

ORIGINAL RESEARCH

Correlation Analysis of Estrogen Levels and Psychological Status Among Patients with Uterine Fibroids

Lianqin Cheng, BM; Mei Cheng, BM; Lijun Ye, BM; Boyao Xia, BM; Shan Xu, BM

ABSTRACT

Objective • This study aims to investigate the correlation between estrogen levels and psychological distress, focusing on depression and anxiety symptoms among patients diagnosed with uterine fibroids.

Methods • The study employed a retrospective design and enrolled a cohort comprising 50 patients diagnosed with uterine fibroids and 50 healthy individuals as controls. Serum estradiol levels were quantified using a chemiluminescent immunoassay technique one month before surgery in the patient group. Depression and anxiety levels were evaluated using the Self-Rating Depression Scale (SDS) and the Self-Rating Anxiety Scale (SAS), respectively.

Results • Significant differences in SDS scores, SAS scores, and serum estradiol levels emerged between the patient and control groups ($P < .05$). Patients exhibited higher SDS and SAS scores alongside elevated serum estradiol levels. Correlation analysis unveiled a negative association between SAS scores and estrogen levels among patients

($r = -0.724$, $P = .013$), suggesting a rise in anxiety levels with declining estrogen levels. Similarly, a negative correlation surfaced between SDS scores and estrogen levels among patients ($r = -0.624$, $P = .016$), indicating increased depressive symptoms as estrogen levels decrease. Conversely, no noteworthy correlations were demonstrated between anxiety or depressive symptoms and estrogen levels in the control group.

Conclusion • Reduced estrogen levels were linked to heightened anxiety and depressive symptoms in patients with uterine fibroids. These findings suggest a plausible connection between estrogen hormone levels and psychological well-being, particularly concerning anxiety and depression. Further exploration of this association is warranted to shed light on potential therapeutic interventions targeting hormonal regulation to improve psychological distress in affected individuals. (*Altern Ther Health Med*. [E-pub ahead of print.])

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INTRODUCTION

Uterine fibroids are the most prevalent benign tumors of the female reproductive system, typically occurring during the childbearing years and rarely before puberty, with a tendency to shrink or disappear after menopause.¹ The development of uterine fibroids is believed to be influenced by female sex hormones, with both clinical and biological studies suggesting that estrogen plays a crucial role in their growth.^{2,3} Common symptoms associated with uterine

fibroids include shortened menstrual cycles, increased menstrual flow, irregular bleeding, and secondary anemia.⁴

Uterine fibroids can significantly impact fertility, potentially resulting in infertility and recurrent miscarriages. During pregnancy, these fibroids have the propensity to grow rapidly and can lead to obstructed labor, often necessitating cesarean section.⁵ Moreover, complications such as postpartum bleeding, fetal malpresentation, and abnormalities may arise, posing substantial risks to women's health.⁶ One of the primary reasons uterine fibroid patients of childbearing age may opt for a hysterectomy is the multitude of effects it can have on their well-being. Hysterectomy can lead to the loss of physiological sensation, evoking a sense of incompleteness, while the accompanying physical changes may induce confusion and negative emotions.⁷

Moreover, hysterectomy can precipitate endocrine disruption. The uterus serves as a vital endocrine organ pivotal in estrogen regulation. However, its removal triggers a sudden decline in estrogen levels among women,

culminating in imbalances within the endocrine system. Consequently, a spectrum of estrogen-related complications may develop, including premature onset of menopause, osteoporosis, and cardiovascular diseases.⁸

Uterine fibroids can exert a notable influence on patients' sexual lives, primarily through their effect on estrogen secretion. Many patients report reduced libido, vaginal dryness, and related concerns attributable to alterations in reproductive organs and decreased estrogen levels.⁹ Consequently, the quality of their sexual experiences may markedly decline. This decline not only impacts personal satisfaction and relationship quality but also contributes to adverse effects on their mental well-being.^{8,9}

Beyond its physiological implications, hysterectomy also encompasses profound psychological and social implications for patients. For numerous women, the uterus symbolizes female identity and embodies feminine characteristics.¹⁰ Therefore, its removal may evoke a sense of identity confusion and self-acceptance challenges, potentially leading to adverse effects on self-esteem and emotional equilibrium. Additionally, societal norms and expectations regarding fertility and motherhood can further exacerbate pressure and distress among affected individuals.¹¹

This study employed an innovative approach to investigating uterine fibroids, conducting a comprehensive analysis that goes beyond the physiological symptoms of these common benign tumors to explore their psychological impact on patients. Previous studies primarily focused on the physical and fertility-related implications of fibroids. However, this study stands out by highlighting the significance of mental health by investigating the relationship between preoperative anxiety, depression, and estrogen levels in patients.

This innovative perspective aims to explore the complex relationship between hormonal imbalances and psychological well-being, providing insights into personalized and comprehensive treatment strategies. By emphasizing the substantial impact of fibroids and their treatment on sexual and reproductive health, as well as their broader implications for patients' overall quality of life, the study establishes a precedent for future research and clinical interventions. These approaches address both the physical symptoms of the condition and the significant psychological distress it can cause. It can pave the way for integrated care strategies that greatly improve patient outcomes.

METHODS

Study Design

This study utilized a retrospective analysis to examine preoperative anxiety, depression status, and estrogen levels among 50 patients diagnosed with uterine fibroids at our hospital. The experimental group comprised individuals treated at our facility from January 2020 to May 2021. A control group consisting of 50 healthy individuals was also included for comparison. Ethical approval was obtained from the Ethics Committee of The First People's Hospital of Linan for this study.

Inclusion and Exclusion Criteria

Inclusion criteria were as follows: (1) a confirmed diagnosis of uterine fibroids through pathological examination conducted by experts; (2) absence of any lesions in the ovaries; (3) no use of hormone drugs or drugs affecting prolactin levels within three months prior to admission; (4) no history of artificial abortion; (5) delivery, or breastfeeding in recent years; (6) clear consciousness; (7) normal speech; and (8) voluntary participation with informed consent. Patients meeting any of the following criteria were excluded from the study: (1) severe cognitive impairment; (2) mental disorders; (3) speech expression defects; (4) presence of tumors in the pelvic appendix resulting from metastasis from other primary tumors; (5) patients undergoing chemotherapy; and (6) those categorized as terminally ill or extremely weak.

Demographics and Clinical Characteristics of Patients

Among the 50 selected inpatients with uterine fibroids, all met the inclusion criteria, with an age range of 18 to 55 years and an average age of 39.5 ± 5.5 years. Educational levels were distributed as follows: 12 cases of primary school, 21 cases of middle school, and 15 cases of junior college or above. At the same time, a control group of 50 healthy individuals who underwent physical examinations during the same period was selected. The control group had an age range of 20 to 54 years and an average age of 38.9 ± 5.2 years. Educational levels in the control group were distributed as follows: 14 cases of primary school, 20 cases of middle school, and 14 cases of junior college or above. No statistically significant differences were observed in age and educational level between the two groups ($P > .05$), refer to Table 1.

Serum Estradiol Measurement

Serum estradiol levels during the follicular phase were measured in the patients one month prior to surgery. Fasting venous blood samples (3 mL) were collected from the elbow vein between 7-8 AM. These samples were centrifuged within 2 hours to separate the serum, which was then stored at -80°C . Serum estradiol levels were measured using a chemiluminescent immunoassay method, employing assay kits provided by Abbott Laboratories, USA.

Assessment of Depression and Anxiety Levels

The depression levels of hospitalized patients with uterine fibroids were evaluated using the Self-Rating Depression Scale (SDS), which comprises 20 items, including 10 reverse-scored

Table 1. Demographic Characteristics of Study Participants

Category	Uterine Fibroids Patients (Experimental Group)	Control Group
Total Number of Participants	50	50
Study Period	January 2020 - May 2021	January 2020 - May 2021
Age Range	18 to 55 years	20 to 54 years
Average Age	39.5 ± 5.5	38.9 ± 5.2
Educational Level - Primary School	12 cases	14 cases
Educational Level - Middle School	21 cases	20 cases
Educational Level - Junior College or Above	15 cases	14 cases

Note: Data presented as mean \pm standard deviation ($\bar{x} \pm s$) or as counts.

Table 2. Comparison of SDS, SAS Scores, and Serum Estradiol Levels Between Experimental and Control Groups

Groups	n	SDS	SAS	Serum Estradiol Levels (ng/L)
Experimental Group	50	50.81±10.71	55.58±11.87	193.48±152.39
Control Group	50	26.65±4.86	25.23±8.34	97.71±52.39
<i>t</i>		15.617	14.632	3.946
<i>P</i> value		.001	.001	.001

Abbreviations: SDS, Self-Rating Depression Scale scores; SAS, Self-Rating Anxiety Scale scores.

questions. Each item is rated on a four-point scale, and the scores are aggregated to obtain a standardized total score. Higher SDS scores indicate greater severity of depression.

Similarly, the anxiety levels of hospitalized patients with gynecological tumors were assessed using the Self-Rating Anxiety Scale (SAS), which consists of 20 items. Each item is rated on a four-point scale, and the scores are totaled to derive a standardized overall score. Elevated SAS scores reflect a higher degree of anxiety.

Statistical Analysis

Data processing and analysis in this study were conducted using SPSS 23.0 software (SPSS Inc., Chicago, IL). Continuous variables are presented as mean ± standard deviation ($\bar{x} \pm s$), and *t* tests were performed for comparative analysis. Categorical variables are expressed as counts or percentages [*n* (%)], and chi-square tests (χ^2) were utilized for comparative analysis. Multivariate linear regression analysis was employed to assess the relationship between SAS and SDS scores and estrogen levels in the two patient groups. A significance level of *P* < .05 was considered statistically significant.

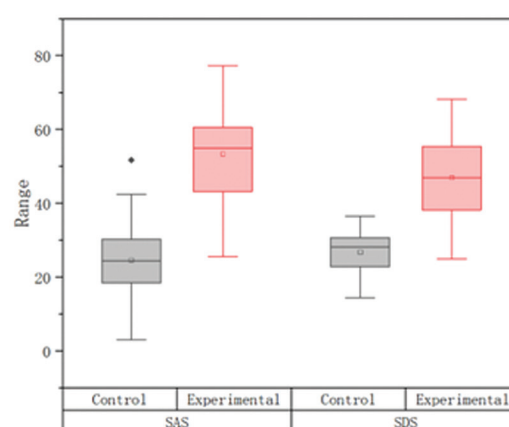
RESULTS

Comparative Analysis of SDS Scores, SAS Scores, and Serum Estradiol Levels

Table 2 presents the results of a study comparing the SDS scores, SAS scores, and serum estradiol levels between the experimental group and a control group. The experimental group comprised 50 participants, with mean SDS scores of 50.81 ± 10.71, refer to Figure 1, mean SAS scores of 55.58 ± 11.87, refer to Figure 1, and mean serum estradiol levels of 193.48 ± 152.39 ng/L, refer to Figure 2. In contrast, the control group also included 50 participants, with lower mean SDS scores of 26.65 ± 4.86, lower mean SAS scores of 25.23 ± 8.34, and lower mean serum estradiol levels of 97.71 ± 52.39 ng/L.

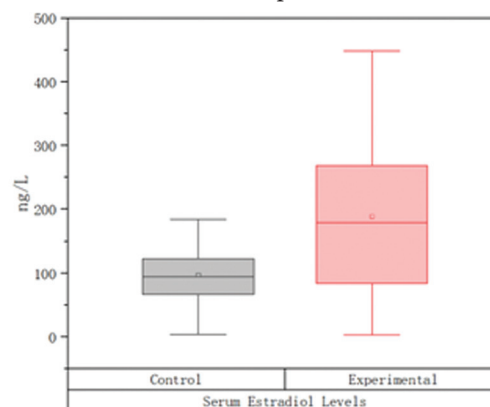
The *t*-test results reveal statistically significant differences between the two groups for all measured variables. The *t*-values are 15.617 for SDS scores, 14.632 for SAS scores, and 3.946 for serum estradiol levels, with *P* = .001 for each variable. These significant differences suggest substantial variations in terms of depression severity (SDS scores), anxiety levels (SAS scores), and estrogen hormone levels between the experimental and control groups.

Based on these findings, it can be inferred that there is a strong relationship between depressive symptoms, anxiety levels, and serum estradiol levels in both groups. The higher SDS and SAS scores in the experimental group, alongside

Figure 1. Comparison of SDS and SAS Scores between Experimental and Control Groups.

Note: The error bars represent the standard deviation.

Abbreviations: SDS, Self-Rating Depression Scale scores; SAS, Self-Rating Anxiety Scale scores.

Figure 2. Comparison of Serum Estradiol Levels between Experimental and Control Groups.

Note: The error bars represent the standard deviation.

Table 3. Correlation Analysis between SAS, SDS Scores, and Estrogen Levels

Groups	n	SAS and Estrogen Levels		SDS and Estrogen Levels	
		<i>r</i>	<i>P</i> value	<i>r</i>	<i>P</i> value
Experimental Group	50	-0.724	.013	-0.624	.016
Control Group	50	0.132	.421	0.151	.432

Abbreviations: SAS, Self-Rating Anxiety Scale scores; SDS, Self-Rating Depression Scale scores; *r*, denotes the correlation coefficient between SAS or SDS scores and estrogen levels.

elevated estradiol levels, indicate a potential association between hormonal factors and psychological distress. However, further analysis and investigation are needed to understand the specific underlying connections and mechanisms involved.

Correlation Analysis between SAS, SDS Scores, and Estrogen Levels

Table 3 presents correlations between SAS scores and estrogen levels, as well as SDS scores and estrogen levels in both the experimental group and the control group.

In the experimental group, consisting of 50 participants, there is a negative correlation between SAS scores and estrogen levels, with a correlation coefficient (r) of -0.724 and $P = .013$. It suggests that as estrogen levels decrease, anxiety levels tend to increase. Similarly, there is a negative correlation between SDS scores and estrogen levels in the experimental group, with a r -value of -0.624 and $P = .016$. This finding indicates that as estrogen levels decrease, depressive symptoms tend to increase.

In the control group, also comprising 50 participants, there is a positive correlation between SAS scores and estrogen levels, although it is relatively weak, with a $r = 0.132$ and $P = .421$. This finding suggests that in the control group, there is no significant relationship between anxiety levels and estrogen levels. Similarly, there is a positive correlation between SDS scores and estrogen levels in the control group, but it is also weak, with a r -value of 0.151 and a $P = .432$. Therefore, in the control group, there is no substantial relationship between depressive symptoms and estrogen levels.

Overall, the findings suggest that in the experimental group, lower estrogen levels are associated with higher anxiety and depressive symptoms. However, in the control group, there is no significant relationship between estrogen levels and anxiety or depressive symptoms. These results imply a potential link between estrogen hormone levels and psychological well-being, particularly in the context of anxiety and depression, but further research is necessary to establish causality and understand the underlying mechanisms.

DISCUSSION

Uterine fibroids have multiple etiological factors, including estrogen and progesterone hormones and their receptors, growth factors and their receptors, cell apoptosis, trace elements, carbon monoxide, leptin, and endothelin-1.¹² Estrogen is a major promoting factor for fibroid growth.¹³ In clinical practice, fibroids rarely occur before puberty, but they tend to grow during pregnancy and shrink after menopause.¹⁴ Biochemical studies have confirmed that fibroids have significantly increased concentrations of estradiol compared to adjacent normal muscle tissue.¹⁵

Additionally, fibroids have significantly higher concentrations of estrogen receptors compared to surrounding tissues. These observations suggest that the local hormonal environment in fibroids is characterized by high estrogen levels.¹⁶ In this study, the estrogen levels in the uterine fibroid group were significantly higher than in the healthy control group ($P < .001$). With the shift from traditional biomedical models to modern medical models, there is a growing focus on the social and psychological well-being of individuals with chronic diseases. When a previously healthy person becomes ill, it inevitably results in corresponding psychological changes.

Patients with chronic diseases often experience symptoms of anxiety and depression.¹⁷ While medication for anxiety and depression can effectively reduce and suppress

tumors, it is unable to eliminate them, making achieving a complete cure challenging.¹⁸

Presently, total hysterectomy or partial myomectomy remains the primary treatment approach for uterine fibroids. However, the uterus is a vital reproductive and endocrine organ in females. Thus, when diagnosed with uterine fibroids, patients face the potential loss of their reproductive organs through surgery, leading to negative emotions such as anxiety, loneliness, depression, fear, and tension.¹⁹

Estrogens, lipid molecules derived from steroids, include estradiol, the most abundant estrogen in the central nervous system.^{20,21} Estrogens have the ability to regulate numerous neurotransmitter systems, such as dopamine, serotonin, norepinephrine, acetylcholine, and glutamate.²⁰ The serotonin system, in particular, has been reported in the literature to play a significant role in mood regulation influenced by estrogen.²¹

Females are more susceptible to depression during periods of drastic estrogen reduction, such as premenstrual, pregnancy, postpartum, and perimenopausal stages.²² In this study, it was observed that patients with uterine fibroids exhibited elevated SAS and SDS scores prior to surgery, confirming the presence of anxiety and depression symptoms in these patients ($P < .05$). Moreover, research has suggested that serum levels of estradiol and other estrogens can modulate various neurotransmitter systems and possess antidepressant effects.²³

Our study findings revealed a surprising trend: patients diagnosed with uterine fibroids displayed symptoms of anxiety and depression despite having elevated estrogen levels. Intriguingly, we observed a distinct negative correlation between their mental well-being and estrogen levels. Essentially, the more severe the patients' psychological distress, the higher their estrogen levels were.

Uterine fibroids represent a complex condition influenced by a multitude of etiological factors, encompassing hormonal dynamics, growth factors, and trace elements. Among these factors, estrogen emerges as a key driver of fibroid proliferation. Elevated estrogen levels within fibroid tissues, alongside an augmented density of estrogen receptors, underscore the hormone's critical role in the pathophysiology of fibroids. Intriguingly, while fibroids exhibit growth during periods of heightened estrogen levels, such as pregnancy, they tend to regress following menopause, further highlighting the significant influence of estrogen on their growth dynamics.

The evolution from traditional to contemporary medical paradigms has expanded the scope of health considerations to encompass not only physical but also psychological well-being, especially among individuals struggling with chronic ailments like uterine fibroids. The diagnosis of uterine fibroids frequently precipitates a profound psychological toll, chiefly resulting from the prospect of losing reproductive function and the organ itself through surgical interventions like hysterectomy or myomectomy. This grim reality often surrounds patients in turbulence of adverse emotions, including anxiety, depression, isolation, and fear.

Estrogens play a multifaceted role beyond reproductive functions, actively influencing neurotransmitter systems associated with mood regulation, notably serotonin. Variations in estrogen levels, particularly during pivotal life phases such as premenstrual, pregnancy, postpartum, and perimenopausal stages, are linked to increased vulnerability to depression among females.

The outcomes of this study, revealing heightened anxiety and depression symptoms as measured by SAS and SDS scores in uterine fibroid patients prior to surgery, contribute further nuance to the intricate relationship between estrogen and mental well-being. The observed negative correlation between estrogen levels and mental state in uterine fibroid patients emphasizes the necessity for a holistic treatment approach that encompasses both the physiological and psychological dimensions of the condition. It challenges the healthcare community to excel in conventional surgical interventions and contemplate strategies that integrate mental health support. Such approaches may include counseling, lifestyle modifications, and potentially pharmacological interventions aimed at stabilizing mood and enhancing overall quality of life.

The precise pathogenesis of uterine fibroids, notably regarding the expression and mechanisms of action of estrogen and progesterone, as well as their receptors, remains unclear. The cyclic fluctuations of estrogen and progesterone levels in these receptors, coupled with the influence of other hormones and enzymes, contribute to the complexity of their regulation, warranting further investigation.²⁴

The study examined the relationship between estrogen levels and uterine fibroids to establish a theoretical basis for more effective drug treatments and management strategies. While surgical interventions remain the primary approach for addressing uterine fibroids, psychological factors can significantly impact surgical outcomes. Thus, understanding the relationship between estrogen levels and psychological well-being is crucial for optimizing treatment outcomes.²⁵

Anxiety and depression symptoms frequently manifest in patients diagnosed with uterine fibroids prior to surgery. It is recommended that psychological intervention be offered by medical professionals who can utilize their medical expertise to educate and counsel patients effectively. This intervention should encompass preoperative guidance, an explanation of the necessity of surgical treatment, and anticipation of potential occurrences during and after surgery.²⁶ Such interventions play a crucial role in helping patients alleviate mental stress, regain a healthy psychological state, and enhance overall quality of life.

Study Limitations

Despite the valuable insights gained from this study, several limitations must be acknowledged. Firstly, the sample size was relatively small, which may limit the generalizability of the findings to broader populations. Additionally, the study primarily relied on self-reported measures for assessing anxiety and depression symptoms, which could introduce

bias or inaccuracies. Furthermore, the cross-sectional design of the study restricts our ability to establish causal relationships between estrogen levels and psychological well-being. Future research employing larger sample sizes, objective measures, and longitudinal designs is warranted to address these limitations and provide more robust evidence in this area.

Future Research Directions

Future research should prioritize exploring the intricate relations among estrogen, neurotransmitter systems, and mood regulation, particularly within the realm of uterine fibroids. Further exploration of the mechanisms behind the perplexing link between heightened estrogen levels and adverse mental health effects presents an opportunity for the development of novel therapeutic strategies. These interventions could extend beyond addressing the physical aspects of uterine fibroids to encompass mitigating the psychological burden associated with this condition, thereby advancing toward a more holistic approach to patient care.\

CONCLUSION

In conclusion, our study sheds light on the complex relationship between estrogen levels and psychological well-being in patients with uterine fibroids. Despite the traditionally understood role of estrogen in mood regulation, our findings reveal a paradoxical association where higher estrogen levels correlate with worsened mental health states in these patients. It highlights the complexity of uterine fibroids and the need for a holistic approach to treatment that addresses both the physical and psychological aspects of the condition. In the future, further research into the underlying mechanisms of this association is warranted, with the aim of developing more effective therapeutic interventions that encompass both realms of patient care.

CONFLICTS OF INTEREST

The authors declared that they have no conflicts of interest regarding this work.

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AUTHORS' CONTRIBUTIONS

LQ and MC wrote the main manuscript. LJ prepared the data collection. BY and SX analyze and interpret the results. All authors reviewed the results and approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

All experimental protocols were observed by the Ethics Committee of the First People's Hospital of Linan. All methods were performed in accordance with the relevant guidelines and regulations. For the ethical research content involved in this project, standardized management and scientific research shall be carried out in strict accordance with relevant national laws, regulations, and international practices. Approval No. XHEC-D-2024-009.

DATA AVAILABILITY

The experimental data used to support the findings of this study are available from the corresponding author upon request.

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