

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, Dys-metabolic 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 ("Major 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
Springer 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

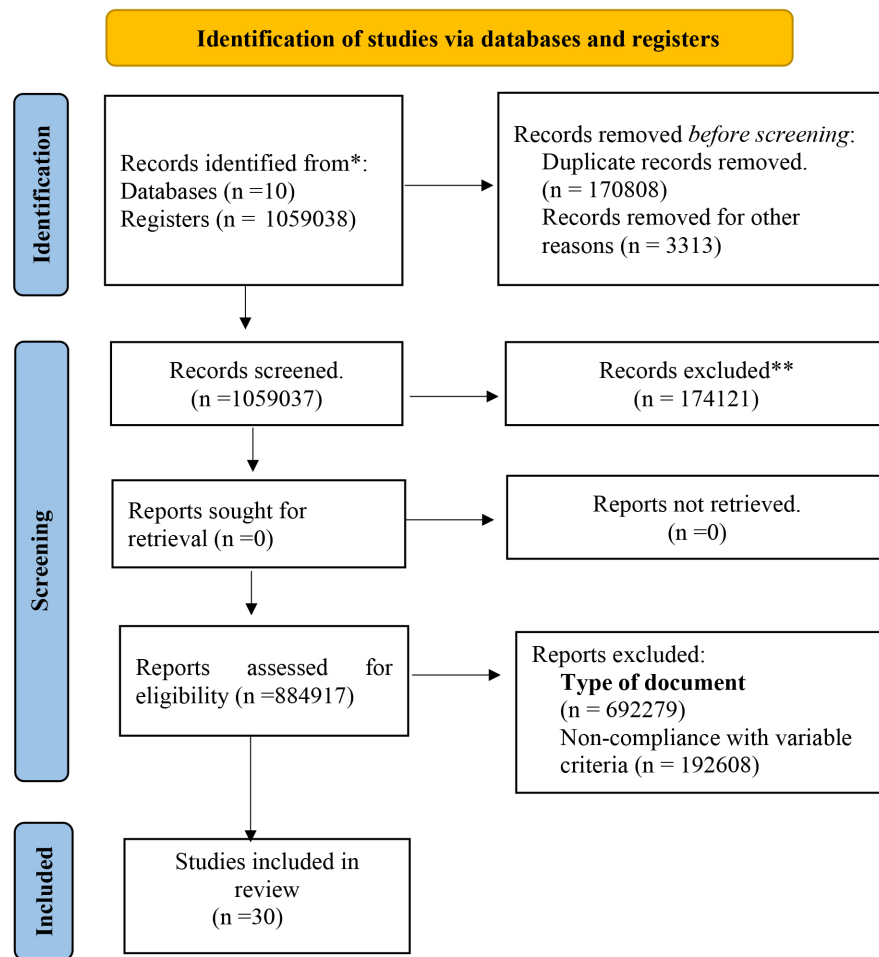


Figure 1. PRISMA flowchart.

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 items.

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-naïve patients with depressive disorders (35).	N a r e s h 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 alterations 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

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...continuation Table 6. Description of items.

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).	M e g a n 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).	Akılhoğlu 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).	P u l k i - 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

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...continuation Table 6. Description of items.

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

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...continuation Table 6. Description of items.

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 affection 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 cardiovascular 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: Duloxetine 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.

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...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).
	No report	Patients with depression often exhibit high levels of Metabolic Syndrome due to their typical lifestyle habits (30).
Woman	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

BIOCHEMICAL AND METABOLIC CHANGES

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 metabolic 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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