Population, Place, and Time (28). Thus, the research question was: What are the factors associated with the political participation of young people?

Eligibility Criteria

To select relevant studies, inclusion and exclusion criteria were established to allow an adequate synthesis of the results. We included articles that met the following criteria: They have been published in the last 15 years (between 2009 and 2024); They address the relationship between political participation, emotions, political feelings, and civic awareness in young people and university students, especially in electoral period; They present empirical results derived from data analysis; They were published until July 2024.

We excluded articles of a theoretical or reflexive nature that did not present empirical results, as well as narrative or systematic reviews or studies that only offered descriptive analyses without providing new data. Additionally, publications outside the selected period were excluded.

Sources of information

The search for relevant studies was conducted in the specialized databases PubMed, Scopus, and Web of Science, chosen for their comprehensive coverage and high quality.

Search strategy

The identification of studies began with the preparation of a table of descriptors, using key terms extracted from the DeCS, MeSH and UNESCO electronic dictionaries (Table 1).

Based on the descriptors found, search algorithms were constructed using the logical/boolean operators 'AND' and 'OR' (Table 2), which were then used to consult the PubMed, Scopus and Web of Science databases

Selection process and data collection

The study selection process was carried out through a preliminary analysis performed independently by two teams of reviewers. Each article was evaluated according to the

Table 1. Descriptors

Spanish term	DeCS	MeSH	UNESCO
Jóvenes	Young people	Youth	Young people
Estudiantes universitarios	University students	College students	Higher education students
Emociones	Emotions	Emotions	Emotions
Respuestas emocionales	Emotional responses	Emotional responses	Emotional responses
Afecto	Affect	Affect	Affect
Sentimientos	Feelings	Feelings	Feelings
Regulación emocional	Emotional regulation	Emotional regulation	Emotional regulation
Procesamiento emocional	Emotional processing	Emotional processing	Emotional processing
Inteligencia emocional	Emotional intelligence	Emotional intelligence	Emotional intelligence
Activismo Político	Political activism	Political activism	Activism, political
Participación Política	Political participation	Political participation	Political participation
Comportamiento Político	Political behavior	Political behavior	Political behavior
Actitud Política	Political attitude	Political attitude	Political attitude
Educación cívica	Civic education	Civic education	Civic education
Educación para la ciudadanía	Citizenship education	Citizenship education	Citizenship education
Competencia cívica	Civic competence	Civic competence	Civic competence
Ciudadanía activa	Active citizenship	Active citizenship	Active citizenship
Participación ciudadana	Citizen participation	Citizen participation	Citizen participation
Conciencia cívica	Civic awareness	Civic awareness	Civic consciousness
Desarrollo político	Political development	Political development	Political development

Table 2. Search Algorithm

N	Search algorithm
1	("Active citizenship" OR "Civic awareness" OR "Civic behavior" OR "Civic competence" OR "Civic education" OR "Citizen participation" OR "Citizenship education" OR "Political activism" OR "Political attitude" OR "Political behavior" OR "Political development" OR "Political participation") AND ("Affect" OR "Emotional intelligence" OR "Emotional processing" OR "Emotional regulation" OR "Emotional responses" OR "Emotions" OR "Feelings") AND ("College students" OR "Higher education students" OR "University students" OR "Young people" OR "Youth")
2	("Ciudadanía activa" O "Conciencia cívica" O "Comportamiento cívico" O "Competencia cívica" O "Educación cívica" O "Participación ciudadana" O "Educación para la ciudadanía" O "Activismo político" O "Actitud política" O "Comportamiento político" O "Desarrollo político" O "Participación política") Y ("Afecto" O "Inteligencia emocional" O "Procesamiento emocional" O "Regulación emocional" O "Respuestas emocionales" O "Emociones" O "Sentimientos") Y ("Estudiantes universitarios " O "Estudiantes de educación superior" O "Estudiantes universitarios" O "Jóvenes" O "Jóvenes")

established inclusion criteria, and the strengths and weaknesses of each study were subsequently discussed to consolidate the final selection in a matrix elaborated in Microsoft Excel.

Data elements

The data was organized into categories that covered both the main results and additional variables necessary to describe the characteristics of the participants, the study contexts, and the methodologies employed. The collection focused on two main areas:

Emotional dimensions: These include emotions, emotional responses, affect, feelings, emotional regulation and processing, and emotional intelligence.

Dimensions of political participation and citizenship: These include political activism, political participation, political behavior and attitudes, civic education, civic competence, active citizenship, civic awareness, and political development.

An attempt was made to compile all available measures related to these dimensions, considering the temporality and the different analyses reported in each study. However, some articles presented ambiguous or incomplete data.

In addition, information was extracted on:

Characteristics of participants: Age, gender, educational level (high school or university), geographic context, electoral periods (when applicable) and sample size.

Methodological characteristics: Research approach (quantitative, qualitative, or mixed), description of the population and sample, data collection instruments, and main findings.

General data of the study: Title, author(s), and year of publication.

When information was insufficient or unclear, assumptions were made based on the context of the study. For example, if an article mentioned "youth" without specifying age ranges, a range that included both adolescence and early youth was assumed; in the absence of disaggregation by gender, a mixed population was considered; and if educational level was not defined, it was inferred from the context (e.g., university studies were classified as college-level education). Likewise, geographic locations were determined from the authors' affiliated institutions or from contextual descriptions present in the studies.

RESULTS

This segment presents the research selection process conducted under pre-established and meticulous criteria. To ensure a systematic and transparent approach, specific search equations were used (Table 3) that facilitated the identification and selection of relevant studies in various scientific databases. The selection procedure was based on the PRISMA flowchart (Figure 1), which illustrates the phases of identification, evaluation, final choice and definitive selection. Finally, Table 4 summarizes the characteristics of the studies included in the review.

Selection of studies

The process of searching and selecting studies involved consulting various databases, including PubMed, Scopus, and Web of Science, using a search equation that combined terms related to active citizenship, emotions, and university students. In total, 458 records were identified (11 from PubMed, 288 from Scopus and 159 from Web of Science). After the initial search, exclusion criteria were applied to reduce the number of studies, eliminating 330 records due to reasons such as duplication, incomplete texts, lack of full access to articles, and other methodological or quality issues. This left a total of 128 records for further review (Table 3).

After a detailed review of the 128 studies, 35 studies were selected for inclusion in the final review, as they met the established inclusion criteria. During this process, some studies initially considered were excluded because they were incomplete, duplicated or did not meet the variables of interest, specifically in relation to active citizenship and the university student population.

Characteristics of the studies

This section presents the main characteristics of the 35 articles selected. These research studies were identified in English-language academic databases, with 23 records in Web of Science and 12 in Scopus. All the studies focused on evaluating the levels of civic awareness and civic education, as well as the emotional reactions of young people in the context of their political participation in various countries in Europe, Africa, Asia, and the Americas (Table 4).

Results of individual studies

In this section, the studies are classified according to various population characteristics.

Table 3. Search equations

N	Search equation	Database	Total found	Documents removed					Total Sample
				Document type	Time period	Incomplete/ duplicated texts	No access	Non-compliance with variable criteria	
1	("Active citizenship" OR "Civic awareness" OR "Civic behavior" OR "Civic competence" OR "Civic education" OR "Citizen participation" OR "Citizenship education" OR "Political activism" OR "Political attitude" OR "Political behavior" OR "Political development" OR "Political participation") AND ("Affect" OR "Emotional intelligence" OR "Emotional processing" OR "Emotional regulation" OR "Emotional responses" OR "Emotions" OR "Feelings") AND ("College students" OR "Higher education students" OR "University students" OR "Young people" OR "Youth")	PubMed	11	0	0	0	0	11	0
2	("Active citizenship" OR "Civic awareness" OR "Civic behavior" OR "Civic competence" OR "Civic education" OR "Citizen participation" OR "Citizenship education" OR "Political activism" OR "Political attitude" OR "Political behavior" OR "Political development" OR "Political participation") AND ("Affect" OR "Emotional intelligence" OR "Emotional processing" OR "Emotional regulation" OR "Emotional responses" OR "Emotions" OR "Emotions" OR "Feelings" AND ("College participation") AND ("Affect" OR "Emotional intelligence" OR "Emotional processing" OR "Emotional regulation" OR "Emotional responses" OR "Emotions" OR "Feelings") AND ("College students" OR "Higher education students" OR "University students" OR "Young people" OR "Youth")	Scopus	288	61	16	11	128	61	11
3	("Active citizenship" OR "Civic awareness" OR "Civic behavior" OR "Civic competence" OR "Civic education" OR "Citizen participation" OR "Citizenship education" OR "Political activism" OR "Political attitude" OR "Political behavior" OR "Political development" OR "Political participation") AND ("Affect" OR "Emotional intelligence" OR "Emotional processing" OR "Emotional regulation" OR "Emotional responses" OR "Emotions" OR "Feelings") AND ("College students" OR "Higher education students" OR "University students" OR "Young people" OR "Youth")	Web of Science	159	3	0	20	91	21	24
	Total		458	64	16	31	219	93	35

Table 5 shows the gender distribution, while Table 6 specifies the age intervals. Table 7 contains information on the educational level of the participants. Additionally, Table 8 provides complementary information on the method used, Table 9 details the country or continent of origin, and Table 10 outlines the electoral period studied.

Table 5 shows the distribution by gender of the population registered in the studies, totaling 693 325 individuals classified in three categories: male, female and unspecified. There were 150 146 male subjects (22 %), 154 504 female subjects (22 %) and 388 675 subjects in the "unspecified" category (56 %).

Table 6 presents the age distribution of the participants, categorized into various age ranges. Most studies reported a range of approximately 18 years of age. Among them, the age group 18 to 24 years is the most common, represented in 5 cases (14 % of the total sample), followed by the group "18 years and over" (4 cases, 11 %). Other groups, such as "15 years and older" (3 cases, 9 %) and "18 to 30 years" (3 cases, 9 %), are also present, indicating that the sample is

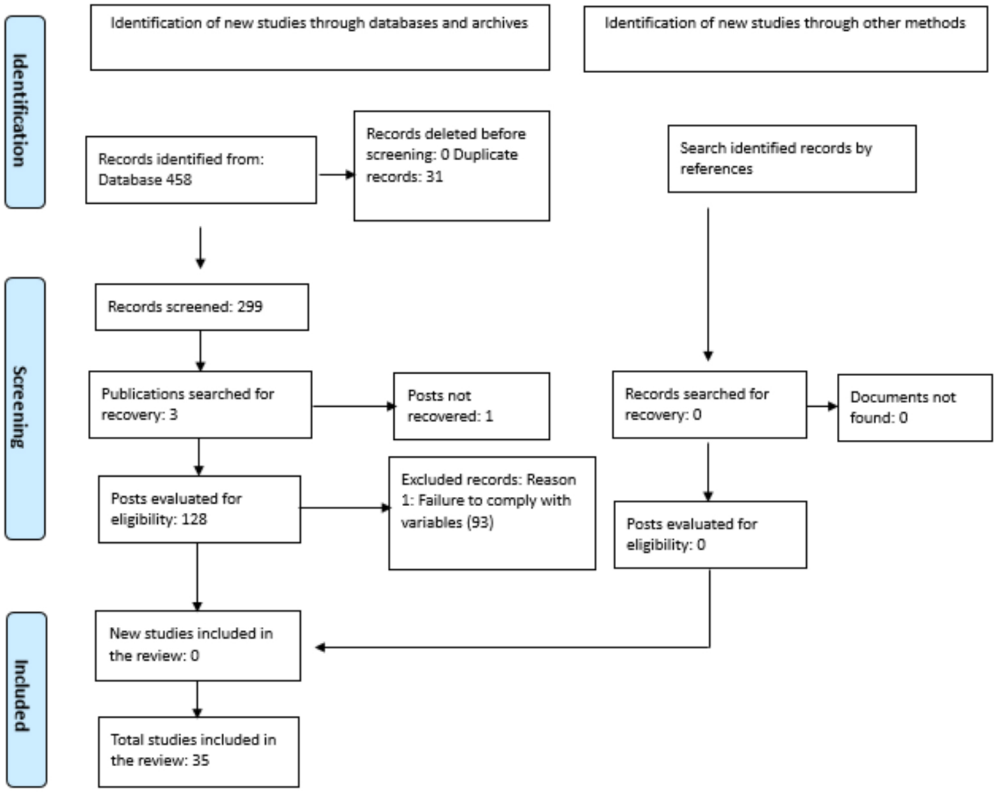


Figure 1. PRISMA Flow Diagram. Sources (27).

mainly composed of young adults. In addition, one case (3 %) is reported in the "Unspecified" category.

Table 7 presents the distribution of educational levels in the studies, distinguishing between secondary and university education. In the secondary education category, 13 studies (37 %) include participants with a high school education, while 11 studies (31 %) do not specify the educational level, and another 11 (31 %) are classified as "Not Applicable". On the other hand, in the university education category, most studies (30,86 %) have participants who have reached this level, and only five studies (14 %) do not specify whether the individuals have university studies

Table 8 summarizes the methodologies employed in the 35 studies, classified into three categories: qualitative, quantitative, and mixed. Of the 35 studies, 6 (17 %) used a qualitative approach, 27 (77 %) relied on quantitative methods, and 2 (6 %) adopted a mixed approach, indicating a predominance of quantitative methodology in the sample analyzed.

Table 9 presents the distribution of countries and regions in the studies, comprising 35 observations. The United States is the country with the highest frequency (17 % or 6 records), followed by countries such as Belgium, China, Portugal and Russia, each with 2 records (6 %). Most countries have a single observation (3 %), including nations from different continents, and

Table 4. Selected studies.

Database	Title	Author(s)	Year	Method	Context, Population & Sample	Results and Findings
Scopus	Youth, Life, and Politics: Examining the Everyday in Comparative Politics.	Ortuoste M (29)	2012	Mixed	√United States, UK, India, Japan, China, Sierra Leone, South Africa, Tanzania, United States, UK √ 60 first-year students	√Greater student engagement and curiosity, improved understanding of concepts, and development of empathy and civic responsibility, but challenges like consistent participation remain. √Promising results in increasing student engagement, improving understanding of comparative politics, and developing empathy and civic responsibility.
Scopus	Current situation of civil awareness of undergraduate and promotion strategy research	Li HM (30)	2017	Quantitative	√ China √ 270 university students	√Students have strong national consciousness and a sense of freedom but low participation in public affairs and an incomplete understanding of social morality. √Emphasizes the need to strengthen civic education to foster greater participation and understanding of citizens' rights and duties.
Scopus	Higher Education Students as Political Actors: Evidence from England and Ireland.	Abrahams J, Brooks R (31).	2019	Qualitative	√ England & Ireland √ 103 undergraduate students (52 in England, 51 in Ireland)	√Notable differences between students in England and Ireland regarding their perceptions of political empowerment and perceived influence. Both groups expressed similar desires for political engagement but differed in how empowered they felt and the scope of influence they perceived. √Increased political empowerment, influence, and participation were found across both countries.
Scopus	Youth Political Participation in Russia Influence of Voluntary Associations	Gukova et al. (32).	2019	Quantitative	√ Russia √ 6,272 youth in Russia aged 18-30	√Participation in voluntary associations and education enhances future political engagement. Employed youth vote less than unemployed youth, and political interest among youth has increased significantly since 2011. √Education is crucial for youth political participation in Russia, and the country has fewer internal inequalities compared to the U.S.
Scopus	Social and Political Attitudes of Moscow Students on the Background of the All-Russia and Regional Youth Studies	Litvinova et al. (33).	2020	Quantitative	√ Russia √ 768 participants, ages 18-30 (49% male, 51% female)	√Technology, trade, and public administration were considered the most promising sectors. 49% of students closely followed political events in Russia; 26% never missed an election. √These results characterize Moscow students as active young citizens, oriented towards family and career, with contemplative political activity and low political participation.
Scopus	Newspaper Exposure, Efficacy Feeling and Political Apathy among	Erubami et al. (34).	2021	Quantitative	√ Nigeria √ 384 youth aged 18-35 years in	√Majority of youth frequently read political news in newspapers (61.2%). Youth show political apathy towards

Continued in pag. 918...

…continuation Table 4. Selected studies.

Database	Title	Author(s)	Year	Method	Context, Population & Sample	Results and Findings
	Youths in South-East Nigeria				Southeastern Nigeria	active participation, but less toward passive participation. They view political reports as biased and filled with scandals. √Newspaper exposure negatively correlates with political apathy among youth.
Scopus	Extreme Pessimists? Expected Socioeconomic Downward Mobility and the Political Attitudes of Young Adults.	Mitrea et al. (35)	2021	Quantitative	√ Austria,Czech Republic,Denmark, Germany,Greece,Hungary,Italy,Spain, Switzerland, Turkey, and the UK √ 1 000 young adults aged 18-35 per European country (11 European countries)	√Young adults expecting to fare worse than their parents in the future are more likely to hold extreme ideological views. √Young adults with lower socioeconomic expectations are more likely to hold extreme political views.
Scopus	College Students' Political Attitudes Affect Negative Stereotypes about Social Groups	Beyer S (36)	2022	Quantitative	√ United States √ 116 psychology students, 79 females, 37 males, average age 18-24.	√Republicans showed more negative stereotypes toward racial, religious, and sexual minorities; Democrats showed negative stereotypes toward more powerful groups like Caucasians and Christians. √Conservatives exhibited more negative stereotypes than liberals,especially toward disadvantaged minorities. Women were more likely to be Democrats, while men were more likely to be Republicans.
Scopus	Youth Political Participation on Social Media and Its Effect on Political Disaffection	Berlanga Ramírez et al. (37)	2023	Quantitative	√ Mexico √ 900 students from the Faculty of Political Science and International Relations	√48% of students occasionally post political opinions, 63% like political comments, 50% think politicians care little about citizens, but 70% believe politicians consider social media expressions. √Significant relationship between political participation on social media and trust in political actors. Students recognize the power of social media in electoral campaigns.
Scopus	Information, perceptions, and electoral behavior of young voters: A randomised controlled experiment.	Carvalho et al. (38)	2023	Quantitative	√ Portugal √ 1 799 university students, average age 21.3 years.	√Undecided voters exposed to negative information were less likely to vote and more likely to vote for opposition parties. First-time voters showed a more pronounced negativity bias, reacting strongly to negative information. √High negativity bias, with undecided voters and first-time voters more susceptible to manipulation.
Scopus	The Stubborn Unresponsiveness of Youth Voter Turnout to Civic Education: Quasi-Experimental Evidence From State-Mandated Civics Tests	Jung, and Gopalan (39)	2023	Quantitative	√ United States √ 36 627 participants, all U.S. citizens aged 18-22	√Civic tests based on memorization do not significantly increase youth voter turnout. Applied civic education and practical interventions, like voter registration campaigns, are more effective. √A need to reevaluate civic education strategies and consider more practical approaches to foster youth electoral participation.

Continued in pag. 919…

…continuation Table 4. Selected studies.

Database	Title	Author(s	Year	Method	Context, Population & Sample	Results and Findings
Scopus	Null effects of social media ads on voter registration: Three digital field experiments.	Unan et al. (40)	2024	Quantitative	√ United Kingdom √ 9 290 participants	√Social media ads (Instagram, Snapchat, Facebook) did not significantly increase voter registration. √The results challenge the effectiveness of digital advertising strategies used to boost voter participation.
Scopus	ICTs Changing Youths' Political Attitudes and Behaviors in Bangladesh	Ullah MS (41)	2013	Qualitative	√ Bangladesh √ 92 youth in Bangladesh	√Youth reject traditional politics and prefer virtual participation, though this has a limited impact on decision-making. √ICTs are transforming political participation, highlighting both opportunities and challenges.
Web of Science	The Concept and Determinants of Civic Engagement	Arvanitidis PA (42)	2017	Quantitative	√ Greece √ 2 843 university students, aged 17-55, 43.3% male, 56.7% female.	√Low levels of civic participation; only 11.3% engaged in volunteering, and 19.5% in associations. Protest was the most common form of activism (38.7%). √Sociodemographic and personal factors are crucial for university students' civic engagement in Greece.
Web of Science	Lessons on Citizenship and Democratic Power Literacy from Undocumented Youth	Parkhouse H (43)	2017	Qualitative	√ United States √ 4 undocumented youth in the United States	√The youth developed a deep understanding of power and engaged in political activities, showing resilience and empowerment. They sought significant social change, suggesting civic education should focus on political tools for social change. √Undocumented youth can become agents of change through self-education and activism.
Web of Science	Mediated and moderated effects of political communication on civic participation	Reichert and Print (44)	2017	Quantitative	√ Australia √ 3 513 10th grade students, ages 15-16 (51.8% male, 48.2% female)	√Media use stimulates civic discussions, with varied effects based on the medium. Civic discussions, especially with friends and online, positively affect future civic participation. √Discussions on civic topics, particularly online, are crucial for encouraging youth civic engagement.
Web of Science	Evidence of the validity and accuracy of the Brazilian social attitude of students scale towards politics	Coelho Junior et al. (45)	2018	Quantitative	√ Brazil √ 445 Brazilian students	√Factor analysis revealed three main factors: political knowledge (15 items, Cronbach's alpha 0.82), political emotions (7 items, Cronbach's alpha 0.72), and political behavior intentions (2 items, Cronbach's alpha 0.80). √The scale is valid and accurate for measuring Brazilian students' political attitudes.
Web of Science	Factors affecting political participation (Jordanian universities students' voting: field study 2017-2018).	Alelaimat MS (46)	2019	Quantitative	√ Jordan √ 900 students from three Jordanian universities	√Gender, age, family income, and regional affiliation affect the voting behavior of Jordanian university students. √Social and economic factors, such as gender, age, family income, and regional affiliation, led to different voting patterns in national and local elections.

Continued in pag. 920…

…continuation Table 4. Selected studies.

Database	Title	Author(s	Year	Method	Context, Population & Sample	Results and Findings
Web of Science	Nation-building among youth in Malaysia: The civic education approach.	Ismail et al. (47).	2019	Quantitative	√ Malaysia √ 431 youth in Malaysia	√Both Malay and Chinese youth exhibited high levels of civic education and awareness. Specifically, 94.6% of Malay students and 83.7% of Chinese students demonstrated high civic education intensity. √Civic education in Malaysia is effective in cultivating strong civic awareness among youth, vital for integration and a sense of belonging in a multi-ethnic society.
Web of Science	Standing still or ascending in the social media political participation ladder? Evidence from Iran	Da Silva Nogueira et al. (48)	2020	Quantitative	√ Iran √ 110 participants in Iran	√Social media serves as a primary source of political information for many Iranians, improving the sense of being informed, though online political participation is moderate and offline participation is low. √Censorship and restrictions in Iran limit social media's ability to promote more active and meaningful political participation.
Web of Science	Rock the Vote or Block the Vote? How the Cost of Voting Affects the Voting Behavior of American Youth	Juelich and Coll (49)	2020	Quantitative	√ United States √ 368,439 young adults, ages 18-29	√Restrictive voting laws reduce youth participation more than older age groups, with a 16-percentage point decrease in the most restrictive states. √The findings highlight the importance of considering how electoral laws affect different demographic groups and the need for policies that facilitate youth voter participation.
Web of Science	Deliberative Walks: citizen participation in local-level planning processes	Lindell and Ehrström (50)	2020	Qualitative	√ Finland √ 19 students	√Over 83% of participants felt heard, although 50% noticed dominance in discussions. There was a significant increase in knowledge and interest in deliberate methods. Participants gained confidence in influencing political decisions and developed civic skills. √Effective facilitation was crucial for inclusion and equity in discussions. Deliberative and participatory methods promoted inclusion, learning, and empowerment.
Web of Science	Promoting the Youth Vote: The Role of Informational Cues and Social Pressure.	Bergan et al. (51).	2021	Quantitative	√ United States √ 2 801 university students	√Classroom interventions significantly increased electoral participation among students already registered to vote. Social pressure was especially effective in increasing voting likelihood. √Classroom interventions, especially with social pressure, can increase youth electoral participation. Facilitating voter registration and public engagement are also crucial.
Web of Science	Resentment and Coping with the Democratic Dilemma	Celis et al. (52)	2021	Qualitative	√ Belgium √ 19 participants	√Participants were deeply dissatisfied with democracy's functioning but did not reject democracy as a principle. √Citizens face a "democratic dilemma," balancing disillusionment with hope in the system. Some protest, others advocate alternatives, while others believe in the current system.

Continued in pag. 921…

…continuation Table 4. Selected studies.

Database	Title	Author(s	Year	Method	Context, Population & Sample	Results and Findings
Web of Science	Does youth civic engagement enhance social and academic performance?	Fernandes et al. (53)	2021	Quantitative	√ Portugal √ 370 university students, ages 18-24	√Students highlighted expressive motivations such as social recognition and personal development. Youth civic engagement improves social performance, with expressive motivations as key predictors. √Civic engagement can benefit both social and academic development, emphasizing the need to promote such activities in educational institutions.
Web of Science	Pedagogies of agonistic democracy and citizenship education	Sant et al. (54)	2021	Qualitative	√ England √ 44 university and primary school students	√The pluralism of participants and the conflict-oriented nature of the activities facilitated the normalization of conflict and emotional engagement with other social imaginaries. √Older participants exhibited fewer positive attitudes toward conflict-oriented pedagogies.
Web of Science	Psychosocial Factors Associated with Non-Conventional Political Participation Among Young Citizens in Lima, Peru	Tintaya Orihuela and Cueto Saldivar (55)	2021	Mixed	√ Peru √ 132 young people from Lima, Peru	√The qualitative study revealed that youth see political participation as a means of social change, motivated by social awareness and peer support, but limited by responsibilities and cynicism. The quantitative study identified that internal political efficacy and interest in politics increase participation, while political cynicism decreases it. √Highlights the complexity and multidimensionality of youth political participation, as well as the importance of emotional, cognitive, and contextual factors in motivating and limiting participation.
Web of Science	Contagious Politics: Tie Strength and the Spread of Political Knowledge	Ognyanova K (56)	2022	Quantitative	√ United States √ 390 students from 13 residential communities in a large public university	√Political knowledge was predicted by the knowledge of participants' strong social ties, but not by their political or close ties. Strong, redundant ties (many shared contacts) also influenced political knowledge. √Peer ties can play a significant role in the diffusion of political knowledge among youth.
Web of Science	Radicalisation, Exhaustion, and Networked Movement in Abeyance: Hong Kong University Students' Localist Identification after the Umbrella Movement.	Tang and Chung (57)	2022	Quantitative	√ Hong Kong √ 1,365 university students	√Social media promoted localist identification, with localists showing greater collective efficacy but lower trust in political parties. √Political emotions and media use are key to forming political identities.
Web of Science	Youth voting and institutional change in the post-Arab Spring MENA region	Fakih et al. (58)	2023	Quantitative	√ Lebanon, Egypt, Algeria, Tunisia, Morocco √ 9 860 young people surveyed	√There were gender and country differences, with personal beliefs and institutional variables becoming more significant in upcoming elections. √Socioeconomic characteristics, trust in institutions, and personal beliefs play a crucial role in determining youth voting behavior in the MENA region.

Continued in pag. 922…

…continuation Table 4. Selected studies.

Database	Title	Author(s	Year	Method	Context, Population & Sample	Results and Findings
Web of Science	Influencers as Empowering Agents? Following Political Influencers, Internal Political Efficacy and Participation among Youth.	Harff, and Schmuck (59)	2023	Quantitative	√ Germany √ Young people aged 16-25 in Germany (1st wave: 1007 participants, 2nd wave: 496 participants)	√A significant relationship was found between following political influencers and higher political participation, both online and offline, among youth. √Political influencers can increase youth political participation, particularly when simplifying politics, though they don't necessarily increase internal political efficacy.
Web of Science	Physical health conditions and political participation in Europe: the moderating effects of age	Kirbiš et al. (60).	2023	Quantitative	√ Europe (20 countries) √ 34,913 adults in Europe	√Most physical health conditions are related to political participation, but the effect varies by type of participation. Physical health conditions tend to mobilize individuals, especially among the youth. √Physical health conditions may have a greater negative impact on political participation among older adults than among the youth.
Web of Science	Does cohort size matter? Assessing the effect of youth cohort size and peer influence on young people's electoral participation.	Nkansah and Papp (61)	2023	Quantitative	√ Japan, Germany, Malaysia, Philippines, South Africa, Pakistan, Ghana, and more √ 10 933 participants	√Larger youth cohort size reduces the likelihood of youth participating in national elections. √The study enhances understanding of cohort size effects on youth political behavior.
Web of Science	Future Time Perspective and Trust in Government: The Mediation of the consideration of future Consequences.	Zhi et al. (62).	2023	Quantitative	√ China √ 1,617 participants	√The future time perspective influences trust in government through the consideration of future consequences. √A future time perspective influences trust in government through consideration of future consequences.
Web of Science	Social media as an exit strategy? The role of attitudes of discontent in explaining non-electoral political participation among Belgian young adults	Waeterloos, C., Walrave, M., & Ponnet, K. (63)	2024	Quantitative	√ Belgium √ 720 young adults in Belgium	√No significant association between electoral abstention and non-electoral participation. Trust in political institutions and populist attitudes encouraged participation, while political despair reduced it. √Highlights the complexity of the relationship between political discontent attitudes and various forms of political participation among Belgian young adults.

Table 5. Gender

Gender	Frequency	Percentage (%)
Male 150,146	22	
Female	154,504	22
Unspecified	388,675	56
Total	693,325	100

Table 6. Age ranges in the population

Age Ranges in Population	Frequency	Percentage (%)
10 years and older	1	3
15 to 29 years	1	3
15 years and older	3	9
16 to 25 years	1	3
16 years and older	2	6
17 to 21 years	1	3
17 to 31 years	1	3
18 to 24 years	5	14
18 to 25 years	2	6
18 to 29 years	2	6
18 to 30 years	3	9
18 to 32 years	1	3
18 to 35 years	2	6
18 years and older	4	11
18 and 19 years	2	6
18 and 25 years	1	3
18 and 35 years	1	3
21 years and older	1	3
Not specified	1	3
Total	35	100

Table 7. Educational Level

Education Level		Frequency	Percentage (%)	
High School Education	Medium	13	37	
	Not Applicable	11	31	
	Not Specified	11	31	
	Total		35	100
University Education	Not Specified	5	14	
	University	30	86	
	Total	35	100	

Table 8. Methodology

Methodology	Frequency	Percentage (%)
Qualitative	6	17
Quantitative	27	77
Mixed	2	6
Total	35	100

Table 9. Country/Continent.

Country/Continent	Frequency	Percentage (%)
Germany	1	3
Australia	1	3
Austria, the Czech Republic, Denmark, Germany, Greece, Hungary, Italy, Spain, Switzerland, Turkey, and the UK	1	3
Bangladesh	1	3
Belgium	2	6
Brazil	1	3
China	2	6
United States	6	17
United States, United Kingdom, India, Japan, China, Sierra Leone, South Africa, and Tanzania	1	3
Europe	1	3
Finland	1	3
Greece	1	3
Hong Kong	1	3
England	1	3
England and Ireland	1	3
Iran	1	3
Japan, Germany, Malaysia, Philippines, South Africa, Pakistan, and Ghana, among others.	1	3
Jordan	1	3
Lebanon, Egypt, Algeria, Tunisia, and Morocco	1	3
Malaysia	1	3
Mexico	1	3
Nigeria	1	3
Peru	1	3
Portugal	2	6
United Kingdom	1	3
Russia	2	6
Total	35	100

Table 10. Electoral period.

Election Period	Frequency	Percentage (%)
1093 onwards	1	3
1996 to 2020	1	3
1999 to 2019	1	3
2004 to 2016	1	3
2008 to 2010	1	3
2011 to 2018	1	3
2011 onwards	1	3
2016	1	3
2017	1	3
2018	1	3
2018 to 2019	1	3
2019 to 2021	1	3
Not specified	23	66
Total	35	100

some studies group several countries into a single category.

Table 10 presents the data related to the electoral period. It was observed that in 23 cases (66 %) a specific electoral period is not specified, being labeled as "Not specified". Electoral period that are mentioned specifically, either in intervals of years or individual years, are presented with a frequency of 1 case each (3 % in each category).

Dimensions of political participation among young people

The political participation of young people is influenced by various personal, sociocultural and emotional elements, which determine both their involvement in the public sphere and their commitment to citizenship. In this context, three fundamental dimensions were identified:

1. **Political involvement:** Table 11 addresses factors related to activism and mobilization through social networks.
2. **Political emotions and feelings:** Table 12 examines the effects of trust, political efficacy and emotions associated with political activity. (Political emotions and feelings).
3. **Civic awareness:** Table 13 focuses on citizen engagement, education and civic culture, essential aspects to promote a participatory and informed citizenry.

Individual and sociocultural factors associated with political participation

Various individual and sociocultural factors determine political participation among young people. Sociodemographic factors, such as gender, age and income, influence electoral participation and populist inclinations (46,58). It is observed that men have a greater tendency to participate in conventional political activities compared to women, due to the structural limitations that have historically affected the latter (46,58). In addition, less political engagement is evident among young people in contrast to older adults. Health is also a determinant, since young people with better physical condition are oriented toward electoral participation, while those with health problems opt for unconventional forms of participation (60,49). As for political attitudes, these contribute to the formation of social stereotypes and motivate participation in political activities (36).

Table 11. Factors involved in Political Participation.

Political participation in youth	Findings
Individual and socio-cultural factors associated with political participation.	√ Social and economic factors such as gender, age, income and family dynamics determine voter turnout and susceptibility to populism (46,58. √ Healthier people tend to participate more in elections, while poor health may drive non-electoral political action (60). √ Peer influence and interpersonal relationships have a positive effect on young people's political knowledge and electoral participation (61,56). √ Political participation can be conventional (voting) or unconventional (protests, volunteering) motivated by social interests (55) √ Exposure to political news and the use of social media impact political efficacy and participation and are key for young people to express their voice and lobby political actors (34,48,63). √ Political attitudes can influence stereotypes and how young people engage in politics (36) √ Beliefs in democratic values and gender equality influence youth voter turnout (58) √ Political influencers can empower young people and increase their political participation (59,44) √ Developing leadership and organizational skills through activism (43).
Political activism	√ Protest as a predominant form of activism among students in specific contexts (42). √ The relationship between localism and political autonomy among students following mobilization events (57). √ Participation in local planning processes affects perceptions of knowledge and subjective experiences (50).
Political mobilization in social networks	√ Social media advertising campaigns targeting unregistered groups fail to increase voter registration (40). Young people are more susceptible to the influence of social media in forming political opinions and voting decisions (38). √ Despite low offline participation in Iran, the use of social media has increased political information and participation (48). √ Despite access to online political news, dialogue about politics is scarce among young people (45). √ There is a relationship between young people's political participation in social networks and their level of trust in political actors (37).

Likewise, beliefs in democratic values and support for gender equality enhance electoral participation (58). The role of political influencers in social networks has also empowered young people in addressing political issues (59,44).

Political activism

Political activism is associated with dynamics that favor the development of leadership and organizational skills. Protest, recognized as a form of activism, contributes to the formation of political identity in contexts where young people express their uncertainty and demand structural changes (42). This activism has been viewed as a learning opportunity for young people, including those in irregular situations, who develop organizational and leadership skills in the defense of human rights and civic participation (43). For example, in the context of Hong Kong, following the Umbrella Movement, a localist identification was evidenced that fostered political autonomy (57).

In addition, the relevance of compliance with legal norms in demonstrations is highlighted, which ensures the safety and sustainability of activism in politically tense environments (57). In conclusion, political activism integrates organizational skills, meaningful protests, local identities, emotions, and legal strategies, enriching the understanding of the current democratic landscape (50).

Political mobilization in social media

Political mobilization through social media presents a complex and ambivalent dynamic. While these platforms have allowed the expression of opinions and electoral decisions among young people, their effectiveness in increasing voter registration has been limited (40,48). On the other hand, social networks facilitate access to political information and strengthen trust in political actors, contributing to the construction of a perception of legality in institutions (38,37). It has also been observed that participation in networks can be hindered by the feeling of a lack of recognition and empowerment, which limits their long-term impact on political engagement (45).

Trust and political effectiveness

The perception of trust and political efficacy is a key determinant of civic participation. Low literacy and uncertainty, especially in contexts marked by corruption, are associated with reduced levels of trust and political efficacy, which in turn decrease civic participation (58). In contrast, political influencers have contributed positively to young people's political self-confidence, particularly through the use of social media (59). Furthermore, university students with a positive future orientation were found to exhibit higher levels of political confidence (62).

Table 12. Political Emotions and Feelings.

Emotions and political feelings	Findings
Trust and political effectiveness	√ Lack of trust in government and concerns about corruption hinder electoral participation (58). √ Following political influencers increases young people's internal political efficacy (59). √ University students with a positive future orientation in government have a higher level of trust in government (62).
Emotions and political feelings	√ Students demonstrated empathy by recognising the struggles of other young people, which fuels their ability to create change (29). √ Political awareness in Iran has been influenced using social media (48) √ Resentment mixes perceptions of injustice and anger, which affects participation (52). √ Students are motivated by social recognition and personal development in their civic engagement (53).

Emotions and political feelings

Political emotions and feelings are determinant in the mobilization and participation of young people. Empathy generates solidarity and encourages support for social transformation, whereas resentment, derived from perceptions of injustice, drives mobilization in response to dissatisfaction with democratic processes (29,52). In the Iranian context, for example, social networks have amplified the expression of political emotions, favoring the formation of collective opinions (48). Similarly, the search for social recognition and personal development is a driving force behind the formation of a political identity, with social change serving as the foundation for the demonstrations (53).

Table 13. Civic Awareness.

Civic awareness		Findings
Civic Engagement	√	University students in Greece show low civic engagement (42).
	√	There is a trend of 83.3% marking low civic engagement among Brazilian students (45).
	√	Higher education limits students' political engagement (31).
	√	Civic engagement influenced by parental education improves young people's social performance (53).
	√	Trust in government institutions and national elections influences civic engagement (58).
	√	Exposure to political news in newspapers has a positive impact on young people's civic engagement (56).
	√	Influence of social ties on political behavior and informed citizenship (56).
	√	Undocumented youth develop key skills and a sense of political empowerment by participating in migrant advocacy organizations (43).
	√	Compulsory civic education in schools does not necessarily increase youth voter turnout in the short term (39).
	√	Classroom interventions that combine information and social pressure can be effective in motivating young people towards political engagement (51,29).
Civic Education	√	Civic awareness among university students is still at a relatively low level, with deficiencies in areas such as civic knowledge, civic participation and civic responsibility (30).
	√	The teaching of comparative politics must address young people's concerns to improve political engagement (29).
	√	Civic education is central to national development, political engagement and youth unity in specific contexts, such as in Malaysia (47).
	√	Participation in voluntary political associations during education is more important than leadership in them (32).
	√	Democratic literacy develops in difficult contexts, as evidenced by undocumented youth navigating political systems (43).
	√	Differences in education and social background influence students' political attitudes, as observed in different academic disciplines (33).
Civic culture	√	Family upbringing, school education and media consumption are important determinants of students' civic awareness (30,34).
	√	Institutional barriers and the electoral context negatively affect youth political participation (49).
	√	Moral emotions in social movements influence the mobilisation of young people and their identification with causes (57).
	√	Social peer pressure can increase debate and participation in elections (51).

Civic engagement Civic engagement is defined by factors such as education, literacy, use of social networks, health and trust in institutions. Low civic engagement among young university students has been identified, especially in countries such as Greece and Brazil, where 83.3 % of students exhibit low engagement, which is attributed to a lack of political involvement in the school context (42,45). In contrast, in England and Ireland, it has been suggested that academic pressures in higher education limit civic engagement, while the educational level of parents has a positive influence over it (31,53). In addition, trust in government institutions and electoral processes motivates political participation, and the media and social networks contribute to the development of political skills and empowerment for social transformation (34,43,56,58).

Civic education

Although the importance of civic education is recognized, its compulsory nature does not necessarily guarantee an increase in electoral

participation, which suggests the limitations of educational policies in transforming political behavior (39). In countries such as Malaysia, civic education has proven effective in promoting social cohesion and responsible citizenship by identifying stimuli relevant to the context and cultural realities (47,51,29,33). In addition, differences have been observed in the way students access and use participation channels, which may be related to inequalities in the development of civic knowledge and skills, reflecting low civic awareness and representing an opportunity to implement more effective educational programs (30).

Civic culture

The formation of civic culture is influenced by family, educational, and social factors. The school context and the media are key elements for developing civic attitudes and awareness (34).

DISCUSSION

This systematic review analyzed the relationship between the factors that influence youth political participation, considering variables such as emotions, political feelings and civic awareness in young university students. The analysis was organized according to the main themes identified.

Factors associated with youth political participation

Sociodemographic factors, such as gender, age, and income, influence the political participation of young people, both in their conventional (voting) and unconventional forms (protests) (46). Likewise, health has emerged as a determining factor: young people with better physical condition tend to participate more in voting. In contrast, individuals with health problems tend to express their opinions through digital platforms, thereby reducing their impact on electoral decision-making (60).

Young people develop their attitudes, thoughts, and emotions toward political participation through their family environment, the media, cultural context, and personal experiences (64,65).

The influence of social media in political mobilization

Several studies have shown that greater involvement in political debates through social networks, utilizing memes, messages, and other digital materials, is positively correlated with increased participation in political campaigns and elections, thereby reinforcing the perception of political efficacy (49,56,61,63).

In addition, it has been observed that digital interactions strengthen group social cohesion and facilitate access to political information. They also allow greater rapprochement between political figures and young people, which could enhance electoral participation. However, this impact is contingent upon factors such as the cultural context and the emotional responses elicited in these exchanges (65). Likewise, youth political participation through social networks can foster the generation of innovative solutions in the field of activism and political communication, contributing to the strengthening of democracy (66).

However, the articulation between social networks and political participation is not uniform. Significant limitations have also been observed in countries such as France and Iran, where social networks have been a vehicle for political mobilization (67, 48). In this sense, the socio-political context is a key factor in empowering young people to feel recognized as agents of change in political processes (45).

Emotional experiences in political participation

The analysis of the relationship between emotions and political participation has revealed differences and similarities across various environments. Some studies highlight the role of social networks in fostering political trust and mobilizing participation through emotional engagement (59,48). Others, on the other hand, stress the influence of emotional contagion and individual and social experiences on the permanence of political activism (68,69).

In this sense, experiences of violence or trauma can motivate electoral participation, since voters seek candidates who validate their experience and propose protection and reparation policies (69,70). Additionally, it has been observed that evoking past political memories can be an effective strategy to encourage electoral participation, especially among first-time and young voters (71).

On the other hand, a positive relationship has been identified between emotional bonds and young people's political activism (72). In this framework, the concept of "affective solidarity" has been defined as the generation of shared emotions during activism, which is more relevant for the permanence of political action than ideological values *per se* (29,68).

Likewise, the importance of political ambivalence, understood as an emotional state of uncertainty regarding the decision to vote regardless of political affiliation, has been highlighted. This phenomenon demonstrates that attitudes towards political leaders are not necessarily unidimensional and can be marked by complex emotional factors (73,48).

Physiology, emotion, and influence on political behavior

The research reviewed suggests that physiological states associated with emotions have a significant influence on political decisions and behaviors (52). Prolonged exposure to stress can impair the ability to manage emotional responses adaptively, which in turn affects political preferences and decision-making (74). It has been reported that political contexts marked by uncertainty and fear can generate a preference for political leaders perceived as trustworthy and less authoritarian (74,75). Likewise, an association has been identified between anger and an inclination towards more conservative economic positions, modulated by the availability of resources in the environment (76).

Additionally, political events can impact the health and psychological well-being of young adults. Emotional and physiological responses to these events are mediated by factors such as gender, ethnicity, and political attitudes (77).

Civic awareness: education and civic culture

Civic awareness is shaped by civic education and civic culture, both of which are fundamental for the formation of active and committed citizens (78). Studies have shown that civic education promotes political participation, youth empowerment, and social cohesion (47,79,80,81).

The family and school environments play a key role in shaping civic culture. It has been found that parents' educational level has a positive influence on young people's civic participation (53,82,83). However, discrepancies persist in the real impact of civic education on electoral participation (39).

CONCLUSIONS

This review identified a line of research examining the factors influencing youth political participation, including emotional, educational, and civic awareness aspects.

The findings suggest that sociodemographic factors, including family background, age, gender, and health status, have a significant impact on political activism. Additionally, political ideology influences the perception and processing of emotional information, while emotional states impact the appraisal of political events.

Finally, the interaction between emotions, education, and civic awareness, mediated by social networks, conditions the ways of youth political participation, influencing their political decisions and behaviors.

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Psychosocial Autopsy-Based Predictive Models of Suicidal Behavior: Systematic Review of Approaches and Recent Evidence

Modelos Predictivos de la Conducta Suicida Basados en la Autopsia Psicosocial: Revisión Sistemática de Enfoques y Evidencia Reciente

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SUMMARY

The purpose of this study was to analyze the recent scientific literature on predictive models of suicidal behavior based on psychosocial autopsy. The methodology used was based on PRISMA guidelines, complemented with a quantitative approach typical of exploratory systematic reviews. For the collection of information, publications in English and Spanish corresponding to the period 2020 - 2025 were considered. Sixteen relevant studies were selected, located through the Scopus, PubMed, and Web of Science databases. The findings indicate that the integration of psychosocial autopsies with artificial intelligence models allows the development of more accurate and contextualized predictors of suicide risk, thus strengthening prevention and early intervention strategies.

Keywords: *Models, prediction, suicide, psychosocial autopsy.*

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RESUMEN

Este estudio tuvo como propósito analizar la literatura científica reciente sobre los modelos predictivos de la conducta suicida basados en la autopsia psicosocial. La metodología empleada se basó en los lineamientos de PRISMA, complementada con un enfoque cuantitativo propio de las revisiones sistemáticas de tipo exploratorio. Para la recolección de información, se consideraron publicaciones en inglés y español correspondientes al periodo 2020 – 2025. Se seleccionaron 16 estudios relevantes, localizados a través de las bases de datos Scopus, PubMed y Web of Science. Los hallazgos indican que, la integración de autopsias psicosociales con modelos de inteligencia artificial permite desarrollar predictores más precisos y contextualizados del riesgo suicida, fortaleciendo así las estrategias de prevención e intervención temprana.

Palabras clave: *Modelos, predicción, suicidio, autopsia psicosocial.*

INTRODUCTION

Suicide is a complex, multifactorial, and multicultural phenomenon worldwide, and its approach represents a major concern for many public health systems. According to the World Health Organization (WHO), it indicates that statistically, 700 000 people die by suicide each year, being the fourth leading cause of death among young people aged 15-29 years, and the leading cause of premature mortality in several high and middle-income countries (1). This results in irreparable loss and high social, emotional, and economic costs for individuals, families, and healthcare systems.

Despite significant advances in the identification of risk factors associated with this problem, suicide rates have not declined in a representative manner worldwide. In countries such as South Korea, suicide has remained the leading cause of death in adolescents and young adults for decades, reflecting persistent challenges in prevention and intervention strategies (2). Similarly, in China, despite an overall reduction in suicide rates, it remains a significant public health threat, especially in rural and vulnerable populations (3). This persistence highlights the urgent need for a deeper understanding of the contextual and longitudinal factors surrounding this phenomenon. To this end, several research methodologies have been developed. Among them, psychosocial autopsy emerges as a fundamental tool, allowing a detailed reconstruction of the circumstances before the suicide through structured interviews with relatives and the review of medical records and other relevant documents. This retrospective approach offers crucial insight into the interaction of risk and protective factors over time (4).

In coherence with this, different theoretical models have joined efforts to explain suicide from multiple perspectives at the psychological, historical, biological, and social levels. In this sense, one of the approaches with the greatest integration of variables is the biopsychosocial model proposed by Turecki at al. (5) which distinguishes between distal risk factors such as genetics, family history, and childhood trauma; developmental factors such as impulsivity and substance use; and proximal factors such as hopelessness, emotional dysregulation, and stressful life events.

Despite the reported studies on these factors, the integration of this knowledge into clinical and community resources for the timely identification and management of this problem remains limited. This is due, in part, to the fact that conventional predictive models have relied predominantly on traditional statistical approaches, such as logistic regression. These methodologies exhibit strong difficulties in recording nonlinear relationships, complex interactions, and temporal dynamics among the multiple variables associated with suicidal behavior (6). This situation has limited the ability to generate effective and generalizable predictive models, especially in populations with high psychosocial vulnerability, such as children, adolescents, and young adults (7). It is in this context that the psychosocial autopsy acquires particular relevance, given that the qualitative and contextual data of high granularity derived from it can significantly enrich the information used by predictive models, allowing a more holistic and personalized view of suicidal risk by capturing the life trajectory and precipitating events (8).

Currently, advances in artificial intelligence (AI) and machine learning (ML) have expanded the possibilities for developing more accurate predictive models, enabling the identification

of complex patterns that are not readily apparent to the naked eye. In particular, the integration of data obtained from psychosocial autopsies, including detailed narratives, contextual factors, psychopathological history and critical life events of the deceased individual, can enhance the ability of these algorithms to build more robust risk models. Models such as artificial neural networks, multilayer perceptrons, and backpropagation algorithms have demonstrated greater predictive capacity compared to traditional approaches when processing high-dimensional and heterogeneous information, achieving accuracy levels above 90 % in some studies that combine clinical and sociodemographic data (6,9).

Given this scenario and recognizing the potential of psychosocial autopsy to generate valuable data on the etiology of suicide, it is imperative to review how these elements can be integrated in the development of predictive models that allow early identification of at-risk populations and the design of early intervention strategies. Artificial intelligence and machine learning have proven to be effective tools for the prediction of suicidal behaviors in adolescents and young adults (9,10). It is crucial to understand how these models can be informed and refined by detailed information obtained from psychosocial autopsies, enabling the identification of behavioral, psychological, and social biomarkers with greater specificity (11).

Considering the above elements, the purpose of this study was to synthesize the current knowledge on predictive models of suicidal behavior based on psychosocial autopsy, analyzing their methodological approaches, diagnostic accuracy, variables used and potential for clinical and preventive application.

Predictive models of suicide based on psychosocial autopsy.

In the last two decades, the prediction of suicidal behavior has gained prominence as a crucial strategy for prevention and care in mental health. One of the most promising approaches has been the development of predictive models based on psychosocial autopsies. Although traditionally used for epidemiological research and etiological understanding of suicide, this technique allows the identification of risk factors from retrospective analysis of completed suicide cases. This methodology, originally designed to explore psychological and social circumstances before death, has evolved into a valuable resource for feeding artificial intelligence (AI) and machine learning (ML) systems, given its ability to generate rich, detailed, and contextualized data on the life course and precipitants of suicidal risk (5,12).

Psychosocial autopsy, also known as psychological autopsy, involves the systematic collection of information about the deceased's life, mental health, social relationships, life events, and behavior through structured interviews with close people, as well as the analysis of medical, school, and social records (13). This methodology has been fundamental for the identification of proximal factors and triggers of suicide, such as depressive symptoms, hopelessness, social isolation, family dysfunction, and exposure to traumatic events (7,12). The richness of retrospective data and the contextualization it provides are crucial for capturing the complexity of suicidal patterns that are not evident with cross-sectional data alone, allowing a deeper understanding of the dynamics of suicidal risk (4).

Recent studies in South Korea have shown that up to 97 % of adolescents who died by suicide had at least one diagnosable mental disorder, and more than 80 % had manifested warning signs in the year before their death. However, many of these signs were not recognized by their families or educational institutions, evidencing the need for more sensitive predictive models that integrate this qualitative and contextual information provided by psychosocial autopsy (12). The ability of psychosocial autopsy to uncover subtle or previously uninterpreted signals, when combined with the capacity of machine learning algorithms to identify complex patterns, represents a promising avenue for overcoming current limitations in risk detection by enabling the identification of behavioral, psychological, and social biomarkers with greater specificity (14).

From this empirical basis, several researchers have begun to build predictive models of suicide using artificial intelligence algorithms that incorporate psychosocial autopsy data. For example, Lyu et al. (3) utilized data collected

in rural China through psychological autopsies to train artificial neural networks (including backpropagation and multilayer perceptrons). Their results showed accuracy rates above 90 %, significantly exceeding those of traditional logistic regression models. This research highlights that the richness of qualitative data, when processed by nonlinear algorithms, can substantially improve predictive ability. In addition, other research has explored the use of longitudinal and clinical data, sometimes resembling the granularity obtained in psychosocial autopsies, to feed machine learning models in the prediction of suicide in young populations, achieving high accuracy and area under the curve (AUC) values above 0.90 (11).

Likewise, the use of structural models, such as the one proposed by Lievano-Ruiz et al. (7), in Mexican university students, has allowed the identification of proximal risk factors such as hopelessness, emotional dysregulation, social isolation and family dysfunction, all extracted from self-reported information and interviews that simulate the structure of a psychosocial autopsy. Although these structural models do not employ machine learning algorithms directly for prediction, their value lies in the empirical validation of the interrelationship of these risk factors. Such validation is critical for variable selection and conceptualization of more complex AI/ML-based predictive models, ensuring that the features used are theoretically sound and clinically relevant (15).

Despite these advances, important methodological challenges remain. These include the standardization of psychosocial autopsy protocols, the inherent subjectivity of interviews with family members and close associates, and the difficulty in accessing sensitive data in sociocultural contexts where suicide remains a stigmatized topic (5). Additionally, the scarcity of large psychosocial autopsy datasets that can be systematically integrated into machine learning models limits their generalization, and efforts are required to develop methodologies that enable interoperability and analysis of large-scale qualitative information (14). Nevertheless, the heuristic value of this tool remains indisputable, especially when articulated with emerging technologies for suicide detection and prevention (5).

METHODOLOGY

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. It had an exploratory quantitative approach. For the structuring and delimitation of the research, Boolean operators were used to ensure the consolidation of a robust and coherent search, taking into account the study's purposes.

A systematic literature search was conducted in high-impact databases, including Springer Open, Web of Science, and Scopus, which were selected for their comprehensive coverage of the social sciences, psychology, and applied informatics. The search strategy incorporated a combination of keywords, linked by Boolean operators AND, OR, NOT, in order to maximize the relevance of the results (Table 1).

Table 1. Controlled terms and Boolean operators

("psychological autopsy" and "prediction" or = "suicide" not = "disability" "psychosocial" and "behavior" or "Suicidal" or "predictive" not = = "elderly" ("psychological autopsy" and "prediction" or = "suicide" not = "disability" "psychosocial" and "behavior" or "suicidal" or "predictive" not = "elderly")

Inclusion and exclusion criteria

In this study, clear criteria were defined that responded to the nature of the research, the period of publication, and the variables involved. These guidelines helped to minimize possible biases and strengthen the validity of the results obtained.

The search focused on articles published between 2020 and 2025, in English, Spanish, and Portuguese, selected from journals indexed in specialized databases. Duplicate papers, abstracts, and brief notes were discarded, always prioritizing those that offered the full text. Key information was extracted from each study chosen, such as the title, objective, authors, country, year of publication, sample, methodology, instruments used, main findings and theoretical gaps, which allowed the construction of a solid background matrix, facilitating a deeper, more current and contextualized understanding of the variables analyzed.

Table 2. Cross-referencing of search terms in databases

Search	Data base	Final Results Algorithms			
"psychological autopsy" and "prediction" or = "suicide" not = "disability", "psychosocial" and "behavior" or "suicidal" or "predictive" not = "elderly" ("psychological autopsy" and "prediction" or = "suicide" not = "disability" "psychosocial" and "behavior" or "suicidal" or "predictive" not = "elderly").	Scopus	90	75	35	200
	PubMed	78	52	45	175
	Web of Science	120	58	62	240
	Total	288	185	142	615

Table 3. Final research results by database

Database	Final Results
Scopus	200
PubMed	175
Web of Science	240
Total	615

Choice of studies

For the selection of documents for the review, the time window of the last five years was taken into account, without considering articles linked to scientific platforms or journals that were in closed access, in addition to duplicate texts, which fell outside the categories established for the search, in addition to abstracts and research notes.

RESULTS

For the consolidation of the review, the criteria described in the PRISMA methodology were followed. Boolean operators AND, OR and NOT were used to perform the searches: "psychological autopsy" AND "prediction" OR = "suicide" NOT = "disability" "psychosocial " AND "behavior" OR "Suicidal" OR "predictive"

Table 4. Process of identification, elimination and selection of items

Equations	**AND, OR and NOT operators**			
No Articles in the Language	**Spanish**		**English**	
		295	320	
Databases	**Scopus**	**PubMed**	**Web of Science**	**Total**
No Filter	200	175	240	615
No Access	100	90	140	330
R/ Incomplete/ Duplicates	50	40	73	163
Do Not Meet Criteria	45	40	21	106
Election	5	5	6	16

NOT = "elderly" ("psychological autopsy" AND "prediction" OR = "suicide" NOT = "disability" "psychosocial" AND "behavior" OR "suicidal" OR "predictive" NOT = "elderly" (Table 1). Reference lists of the most relevant systematic reviews to be considered in this study were also reviewed. Eligible publications were those that were limited to reporting predictive models of suicidal behavior and psychosocial autopsies in cases of completed suicides.

Relevant documents were selected from scientific databases, such as Scopus, PubMed, and Web of Science. The search included publications in English and Spanish, focusing on the last five years (2020 - 2025) to compile the most recent research in this thematic line (Table 2 and 3).

Similarly, all the articles taken from the indexed journals were downloaded and those that were duplicates or did not meet the criteria were eliminated. Priority was given to publications with full text, and the abstracts and research notes were excluded; the key information of the articles was extracted. As an initial result of this search, 615 files were obtained, comprising 32.5 % from Scopus, 28.4 % from PubMed, and 39 % from Web of Science. Of these, 47 % are in Spanish and 52 % in English (Table 4).

The following is a summary of the most important findings of the studies reviewed through the search in different scientific databases, which allow the foundation and support for the approaches of this research related to predictive models of suicide based on artificial intelligence and machine learning and psychological autopsy, thus allowing the knowledge of the problem in a current manner in the last five years, in addition to the relationship that is found with the objectives set out in this project.

Accordingly, López-Villalobos et al. (17) examined the prevalence and prediction of suicidal behavior in Spanish adolescents through the Millon Clinical Inventory. For this purpose, they designed statistical models to predict suicidal tendency, ideation, planning and attempts. In this study, child abuse was found to be a variable present in all models. At the same time, family conflicts, pessimism, oppositional or impulsive personality were associated with an increased risk of suicide in the population.

In a study conducted by Barajas-Aranda et al. (13), Machine Learning models were compared and explained to predict suicide. Within this research, they evaluated artificial neural networks, logistic regressions, and decision trees, noting that the neural network technique yielded the best performance in predicting 82 %. However, the study places special emphasis on its practical use in clinical and healthcare scenarios. Therefore, SHAP (SHapley Additive exPlanations) and LIME (Local Interpretable Model-agnostic Explanations) techniques were also employed to achieve a more precise definition of the model. This study is situated at the exact crossroads between artificial intelligence and mental health in clinical contexts.

In line with this, Patel et al. (18) developed a machine learning-based approach to predict weekly state suicide rates in individual states, incorporating real-world data from social media, emergency room visits, specialized search engines, and mental health self-assessments. Within the state, the model achieved high accuracy in four different states, outperforming conventional models, demonstrating its value in integrating digital signals for monitoring suicide trends in the population. Arunpongpaisal et al. (19) conducted a predictive model for the risk of death in the first suicide attempt, considering records from the national suicide surveillance system in Thailand. The design was based on the multivariable logistic regression method, identifying variables such as advanced age, male sex, presence of mental disorders, unemployment and warning signs of suicidal behavior as one of the main predictors, obtaining a high level of accuracy. This model has been applied within the clinical field to enhance suicide risk assessment and prevention in hospital and healthcare settings.

In contrast, Núñez et al. (20) conducted a scientometric analysis of research trends using a meta-investigative approach to examine the suicide risk variable in children and adolescents, employing a graph theoretical model and citation networks. The study identified trends related to non-suicidal self-injury, psychiatric factors, antidepressant use and child abuse. The research made a map of specific knowledge from the area, highlighting theoretical gaps, authors and patterns of scientific articulation where they establish the need to use models that allow the prediction of suicide in vulnerable populations. Similarly, Cifuentes et al. (21) developed a module for forecasting suicide predictions using time series data in the city of Medellín, Colombia. They evaluated Holt-Winters, Box-Jenkins, and a seasonal parametric model with ARMA 0.5 errors, which incorporates both autoregressive (AR) and moving average (MA) components, where the latter proved to be the most effective.

Lievano-Ruiz et al. (7) carried out research focused on the validation of Turecki's biopsychosocial model of suicidal ideation in Mexican university students. The study took into account the structural equations in a sample of 165 young students, where they found very good levels of adjustment in the proposed model, identifying emotional dysregulation, depressive symptoms, feelings of hopelessness, social isolation and family dysfunction as risk factors. Lee et al. (2) developed an investigation considering the psychological autopsy in South Korean adolescents in cases of completed suicides, to explore psychiatric diagnoses, personality traits, risk factors, life histories and warning signs in 36 adolescents who died between 2015 and 2021, using interviews with their parents and the application of standardized analyses. In the main results, they found that 97.2 % presented a psychiatric disorder, with the most prevalent being depression. In addition, most had manifested warning signs that were complex to identify, due to personality characteristics of submission or avoidance.

Núñez et al. (20) designed and validated a model to predict suicide in young people in Colombia, where they identified that variables such as anxiety, depression, and hopelessness explain more than 50 % of the risk of suicide. In addition, substance use, especially alcohol, acts as a mediator of affective variables related to suicide, suggesting the importance of interventions for emotional regulation and substance use in the youth population. Underwood et al. (22) studied the relationship between stress, early adversity, and suicidal behavior, also reviewing the levels of HPA axis-associated proteins cortisol and BDNF in postmortem samples of prefrontal and anterior cingulate cortex in 52 people distributed between suicidal patients and a sex- and age-matched control group. The results of the study indicate that high levels of recent stress, rather than early stress, biologically influence the risk of suicide.

In the same vein, Lyu et al. (6) conducted a study in which they developed a model to predict suicide through the implementation of neural networks, using psychosocial autopsies in rural areas of China as a database. For this, two artificial intelligence models were considered: the backpropagation neural network and the multilayer perceptron, which were compared using traditional logistic regression. The main findings showed that the model achieved an accuracy of over 90 %. In comparison, the other method attained a rate of 82 %, demonstrating the effectiveness of models based on machine learning in predicting risk and suicidal behavior, and highlighting the relevance of implementing

them in clinical scenarios to support automated diagnoses.

On the other hand, Pérez-Martínez and Rodríguez-Fernández (10) analyzed the psychosocial autopsy as a technique to explore the causes of violent deaths, with special emphasis on cases of completed suicides, reconstructing a psychological profile of the deceased, positioning this tool as a key resource for the investigation of self-inflicted deaths.

Bae et al. (23) performed psychosocial autopsies in 48 suicide cases in South Korea to identify psychosocial and psychiatric factors in the deceased and their family members, using the Korea Psychological Autopsy Checklist (K-PAC) to collect information on mental health status, stressful life events, and warning signs. The findings indicate that in 87 % of cases, a previous psychiatric diagnosis was present. Still, in only 15 % of the cases, the current treatment was ongoing, and some instances exhibited warning signs that family members did not detect. Valdés-García et al. (24) implemented psychological autopsies to analyze the factors associated with suicide in two members of the same family. In the investigation, precipitating factors such as love breakups, suicidal ideation, and the method of hanging were found. In this study, the authors conclude that couple conflicts and a history of suicidal behavior in the family are factors that increase the vulnerability to suicide within the family nucleus.

Pérez-Martínez and Rodríguez-Fernández (10) explored the application of psychological autopsies to clarify doubts about suicide. From this study, the autopsy was explored as a fundamental resource to perform retrospective analysis in the psychological state of people who have died. The research highlights its employability to establish risk factors and distinguish the difference between suicidal acts, accidental death, and homicide.

Kim at al. (11) analyzed 23 000 cases of suicide in South Korea, where they found that hanging was the most frequent method of suicide in this population, and that certain variables such as age, the presence of psychopathology such as schizophrenia, substance use, especially alcohol, and psychopathological history in the family are closely related to the selection of the method. This research allows for the establishment of a risk profile associated with different forms of suicide, which provides inputs for the design and implementation of contextualized interventions.

Finally, the studies analyzed show that suicide is the product of an interaction between multiple psychosocial risk factors at the psychiatric, biological, social, and personality levels. They also highlight the need to design and implement predictive models of suicide that integrate the resources derived from psychosocial autopsies,

Based on these findings, the need arises to design a predictive model of suicide that integrates the inputs obtained through psychosocial autopsies, taking advantage of the capabilities of artificial intelligence to analyze complex patterns, detect risk factors, predict suicidal behaviors, and generate diagnostic support tools. It is essential to recognize the strategic value of psychosocial autopsies as a critical resource in this process, since they allow the construction of more accurate predictive models, contextualized and based on real information, contributing to improving the response capacity of the health system to risk cases detected early and strengthening suicide prevention strategies.

DISCUSSION

The results obtained in the present study highlight the remarkable progress in the study of suicidal behavior from a predictive approach supported by psychosocial autopsies and AI artificial intelligence models. The affinity between classical methodologies such as psychological autopsy and contemporary computational approaches such as machine learning enhances an epistemological transition in the approach to suicide as a global public health problem. This discussion presents the results obtained in light of the theoretical background, the empirical literature, and the clinical and preventive implications that emerge from this synthesis.

First, the analysis reveals a growing trend towards the use of algorithmic models for predicting suicidal behavior, as highlighted in studies such as those of Barajas-Aranda et

al. (13), where artificial neural networks achieved predictive accuracy above 80 %, even reaching 90 % in rural contexts. These findings reinforce the effectiveness of deep learning for processing large volumes of clinical and psychosocial data, outperforming traditional statistical models in many cases. Similar results have been reported by Kessler et al. (25), who, by applying predictive models, found accuracies of 85 % in predicting suicidal risk based on longitudinal data. However, these models present limitations in their real-world applicability if they are not accompanied by interpretative tools such as SHAP or LIME7(13), which enable the translation of algorithmic findings into understandable variables for clinical staff, a necessity in the healthcare context.

Regarding the population variable, there is a marked concern for suicide in vulnerable populations such as children, adolescents, and young people, especially in Latin American and Asian contexts (12,17,20). Childhood abuse, family conflict, impulsivity, and hopelessness emerge as highly predictive variables of suicidal risk, being constant in several models. Parallel studies, such as Walsh et al. (27), focused on North American adolescents, also identified depressive symptomatology and family problems as key predictors, validating the international consistency of these factors.

However, the study by Lievano-Ruiz et al. (7) validates Turecki's biopsychosocial model, providing empirical evidence on the interaction between emotional, family, and social variables. This comprehensive approach reaffirms that a single dimension cannot explain suicidal behavior, but rather a complex web of factors. Similarly, Franklin et al. (27) in their literature review on predictors of suicide, concluded that the most robust models are those that combine multiple dimensions (clinical, social, and cognitive), which converges with the findings of the present review.

The contributions of studies such as that of Underwood et al. (22) show a relevant biological component by identifying neurochemical alterations linked to the HPA axis and BDNF in people who have died by suicide. This line of research opens the possibility of integrating objective biomarkers into predictive models, thereby enriching diagnostic precision and depth. Research such as Neupane et al. (28) has also explored this approach, identifying several biomarkers in suicides, which reinforces the role of the biological component in prediction.

From the methodological point of view, the review confirms the richness of psychological autopsy as a retrospective technique for in-depth exploration of risk factors. Studies (2,23,24) highlight its usefulness in reconstructing the emotional and behavioral profiles of deceased people. Similarly, recent reviews such as Favril et al. (29) also highlight the usefulness of psychological autopsy to understand the underlying causes of suicide, which remains valid and of practical value.

Another notable finding is the exploration of alternative data sources in predictive models, as evidenced by the study by Patel et al. (18), which integrates information from social networks, search engines, and emergency records. This approach, which can be termed "applied psychoinformatics," allows for more proactive surveillance of suicidal tendencies. Similar findings were reported by Soron and Pagliari (30), who demonstrated that the analysis of social network data allows the detection of early signs of suicidal risk.

From the perspective of population prediction, research such as that of Cifuentes et al. (21) explores time series models. In this regard, previous studies such as Yan et al. (31) have already noted the importance of monitoring temporal patterns of suicide to adjust public health strategies. This distinction between individual and ecological prediction reinforces the need for a multilevel approach. It also highlights the potential of predictive models to profile specific suicide patterns, as seen in the study by Kim et al. (32). Park et al. (33) have also explored the choice of suicidal method as an indicator of risk, highlighting the importance of considering these variables to improve preventive intervention. Despite these advances, gaps in the literature have also been identified, as noted by the scientometric analysis of Núñez et al. (34). This issue could be addressed through transdisciplinary research that integrates mental health, data science, and social sciences.

In summary, the results of this review allow us to conclude that suicide prediction has moved

from purely clinical approaches to hybrid models, where psychological autopsies provide contextual depth, while AI algorithms provide analytical power. This pairing offers a glimpse of a future where healthcare systems can anticipate suicide attempts, acting in a preventive and personalized manner. To this end, it is essential to move towards predictive models that integrate clinical, social, digital, and biological data, always under principles of ethics, confidentiality, and equity. In addition, the training of mental health professionals should include competencies in the interpretation of algorithmic models and the responsible use of technology in clinical contexts. Finally, it is recommended that suicide epidemiological surveillance systems be strengthened to incorporate these findings and become effective tools for the design of sensitive, evidence-based public policies aimed at early prevention.

CONCLUSIONS

Integrating psychosocial autopsy as an input for the design of predictive models of suicide represents a key epistemological advance in suicide prevention, by articulating qualitative dimensions with quantitative data processing through artificial intelligence and machine learning. This methodological convergence enables the overcoming of the limitations of traditional approaches, providing a more contextualized, personalized, and dynamic understanding of suicide risk factors (2,3).

One of the main conclusions derived from the study is that AI-based models, particularly artificial neural networks and multilayer perceptrons, significantly outperform classical statistical models, such as logistic regressions, in accuracy, especially when fed with data derived from psychosocial autopsies (3). This finding not only highlights the technical efficacy of these algorithms but also underscores the relevance of contextual, narrative, and longitudinal data that only psychosocial autopsy can provide.

Another relevant contribution of the study lies in the validation of the biopsychosocial model of suicide (5), which recognizes the interaction of factors such as genetic and historical factors, impulsivity, life events and hopelessness as a complex explanatory network of suicidal behavior. The literature reviewed confirms the repeated presence of variables such as depressive symptomatology, social isolation, family dysfunction and child abuse, especially in adolescents and young adults, as strong predictors of suicidal risk (17,20). These variables not only have international empirical support (26) but also confirm the need for multi-systemic and interdisciplinary approaches.

In addition, progress has been made in utilizing alternative data sources to inform predictive models, such as digital records, social networks, and web searches, which expands the possibilities for proactive monitoring of suicide risk (35). This could complement classical techniques and generate real-time early warning systems, with high value in public health contexts.

Likewise, the study confirms the clinical and forensic value of psychosocial autopsy, not only as a tool for reconstructing the mental state before suicide, but also as a method for generating predictive profiles applicable in clinical and community settings (4,10). Its rigorous and systematic implementation, however, is hampered by ethical, cultural, and methodological barriers, such as the standardization of protocols, access to sensitive information, and the specialized training of professionals (5).

Finally, from an applied perspective, the inclusion of alternative data sources, such as social networks, digital medical records, and search engines, in predictive models is also noteworthy (30,35). These emerging sources constitute an expanding frontier in the field of psychoinformatics and open unprecedented opportunities for proactive detection of suicide risk at the population level, especially among young digital natives.

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Efectividad del uso de la tecnología en el cuidado de enfermería: Revisión integrativa

Effectiveness of technology used in nursing care: An integrative review

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RESUMEN

El avance tecnológico ha transformado el cuidado en enfermería con herramientas como la telemedicina, dispositivos de monitoreo remoto y registros electrónicos de salud. Estas tecnologías han mejorado la calidad, y eficiencia del cuidado, pero enfrentan desafíos significativos. **Objetivo:** *Analizar la efectividad del uso de las tecnologías en el cuidado de enfermería desde la evidencia científica.* **Método:** *Se realizó una revisión integrativa de artículos publicados entre 2016 y 2023 en PubMed, ScienceDirect y SciELO, en español, inglés y portugués. Se emplearon métodos cualitativos, cuantitativos y mixtos, utilizando la herramienta RAYYAN para la selección y clasificación sistemática de cinco aspectos clave.* **Resultados:** *Se destacaron avances en indicadores clínicos como la reducción de morbilidad y hospitalizaciones, así como mayor satisfacción del paciente. Sin embargo, existen limitaciones relacionadas con mantenimiento, formación y privacidad.* **Conclusión:** *La implementación efectiva de estas tecnologías requiere superar barreras y garantizar equidad en el acceso, optimizando su impacto en la atención de enfermería.*

Palabras clave: *Salud digital, enfermería, atención de enfermería, efectividad.*

SUMMARY

Technological advancements have transformed nursing care with tools such as telemedicine, remote monitoring devices, and electronic health records. These technologies have improved the quality and efficiency of care, but they face significant challenges. **Objective:** *To analyze the effectiveness of technology use in nursing care based on scientific evidence.* **Method:** *An integrative review of articles published between 2016 and 2023 in PubMed, ScienceDirect, and SciELO, in Spanish, English, and Portuguese, was conducted. Qualitative, quantitative, and mixed methods were used, using the RAYYAN tool for the systematic selection and classification of five key aspects.* **Results:** *Advances in clinical indicators,*

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including reduced morbidity and hospitalizations, as well as increased patient satisfaction, were highlighted. However, there are limitations related to maintenance, training, and privacy. **Conclusion:** *The effective implementation of these technologies requires overcoming barriers and ensuring equitable access, thereby optimizing their impact on nursing care.*

Keywords: *Digital health, nursing, nursing care, effectiveness.*

INTRODUCCIÓN

El avance acelerado de la tecnología ha revolucionado múltiples sectores, y el campo de la enfermería se ha transformado significativamente con la integración de herramientas digitales como los registros electrónicos de salud, los sistemas de monitorización remota y la telemedicina. Estas innovaciones han modificado fundamentalmente la forma en que el personal de enfermería proporciona atención, mejorando tanto la calidad como la eficiencia en el cuidado de los pacientes. La evidencia científica ha demostrado que el uso adecuado de estas herramientas puede mejorar la toma de decisiones clínicas, reducir errores médicos y optimizar la coordinación del cuidado, permitiendo una atención más precisa y segura (1-4). En particular, los registros electrónicos de salud han facilitado el acceso inmediato a la información del paciente, mejorando significativamente la comunicación entre profesionales y, en consecuencia, la calidad de la atención brindada (5).

En el contexto de los países en desarrollo, la implementación de estas tecnologías ha mostrado un progreso notable, aunque enfrenta desafíos específicos. En Colombia, por ejemplo, las Tecnologías de la Información y Comunicación (TIC) han demostrado ser herramientas valiosas para la gestión de enfermedades crónicas, facilitando la educación en salud y mejorando la adherencia a tratamientos, lo que ha resultado en una reducción significativa de complicaciones y hospitalizaciones (6,7). La tecnología en salud (TS), según la definición de la Oficina de Evaluación Tecnológica del Congreso de Estados Unidos, abarca no solo medicamentos y dispositivos médicos, sino también sistemas organizacionales y de soporte, requiriendo una considerable especialización del personal sanitario para su implementación efectiva (8,9).

Sin embargo, estas innovaciones tecnológicas presentan desafíos significativos que deben ser considerados. Entre las vulnerabilidades más notables se encuentran los posibles fallos técnicos o interrupciones en los sistemas informáticos, que podrían comprometer la disponibilidad de datos críticos para la atención al paciente. Además, existe la preocupación por la dependencia excesiva de la tecnología, que podría limitar la capacidad de los profesionales de enfermería para confiar en sus habilidades clínicas y juicio profesional (10,11). La brecha digital también representa un obstáculo significativo, especialmente para aquellos pacientes que no tienen acceso o no están familiarizados con la tecnología, lo que puede limitar su participación en su propio cuidado (12).

A nivel internacional, el panorama es diverso. En España, el 8,2 % del gasto total en el sistema de salud se ha destinado a la adquisición de tecnologías sanitarias en la última década, lo que ha generado una mayor implementación de estas herramientas en distintos entornos sanitarios (9). En América Latina, países como México, Chile y Cuba han demostrado avances significativos, destacándose iniciativas como el Centro de Evolución de Tecnología (CENETEC) en México (13). Brasil, por su parte, ha implementado sistemas de información sanitaria y telemedicina para mejorar la accesibilidad en zonas remotas, mientras que a nivel nacional se esperan cambios significativos en la cultura de evaluación de TS con la implementación de centros especializados (9,14).

En este contexto, resulta fundamental evaluar la viabilidad y efectividad de la tele-enfermería, considerando no solo los beneficios potenciales en términos de eficiencia y calidad, sino también su adaptabilidad a la práctica clínica. Es crucial examinar los tipos específicos de tecnología utilizados para brindar cuidado, así como los resultados de salud asociados con su uso y su impacto en la calidad del cuidado (11,12,14). Esta evaluación se vuelve particularmente relevante en un entorno donde la demanda de servicios de salud eficientes y accesibles continúa creciendo, y donde la tecnología juega un papel cada vez más crucial en la prestación de cuidados de enfermería.

Por lo tanto, este estudio se propone analizar la efectividad del uso de las tecnologías en el cuidado de enfermería desde la evidencia científica, con objetivos específicos que incluyen: identificar los tipos específicos de tecnología utilizados en el cuidado de enfermería, distinguir los resultados de salud relacionados con su uso, tanto en términos de resultados clínicos como de experiencia del paciente, y explorar la evidencia relacionada con la efectividad de la tecnología del cuidado de enfermería según el entorno de atención. Esta investigación busca contribuir al conocimiento existente sobre la implementación efectiva de tecnologías en el cuidado de enfermería, proporcionando información valiosa para la toma de decisiones en la práctica clínica y el desarrollo de políticas sanitarias.

METODOLOGÍA

Diseño

Cualitativa, tipo revisión integrativa. Se llevó a cabo una revisión integrativa que abarcó artículos con metodologías cuantitativas, cualitativas y mixtas. La búsqueda de referencias se realizó en publicaciones en español, inglés y portugués, utilizando bases de datos como PubMed, Science Direct y SciELO. Para mejorar la búsqueda, se utilizaron operadores booleanos (AND, OR, NOT) y se aplicaron descriptores clave en los títulos, resúmenes y palabras clave de los artículos. Además, se ajustaron filtros específicos en cada base de datos para garantizar la sensibilidad y especificidad, limitando la búsqueda a textos completos publicados entre 2016 y 2023. El proceso de selección de artículos comenzó con la identificación inicial a partir de los títulos; los artículos seleccionados debían contener al menos dos de las palabras clave. Se revisaron los resúmenes, y aquellos que incluían información relevante sobre la efectividad de la tecnología y su aplicación en el cuidado de enfermería fueron seleccionados, para lectura completa y valorar la calidad de los mismos se analizaron a partir de cinco de los siguientes aspectos : claridad en los fines u objetivos, pertinencia de los criterios para la selección como parte de la metodología implementada, estrategias de búsqueda, términos de búsqueda apropiados, criterios utilizados para la evaluación de la calidad de los artículos, y modo en que los autores analizaron la información para presentar los hallazgos.

Criterios de Legibilidad

Desenlace

La investigación revela las tecnologías más comúnmente utilizadas, sus efectos en los resultados clínicos de los pacientes y cómo varía su efectividad según el entorno de atención. Proporciona una comprensión completa de cómo las tecnologías están influyendo en la práctica de enfermería y sugiere recomendaciones para optimizar su implementación y uso, maximizando beneficios y minimizando desafíos. Con el objetivo de analizar la efectividad del uso de las tecnologías en el cuidado de enfermería desde la evidencia científica.

Tipos de estudios

Se fundamenta en una variedad de enfoques metodológicos, que abarcan desde artículos originales hasta reportes de casos y revisiones bibliográficas. Estos estudios, realizados por profesionales del ámbito de la salud (enfermería), y artículos que analizaron alguno de los siguientes aspectos: Tecnología robótica del cuidado, la formación del personal de enfermería en el uso de tecnología, relación enfermería-tecnología-paciente, la ética del cuidado con la tecnología.

Los idiomas considerados para la inclusión de artículos fueron artículos publicados en idioma español, inglés y/o portugués. Los artículos considerados para la inclusión fueron artículos publicados entre el período 2016 hasta 2023.

Criterios de Exclusión. Durante el proceso de revisión integrativa, se excluyeron los artículos que presentaban una calidad científico-técnica deficiente, tras aplicar las herramientas de evaluación correspondientes a cada tipo de estudio, así como aquellos que no abordaban la pregunta de investigación y los objetivos establecidos para esta revisión. Además, se descartaron los artículos según su tipología como opiniones, editoriales, cartas al director o editor, con el fin de garantizar la selección de estudios

que proporcionaran evidencia sólida y relevante para el análisis.

Estrategias de Búsqueda

La búsqueda se llevó a cabo en las bases de datos: PubMed, ScienceDirect y SciELO, utilizando las palabras clave MESH "Health Technology" y "Nursing Care", así como términos de descriptores de la BIREME para maximizar la exhaustividad de la búsqueda (Cuadro 1).

El proceso de búsqueda se llevó a cabo entre los meses de febrero y abril de 2024, se aplicó estrategias de búsqueda según las bases de datos.

Se llevó a cabo una búsqueda exhaustiva de literatura donde se publica evidencia científica relevante sobre el tema. Además, se exploraron otras fuentes, incluyendo el uso de la ecuación de búsqueda en Google Académico. Este enfoque amplio permitió obtener una variedad de resultados, con un total de 2 hallazgos relevantes.

La información recopilada se sometió a un análisis utilizando la herramienta Rayyan. Esta plataforma facilitó la revisión y clasificación de los artículos seleccionados. Se incluyeron artículos publicados desde 2016 hasta 2023 para asegurar que los datos recopilados sean actuales y relevantes.

Cuadro 1. Bases de datos y algoritmos utilizados

Base de datos	Ecuación de búsqueda	Resultados
PubMed	("biomedical technology"[All Fields]) AND ("nursing care"[All Fields])	19
Science Direct	biomedical technology AND nursing care	181
SciELO	(biomedical technology) AND (nursing care)	38
OTRAS FUENTES	Google Académico	2

RESULTADOS

Una vez eliminadas las referencias duplicadas, se procedió con el tamizaje de los registros mediante la lectura de títulos y resumen, donde se aplicaron criterios de inclusión (Cuadro 2) y se definieron referencias para lectura completa, a los cuales se les aplican criterios de exclusión y se eligieron los registros que hacen parte de la revisión (Cuadro 3) (Figura 1).

Se identificaron tres tipos de estudios principales: cualitativos, cuantitativos y mixtos, obteniendo un total de 22 estudios cualitativos, 7 estudios cuantitativos y 3 estudios mixtos, para un total de 32 artículos, lo que proporcionará una amplia gama de perspectivas para abordar el tema de investigación. A su vez, se examinarán los hallazgos de cada estudio para identificar patrones, tendencias y relaciones significativas entre la tecnología de la salud y el cuidado de enfermería. Este enfoque metodológico riguroso garantiza la integridad y validez de los resultados obtenidos, permitiendo una comprensión integral de la interacción entre la tecnología y la práctica de enfermería. La información de los artículos fue extraída por un revisor de manera independiente, utilizando una tabla de extracción de datos que contiene las variables: autor, año del estudio, país, continente, idioma, población tipo de estudio, instrumento utilizado.

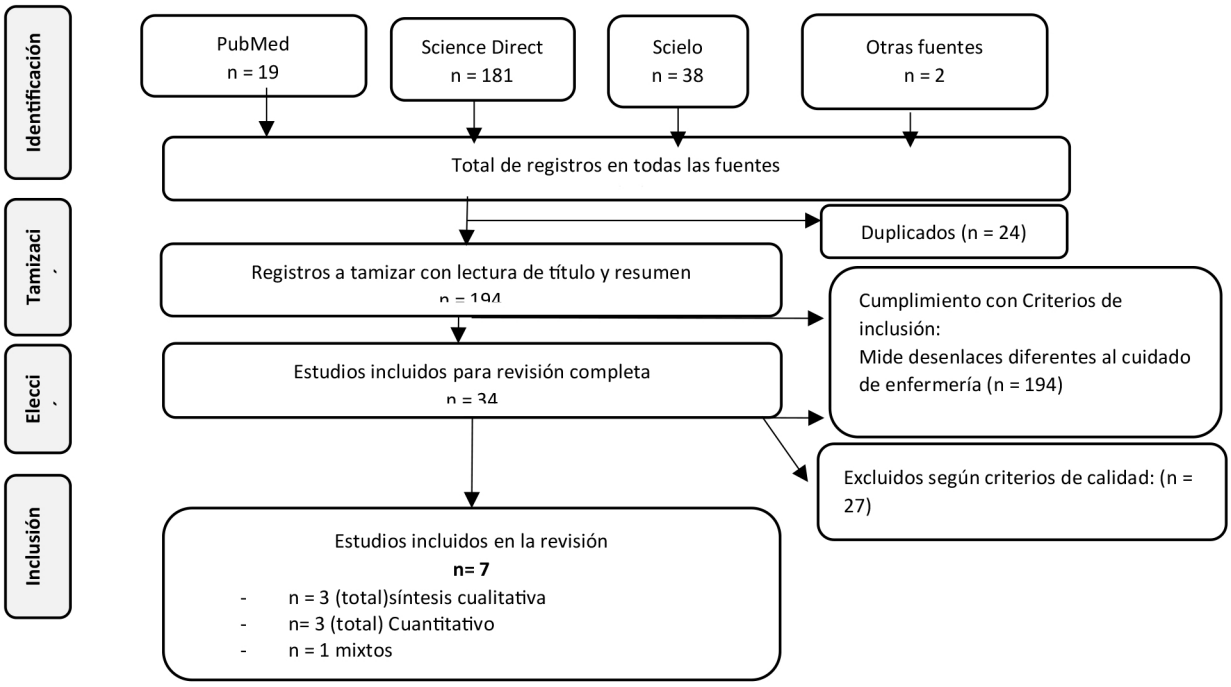


Figura 1. Flujograma de proceso de búsqueda de artículos.

El Cuadro 2 ofrece una visión integral de las distintas tecnologías utilizadas en el ámbito del cuidado de enfermería, destacando la diversidad y especificidad de cada una. Las tecnologías se clasifican en varias categorías, como tecnologías de producto, monitorización, gestión operativa, aplicaciones móviles y más. Cada categoría se desglosa en tipos específicos de tecnología con ejemplos concretos que ilustran su aplicación en el entorno clínico. En resumen, el Cuadro 2 refleja cómo la integración de diversas TS no solo incrementa la eficiencia y precisión de las intervenciones clínicas, sino que además contribuye a un entorno de atención más seguro y centrado en el paciente.

El análisis del Cuadro 3 revela el impacto significativo que tiene la implementación de tecnologías en los resultados clínicos dentro del cuidado de enfermería. Cada tecnología está asociada a mejoras específicas en la atención al paciente, lo que lleva a una reducción en la morbilidad y hospitalizaciones. Asimismo, se destaca los desafíos que acompañan el uso de estas tecnologías, como la necesidad de un mantenimiento constante de los equipos, la capacitación continua del personal, y las medidas para proteger la privacidad y seguridad de la información médica. En conclusión, el Cuadro 3 subraya cómo las tecnologías pueden transformar el cuidado de enfermería al mejorar los resultados de salud, pero también enfatiza la importancia de abordar los desafíos operacionales y de seguridad para maximizar su eficacia.

El Cuadro 4 presenta un análisis exhaustivo de la efectividad de las tecnologías en distintos entornos de atención, tales como hospitales, áreas rurales, y entornos ambulatorios. Han demostrado ser efectivas en la mejora de la calidad del cuidado de enfermería, con beneficios que van desde la reducción de la mortalidad materna hasta el mejor control de enfermedades crónicas. Además, estas tecnologías destacan por su importancia en el acceso a la atención médica en regiones remotas, lo que ha resultado en un aumento en la accesibilidad y eficiencia de los servicios. El Cuadro 4 también resalta la importancia de las referencias académicas para validar la efectividad de estas tecnologías en la práctica clínica.

Cuadro 2. Identificación de los tipos específicos de tecnología en el cuidado de enfermería.

Categoría de Tecnología	Tipo de Tecnología	Descripción	Ejemplos	Uso Principal
Tecnologías de Producto	Dispositivos de Recolección (DR)	Medir y cuantificar la pérdida de sangre durante y después del parto.	-Saco recolector plástico transparente (recolector de sangre)	-Monitoreo de la pérdida de sangre para prevenir y controlar la hemorragia posparto.
Tecnologías de Monitorización	Monitorización Remota de Pacientes (MRP)	Recolección y envió de datos biométricos, como constantes vitales y control de glucosa, a un centro remoto para su análisis.	Teleasistencia domiciliaria,	-Monitoreo continuo de pacientes en su hogar para gestionar su salud de forma remota.
Registros Electrónicos	Historia clínica electrónica (HE)	Almacenamiento, gestión y acceso a la información de salud de los pacientes.	Historia clínica de pacientes	-Sistema digital de almacenamiento y acceso a la información médica .
Tecnología de Comunicación	Telesalud y Teleconsulta (TE-TC)	Uso de telecomunicaciones para proveer atención médica a distancia.	-Videollamadas, -teleconsultas -programas de mensajería electrónica	-Facilitar el acceso a consultas médicas sin la necesidad de visitas presenciales.
Aplicaciones de Salud	Aplicaciones móviles (AM)	Diseñado para el seguimiento y cuidado de bebés y madres	Aplicación (Baby Tracker, UW Baby)	-Monitoreo de lactancia -Registro de datos de recién nacido (peso, vacunas, temperatura, medicamento…)
Aplicaciones de Salud	Aplicaciones móviles (AM)	Permite hacer registros, y monitorio de la salud posparto.	LactApp+, FitMama Lite 5 Minute Workouts	-Monitoreo de estado salud. -Monitoreo recuperación posparto.
Tecnología de sensores	Sensores inerciales adheridos a la ropa (SEN)	-Descripción de la postura del paciente -Orientación de las zonas del cuerpo con precisión y de forma no invasiva -Calcula prioridad de los cambios posturales	Tactigon ONE acelerómetros Giroscopios	-Monitorear los cambios posturales en la cama para la prevención de UPP.
Gestión de Enfermería	Tecnología de Gestión Operativa en Enfermería (TG)	- Mejora del desempeño organizacional, apoyo en la toma de decisiones clínicas, planificación, y administración en servicio de enfermería	Modelo explicativo de matriz de gestión operativa Lista verificación (checklist)	- Supervisión y evaluación de la gestión de la sistematización de la atención de enfermería en los servicios.
Aplicaciones de salud	Aplicación móvil (AM)	- Ofrecer apoyo en el proceso de atención de enfermería para mujeres que han experimentado violencia sexual.	“CuidarTech EnfporElas”	Brindar apoyo al proceso de atención de enfermería y a la toma de decisiones clínicas en situaciones de violencia sexual.
Tecnología educativa -Gammificación	Gerontología (G)	-Uso de juegos de mesa como herramienta de cuidado gerontológico en el contexto de la atención de enfermería	Diseñado para personas mayores	-Interacción social y el bienestar cognitivo de personas mayores en el cuidado de enfermería

Cuadro 3. Resultados de salud relacionados con el uso de tecnologías en el cuidado de enfermería.

Tipo de Tecnología	Resultado Clínico	Impacto General	Medición de Resultados	Observaciones
Monitorización Remota de Pacientes (MRP)	-Mejora en la precisión de la medición de la pérdida de sangre -Identificación tempra-na de intervenciones.	-Reducción de la morbilidad materna mediante la detección temprana de la (HPP)	-Cantidad de sangre recolectada y comparada con la evaluación visual; tasas de intervención para la hemorragia posparto.	-Requiere constante mantenimiento
Historia clínica electrónica (HE)	-Mejora en la identifi-cación temprana de complicaciones -Reducción de hospita-lizaciones	-Disminución en la tasa de reingresos hospitalarios y en los costos de atención médica.	-Reducción de Tasa de complicaciones y de hospitalizaciones, adherencia al moni-toreo remoto.	-Requiere conecti-vidad y un buen soporte técnico para evitar fallos en la transmisión de datos
Telesalud y Teleconsulta (TE-TC)	-Acceso rápido a la información médica del paciente -Mejora coordinación entre equipos de salud.	-Incremento en la excelencia y efectividad de la atención brindada a los pacientes. -Reducción de errores médicos - Optimización de los procesos y recursos para un funcionamiento más eficaz del sistema de salud.	-Tasa de errores médicos -Tiempo de acceso a la información -Satisfacción del personal médico.	-Capacitaciones constantes -Riesgos asociados con la seguridad y privacidad de la información.
Aplicaciones móviles (AM)	-Facilita el acceso a cuidados médicos a distancia -Manteniendo la calidad del cuidado.	-Aumento en el acceso a servicios de salud, en áreas rurales -Reducción en los tiempos de espera para consultas.	-Cantidad de datos biométricos monitoreados -Reducción en la tasa de hospitalización	-Regulaciones para el manejo de datos sensibles recolectados.
Aplicaciones móviles (AM)	-Mejora en el seguimiento de la lactancia y cuidados del RN	-Reducción en la tasa de consultas innecesarias -Mejora en la adherencia al cuidado	-Tasa de uso de la app -Reducción de visitas médicas	-Compatibilidad de la aplicación con diferentes dispositivos
Sensores inerciales adheridos a la ropa (SEN)	-Detección temprana de posibles complicaciones posparto	-Mejora en la detección temprana -Reducción de complicaciones	-Tasa de detección de complicaciones -Satisfacción del paciente	-Capacitaciones continuas
Tecnología de Gestión Operativa en Enfermería (TG)	-Mejora en la detención temprana de áreas de alta presión -Permite tomar medidas preventivas para evitar la formación de UPP	-Reducción de morbilidad -Disminución del número de casos de UPP	-Gravedad y severidad de la úlcera según la clasificación de la National Pressure Injury Advisory Panel NPIAP)	-Seguimiento constante
Aplicación móvil (AM)	-Mejora en los indicadores de salud y desempeño organizacional	-Apoya la toma de decisiones clínicas -Mejora la planificación y administración de servicios de enfermería	- Uso de matrices de gestión -Listas de verificación para el monitoreo de la implementación del SNC.	-Limita el sesgo de medición -favorece la visibi-lidad y gobernabilidad del personal de enfermería.
Gerontología (G)	-Orienta la asistencia a mujeres en situación de violencia sexual a través del proceso de enfermería.	-Brindar atención sistemática y calificada -Facilitar la documentación, comu-nicación y la toma de decisiones en el cuidado	-Tasa de uso de la app	-Requiere de confidencialidad -Seguridad para proteger la privacidad
Monitorización Remota de Pacientes (MRP)	-Promover el envejeci-miento activo y saludable	-Promueve la interacción entre los adultos mayores fomentando el pensamiento creativo	-Tasa de uso de la app	-Entendimiento de la app debe ser fácil -Usar sin requerir habilidades tecnoló-gicas avanzadas

Cuadro 4. Evidencia sobre la efectividad de la tecnología en el cuidado de enfermería según el entorno de atención.

Entorno de Atención	Tipo de Tecnología	Evidencia de Efectividad	Beneficios Observados
Hospitalario	Monitorización Remota de Pacientes (MRP)	-Mejora la seguridad y efectividad del tratamiento, -Disminuyendo la mortalidad materna.	-Reducción significativa en la mortalidad materna relacionada con HPP.
Hospitalario	Historia clínica electrónica (HE)	-Reducción en la tasa de reingresos hospitalarios -Mejora en la gestión de enfermedades crónicas.	-Mejora en el control de enfermedades crónicas, reducción de complicaciones y mayor adherencia al tratamiento.
Hospitalario	Telesalud y Teleconsulta (TE-TC)	-Incremento en la precisión diagnóstica y reducción de errores médicos	-Mejora en la calidad y seguridad de la atención al paciente
Áreas Rurales, Hospitales	Aplicaciones móviles (AM)	-Mejora en el acceso a la atención médica en áreas remotas.	-Aumento en la accesibilidad y eficiencia de la atención
Atención ambulatoria, seguimiento a domicilio	Aplicaciones móviles (AM)	-Mejora en el seguimiento de condiciones crónicas y de la salud materno-infantil	-Reducción de la tasa de hospitalizaciones
Hospitales, atención domiciliaria	Sensores inerciales adheridos a la ropa (SEN)	-Detección temprana de complicaciones	-Mejora en la respuesta médica
Hospitalario Geriátricos viviendas particulares	Tecnología de Gestión Operativa en Enfermería (TG)	- Reducción notable en la incidencia de úlceras por presión en pacientes que emplean sensores inerciales.	-Evita la formación de UPP
Entornos hospitalarios y clínicos	Aplicación móvil (AM)	- Avances en la organización, coordinación y realización de la atención de enfermería. -Disminución de errores clínicos.	-Incremento en la eficiencia operativa -Aumento en la satisfacción del personal y la calidad de la atención brindada
Hospitalario	Gerontología (G)	-Mejora en la atención y brindar apoyo	- Confiable y adecuada
Geriátrico	Monitorización Remota de Pacientes (MRP)	-Mejora la calidad del cuidado	-Fácil adaptabilidad

DISCUSIÓN

Con el análisis de la pesquisa se logró identificar diversas tecnologías específicas utilizadas en el cuidado de enfermería, como los dispositivos de recolección de sangre, los sistemas de monitorización remota de pacientes, los registros electrónicos de salud y las plataformas de telesalud. Estos hallazgos coinciden con lo descrito por Glasgow y col. (1) y Quille y col. (6) quienes destacan la integración de tecnologías avanzadas como los registros electrónicos para mejorar la precisión y eficiencia en la atención

al paciente (6,15-24). Ambos estudios subrayan la importancia de los registros electrónicos para optimizar la coordinación del cuidado y reducir errores médicos, resaltando así un punto de convergencia significativo entre nuestra investigación y la literatura existente (1,6). Adicionalmente, un análisis reciente también refuerza la efectividad de las tecnologías digitales, incluyendo los sistemas de monitorización y la telemedicina, en la mejora de los resultados de salud en diversos entornos de atención (5,25,26).

Por otra parte, en cuanto a los resultados de salud relacionados con el uso de tecnologías, la evidencia reveló mejoras en la precisión de las intervenciones, una reducción en la morbilidad y las hospitalizaciones, así como una mejor coordinación del cuidado gracias a la implementación tecnológica en el ámbito sanitario, lo que ha sido ampliamente promovida como una vía para mejorar la calidad del cuidado, optimizar los recursos y reducir la carga sobre los sistemas de salud. Los estudios evidencian beneficios significativos, aunque también reflejan la complejidad de estos procesos y sus desafíos contextuales. Por ejemplo, Liang y col. (27) concluyen, a partir de un metaanálisis, que los modelos de atención integrada soportados por tecnologías de la información y comunicación (TIC) mejoran significativamente la calidad de vida y reducen las re-hospitalizaciones en adultos mayores. Este hallazgo coincide con el estudio De Lathauwer y col. (28) en el que se confirma la eficacia la monitorización remota de pacientes reduce las hospitalizaciones y la mortalidad relacionadas con la IC. Entre los componentes eficaces se incluyen la autogestión, los módulos educativos y la comunicación por vídeo. Sin embargo, la heterogeneidad entre las intervenciones dificulta la evaluación global. La modernización del monitoreo con tecnologías avanzadas como sensores no invasivos, inteligencia artificial y tele-rehabilitación cardíaca podría aumentar su potencial. Con ello se refuerza el valor del monitoreo continuo y la comunicación digital en la prevención de complicaciones. En contraste, el análisis de Piroddi y col. (29) demuestra que, si bien un programa de atención integrada redujo admisiones hospitalarias y mortalidad en comunidades vulnerables en Inglaterra, los resultados fueron sensibles al contexto socioeconómico local. Este enfoque contrasta con la visión más generalizada que la tecnología *per se* mejora los resultados, subrayando la necesidad de adaptar las estrategias a las realidades comunitarias.

Asimismo, el estudio de Morciano y col. (30) aporta un enfoque comparativo entre programas nacionales, revelando que no todos los modelos de integración tecnológica generan efectos uniformes en la reducción de admisiones de urgencia. Esto evidencia que el diseño del programa, su implementación y el nivel de adopción tecnológica por los equipos clínicos son factores críticos que pueden modular los resultados esperados. Por su parte, Endalamaw y col. (31), en una revisión global sobre tecnologías aplicadas a la multimorbilidad, identificaron que las barreras técnicas, la inter-operabilidad limitada, la falta de capacitación y la resistencia institucional pueden contrarrestar los beneficios esperados. Sin embargo, cuando se integran correctamente, estas tecnologías logran intervenciones más precisas, menos eventos adversos y mejor coordinación entre niveles de atención (31).

La evidencia sugiere que la tecnología, cuando es implementada estratégicamente y con base en las necesidades contextuales, puede mejorar la precisión de las intervenciones, reducir la morbilidad y optimizar la coordinación del cuidado. No obstante, la heterogeneidad en los resultados plantea la necesidad de marcos de evaluación más sólidos, enfoques adaptativos, y una visión centrada tanto en el paciente como en la sostenibilidad del sistema. La tecnología no debe verse como una solución universal, sino como una herramienta cuyo impacto depende de su integración eficaz en procesos clínicos y sociales existentes.

Finalmente, los hallazgos evidencian que la tecnología es altamente efectiva tanto en entornos hospitalarios como en áreas rurales, mejorando significativamente la calidad del cuidado y reduciendo la mortalidad materna. Estos hallazgos son respaldados por Barrientos y col. (7), quienes reportan que la tecnología ofrece beneficios significativos al ampliar el acceso a servicios de salud en zonas remotas y optimizar la gestión de enfermedades crónicas. No obstante, también advierte que su efectividad varía considerablemente según el contexto

regional, debido a diferencias en la forma en que estas herramientas son implementadas y adaptadas. Esta observación coincide con los hallazgos del presente análisis, que evidencian una marcada variabilidad en los resultados según el entorno de atención. Así se demuestra que la tecnología es altamente efectiva para mejorar la calidad del cuidado y reducir la mortalidad materna tanto en entornos hospitalarios como rurales. En regiones remotas de Nepal, la telemedicina ha facilitado la detección temprana de riesgos obstétricos, mejorando el acceso a atención especializada (32). Estudios en países con sistemas desarrollados han mostrado que la monitorización remota en embarazos complicados es tan segura como la hospitalaria, aumentando la satisfacción y reduciendo costos (33). En el manejo de la diabetes gestacional, la telemedicina ha logrado un mejor control glucémico y reducción de complicaciones materno-fetales (34,35). En zonas de bajos recursos, programas combinados de *Telehealth* y educación han mejorado indicadores maternos y perinatales, disminuyendo la mortalidad (36). Además, las intervenciones móviles (mHealth) en países de ingresos bajos y medios aumentan la adherencia a controles prenatales y la detección precoz de riesgos, impactando positivamente en la mortalidad materna (37). Estos hallazgos resaltan la importancia de integrar la tecnología con políticas y modelos de atención centrados en el paciente para maximizar su impacto.

La evidencia reciente respalda la efectividad de la tecnología en el cuidado de enfermería, destacando su impacto positivo en distintos entornos de atención. Intervenciones telemáticas lideradas por enfermeras han demostrado ser efectivas en la reducción de la hipertensión, mejorando la gestión clínica en pacientes atendidos de forma remota (38). Además, la telerehabilitación dirigida por enfermería en pacientes con enfermedades crónicas que viven en la comunidad ha mostrado beneficios significativos en la mejora de la funcionalidad y la calidad de vida, demostrando que la atención a distancia puede ser tan eficaz como la presencial (39). Por último, los sistemas de gestión de enfermedades crónicas mediante *Telehealth* han mostrado mejoras notables en la calidad de vida física, mental y social de los pacientes, reforzando el papel de la tecnología como herramienta clave para el cuidado integral en distintos contextos (40). En conjunto, estos estudios sugieren que la integración de tecnologías digitales en el cuidado de enfermería puede optimizar resultados clínicos y de bienestar, independientemente del entorno donde se implemente.

CONCLUSIONES

La investigación sobre la efectividad de la tecnología en el cuidado de enfermería muestra que herramientas como dispositivos de recolección de datos, monitoreo remoto, registros electrónicos y telemedicina han mejorado la precisión, eficiencia y coordinación clínica, reduciendo errores y mejorando la satisfacción de pacientes y profesionales. Estas tecnologías amplían el acceso a servicios de calidad, especialmente en zonas rurales, disminuyen hospitalizaciones y facilitan un seguimiento oportuno de enfermedades crónicas mediante intervenciones rápidas y personalizadas. Sin embargo, su eficacia depende de la capacitación continua del personal, mantenimiento adecuado de equipos y protección de datos, desafíos acentuados en contextos con infraestructura limitada. Además, el impacto varía según el entorno: en hospitales mejora la eficiencia y reduce errores, mientras que en áreas rurales limita la conectividad, requiriendo adaptaciones locales. En conclusión, la tecnología es clave para optimizar la atención de enfermería, siempre que se implemente con formación, soporte técnico y adaptación al contexto, garantizando un sistema de salud accesible, eficiente y centrado en el paciente.

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ARTÍCULO DE REVISIÓN

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Guided Imagery Intervention Improves the Quality of Life in Breast Cancer Patients: A Literature Review

La intervención con imágenes guiadas mejora la calidad de vida en pacientes con cáncer de mama: Una revisión bibliográfica

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SUMMARY

Introduction: *Breast cancer is the most common malignancy affecting women. The disease and its treatment can significantly impact patients' health-related quality of life, requiring further supportive interventions. Breast cancer management includes both pharmacological and non-pharmacological approaches. Among non-pharmacological interventions, guided imagery is a nursing intervention that has been explored for its potential benefits.* **Objective:** *This study aims to identify and provide an overview of evidence-based practices related to the development and implementation of guided imagery nursing interventions to improve the health-related quality of life in breast cancer patients.* **Methods:** *A comprehensive literature search was conducted using electronic databases, including PubMed, EBSCO, ScienceDirect, ProQuest, and the Cancer Journal. The PICO (Population, Intervention, Comparison, Outcome) framework was used to formulate the search strategy, utilizing Boolean operators to refine results. The inclusion criteria included full-text research articles published within the last ten years.* **Result:** *A total of 43 articles were initially retrieved for full-text review. After screening, 33 articles were excluded due to the absence of guided imagery interventions, lack of full-text availability, or irrelevance to the study objective. Ultimately, 10 articles met the inclusion criteria and were reviewed.* **Conclusions:** *Guided imagery is a viable nursing intervention that helps alleviate symptoms and improve the health-related quality of life in breast cancer patients undergoing treatment. The findings suggest that guided imagery may serve as a supportive care strategy to improve overall well-being in this patient population.*

Keywords: *Guided imagery, breast cancer, quality of life.*

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RESUMEN

Introducción: *El cáncer de mama es la neoplasia maligna más común que afecta a las mujeres. La enfermedad y su tratamiento pueden afectar significativamente la calidad de vida relacionada con la salud de las pacientes, lo que requiere intervenciones de apoyo adicionales. El manejo del cáncer de mama incluye enfoques farmacológicos y no farmacológicos.*

Entre las intervenciones no farmacológicas, la imaginería guiada es una intervención de enfermería que se ha explorado por sus posibles beneficios. **Objetivo:** *Este estudio busca identificar y proporcionar una visión general de la práctica basada en la evidencia relacionada con el desarrollo de la implementación de intervenciones de enfermería con imaginería guiada para mejorar la calidad de vida relacionada con la salud en pacientes con cáncer de mama.* **Métodos:** *Se realizó una búsqueda bibliográfica exhaustiva utilizando bases de datos electrónicas, como PubMed, EBSCO, ScienceDirect, ProQuest, Cancer Journal. Se utilizó el marco PICO (Población, Intervención, Comparación, Resultado) para formular la estrategia de búsqueda, utilizando operadores booleanos para refinar los resultados. Los criterios de inclusión incluyeron artículos de investigación a texto completo publicados en los últimos diez años.* **Resultado:** *Se recuperaron inicialmente 43 artículos para su revisión completa. Tras la selección, se excluyeron 33 artículos debido a la ausencia de intervenciones de imaginería guiada, la falta de disponibilidad de texto completo o su irrelevancia para el objetivo del estudio. Finalmente, 10 artículos cumplieron los criterios de inclusión y fueron revisados.* **Conclusiones:** *La imaginería guiada es una intervención de enfermería viable que ayuda a aliviar los síntomas y a mejorar la calidad de vida relacionada con la salud en pacientes con cáncer de mama en tratamiento. Los hallazgos sugieren que la imaginería guiada puede servir como una estrategia de cuidados de apoyo para mejorar el bienestar general en esta población de pacientes.*

Palabras clave: *Imaginería guiada, cáncer de mama, calidad de vida.*

INTRODUCTION

Breast cancer is one of the most common malignancies in women, second only to cervical cancer, accounting for 11.7 % of the 19.3 million cancer cases worldwide, or 2 261 419 out of 19 292 789 cases (1). In Indonesia, breast cancer represents 16.6% (68 858 cases) of the total 396 914 newly diagnosed cancer cases (2). These statistics indicate that the incidence of breast cancer remains significant both globally and nationally.

The medical management of breast cancer typically involves a combination of treatment modalities, including radiation therapy, chemotherapy, surgery, or multimodal approaches. However, these treatments often have adverse effects that can negatively impact patients' health-related quality of life (3). Physical side effects include pain, fatigue, decreased muscle strength, loss of appetite, poor sleep quality, changes in body composition, and reduced daily activity levels (4,5). Psychological side effects may include anxiety, fear, depression, cognitive decline, reduced concentration, limited comprehension, and decreased sexual function (4).

Managing these side effects requires a combination of pharmacological and non-pharmacological interventions. According to World Health Organization (WHO) guidelines, pharmacological treatments are administered based on the patient's specific symptoms and complaints (6). In contrast, non-pharmacological interventions, which can be implemented independently by nurses and healthcare professionals, aim to provide a holistic approach that minimizes drug side effects and dependency (7). One such intervention is guided imagery.

Given the potential benefits of guided imagery, this article aims to conduct a literature review on the effectiveness of guided imagery interventions in improving the quality of life of breast cancer patients.

METHODS

Search strategy and selection

A systematic literature search was conducted using the following electronic databases: PubMed, EBSCO, ScienceDirect, ProQuest, Cancer Journal, and Google Scholar. The keywords used in the search strategy included: "Cancer OR Breast Cancer AND Complementary Nursing OR Guided Imagery AND Pain Reduction AND Anxiety AND Vomit AND Health-Related Quality of Life". Boolean operators were applied to refine the search results. The inclusion criteria included full-text research articles published within the last ten years. All selected references were systematically managed using Mendeley for citation and referencing purposes.

Eligibility criteria

The PICO (Population, Intervention, Comparison, Outcome) framework was used to define the eligibility criteria. The population focus of this literature review was breast cancer patients who received guided imagery interventions aimed at improving their health-related quality of life. The review was not restricted to specific healthcare settings and included both inpatient and outpatient populations.

Data extraction and reporting

The extracted data from each study included key characteristics such as study design, research objectives, population, methodology, intervention details, outcomes of guided imagery, and significant findings. These data were systematically organized and summarized in Table 1. The information was then synthesized and expanded upon in the Results section to provide a comprehensive analysis of the findings. The initial literature search yielded a total of 297 articles, distributed as follows: 98 from PubMed, 24 from EBSCO, 87 from ScienceDirect, 64 from ProQuest, and 24 from the Cancer Journal, as shown in Figure 1. After screening the abstracts for relevance and adherence to the inclusion criteria, 43 articles were selected for full-text review. Of these, 33 articles were excluded because they lacked guided imagery interventions or were not available in full text. Ultimately, 10 articles met the eligibility criteria and were included in the final review, as summarized in Table 1.

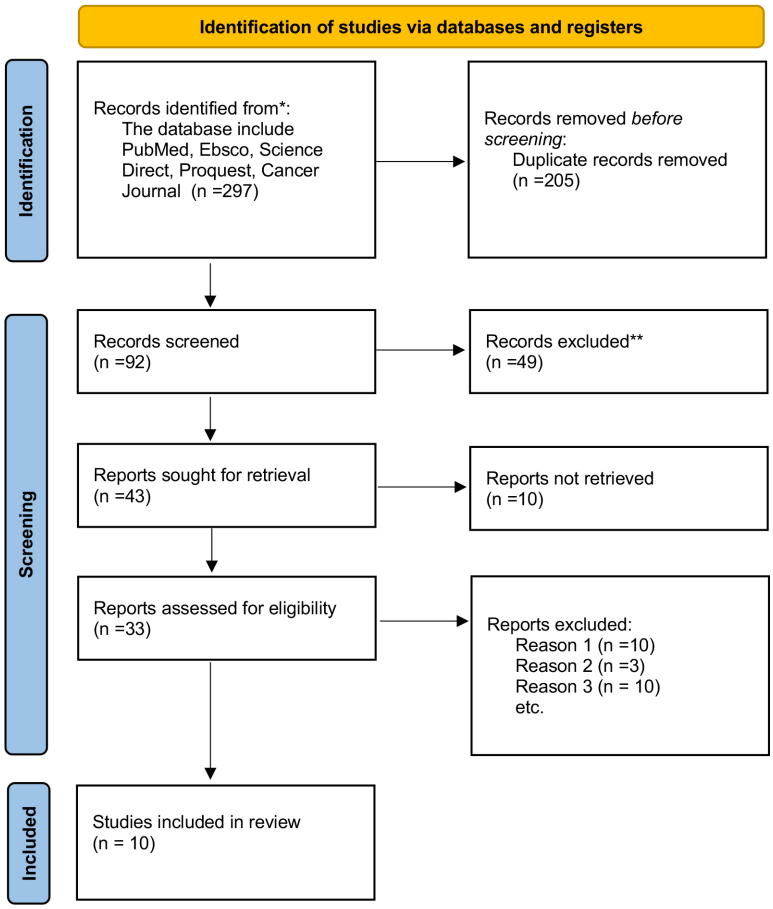


Figure 1. PRISMA Flow Diagram.

Table 1. Articles met the eligibility criteria and were included in the final review.

NO	TITLE	OBJECTIVE	METHOD	RESULTS
1	Guided Imagery Relaxation in Quality of Life of Patients Undergoing Hematopoietic Stem Cell Transplantation: A Quasi-Experiment (8)	To explore the effect of guided imagery relaxation on the quality of life of patients undergoing hematopoietic stem cell transplantation.	1. Quasi-experimental, longitudinal, and analytical study. 2. Sample: 42 participants (35 in the intervention group, 7 in the control group). 3. Instruments: a. Functional Assessment of Cancer Therapy–Bone Marrow Transplantation (FACT-BMT) b. Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-Fatigue) c. Functional Assessment of Cancer Therapy–Neutropenia (FACT-N) 4. Intervention: Guided imagery relaxation with audio accompanied by 360° nature images. 5. Duration: 10 minutes, 3 times a week.	Health-related quality of life scores increased in both groups. The study indicates that patients undergoing hematopoietic stem cell transplantation experienced significant changes in their quality of life.
2	The Effects of Guided Imagery on State and Trait Anxiety and Sleep Quality Among Patients Receiving Haemodialysis: A Randomized Controlled Trial (9)	To determine the effect of guided imagery on anxiety traits and sleep quality in haemodialysis patients.	1. Randomized controlled trial (RCT). 2. Sample: 70 participants (35 in the intervention group, 35 in the control group). 3. Instruments: Spielberger State-Trait Anxiety Inventory (STAI), Pittsburgh Sleep Quality Index (PSQI) 4. Intervention: Guided imagery using a compact disc (CD). 5. Duration: 25 minutes, 6 times a week for four consecutive weeks, performed twice daily.	Guided imagery has been shown to significantly reduce anxiety and improve sleep quality in patients undergoing haemodialysis.
3	Guided Imagery Improves Mood, Fatigue, and Quality of Life in Individuals with Multiple Sclerosis: An Exploratory Efficacy Trial of Healing Light Guided Imagery (10)	To assess the potential of Healing Light (HL) Guided Imagery in improving patient-reported quality of life.	1. Exploratory study. 2. Sample: 23 participants. 3. Instrument: Patient journal or recorded self-reports. 4. Intervention: Guided imagery facilitated through visual cues by healthcare staff. 5. Duration: Once a week for 10 weeks.	Healing Light Guided Imagery improves patient-reported physical and mental health.
4	The Effects of Guided Imagery on Comfort in Palliative Care (11)	To evaluate the effect of guided imagery on patient comfort in palliative care.	1. Pre-posttest pre-experimental one-group study. 2. Sample: 28 participants. 3. Instruments: Heart rate (HR), respiratory rate (RR), pain (VAS), and comfort (VAS); The Holistic Comfort Scale (HCQ-PT-DC). 4. Intervention: Guided imagery script accompanied by music. 5. Duration: Two sessions of 17 minutes over two days.	Guided imagery intervention increased patient comfort levels and reduced heart rate, respiratory rate, and pain in palliative care patients.
5	The Effects of Guided Imagery and Hand Massage on Well-Being and Pain in Palliative Care: Evaluation of a Pilot Study (12)	To evaluate the effects of guided imagery and hand massage on well-being and pain in palliative care patients.	1. Pre-posttest quasi-experimental one-group study. 2. Sample: 20 participants. 3. Instrument: Functional Assessment of Chronic Illness Therapy–Palliative Care (FACIT-Pal-14, 14-item version 4). 4. Intervention: Guided imagery script facilitated by a trained professional. 5. Duration: 20 minutes.	Guided imagery and hand massage interventions led to significant improvements in self-reported well-being and reductions in self-reported pain among palliative care patients.
6.	The Meaning of Integrative Guided Imagery Relaxation Therapy for Women with Breast Cancer (13)	To understand the significance of guided imagery relaxation for women with breast cancer, including how patients visualize	1. Qualitative study with a phenomenological approach. 2. Sample: 9 participants. 3. Instruments: Not specified.	Guided imagery provides meaningful therapeutic benefits, reinforcing its importance in nursing intervention

Continued in pag. 963…

…continuation Table 1. Articles met the eligibility criteria and were included in the final review.

NO	TITLE	OBJECTIVE	METHOD	RESULTS
		their cancer and immune system during guided imagery sessions, and how they feel afterward.	4. Intervention: Guided imagery using a compact disc (CD) with visualization. 5. Duration: 15 minutes.	for women with breast cancer by fostering self-reflection and emotional well-being.
7.	Feasibility and Acceptability of i-Restoring Body Image After Cancer (i-ReBIC): A Pilot Trial for Female Cancer Survivors (14)	To evaluate the feasibility, acceptability, and psychosocial outcomes of a text-based online group therapy intervention, i-ReBIC, designed to reduce body image disturbance and psychosexual dysfunction in women diagnosed and treated for breast or gynecologic cancer.	1. Face-to-face group therapy intervention study. 2. Sample: 47 participants. 3. Instruments: Quality of life instrument, The Functional Assessment of Cancer Therapy–General (FACT-G), Patient journals. 4. Intervention: Text-based guided imagery covering nine themes. 5. Duration: 90 minutes per session, once a week for 8 weeks.	The i-ReBIC intervention was well-received and effective in addressing body image issues experienced by women treated for breast and gynecologic cancer.
8.	Restoring Body Image After Cancer (ReBIC): Results of a Randomized Controlled Trial (15)	To test a group psychosocial intervention aimed at improving body image disturbance, sexual function, and quality of life in breast cancer survivors.	1. Prospective randomized controlled trial (RCT). 2. Sample: 194 participants. 3. Instruments: a. Body Image: Body Image Scale (BIS), Body Image After Breast Cancer Questionnaire (BIBCQ). b. Sexual Function: Female Sexual Function Index (FSFI). c. Quality of Life: Functional Assessment of Cancer Therapy (FACT). 4. Intervention: Text-based guided imagery. 5. Duration: 90 minutes per session, once a week for 8 weeks.	Restoring Body Image After Cancer (ReBIC), a group therapy intervention using guided imagery, effectively improves body image perception and quality of life in breast cancer survivors.
9.	Effectiveness of a Self-Care Toolkit for Surgical Breast Cancer Patients in a Military Treatment Facility (7)	To assess whether a self-care toolkit (SCT) provided to breast cancer patients undergoing surgery can reduce distress and alleviate symptoms associated with surgery.	1. Randomized controlled trial (RCT) with two non-blinded groups. 2. Sample: 100 participants (SCT: 51, TAU: 49). 3. Instruments: DVRPS Pain Scale, Visual Analog Scale (VAS) for anxiety and nausea. 4. Intervention: Guided imagery script in MP3 format, covering seven themes. 5. Duration: Varies by theme; recommended use is once per week and as often as desired, starting two weeks before surgery.	Patients using a self-care toolkit (SCT) in the perioperative period experienced reduced pain perception, fatigue, and inflammatory cytokine secretion.
10	Efektivitas Teknik Guided Imagery dalam Menurunkan Nyeri terhadap Kadar Endorfin pada Pasien Breast Cancer (The Effectiveness of Guided Imagery Techniques in Reducing Pain and Endorphin Levels in Breast Cancer Patients) (16)	To examine the effectiveness of guided imagery in reducing pain and increasing endorphin levels in breast cancer patients.	1. Quasi-experimental, non-randomized study. 2. Sample: 16 participants (10 in the intervention group, 6 in the control group). 3. Instruments: a. McGill Pain Rating Index (PRI). b. McGill Present Pain Intensity (PPI). c. Visual Analog Scale (VAS). 4. Intervention: Guided imagery script in MP3 format (15-minute duration). 5. Duration: Administered twice over two days while the patient is hospitalized.	Guided imagery intervention effectively reduces pain scores in breast cancer patients and is more effective in increasing serum endorphin levels in the treatment group.

DISCUSSION

Cancer and its treatment significantly impact patients' health-related quality of life (HRQoL) due to the associated side effects (3). These symptoms can profoundly affect various aspects of a patient's well-being, including physical, psychological, social, and spiritual dimensions (17). Pain and physical discomfort are among the most common complaints in breast cancer patients, manifesting as subjective sensory experiences (18). Pain in breast cancer, like in other malignancies, can lead to multidimensional distress, affecting psychological well-being, social interactions, spiritual beliefs, and most prominently, physical functioning (19). Other physical side effects include fatigue, weakness, reduced muscle strength, loss of appetite, sleep disturbances, and decreased daily activity levels. Psychological effects often include anxiety, fear, loss of concentration, and depression, while social consequences may involve diminished interpersonal relationships and concerns about physical appearance. The spiritual impact can include increased existential distress, a loss of meaning or purpose in life, and challenges in religious or personal beliefs (20,21).

Non-pharmacological interventions serve as complementary therapeutic options that nurses can independently implement. These interventions often include biobehavioural and cognitive-behavioural techniques, one of which is guided imagery (22,23). Guided imagery is a cost-effective complementary therapy used in healthcare systems to improve patient health promotion, function, and overall well-being (24). It has been shown to improve immune function, enhance sleep quality, and reduce adverse effects associated with cancer treatments such as chemotherapy and radiation therapy (25). Guided imagery involves the cognitive process of creating vivid mental images that engage multiple senses, influencing psychophysiological responses and promoting behavioural, perceptual, or physiological changes facilitated by a person (trained practitioner) or delivered through various media (26). Similarly, a study by Corpora et al. (12) indicated that combining guided imagery with hand massage interventions led to notable improvements in self-reported well-being and reductions in self-reported pain among palliative care patients.

Guided imagery is a cognitive technique involving deliberately structured imagination to elicit positive and pleasant effects (27). By visualizing pleasant scenarios, tense muscles can undergo relaxation due to changes in motor activity. This occurs as the stimulus of pleasant imagery is processed through the brainstem and transmitted to the sensory thalamus for further integration and processing. The stimulus is then relayed to both the amygdala and hippocampus, as well as the cerebral cortex. Within the cerebral cortex, sensory and associative processing occur. In the hippocampus, these pleasant images are encoded into memory. When an individual engages in guided imagery, previously stored positive memories can be recalled, influencing perception. The hippocampus then transmits this meaningful stimulus to the amygdala, which generates an appropriate emotional and physiological response based on the interpreted meaning (28,29).

Guided imagery interventions have been shown to reduce pain by stimulating the pituitary gland to release endorphins, which induce feelings of calm, pleasure, and happiness (30). This aligns with a study by Sulastri et al. (16), which demonstrated that guided imagery is effective in reducing pain scores in breast cancer patients and is empirically more effective in increasing serum endorphin levels in the treatment group, which demonstrated that guided imagery is effective in reducing pain scores in breast cancer patients and is empirically more effective in increasing serum endorphin levels in the treatment group. Endorphins function as excitatory neurotransmitters that activate the brain's analgesic pathways, producing effects similar to those of morphine (31). The resulting sensations of calmness, pleasure, and happiness (comfort) are associated with psychobiological interactions involving endorphins, which contribute to improved physical well-being and emotional stability. Consequently, these effects have a positive impact on patients' overall quality of life. A study by Alves da Silva et al. (32) reported improvements in health-related quality of life scores among patients undergoing hematopoietic stem cell transplantation, highlighting significant

changes in their perceived well-being. Similarly, a study by Afshar et al. (9) suggested that guided imagery significantly reduces anxiety and improves sleep quality in patients undergoing haemodialysis.

Guided imagery interventions are effective in managing pain, anxiety, reduced sleep quality, and other side effects associated with cancer treatment. Studies indicate that listening to guided imagery for 10-30 minutes daily can significantly alleviate pain, anxiety, depression, nausea, loss of appetite, and other treatment-related adverse effects. Cancer and its treatments profoundly impact patients' mental health and psychological well-being, often leading to symptoms such as insomnia, nausea, decreased appetite, and neuropathy. Guided imagery aids in symptom management by redirecting patients' attention away from their illness, treatment side effects, and distressing emotions, instead encouraging a focus on calming and pleasant mental imagery (7,9,10,12).

CONCLUSION

Guided imagery is a biobehavioural therapy used as a nursing intervention to alleviate complaints experienced by breast cancer patients due to the disease and its treatment. By integrating guided imagery into patient care, it can contribute to improving health-related quality of life. As a mind-body intervention, guided imagery is recognized as a complementary and alternative therapy within the healthcare field. Its application as a non-pharmacological approach offers an alternative option for nursing interventions aimed at improving the well-being of cancer patients undergoing treatment.

Conflict of interest

All authors declare that there are no conflicts of interest in connection with the publication of this article.

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Management of soft tissues in post-extraction dental implant with connective tissue graft. Case report

Manejo de tejidos blandos en implante dental pos-extracción con injerto de tejido conectivo. Informe de un caso

Enrique Nuñez[1], Suani Torres-Tom[4], Brian Espinosa-Segira[2], Antonio Diaz-Caballero[3]

SUMMARY

Dental implants are a crucial component of dentistry, and the protocols for their use are continually evolving. One crucial aspect of success is the relationship between the implant and the surrounding tissue. Grafting procedures have shown potential benefits, although limited evidence is available. This article presents a 30-year-old patient who had to undergo exodontia due to failed internal tooth bleaching that caused internal radicular resorption. Patient's soft tissues were managed with connective tissue grafting, and a dental implant was successfully placed. Tissue grafts during immediate post-extraction implant placement are deemed effective and esthetically favorable, supporting their incorporation into clinical practice.

Keyword: *Surgery, dental implant, periodontics, aesthetics, graft.*

RESUMEN

Los implantes dentales son una parte importante de la odontología, y los protocolos para su uso mejoran constantemente. Un aspecto crucial para el éxito es la relación entre el implante y el tejido circundante. Los procedimientos de injerto han mostrado beneficios potenciales, aunque la evidencia disponible es limitada. Este artículo presenta a una paciente de 30 años que tuvo que someterse a una exodoncia debido a un blanqueamiento dental interno fallido que causó una reabsorción radicular interna. Los tejidos blandos de la paciente se trataron con injertos de tejido conjuntivo, y se colocó con éxito un implante dental. Los injertos de tejido durante la colocación de implantes pos-extracción inmediata se consideran eficaces y estéticamente favorables, lo que respalda su incorporación a la práctica clínica.

Palabras clave: *Cirugía, implante dental, periodoncia, estética, injerto.*

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INTRODUCTION

Dental implants function as a medical device in relation to the lower jaw, often facilitating the phenomenon of osseointegration, which provides optimal fixation to withstand masticatory and occlusal forces, and promotes patient rehabilitation in both functional and aesthetic aspects. The use of implants in the oral cavity is determined by the specific conditions present in each patient, such as restoring a dental organ or serving as a pillar for supporting two or more teeth in the mouth (1).

Among the first standard protocols dictated for dental implant placement, the importance of site healing after extraction was highlighted, followed by osteotomy and subsequent implant placement, designed to ensure maximum bone-implant contact by adapting the work site to the implant to be placed. The final protocols in the 1970s and 1980s advocated for dental implant placement exclusively in completely healed edentulous ridges. A 6 to 12-month healing period was also recommended before loading (2,3).

Currently, four different protocols for implant placement in the extraction socket are highlighted. Type 1 refers to immediate placement after tooth extraction, type 2 is considered when implants are placed after 4 to 8 weeks, achieving complete soft tissue coverage, type 3 consists of implants placed after 12 to 16 weeks when substantial clinical and/or radiographic bone fill has occurred, and type 4 refers to implants placed in healed sites (3).

The new balance established between the patient's needs and rehabilitation tilts the scale in such a way that dentists must investigate and use these new treatment techniques regarding dental implants. Among these is post-extraction implant placement, where the marked difference from original postulates is the absence of the extraction socket healing period, changing the original idea of alveolar remodeling for the implant by using irregular conditions for implant placement. Fortunately, in addition to innovation in implant placement techniques, research on new implant surface methods, implant designs, and biomaterials that aid the healing and fixation process reduces operative times, ensuring the success of these new techniques. Clinical data demonstrate that immediate post-extraction implants can undergo osseointegration, but the biomechanical mechanisms responsible for this success are not entirely clear (2,3).

In literature, the relationship between the wall space and the alveolus is a determining factor in ensuring implant success. If this peri-implant space is ≤ 2 mm, bone growth occurs naturally, and therefore, no regenerative bone material is required. However, if this space exceeds 2 mm, the use of regenerative material with or without a resorbable membrane is recommended to ensure better implant stability. Plastic periodontal procedures have been used to establish functional and biological stability around teeth and implants, such as the use of subepithelial connective tissue graft (SCTG). Additionally, various studies have associated this technique with the relief of soft tissue recession and marginal bone loss when used in immediate implant placement. However, there is a lack of clear evidence regarding the clinical and aesthetic benefits of simultaneous soft tissue augmentation around immediate or delayed dental implant placement using SCTG (4-6).

This report aims to demonstrate the clinical management of a post-extraction implant by outlining the surgical protocol used, which involves a subepithelial connective tissue graft (SCTG).

CLINICAL CASE

A 30-year-old female patient attends a dental consultation reporting pain in an anterior tooth. The patient mentions having undergone an internal dental whitening procedure, but upon the procedure's failure, internal root resorption was subsequently observed (Figure 1, A trough C). Upon evaluating and investigating her medical history, it is noted that the patient does not have any systemic diseases or clinically significant conditions.

Informed consent was obtained from the patient. An extraction was performed as atraumatically as possible to preserve the integrity of both hard and soft tissues. The patient's natural tooth crown was used to create an immediate provisional restoration. Subsequently, an exhaustive curettage of the socket was performed to remove ligament remnants and any remaining fibers. A computer-guided surgery was performed

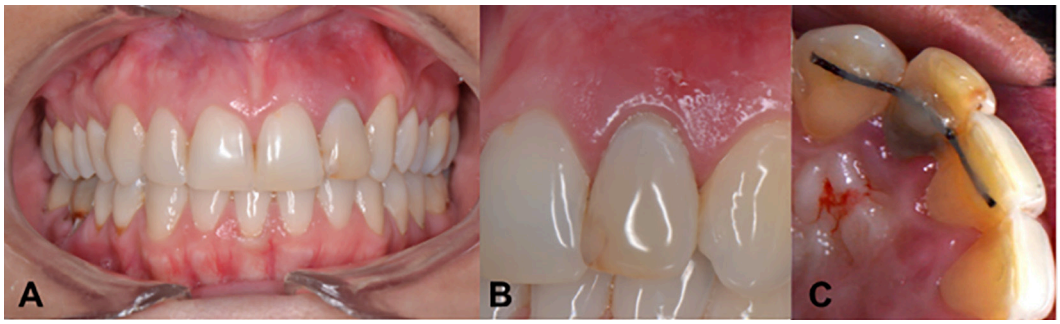


Figure 1. **A.** Initial aspect of the patient's condition. **B.** Detailed view of the periodontal phenotype of the area to be intervened. **C.** Splinting of the fractured tooth with a Maryland-type structure

since the space in this lateral area is very tight. The Implant Station software was used to plan the case to operate through the precise Galimplant 3D system. A Galimplant 4x12 implant was placed, filling the gap with Apatoss (osteobiol). At the exact moment, a 3mm straight aesthetic transepithelial was placed, taking into account that this transepithelial will create the subcritical zone of the implant crown. The transepithelial was fixed at 35N. Additionally, we placed an immediate loading abutment (Figure 2, A through D).

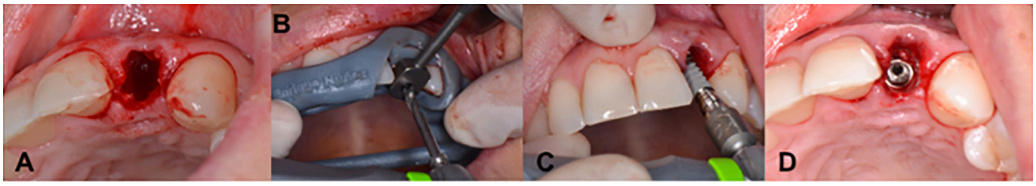


Figure 2. **A.** Post-extraction socket with closed method, attempting to preserve the maximum amount of bone and gingival tissue. **B.** Restrictive surgical guide in position during the drilling protocol and palatal approach. **C.** Implant placement. **D.** Implant placed, a wide space or gap is observed on the buccal side.

Subsequently, a detachment of the area was performed to prepare the bed that will receive the connective graft taken from the palatal area using a U-envelope technique, in order to suture the area after obtaining the graft. We place the graft in the most coronal area possible to provide stability and aesthetics through tunnelization (Figure 3, A through D).

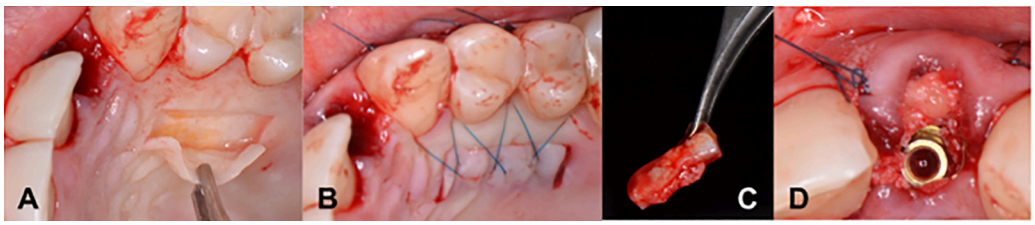


Figure 3. **A.** Connective tissue harvesting from the palate in the premolar area, with a window technique to avoid the epithelium. **B.** The donor site is sutured with 5-0 nylon. **C.** Connective tissue before placement in the gap area. **D.** Tunneling technique to position the graft in the desired location using sutures.

We adapted the patient's crown to serve as a provisional restoration, carefully polishing the area that will form the critical profile. The provisional crown, previously made to match the patient's crown, was placed and tightened onto the transepithelial area at 25 N. We remove the suture at 2 weeks and take impressions for the definitive crown at 4 months (Figure 4, A through D).

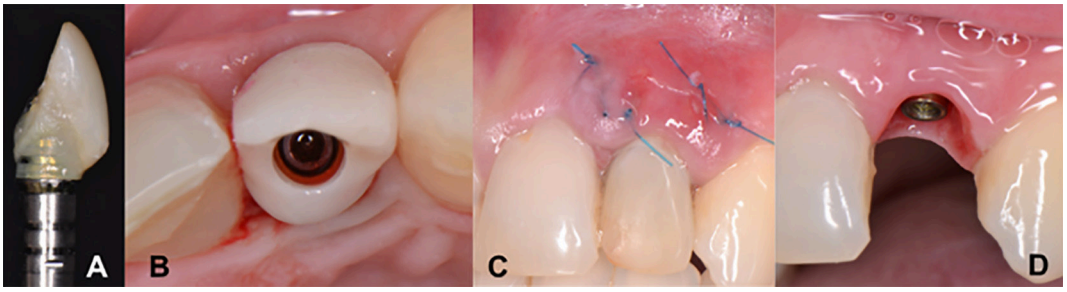


Figure 4. **A.** Crown integrated with the implant abutment to perform immediate loading. **B.** The coronal aspect of the crown is screwed to the abutment to initiate healing. **C.** Healing appearance at 10 days post-operation. **D.** healing conditions with maintenance of papillary height.

The emergence profile was replicated as it has been maintained. Once the provisional crown has fulfilled its function, it is dismounted and fixed to an implant analog. This entire structure was introduced into a heavy silicone ball and set. After setting it up, the provisional crown was removed, leaving the analog in the silicone ball. A transfer impression was placed on this analog, and the GAP left by the impression of the provisional crown on the silicone was filled with flowable composite. Upon polymerization, the transfer was removed from the silicone, yielding a personalized transfer that replicates the achieved emergence profile. It was placed in the mouth in the correct position, and both a heavy and a light silicone impression were taken. The laboratory sent a crown mockup for in-mouth adjustment. It was tried on, and after making the pertinent modifications, it was sent back to the laboratory to finish the crown, which was placed and fixed at 25 N onto the transepithelial (Figures 5.1 and 5.2).

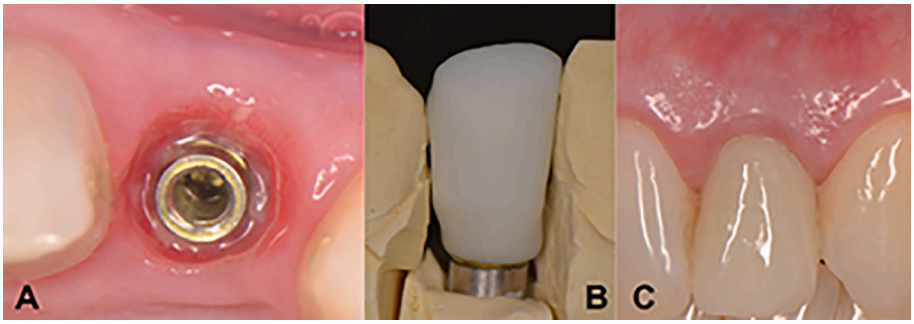


Figure 5.1. **A.** Appearance of peri-implant tissue maturation, maintaining a natural look. **B.** Laboratory handling of the definitive crown. **C.** Healing appearance with the crown already in position, after several months of healing.



Figure 5.2. Healing appearance with the crown already in position, after several months of healing.

DISCUSSION

The subepithelial connective tissue graft (SCTG) is a procedure that involves harvesting a portion of connective tissue from the hard palate or tuberosity region to thicken the peri-implant tissue and increase the amount of keratinized tissue. The connective tissue graft for covering implants affected by peri-implantitis is also favorable, with more favorable peri-implant health (including gain of keratinized mucosa, improved bleeding indices, and higher marginal bone levels) and aesthetic improvement. Among the results of various studies focused on this technique, many agree on the aesthetic results and its good management for alleviating soft tissue recession and marginal bone loss, especially in immediate post-extraction implants. The low percentage reported in healing problems and donor area necrosis is not excluded (4,7).

De Angelis et al. (8), indicate through a meta-analysis that the use of SCTG guarantees a statistically significant increase in the stability of the mean buccal marginal level, showing greater thickness and a better result in stability and aesthetics in periodontal plastic procedures related to dental implants, especially in thin periodontal phenotypes where achieving a high aesthetic result after an invasive procedure is complicated. This is where surgical and postoperative complications come into consideration. In the same research, the author highlights that complications such as bleeding, swelling, graft necrosis, and patient morbidity are factors to consider. However, proposals such as using a xenogenic collagen matrix (XCM) as a viable solution to avoid the aforementioned complications lack scientific support when comparing results, as they are unable to make a risk-benefit comparison of these two techniques due to a lack of evidence (8).

It has been demonstrated that immediate post-extraction implants yield favorable results in the osseointegration process and the resulting aesthetics, even when discussing immediate provisionalization. Groenendijk et al. (9) analyzed the aesthetic outcome one year after, in a prospective multicenter series of consecutive cases, in 100 patients undergoing immediate post-extraction implant placement and immediate provisionalization. Using the Chi-Square test, the overall changes in aesthetic scores between various points in time were examined using a mixed model with a random intercept for treatment center. They determined that throughout the year of study, 93 % of participants fell within the satisfied and acceptable range for the aesthetic result obtained, indicating that a high aesthetic outcome was achieved (9).

Regarding the aesthetic results that can be achieved by combining immediate post-dental organ extraction implant placement and SCTG use, there is a disparity in understanding whether this technique, characterized by increasing thickness in periodontally related procedures, manages an aesthetic margin that is comfortable for the patient and makes them feel satisfied with the results. De Angelis et al. (10) demonstrated in another investigation that patients reported high levels of satisfaction regarding aesthetic results in immediate implant placement procedures with provisionalization and SCTG use. It also records a reduction in operative time for patients who did not undergo soft tissue augmentation, while resorting to XCM resulted in an easier and faster solution than subepithelial connective tissue grafting.

CONCLUSION

Based on the evidence, the authors of this report agree that the use of SCTG in immediate

post-extraction implant placement and immediate provisionalization is adequate and effective, provided that the healthcare professional has optimal management of the subject and is familiar with the anatomical relationships and potential surgical complications. The cost-benefit ratio, as evidenced in the literature and studies, promotes this practice based on the success of its results and the aesthetic benefits obtained after communicating and explaining such information to the patient. In the present case, healing was achieved without any inconvenience, both at the donor site and in the final result after patient rehabilitation, yielding a favorable and expected aesthetic outcome.

Conflict of Interest Statement: No conflicts to declare.

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Linfoma de células grandes anaplásicas asociado a prótesis mamarias, a propósito del primer caso diagnosticado en Venezuela. Propuesta para la evaluación de las muestras

Anaplastic large cell lymphoma associated with mammary prostheses, relating to the first case diagnosed in Venezuela. Proposal for the evaluation of the samples

Enrique Santiago López-Loyo

RESUMEN

El linfoma de células grandes anaplásicas asociado a prótesis mamarias (LCGA-APM) es un tipo de linfoma no Hodgkin, considerado una rara entidad descrita inicialmente en 1977, que se caracteriza por expresar siempre el anticuerpo CD30 con negatividad para el anticuerpo ALK. Presentamos el primer caso de LCGA-APM diagnosticado en Venezuela, a partir del estudio de muestras de una paciente de 38 años, portadora de implantes mamarios texturizados de 320 mL, sometida a capsulectomía bilateral, mostrando las evidencias morfológicas con evaluación citológica, del bloque celular, de la biopsia y con la determinación de su patrón de inmunofenotipo, con hallazgos de la neoplasia en la muestra de cápsula periprotésica izquierda. Este trabajo evalúa la evolución de los procedimientos de diagnóstico y tratamiento de esta entidad relacionada con procesos irritativos locales y el uso de prótesis texturizadas, y se presenta una propuesta para el manejo histocitológico de los especímenes de líquido y cápsulas periprotésicas adaptada a nuestro medio con muchas limitaciones de recursos. Dado el aumento de la colocación de prótesis mamarias, esta neoplasia ha adquirido una importancia significativa en la valoración del seguimiento de las pacientes que han sido sometidas a estos procedimientos. La metaplasia sinovial es el hallazgo histopatológico clave en esta entidad, ya que genera la secreción líquida responsable del seroma, previa colonización bacteriana. El caso que presentamos tiene el valor de ser el primero que se tiene registro de que fue diagnosticado en el país, sabiendo que Venezuela tiene alta incidencia de procedimientos protésicos, con predominio de la utilización de implantes mamarios, en medio de un culto a la belleza que ha caracterizado a nuestra sociedad, sobre todo en las últimas cuatro décadas. Por lo tanto, la identificación de este tipo de patologías tiene importancia en el seguimiento de los problemas de salud pública, aun con su baja morbimortalidad, porque además es una alerta a los equipos médicos en las especialidades de patología, oncología y cirugía plástica, estética y reconstructiva.

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Palabras clave: *Linfoma de células grandes anaplásicas, cápsula periprotésica, mama, metaplasia sinovial.*

SUMMARY

Anaplastic large cell lymphoma associated with breast prostheses (ALCL-APM) is a type of non-Hodgkin lymphoma, considered a rare entity initially described in 1977, which is characterized by always expressing the CD30 antibody with negativity for the ALK antibody. We present the first case of LCGA-APM diagnosed in Venezuela, based on the study of samples from a 38-year-old patient, carrier of 320 mL textured breast implants, who underwent bilateral capsulectomy, showing morphological evidence with cytological evaluation of the cell block, from the biopsy and with the determination of its immunophenotype pattern, with findings of the neoplasia in the left periprosthetic capsule sample. This work evaluates the evolution of diagnostic and treatment procedures for this entity, focusing on local irritative processes and the use of textured prostheses. It presents a proposal for adapting histocytological management of fluid specimens and periprosthetic capsules to our environment, which faces numerous resource limitations. Given the increase in the placement of breast prostheses, this neoplasia has acquired significant importance in the follow-up assessment of patients who have undergone these procedures. Synovial metaplasia is the key histopathological finding in this entity, since it generates the liquid secretion responsible for the seroma, after bacterial colonization. The case we present has the value of being the first on record that was diagnosed in the country, knowing that Venezuela has a high incidence of prosthetic procedures, with a predominance of the use of breast implants, in the midst of a cult of beauty that has characterized our society, especially in the last four decades. Therefore, identifying this type of pathology is crucial for monitoring public health problems, even with its relatively low morbidity and mortality, as it also alerts medical equipment specialists in pathology, oncology, and plastic, aesthetic, and reconstructive surgery.

Keywords: *Anaplastic large cell lymphoma, periprosthetic capsule, breast, sinovial metaplasia.*

INTRODUCCIÓN

La relación entre linfomas e implantes mamarios se describió en 1995 por Duvic y col. (1). Se publicaron tres casos de linfomas cutáneos de células T que se originaron coincidentemente en mujeres portadoras de implantes protésicos mamarios. En uno de estos casos el linfoma hizo remisión una vez fue retirado el implante, con curación de la infección cutánea estafilocócica crónica en la piel de la mama intervenida, también se utilizó la terapia con interferón alfa y el procedimiento de fotoforesis extracorpórea, el cual es un protocolo terapéutico fundamentado en el efecto biológico del psoraleno y la luz ultravioleta A, sobre las células mononucleares recogidas mediante aféresis y reinfundidas posteriormente al paciente. Otra de las pacientes tenía enfermedad progresiva de linfoma. Esta publicación estableció que los linfomas de células T podrían ocurrir asociados con implantes mamarios en mujeres jóvenes; sin embargo, no estaba clara la etiopatogenia que pudiese explicar este fenómeno (1).

El linfoma de células grandes anaplásicas asociado a prótesis mamarias (LCGA-APM) es un tipo de linfoma no Hodgkin considerado como una rara entidad clínico-patológica que fue descrita inicialmente en 1977, sin identificar una asociación con procedimientos de cirugía estética. Se caracteriza por expresar siempre el anticuerpo CD30 con negatividad para el anticuerpo ALK, el cual es la denominación para designar el gen del receptor de la tirosina quinasa del linfoma anaplásico, que al estar activo actúa generando un mecanismo de bloqueo. El primer caso se describió en una paciente de 41 años con una masa incluida en la cápsula de una prótesis colocada con propósitos estéticos.

Un informe inicial daba cuenta de la comunicación de más de 500 casos en 23 países, siendo la mayor serie una publicación de 173 casos recogidos de la literatura mundial en la que todas las pacientes presentaron implantes mamarios texturizados. Más recientemente, la Sociedad Estadounidense de Cirujanos Plásticos (ASPS) ha establecido una red global para compartir casos de linfomas asociados a implantes mamarios y, para el primero de abril de 2024, reconoció aproximadamente 1 358 casos de esta patología en todo el mundo (2-4).

Este linfoma es también considerado una entidad provisional reconocida en la revisión de 2017 de la Clasificación de tumores de tejidos hematopoyéticos y linfoides de la Organización

Mundial de la Salud, con un característico crecimiento y con morfología e inmunofenotipo similar al linfoma anaplásico llamado cinasa negativa, también de células grandes; pero con una presentación y significación pronóstica única. Aunque generalmente sigue un curso clínico indolente, este linfoma anaplásico de células grandes asociado con implantes mamarios tiene el potencial de formar una masa e invadir localmente a través de la cápsula hacia el parénquima mamario o el tejido blando y/o diseminarse a los ganglios linfáticos regionales. En la mayoría de los casos, una resección quirúrgica con una capsulectomía completa donde se extraiga toda la lesión morfológicamente detectada como expresión de la enfermedad, sin aplicación de quimioterapia, se considera curativa y confiere una excelente supervivencia libre de recidivas o recurrencias locales (5).

Dentro de sus antecedentes se consideró el punto de partida en la infección crónica de la biopelícula o *biofilm* de los implantes mamarios como un detonante que potencia significativamente la contractura capsular y que fisiopatológicamente promueve la proliferación hiperplásica de las células T. Las biopelículas son colonias microbianas localizadas en la superficie, adheridas a la matriz extracelular autosecretada. Una propiedad importante del *biofilm* es el aumento de la resistencia a la fagocitosis y a los antisépticos, lo que, en un contexto clínico, conduce a la resistencia a los mecanismos de defensa del huésped y a los antimicrobianos. En consecuencia, la biopelícula bacteriana puede estimular crónicamente el sistema inmunológico del huésped y su proceso inflamatorio secundario (6).

La observación de metaplasia sinovial en la zona de contacto de las prótesis con el tejido circundante sugiere que la funcionalidad que provee una "corredera de deslizamiento" también produce una secreción de líquido "tipo sinovial" que sirve de base para la generación de los seromas al producirse la colonización de agentes microbianos. Esto se comprobó en un estudio publicado por Hu y col. (7) en cerdos y humanos. En los cerdos se insertaron 12 implantes texturizados y 12 lisos en tres cerdos adultos. Este material implantado se mantuvo *in situ* durante un período medio de 8,75 meses. Para un ensayo prospectivo en humanos, se evaluaron 57 cápsulas de pacientes con contractura de grado IV de Baker durante un período de 4 años. En ambos casos, tanto la biopelícula capsular como los linfocitos circundantes se analizaron mediante técnicas de cultivo, determinación de ácidos nucleicos y por visualización directa.

Al analizar el ensayo con los cerdos se comprobó que todas las muestras mostraron infección bacteriana de la biopelícula de la cubierta, con una correlación significativa entre el número de bacterias y el grado de contractura de la cápsula. La reacción en cadena de la polimerasa cuantitativa en tiempo real (PCR-RT) mostró que las células T eran las predominantes y que ese infiltrado linfocitario se mostró en mayor número en aquellos implantes texturizados, en comparación con los lisos. Esto determinó que la infección crónica genera una respuesta de las células T en la biopelícula alrededor de las prótesis mamarias tanto en cerdos como en humanos, siendo el elemento fisiopatológico clave en la aparición del linfoma de células grandes anaplásicas asociado con implantes mamarios. Adicionalmente encuentran, en el ensayo referido, una bacteria, la *Ralstonia sp*., con mayor frecuencia en las cápsulas de las pacientes diagnosticadas con LCGA (7).

Se ha determinado la mayor tendencia del *biofilm* bacteriano a colonizar la superficie de los implantes texturizados en comparación con los implantes lisos y la consiguiente inflamación crónica que, en pacientes predispuestos, es un disparador de tumorigénesis. Las biopelículas son colonias microbianas asociadas a la superficie, incrustadas en una matriz extracelular autosecretada, a partir del líquido del sinoviocito en la metaplasia sinovial como fenómeno adaptativo de la prótesis encapsulada (8).

James y col. confirmaron que los implantes mamarios rugosos, que les generan más superficie, pueden albergar una mayor cantidad de biopelícula bacteriana, que incluye agentes como *Staphylococcus epidermidis, Pseudomonas aeruginosa* y *Ralstonia pickettii,* en comparación con los implantes más lisos (9).

Para abril de 2022, la Administración de Alimentos y Medicamentos (FDA) anunció el registro de 1 130 informes médicos diagnósticos tanto de Estados Unidos, como de todo el mundo sobre linfoma de células grandes anaplásico

asociado a implantes mamarios (LCGA-APM). Este total incluye todos los procedimientos relacionados con implantes mamarios que recibió la FDA con alguna mención de "LCGA" u otras variaciones de la descripción de la patología, tales como "linfoma anaplásico", dentro de los informes recibidos. Sin embargo, solo fueron aceptados aquellos informes clínicos o patológicos con un diagnóstico o tratamiento instaurado por LCGA-APM, o con pruebas de citologías o biopsias confirmadas, o con biomarcadores de quinasa de linfoma anaplásico negativo (ALK-) y CD30 positivo, en lugar de solo mencionar LCGA (10).

En un grupo de estudio multicéntrico en Estados Unidos fueron evaluadas 87 pacientes femeninas que correspondieron a 50 pacientes ya publicados y a 37 pacientes con datos no publicados seleccionados de muchas instituciones participantes. El promedio de edad fue de 54 años, con un rango entre los 28 y los 87 años. El intervalo medio desde la implantación hasta el diagnóstico de LCGA-APM fue de 8 años, con un rango entre los 2 y los 25 años. Cincuenta y dos pacientes (59,8 %) presentaron un derrame alrededor del implante, que se identificó como seroma, 17 pacientes (19,5 %) mostraron una masa mamaria y derrame, 15 pacientes (17,2 %) presentaron una masa mamaria y tres pacientes (3,5 %) no tenían ningún hallazgo morfológico. Cincuenta y siete pacientes (65,5 %) tenían linfoma confinado por la cápsula fibrosa y 30 pacientes (34,5 %) tenían infiltración de linfoma más allá de la cápsula. Considerando los ganglios linfáticos axilares, 13 (14,9 %) de los 87 pacientes resultaron positivos para linfoma, ya sea para el momento del diagnóstico o posteriormente. El tiempo promedio de seguimiento fue de 30 meses. Los hallazgos patológicos de las 87 pacientes se revisaron centralmente. El tiempo de supervivencia general (SG) media después del diagnóstico de LCGA-APM fue de 13 años, con el hallazgo de una tasa de SG del 93 % y del 89 % a los 3 y 5 años, respectivamente. Las pacientes con linfoma que se mantuvieron confinadas en la cápsula fibrosa que rodea el implante mostraron una mejor supervivencia sin complicaciones (SSC) y SG que los pacientes con linfoma que se había propagado más allá de la cápsula. Las pacientes sometidas a cirugía consistente en una capsulectomía total con extracción de implantes mamarios presentaron una mejor SG y una SSC, en comparación con las pacientes a las cuales se practicó procedimiento de capsulectomía parcial, quimioterapia sistémica o radioterapia. Esta revisión permitió establecer que la terapia fundamental para asegurar una supervivencia sin complicaciones y óptimas, la constituye el procedimiento quirúrgico con escisión completa de la cápsula periprotésica en las pacientes con LCGA-APM (11).

Se presenta el primer caso de LCGA-APM diagnosticado en Venezuela, el cual fue realizado en 2017, mostrando las evidencias de todos los pasos del procedimiento diagnóstico morfológico que incluyó evaluación citológica, del bloque celular y de la biopsia de capsulectomía bilateral, con hallazgos de la neoplasia en la muestra de cápsula periprotésica izquierda.

Las estrategias diagnósticas

De acuerdo con las directrices del Consenso español, en presencia de cualquier derrame periprotésico subagudo o tardío, excluyendo las rupturas de prótesis, traumatismos recientes e infecciones, se debe investigar la posibilidad de LCGA-APM. Puede encontrarse incidentalmente el hallazgo de mínima cantidad de líquido periprotésico, entre 5-10 mL, en implantes en pacientes asintomáticos y que no requiere más investigación. Aquellos cuyas cantidades oscilan entre 200 y 1 000 mL deben ser investigados para descartar linfoma.

Ante la sospecha clínica, el estudio fundamental lo constituye la ecografía para evaluar la presencia de derrame periprotésico, o hallazgo de nódulos, masas mamarias o adenopatías, siendo las axilares las más frecuentes hasta en 93 %. El estudio ecográfico presenta una sensibilidad del 84 % y una especificidad del 75 % para la detección de derrame y una sensibilidad del 46 % y una especificidad del 100 % para la detección de masas. Presenta también utilidad para guiar la toma de muestras para citología o biopsia ante la sospecha de LCGA-APM. Se indica Resonancia Magnética (RM) en caso de no ser concluyente la ecografía. La RM con o sin contraste intravenoso, tiene una sensibilidad del 82 % y una especificidad del 33 % para la detección de derrame, y una sensibilidad del 50 % y una especificidad del 93 % para la detección de masas.

La punción con aguja fina (PAAF) complementa la evaluación como el próximo paso, también guiada por ecografía, lo cual permitirá valorar en todo momento la posición del implante, así como su integridad. Idealmente se deben extraer un mínimo de 10 mL, siendo la cantidad ideal desde 50 mL, sin embargo, la mayor cantidad posible de líquido extraído facilita disponer de muestra suficiente para el estudio de Anatomía Patológica, que incluirá citología, posible bloque celular y una citometría de flujo para la determinación de CD30. Ante la detección de masa tumoral es necesario realizar una biopsia con aguja gruesa (BAG), preferentemente con calibre 14G, también guiada por ecografía. Es importante tomar en cuenta que, en presencia de adenopatías, hay que programar una biopsia inicialmente mediante BAG guiada por ecosonograma, o si es posible realizar biopsia escisional. Los estudios de extensión pueden incluir PET-CT, cuya aplicación es útil para valorar otras localizaciones y secundariamente hacer seguimiento de la terapia (12).

Han sido evaluados los hallazgos clínicos y las características histopatológicas de los ganglios linfáticos en 70 pacientes con LACG-APM, definiendo aquellos ganglios infiltrados por este tumor. El 20 % de los pacientes (14) mostraron invasión linfática regional, con incidencia mayor en ganglios axilares (93 %) y presencia predominante en la sinusoide ganglionar (92,9 %). Dos casos tenían patrones similares a los Linfomas de Hodgkin. Esta investigación estableció que el LCGA-APM más allá de la cápsula se relaciona con un mayor riesgo de afectación de ganglios linfáticos regionales, lo cual se asocia directamente con una disminución de la supervivencia global y se describe también que tal infiltración a ganglios linfático puede confundir con Linfoma No Hodgkin, más aún con la positividad al CD30 que comparten (13).

La estadiación del LACG-APM ha evolucionado de un modelo de "tumor líquido" a una clasificación de "tumor sólido" (14).

La Red Nacional Integral del Cáncer (NCCN) que establece el consenso de atención para el diagnóstico y el tratamiento de la mayoría de las neoplasias malignas conocidas, dio a conocer sus pautas sobre el linfoma anaplásico de células grandes asociado con prótesis mamarias, que han sido reconocidas por la Administración de Drogas y Alimentos de EE.UU y aceptadas por las sociedades especializadas nacionales. Las recomendaciones centran sus puntos clave en parámetros para lograr un diagnóstico y manejo de la enfermedad confiables y enfatizan el papel fundamental de la ablación quirúrgica completa. Se incluye la Clasificación TNM (Cuadro 1) y sugerencias para tratamientos complementarios y regímenes de quimioterapia para LACG-

Cuadro 1. Clasificación TNM del Linfoma de Células Grandes Anaplásicas Asociado a Prótesis Mamarias (LCGA-APM)*

PARAMETRO	HALLAZGO MORFOLÓGICO	ESTADIO TNM
TUMOR EXTENSIÓN (T)		**IA T1 N0 MO**
T1	Tumor confinado al seroma	
T2	Infiltración capsular temprana	**IB T2 N0 M0**
T3	Agregados celulares infiltran la cápsula	
T4	Linfoma infiltra más allá de la cápsula	**IC T3 N0 M0**
NODULO LINFÁTICO (N)		**IIA T4 NO MO**
N0	Sin evidencias de ganglios linfáticos	
N1	Solo 1 ganglio linfático regional	**IIB T1-3 N1 M0**
N2	Más de 1 ganglio linfático regional	
METASTASIS (M)		**III T4 N1-2 M0**
M0	Sin evidencias de metástasis	
M1	Metástasis distal o a otros órganos	**IV ALGÚN T ó N y M1**

*Modificado de (11)

*Fuente: Clemens y col. (1)

APM avanzado con afectación de los ganglios linfáticos. Se abordan tanto la recurrencia de esta neoplasia, como el manejo de la enfermedad irresecable, así como las metástasis a órganos. Estas pautas garantizan que los pacientes reciban el tratamiento eficaz y más actualizado de los que se dispone.

Se puede requerir de otros biomarcadores adicionales para establecer el diagnóstico y excluir otras neoplasias malignas, que incluyen el CD45 como marcador genérico de linfocitos T, así como a las subpoblaciones de linfocitos T que representan el CD2, CD3, CD4, CD5, CD7 y el llamado "natural killer o T-helper", CD8, el cual se asocia a etiologías infecciosas de base. Por supuesto, es fundamental determinar si hay expresión de quinasa de linfoma anaplásico (ALK). Los LACG-APM siempre son ALK negativos; sin embargo, debido a que otras formas sistémicas y cutáneas de LACG son con frecuencia ALK negativas, este hallazgo por sí solo no establece un diagnóstico de certeza. Deben ser integrados los hallazgos tanto clínicos como histopatológicos, proteómicos de inmunohistoquímica y genómicos. La expresión del marcador CD30 completa los requerimientos diagnósticos de esta entidad (15).

PACIENTE Y MÉTODOS

Presentación del caso

Paciente femenina de 38 años, portadora de implantes mamarios texturizados con un volumen de 320 mL desde el año 2013. Presentó un cuadro clínico con tres meses de evolución, caracterizado por aumento de volumen de la mama izquierda, dolor y rubor de la superficie de la piel. Se inicia la evaluación especializada por cirugía plástica, practicando estudio de resonancia magnética de ambas glándulas mamarias, tórax, axilas, con contraste, sin hallazgos de evidencia de patología específica. Por persistir el signo-sintomatología se programa para intervención quirúrgica para retiro de implantes y cápsulas bilaterales, en julio de 2017.

Procesamiento histo-citológico de las muestras

Las muestras fueron recibidas en el Servicio de Patología del Urológico San Román de Caracas desde un centro privado de Cirugía Plástica y Reconstructiva. Consistieron en los especímenes de capsulectomía derecha e izquierda, además de los líquidos obtenidos por Punción Aspiración con Aguja Fina (PAAF) de los seromas pericapsulares de ambos lados.

Las cápsulas fueron debidamente fijadas con formalina buffer al 10 %, con un tiempo máximo de fijación no mayor de 24 horas. Paralelamente se realizó la evaluación macroscópica, identificando las características de tamaño, superficie externa e interna, color, variaciones de espesor parietal y consistencia. Posteriormente se realizaron los cortes de las muestras con prioridad en zonas de mayor espesor, con poca hemorragia y sin calcificaciones. Las muestras fueron colocadas en casetes para completar la fijación y realizar el procesamiento del tejido, inclusión en bloques de parafina, cortes sobre láminas portaobjetos, coloración con hematoxilina-eosina y evaluación con microscopia de luz.

El líquido fue sometido a caracterización morfológica con medición de cantidad, color, aspecto y contenido de sedimento y sobrenadante. Luego se colocó en centrifugación prolongada para obtener material de bloque celular y extendidos citológicos para evaluación.

Procesamiento inmunohistoquímico

Se siguió el procedimiento convencional para el estudio inmunohistoquímico. Se escogieron los bloques y se procedió a realizar cortes de dos micras de espesor, sobre láminas previamente tratadas con poli-L-lisina (Sigma®), se secaron en estufa con temperatura de 56ºC por un lapso de 30 minutos. Fueron desparafinados en tres baños de xileno por un tiempo de 5 minutos cada uno y luego por tres baños de alcoholes de concentración decrecientes (90 %, 80 %, 70 %) hasta hidratar en agua. Finalmente se cumplió la recuperación antigénica con *Dako Target Retrieval Solution Low,* pH 6,0 (Dakocytomation cat K8005®) en una *Decloaking Chamber TX Nx Gen* (Biocare cat. DC2012®) con un protocolo de 110°C por treinta minutos. Una vez finalizada la recuperación, se procedió a la inhibición de la peroxidasa endógena por diez minutos con peróxido de hidrógeno al 2 %. Se escogieron casos controles adecuados.

Los anticuerpos seleccionados para detectar los antígenos fueron CD30 (Biocare cat. CM346C®) dilución 1:150, ALK (Biocare cat. ACI3041B®) dilución 1:150, Mo a Hu CD3 (DAKO M7254®) dilución 1:100, CD4 (Biocare cat. RMAB083-05®) dilución 1:100, CD20 (L26) (Biocare cat. CM004C®) dilución 1:150, CD15 (Concentrate-Dako - CiteAb M3631®) dilución 1:150, CD45ro (UCHL-1) (Biocare cat. CM006C®) dilución 1:150, CD68 Antibody (Dako Omnis®) dilución 1:150, CD8 (Concentrate Dako – CiteAb M7103®) dilución 1:100. Fueron incubados por 1 hora a temperatura ambiente. El sistema de detección usado fue de streptavidina –HRP, Starr Trekk Universal HRP system (Biocare cat STUHRP700®) se hizo el revelado con DAB y contrastado con Hematoxilina de Meyer.

Estudio de Anatomía Patológica

Evaluación macroscópica de las muestras

Cápsula periprotésica derecha. Se recibe un espécimen que consiste en una estructura membranosa plegada sobre su propio eje, que mide 12x10 cm, con un espesor que oscila entre 0,3 y 0,8 cm. Color pardo claro y oscuro, con adherencias fibrosas periféricas, al corte homogéneo, con hemorragia reciente y placas de calcificación. Consistencia firme y pétrea en zonas calcificadas. Se incluyen muestras representativas para evaluación histopatológica (Figura 1).



Figura 1. Cápsula periprotésica derecha.

Referido como líquido de colección por seroma periprotésico derecho. 50 mL de líquido de color pardo claro, con aspecto turbio y viscoso. Se procede a la realización de extendidos citológicos y bloque celular previa centrifugación extendida de 2 horas.

Cápsula periprotésica izquierda. El espécimen es un fragmento de tejido plegado y de forma sacular, más irregular que el derecho, que midió 9x19 cm, cuya pared muestra un espesor entre 0,5 y 1,5 cm. Superficie con fibrosis, pardo claro con áreas de hemorragia reciente, con adherencias fibrosas periféricas, placas de calcificación, al corte es homogéneo y de consistencia firme y pétreo en zonas calcificadas. Se incluyen muestras representativas para evaluación histopatológica (Figura 2).



Figura 2. Cápsula periprotésica izquierda.

Referido como líquido de colección por seroma periprotésico izquierdo. 200 mL de líquido de color pardo claro, con aspecto turbio viscoso. Se procede a la realización de extendidos citológicos y bloque celular previa centrifugación extendida de 2 horas.

RESULTADOS

1. Cápsula periprotésica derecha. Fragmentos de tejido fibroconectivo con inflamación crónica y con presencia de células linfocitarias en

cúmulos, sin atipias. Se identifican células de metaplasia sinovial. Cambios de fibrosis laminar, edema y neovascularización (Figura 3).

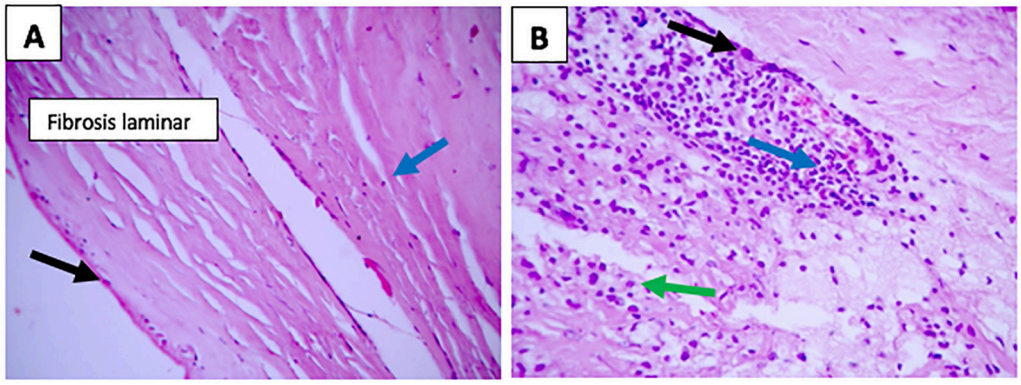


Figura 3. **(A)** Corte longitudinal de cápsula periprotésica. Se observa fibrosis laminar, zonas periféricas de metaplasia sinovial (flecha negra) y presencia de grupos aislados de linfocitos sin atipias (flecha azul). HE. 40X. **(B)** Se identifican varios estadios de inflamación activa. Infiltrado linfoplasmocitario (flecha negra), histiocitos/macrófagos (flecha verde) y leucocitos polimorfonucleares neutrófilos focales (flecha azul). HE. 20X.

2. Referido como líquido de colección por seroma periprotésico derecho. Restos de estroma y fibrina con infiltrado linfocitario con cambios reactivos. Hematíes. Histiocitos. Compatible con citología inflamatoria.
3. Cápsula periprotésica izquierda. Tejido fibroconectivo con cúmulos de inflamación crónica granulomatosa, focos de reagudización y presencia de linfocitos de aspecto neoplásico, con predominio de células grandes. Se identifican folículos linfoides. Cambios de metaplasia sinovial en la periferia. Se solicita estudio de inmunohistoquímica para descartar neoproliferación tumoral (Figura 4).

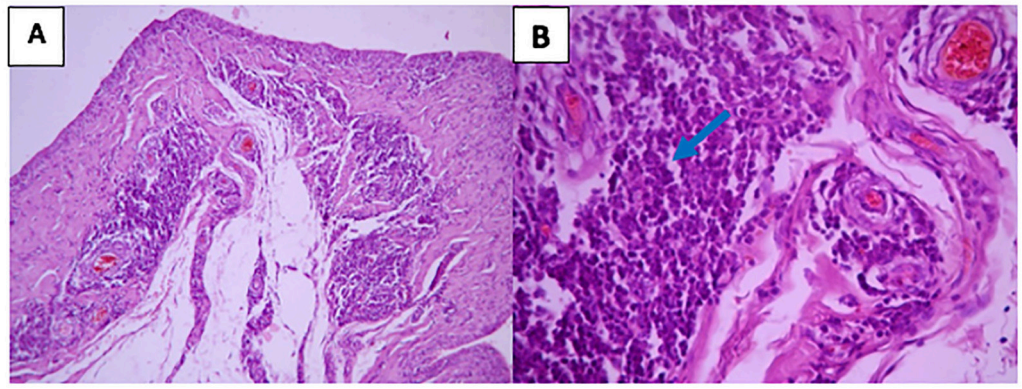


Figura 4. Estructura histológica de la cápsula protésica con cambios de inflamación crónica y aguda con presencia de infiltración por células de aspecto linfoide tumorales (A, HE. 20X). Las células tumorales se corresponden con linfocitos grandes de aspecto pleomórfico sugestivos de linfoma de células grandes anaplásicas. (B, HE. 40X).

4. Referido como líquido de colección por seroma periprotésico izquierdo. Frotis y bloque celular con linfocitos que muestran alteración de su forma y tamaño o pleomórficos. Restos de estroma y fibrina. Hematíes. Histiocitos. Se concluye: Positivo para malignidad y se solicita estudio de inmunohistoquímica del bloque celular para descartar neoproliferación tumoral (Figura 5).

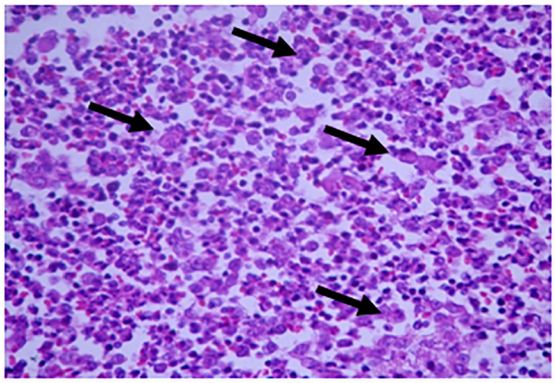


Figura 5. Bloque celular donde se identifican linfocitos grandes de aspecto pleomórfico, hematíes y grupos de histiocitos. HE. 20X.

Resultados de evaluación Inmunohistoquímica

Se procedió a practicar el perfil inmunohistoquímico a la muestra de la cápsula periprotésica izquierda, por presentar los hallazgos sugestivos de neoplasia. La sospecha de que se tratase de un LCGA-APM, como una entidad nueva, la presencia de linfocitos grandes con marcado polimorfismo justificó la extensión de los estudios diagnósticos con la realización del marcaje de anticuerpos específicos, que descartasen linfocitos B, histiocitos y sobre todo variantes de linfocitos T, para la identificación del inmunofenotipo.

Los marcadores investigados incluyeron los anticuerpos CD30, ALK, CD20 para la identificación de linfocitos B, CD68 para los histiocitos de la inflamación crónica y los anticuerpos para caracterizar a los linfocitos T, a saber, CD45ro, CD3, CD5 y CD8 (Cuadro 2).

Cuadro 2. Resultados del estudio inmunohistoquímico de la cápsula periprotésica izquierda.

ANTICUERPO	RESULTADOS
ALK	Inmunoreacción negativa en las células tumorales
CD30	Inmunoreacción positiva en las células tumorales
CD45ro	Inmunoreacción positiva en las células tumorales
CD3	Inmunoreacción positiva en las células tumorales
CD5	Inmunoreacción positiva en las células tumorales
CD8	Inmunoreacción positiva en las células tumorales
CD68	Inmunoreacción positiva en grupos de histiocitos
CD20	Inmunoreacción positiva en aislados y escasos linfocitos B.

La inmunorreacción para el anticuerpo CD30 resultó positiva con el marcaje de membrana, limitado a las células linfoides grandes tumorales, en contraste, el marcaje para la quinasa de linfoma anaplásico (ALK) resultó negativo en las células neoplásicas (Cuadro 2, Figura 6).

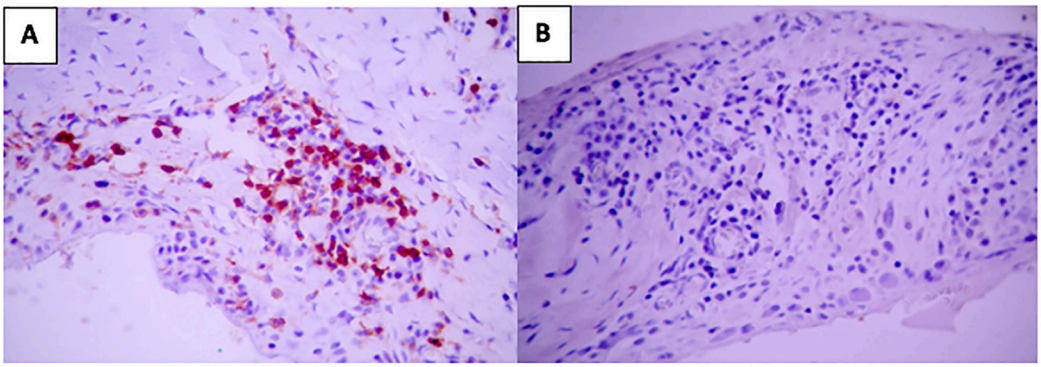


Figura 6. Positividad del anticuerpo CD30, elemento fundamental en la complementación diagnóstica de esta variedad de linfoma de células grandes anaplásicas. CD30. 20X (A). Al investigar la expresión del anticuerpo ALK se comprueba su inmunoreacción negativa. ALK. 40X (B).

Con la positividad para los anticuerpos CD3, CD5 y CD8 se demostró que el tumor se deriva de los linfocitos T, al identificarse en tales marcadores de subpoblaciones de esta estirpe y confirmada por igual positividad del CD45. Los linfocitos B de predominio centrolobulillar se identificaron con el anticuerpo CD20 en los folículos linfoides peritumorales reactivos de inflamación crónica (Cuadro 2, Figuras 7 y 8).

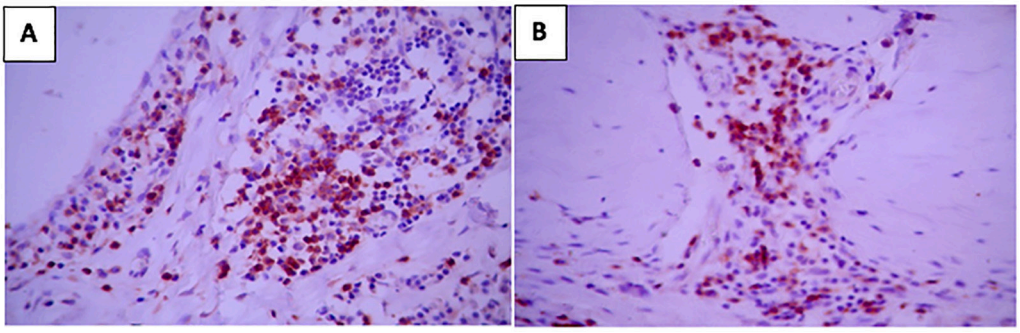


Figura 7. Con la positividad en células grandes anaplásicas de los anticuerpos CD3 (A) y CD5 (B) se comprueba el origen del tumor a partir de linfocitos T, CD3/CD4. 20X.

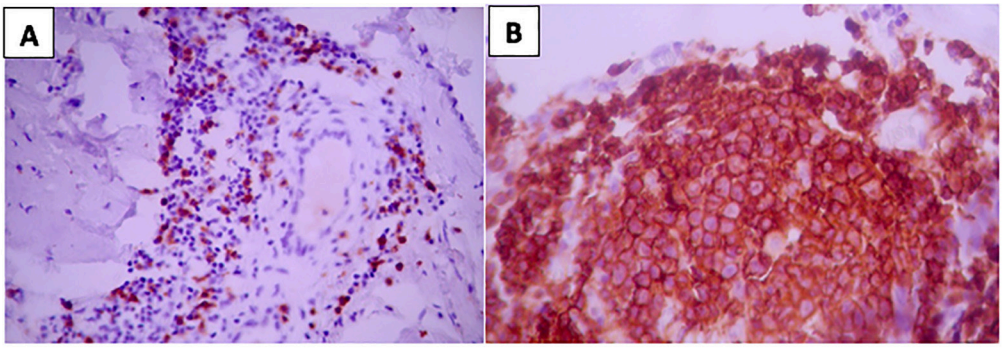


Figura 8. Positividad para el anticuerpo CD8 que identifica al linfocito T citotóxico, también conocido como célula NK o Natural Killer, CD8. 20X (A). Folículos linfoides en la periferia de la proliferación neoplásica con positividad al CD20, identificando los linfocitos B centro-foliculares, CD20. 40X (B).

Propuesta para la Evaluación del Linfoma de Células Grandes Anaplásicas asociado a Prótesis Mamarias (LCGA-APM)

Procesamiento del líquido periprotésico

El material obtenido por la punción debe ser remitido al laboratorio de patología en un tiempo ideal máximo de 2 horas luego del procedimiento, libre de aplicación de fijador inicialmente, en un envase que sea adecuado a su volumen.

El laboratorio debe ser notificado que le será referida la muestra a fin de proceder a la obtención tanto de extendidos celulares sobre láminas porta objetos para análisis citológico convencional, así como de uno o dos bloques celulares que puedan tener utilidad para análisis histológico con hematoxilina-eosina y posterior aplicación de estudios proteómicos de inmunohistoquímica

Una vez obtenida la muestra suficiente para realizar los extendidos y los bloques celulares, y quedando aún material, este remanente debe ser preservado bajo refrigeración a 5 °C, luego de agregar 1 gota de fijador de Formalina Buffer al 10 % por cada mL de líquido periprotésico.

En principio, cualquier cantidad de líquido obtenido para estudio puede ser de utilidad, pero cantidades superiores a 5 mL son las que pueden ayudar a obtener mejores resultados por disponer de mayor material, sobre todo si el objetivo es obtener al menos un bloque de tejido para incluir en parafina.

Cuando se dispone de citocentrífuga o si existe y se dispone en los centros receptores de la muestra de citología en base líquida, no habría problema en obtener un extendido de calidad y con adherencia adecuada a la lámina, sin embargo en nuestro país la mayoría de los laboratorios cuentan con centrífugas convencionales, por lo cual, para obtener los extendidos y los bloques de tejido para incluir en parafina se debe proceder a la centrifugación del líquido periprotésico vertido en, al menos, dos tubos de ensayo. Para el logro del bloque se debe procurar una centrifugación extendida para buscar la estabilidad del material, con duración no menor de 45 minutos y hasta 2 horas.

La preferencia por la obtención del o los bloques celulares está fundamentada en que se pueden lograr cortes que sean utilizados para aplicar inmunohistoquímica, ya que solo el extendido o la citología convencional tienen una alta probabilidad de desprenderse, lo que hace inviable este estudio.

Los líquidos mezclados con componente inflamatorio supurativo (pus) pueden hacer muy difícil la obtención de un bloque de tejido estable. Para la compactación es importante el componente de fibrina y conocer si la (el) paciente mantiene terapia de anticoagulación.

Una vez transcurrida la etapa de centrifugación, se debe extraer el bloque y colocarlo envuelto en un papel filtro, debidamente identificado en un casete de procesamiento de tejido, sometido

previamente a fijación inicial con formalina buffer al 10 %. Con la fracción líquida espesa se procede a realizar al menos dos extendidos sobre láminas portaobjetos.

Finalmente, la evaluación microscópica más efectiva se logra en áreas de la periferia, que por lo general son zonas de menor densidad celular y no compactadas.

Protocolo de estudio de biopsia de cápsula periprotésica

Una vez obtenida la muestra, esta debe ser colocada en fijación utilizando solución de formalina tamponada al 10 % o formol buffer, como también se conoce. Debe estar identificada adecuadamente con los datos de la (el) paciente y la localización exacta de la misma.

Se procede a su estudio macroscópico, describiendo el tamaño de la(s) muestra(s) recibida(s), su aspecto superficial, color y consistencia.

Los cortes, de ser posible, deben contener los extremos de la muestra para incluir las zonas distales y proximales de la cápsula, evitando las áreas con mayor hemorragia o de aspecto necrótico y las zonas calcificadas. Se deben al menos obtener dos bloques de tejido conteniendo cada uno 4 cortes del tejido referido para estudio.

Se recomiendan fragmentos de tejido de 1,5 a 2 cm de longitud por un espesor que represente el de la muestra, cuya fijación máxima no debe exceder las 48 horas, debido a que la sobrefijación puede afectar la posibilidad de obtener buenos resultados en la inmunohistoquímica.

Una vez obtenidas las láminas teñidas con hematoxilina-eosina, en el estudio microscópico se debe evaluar el tipo de celularidad presente en el tejido, buscando identificar, sobre todo en la periferia de la región capsular, las células compatibles con LCGA-APM. Se debe descartar la presencia de enfermedad granulomatosa o la mezcla de componente granulomatoso asociado a células de aspecto neoplásico.

Ante la sospecha, los anticuerpos que forman el panel básico para la investigación lo constituyen el anticuerpo policlonal Pan-T CD45, el ALK y el CD30, los cuales se pueden complementar con el CD68 para los histiocitos y los que complementan familias de linfocitos T, tales como CD2, CD3, CD4, CD5, CD7 y CD8.

Se considera un panel de inmunofenotipo compatible con LCGA-APM si se comprueba positividad para CD45 o con la combinación de otros marcadores de linfocitos T, junto a la positividad del CD30 y la negatividad para el ALK.

DISCUSIÓN

El caso que se presenta tiene el valor de ser el primero que se tiene registro haya sido diagnosticado en el país, en el año 2017, en una paciente de la cuarta década de la vida con antecedente clínico de colocación de prótesis mamaria con superficie texturizada, de 320 mL de volumen desde 2013 y un aumento de volumen mamario bilateral, con sensación de tensión superficial, dolor al tacto y evidencias de seroma de tres meses de evolución. El promedio de aparición del LCGA-APM informado en los estudios internacionales es de ocho años posteriores al procedimiento de colocación protésica, aunque se encuentra en el rango de aparición informado entre 2 y 25 años. Sin embargo, se debe tomar en cuenta la confluencia de aspectos etiopatogénicos de carácter epigenéticos, tales como el uso de prótesis texturizadas, colección líquida o seroma periprotésico, además de la predisposición genética con potencial de mutación que ha sido descrita en un importante número de pacientes.

Di Napoli y col. (6) aportan nuevos conocimientos sobre las bases biológicas de esta nueva entidad patológica, estableciendo que el linfoma anaplásico de células grandes asociado con implantes mamarios representa una entidad distinta de linfoma de células T periféricas. Este grupo investigó los perfiles de expresión genética de muestras de linfoma anaplásico de células grandes asociado a implantes mamarios tomados por microdisección y se compararon también sus perfiles transcripcionales con los que se han obtenido previamente tanto de células T normales, como de otros linfomas de células T periféricos. Esto permitió validar la expresión de marcadores que fueron seleccionados utilizando

estudios de inmunohistoquímica. Establecieron que la mayoría de los linfomas anaplásicos de células grandes asociados con prótesis mamarias exhiben un fenotipo de células T de memoria CD4+ activado, que está asociado además con la expresión de CD25 y FoxP3. Con procesos de ontología genética identificaron que muestran una regulación positiva de los genes implicados en la programación de la motilidad celular, en esta variante de linfomas que incluyen CCR6, MET, HGF y CXCL14, de acuerdo con sus siglas en inglés, cuando se comparan con las células T CD4+ normales y también otra regulación positiva de los genes implicados en la diferenciación de células mieloides, entre ellos PPARg, JAK2, SPI-1 y GAB2. Por otra parte, fue identificada una transcripción de genes virales del tipo RPS10, RPL17, RPS29 y RPL18A, a diferencia de otras variantes de linfomas de células T periféricas.

Por análisis de enriquecimiento de conjuntos de genes se identificaron también características compartidas entre los perfiles moleculares de los linfomas anaplásicos de células grandes asociados con implantes mamarios y otros tipos de linfomas anaplásicos de células grandes, que incluyeron la regulación a la baja de la señalización del receptor de células T y la activación de STAT3 (15).

La investigación sobre los LCGA-APM, dado lo novedoso de esta entidad tumoral, también ha ahondado en aspectos de su clasificación genético-molecular con pertinencia en la progresión pronóstica de la terapéutica (7). Esto ha definido que hasta ahora muestran un perfil genético "triple negativo", por ser negativo para los reordenamientos de ALK, DUSP22 y TP63, caracterizándose por perfiles mutacionales y de expresión genética que muestran una activación aberrante de la vía JAK/STAT. La forma activa de STAT3 (pSTAT3) se expresa constantemente en los LPCG-APM y puede ayudar a un mecanismo de escape inmunitario del tumor por desencadenar la transcripción de PDL1 (CD274), gen encargado de codificar la molécula de punto de control inmunitario que lo define como Ligando de Muerte Celular Programada-1 (PDL1). De acuerdo con esto, se determinó que estos tumores expresan con frecuencia PDL1 y albergan alteraciones recurrentes del número de copias de este ligando. En el análisis del microambiente del LCGA-APM se identificó señalización predominante por la vía JAK/STAT y refleja un eje PD1/PDL1 activo. Estos hallazgos tienen valor terapéutico para pacientes en etapa avanzada, quienes podrían beneficiarse de una estrategia terapéutica de bloqueo de PD1/PDL1 (17).

En una serie de 29 casos en 2020, Los-de Vries y col. (8) realizaron un análisis genético completo y determinaron las aberraciones del número de copias cromosómicas (CNA) de todo el genoma, así como los perfiles mutacionales. Se detectó la pérdida característica del cromosoma 20 en los LCGA-APM, lo cual proporciona información para una justificación adicional para reconocerlo como una entidad independiente. Por otra parte, el análisis de CNA puede servir como parámetro para futuros ensayos de diagnóstico para mujeres con implantes mamarios a fin de distinguir el seroma producido por LCGA-APM de otras causas de acumulación de seroma, como la infección o el trauma (18).

Consideramos que el proceso de metaplasia sinovial es un hallazgo histopatológico que condiciona la acumulación de líquido, secundariamente colonizado por bacterias, generando la expresión clínica fundamental de la patología que la constituye el seroma.

Esta neoplasia, a la luz de una proliferación incontrolada de la colocación de prótesis mamarias, ha adquirido una importancia significativa en la valoración del seguimiento de las pacientes que han sido sometidas a estos procedimientos. Para 2019 se registraban, de acuerdo con un estudio de Australia, 35 millones de pacientes con implantes en el mundo. Ya la Guía Práctica Clínica en Oncología (NCCN, de acuerdo con sus siglas en inglés) ha establecido una serie de pautas con pertinencia en el diagnóstico y el tratamiento, siendo la posibilidad de un diagnóstico temprano la clave para asegurar su curación. En una etapa temprana y para el mayor porcentaje de pacientes, la conducta es la capsulectomía y extracción del implante. Pero en los estadios II a IV, se justifica un tratamiento sistémico que incluya quimioterapia, radioterapia en presencia de enfermedad residual y terapia inmunológica con Brentuximab Vedotin, cuya presentación comercial es ADCETRIS®, el cual está indicado para el tratamiento de pacientes adultos con LCGA-APM sistémico en recaída o refractario. Esta formulación es un anticuerpo sintético que induce al sistema inmunitario a

atacar a las células del linfoma que contienen la proteína CD30, el cual también es utilizado en la terapia inmunológica del linfoma de Hodgkin (19).

La clasificación TNM es un sistema usado para describir la extensión de un tumor canceroso. Evalúa tres aspectos principales: el tamaño del tumor (T), la afectación de los ganglios linfáticos (N), y la presencia de metástasis a distancia (M). De acuerdo con la Clasificación TNM propuesta para esta entidad, el caso presentado se corresponde con un estadio T4 N0 M0, por presentar un tumor que infiltra más allá de la cápsula sin evidencias de presencia de ganglios linfáticos infiltrados ni metástasis a distancia (Cuadro 1). La paciente del caso presentado fue remitida a quimioterapia y terapia de anticuerpos monoclonales. De acuerdo con la información clínica, ha evolucionado satisfactoriamente.

Para 2019, se estableció que solo 33 pacientes murieron por LCGA-APM en todo el mundo. Se comprobó que dichas muertes se relacionaron con el retraso en el diagnóstico y el tratamiento. Los implantes texturizados han estado en medio de la reciente crisis internacional de los implantes de mama, y el principal producto llamado "Biocell" fue retirado del mercado en todo el mundo después de la última actualización de la FDA sobre la enfermedad. Esta problemática plantea un seguimiento y registro de los aspectos cualitativos y cuantitativos relacionados con la distribución y uso de los productos de implantes disponibles en el mercado (20).

Ha sido reportado un caso en un masculino de 76 años con un seroma tardío, con antecedente de cirugía estética de tórax con implantes pectorales de silicona de 9 años de evolución, con informes de estudios citológicos previos negativos de malignidad, sin embargo, el estudio repetido a las 6 semanas por el seroma recurrente demostró clones de células T CD30+ característicos. Se le realizó cirugía con capsulectomía bilateral completa y retirada del implante. Debido a que esta patología en etapa temprana se limita solo a la cápsula y no hubo evidencia de enfermedad sistémica, no se consideró necesario el tratamiento adyuvante. Esto ejemplifica que no es exclusiva la presentación solo relacionada con sexo y con implantes mamarios, ya que todos los procedimientos estéticos de esta naturaleza con material texturizado pueden generar esta forma especial de linfoma de células grandes anaplásicas dependiente de la célula T.

Esto fundamenta el hecho de que es importante recalcar que cualquier seroma persistente de aparición tardía también en pacientes masculinos con implantes pectorales debe generar sospecha de esta entidad como diagnóstico diferencial y debe ser evaluado con examen citológico inicial y considerar la extracción de la prótesis (21).

Venezuela es un país con alta incidencia de procedimientos protésicos, con predominio de la utilización de implantes mamarios, en medio de un culto a la belleza que ha caracterizado a nuestra sociedad en las últimas cuatro décadas, por lo tanto la identificación de este tipo de patologías tiene importancia en el seguimiento de los problemas de salud pública, aún con su baja morbimortalidad, además identificar su presencia en el país es un alerta a los equipos médicos que realizan estos procedimientos, básicamente en el área oncológica y de medicina estética y reconstructiva.

Recomendaciones

Es fundamental insistir en la educación médica continua para dar a conocer la importancia de esta neoplasia de relativa reciente aparición en el equipo de salud responsable de la realización de procedimientos protésicos de mama.

Hacer entender que en presencia de aspectos clínicos y patológicos específicos de sospecha se debe pensar en esta entidad y aplicar el procedimiento diagnóstico recomendado.

El especialista debe tener pleno conocimiento sobre cómo trabajar con las muestras para asegurar el éxito de los estudios histológicos y proteómicos de inmunohistoquímica.

La obtención de bloques celulares en el procesamiento de los líquidos periprotésicos, además de la cantidad y calidad de la muestra, puede depender de la cantidad de fibrina de la misma, la cual favorece la agregación y compactación del líquido sometido a centrifugación extendida.

El diagnóstico depende exclusivamente del perfil de inmunohistoquímica, por lo cual en presencia de grupos de linfocitos atípicos

en agregados focales o difusos se recomienda completar este estudio proteómico, dado el curso de bajo nivel clínico o indolente, que puede presentar esta neoplasia.

Debe asegurarse que este tipo de casos sean canalizados por especialistas experimentados en la aplicación de los protocolos de estudios recomendados.

Se debe mantener una comunicación continua entre el cirujano y el patólogo responsable del procedimiento diagnóstico de los especímenes.

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Conflicto de interés

El autor declara no tener conflictos de interés.

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Dr. José Gregorio Hernández (1864-1919): una nueva visión de la bacteriología

Dr. José Gregorio Hernández (1864-1919): A new vision of bacteriology

Tomás González[1], Cynthia Verónica Hernández Campuzano[2]

RESUMEN

La reciente canonización del Dr. José Gregorio Hernández avivará con fervor el interés por investigar su vida y obra tratando de dar a conocer nuevos datos. Desde la Cátedra de Historia de la Medicina de la Escuela Dr. Luis Razetti de la Universidad Central de Venezuela, nos propusimos examinar su libro Elementos de Bacteriología (1906) y hacer una exégesis del mismo para determinar los aportes concretos en esta disciplina de la medicina en Venezuela. Hernández, tras su formación en París, introdujo en Venezuela el uso del microscopio y técnicas de estudio de microorganismos, marcando el inicio de la microbiología científica en el país. "Elementos de Bacteriología" es un compendio de sus lecciones, adaptadas al programa de estudios médicos de la época. En él aborda la bacteriología general y especial, así como técnicas de laboratorio y enfermedades infecciosas. Su obra no solo fue un texto didáctico, sino también una herramienta para modernizar la medicina venezolana en la cual, con su enfoque pedagógico y su visión innovadora, dejó un legado duradero.

Palabras clave: *Bacteriología, historia de la medicina, microbiología, cátedra, modernidad.*

SUMMARY

The recent canonization of Dr. José Gregorio Hernández will fervently rekindle interest in researching his life and work, and in seeking to shed new light on his life and legacy. From the Chair of History of Medicine at the Dr. Luis Razetti School of the Central University of Venezuela, we set out to examine his book, Elements of Bacteriology (1906), and conduct an exegesis to determine its specific contributions to the field of bacteriology in Venezuela. After his training in Paris, Hernández introduced the use of the microscope and techniques for studying microorganisms to Venezuela, marking the beginning of scientific microbiology in the country. "Elements of Bacteriology" is a compendium of his lectures, adapted to the medical curriculum of the time. It covers general and specialized bacteriology, as well as laboratory techniques and infectious diseases. His work was not only an educational text but also a tool for modernizing Venezuelan medicine, in which, with his pedagogical approach and innovative vision, he left a lasting legacy.

Keywords: *Bacteriology, history of medicine, microbiology, chair, modernity.*

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INTRODUCCIÓN

La microbiología es el estudio de los seres vivos que se encuentran por debajo del poder resolutivo del ojo humano. Para destacar sus períodos evolutivos, Collard (1) presenta un esquema donde el primer período, eminentemente especulativo, se extiende desde la antigüedad hasta llegar al que se considera el primer microscopista, Cornelis Drebbel (1572 - 1633). El segundo período, va desde 1675 que inicia con el descubrimiento de los microorganismos por Antón van Leeuwenhoek (1632 – 1723) hasta la mitad del siglo XIX. El tercer período, de cultivo de microorganismos, llega hasta finales del siglo XIX, donde las figuras de Louis Pasteur (1822 – 1895) y Robert Koch (1843 – 1910) encabezan el logro de cristalizar a la microbiología como ciencia experimental bien asentada. Y por último, el cuarto período, desde principios del siglo XX hasta nuestros días, en el cual los microorganismos se estudian en toda su complejidad fisiológica, bioquímica, genética, y surgen disciplinas microbiológicas especializadas como la virología y la inmunología (2). En Venezuela se estrena la microbiología en el tercer período en 1891 cuando el Dr. José Gregorio Hernández introdujo la enseñanza del uso y manejo del microscopio, así como las técnicas de estudio de tejidos y cultivos de los microbios, es desde entonces, cuando se empieza a hacer verdaderamente científica esta rama de la medicina. En la Memoria de Instrucción Pública de 1892, el ministro Dr. Eduardo Blanco afirma que "si ninguna reforma estudiantil ha hecho el Ejecutivo, sí ha favorecido con atención constante a los Institutos referidos, proveyendo a todas sus necesidades y ha mejorado los estudios médicos en la Universidad Central con varias medidas oportunas y con el establecimiento del laboratorio de Histología Normal y Patológica, Fisiología Experimental y Bacteriología, organizado con todos los elementos, aparatos e instrumentos necesarios. La dirección de este laboratorio y las cátedras de enseñanza experimental que en él se dan están a cargo del Doctor José Gregorio Hernández, especialista aprovechado que perfeccionó sus estudios en Europa para hoy generalizarlos entre sus compatriotas, y los gastos ocasionados por la fundación de tan útil departamento en los estudios médicos, alcanzan a la suma de Bs. 14 772,49" (3).

Tiempo y época del Dr. José Gregorio Hernández

José Gregorio Hernández nació el 26 de octubre de 1864 en Isnotú, Estado Trujillo, Venezuela, donde vivió durante su infancia junto a su familia. Una vez alcanzada la edad escolar, su padre lo inscribe en la única escuela del pueblo, dirigida por el maestro Pedro Celestino Sánchez. Cuando el alumno cumplía cinco años de asistencia a clases, se dio cuenta que sus lecciones se habían agotado y le convenía seguir sus estudios en Caracas (4).

Es así como el padre de José Gregorio, una vez que cumplió los 13 años, lo inscribe en calidad de interno en el Colegio Villegas de Caracas donde se gradúa de Bachiller en Filosofía en junio 1882 e ingresa a la Facultad Médica de la Universidad Central, donde a la usanza de la época, primero obtiene el título de Bachiller en Ciencias Médicas y luego el de Doctor en Ciencias Médicas el 29 de junio de 1888 (5).

El 31 de julio de 1889, el presidente Juan Pablo Rojas Paúl dispone enviar a París "por cuenta del Gobierno Nacional (…) a un joven médico de nacionalidad venezolana, graduado de Doctor en la Universidad Central, de buena conducta y de aptitudes reconocidas, con el fin de que curse allí las siguientes especialidades: Microscopía, Bacteriología, Histología Normal y Patológica y Fisiología Experimental. Se le asigna, al efecto, la pensión mensual de seiscientos bolívares (Bs. 600,oo), que se pagará por la Tesorería General de Instrucción Pública", y para cumplir esta misión se decide enviar al Dr. José Gregorio Hernández (6).

El Dr. Hernández inicia su formación desde los primeros días de noviembre de 1889 en la Facultad Médica de París en el Laboratorio de Histología a cargo del Dr. Mathias Duval, quien señala "Es para mí un deber y un placer agregar que él se ocupa en el estudio de la histología con actividad y gran éxito; y no dudo que un día yo estaré orgulloso de tenerlo como discípulo" (7). Una vez terminada su labor, regresa a Venezuela donde instala el Laboratorio de Fisiología Experimental y Bacteriología con los equipos

que había traído de Francia, dice el historiador Plácido Daniel Rodríguez Rivero "como corolario obligado de la teoría pasteuriana aceptada desde su creación como una verdad inconcusa, se fundó junto con un laboratorio anexo, la Cátedra de Bacteriología, el 6 de noviembre de 1891, y se puso a cargo del joven, sabio y justo doctor José Gregorio Hernández, de tan eximias virtudes y de conocimientos tan hondos" (8).

Elementos de bacteriología: una nueva visión de la ciencia

El 15 de junio de 1906, en ocasión de solicitar su jubilación como profesor universitario, el Dr. Hernández "fundador de la Cátedra de Bacteriología, Histología y Fisiología Experimental en la Universidad Central desde el mes de noviembre de 1891, adjunto a esta representación tengo a honra enviar a usted un ejemplar de una obra titulada *Elementos de Bacteriología* que acabo de escribir para la expresada Cátedra, pues aspiro a que, de acuerdo con el artículo 15 del Código de Instrucción Pública, se me conceda la jubilación de ley, conmutándose dicho trabajo por los seis años que me faltan para los veinte que al efecto señala el artículo 14 del citado código" (9). La respuesta oficial es del 20 de junio y se le comunica que por disposición del general Juan Vicente Gómez se le concede la jubilación solicitada con la asignación de doscientos bolívares (Bs. 200,oo) mensuales y que del Ministerio de Hacienda se le libraría la cantidad de mil bolívares (Bs. 1.000,oo) para pagar la impresión de su libro reconocido como de "utilidad pública" (10).

El libro fue publicado en Caracas por la Tipografía Herrera Irigoyen en 1906. Es un compendio de las lecciones dictadas en clase ordenadas según el programa de estudios médicos de la época, por lo que el alcance de esa obra fue servir de apoyo para los estudiantes proveyéndoles un material didáctico, sencillo y sistematizado acerca de la bacteriología teórica general, las técnicas de laboratorio y las enfermedades infecciosas más comunes en el hombre y los animales. En el prólogo del libro *Elementos de Bacteriología*, el Dr. Hernández escribe "la enseñanza dada durante estos quince años ha sido bastante laboriosa para nosotros, porque, aunque hay un crecido número de obras de bacteriología, muchas de ellas con gran valor científico, ninguna está completamente acomodada a las necesidades de nuestro programa universitario" (11).

Primera parte: Bacteriología general. Tratado Primero: Bacteriología Teórica General.

La microbiología o la patología experimental bacteriológica se centra en la idea de que los microbios son seres vivos elementales muy pequeños que se observan con microscopio. Esta ciencia se divide en bacteriología general donde todos los microbios tienen características comunes. En la bacteriología especial cada microbio resalta individualmente y la técnica especial estudia un solo microbio determinado según el método experimental. Su antecesor, Leeuwenhoeck con ayuda de lentes biconvexos vio este pequeño mundo de organismos, los dibujó y consideró que eran agentes de putrefacción. Müller (1786) y Ehrenberg (1833) los clasificaron y, en 1860, Pasteur atribuye que las fermentaciones eran producidas por los seres microscópicos e inventa la técnica para su estudio que más adelante fue perfeccionada por Koch en Alemania. Davaine (1863) señaló el primer microbio, el *Bacillus Anthracis,* y lo asoció a enfermedad en la pústula maligna (12).

Los primeros observadores creyeron que pertenecían al reino animal por eso el nombre de animáculos, posteriormente se dividen en reino animal y vegetal. Se diferencian ya que los microbios vegetales tienen forma de cristal, con caras planas, ángulos y aristas muy pronunciadas, ellos elaboran celulosa, féculas y pigmentos análogos a la clorofila, se reproducen por medio de espórulos, son inmóviles en su mayor parte y los que se mueven lo hacen por pestañas vibrátiles, el arsénico es tóxico para este tipo de microorganismos. En contraparte, los microbios animales son de forma irregular de líneas menos geométricas que se reproducen por división, todos se mueven por pseudópodos [Sic.] (ameboideo) y la estricnina conjunta a la quinina son venenosas para este tipo de microbios (13). Al hacer referencia a la reproducción bacteriana, en el capítulo V, en la sección de espórulo, Hernández describe que en los *Bacillus* el espórulo tiene aspecto de gota de grasa pequeña,

tal como lo refiere Koch. Sin embargo, otros autores describieron que la gota estaba formada por una sustancia albuminoidea (14).

Tratado segundo: Técnica bacteriológica general

Los colores de anilina se dividen según Ehrlich en colores ácidos, básicos y neutros. Los colores ácidos son aquellos formados por un ácido colorante, unido a una base coloreada o no; son los colorantes que tiñen difusamente el protoplasma celular, es decir, que no son colores electivos. Los más usados son la eosina, fluoresceína, la aurancia, la coccinina, la fucsina ácida, y el orange G. El picrocarmín de índigo es también colorante ácido, derivado del carmín. Los colores básicos son aquellos producidos por un ácido incoloro y una base colorante. Los colorantes básicos, que son sales con una base coloreada y un ácido incoloro, se unen a componentes celulares con carga negativa, como los ácidos nucleicos (ADN y ARN), que se encuentran principalmente en el núcleo, y son los propios colorantes de los microbios, los cuales toman el color a la manera de los núcleos celulares. Son muy numerosos y se dividen en violetas azules, rojos, verdes, brunos y negros. Los violetas más usados son el violeta de genciana, la tionina, el cristal violeta (violeta de genciana), el violeta de metilo B, el violeta de metilo 6B, el violeta Dahlia, y el violeta de París. Los azules son: el azul de metileno, el azul de quinoleína, el azul Victoria, y el azul policromático de Unna. Los rojos son la fucsina [Sic.], la rubina, el neutral Rotch y la safranina (15). Los verdes son el verde de metilo y la verde malaquita. Los brunos son el Bruno de bismarck y la vesuviana. Los negros son el negro colín y la indulina. Los colores neutros vienen de la mezcla de los ácidos y de los básicos. Para el empleo de soluciones que aumentaban la intensidad de coloración se usaban los mordientes, haciendo énfasis en la fucsina de Ziehl, el azul de metileno fenicado y azul alcalino de Kühne, el azul policromático fenicado de Unna, la tionina fenicada de Nicolle, el azul alcalino de Löffler, azul compuesto de Roux, el violeta anilinado de Erlich y el azul de borrel (16).

En este capítulo Hernández hace uso del método más utilizado hasta la fecha, la tinción de Gram que consiste en la colocación, fijación, coloración y decoloración, usando Violeta de genciana anilinado de Erlich. Esta se utilizada para diferenciar bacterias en dos grandes grupos: Gram positivas y Gram negativas, basándose en las propiedades de sus paredes celulares. El procedimiento implica la aplicación secuencial de un colorante primario, la violeta de genciana anilinado de Erlich, un mordiente el lugol, un decolorante como el alcohol o la acetona y un colorante de contraste como la safranina o fucsina. También era utilizado el método de Claudius que sigue la misma idea del método de Gram y es preparado con violeta de metilo 6B, solución saturada de ácido pícrico, agua destilada y cloroformo (17).

Para la coloración de los bacilos vivos se usaba el método tinción de Strauss que permite la visualización de flagelos bacterianos, mediante el uso de la solución de Ziehl diluida con tres o cuatro partes de agua colocada sobre la excavada de Koch y examinada al microscopio. Para colorear las pestañas de los bacilos, los más empleado era el método de Nicolle-Morat, una técnica microbiológica clásica utilizada para la visualización de bacterias intracelulares, especialmente en el estudio de *Brucella spp*. y otros microorganismos que se alojan dentro de células fagocíticas. Consiste en la toma de una pequeña cantidad de cultivo, se diluye con agua, luego se toma una gota y se extiende en una laminilla con alcohol el cual es flambeado y se deja secar a temperatura ambiente. Luego se tiñe con una mezcla de fucsina básica diluida en fenol y agua destilada [Sic.] y se calienta con el mechero de bunsen, se lava, se colorea con la solución de Ziehl y se observa el microscopio (18).

El método de Van Ermengen también conocido como tinción de Dieterle, es una técnica de tinción especial utilizada para visualizar microorganismos, específicamente espiroquetas, en muestras histológicas. Se basa en la impregnación argéntica de las espiroquetas, lo que significa que utiliza sales de plata para teñir y hacer visibles estas bacterias delgadas y difíciles de ver. El procedimiento implica varios pasos, incluyendo la fijación de la muestra, la impregnación con sales de plata, y el revelado para visualizar las espiroquetas. Este método de tinción es usado para estudiar bacilos preparando una emulsión de los microbios donde se fijan con ácido ósmico al 2 %, solución de tanino al 10 %,

ácido acético cristalizable, se lava en agua y en alcohol absoluto; una vez fijada la muestra se añade nitrato de plata cristalizado, agua destilada, ácido gálico, tanino, acetato de soda fundido, agua destilada y se agita hasta que adquiera un tinte negro, por último, se observa la muestra al microscopio (19).

José Gregorio Hernández describe en este capítulo el método para realizar preparaciones microscópicas de los tejidos (técnica histológica) que consiste en la fijación, inclusión, cortes con el microtomo y coloración simple o triple. Hacía uso del microtomo de Cambridge o el de Reichert donde se hacían finos cortes para adherirse a la lámina portaobjetos (20).

En el apartado del Método del Balón Común, el Dr. Hernández describe que en esta técnica se puede hacer el cultivo en la pipeta de Roux sin necesidad de hacer un vacío, para lo cual se debe enfriar bruscamente la probeta de caldo antes de sembrar los microbios. También acotó que en métodos de cultivo para anaerobios en medios sólidos se pueden añadir sustancias oxidables para favorecer su germinación (21). Al explicar la experimentación con animales, describe técnicas de contención como el uso del aparato de Czermak, en lugar de sostenerlos de forma manual. Así como el uso de mesas de vivisección de Jollyet, empleadas en la técnica fisiológica, para la experimentación con perros (22).

Al mencionar los microscopios, el Dr. Hernández incentiva su uso en la bacteriología, pero refiere que los microscopios de Zeiss en Yena y los de Leitz en Wetzlar son los mejores para esta área, además de resaltar la necesidad de que todos deben tener diafragma-iris, un iluminador de Abbe y un revólver, más oculares de Huygens del número 1 al 5, para que puedan ser de verdadera utilidad. A estas características se le suman los instrumentos empleados en histología, como láminas y laminillas, para poder realizar las preparaciones microscópicas (23).

Segunda parte: Bacteriología especial. Enfermedades comunes al hombre y los animales - Enfermedades propias del hombre.

En la segunda parte de *Elementos de Bacteriología*, el Dr. Hernández describe las enfermedades conocidas para la época y logra explicarlas de una manera didáctica al subdividir la información conocida en: Definición, enfermedad espontánea (en el humano) y experimental (inoculada en los animales del laboratorio), morfología del microorganismo, coloración, cultivos, biología, vacuna y seroterapia. Le atribuye el descubrimiento de la tuberculosis a Koch y describe que experimentalmente se pueden producir los tipos de enfermedad en animales. El tipo de Villemin: inoculando bajo la piel y el tipo de Gersin: inoculando de manera intravenosa. Describe que el bacilo se tiñe con coloración de Ziehl y Ehrlich y él añade los métodos de Gabbé y Fränkel para la doble coloración. Para la prueba de esputo se usa el método de Biedert y el método de Jousset es aplicado en sangre, pus y exudados serosos (24).

En el capítulo IV, Hernández habla de las "Estreptoccias" donde destaca que el suero de Marmorek contra este tipo de patógenos dan buenos resultados, pero en ocasiones no tanto, indica que en dos condiciones se obtiene éxito: realizar la inyección lo más pronto posible en el comienzo de la infección y continuar las inyecciones por mucho tiempo hasta que el microbio desaparezca (25).

El Capítulo V trata acerca del descubrimiento del bacilo del tétanos, obra del médico alemán Arthur Nicolaïer, quien, en 1885, logró aislar el agente causante de esta enfermedad: *Clostridium tetani,* y para separarlo de otros microbios se guía de la técnica de Kitasato, relata que adicional a la toxina "tetanina" hay un fermento o diastasa descoagulante llamado tetanolisina. Con respecto a la vacuna está de acuerdo con el método de Roux y Vaillard el cual combina la toxina antes mencionada con yodo; y finalizando el capítulo menciona que la curación del tétanos es muy difícil de impedir ya que se debe inocular el suero en la sustancia nerviosa (26).

Hernández hace alusión al Muermo donde no refiere información con respecto a la sintomatología y solo nombra dos casos: Kalming y Protopopoff (27). En el Capítulo VII hace referencia a la septicemia gangrenosa descubierta por Louis Pasteur en 1875 como complicación de traumatismos en el hombre y concluye en la sueroterapia que el suero de asno inmunizado hecho por Leclainche es antitóxico (28).

La difteria producida por el bacilo *Corynebacterium diphtheriae,* forma parte del Capítulo VIII, descubierto por Theodor Albrecht Edwin Klebs en 1883 y descrito por Loëffler. El Dr. José Gregorio Hernández propone el diagnóstico bacteriológico por examen microscópico, cultivos e inoculaciones y en cuanto a la vacuna destaca diferentes autores siendo el método de Roux y Nocard el indicado (29).

En el Capítulo IX la fiebre tifoidea se basa mayormente en la información proporcionada por Chantemesse y Widal (30). En la seroterapia de la fiebre tifoidea, describe que además del cultivo tífico, se puede utilizar sangre desecada disuelta con agua y caldo para cultivo para observar los bacilos aglutinados (31). Con respecto a la peste bubónica, caracteriza al suero antipestoso como aglutinante, diferenciándolo así del suero del enfermo, el cual puede o no aglutinar, y notando que es más probable que aglutine en las personas convalecientes (32).

Al describir el paludismo, hace referencia al doctor Santos A. Dominici, quien demostró en su trabajo "Contribución al estudio del hematozoario de Laveran en Venezuela" que el *Plasmodium vivax* es el microorganismo causante de la enfermedad en Venezuela. También describe el Método de Romanowsky como la mejor técnica de coloración para detectar la enfermedad (33). Otro trabajo al que hace referencia al hablar sobre la enfermedad del sueño (actual tripanosomiasis africana) es a la "Nota preliminar sobre la peste boba y la derrengadera de los equídeos de los Llanos de Venezuela'', publicado por el bachiller Rafael Rangel, en el cual demuestra que los tripanosomas son los causantes de dichas enfermedades (34).

CONCLUSIÓN

El Dr. José Gregorio Hernández fue el encargado de traer a Venezuela las bases fundamentales para la enseñanza de la medicina científica. Además, transmitió a sus estudiantes lo que hoy en día se conoce como los principios de bioética de la investigación científica, siendo considerado un médico adelantado para su época. La incorporación de dicha disciplina marcó un hito en la modernización de la medicina venezolana, contribuyendo a mejorar la salud pública y reducir la mortalidad causada por enfermedades infecciosas para la época, tales como la tuberculosis y la fiebre amarilla (35).

Él mismo cierra el prólogo de *Elementos de Bacteriología* diciendo: "Siempre hemos tenido el pensamiento con que Cruveilhier termina el prólogo de su Tratado de Anatomía: Que escribir una obra científica es propiamente entonar un canto de alabanza a la Gloria infinita de Dios, Creador del Universo" (36).

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La Gaceta Médica de Caracas hace 100, 50 y 25 años

The Gaceta Medica de Caracas 100, 50, 25 years ago

Dr. Enrique Santiago López-Loyo

Individuo de Número Sillón XXXI

Hace 100 años: julio – septiembre de 1925

El día 7 de julio de 1925 se publica el Número 13 del año XXXII de nuestra Gaceta Médica de Caracas, en la cual destaca una publicación intitulada "Malaria. Apuntes sobre su morbosidad, profilaxis y tratamiento en la cuenca del Lago de Maracaibo" bajo la autoría del Dr. Eugenio Pignat de Bellard Maldonado (Figura 1) quien era el director de los Hospitales de la Compañía petrolera estadounidense Beacon-Sun, incluyendo sus campos en los estados Zulia, Falcón, Trujillo, Mérida y Táchira. Describe que la topografía de la cuenca del Lago de Maracaibo tiene características distintivas al norte y al sur, mientras que al norte es selvática y de clima frío, el borde sur es caluroso y con áreas semidesérticas. El paludismo es endémico en la zona sur del lago y en la misma se despliegan continuas campañas de profilaxis con la distribución de dosis de quinina, a saber, de 0,65 g en obreros y entre 0,65 y 1,5 g a los extranjeros. Determina que como profiláctico la quinina falla en presencia de infecciones masivas de malaria. Se hace más difícil aún evitar las recidivas una vez que se infectan los individuos y adquieren resistencia al hematozoario. Describe las formas clínicas de infección por *Plasmodium vivax* y *falciparum*, siendo esta última la menos frecuente, ocupando el 16 % de todos los casos. Manifiesta que el tratamiento complementario se realiza con compuestos orgánicos de arsénico. Una de las complicaciones de la patología es la parálisis general y mencionan que para esta complicación ya en Estados Unidos y Europa se utiliza la inoculación artificial con "paludismo benigno" (1).



Figura 1. Eugenio Pignat de Bellard Maldonado (1883 - 1969)

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En el número 14 de la revista leemos un trabajo sobre "Gastrotomía por úlcera del estómago. Curación" bajo la firma del Dr. Henrique Toledo Trujillo (Figura 2). Presenta un caso clínico de una paciente femenina de 27 años con antecedentes de tuberculosis y dos partos. La paciente mostró un cuadro de dolor abdominal en el área epigástrica, inducido por la ingesta de sólidos. Se determina cuadro de hemorragia intestinal con abdomen agudo quirúrgico que motivó una intervención quirúrgica con resección de un tercio del estómago con el Método de Billroth con gastro-yeyunostomía transmesocólica de asa corta. Narra lo que fue una evolución satisfactoria. El Dr. Henrique Toledo Trujillo ingresó como miembro de la Academia Nacional de Medicina, ocupando el Sillón XIII, vacante por el fallecimiento del Dr. Luis Razetti, se incorporó en 1940 con el trabajo "Tratamiento actual del cáncer del cuello uterino". Por cierto, el Dr. Toledo Trujillo tuvo una destacada actuación en el cuidado del General Gómez, a través de numerosos cateterismos y atención de sus trastornos obstructivos prostáticos, y fue premiado con el otorgamiento del Ministerio de Salubridad, Agricultura y Cría, una vez dictado el Decreto Presidencial que creó el nuevo despacho. Al morir el General Juan Vicente Gómez, en diciembre de 1935, fue el encargado de embalsamar su cadáver. Se mantuvo en su cargo de Ministro de Salubridad, Agricultura y Cría en el primer gabinete del General Eleazar López Contreras hasta febrero de 1936 (2).

El 15 de agosto de 1925 se emite el número 15 y abre su edición con el Trabajo de Incorporación del Dr. Julio Carlos Rivas Morales, titulado "Simpatectomía Peri-arterial". En los primeros 4 capítulos se desarrollan los aspectos más importantes de esta técnica quirúrgica. En el primero se describen las reacciones fisiológicas y la génesis de la simpatectomía peri-arterial. Luego describe la técnica del procedimiento, en el capítulo 3 establece las indicaciones de la simpatectomía peri-arterial, para que en un cuarto capítulo haga un análisis de los casos tratados por él y sus observaciones (3).

La última edición de agosto de 1925, el número 16, completa el Trabajo de Incorporación antes descrito, describiendo su capítulo quinto para definir las afecciones en que la simpatectomía peri-arterial ha sido empleada (4).

En el número 17 de fecha 15 de septiembre de 1925, se identifica como contenido predominante el Juicio Crítico del Trabajo de Incorporación del Dr. Julio Carlos Rivas Morales, a cargo del Dr. Domingo Luciani (Figura 3). Destaca que el Recipiendario fue el primero en Venezuela



Figura 2. Dr. Henrique Toledo Trujillo (1885-1986).



Figura 3. Dr. Domingo Luciani (1886-1979).

en realizar este procedimiento quirúrgico, considerado muy avanzado en el primer tercio del siglo XX. Describe que la intervención fue radical en todos sus casos, como se atestigua en la doble reacción de vasoconstricción inicial y vasodilatación final, lo cual es un signo inequívoco de que la extirpación de la adventicia ha sido llevada a cabo en toda la periferia del tronco arterial. Con una dimensión de la zona denudada de 12 centímetros en 4 casos y de 10 cm en los dos restantes. Sin evidencias de complicaciones quirúrgicas (5).

La edición del número 18 se imprime el 30 de septiembre de 1925. Destaca el escrito del Dr. Juan de Dios Villegas Ruíz (Figura 4), Presidente en funciones de la Academia Nacional de Medicina, que lleva por título "La alimentación de los débiles y el tratamiento de la debilidad congénita". Inicia destacando que el fundamento de la terapia de los recién nacidos débiles estaba basado en el aseguramiento de un esquema de alimentación que permita su plena funcionalidad, desde recuperar el estado de óptima temperatura en condición de hipotermia, hasta la aplicación de terapias de suplementación de proteínas, o de antibióticos para combatir las infecciones oportunistas. Se debe considerar que el recién nacido débil no solo toma el seno o biberón igual al recién nacido normal, sino que en su estado de debilidad carece de fuerzas para chupar, mamar y deglutir. Ante esta realidad, el Dr. Villegas Ruíz define que el objetivo del equipo médico debe ser el rescate de estos pequeños pacientes para recuperar su potencialidad y así fortalecer su estado clínico que le permita retomar un adecuado crecimiento y desarrollo futuros (6).

Hace 50 años: julio – septiembre de 1975

En el libro que incluye los números 7, 8 y 9 de la Gaceta Médica de Caracas para su año LXXXII, encontramos un interesante trabajo bajo la autoría del Dr. Dante Borelli (Figura 5), nacido en la ciudad italiana de Parma y para el momento Profesor de la Cátedra de Micología Médica del Instituto de Medicina Tropical de la Universidad Central de Venezuela, considerado el padre de la micología médica venezolana. Este artículo lo titula "Tratamiento de las micosis" y en su contenido va clasificando las micosis y describiendo los tratamientos requeridos. Inicia con las micosis superficiales, las cuales requieren terapias tópicas por ser variadas y económicas, destacando el uso combinado de



Figura 4. Dr. Juan de Dios Villegas Ruíz (1868 - 1928).



Figura 5. Dr. Dante Borelli (1920-1998).

antisépticos queratolíticos, antisépticos sintéticos o semisintéticos que incluyen el tolnaftato, compuestos de pirrolnitrina. Otros usados son derivados sintéticos del imidazol como el miconazol y el clotrimazol, el antibiótico natamicina (Pinafucina) y el iodado haloprogin (Polik). Según su trabajo en el caso de la tiña, estas requieren complemento con aplicación de terapias sistémicas, siendo usada la griseolfulvina para la *tiña cápitis* no inflamatoria y la depilación manual con compresas boricadas con pomada queratolítica en los casos de *tiña cápitis* inflamatoria. Otras combinaciones se realizan en tratamientos de *tiña corporis*. Describe seguidamente la terapia de Pitiriasis versicolor con el uso fundamental de solución de hiposulfito por dos semanas con dos dosis por día. Por otra parte, en el eritrasma se recomienda el uso de loción queratolítica dos veces por día, en la pilonodosis se combinan lociones de sublimado corrosivo con loción queratolítica, en la candidiasis una variedad de opciones que incluyen solución bórica, nistatina, anfotericina B, miconazol, clotrimazol, natamicina y bioformo. En el caso de micosis profundas destaca la variedad de terapias que por su efecto sistémico de toxicidad deben ser adecuadamente indicadas y cuya duración de aplicación de las terapias es muy controlada. Por último, se estima que la cirugía puede ser una alternativa en lesiones de aspecto tumoral que pueden incluir la limpieza quirúrgica o las resecciones parciales o totales (7).

Hace 25 años: julio – septiembre de 2000

Para este período del año 2000, el número 3 de nuestra Gaceta Médica de Caracas se publica bajo la dirección del Dr. Oscar Agüero y la Presidencia de la Academia Nacional de Medicina del Dr. Pedro Manrique Lander (Figura 6). Podemos leer un artículo de los Dres. María Isabel Herrera y Francisco Herrera titulado "Apoptosis". Describen que la apoptosis es un término introducido en 1972 para designar la forma de muerte celular que se caracteriza por ser prolongada, morfológica y bioquímicamente diferente a la necrosis. Esta última se considera una forma de muerte violenta con hinchamiento celular, fragmentación del núcleo y ruptura final de la membrana. La definición de apoptosis se acuña como "muerte celular programada" y forma parte de la homeostasis celular como un proceso fisiológico que puede observarse en la organogénesis, en los tejidos dependientes de hormonas como el endometrio, las mamas y en la eliminación de timocitos reactivos, con destrucción selectiva de linfocitos T y B. También puede ser observada la apoptosis en las enfermedades neurodegenerativas, inmunológicas, virales y neoplásicas, eliminando células anormales o lesionadas por fenómenos físicos, químicos o biológicos.

Establecen que a diferencia de la necrosis, la apoptosis consume energía en forma de ATP y produce activación de las caspasas, que secuencialmente actúan degradando proteínas. La activación del sistema de caspasas para generar la apoptosis se hace por la intermediación de receptores específicos de las membranas celulares denominados "receptores de muerte celular". La destrucción celular pasa por cambios de su membrana con "arrugamiento" de su superficie, la cual genera segmentos empaquetados revestidos de esa membrana que se denominan "cuerpos apoptóticos". Por cierto, un aspecto que hoy se



Figura 6. Dr. Pedro Manrique Lander (1928-2007).

reconoce como una característica distintiva de la apoptosis en relación con la necrosis es que no produce una reacción inflamatoria en su proceso de cambios morfológicos (8).

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Vida de la Academia, Resúmenes de los trabajos presentados y Notas Bibliográficas

Life of the Academy, Summary of the papers presented and the Bibliographic Notes

Enrique Santiago López-Loyo

Individuo de Número, Sillón XXXI

VIDA DE LA ACADEMIA

FORO DE LA COMISIÓN DE PUERICULTURA Y PEDIATRÍA JUEVES 29 DE JUNIO DE 2025.

Conferencia 1: Biopsia líquida de leche.

Ponente: Dra. Elvia Badell Madrid (Figura 1).

Resumen

El cáncer de mama (C.A. de mama) es la neoplasia más frecuente en mujeres. En 2023, la Organización Mundial de la Salud (OMS) registró 144 casos/100 000 mujeres (mortalidad 22,7/100 000 habitantes). En Venezuela es la principal causa de muerte oncológica, con una incidencia de 8 691 casos y 3 515 muertes en 2023. La biopsia líquida (Bx. líquida), técnica para detección temprana de biomarcadores tumorales: ADN tumoral circulante (ADNct), en fluidos corporales como sangre, médula ósea y leche, identifica mutaciones asociadas al C.A. de mama 1 a 6 meses antes que métodos tradicionales hasta en 87 %, mejorando posibilidades de tratamiento y supervivencia. El C.A. de mama durante el embarazo o posparto tiene incidencia de 1/3 000 a 1/10 000 gestantes. De diagnóstico tardío con mayor riesgo de mortalidad. La lactancia reduce el riesgo de C.A. de mama en 4,3 % cada 12 meses, por la diferenciación celular y la apoptosis inducida durante este proceso. El microentorno de la mama lactante, rico en nutrientes y factores de crecimiento, favorece la proliferación de células tumorales existentes. La leche contiene la proteína inducida por prolactina (PIP), biomarcador útil en el diagnóstico histopatológico, y el ADNct, refleja alteraciones genómicas tumorales. La secuenciación de próxima generación (NGS) y la reacción en cadena de polimerasa (PCR) digital (ddPCR) permiten analizar mutaciones específicas en la leche con una sensibilidad de 71 % y especificidad de 100 %. La NGS identifica mutaciones subclonales responsables de recaídas; la ddPCR cuantifica ADNct con alta precisión. La OMS con la Iniciativa Global de Cáncer de Mama promueve reducir la mortalidad en 2,5 % anual para 2040, priorizando estos

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métodos. Futuras investigaciones explorarán: biomarcadores emergentes, integración clínica, inteligencia artificial. Conclusiones: El C.A. de mama en embarazo y posparto exige enfoques multidisciplinarios y técnicas adaptadas a poblaciones vulnerables. La biopsia líquida es un avance significativo en el diagnóstico precoz, no invasivo y accesible. Su implementación transforma la oncología mamaria en mujeres jóvenes, reduciendo la morbimortalidad asociada a diagnósticos tardíos.



Figura 1. Dra. Elvia Badell Madrid.

Conferencia 2: Calidad asistencial y seguridad del niño y adolescente hospitalizados

Ponente: Dr. Germán Rojas Loyola (Figura 2).

Resumen

La mejora de la calidad en la atención en salud es un proceso sistemático que busca identificar problemas, implementar cambios y elevar los



Figura 2. Dr. Germán Rojas Loyola.

estándares, con el objetivo de incrementar la seguridad, mejorar la coordinación de la atención y lograr mayor satisfacción tanto de pacientes como de profesionales. La Organización Mundial de la Salud (2020) definió la atención de alta calidad como aquella que es correcta, coordinada, responde a las necesidades y preferencias de los usuarios y minimiza daños y desperdicios de recursos, optimizando los resultados en salud. Por ello, la calidad debe ser una prioridad en la atención pediátrica, considerando que los niños también están expuestos a eventos adversos (EA). Aunque la incidencia de EA en niños es menor que en adultos, la proporción de casos evitables en el grupo pediátrico es mayor, debido a su vulnerabilidad y a la presencia de factores de riesgo intrínsecos que aumentan la probabilidad de EA ligados a la atención sanitaria. Sin embargo, existe una subestimación generalizada del problema de seguridad del paciente pediátrico (SPP). La Academia Americana de Pediatría (2011) recomendó no solo prevenir los EA, sino también identificarlos y notificarlos oportunamente. Además, abogó por promover las mejores prácticas, fomentar una cultura de seguridad y fortalecer la formación educativa de todos los profesionales sanitarios, incluyendo aquellos en formación, para reducir estos eventos

y garantizar una atención más segura y de calidad en la pediatría. La complejidad del sistema de salud actual aumenta el riesgo de errores, lo que hace esencial la implementación de una cultura de seguridad del paciente. La responsabilidad de los EA recae más en el diseño del sistema que en las acciones individuales. El daño en la atención sanitaria afecta a pacientes, profesionales y organizaciones. La seguridad del paciente debe estar en la agenda política para mitigar daños. Se necesita un liderazgo político claro y alianzas con actores clave para el éxito.

Presentación de un Aspirante a Invitado de Cortesía.

Conferencia 2: La medicina alemana como instrumento político del III Reich.

Ponente: Dr. Eliéxer Urdaneta.

Resumen

Adolf Hitler en su obra Mi Lucha (1925) expresó el concepto de «pueblo germano» como un organismo infectado que necesitaba ser purificado y sanado. Utilizó como referentes: El evolucionismo de Darwin, como primacía de la raza aria sobre las demás; y el eugenismo social, como la superioridad del más fuerte. Años después, en el poder, la terminología médica se incorporó a la ideología nazi, para medicalizar las políticas de Estado del III Reich y los judíos fueron señalados como parásitos, bacterias y raza enferma. Las Leyes de Núremberg (1935) proclamaron la depuración de la sangre del pueblo germano y con ello, el nazismo fundamentó el concepto de raza, al otorgarle a sus ciudadanos: carácter espiritual a su cuerpo y forma biológica a su alma, a fin de adquirir su identidad ideal. Así, el exterminio de los judíos se concibió como necesidad imperiosa del III Reich, ya que al cercenar el tejido social corrompido por ellos, Alemania obtendría su sanación. Además, la destrucción del judaísmo por la depuración racial a través de la Medicina, la Biología, la Filosofía y el Derecho juntos permitiría obtener la superioridad de Alemania y, con ello, remodelar la humanidad. En el siglo XX, el Holocausto, como fenómeno político-social inédito hasta entonces, reveló con todo su horror: el lado oscuro de la modernidad, los extremos de la inhumanidad del hombre y la débil estructura moral en la que se cimentaba la civilización.

SIMPOSIO DE LA COMISIÓN DE INTELIGENCIA ARTIFICIAL DE LA ACADEMIA NACIONAL DE MEDICINA: MEDICINA E INTELIGENCIA ARTIFICIAL

JUEVES 17 DE JULIO DE 2025.

Conferencia: La inteligencia artificial en la oftalmología.

Ponente: Dr. Oscar Beaujón Rubín (Figura 3)

Resumen

La inteligencia artificial (IA) está revolucionando el campo de la medicina, y la oftalmología no es la excepción. Su importancia radica en la capacidad de procesar vastas cantidades de datos con rapidez y precisión, permitiendo diagnósticos más certeros y tratamientos personalizados. Uno de los usos más destacados de la IA en oftalmología es el análisis de imágenes. Algoritmos avanzados pueden evaluar escáneres de retina, detectando signos tempranos de enfermedades como la retinopatía diabética, el glaucoma y la degeneración macular. Estos sistemas de IA suelen superar en precisión a los especialistas humanos, reduciendo así el margen de error y mejorando los resultados para el paciente. Además, la IA facilita el acceso y la democratización de servicios oftalmológicos de alta calidad en áreas remotas. Aplicaciones móviles conectadas a sistemas de IA permiten realizar evaluaciones oculares preliminares, disminuyendo la carga sobre los profesionales y enfocando los recursos en casos más críticos. El alcance de la IA en oftalmología también abarca la investigación y el desarrollo de nuevos tratamientos. Modelos predictivos ayudan a identificar moléculas efectivas para el desarrollo de fármacos o terapias innovadoras. Esto acelera el tiempo de investigación y desarrollo, abaratando costos y mejorando el acceso al tratamiento. En

el ámbito quirúrgico, la IA también juega un papel fundamental. Su aplicación en los microscopios quirúrgicos permite una mayor, mejor y más detallada visualización de las estructuras oculares, determinando una mejoría en los resultados finales. Sin embargo, la implementación de IA no está exenta de desafíos. La ética y la privacidad de los datos siguen siendo preocupación principal. Es vital asegurar que los datos utilizados para entrenar modelos de IA se manejen con el máximo cuidado, garantizando la confidencialidad del paciente. En conclusión, la inteligencia artificial está transformando la práctica oftalmológica, ofreciendo diagnósticos más rápidos, precisos y accesibles. A medida que la tecnología continúa avanzando, es esencial fomentar una colaboración estrecha entre tecnólogos y oftalmólogos para maximizar los beneficios y mitigar los riesgos, todo en favor de una atención ocular más eficaz y equitativa.



Figura 3. Dr. Oscar Beaujón Rubín.

PRESENTACIÓN DEL TRABAJO DE INCORPORACIÓN DEL DR. JOSÉ RODRÍGUEZ CASAS COMO INDIVIDUO DE NÚMERO PARA OCUPAR EL SILLÓN XXXVI

En Sesión Extraordinaria realizada el jueves 31 de julio de 2025 en las modalidades presencial en el Salón de Sesiones de la Academia Nacional de Medicina y virtual por las plataformas ZOOM y YouTube se procedió a la presentación del Trabajo de incorporación del Dr. José Rodríguez Casas (Figura 4) como Individuo de Número para ocupar el Sillón XXXVI, vacante por el fallecimiento del Académico Dr. Antonio Clemente H.

Se inicia la sesión con la verificación del quórum por parte del Secretario Académico Dr. Andrés Soyano López. El Presidente pronuncia las palabras de bienvenida y concede el derecho de palabra al Dr. Rodríguez Casas para la presentación de su Trabajo intitulado "Medicina, Mente Cuerpo y Psiconeuroinmunología".

En su trabajo propone una visión integral de la salud basada en la interrelación entre procesos psicológicos, neuroendocrinos e inmunológicos. Se fundamenta en décadas de experiencia clínica y académica, y expone cómo el estrés, las emociones y los factores psicosociales influyen en el desarrollo de enfermedades físicas. El autor recorre desde los inicios de la medicina psicosomática hasta los avances de la física cuántica, proponiendo una medicina holística que considere también la dimensión espiritual del ser humano. El trabajo se apoya en investigación clínica, evidencia científica y reflexiones personales.

Una vez culminada la presentación del trabajo, el Académico Dr. Marco Sorgi Venturoni, Individuo de Número Sillón III, procedió a realizar el juicio crítico al trabajo de incorporación. Incluye dentro de sus consideraciones que el trabajo de incorporación a la Academia Nacional de Medicina titulado "Medicina Mente-Cuerpo y Psiconeuroinmunología", escrito por el Académico Dr. José Rodríguez Casas, propone una visión integral de la salud basada en la interrelación entre procesos psicológicos, neuroendocrinos e inmunológicos. Se fundamenta en décadas de experiencia clínica y académica, y expone cómo el estrés, las emociones y los

factores psicosociales influyen en el desarrollo de enfermedades físicas. El autor recorre desde los inicios de la medicina psicosomática hasta los avances de la física cuántica, proponiendo una medicina holística que considere también la dimensión espiritual del ser humano. El trabajo se apoya en investigación clínica, evidencia científica y reflexiones personales. El trabajo se delinea como un mensaje impregnado de una invitación sutil y visión de progreso a una atención médica humana, progresista, optimista, ambiciosa en intenciones puras y profundamente personal, que recoge más de cinco décadas de experiencia clínica y académica en un campo aún poco explorado en la formación médica tradicional.

La psiconeuroinmunología es una nueva parcela de la ciencia que apenas lleva tres décadas, pero que en los últimos años ha sido objeto de una enorme atención por diversos grupos de investigación. El autor reivindica la dimensión espiritual como parte esencial de la experiencia humana y del proceso salud-enfermedad. Se propone integrar este aspecto dentro del modelo médico, superando la dicotomía entre cuerpo y alma. Se argumenta que la espiritualidad, entendida como búsqueda de sentido, conexión trascendente y reconocimiento de lo sagrado en la vida, puede fortalecer la resiliencia, el bienestar emocional y la capacidad de recuperación ante la enfermedad.

El Dr. Rodríguez Casas ha sido un defensor de la psiconeuroinmunología, una disciplina que estudia cómo los procesos emocionales, mentales y psicológicos impactan en el sistema inmunológico y, por ende, en la salud general del individuo. Ha propuesto que, mediante técnicas como la meditación, la visualización y la relajación, se puede potenciar la respuesta inmunológica, mejorando los resultados en pacientes con cáncer y enfermedades autoinmunes. Su trabajo clínico ha demostrado que estos enfoques conductuales pueden ser efectivos cuando se combinan con los tratamientos médicos convencionales. Sin embargo, los resultados de sus primeros estudios son limitados debido a muestras reducidas y carecen de validación estadística más amplia. A pesar de ello, su enfoque innovador ha generado interés y reconocimiento en el ámbito académico y médico venezolano.

Una vez terminadas ambas ponencias, se dio por terminada la sesión.

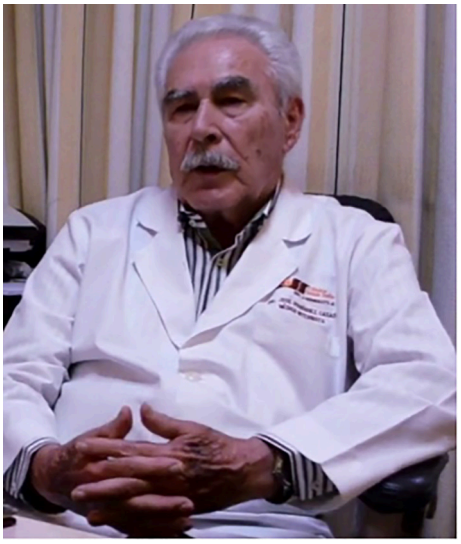


Figura 4. Dr. José Rodríguez Casas.

SESIÓN SOLEMNE DE JURAMENTACIÓN Y DISCURSOS DE INCORPORACIÓN Y RECEPCIÓN DEL DR. JOSÉ RODRÍGUEZ CASAS COMO INDIVIDUO DE NÚMERO SILLÓN XXXVI

En Sesión Solemne celebrada en el Paraninfo del Palacio de las Academias el jueves 7 de agosto de 2025, se procedió a la Juramentación y Discurso de Incorporación del Dr. José Rodríguez Casas (Figura 5) para ocupar el Sillón XXXVI como Individuo de Número. Para iniciar el protocolo de rigor, se procedió a realizar desde el pasillo de entrada de la Academia Nacional de Medicina la Marcha Académica encabezada por el recipiendario, acompañando a la Junta Directiva y al Cuerpo de Académicos, la cual culminó con su entrada al Paraninfo del Palacio de las Academias.

El Secretario informó que había cuórum para iniciar el acto y leyó el orden del día. El Presidente inició la Sesión y designó a dos

Individuos de Número para que acompañaran al Dr. José Rodríguez Casas al pódium, a fin de realizar su Juramentación y entrega del Diploma que le acredita como Individuo de Número Sillón XXXVI.

Seguidamente fue acompañado para pronunciar su Discurso de Incorporación desde el Púlpito de Santo Tomás. Inicia su discurso y destaca que es tradición reconocer a las personas que le han precedido en este sillón y han honrado esta Academia; faltan palabras para exaltar los méritos de ellos, los doctores David Iriarte y Antonio Clemente, excelsos médicos que han ocupado este sillón. El Dr. David Iriarte (1903-1994) nació en Maracaibo en 1903, fue director de la Gaceta Médica de Caracas, Tesorero de la Junta Directiva de la Academia de Medicina, Otorrinolaringólogo, Laboratorista Clínico, uno de sus estudios se basó en la contribución al estudio de la Flageliosis de las plantas en Venezuela. Ejerció en Maracaibo. Hizo cursos en Europa. Fundador del Laboratorio de la Clínica Razetti. Médico del Ministerio de Sanidad y Asistencia Social, jefe de la cátedra de ORL de la UCV, jefe de la cátedra de Microbiología y Parasitología de la Facultad de Odontología, publicó más de cien trabajos y cinco libros, Premios José Gregorio Hernández y Próspero Reverend. Orden del Libertador, Andrés Bello y José María Vargas. El Dr. Antonio Clemente (1927-2023), graduado de médico en la UCV, posgrado de Cirugía en la Universidad de Nueva York, Hospital San Vicente, Doctor en Ciencias Médicas de la UCV en 1962, Profesor del Servicio de Cirugía I del Hospital Universitario, jefe de cátedra de Cirugía III por concurso, jefe del Servicio de Cirugía IV del Hospital Miguel Pérez Carreño, vicepresidente del Instituto Venezolano de los Seguros Sociales, del cual fue su director de Docencia e Investigación, Presidente de la Academia Nacional de Medicina, con más de cuatrocientos trabajos publicados y veinticuatro condecoraciones.

A continuación, realizó un recuento histórico de su vida familiar y posterior fase profesional, destacando el importante papel de maestros como el Dr. Otto Lima Gómez como su gran ductor y ejemplo de compromiso y lealtad con la profesión y en especial con su especialidad.

Se pregunta: ¿por qué mi pasión hacia la Medicina Psicosomática?, para luego argumentar "Cuando estudiaba medicina en Buenos Aires, al hacer mi pasantía por la materia Psiquiatría, visité el Hospital Psiquiátrico y viví la experiencia en aquella época de los enfermos mentales, prácticamente en un hospicio, abandonados a los precarios tratamientos, donde la existencia de las drogas psicotrópicas era casi inexistente. A mi regreso, e iniciar mi experiencia con la Medicina Psicosomática, entendí, que los procesos de la mente, eran mucho más que los cuadros psicóticos, que existía otra forma de abordar los procesos de la salud mental mediante el diálogo e historia llamada Patobiográfica, introducida por Clauser; aprendí que el estrés puede causar enfermedad y trastornos mentales; que la palabra del médico puede curar, aliviar o enfermar, en fin, que nuestra presencia ante el enfermo es factor de curación y la misma, no puede ser sustituida por la tecnología, ni la cibernética. La relación médico-paciente es fundamental, única en medicina clínica y nunca podrá ser virtual".

Continúa su discurso manifestando que "Los procesos de la mente se elaboran en el llamado sistema límbico; las moléculas de neurotransmisores se liberan a ese nivel del cerebro para dar las respuestas sistémicas desde el punto de vista orgánico". Nuestras emociones y pensamientos no son materia, son energía y en consecuencia tenemos que aceptar que esos procesos se realizan en la dimensión cuántica, es decir, subatómica, en la cual se liberan las moléculas causantes de nuestras respuestas físicas, los síntomas, la alteración funcional y por qué no, la enfermedad".

Relató a continuación una experiencia personal muy determinante: "El otro aspecto que deseo relatar, es haber vivido la experiencia del médico como paciente; si, en cinco ocasiones muy graves, sufrí la experiencia y las angustias del paciente, la atención del médico en mi persona y ello me llevó a manifestar posteriormente, el agradecimiento hacia mis colegas y personal de enfermería, en el sentimiento de haber vivido mi papel de paciente, la atención y el apoyo ante la angustia y el temor que produce la enfermedad y sentir el don de la curación y satisfacción de recuperar la salud".

Para finalizar, destacó que "Estamos en el devenir de nuevos paradigmas médicos y, en consecuencia, somos espectadores y actores de una nueva medicina, donde el objetivo será el paciente en toda su integridad, un ser humano". La síntesis de esta integración es el amor que damos en la atención de nuestros pacientes. Amor que debe centrar todos nuestros actos de vida".

Al terminar este discurso, fue conducido a su asiento protocolar de donde fue retirada la cinta tricolor, significando la llegada del nuevo ocupante del Sillón XXXVI.



Figura 5. Dr. José Rodríguez Casas.

Seguidamente el Académico Dr. Rafael Muci-Mendoza (Figura 6), Individuo de Número Sillón XXII procedió a dar el Discurso de Bienvenida al Recipiendario.

El Dr. Muci-Mendoza inicia su discurso con una interrogante: "¿Qué es el médico?, "*Vir bonus medendi peritus*" es una frase latina que significa "un hombre bueno experto en curar". Se refiere a la idea de que un buen médico no solo debe poseer habilidades técnicas y conocimientos médicos, sino también cualidades morales y éticas, como la bondad, la empatía y la compasión, decían los antiguos, «perito en el arte de curar». El verdadero médico no puede serlo si en alguna medida no es también "patólogo", es decir, un hombre capaz de hablar adecuadamente de la enfermedad y del enfermo: unos, aspirantes a la originalidad: los genios creadores; otros, resignados a la epigonía: vale decir, a seguir las huellas de otro. Sin una constante alusión al hombre como un todo, con su psiquis, su soma y su mundo externo, al arte del diagnóstico, a la clasificación de las dolencias, a la teoría de la enfermedad, no es posible entender la estructura, el contenido y la intención de nuestra profesión".

Seguidamente relata la historia del Paraninfo del hoy Palacio de las Academias y del Púlpito de Santo Tomás. Describe los orígenes y la vida familiar del Dr. José Rodríguez Casas en un hogar donde las virtudes de honestidad, trabajo y compasión forjaron su personalidad y le prepararon para el reto de su formación como médico.

Describe que el doctor Rodríguez Casas es un «homo humanus de la antigüedad» a quien nada de lo humano parece serle ajeno, quien posee un «inquietum corda» llevando como blasón una vida ejemplar.

Destaca que llega el doctor Rodríguez Casas a la Academia en momentos críticos y dolorosos para la Medicina y, en general, para la ciencia y el academicismo nacionales. "El sistemático estrangulamiento de las academias y las universidades nacionales, y especialmente de la Universidad Central de Venezuela a través del regateo de recursos, la amenaza de la rapacería y la rastrera descalificación de sus autoridades, nos invita a resistir, a no permitir que nos invada el desánimo, a no flejar; la canalla ha querido, pero no ha podido vencer la reciedumbre de nuestras bases fundacionales, éticas y morales y, algún día, almorzarán festivos y despreocupados con sus compinches y cenarán en la noche con sus antepasados porque puedo asegurar que su futuro está detrás de ellos, porque son los platelmintos carnívoros más simples y probablemente los más primitivos".

Finaliza diciéndole al Doctor Rodríguez Casas que "la Academia Nacional de Medicina de Venezuela, cuerpo colegiado y máxima institución científica de la medicina nacional le abre de par en par sus puertas con la seguridad de que usted seguirá honrando lealmente el Sillón XXXVI que ocupó nuestro querido, admirado y bien recordado académico, hombre de bien, doctor Antonio Clemente Heimerdinger; y para todos y cada uno de nosotros, es motivo de justificado orgullo recibir a una personalidad de su talla moral y científica, y con ello, entregarle a nuestra querida patria su noble vocación de servicio y lo mejor de su talento".

Terminados los discursos, el Secretario Académico informa que se ha cumplido la agenda programada para esta Sesión Solemne y posteriormente el Señor Presidente anunció su finalización, invitando a un vino de honor a nombre del Recipiendario.



Figura 6. Dr. Rafael Muci-Mendoza.

RESÚMENES DE LOS TRABAJOS PRESENTADOS

Sesión Ordinaria del jueves 03 de julio de 2025

Preside: Dr. Huniades Urbina-Medina

Conferencia 1: Origen, evolución y razón de ser del Hospital Ortopédico Infantil, con motivo de su 80vo aniversario.

Ponente: Dr. Pablo Pulido Musche. Presidente de la Fundación HOI (Figura 7).

Resumen

Atendiendo la invitación de la Academia Nacional de Medicina, con motivo de los 80 años del Hospital Ortopédico Infantil, haremos una exposición del origen, evolución y razón de ser de la institución, la cual se inició en 1942, dadas las circunstancias por la epidemia de polio en el país. Surge la idea de Don Eugenio Mendoza y un grupo de colaboradores de abordar el mal que afectaba a los niños. La Fundación Venezolana contra la Parálisis Infantil se creó en 1945 con el fin de contribuir al estudio de acciones para combatir la pandemia. En el transcurso de los años, el Hospital fue creciendo hacia la especialización en Traumatología, desarrollándose como una institución privada, sin fines de lucro, sin ánimo de pérdida, cuyo objetivo primordial es la atención de niños y jóvenes entre 0 y 16 años, de limitados recursos económicos con problemas osteomusculares, así como adultos que solidariamente así lo requieran. Actualmente, cuenta con 47 especialidades médicas y servicios, contribuyendo a la atención en comunidades aledañas y provenientes de todo el territorio nacional. En Educación e Investigación, desde 1970, se cumplen las actividades educativas, en 1974, se crea el Posgrado Ortopedia Infantil y en 2003, los Programas de formación continua de "Fellowship" en Miembros Inferiores, en adición a otras actividades, así como reconocimientos por parte de instituciones colegiadas en medicina. El hospital hoy es un centro de referencia nacional en ortopedia, adecuándose a las necesidades reales de la población con innovación, educación

y tecnología de punta, reformulando su esquema operativo hacia la autosustentabilidad financiera. 80 años de labores ininterrumpidas, con más de 7 335 673 pacientes atendidos.



Figura 7. Dr. Pablo Pulido Musche.

Conferencia 2: Campamento Universitario Multidisciplinario de Investigación y Servicio, CUMIS UCV (Figura 8).

Ponente: Br. Andrés Sánchez Rodríguez.

Resumen

El Campamento Universitario Multidisciplinario de Investigación y Servicio (CUMIS) es un proyecto sin fines de lucro creado en 2014 por estudiantes de medicina de la Universidad Central de Venezuela, cuyo propósito es brindar asistencia sanitaria gratuita y especializada a las comunidades rurales e indígenas más vulnerables de nuestro país. Desde su fundación en 2014, CUMIS UCV ha realizado 30 jornadas, donde ha tenido la oportunidad de atender 23 859 pacientes, ofrecer 39 955 consultas gratis y especializadas. CUMIS se ha convertido en una ONG que visita 8 destinos diferentes en Venezuela, cuida de más de 5 etnias indígenas y que no solo ofrece atención médica, sino que incorpora a su equipo odontólogos y psicólogos. Actualmente, el equipo está conformado por estudiantes de medicina, odontología y psicología de destacadas universidades del país, que junto con especialistas de diversas áreas llevan a cabo jornadas para brindar atención integral a todos nuestros pacientes. La educación es una herramienta que transforma comunidades enteras; es por esto que, a través de charlas educativas en las tres áreas, medicina, odontología y psicología, logramos un cambio que perdure en el tiempo.



Figura 8. CUMIS: atención sanitaria en la población desasistida.