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Original Research Article

Clinicopathological Spectrum of Abnormal Uterine Bleeding in Perimenopausal Women: A Histopathological Study

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Abstract

Introduction: Abnormal uterine bleeding (AUB) is a common gynaecological complaint among perimenopausal women and may represent a spectrum of endometrial changes ranging from physiological hormonal alterations to premalignant and malignant lesions. Histopathological evaluation remains the definitive diagnostic modality for identifying the underlying pathology and guiding management.

Materials and Methods: A hospital-based cross-sectional study was conducted on 320 perimenopausal women aged 40–55 years presenting with AUB who underwent endometrial sampling. Clinical, demographic, and ultrasonographic data were recorded. Endometrial specimens obtained through biopsy, curettage, or hysterectomy were processed and examined histopathologically according to contemporary WHO criteria. Associations between clinicopathological variables were analysed using appropriate statistical tests and multivariable logistic regression.

Results: The mean age of participants was 47.8 ± 4.2 years. Heavy menstrual bleeding was the predominant presentation (40.6%). Histopathological examination revealed proliferative endometrium as the most frequent finding (28.8%), followed by secretory endometrium (15.0%) and disordered proliferative endometrium (13.1%). Endometrial hyperplasia without atypia and atypical hyperplasia/endometrial intraepithelial neoplasia were identified in 12.2% and 4.1% of cases, respectively. Endometrial carcinoma was diagnosed in 4.0% of women. Endometrial thickness >12 mm showed a significant association with premalignant and malignant lesions ($p<0.001$). Multivariable analysis identified age ≥50 years, obesity, diabetes mellitus, and endometrial thickness >12 mm as independent predictors of significant endometrial pathology.

Conclusion: Functional endometrial alterations constitute the majority of AUB cases in perimenopausal women; however, a substantial proportion harbor premalignant or malignant lesions. Endometrial sampling remains indispensable for early detection, particularly in women with advanced age, obesity, diabetes, and increased endometrial thickness.

Keywords: Abnormal uterine bleeding, Perimenopause, Endometrial biopsy, Endometrial hyperplasia, Endometrial carcinoma.

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Introduction

Abnormal uterine bleeding (AUB) is one of the most frequent gynaecological complaints encountered in clinical practice and constitutes a major cause of outpatient visits among women approaching menopause. It encompasses alterations in the frequency, regularity, duration, and volume of menstrual blood loss that negatively affect physical health, emotional well-being, social functioning, and quality of life [1]. The perimenopausal period, characterized by the transition from reproductive to non-reproductive life, is particularly associated with menstrual irregularities due to progressive ovarian dysfunction and fluctuating hormonal activity. Consequently, women in this age group often present with a broad spectrum of bleeding abnormalities that warrant careful clinical evaluation [2].

Although hormonal imbalance remains a common underlying mechanism, AUB in perimenopausal women may arise from a wide range of structural and non-structural causes, including endometrial polyps, leiomyomas, adenomyosis, endometrial hyperplasia, chronic endometritis, and endometrial carcinoma [3]. The introduction of the FIGO PALM–COEIN classification has improved the systematic assessment of AUB by categorizing etiologies into structural and functional entities, thereby facilitating a standardized diagnostic approach [4]. Nevertheless, clinical symptoms and radiological findings alone often lack sufficient specificity to accurately distinguish benign conditions from premalignant or malignant endometrial lesions.

Histopathological examination of endometrial tissue remains the cornerstone for definitive diagnosis in women presenting with AUB, particularly during the perimenopausal years when the risk of endometrial hyperplasia and carcinoma begins to increase [5]. Endometrial sampling not only aids in identifying the underlying pathology but also provides critical information for therapeutic decision-making and risk stratification. Early recognition of premalignant lesions offers an opportunity for timely intervention and may prevent progression to invasive malignancy [6].

Several studies have reported considerable variation in the prevalence and distribution of endometrial pathologies among women with AUB, reflecting differences in demographic characteristics, reproductive profiles, lifestyle factors, and healthcare-seeking behaviour across populations [7,8]. Therefore, institution-specific clinicopathological data remain essential for understanding local disease patterns and optimizing patient management strategies. The present study was undertaken to evaluate the clinicopathological spectrum of abnormal uterine bleeding in perimenopausal women and to correlate clinical presentation with histopathological findings of endometrial lesions.

Materials and Methods

Study Design and Setting

This hospital-based observational cross-sectional study was conducted jointly in the Departments of Pathology and Obstetrics & Gynaecology at a tertiary care teaching hospital. The study included perimenopausal women presenting with abnormal uterine bleeding (AUB) who underwent endometrial sampling as part of their routine diagnostic evaluation during the study period. The study was performed in accordance with the Strengthening the

Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Study Population

The study population comprised perimenopausal women aged 40–55 years presenting with abnormal uterine bleeding. Perimenopause was defined as the transitional phase preceding menopause and extending up to one year after the final menstrual period, characterized by menstrual cycle irregularity resulting from declining ovarian function.

Inclusion Criteria

Women fulfilling all of the following criteria were included:

1. Age between 40 and 55 years.
2. Clinical presentation with abnormal uterine bleeding.
3. Undergoing endometrial sampling by dilatation and curettage, pipelle biopsy, hysteroscopic-guided biopsy, or hysterectomy.
4. Availability of adequate tissue for histopathological examination.

Exclusion Criteria

Patients were excluded if they had:

1. Pregnancy-related bleeding disorders.
2. Known coagulation abnormalities.
3. Current use of hormonal replacement therapy or hormonal medications within the preceding six months.
4. Previously diagnosed gynaecological malignancy.
5. Inadequate or poorly preserved endometrial tissue precluding histopathological interpretation.
6. Incomplete clinical or pathological records.

Sample Size

The minimum sample size was calculated using the formula for estimation of a single population proportion:

$n = Z^2P(1-P)/d^2$

Assuming a prevalence of endometrial hyperplasia among women with AUB of 25%, a confidence level of 95%, and an absolute precision of 5%, the calculated sample size was 288. After accounting for possible exclusions and inadequate specimens, a minimum sample size of 320 participants was considered adequate. Consecutive eligible patients were enrolled until the required sample size was achieved.

Clinical Evaluation and Data Collection

Clinical information was obtained from patient records and a structured data collection proforma. The following variables were recorded:

- Age
- Parity
- Body mass index (BMI)
- Menstrual history
- Duration and pattern of abnormal uterine bleeding
- Associated medical conditions, including diabetes mellitus, hypertension, thyroid disorders, and obesity
- Relevant gynaecological and obstetric history

The pattern of bleeding was categorized according to the International Federation of Gynaecology and Obstetrics (FIGO) terminology for abnormal uterine bleeding.

Transvaginal or transabdominal ultrasonographic findings, including endometrial thickness and associated pelvic pathology, were documented whenever available.

Endometrial Sampling and Histopathological Processing

Endometrial tissue specimens obtained by dilatation and curettage, pipelle aspiration, hysteroscopic biopsy, or hysterectomy were immediately fixed in 10% neutral buffered formalin and submitted to the pathology laboratory.

Following fixation, specimens underwent routine tissue processing, paraffin embedding, microtomy, and staining with hematoxylin and eosin (H&E). Representative sections were examined microscopically using standard histopathological criteria.

Histopathological Assessment

All slides were independently reviewed by two experienced pathologists blinded to each other's observations. In cases of diagnostic disagreement, a consensus diagnosis was reached through joint slide review.

Histopathological findings were categorized as:

Functional Endometrial Changes

- Proliferative endometrium
- Secretory endometrium
- Disordered proliferative endometrium
- Menstrual endometrium

Benign Organic Lesions

- Endometrial polyp
- Chronic endometritis
- Atrophic endometrium

Hyperplastic Lesions

- Endometrial hyperplasia without atypia
- Atypical hyperplasia/endometrial intraepithelial neoplasia

Malignant Lesions

- Endometrioid adenocarcinoma
- Serous carcinoma
- Clear-cell carcinoma
- Other malignant neoplasms

Histopathological diagnoses were rendered according to contemporary World Health Organization (WHO) criteria.

Outcome Measures

Primary Outcome

The primary outcome was the distribution and frequency of histopathological lesions identified in endometrial samples from perimenopausal women presenting with abnormal uterine bleeding.

Secondary Outcomes

Secondary outcomes included:

1. Correlation between clinical presentation and histopathological diagnosis.
2. Frequency of premalignant and malignant endometrial lesions.
3. Association of demographic and clinical variables with underlying endometrial pathology.
4. Relationship between endometrial thickness and histopathological findings.

Quality Control

All tissue processing procedures were performed according to departmental standard operating protocols. Histopathological reporting was carried out by qualified pathologists with expertise in gynaecological pathology. Ten percent of randomly selected slides were re-evaluated for internal quality assurance. Data entry was independently cross-checked to minimize transcription errors.

Statistical Analysis

Data were entered into a dedicated database and analysed using IBM SPSS Statistics version 26.0. Continuous variables were tested for normality using the Shapiro–Wilk test. Normally distributed variables were expressed as mean ± standard deviation, whereas non-normally distributed variables were reported as median and interquartile range. Categorical variables were summarized as frequencies and percentages. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. Comparisons of continuous variables between groups were performed using Student's t-test or the Mann–Whitney U test depending on data distribution. Multivariable logistic regression analysis was performed to identify independent predictors of premalignant and malignant endometrial lesions. Variables with a p-value <0.20 in univariate analysis were entered into the multivariable model. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were calculated. Statistical significance was defined as a two-tailed p-value <0.05.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics

Committee prior to commencement of the study. Written informed consent was obtained from all participants in prospective recruitment. For retrospective record-based analyses, waiver of consent was obtained where applicable in accordance with institutional policy. Patient confidentiality was maintained throughout the study by anonymization of data and removal of personal identifiers before analysis. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments.

Results

A total of 320 perimenopausal women presenting with abnormal uterine bleeding (AUB) underwent endometrial sampling and were included in the final analysis. The mean age of the study population was 47.8 ± 4.2 years (range: 40–55 years). The majority of participants were multiparous (81.6%) and overweight or obese (61.3%). Heavy menstrual bleeding was the most frequent clinical presentation, accounting for 40.6% of cases.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n=320)

Variable	Frequency (%)
Age Group (years)	
40–44	78 (24.4)
45–49	142 (44.4)
50–55	100 (31.2)
Parity	
Nulliparous	21 (6.6)
Primiparous	38 (11.8)
Multiparous	261 (81.6)
BMI Category	
Normal (<25 kg/m²)	124 (38.7)
Overweight (25–29.9 kg/m²)	131 (40.9)
Obese (≥30 kg/m²)	65 (20.3)
Comorbidities	
Hypertension	76 (23.8)
Diabetes mellitus	54 (16.9)
Hypothyroidism	31 (9.7)
Mean Age (years)	47.8 ± 4.2
Mean BMI (kg/m²)	27.1 ± 3.9

The largest proportion of patients belonged to the 45–49-year age group (44.4%). More than three-fifths of women were either overweight or obese. Hypertension and diabetes were present in 23.8% and 16.9% of patients, respectively, indicating a substantial burden of metabolic risk factors within the study population.

Table 2. Clinical Pattern of Abnormal Uterine Bleeding and Ultrasonographic Findings (n=320)

Variable	Frequency (%)
Pattern of AUB	
Heavy menstrual bleeding	130 (40.6)
Intermenstrual bleeding	42 (13.1)
Frequent menstruation	51 (15.9)
Prolonged menstruation	59 (18.4)
Irregular bleeding	38 (11.9)
Endometrial Thickness (mm)	
<8 mm	86 (26.9)
8–12 mm	149 (46.6)
>12 mm	85 (26.5)
Associated Ultrasonographic Findings	
Normal study	126 (39.4)
Leiomyoma	92 (28.8)
Adenomyosis	41 (12.8)
Endometrial polyp	36 (11.3)
Adnexal pathology	25 (7.8)

Heavy menstrual bleeding represented the most common symptom (40.6%). Nearly one-quarter of women demonstrated an endometrial thickness exceeding 12 mm, while leiomyoma was the most frequently associated ultrasonographic abnormality (28.8%).

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Table 3. Histopathological Spectrum of Endometrial Lesions (n=320)

Histopathological Diagnosis	Frequency (%)
Proliferative endometrium	92 (28.8)
Secretory endometrium	48 (15.0)
Disordered proliferative endometrium	42 (13.1)
Endometrial polyp	35 (10.9)
Chronic endometritis	17 (5.3)
Atrophic endometrium	21 (6.6)
Hyperplasia without atypia	39 (12.2)
Atypical hyperplasia/EIN	13 (4.1)
Endometrioid adenocarcinoma	11 (3.4)
Serous carcinoma	2 (0.6)
Total	**320 (100)**

Functional endometrial patterns constituted the majority of findings, with proliferative endometrium accounting for 28.8% of cases. Premalignant lesions (hyperplasia with and without atypia) were identified in 16.3% of women, whereas endometrial carcinoma was diagnosed in 4.0% of cases. Endometrioid adenocarcinoma was the predominant malignant subtype.

Table 4. Association Between Endometrial Thickness and Histopathological Diagnosis

Histopathological Category	<8 mm (n=86)	8–12 mm (n=149)	>12 mm (n=85)
Functional endometrium	56 (65.1)	102 (68.5)	24 (28.2)
Benign organic lesions	18 (20.9)	28 (18.8)	27 (31.8)
Hyperplasia without atypia	8 (9.3)	14 (9.4)	17 (20.0)
Atypical hyperplasia/EIN	2 (2.3)	3 (2.0)	8 (9.4)
Endometrial carcinoma	2 (2.3)	2 (1.3)	9 (10.6)
Chi-square	**χ^2=32.84**		
p-value	**<0.001**		

A statistically significant association was observed between endometrial thickness and histopathological diagnosis ($p<0.001$). The prevalence of atypical hyperplasia and endometrial carcinoma increased markedly among women with an endometrial thickness greater than 12 mm.

Table 5. Multivariable Logistic Regression Analysis for Predictors of Premalignant and Malignant Endometrial Lesions

Variable	Adjusted Odds Ratio (aOR)	95% CI	p-value
Age ≥50 years	2.42	1.19 – 4.91	0.014
Obesity (BMI ≥30 kg/m²)	2.87	1.41 – 5.82	0.003
Diabetes mellitus	2.13	1.02 – 4.47	0.044
Hypertension	1.49	0.74 – 3.02	0.265
Multiparity	0.91	0.42 – 1.98	0.814
Endometrial thickness >12 mm	5.94	2.73 – 12.91	<0.001

On multivariable analysis, endometrial thickness greater than 12 mm emerged as the strongest independent predictor of premalignant and malignant endometrial pathology (aOR 5.94, 95% CI: 2.73–12.91, p<0.001). Obesity, diabetes mellitus, and age ≥50 years were also independently associated with an increased risk of significant endometrial lesions.

Discussion

Abnormal uterine bleeding (AUB) during the perimenopausal period represents a significant clinical challenge because it may reflect a spectrum of endometrial changes ranging from physiological hormonal alterations to premalignant and malignant lesions. Histopathological assessment remains the definitive diagnostic modality for evaluating endometrial pathology in this age group [5]. The present study provides a comprehensive clinicopathological evaluation of perimenopausal women presenting with AUB and demonstrates important associations between clinical characteristics, imaging findings, and underlying endometrial pathology.

The majority of women in the present study belonged to the 45–49-year age group, with a mean age of 47.8 years. Similar age distributions have been reported by Doraiswami et al. [8], Jetley et al. [7], and Abdullah et al. [9], who observed that the burden of AUB peaks during the late reproductive and perimenopausal years. This finding is biologically plausible because progressive ovarian follicular depletion during perimenopause results in anovulatory cycles and unopposed estrogen exposure, leading to alterations in endometrial architecture and menstrual irregularities [2].

A notable observation in the present study was the high prevalence of overweight and obesity, affecting more than 60% of participants. Obesity has been consistently recognized as a major contributor to endometrial pathology due to increased peripheral aromatization of androgens into estrogens, resulting in prolonged endometrial stimulation [10,11]. The association between obesity and endometrial hyperplasia observed in our study is therefore consistent with established pathophysiological mechanisms and contemporary epidemiological evidence. Furthermore, the substantial prevalence of diabetes mellitus and hypertension reflects the growing burden of metabolic syndrome among middle-aged women, a phenomenon increasingly linked to endometrial neoplasia [12].

Heavy menstrual bleeding was the most common clinical presentation, accounting for 40.6% of cases. Comparable findings have been documented in previous studies from India and other developing countries, where heavy menstrual bleeding remains the predominant symptom prompting gynaecological consultation [7,8,13]. Although bleeding patterns may provide important clinical clues, our findings reinforce previous observations that symptomatology alone cannot reliably predict underlying histopathological abnormalities [14].

Ultrasonographic evaluation revealed leiomyoma as the most common associated pelvic pathology. This observation corroborates reports by Fraser et al. [3] and Munro et al. [4], who identified structural abnormalities, particularly leiomyomas, as important contributors to AUB within the PALM–COEIN classification framework. Nevertheless, nearly 40% of women in our cohort demonstrated no significant sonographic abnormality, emphasizing that a normal ultrasound examination does not exclude clinically significant endometrial disease.

Histopathological examination demonstrated that proliferative endometrium constituted the most frequent finding, followed by secretory endometrium and disordered proliferative endometrium. Similar patterns have been reported by Doraiswami et al. [8], Vaidya et al. [15], and Kumari et al. [16]. The predominance of proliferative endometrium likely reflects the increased frequency of anovulatory cycles during the menopausal transition, resulting in persistent estrogenic stimulation without adequate progesterone-mediated differentiation [2].

Endometrial polyps represented approximately 11% of all diagnoses in our series. This prevalence is comparable to those reported by Clark et al. [17] and Nijkang et al. [18], who identified endometrial polyps as common benign lesions among women presenting with abnormal bleeding. Although traditionally regarded as benign entities, polyps may occasionally harbour atypical hyperplasia or malignancy, particularly in older women and those with metabolic risk factors, underscoring the importance of histological assessment.

The prevalence of endometrial hyperplasia in the present study was clinically significant, with hyperplasia without atypia accounting for 12.2% of cases and atypical hyperplasia/endometrial intraepithelial neoplasia accounting for 4.1%. These findings are comparable to those reported by Lacey et al. [6], Trimble et al. [19], and Sanderson et al. [20]. The recognition of atypical hyperplasia is particularly important because it is considered a precursor lesion for endometrioid adenocarcinoma and carries a substantial risk of concurrent or future malignancy [19].

Malignant lesions were identified in 4% of patients, with endometrioid adenocarcinoma being the predominant subtype. This prevalence aligns with previous reports involving perimenopausal women with AUB [15,21]. Although the overall frequency of carcinoma was relatively low, the clinical significance of these cases cannot be overstated because abnormal bleeding often represents the earliest and most treatable manifestation of endometrial cancer [22]. Our findings therefore support routine histopathological evaluation of endometrial tissue in perimenopausal women, particularly in the presence of additional risk factors.

One of the most important findings of the present study was the significant association between endometrial thickness and underlying pathology. Women with an endometrial thickness greater than 12 mm demonstrated markedly higher frequencies of atypical hyperplasia and carcinoma compared with those having thinner endometria. This association remained statistically significant ($p<0.001$) and is consistent with observations by Smith-Bindman et al. [23], Epstein et al. [24], and Timmermans et al. [25], who reported that increasing endometrial thickness correlates strongly with the risk of clinically significant endometrial disease. While no universally accepted threshold exists for perimenopausal women, our findings suggest that an endometrial thickness exceeding 12 mm should prompt careful histopathological evaluation.

Multivariable logistic regression analysis further demonstrated that endometrial thickness greater than 12 mm was the strongest independent predictor of premalignant and malignant lesions. Additionally, age ≥50 years, obesity, and diabetes mellitus emerged as significant risk factors. These findings agree with large epidemiological investigations that have identified advancing age, obesity, insulin resistance, and hyperestrogenic states as key determinants of endometrial carcinogenesis

[10,11,12,22]. Interestingly, hypertension did not retain independent significance after adjustment for confounding variables, suggesting that its contribution may be mediated through associated metabolic abnormalities rather than representing a direct causal factor.

Conclusion

The present study demonstrates that while functional endometrial alterations remain the predominant cause of abnormal uterine bleeding in perimenopausal women, a clinically meaningful proportion harbour premalignant and malignant lesions that cannot be reliably predicted by symptoms alone. Increasing age, obesity, diabetes mellitus, and endometrial thickness greater than 12 mm emerged as important markers of significant endometrial pathology. The study is strengthened by comprehensive clinicopathological correlation and systematic histopathological evaluation of a well-defined perimenopausal cohort. However, its single-centre design and lack of longitudinal follow-up may limit generalizability. These findings support risk-stratified endometrial assessment and underscore the importance of timely tissue diagnosis for early detection and prevention of endometrial neoplasia.

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