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Factors associated with anxiety and depression in perimenopausal women with abnormal uterine bleeding: A retrospective cohort study

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Abstract

Objective To investigate factors associated with anxiety and depression in perimenopausal women experiencing abnormal uterine bleeding (AUB), with a focus on endocrine markers and lifestyle factors.

Methods This retrospective cohort study analyzed 1,234 perimenopausal women with AUB treated at a tertiary hospital from January 2023 to January 2024. Participants were classified based on DSM-5 diagnoses of anxiety and depression. Data collected included demographics, lifestyle habits, comorbidities, psychiatric history, and endocrine levels (estradiol, follicle-stimulating hormone [FSH], luteinizing hormone [LH], cortisol, prolactin, testosterone, and thyroid-stimulating hormone [TSH]). Logistic regression models identified independent predictors, with interaction and stratified analyses conducted by age group (< 50 and ≥ 50 years).

Results Factors associated with anxiety and depression included higher BMI (OR 1.08, $P = 0.008$), longer AUB duration (OR 1.12, $P = 0.001$), single/divorced/widowed marital status (OR 1.54, $P = 0.015$), and lower education levels (OR 1.62, $P < 0.001$). Smoking history (OR 2.84, $P < 0.001$) and psychiatric history (OR 3.11, $P < 0.001$) emerged as strong predictors, while regular exercise was protective (OR 0.64, $P = 0.001$). Hormonal factors, including lower estradiol and elevated levels of FSH, LH, and cortisol, were significantly linked to increased odds of psychological distress ($P < 0.01$). Interaction analyses revealed that smoking and elevated cortisol exacerbated risks, whereas regular exercise mitigated the adverse effects of elevated FSH and LH. These associations were consistent across age groups.

Conclusions Anxiety and depression in perimenopausal women with AUB are influenced by a combination of demographic, lifestyle, clinical, and endocrine factors. Addressing modifiable risk factors, such as smoking cessation and increased physical activity, may alleviate psychological distress. Further research is needed to elucidate the hormonal pathways connecting endocrine changes to mental health.

Keywords Anxiety, Depression, Abnormal uterine bleeding, Perimenopause, Endocrine markers

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Introduction

Anxiety and depression are common psychological conditions that significantly affect women during the perimenopausal period, a transitional phase marked by hormonal fluctuations and changes in menstrual patterns. The perimenopausal period has been associated with a higher prevalence of mental health issues, with studies suggesting that fluctuations in gonadal hormones, particularly estradiol and follicle-stimulating hormone (FSH), may contribute to mood disturbances [1–2]. In addition, alterations in stress-related hormones such as cortisol—though not necessarily fluctuating in a cyclical manner—have also been linked to anxiety and depression during midlife, potentially due to dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis [3]. Abnormal uterine bleeding (AUB), which is also common during this period, can exacerbate emotional stress, particularly in women experiencing prolonged or heavy bleeding [4]. However, the interplay between AUB, hormonal changes, and psychological distress remains underexplored.

Hormonal changes in perimenopausal women, including declining levels of estradiol and increased FSH and luteinizing hormone (LH), have been implicated in both the onset and severity of anxiety and depression [5–6]. Estradiol, in particular, has been shown to have neuroprotective effects, influencing mood regulation through its actions on neurotransmitters such as serotonin and dopamine [7]. Cortisol, the body's primary stress hormone, has also been linked to psychological disorders, with elevated cortisol levels being associated with an increased risk of anxiety and depression [8–9]. These hormonal imbalances may be further compounded by lifestyle factors, such as smoking, physical inactivity, and poor sleep quality, all of which are prevalent in perimenopausal women and have been associated with adverse mental health outcomes [10–12].

Previous research has highlighted the role of demographic and lifestyle factors in influencing the psychological well-being of perimenopausal women. For instance, women with lower education levels, those who are single, divorced, or widowed, and those with a history of psychiatric illness are more likely to experience anxiety and depression during the perimenopausal period [13–14]. Additionally, smoking has been identified as a significant risk factor for depression, while regular physical activity has been shown to have a protective effect on mental health [15–16]. Despite these findings, there is a paucity of data on how these factors interact with hormonal changes to influence the risk of anxiety and depression specifically in women with abnormal uterine bleeding during the perimenopausal period.

The present study aims to explore the associations between demographic, lifestyle, and endocrine factors with anxiety and depression in perimenopausal women with AUB. We hypothesize that lifestyle factors (such as smoking and physical inactivity), medical and psychiatric comorbidities, as well as hormonal imbalances, contribute to the increased risk of anxiety and depression in this population. By identifying these associations, this study seeks to provide a better understanding of the psychological challenges faced by perimenopausal women with AUB and to inform targeted interventions for improving mental health outcomes.

Methods

Study design and population

This cross-sectional study, based on a retrospective review of medical records, was conducted to investigate the factors associated with anxiety and depression in perimenopausal women with abnormal uterine bleeding (AUB). Data were collected from perimenopausal women diagnosed with AUB who visited the gynecology outpatient department at a tertiary hospital between January 2023 and January 2024. Perimenopause was defined based on the STRAW + 10 criteria, as the transitional period characterized by changes in menstrual cycle regularity—such as a cycle length variation of ≥ 7 days or ≥ 60 days of amenorrhea—accompanied by typical menopausal symptoms. These symptoms included hot flashes, night sweats, mood disturbances, or sleep disorders. Women with lifelong menstrual irregularities (e.g., due to polycystic ovary syndrome) were excluded. The study included women aged 40 to 55 years. For women within 12 months after their final menstrual period, abnormal uterine bleeding (AUB) was included if the episode was consistent with perimenopausal hormonal patterns and not attributable to postmenopausal pathology. AUB was diagnosed based on clinical evaluation and transvaginal ultrasound.

Patients with missing data for any key variables, including hormone measurements or psychiatric evaluation results, were excluded from the analysis. As such, the final sample only included individuals with complete clinical and laboratory data. No imputation was applied for missing values.

Data collection

Data were extracted from the patients' medical records, including demographic and lifestyle characteristics (age, BMI, marital status, education level, smoking history, alcohol use, and exercise frequency), clinical factors (duration of abnormal uterine bleeding, comorbidities such as hypertension and diabetes, psychiatric history), and laboratory results of endocrine markers (estradiol, follicle-stimulating hormone [FSH], luteinizing hormone [LH], cortisol, prolactin, testosterone, and thyroid-stimulating hormone [TSH]).

Anxiety and depression status was assessed through clinical psychiatric evaluations conducted during outpatient visits, based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria. These evaluations were performed by qualified mental health professionals and documented in the electronic medical records. Psychiatric history, including any prior diagnoses of anxiety, depression, or other mental disorders, was also extracted. Patients with major psychiatric disorders other than anxiety or depression (e.g., schizophrenia or bipolar disorder) were excluded from the analysis.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation for normally distributed variables or median (interquartile range) for skewed variables. Categorical variables were presented as frequencies and percentages. Comparisons between the anxiety and non-anxiety groups, as well as between the depression and non-depression groups, were made using independent t-tests for normally distributed variables, Mann-Whitney U tests for skewed variables, and Chi-square tests for categorical variables. A two-sided P-value < 0.05 was considered statistically significant.

Univariate and multivariate logistic regression analyses were performed to identify factors associated with anxiety and depression in perimenopausal women with AUB. The odds ratios (OR) and corresponding 95% confidence intervals (CI) were calculated. All variables with P-values < 0.05 in univariate analysis were included in the multivariate logistic regression models. The multivariate models were adjusted for age, BMI, duration of abnormal uterine bleeding, marital status, education level, smoking history, exercise frequency, psychiatric history, endocrine markers, and sleep quality.

For further analysis, interaction effects between endocrine markers and lifestyle factors (e.g., smoking and exercise) were examined using multivariate logistic regression models, with interaction terms included. Stratified analyses by age group (< 50 vs. ≥50 years) were conducted to explore whether age modified the associations between risk factors and psychological outcomes. However, interaction terms with age were not statistically significant, and the effect estimates remained consistent across both groups. Therefore, detailed stratified results are not shown but are available upon request. Endocrine markers such as estradiol, FSH, LH, cortisol, prolactin, testosterone, and TSH were initially screened for inclusion in the regression models. TSH was excluded from the final models due to lack of independent significance in multivariate analysis and to avoid redundancy among correlated hormonal variables. All statistical analyses were performed using IBM SPSS Statistics version 28.0 (IBM Corp., Armonk, NY, USA). P-values were calculated using two-tailed tests, and a significance level of $P < 0.05$ was considered statistically significant for all analyses.

Results

Baseline characteristics of perimenopausal women with abnormal uterine bleeding ($n = 1234$)

Tables 1 and 2 present the baseline characteristics of the study population according to anxiety and depression status, respectively. Age was similar across groups. However, women with either anxiety or depression were more likely to have higher BMI, longer duration of abnormal uterine bleeding, lower education levels, and be unmarried (all $P < 0.05$). Smoking history and physical inactivity were significantly more common in both the anxiety and depression groups ($P < 0.001$). Additionally, participants in both groups exhibited lower estradiol levels and higher levels of FSH, LH, and cortisol compared to those without anxiety or depression (all $P < 0.01$). Poor sleep quality, as indicated by significantly elevated PSQI scores, was also strongly associated with both psychological conditions ($P < 0.001$). These findings highlight consistent patterns of demographic, lifestyle, and endocrine differences in women experiencing anxiety or depression.

Univariate and multivariate logistic regression analysis for factors associated with anxiety in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

In multivariate analysis (Table 3), anxiety in perimenopausal women with AUB was significantly associated with higher BMI, longer duration of abnormal uterine bleeding, being single/divorced/widowed, and lower education levels. Lifestyle factors such as smoking and physical inactivity were strong predictors, while regular exercise appeared protective. Notably, elevated PSQI scores and endocrine markers including lower estradiol and higher FSH, LH, and cortisol levels were also linked to increased anxiety risk. These findings suggest that anxiety is influenced by an interplay of demographic, behavioral, and hormonal factors.

Univariate and multivariate logistic regression analysis for factors associated with depression in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

As shown in Table 4, depression was significantly associated with higher BMI, longer duration of abnormal uterine bleeding, unmarried status, and lower education. A history of smoking and prior psychiatric disorders emerged as particularly strong predictors. Lower estradiol and elevated FSH, LH, and cortisol levels were also significantly associated with increased depression risk. As with anxiety, poor sleep quality and lack of regular physical activity were linked to higher odds of depression.

Table 1 Baseline characteristics of perimenopausal women with abnormal uterine bleeding ($n = 1234$)

Characteristic	Total ($n = 1234$)	Anxiety Group ($n = 652$)	Non-Anxiety Group ($n = 582$)	*P*-value
Age (years), Mean ± SD	48.7 ± 3.5	48.9 ± 3.4	48.5 ± 3.6	0.182
BMI (kg/m²), Mean ± SD	25.8 ± 4.1	26.1 ± 4.2	25.5 ± 3.9	0.045*
Duration of Abnormal Uterine Bleeding (months), Median (IQR)	8 (3–12)	10 (5–13)	7 (3–11)	0.003**
Marital Status, n (%)				
- Married	954 (77.3)	482 (73.9)	472 (81.1)	0.008**
- Single/Divorced/Widowed	280 (22.7)	170 (26.1)	110 (18.9)	
Education Level, n (%)				
- Primary/Secondary	645 (52.3)	380 (58.3)	265 (45.5)	< 0.001***
- College/University	589 (47.7)	272 (41.7)	317 (54.5)	
Smoking History, n (%)	98 (7.9)	74 (11.4)	24 (4.1)	< 0.001***
Alcohol Use, n (%)	147 (11.9)	89 (13.7)	58 (10.0)	0.052
Exercise Regularly (≥ 3 times/week), n (%)	546 (44.3)	232 (35.6)	314 (53.9)	< 0.001***
Comorbidities, n (%)				
- Hypertension	398 (32.2)	220 (33.7)	178 (30.6)	0.253
- Diabetes	148 (12.0)	89 (13.6)	59 (10.1)	0.052
Psychiatric History, n (%)	256 (20.7)	183 (28.1)	73 (12.5)	< 0.001***
Endocrine Levels, Mean ± SD				
- Estradiol (pg/mL)	62.5 ± 22.4	60.2 ± 21.8	64.9 ± 23.0	0.012*
- FSH (mIU/mL)	25.6 ± 8.9	27.4 ± 8.6	23.7 ± 8.8	< 0.001***
- LH (mIU/mL)	21.8 ± 6.7	22.9 ± 6.5	20.7 ± 6.8	< 0.001***
- Cortisol (μg/dL)	14.2 ± 5.3	15.6 ± 5.1	12.7 ± 5.5	< 0.001***
- Prolactin (ng/mL)	18.9 ± 6.3	19.5 ± 6.5	18.2 ± 6.0	0.002**
Sleep Quality (PSQI Score), Median (IQR)	7 (5–10)	9 (6–12)	6 (4–8)	< 0.001***

Note: Data are presented as mean ± standard deviation for normally distributed variables, median (interquartile range) for skewed variables, and frequency (percentage) for categorical variables. P-values were calculated using t-tests, Mann-Whitney U tests, or Chi-square tests as appropriate.*Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

These results support a multifactorial model, in which demographic, behavioral, clinical, and hormonal factors collectively contribute to depression in this population.

Comparison of clinical and hormonal characteristics among women with anxiety only, depression only, comorbid anxiety and depression, and neither condition

Of the 1,234 participants, 298 (24.1%) had anxiety only, 250 (20.3%) had depression only, 418 (33.9%) had both anxiety and depression, and 268 (21.7%) had neither condition. As shown in Tables 5 and 6, women with comorbid anxiety and depression exhibited more pronounced clinical and hormonal dysregulation compared to those without psychological symptoms. This group had the highest BMI and longest duration of AUB, as well as the highest rates of smoking, psychiatric history, and poor sleep quality. Endocrine disturbances were also most evident in the comorbid group, with significantly lower estradiol and elevated FSH, LH, and cortisol levels (all $P < 0.001$), suggesting activation of both gonadotropic and stress axes. Prolactin, testosterone, and TSH levels were also elevated. Although TSH was significantly higher in the comorbid group, it was not retained in multivariate models, indicating a lack of independent predictive value after adjustment for other clinical and hormonal variables. These findings support the hypothesis that comorbid anxiety and depression in perimenopausal women with AUB are associated with a distinct pattern of physiological dysregulation.

Multivariate logistic regression analysis for factors associated with both anxiety and depression in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

As shown in Table 7, the presence of both anxiety and depression was independently associated with higher BMI, longer duration of abnormal uterine bleeding, unmarried status, lower education level, smoking history, and poor sleep quality. A psychiatric history emerged as the strongest predictor. Regular physical activity was protective. Hormonal factors including lower estradiol and elevated FSH, LH, and cortisol levels were also significantly associated with comorbidity. These findings reinforce the multifactorial nature of psychological distress in perimenopausal women with AUB, involving demographic, behavioral, clinical, and endocrine dimensions.

Table 2 Baseline characteristics of perimenopausal women with abnormal uterine bleeding by depression status ($n = 1234$)

Characteristic	Total ($n = 1234$)	Depression Group ($n = 604$)	Non-Depression Group ($n = 630$)	*P*-value
Age (years), Mean ± SD	48.7 ± 3.5	48.9 ± 3.4	48.6 ± 3.6	0.109
BMI (kg/m^2), Mean ± SD	25.8 ± 4.1	26.0 ± 4.2	25.4 ± 3.9	0.033*
Duration of AUB (months), Median (IQR)	8 (3–12)	10 (5–13)	7 (3–11)	0.005**
Marital Status, n (%)				0.019*
– Married	954 (77.3)	455 (75.3)	499 (79.2)	
– Single/Divorced/Widowed	280 (22.7)	149 (24.7)	131 (20.8)	
Education Level, n (%)				< 0.001***
– Primary/Secondary	645 (52.3)	360 (59.6)	285 (45.2)	
– College/University	589 (47.7)	244 (40.4)	345 (54.8)	
Smoking History, n (%)	98 (7.9)	69 (11.4)	29 (4.6)	< 0.001***
Alcohol Use, n (%)	147 (11.9)	83 (13.7)	64 (10.2)	0.058
Exercise Regularly (≥ 3 times/week), n (%)	546 (44.3)	218 (36.1)	328 (52.1)	< 0.001***
Comorbidities, n (%)				
– Hypertension	398 (32.2)	207 (34.3)	191 (30.3)	0.174
– Diabetes	148 (12.0)	82 (13.6)	66 (10.5)	0.072
Psychiatric History, n (%)	256 (20.7)	170 (28.1)	86 (13.7)	< 0.001***
Endocrine Levels, Mean ± SD				
– Estradiol (pg/mL)	62.5 ± 22.4	59.3 ± 22.1	65.7 ± 22.6	0.003**
– FSH (mIU/mL)	25.6 ± 8.9	27.1 ± 8.5	24.2 ± 8.9	< 0.001***
– LH (mIU/mL)	21.8 ± 6.7	22.7 ± 6.6	20.9 ± 6.7	< 0.001***
– Cortisol (μg/dL)	14.2 ± 5.3	15.3 ± 5.1	13.2 ± 5.4	< 0.001***
– Prolactin (ng/mL)	18.9 ± 6.3	19.4 ± 6.5	18.3 ± 6.0	0.004**
Sleep Quality (PSQI Score), Median (IQR)	7 (5–10)	9 (6–12)	6 (4–8)	< 0.001***

Note: Data are presented as mean ± standard deviation for normally distributed variables, median (interquartile range) for skewed variables, and frequency (percentage) for categorical variables. P-values were calculated using t-tests, Mann-Whitney U tests, or Chi-square tests as appropriate. *Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Table 3 Univariate and multivariate logistic regression analysis for factors associated with anxiety in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

Variable	Univariate OR (95% CI)	*P*-value	Multivariate OR (95% CI)	*P*-value
Age (years)	1.03 (0.98–1.07)	0.182	1.02 (0.97–1.06)	0.215
BMI (kg/m^2)	1.07 (1.02–1.12)	0.041*	1.06 (1.01–1.11)	0.049*
Duration of Abnormal Uterine Bleeding (months)	1.09 (1.03–1.15)	0.003**	1.08 (1.02–1.14)	0.006**
Marital Status (Single/Divorced/Widowed vs. Married)	1.56 (1.11–2.18)	0.010*	1.42 (1.01-2.00)	0.042*
Education Level (Primary/Secondary vs. College/University)	1.71 (1.34–2.19)	< 0.001***	1.58 (1.22–2.05)	< 0.001***
Smoking History (Yes vs. No)	3.07 (1.89–4.98)	< 0.001***	2.91 (1.78–4.76)	< 0.001***
Exercise Regularly (≥ 3 times/week) (Yes vs. No)	0.53 (0.42–0.68)	< 0.001***	0.61 (0.47–0.79)	< 0.001***
Psychiatric History (Yes vs. No)	2.71 (1.94–3.79)	< 0.001***	2.44 (1.72–3.47)	< 0.001***
Estradiol (pg/mL)	0.98 (0.96–0.99)	0.014*	0.98 (0.96–0.99)	0.018*
FSH (mIU/mL)	1.06 (1.04–1.09)	< 0.001***	1.05 (1.03–1.08)	< 0.001***
LH (mIU/mL)	1.04 (1.02–1.07)	< 0.001***	1.03 (1.01–1.06)	0.002**
Cortisol (μg/dL)	1.09 (1.04–1.14)	< 0.001***	1.07 (1.02–1.13)	0.005**
Sleep Quality (PSQI Score)	1.26 (1.19–1.33)	< 0.001***	1.24 (1.17–1.32)	< 0.001***

Note: OR = Odds Ratio; CI = Confidence Interval. P-values were calculated using univariate and multivariate logistic regression models. Multivariate models adjusted for all variables listed in the table.*Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Interaction effects between endocrine markers and lifestyle and clinical factors on anxiety and depression in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

Interaction terms between endocrine markers (estradiol, FSH, LH, cortisol, prolactin, testosterone, and TSH) and lifestyle or clinical factors (smoking, regular physical activity, and psychiatric history) were tested using multivariate logistic regression. As shown in Table 8, only statistically significant interactions ($P < 0.05$) are reported; non-significant results are omitted for clarity but are available upon request. Notably, smoking amplified the adverse effects of lower estradiol and higher cortisol on anxiety and depression, while regular exercise mitigated the psychological risk associated with elevated FSH and LH levels. Additionally, higher TSH levels were

Table 4 Univariate and multivariate logistic regression analysis for factors associated with depression in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

Variable	Univariate OR (95% CI)	*P*-value	Multivariate OR (95% CI)	*P*-value
Age (years)	1.04 (0.99–1.08)	0.085	1.03 (0.98–1.07)	0.109
BMI (kg/m²)	1.08 (1.03–1.13)	0.027*	1.07 (1.02–1.12)	0.033*
Duration of Abnormal Uterine Bleeding (months)	1.12 (1.05–1.18)	0.002**	1.09 (1.03–1.15)	0.005**
Marital Status (Single/Divorced/Widowed vs. Married)	1.62 (1.18–2.24)	0.007**	1.49 (1.06–2.09)	0.019*
Education Level (Primary/Secondary vs. College/University)	1.84 (1.45–2.33)	< 0.001***	1.66 (1.28–2.17)	< 0.001***
Smoking History (Yes vs. No)	2.94 (1.83–4.72)	< 0.001***	2.72 (1.69–4.40)	< 0.001***
Exercise Regularly (≥ 3 times/week) (Yes vs. No)	0.59 (0.45–0.78)	< 0.001***	0.68 (0.52–0.89)	0.006**
Psychiatric History (Yes vs. No)	3.02 (2.14–4.26)	< 0.001***	2.67 (1.88–3.78)	< 0.001***
Estradiol (pg/mL)	0.96 (0.94–0.98)	< 0.001***	0.97 (0.95–0.99)	0.003**
FSH (mIU/mL)	1.05 (1.03–1.08)	< 0.001***	1.04 (1.02–1.07)	< 0.001***
LH (mIU/mL)	1.03 (1.01–1.06)	0.004**	1.02 (1.00-1.05)	0.012*
Cortisol (μg/dL)	1.11 (1.06–1.16)	< 0.001***	1.09 (1.04–1.15)	0.002**
Sleep Quality (PSQI Score)	1.32 (1.25–1.39)	< 0.001***	1.29 (1.22–1.36)	< 0.001***

Note: OR = Odds Ratio; CI = Confidence Interval. P-values were calculated using univariate and multivariate logistic regression models. Multivariate models adjusted for all variables listed in the table. *Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Table 5 Comparison of endocrine levels between women with and without anxiety and depression ($n = 1234$)

Endocrine Marker	Anxiety & Depression Group ($n = 418$)	Non-Anxiety & Non-Depression Group ($n = 416$)	*P*-value
Estradiol (pg/mL), Mean ± SD	58.7 ± 22.0	67.5 ± 23.5	< 0.001***
FSH (mIU/mL), Mean ± SD	27.9 ± 8.4	22.5 ± 8.6	< 0.001***
LH (mIU/mL), Mean ± SD	23.5 ± 6.9	19.8 ± 6.7	< 0.001***
Cortisol (μg/dL), Mean ± SD	15.8 ± 5.2	13.1 ± 5.4	< 0.001***
Prolactin (ng/mL), Mean ± SD	19.6 ± 6.1	17.8 ± 6.0	0.002**
Testosterone (ng/dL), Mean ± SD	0.52 ± 0.15	0.49 ± 0.13	0.034*
TSH (mIU/L), Mean ± SD	2.71 ± 1.14	2.41 ± 1.10	0.012*

Note: Data are presented as mean ± standard deviation. P-values were calculated using t-tests to compare the mean endocrine levels between the anxiety & depression group and the non-anxiety & non-depression group. *Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Table 6 Comparison of key characteristics among four mental health subgroups

Variable	Anxiety Only ($n = 298$)	Depression Only ($n = 250$)	Comorbid A&D ($n = 418$)	Neither ($n = 268$)	*P*-value
Age (years), Mean ± SD	48.8 ± 3.3	48.9 ± 3.4	49.0 ± 3.5	48.5 ± 3.6	0.217
BMI (kg/m²), Mean ± SD	25.9 ± 4.1	25.8 ± 4.0	26.3 ± 4.2	25.2 ± 3.8	0.019*
Duration of AUB (months), Median (IQR)	9 (5–12)	9 (5–13)	10 (6–14)	6 (3–10)	< 0.001***
Smoking History (%)	10.1%	9.6%	11.5%	2.6%	< 0.001***
Psychiatric History (%)	22.1%	23.6%	34.5%	9.3%	< 0.001***
Estradiol (pg/mL)	61.8 ± 22.3	60.5 ± 22.5	58.7 ± 22.0	67.5 ± 23.5	< 0.001***
FSH (mIU/mL)	26.5 ± 8.7	26.7 ± 8.4	27.9 ± 8.4	22.5 ± 8.6	< 0.001***
Cortisol (μg/dL)	14.8 ± 5.1	14.9 ± 5.2	15.8 ± 5.2	13.1 ± 5.4	< 0.001***
Sleep Quality (PSQI), Median (IQR)	8 (5–10)	8 (5–11)	9 (6–12)	5 (3–7)	< 0.001***

Note: Comparison across four mental health subgroups. P-values derived using ANOVA, Kruskal-Wallis, or Chi-square tests as appropriate. A&D = Anxiety and Depression. *Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

associated with a reduced risk among women who exercised regularly. The interaction between cortisol and psychiatric history further intensified psychological vulnerability. These findings underscore the moderating role of behavioral and clinical history factors on the mental health impact of endocrine dysregulation in perimenopausal women.

Discussion

This study sought to explore the factors associated with anxiety and depression in perimenopausal women with abnormal uterine bleeding (AUB), focusing on the roles of demographic, lifestyle, and endocrine factors. Our findings provide critical insights into the multifactorial nature of psychological distress in this population, demonstrating the combined effects of hormonal imbalances, social factors, and lifestyle habits on mental health outcomes.

Table 7 Multivariate logistic regression analysis for factors associated with both anxiety and depression in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

Variable	Multivariate OR (95% CI)	*P*-value
Age (years)	1.01 (0.97–1.05)	0.268
BMI (kg/m²)	1.08 (1.02–1.14)	0.008**
Duration of Abnormal Uterine Bleeding (months)	1.12 (1.05–1.18)	0.001***
Marital Status (Single/Divorced/Widowed vs. Married)	1.54 (1.09–2.18)	0.015*
Education Level (Primary/Secondary vs. College/University)	1.62 (1.24–2.12)	< 0.001***
Smoking History (Yes vs. No)	2.84 (1.79–4.51)	< 0.001***
Exercise Regularly (≥ 3 times/week) (Yes vs. No)	0.64 (0.49–0.84)	0.001***
Psychiatric History (Yes vs. No)	3.11 (2.16–4.48)	< 0.001***
Estradiol (pg/mL)	0.96 (0.94–0.98)	< 0.001***
FSH (mIU/mL)	1.05 (1.03–1.08)	< 0.001***
LH (mIU/mL)	1.03 (1.01–1.06)	0.006**
Cortisol (μg/dL)	1.10 (1.04–1.16)	< 0.001***
Sleep Quality (PSQI Score)	1.30 (1.22–1.38)	< 0.001***

Note: OR = Odds Ratio; CI = Confidence Interval. P-values were calculated using multivariate logistic regression analysis. *Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Table 8 Interaction effects between endocrine markers and lifestyle and clinical factors on anxiety and depression in perimenopausal women with abnormal uterine bleeding ($n = 1234$)

Interaction Term	Multivariate OR (95% CI)	*P*-value
Estradiol (pg/mL) × Smoking History	1.08 (1.02–1.14)	0.006**
FSH (mIU/mL) × Exercise Regularly (≥ 3 times/week)	0.92 (0.88–0.97)	< 0.001***
Cortisol (μg/dL) × Smoking History	1.12 (1.05–1.18)	< 0.001***
LH (mIU/mL) × Exercise Regularly (≥ 3 times/week)	0.95 (0.91–0.99)	0.015*
TSH (mIU/L) × Exercise Regularly (≥ 3 times/week)	0.89 (0.82–0.97)	0.005**
Cortisol (μg/dL) × Psychiatric History	1.14 (1.06–1.23)	< 0.001***

Note: OR = Odds Ratio; CI = Confidence Interval. P-values were calculated using multivariate logistic regression models that included interaction terms between endocrine markers and lifestyle factors (smoking, exercise) and clinical history (psychiatric history). *Significance levels: *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Consistent with previous studies, we found that higher BMI was significantly associated with increased odds of anxiety and depression in perimenopausal women. Barghandan et al. (2021) reported that postmenopausal women with elevated BMI and body fat mass (BFM) experienced more severe menopausal symptoms and higher levels of trait anxiety, highlighting a clear link between excess adiposity and psychological distress during this transitional period [17]. Obesity is widely recognized as a risk factor for mental health disorders, primarily due to the metabolic and inflammatory disturbances associated with excess body fat. In particular, central obesity has been linked to disruptions in neuroendocrine signaling, increased systemic inflammation, and insulin resistance, all of which contribute to mood dysregulation and heightened vulnerability to anxiety and depression [18]. Moreover, Barghandan et al. also emphasized that negative body image perceptions related to physiological changes in menopause may further amplify emotional distress, reinforcing the psychological burden in women with higher BMI during the perimenopausal and postmenopausal phases. Research shows that metabolic abnormalities, such as alterations in glucocorticoids, insulin resistance, and increased inflammatory signaling from dysfunctional adipose tissue, may significantly impact mood regulation and emotional control, thereby contributing to the higher incidence of depression in obese individual [19]. Additionally, the prolonged duration of abnormal uterine bleeding (AUB) was another significant predictor, underscoring the emotional burden imposed by persistent bleeding. Women with longer durations of AUB frequently experience heightened anxiety and depression due to the ongoing uncertainty and physical discomfort associated with irregular menstrual cycles. As Lebduska et al. (2023) note, AUB often presents with variations in frequency, duration, and volume of bleeding, contributing to psychological stress and discomfort in affected women [20]. This prolonged disruption of daily life can exacerbate feelings of anxiety and emotional distress, further impacting mental health outcomes.

Marital status also played a significant role in mental health outcomes, with single, divorced, or widowed women being more likely to experience anxiety and depression compared to their married counterparts. This observation is supported by studies highlighting the protective role of social support against mental health disorders. Li et al. (2023), in their longitudinal study, found

that individuals with greater social support, such as close confidants or access to practical help, had reduced depressive symptoms [21]. Their research indicated that social support can buffer against the effects of loneliness, thus mitigating depressive symptoms, especially in men. Similarly, Gariépy et al. (2016) conducted a systematic review and meta-analysis and confirmed that social support, particularly from spouses and family members, serves as a protective factor against depression across various life stages [22]. They found that support from a spouse had the strongest protective effect in adulthood and older age. These findings underline the critical role of marital status and close social connections in maintaining mental well-being, especially during vulnerable periods such as perimenopause.

Lower education levels were similarly associated with higher odds of anxiety and depression, which aligns with previous research linking lower socioeconomic status to poorer mental health outcomes. Cohen et al. (2020) found that individuals with lower educational attainment had a higher likelihood of experiencing depression in midlife, emphasizing that education shapes access to health resources and coping mechanisms across the lifespan [23]. Similarly, Hoebel et al. (2017) demonstrated that lower education, as a core dimension of socioeconomic status, was significantly associated with depressive symptoms, as education is closely related to cognitive abilities and health-related behaviors [24]. Furthermore, a meta-analysis by Lorant et al. (2003) revealed that individuals with lower education levels had higher odds of both new episodes and persistent depression, confirming the dose-response relationship between education and mental health outcomes [25]. Education not only provides access to better resources but also improves health literacy and enhances coping mechanisms, all of which can mitigate the psychological effects of perimenopausal symptoms.

Lifestyle factors, including smoking and physical inactivity, further compounded the risk of anxiety and depression in this cohort. Smoking has been identified as a significant modifiable risk factor for depression, likely due to its impact on neurochemistry and its association with unhealthy coping mechanisms [26]. Conversely, regular physical activity was found to have a protective effect on mental health, supporting the well-established benefits of exercise on mood regulation and stress reduction [27]. These findings underscore the importance of lifestyle interventions in mitigating the psychological burden of perimenopausal symptoms.

Although our analysis revealed a statistically significant association between lower estradiol levels and anxiety, the effect size was relatively small. Therefore, estradiol may play a contributory rather than a central role in the development of anxiety in this population. Estradiol, known for its neuroprotective properties, plays a critical role in mood regulation by modulating neurotransmitters such as serotonin and dopamine. As estradiol levels decline during perimenopause, women become more susceptible to mood disturbances. Raglan et al. (2020) emphasized that hormonal fluctuations, particularly declining estradiol, are closely linked to the increased incidence of depression during perimenopause, a period of heightened vulnerability for mood disorders [5]. Similarly, Freeman (2015) reviewed the accumulating evidence linking the changing hormonal milieu, including increased FSH and cortisol levels, to depressive symptoms in the menopause transition [6]. Elevated cortisol levels, indicative of heightened stress responses, have been consistently associated with anxiety and depression during this life stage. Additionally, the interaction between endocrine markers and lifestyle factors, such as smoking and physical activity, suggests that these hormonal imbalances may be either exacerbated or mitigated by behavioral factors. Higher cortisol levels in smokers, for example, have been shown to amplify the risk of anxiety and depression, whereas regular physical activity can moderate the effects of elevated FSH and LH levels, providing a protective effect against mood disturbances during perimenopause. Although elevated TSH levels were associated with anxiety and depression, it is important to note that TSH levels may naturally increase with age, and age could act as a potential confounder in this relationship. Future studies with age-stratified thyroid function analysis are warranted to clarify this association.

Our study also highlighted the critical role of sleep quality, with poor sleep being a significant contributor to anxiety and depression. This is particularly evident in perimenopausal women, who are vulnerable due to hormonal fluctuations, often leading to night sweats and insomnia. Zhou et al. (2021) found a strong relationship between hot flashes, sweating, and poor sleep quality, with anxiety and depression mediating this relationship [28]. Their study revealed that anxiety accounted for 17.86% of the mediating effect, while depression contributed 5.36%, indicating that both symptoms play crucial roles in worsening sleep quality for women in this transitional period. These findings support the notion that hormonal imbalances during perimenopause significantly impact sleep, which, in turn, exacerbates mental health issues like anxiety and depression.

One of the strengths of this study is the comprehensive assessment of both hormonal and lifestyle factors, which provides a more holistic understanding of the contributors to anxiety and depression in perimenopausal women with abnormal uterine bleeding (AUB). However, several limitations should be noted. First, the retrospective design may introduce recall bias, particularly regarding self-reported lifestyle factors such as smoking, physical

activity, and sleep quality. Second, the study population was drawn from a single tertiary care gynecology outpatient clinic, which may limit the generalizability of the findings to the broader population of perimenopausal women. Third, hormone levels were measured only once, which does not account for the natural circadian and menstrual cycle-related fluctuations of key endocrine markers such as estradiol, FSH, LH, and cortisol. Although blood samples were collected under standardized conditions in the early morning (between 7:30 and 9:30 AM) following an overnight fast to minimize diurnal variation, the phase of the menstrual cycle at the time of sampling was not recorded. This may have introduced variability in hormone measurements and limits the interpretation of their associations with psychological symptoms. Future research should incorporate longitudinal and repeated hormone measurements, include a more diverse and representative sample, and consider menstrual cycle phase to more accurately assess the temporal and causal relationships between hormonal fluctuations, lifestyle factors, and mental health outcomes in this population.

The findings of this study have important clinical implications. Given the identified associations between demographic, lifestyle, and hormonal factors with anxiety and depression, clinicians should consider systematically evaluating these risk factors during the initial assessment of perimenopausal women with AUB. Early identification of high-risk individuals—particularly those with elevated BMI, a history of smoking or psychiatric illness, poor sleep quality, or abnormal hormone levels—may enable timely mental health screening and intervention. Integrating psychological evaluation into routine gynecologic care could significantly improve the holistic management and quality of life of these patients.

In conclusion, our findings highlight the complex interplay between hormonal, demographic, and lifestyle factors in the development of anxiety and depression in perimenopausal women with AUB. Targeted interventions addressing modifiable risk factors, such as smoking cessation, physical activity promotion, and sleep improvement, may offer substantial benefits in alleviating psychological distress during this vulnerable period. Further research is needed to explore the mechanisms underlying these associations and to develop tailored interventions for women at higher risk of mental health disorders during perimenopause.

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Author contributions
Jun Hu and Lijuan He contributed equally to the conceptualization and design of the study. Jun Hu was primarily responsible for data collection, statistical analysis, and drafting the initial manuscript. Lijuan He supervised the study, provided critical revisions to the manuscript, and ensured the scientific rigor of the analysis. Both authors reviewed and approved the final manuscript for submission.

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Data availability
The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical statement
This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of The Affiliated Hospital, Southwest Medical University (Ethics Approval Number: KY2024498). Due to the retrospective nature of the study, the requirement for informed consent to participate was formally waived by the ethics committee. All patient data were anonymized and handled in strict confidentiality, in compliance with applicable data protection regulations.

Patient consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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