

Biopsychosocial determinants of cortisol levels in cervical cancer patients: the roles of spirituality, anxiety, and depression undergoing chemotherapy

Determinantes biopsicosociales de los niveles de cortisol en pacientes con cáncer de cuello uterino: el papel de la espiritualidad, la ansiedad y la depresión durante el tratamiento con quimioterapia

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SUMMARY

Introduction: In patients with cancer, spirituality plays a central role in coping with the emotional, psychological, and existential burdens associated with the disease. **Objectives:** This study aimed to examine the relationships between spiritual well-being and psychological outcomes, specifically anxiety and depression, as well as serum cortisol levels, as physiological stress markers, in cervical cancer patients undergoing chemotherapy. **Methods:** Employing a cross-sectional observational design, we included patients diagnosed with advanced-stage cervical cancer at a tertiary referral hospital, Dr. Wahidin Sudirohusodo General Teaching Hospital in Makassar, Indonesia. Data were assessed using validated instruments, i.e., the Zung Self-rating Anxiety Scale (SAS), the Zung Self-rating Depression Scale

(SDS), the Daily Spiritual Experience Scale (DSES), and laboratory measurements of serum cortisol levels.

Results: Of 56 female patients with advanced cervical cancer, the mean age was 44.4 ± 9.1 years. Most patients reported mild to moderate anxiety (55.4%) and mild depressive symptoms (62.5%). Additionally, the majority demonstrated moderate to high levels of spirituality (94.6%), and 80.4% had cortisol levels within the normal range. Bivariate analyses revealed significant inverse associations between spiritual well-being and both anxiety ($p = 0.019$) and depression ($p = 0.011$); however, the association with cortisol levels was not statistically significant ($p = 0.361$). Although multivariate analyses did not yield statistically significant results ($p > 0.05$), the overall trends suggested a potential protective effect of spirituality. **Conclusions:** Our findings indicate that spirituality may play a protective role in psychological well-being and stress regulation, although further research is required to elucidate its independent effects. Incorporating spiritual assessment and supportive interventions into holistic cancer care may help enhance mental health outcomes and overall quality of life during patients' treatment.

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RESUMEN

Introducción: *En los pacientes con cáncer, la espiritualidad desempeña un papel fundamental en el afrontamiento de las cargas emocionales, psicológicas y existenciales asociadas a la enfermedad.* **Objetivos:** *Este estudio tuvo como objetivo analizar las relaciones entre el bienestar espiritual y los resultados psicológicos —específicamente, la ansiedad y la depresión—, así como los niveles séricos de cortisol, marcadores fisiológicos de estrés, en pacientes con cáncer de cuello uterino sometidas a quimioterapia.* **Métodos:** *Se incluyeron pacientes diagnosticadas con cáncer de cuello uterino en estadio avanzado mediante un diseño observacional transversal en el Hospital General de Enseñanza Dr. Wahidin Sudirohusodo, un hospital terciario de referencia en Makassar, Indonesia. Los datos se evaluaron mediante instrumentos validados: la Zung Self-Rating Anxiety Scale (SAS), la Zung Self-Rating Depression Scale (SDS), la Daily Spiritual Experience Scale (DSES) y las determinaciones de laboratorio de los niveles séricos de cortisol.* **Resultados:** *De 56 pacientes con cáncer cervicouterino avanzado, la edad media fue de $44,4 \pm 9,1$ años. La mayoría presentó niveles de ansiedad de leves a moderados (55,4%) y síntomas depresivos leves (62,5%). Asimismo, la mayoría mostró niveles de espiritualidad moderados a altos (94,6%) y el 80,4% presentó niveles de cortisol dentro del rango normal. Los análisis bivariados revelaron asociaciones inversas significativas entre el bienestar espiritual y tanto la ansiedad ($p = 0,019$) como la depresión ($p = 0,011$); sin embargo, la asociación con los niveles de cortisol no fue estadísticamente significativa ($p = 0,361$). Aunque los análisis multivariados no mostraron resultados estadísticamente significativos ($p > 0,05$), las tendencias observadas sugirieron un posible efecto protector de la espiritualidad.* **Conclusiones:** *Nuestros hallazgos indican que la espiritualidad puede desempeñar un papel protector en el bienestar psicológico y en la regulación del estrés, aunque se requiere investigación adicional para esclarecer sus efectos independientes. La incorporación de la evaluación espiritual y de intervenciones de apoyo en un enfoque holístico de la atención oncológica podría mejorar los resultados en salud mental y la calidad de vida de las pacientes durante el tratamiento.*

Palabras clave: *Espiritualidad; Ansiedad; Depresión; Cortisol; Cáncer de cuello uterino; Quimioterapia*

INTRODUCTION

Mental health is a dynamic state of well-being that enables individuals to cope with life stressors, realize their abilities, learn, work productively, and contribute meaningfully to their communities. It encompasses more than the mere absence of mental disorders and is fundamental to overall

health and quality of life. In 2019, approximately 970 million people worldwide were affected by mental disorders, with a notable increase following the COVID-19 pandemic. Mental health is influenced by individual vulnerability and exposure to life stressors, including chronic illnesses such as cancer (1). Cervical cancer is a malignancy affecting the uterine cervix, with infection by the human papillomavirus (HPV) accounting for approximately 70% of cases. In 2020, cervical cancer was the fourth most common cancer among women globally, with an estimated 604,000 new cases and 342,000 deaths, predominantly in low- and middle-income countries. In Indonesia, there were 32,469 new cases and 18,279 deaths reported in the same year (2).

Cervical cancer not only increases mortality but also adversely affects the quality of life of survivors. Patients may experience sleep disturbances, fatigue, urological and gastrointestinal problems, sexual dysfunction, and psychological issues such as anxiety and depression. Anxiety and depression are highly prevalent among cancer patients, with a substantial burden observed in cervical cancer survivors (3,4).

If left unaddressed, anxiety and depression can exacerbate patients' conditions, reduce treatment adherence, and further impair quality of life. Survivors may experience persistent fatigue, heightened anxiety, and difficulties with concentration, which negatively impact both physical well-being and social functioning. Early identification of psychological disorders is therefore critical, despite challenges such as social stigma and limited time for healthcare providers (5). Screening and timely interventions for anxiety and depression are essential to optimize patient outcomes. Moreover, spirituality has been shown to alleviate anxiety and may contribute to improved survival and quality of life (6). Currently, data on anxiety, depression, and spiritual well-being among cervical cancer patients in Indonesia are limited. This study aimed to evaluate anxiety, depression, spirituality, and cortisol levels in patients before undergoing chemotherapy.

METHODS

This single-center, cross-sectional study included patients with advanced-stage cervical cancer who were consecutively recruited at the tertiary referral Dr. Wahidin Sudirohusodo General Teaching Hospital in Makassar, Indonesia, between January 2024 and January 2025. Psychological and spiritual assessments were conducted using validated instruments, including the Zung Self-Rating Anxiety Scale (SAS), the Zung Self-Rating Depression Scale (SDS), and the Daily Spiritual Experience Scale (DSES), as well as laboratory measurement of serum cortisol levels.

The study protocol was approved by the Biomedical Research Ethics Commission on Humans, Faculty of Medicine, Hasanuddin University, Makassar (Letter of Recommendation No. 263/UN4.6.4.5.31/PP36/2022; Protocol No. UH22050205), and was conducted in accordance with ethical standards for research involving human participants.

Statistical Analysis

Univariate analysis was performed to examine the distribution and frequency of the variables, and the results were presented in tabular form. In addition, bivariate analyses were conducted to assess relationships between variables. The Chi-square test was used to evaluate associations between categorical variables; if these assumptions were not met, Fisher's Exact test was applied. For numerical variables, Pearson correlation was used when the data were normally distributed, whereas Spearman's rank correlation was applied for non-normally distributed data. A p-value < 0.05 indicated a statistically significant result. All data were analyzed using SPSS ver.26.

RESULTS

Of 56 female patients with advanced cervical cancer, the mean age was 44.4 ± 9.1 years. Most patients were aged 40-60 years, accounting for

66.1% of the group. Most patients had a history of multiple births (multiparity and grand multiparity). Many patients started sexual intercourse at a young age, with 45.6% at age ≤ 18 years. The majority of patients were married (69.6%) and had more than 9 years of education. More than half of the patients were unemployed, as presented in Table 1.

Table 1. Baseline Characteristics of Study Participants

Characteristics	N = 56
Age (years)	44.4 \pm 9.1
• Adults (18-39 Years)	17 (30.4%)
• Middle Age (40-60 Years)	37 (66.1%)
• Elderly (> 60 years)	2 (3.5%)
Parity (ACOG)	
• Nulliparous (P0)	6 (10.7%)
• Primipara (P1)	4 (7.1%)
• Multipara (P2 – P4)	24 (42.9%)
• Grand Multipara (\geq P5)	22 (39.3%)
Age of First Sex	
• Never	1 (1.8%)
• Middle Age (≤ 18 years)	25 (44.6%)
• Early adulthood (19 – 24 years)	25 (44.6%)
• Adult age (≥ 25 years)	5 (8.9%)
Marital status	
• Not married yet	2 (3.6%)
• First	39 (69.6%)
• Second	15 (26.8%)
Education	
• ≤ 9 Years	21 (37.5%)
• > 9 Years	35 (62.5%)
Employment status	
• Employed	32 (57.1%)
• Unemployed	24 (42.9%)

Values are n (%) and mean \pm SD

Table 2 shows the distribution of anxiety, depression, spirituality, and cortisol levels among study participants. The psychospiritual health characteristics of cervical cancer patients show

Table 2. Distribution of Anxiety, Depression, Spiritual, and Cortisol Level among Study Participants

Characteristics	N = 56
Anxiety Level (SAS)	
• Normal (< 45)	16 (28.6%)
• Mild to Moderate (45-59)	31 (55.4%)
• Severe (60 – 74)	9 (16.1%)
Depression Level (SDS)	
• Normal (< 50)	12 (21.4%)
• Mild (50 – 59)	35 (62.5%)
• Moderate to Severe (60 – 69)	9 (16.1%)
Spiritual Aspects (DSES)	
• Low (15 – 40)	3 (5.4%)
• Intermediate (41-65)	26 (46.4%)
• High (66 – 90)	27 (48.2%)
Cortisol Levels	15.32 (0.76-50.97)
• Low (< 3.95 g/dL)	3 (5.4%)
• Normal (3.95-28.0 g/dL)	45 (80.4%)
• High (> 28.00 g/dL)	8 (14.3%)

Values are n (%) and median (Q1-Q3)

that most patients experience mild to moderate anxiety (55.4%), while 28.6% have normal anxiety levels, and 16.1% experience severe anxiety. Depression levels are more dominant in the mild category (62.5%), followed by normal depression (21.4%) and moderate-to-severe depression (16.1%). In terms of spirituality, the majority of patients have high (48.2%) or intermediate (46.4%) levels, with only 5.4% having low spirituality. Patients' cortisol levels were generally normal (80.4%), while 18.6% had abnormal cortisol levels, indicating stress-response problems.

The relationship analysis showed that patients with lower spirituality were more likely to experience higher levels of anxiety and depression, as presented in Tables 3 and 4. Patients with low spirituality also tended to have higher cortisol levels, although this relationship was not statistically significant.

Table 5 showed the logistic regression analysis with anxiety and depression levels as determinants and spiritual aspects as outcomes; the results were not significant.

DISCUSSION

Spirituality can protect individuals from anxiety and depression by increasing resilience to stress through social, emotional, and cognitive aspects. Spiritual practices, including meditation and prayer, have been shown to mitigate stress by activating the parasympathetic nervous system, thereby promoting physiological relaxation and emotional regulation. Cortisol, a hormone closely linked to the physiological stress response, can disrupt multiple aspects of brain function when elevated. Dysregulation of cortisol secretion has been associated with increased vulnerability to anxiety and depressive symptoms, underscoring its detrimental impact on mental health (6,7).

The results of the study show that most cervical cancer patients are aged 40–60 years, with a proportion of 66.1%. Cervical cancer is often diagnosed in women aged 35 to 44 years. The main risk factors include Human Papillomavirus (HPV) infection, hormonal changes, and lifestyle. Many patients began sexual activity at a young age. The majority of patients in this study were multiparous and grand multiparous, who are at higher risk due to physical changes caused by pregnancy. Marital status also had an effect, with married patients having a better prognosis. Most patients had more than 9 years of education, but many were unemployed. The low rate of early detection was due to limited awareness and access to health services (8).

Table 3. Relationship between Spiritual Aspects and Anxiety Levels in Cervical Cancer Patients

Normal		Anxiety Level			Total	p-value
		Mild to Moderate	Severe			
Spiritual Aspect	Low	0 (0.0)	1 (1.8)	2 (3.6)	3 (5.4)	0.019*
	Intermediate	4 (7.1)	18 (32.1)	4 (7.1)	26 (46.4)	
	High	12 (21.4)	12 (21.4)	3 (5.4)	27 (48.2)	
Total		16 (28.6)	31 (55.3)	9 (16.1)	56 (100.0)	

Values are n (%). *p<0.05

Table 4. Relationship between Spiritual Aspects and Depression Levels in Cervical Cancer Patients

Normal		Depression Level			Total	p-value
		Mild	Moderate to Severe			
Spiritual Aspect	Low	0 (0.0)	1 (1.8)	2 (3.6)	3 (5.4)	0.011*
	Intermediate	2 (3.6)	20 (35.7)	4 (7.1)	26 (46.4)	
	High	10 (17.9)	14 (25.0)	3 (5.4)	27 (48.2)	
Total		12 (21.4)	35 (62.5)	9 (16.1)	56 (100.0)	

Values are n (%). *p<0.05

Evidence suggests a significant association between spirituality and psychological well-being in cancer patients. Several studies report that individuals with higher levels of spirituality tend to exhibit lower levels of anxiety and depression. However, this relationship is not consistently observed across all investigations, indicating that the influence of spirituality on mental health may vary depending on methodological and contextual factors. Cortisol, a biomarker closely linked to stress, has also been associated with anxiety and depressive symptoms. Higher levels of spirituality have been shown to reduce cortisol concentrations, although these effects are not always statistically significant (9,10).

Research indicates that cancer patients with higher levels of spirituality tend to report lower levels of anxiety and depression. Anxiety commonly intensifies at the time of diagnosis, and adverse experiences during treatment further contribute to psychological distress and depressive symptoms. Spirituality appears to buffer these effects by fostering a sense of calm, enhancing meaning-making, and helping patients reinterpret their life purpose, thereby reducing anxiety. Similarly, spiritual beliefs and practices promote a more positive outlook that can mitigate depressive symptoms and improve overall quality of life. Despite these benefits, studies have not consistently demonstrated a

Table 5. Relationship between Anxiety Level and Depression Level with Spiritual

Variables	OR (95% CI)	Exp(B)	p-value
Anxiety level	0.826 (0.565—9.241)	2,285	0.246
Depression Level	1.753 (0.985—33.833)	5,773	0.052

significant association between spirituality and cortisol levels, even though spirituality is known to reduce perceived stress. Moreover, anxiety and depression do not appear to influence levels of spirituality, as patients often remain primarily focused on their illness. Neurobiological evidence suggests that spiritual activities—such as prayer and meditation—stimulate the release of neurotransmitters involved in mood regulation, attenuate stress responses, and enhance autonomic balance, thereby supporting more effective stress management and emotional regulation (11).

This study highlights the importance of a holistic approach to cervical cancer care, emphasizing the role of spirituality in reducing anxiety and depression. Spiritual support programs and psychosocial counseling can improve patients' quality of life. Policies should also focus on early detection and patient nutritional status. Research suggests a link between spirituality and anxiety, but some cases show discrepancies. Other factors, such as socioeconomic status and family support, may also influence outcomes. Further analysis is needed to understand this relationship (12).

CONCLUSION

These findings suggest that spirituality may play a protective role in psychological well-being and stress regulation, though further research is needed to confirm its independent effect. Incorporating spiritual assessments and interventions into holistic cancer care may help improve patients' mental health outcomes and overall quality of life during treatment.

ABBREVIATIONS

BDNF	Brain-derived neurotrophic factor
CIN	Cervical intraepithelial neoplasia
DSM-5:	Diagnostic and statistical manual of mental disorders
HADS	Hospital anxiety and depression scale
HPV	Human papillomavirus
HR-HPV	High-risk Human Papillomavirus
IMS	Sexually transmitted infections
LCR	Long control region
MDD	Major depressive disorder
PPDGJ	Guidelines for the classification and diagnosis of mental disorders in Indonesia
QoL	Quality of life
SAD	Separation anxiety disorder
SAS	Zung's Self-rating Anxiety Scale
SDS	Self-Rating Depression Scale
SIL	Squamous intraepithelial lesions
SSRI	Selective serotonin receptor inhibitors

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Authors' contribution

Conceptualization: VL, AMT, SR; Methodology: SNA; formal analysis and investigation: VL; writing-original draft: VL; writing—review and editing: VL, AMT, SR; resources and supervision: AMT, SR, SNA, SA, and RP; Validation: SA and RP. The authors read and approved the final manuscript.

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Availability of data and materials

Applicable upon request.

DECLARATIONS

Ethics approval and consent to participate

This research was approved by the Biomedical Research Ethics Commission on Humans of the Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia. Based on a letter of recommendation number: 263/UN4.6.4.5.31/PP36/ 2022, protocol number: UH22050205.

Competing interest

The authors declare that they have no competing interests.

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