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Association of Spirituality and Family Support with Depression and Serum Serotonin Levels in Cervical Cancer Patients: a Cross-Sectional Study

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KEYWORDS

Spirituality; Family Support; Serotonin; Depression; Cervical Cancer

ABSTRACT:

Introduction: Substantial physical, psychological, and social burden. Chemotherapy can trigger significant emotional distress, placing patients at increased risk of developing depression by underlying biological mechanisms. Serotonin, a key neurotransmitter involved in mood regulation, has been implicated in the pathophysiology of depression and may serve as a biological indicator linking cervical cancer–related stress and depressive symptoms.

Objectives: This study aimed to evaluate the association of spiritual aspects and family support with serum serotonin levels and depression status among cervical cancer patients following chemotherapy.

Methods: This cross-sectional study included cervical cancer patients who had completed two cycles of chemotherapy. Spirituality was assessed using the Daily Spiritual Experience Scale (DSES), family support was evaluated with the Family APGAR Score, and depression status was measured using the Zung Self-Rating Depression Scale (SDS). Serum serotonin levels were determined through laboratory analysis. Associations between variables were analyzed using Kruskal–Wallis and Chi-square tests, with statistical significance of $p<0.05$.

Results: Higher levels of spirituality were significantly associated with increased serum serotonin levels ($p = 0.012$) and lower depression severity ($p = 0.001$). Patients with healthy family function demonstrated significantly higher median serotonin levels compared with those with moderate or severe family dysfunction ($p < 0.001$). In addition, increasing depression severity was associated with progressively lower serotonin levels ($p < 0.001$).

Conclusions: Spirituality and family support are significantly associated with both biological (serotonin levels) and psychological (depression status) outcomes in cervical cancer patients after chemotherapy. These findings support a biopsychosocial–clinical approach to comprehensive cancer care.

1. Introduction

Cervical cancer remains a major global health burden and one of the leading causes of cancer-related morbidity and mortality among women worldwide [1, 2, 3]. Persistent infection with high-risk human papillomavirus is responsible for most cases [4, 5, 6]. Despite advances in screening and treatment, cervical cancer continues to disproportionately affect women in low- and middle-income countries [7, 8, 9]. Beyond its physical impact, cervical cancer is frequently associated with significant psychological distress. Depression is one of the most common mental health disorders in cancer patients and is known to negatively affect quality of life, treatment adherence, and clinical outcomes [10, 11, 12,

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13, 14, 15]. From a biological perspective, depression has been linked to dysregulation of neurotransmitters, particularly serotonin. Alterations in serotonin metabolism may reflect the interaction between psychological stress and neurobiological changes in cancer patients [16, 17].

In addition, psychosocial factors such as family support and spirituality play an important role in emotional well-being. Family support has been shown to improve coping mechanisms and psychological resilience, while spirituality provides meaning and emotional comfort during illness [18, 19, 20, 21]. However, studies integrating biological, psychological, and social aspects in cervical cancer patients remain limited. Therefore, this study aimed to evaluate the association of spirituality and family support with serum serotonin levels and depression status using a biopsychosocial approach.

2. Methods

Study Design and Setting

This study was an analytical comparative study using a cross-sectional design. The research was conducted at Dr. Wahidin Sudirohusodo General Hospital and affiliated network hospitals of the Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Hasanuddin. The study was carried out after obtaining approval from the institutional ethics committee of the Faculty of Medicine, Universitas Hasanuddin.

Study Population and Participants

The study population consisted of all patients diagnosed with advanced-stage cervical cancer who underwent chemotherapy at Dr. Wahidin Sudirohusodo Hospital and affiliated network hospitals. Eligible participants were cervical cancer patients with histopathological confirmation and clinical staging determined by gynecologic oncologists, who had completed at least two cycles of chemotherapy. Inclusion criteria were female patients aged >18 years, diagnosed with advanced-stage cervical cancer scheduled for neoadjuvant chemotherapy, without a history of other malignancies, able to read and understand Indonesian, and willing to participate in the study by providing written informed consent.

Exclusion criteria included patients with autoimmune diseases, pituitary tumors, adrenal tumors, other malignancies, diabetes mellitus, Cushing syndrome, impaired consciousness, prior radiotherapy, death before chemotherapy completion, use of medications affecting serotonin levels (such as selective serotonin reuptake inhibitors, serotonin–norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, triptans, or serotonin supplements), medical conditions that may influence serotonin levels (including severe hepatic or renal disorders or specific neuroendocrine diseases), extreme nutritional status, and severe sleep disorders under active treatment.

Participants were recruited consecutively from the accessible population during the study period.

Sample Size

The sample size was calculated using the Lemeshow formula for an unknown population size. With a confidence level of 90% (Z = 1.64), an estimated proportion of 0.5, and a margin of error of 10%, the minimum required sample size was 68 participants. Considering the availability of laboratory kits and potential data loss, a total of 80 participants were included in this study.

Variables and Measurements

The primary outcome variable was depression status, assessed using the Zung Self-Rating Depression Scale and categorized into no depression, mild depression, moderate–severe depression, and severe–extreme depression. Spiritual aspects were measured using the Daily Spiritual Experience Scale and classified as low, moderate, or high. Family support was evaluated using the Family APGAR Score and categorized as healthy family function, moderate dysfunction, or severe dysfunction. Serum serotonin levels were measured in nanograms per milliliter from peripheral blood samples. Sociodemographic and clinical variables included age, parity, age at first sexual intercourse, marital status, smoking history, educational level, nutritional status based on body mass index, occupation, and chemotherapy history.

Data Collection Procedures

Eligible patients were informed about the study objectives and procedures. Written informed consent was obtained prior to participation. Primary data were collected using the Zung Self-Rating Depression Scale, Daily Spiritual Experience Scale, and Family APGAR questionnaires, while secondary data were obtained from medical records. Peripheral blood samples were

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collected using standard procedures and sent to the hospital laboratory for serum serotonin analysis. All data were compiled and recorded for further analysis.

Validity and Reliability of Instruments

Validity and reliability testing were conducted prior to data collection. The Zung Self-Rating Depression Scale demonstrated good validity, with item correlation coefficients exceeding the minimum threshold and statistically significant p-values, and high reliability with a Cronbach's alpha of 0.875. The Daily Spiritual Experience Scale showed good validity and reliability with a Cronbach's alpha of 0.826. The Family APGAR Score demonstrated acceptable validity and reliability with a Cronbach's alpha of 0.770.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences. Univariate analysis was performed to describe the distribution and frequency of patient characteristics and serum serotonin levels. Data normality was assessed using the Shapiro–Wilk test. Bivariate analysis was conducted using the independent sample t-test for normally distributed data, the Mann–Whitney test for non-normally distributed data, and the Chi-square test for categorical variables. Statistical significance was set at a p-value of <0.05.

Ethical Considerations

Ethical approval was obtained from the institutional ethics committee prior to study initiation. Written informed consent was obtained from all participants. Confidentiality and anonymity were ensured by coding all participant data, and participants were allowed to withdraw from the study at any time without any consequences.

3. Results

Participant Characteristics

A total of 88 cervical cancer patients who met the inclusion and exclusion criteria were included in this study. The mean age of participants was 45.24 ± 9.80 years. Most patients were classified as middle-aged (40–60 years), accounting for 57 patients (64.8%), followed by adults aged 18–39 years (27.3%) and geriatric patients aged over 60 years (8.0%). Regarding parity, the majority of patients were multiparous (P2–P4) with 43 patients (48.9%), followed by grand multiparous (P≥5) with 29 patients (33.0%). The mean age at first sexual intercourse was 19.05 ± 4.20 years, with most patients reporting first sexual activity before the age of 18 years (47.7%) or between 19 and 24 years (42.0%).

Table 1. Characteristics of Study Subjects

No	Characteristics	Mean (SD) / n (%)
1	Age (years)	45.24 ± 9.80
	Adult (18–39 years)	24 (27.3%)
	Middle-aged (40–60 years)	57 (64.8%)
	Geriatric (>60 years)	7 (8.0%)
2	Parity	
	Nulliparous (P0)	9 (10.2%)
	Primiparous (P1)	7 (8.0%)
	Multiparous (P2–P4)	43 (48.9%)
	Grand multiparous (P≥5)	29 (33.0%)
3	Age at first sexual intercourse (years)	19.05 ± 4.20
	Never	1 (1.1%)
	Adolescence (<18 years)	42 (47.7%)
	Early adulthood (19–24 years)	37 (42.0%)
	Adulthood (>25 years)	8 (9.1%)
4	Marital status	
	Unmarried	2 (2.3%)
	First marriage	58 (65.9%)
	Second or more	28 (31.8%)
5	Smoking history	
	Non-smoker	76 (86.4%)
	Smoker	12 (13.6%)
6	Educational level	
	Primary education	19 (21.6%)
	Secondary education	41 (46.6%)
	Higher education	28 (31.8%)
7	Nutritional status (BMI)	
	Underweight	12 (13.6%)
	Normal	66 (75.0%)
	Overweight	6 (6.8%)
	Obese I	4 (4.5%)

Most participants were in their first marriage (65.9%), while 31.8% had been married twice or more. The majority of patients were non-smokers (86.4%). In terms of educational level, most patients had secondary education (46.6%), followed by higher education (31.8%). Nutritional status based on body mass index showed that most patients had normal BMI (75.0%). Clinically, 67% of patients reported no complaints during data collection. The majority of cases were classified as advanced-stage cervical cancer (IIB–IVB) (75.0%). Histopathological examination revealed that non-keratinizing squamous cell carcinoma was the most common subtype (50.0%), followed by cervical adenocarcinoma (27.3%).

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Distribution of Spirituality, Family Support, Depression Status, and Serum Serotonin Levels

Assessment of spiritual aspects using the Daily Spiritual Experience Scale showed that most patients had moderate spirituality (56.8%), followed by high spirituality (27.3%) and low spirituality (15.9%). Family support evaluation using the Family APGAR Score indicated that half of the patients had healthy family function (50.0%), while 35.2% had moderate dysfunction and 14.8% had severe dysfunction. Based on the Zung Self-Rating Depression Scale, most patients were classified as not depressed (59.1%). Mild depression was observed in 21.6% of patients, moderate–severe depression in 17.0%, and severe–extreme depression in 2.3%. Serum serotonin analysis demonstrated a mean level of 41.56 ng/mL, with values ranging from 2.35 to 806.40 ng/mL

Table 2 Distribution of Spiritual Aspects, Family Support, Depression Level, and Serotonin Levels

No	Characteristics	Mean (SD) / n (%)
1	**Daily Spiritual Experience Scale (DSES)**	
	Low spirituality	14 (15.9%)
	Moderate spirituality	50 (56.8%)
	High spirituality	24 (27.3%)
2	**Family APGAR Score**	
	Healthy family function	44 (50.0%)
	Moderate dysfunction	31 (35.2%)
	Severe dysfunction	13 (14.8%)
3	**Zung Self-Rating Depression Scale (SDS)**	
	No depression	52 (59.1%)
	Mild depression	19 (21.6%)
	Moderate–severe depression	15 (17.0%)
	Severe–extreme depression	2 (2.3%)
4	**Blood serotonin level (ng/mL)**	41.56 (2.35–806.40)

Association Between Spirituality, Family Support, and Serum Serotonin Levels

Analysis using the Kruskal–Wallis test demonstrated a statistically significant association between spirituality level and serum serotonin levels ($p = 0.012$). Patients with low spirituality had the lowest median serotonin level (4.31 ng/mL), whereas patients with moderate spirituality had a higher median level (8.24 ng/mL). The highest median serotonin level was observed in patients with high spirituality (20.30 ng/mL). Similarly, family support was significantly associated with serum serotonin levels ($p < 0.001$). Patients with healthy family function exhibited the highest median serotonin level (12.50 ng/mL), followed by those with moderate dysfunction (7.22 ng/mL) and severe dysfunction (4.28 ng/mL).

Table 3 Association Between Spiritual Aspects, Family Support, and Serotonin Levels in Cervical Cancer Patients

Category	n	Median	Minimum	Maximum	p-value
Spirituality Level					
Low	14	4.31	2.36	5.37	0.012*
Moderate	50	8.24	5.25	13.87	
High	24	20.30	13.22	806.40	
Family Function					
Healthy	44	12.50	7.01	806.40	
Moderate dysfunction	31	7.22	4.77	68.19	<0.001*
Severe dysfunction	13	4.28	2.36	8.86	

**Kruskal–Wallis analysis, sig. p<0.05.*

Association Between Spirituality, Family Support, and Depression Status

A significant association was observed between spirituality level and depression status ($p = 0.001$). All patients with high spirituality were classified as not depressed. In contrast, patients with low spirituality predominantly experienced moderate–severe or severe–extreme depression. Family support was also significantly associated with depression status ($p = 0.005$). All patients with healthy family function were classified as not depressed. Conversely, patients with severe family dysfunction predominantly experienced moderate–severe or severe–extreme depression.

Table 4 Association Between Spiritual Aspects, Family Support, and Depression Level in Cervical Cancer Patients

Category	No Depression	Mild Depression	Moderate–Severe Depression	Severe–Extreme Depression	p-value
Spirituality Level					
Low	0 (0.0%)	2 (2.3%)	10 (11.4%)	2 (2.3%)	0.001*
Moderate	28 (31.8%)	17 (19.3%)	5 (5.7%)	0 (0.0%)	
High	24 (27.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Family Support					
Healthy	44 (84.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0.005*

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Category	No Depression	Mild Depression	Moderate–Severe Depression	Severe–Extreme Depression	p-value
Moderate dysfunction	8 (15.4%)	19 (100.0%)	4 (26.7%)	0 (0.0%)	
Severe dysfunction	0 (0.0%)	0 (0.0%)	11 (73.3%)	2 (100.0%)	

**Pearson Chi-square analysis, sig. p<0.05.*

Association Between Depression Status and Serum Serotonin Levels

Patients without depression had the highest median serotonin level (12.77 ng/mL). Median serotonin levels progressively decreased with increasing depression severity, reaching the lowest level in patients with severe–extreme depression (3.32 ng/mL). Kruskal–Wallis analysis revealed a statistically significant association between depression status and serum serotonin levels ($p < 0.001$).

Table 5 Association Between Depression Level and Serotonin Levels in Cervical Cancer Patients

Depression Level	n	Median	Minimum	Maximum	p-value
No depression	52	12.77	7.01	806.40	<0.001*
Mild depression	19	7.02	4.77	9.68	
Moderate–severe depression	15	4.70	2.76	8.86	
Severe–extreme depression	2	3.32	2.36	4.28	

**Kruskal–Wallis analysis, sig. p<0.05.*

4. Discussion

The present study demonstrates that spirituality and family support are significantly associated with serum serotonin levels and depression severity among cervical cancer patients following chemotherapy. These findings are broadly consistent with prior psychosocial oncology research showing that non-clinical factors play a substantial role in mental health outcomes among cancer patients; however, this study extends existing evidence by integrating a biological marker serum serotonin into the analysis [22, 23].

Previous studies have consistently reported that spiritual well-being is associated with better psychological outcomes and quality of life in cancer patients. Coleman et al. emphasized that dimensions of spirituality related to meaning and inner peace, rather than religious affiliation or ritual practices, are most strongly associated with reduced depressive symptoms (24). The findings of the present study align with this conceptualization, as higher spirituality levels were associated with lower depression severity. What distinguishes this study from prior work is the demonstration that higher spirituality is also associated with higher serum serotonin levels, suggesting a potential biological pathway through which spiritual coping may influence emotional well-being. Earlier research has largely examined spirituality and depression as psychological constructs without incorporating neurobiological correlates. In contrast, our findings suggest that spirituality may be linked not only to subjective emotional states but also to objective biological regulation. This observation is consistent with evidence showing that stress-reducing psychosocial interventions, such as cognitive behavioral therapy or mindfulness-based approaches, can modulate serotonin levels in cancer patients [25, 26].

The association between family support and depression observed in this study is consistent with a substantial body of literature emphasizing the protective role of family functioning in cancer populations. Prior studies have shown that healthy family dynamics are associated with lower anxiety, lower depression scores, and better overall quality of life among patients with advanced cancer [27, 28, 29]. Our results confirm these associations in cervical cancer patients and further demonstrate that better family support is associated with higher serum serotonin levels. This biological association has been infrequently explored in previous studies, which have predominantly focused on psychosocial outcomes alone.

In contrast to some earlier studies that reported mixed or indirect associations between social support and biological stress markers, the present study identified a clear gradient: patients with healthier family function exhibited higher median serotonin levels, whereas those with severe family dysfunction showed the lowest levels. This finding suggests that sustained emotional and instrumental support from family members may buffer chronic stress responses that are known to disrupt serotonergic regulation [30, 31].

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The observed inverse relationship between serum serotonin levels and depression severity in this study is consistent with established neurobiological models of depression. Reviews by Jauhar et al. have documented consistent abnormalities in serotonergic activity among patients with untreated depression, including reduced presynaptic serotonin signaling and altered tryptophan metabolism [32].

Our findings align with these models and extend them to cervical cancer patients undergoing chemotherapy, a population exposed to additional physiological and psychological stressors. Notably, while previous studies have reported inconsistent associations between peripheral serotonin levels and depressive symptoms, the graded relationship observed in this study strengthens the biological plausibility of serotonin as a relevant marker in this clinical context. Differences across studies may be explained by heterogeneity in patient populations, cancer treatments, timing of measurements, and exclusion of confounding factors such as antidepressant use, which was carefully controlled in the present study [33, 34]. This integrative biopsychosocial–clinical perspective provides a more comprehensive understanding of depression in cervical cancer patients and underscores the importance of holistic care strategies [35, 36].

5. Conclusion

This study demonstrates significant associations between spirituality, family support, serum serotonin levels, and depression status among cervical cancer patients following chemotherapy. Higher levels of spirituality and better family support were associated with higher serum serotonin levels and lower depression severity. Additionally, lower serotonin levels were associated with more severe depressive symptoms. These findings support the relevance of a biopsychosocial–clinical approach in the comprehensive management of cervical cancer patients.

6. Declaration

Conflict of Interest

This study was conducted as part of a postgraduate thesis at the Faculty of Medicine, Universitas Hasanuddin. The authors declare no conflicts of interest related to this study.

Ethical Approval

This study was approved by the Ethics Committee of the Faculty of Medicine, Universitas Hasanuddin. All procedures involving human participants were conducted in accordance with the ethical standards of the institutional research committee and with the principles of the Declaration of Helsinki.

Informed Consent

Written informed consent was obtained from all participants prior to their inclusion in the study.

Data Availability Statement

The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Authors Contribution

RB, RPA, and NUP conceptualized the study and developed its overall design. RB, RPA, and ECJ established the methodology and research planning. Data collection and investigation were carried out by RB, NUP, and LML while NUP, SR, and LML provided clinical supervision and oncological interpretation. Statistical analysis and data interpretation were conducted by RB and ECJ. Validation of instruments and data quality control were performed by RB, ECJ, and RPA. The initial manuscript was drafted by RB, ECJ, SR, and LML while RPA and NUP provided critical revision of the manuscript for important intellectual content. All authors read and approved the final version of the manuscript.

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