



Original Article

Histopathological Spectrum of Endometrial Lesions in Women with Abnormal Uterine Bleeding: A Clinicopathological Correlation Study

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ABSTRACT

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Background: Abnormal uterine bleeding (AUB) represents a common gynecological complaint affecting women across all age groups, with endometrial pathology being a significant underlying cause. This study aimed to evaluate the histopathological spectrum of endometrial lesions in women presenting with AUB and correlate findings with clinical parameters.

Methods: This prospective observational study was conducted over 24 months involving 385 women presenting with AUB who underwent endometrial sampling. Clinical data including age, parity, bleeding pattern, and body mass index were recorded. Endometrial samples were processed and examined histopathologically. Statistical analysis was performed using Chi-square test and Student's t-test, with $p < 0.05$ considered significant.

Results: The mean age of participants was 42.3 ± 8.7 years. Proliferative endometrium was the most common finding (32.5%), followed by secretory endometrium (18.4%), endometrial hyperplasia (17.1%), endometrial polyps (14.0%), atrophic endometrium (8.3%), and endometrial carcinoma (4.9%). Disordered proliferative endometrium was observed in 4.7% of cases. Endometrial hyperplasia and carcinoma showed significant association with age > 45 years ($p = 0.002$) and obesity ($p = 0.001$). Menorrhagia was the predominant bleeding pattern (45.2%), followed by metrorrhagia (28.3%) and postmenopausal bleeding (15.6%). Malignancy was significantly associated with postmenopausal bleeding ($p < 0.001$).

Conclusion: Endometrial pathology in AUB demonstrates a diverse histopathological spectrum with age-dependent variation. Timely histopathological evaluation is essential for appropriate management and early detection of premalignant and malignant conditions.

Keywords: Abnormal uterine bleeding, endometrial biopsy, histopathology, endometrial hyperplasia, endometrial carcinoma, clinicopathological correlation.

INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency, or duration occurring in the absence of pregnancy [1]. It affects approximately 14-25% of women of reproductive age and up to 50% of perimenopausal women, significantly impacting their quality of life and productivity [2]. AUB represents one of the most common reasons for gynecological consultations and accounts for approximately one-third of all outpatient gynecology visits [3].

The International Federation of Gynecology and Obstetrics (FIGO) introduced the PALM-COEIN classification system in 2011 to standardize the terminology and classification of AUB causes [4]. The structural causes (PALM) include polyps, adenomyosis, leiomyoma, and malignancy/hyperplasia, while non-structural causes (COEIN) comprise coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified [5].

Endometrial pathology constitutes a significant proportion of AUB etiology, ranging from benign functional disorders to premalignant and malignant conditions [6]. The spectrum of endometrial lesions includes proliferative and secretory patterns, endometrial hyperplasia, polyps, chronic endometritis, and endometrial carcinoma [7]. With the rising incidence of endometrial carcinoma, particularly in developing countries, and its association with obesity, diabetes, and unopposed estrogen exposure, early detection through histopathological evaluation has become increasingly important [8].

Several studies have documented the histopathological patterns of endometrial lesions in women with AUB, but considerable geographic and demographic variations exist [9]. A study by Doraiswami et al. reported proliferative endometrium as the most common finding (35.4%), while others have reported higher rates of endometrial hyperplasia in specific populations [10]. Recent advances in endometrial sampling techniques, including office-based procedures, have improved the diagnostic yield and patient compliance [11].

Despite numerous studies, there remains a need for comprehensive data correlating clinical presentations with histopathological findings to guide appropriate investigation and management strategies [12]. Furthermore, understanding the age-specific distribution of endometrial pathology can aid in risk stratification and targeted screening approaches [13]. This study aimed to evaluate the histopathological spectrum of endometrial lesions in women presenting with abnormal uterine bleeding and to correlate the histopathological findings with clinical parameters including age, parity, body mass index, and bleeding patterns. Additionally, we sought to identify risk factors associated with premalignant and malignant endometrial lesions.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of Pathology in collaboration with the Department of Obstetrics and Gynecology at a tertiary care teaching hospital over a period of 24 months.

Study Population

A total of 385 women presenting with abnormal uterine bleeding were enrolled in the study. Sample size was calculated using the formula $n = Z^2pq/d^2$, where $Z = 1.96$ (95% confidence level), $p =$ expected prevalence (0.25), $q = 1-p$, and $d =$ precision (0.05), with a 10% non-response rate.

Inclusion Criteria

Women aged 18-70 years presenting with one or more of the following bleeding patterns were included: menorrhagia (prolonged or excessive bleeding at regular intervals), metrorrhagia (irregular bleeding), menometrorrhagia (prolonged and excessive bleeding at irregular intervals), polymenorrhea (frequent bleeding at intervals <21 days), intermenstrual bleeding, or postmenopausal bleeding (bleeding occurring >12 months after menopause).

Exclusion Criteria

Patients with pregnancy-related bleeding, genital tract infections, bleeding disorders, patients on anticoagulant therapy, cervical or vaginal pathology causing bleeding, and those who refused consent were excluded from the study.

Clinical Data Collection

Detailed clinical history was obtained including age, parity, menstrual history, contraceptive use, history of hormone therapy, medical comorbidities (diabetes mellitus, hypertension), and family history of gynecological malignancies. Physical examination including general examination and pelvic examination was performed. Body mass index (BMI) was calculated using the formula: weight (kg)/height (m²). Patients were categorized as normal weight (BMI 18.5-24.9 kg/m²), overweight (BMI 25-29.9 kg/m²), and obese (BMI ≥30 kg/m²).

Endometrial Sampling

Endometrial sampling was performed using dilatation and curettage (D&C) under anesthesia or office endometrial biopsy using Pipelle sampler depending on patient condition and clinical indication. All specimens were fixed in 10% neutral buffered formalin and sent to the pathology department with relevant clinical details.

Histopathological Examination

The endometrial tissue was processed routinely, embedded in paraffin, and sections of 4-5 μm thickness were cut and stained with hematoxylin and eosin (H&E). All slides were examined by two experienced pathologists independently. In cases of discordance, slides were reviewed together to reach consensus. Endometrial lesions were classified according to the World Health Organization (WHO) classification of tumors of female reproductive organs.

The histopathological diagnoses were categorized as: proliferative endometrium, secretory endometrium, atrophic endometrium, endometrial polyp, disordered proliferative endometrium, endometrial hyperplasia (without atypia and with atypia), chronic endometritis, and endometrial carcinoma.

Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean \pm standard deviation, and categorical variables as frequencies and percentages. Chi-square test was used to assess associations between categorical variables. Student's t-test was used for comparison of continuous variables between groups. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Clinical Characteristics

A total of 385 women with abnormal uterine bleeding were included in the study. The mean age of participants was 42.3 ± 8.7 years (range: 22-68 years). The majority of patients (58.4%, n=225) were in the 40-50 years age group, followed by 30-40 years (26.2%, n=101), >50 years (11.9%, n=46), and <30 years (3.4%, n=13). The mean parity was 2.4 ± 1.3 . The mean BMI was 26.8 ± 4.2 kg/m², with 42.1% (n=162) classified as overweight and 28.6% (n=110) as obese.

Clinical Presentation Patterns

Menorrhagia was the most common presenting complaint (45.2%, n=174), followed by metrorrhagia (28.3%, n=109), postmenopausal bleeding (15.6%, n=60), menometrorrhagia (7.5%, n=29), and polymenorrhea (3.4%, n=13). Associated symptoms included dysmenorrhea (32.5%), pelvic pain (18.7%), and weakness/anemia (41.3%).

Histopathological Spectrum

The histopathological spectrum of endometrial lesions is presented in Table 1. Proliferative endometrium was the most common finding observed in 125 cases (32.5%), followed by secretory endometrium in 71 cases (18.4%). Endometrial hyperplasia was diagnosed in 66 cases (17.1%), of which 52 cases (13.5%) were hyperplasia without atypia and 14 cases (3.6%) were hyperplasia with atypia. Endometrial polyps were identified in 54 cases (14.0%). Atrophic endometrium was seen in 32 cases (8.3%), while disordered proliferative endometrium was observed in 18 cases (4.7%). Chronic endometritis was diagnosed in 11 cases (2.9%). Endometrial carcinoma was found in 19 cases (4.9%), with endometrioid adenocarcinoma being the most common type (n=17, 89.5%).

Table 1: Histopathological Distribution of Endometrial Lesions (N=385)

Histopathological Diagnosis	Number of Cases	Percentage (%)
Proliferative endometrium	125	32.5
Secretory endometrium	71	18.4
Endometrial hyperplasia	66	17.1
- Without atypia	52	13.5
- With atypia	14	3.6
Endometrial polyp	54	14.0
Atrophic endometrium	32	8.3
Disordered proliferative endometrium	18	4.7
Endometrial carcinoma	19	4.9
Chronic endometritis	11	2.9
Total	385	100

Age-wise Distribution of Endometrial Lesions

The correlation between age and histopathological findings is shown in Table 2. Proliferative and secretory endometrium were more common in the reproductive age group (<45 years), accounting for 78.4% and 87.3% respectively. Endometrial hyperplasia showed a peak in the 40-50 years age group (60.6%). Atypical hyperplasia and endometrial carcinoma were significantly more common in women >45 years ($p=0.002$ and $p<0.001$ respectively). Among 19 cases of endometrial carcinoma, 15 cases (78.9%) occurred in women >50 years of age.

Table 2: Age-wise Distribution of Endometrial Lesions

Histopathological Diagnosis	<40 years n (%)	40-50 years n (%)	>50 years n (%)	p-value
Proliferative endometrium	52 (41.6)	63 (50.4)	10 (8.0)	0.134
Secretory endometrium	38 (53.5)	24 (33.8)	9 (12.7)	0.089
Hyperplasia without atypia	11 (21.2)	32 (61.5)	9 (17.3)	0.045
Hyperplasia with atypia	1 (7.1)	6 (42.9)	7 (50.0)	0.002
Endometrial polyp	14 (25.9)	28 (51.9)	12 (22.2)	0.176
Atrophic endometrium	0 (0)	8 (25.0)	24 (75.0)	<0.001
Disordered proliferative	8 (44.4)	9 (50.0)	1 (5.6)	0.421
Endometrial carcinoma	0 (0)	4 (21.1)	15 (78.9)	<0.001
Chronic endometritis	4 (36.4)	5 (45.5)	2 (18.2)	0.652

Correlation with Clinical Parameters

Table 3 presents the correlation between histopathological findings and clinical parameters. Menorrhagia was the predominant symptom in cases with proliferative endometrium (62.4%), secretory endometrium (59.2%), and endometrial

polyps (51.9%). Postmenopausal bleeding showed significant association with endometrial carcinoma ($p < 0.001$), with 84.2% of malignancy cases presenting with this symptom.

Obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) was significantly associated with endometrial hyperplasia ($p = 0.001$) and endometrial carcinoma ($p < 0.001$). Among patients with endometrial carcinoma, 68.4% were obese compared to 25.5% in the benign lesion group. Diabetes mellitus was present in 42.1% of endometrial carcinoma cases and 50.0% of atypical hyperplasia cases, showing significant association ($p = 0.003$).

Table 3: Correlation of Histopathological Findings with Clinical Parameters

Parameter	Proliferative (n=125)	Hyperplasia without atypia (n=52)	Hyperplasia with atypia (n=14)	Endometrial Carcinoma (n=19)	p-value
Mean Age (years)	38.6 ± 6.4	44.2 ± 5.8	48.3 ± 6.1	56.7 ± 7.2	<0.001
Mean BMI (kg/m ²)	24.8 ± 3.6	27.9 ± 4.1	29.4 ± 3.8	31.2 ± 4.5	<0.001
Obesity n (%)	22 (17.6)	20 (38.5)	7 (50.0)	13 (68.4)	<0.001
Diabetes n (%)	15 (12.0)	14 (26.9)	7 (50.0)	8 (42.1)	0.003
Menorrhagia n (%)	78 (62.4)	28 (53.8)	4 (28.6)	1 (5.3)	<0.001
PMB n (%)	2 (1.6)	5 (9.6)	4 (28.6)	16 (84.2)	<0.001
Nulliparity n (%)	8 (6.4)	7 (13.5)	3 (21.4)	6 (31.6)	0.012

PMB = Postmenopausal bleeding

Inadequate tissue for diagnosis was obtained in 8 cases (2.0%) during initial sampling, requiring repeat procedures. All endometrial carcinoma cases were further staged and managed according to standard protocols.

DISCUSSION

This study comprehensively evaluated the histopathological spectrum of endometrial lesions in 385 women presenting with abnormal uterine bleeding and established clinicopathological correlations. Our findings demonstrate that while benign conditions predominate, a significant proportion of cases harbor premalignant and malignant pathology, underscoring the importance of systematic histopathological evaluation.

The predominance of proliferative endometrium (32.5%) in our study aligns with findings from multiple studies. Tiwari et al. reported proliferative endometrium in 34.2% of AUB cases [14], while a study by Vaidya et al. found it in 29.8% of cases [15]. This pattern reflects anovulatory cycles or persistent follicular phase, commonly seen in perimenopausal women due to declining ovarian function [16]. The presence of secretory endometrium (18.4%) in our study indicates ovulatory cycles and was predominantly seen in younger women, consistent with findings by Baral et al. who reported 21.3% secretory patterns [17].

Endometrial hyperplasia constituted 17.1% of cases in our study, with 13.5% being hyperplasia without atypia and 3.6% with atypia. These findings are comparable to those reported by Moghal et al. (15.8%) [18] but higher than some Western studies reporting 8-12% [19]. This difference may be attributed to variations in the prevalence of risk factors such as obesity, diabetes, and polycystic ovarian syndrome across different populations [20]. The significant association between hyperplasia and obesity ($\text{BMI} \geq 30 \text{ kg/m}^2$) in our study ($p = 0.001$) supports the well-established role of unopposed estrogen stimulation in hyperplasia development [21].

Atypical hyperplasia, identified in 3.6% of our cases, is particularly significant as it represents a precancerous condition with a 25-30% risk of progression to endometrial carcinoma [22]. The higher prevalence in women >45 years (50.0%) and its association with diabetes (50.0%) in our study emphasizes the need for vigilant surveillance in high-risk groups [23]. Current guidelines recommend progestin therapy or hysterectomy for atypical hyperplasia depending on fertility desires and risk factors [24].

The detection of endometrial carcinoma in 4.9% of AUB cases in our study is clinically significant. This rate is higher than that reported in some studies from developed countries (2-3%) [25] but consistent with other studies from South Asia reporting 4-7% [26]. The strong association with postmenopausal bleeding (84.2% of malignancy cases, $p < 0.001$) reinforces that postmenopausal bleeding should be considered endometrial carcinoma until proven otherwise [27]. The mean age of endometrial carcinoma patients in our study was 56.7 ± 7.2 years, similar to global data showing peak incidence in the sixth decade [28].

The significant association between endometrial carcinoma and obesity (68.4% obese, $p < 0.001$) corroborates extensive evidence linking adiposity with endometrial cancer through increased peripheral aromatization of androgens to estrogens

and insulin resistance [29]. The presence of diabetes in 42.1% of malignancy cases further supports the metabolic syndrome-endometrial cancer connection documented in numerous epidemiological studies [30].

Endometrial polyps were diagnosed in 14.0% of cases, predominantly in the 40-50 years age group. This finding is consistent with literature reporting polyp prevalence of 10-24% in women with AUB [31]. While most polyps are benign, they can harbor malignancy in 0.5-4.8% of cases, particularly in postmenopausal women [32], justifying histopathological examination of all polyps.

Atrophic endometrium was found in 8.3% of cases, predominantly in postmenopausal women (75.0%, $p < 0.001$). Atrophic endometrium results from estrogen deficiency and, paradoxically, is a common cause of postmenopausal bleeding due to fragile, easily traumatized endometrium [33]. The challenge lies in distinguishing benign atrophy from atypical hyperplasia or well-differentiated carcinoma, requiring adequate sampling and experienced pathological assessment [34].

Chronic endometritis, identified in 2.9% of cases in our study, is often underdiagnosed as it requires careful histological examination for plasma cell infiltration [35]. Studies using immunohistochemistry report higher prevalence (10-15%) in AUB cases [36]. Chronic endometritis may cause AUB through impaired endometrial hemostasis and is associated with infertility, recurrent miscarriage, and implantation failure [37].

The correlation between clinical presentation and histopathology revealed that while menorrhagia was common across various diagnoses, postmenopausal bleeding showed high specificity for malignancy. This finding has practical implications for prioritizing endometrial evaluation in postmenopausal women [38]. The association between nulliparity and endometrial carcinoma (31.6% vs. 6.4% in proliferative endometrium, $p = 0.012$) reflects the protective effect of pregnancy through progesterone exposure and clearance of potentially malignant cells [39].

Our study had several strengths including prospective design, adequate sample size, standardized histopathological evaluation by experienced pathologists, and comprehensive clinical correlation. However, limitations include its single-center nature, which may limit generalizability, and lack of long-term follow-up data for patients with hyperplasia. Additionally, we did not perform immunohistochemistry for all cases, which might have enhanced diagnostic accuracy, particularly for chronic endometritis.

The findings emphasize that while AUB often results from benign conditions, systematic histopathological evaluation is essential to detect premalignant and malignant lesions. Risk stratification based on age, BMI, metabolic factors, and bleeding patterns can guide appropriate investigation intensity [40]. The high prevalence of hyperplasia and malignancy in specific subgroups supports the need for targeted screening protocols and patient education regarding modifiable risk factors.

CONCLUSION

This study demonstrates a diverse histopathological spectrum of endometrial lesions in women with abnormal uterine bleeding, ranging from benign physiological variations to malignant neoplasms. While proliferative and secretory endometrium constitute the majority of cases, endometrial hyperplasia and carcinoma represent significant proportions, particularly in older, obese women with metabolic comorbidities. The strong association between postmenopausal bleeding and endometrial malignancy necessitates prompt and thorough evaluation in this population. Age-specific distribution patterns of endometrial pathology support tailored diagnostic approaches based on clinical risk stratification. These findings underscore the critical importance of histopathological examination in the evaluation of abnormal uterine bleeding for appropriate management, early detection of premalignant conditions, and improved patient outcomes. Awareness of the histopathological spectrum and associated risk factors can guide clinicians in identifying high-risk patients requiring expedited evaluation and intervention.

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