



EVALUATION AND HISTOPATHOLOGICAL CORRELATION OF ABNORMAL UTERINE BLEEDING DURING THE MENOPAUSAL TRANSITION AT A TERTIARY CARE HOSPITAL IN NORTH COASTAL ANDHRA PRADESH

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Abstract

Background: The study evaluates abnormal uterine bleeding (AUB) during the menopausal transition in women at a tertiary care hospital in North Coastal Andhra Pradesh, highlighting its clinical presentation and histopathological correlation. AUB is prevalent during this transitional period due to fluctuating hormonal levels, leading to various bleeding patterns, such as heavy, prolonged, and irregular bleeding. The FIGO PALM-COEIN system standardizes the classification of AUB, emphasizing the need to differentiate between physiological irregularity and pathological bleeding, particularly to rule out endometrial hyperplasia and carcinoma.

Methods: Conducted over 18 months, the study included 150 women aged 40-55 years, most of whom presented with heavy menstrual bleeding. Transvaginal ultrasonography revealed increased endometrial thickness and structural lesions such as leiomyoma and endometrial polyps. Histopathological findings indicated that 90.7% of participants had benign conditions, with endometrial hyperplasia observed in 20.7% and malignancies in 3.3%. Prevailing associations were noted between heavy bleeding and significant endometrial pathologies.

Results and Conclusion: The results underscore the importance of comprehensive clinical assessments integrated with imaging and histopathological evaluations to enhance the diagnosis of significant endometrial conditions. Although benign changes were most common, the existence of atypical hyperplasia and carcinoma stresses the necessity for vigilant surveillance in women experiencing AUB during menopause. The findings are particularly relevant for improving clinical practices in managing AUB in this demographic.

Keywords: abnormal uterine bleeding, FIGO PALM-COEIN, histopathological correlation, hyperplasia.

Introduction

Abnormal uterine bleeding (AUB) is a common gynaecologic complaint for women approaching menopause and an important cause of morbidity and healthcare utilisation. It means bleeding that is different from the normal menstrual pattern in frequency, regularity, duration or volume. AUB is most common during the menopausal transition due to progressive alterations in ovarian function, fluctuating levels of oestrogen and progesterone, and higher frequency of anovulatory cycles(1).

The menopausal transition or perimenopausal period is characterised by dramatic fluctuations in ovarian hormonal activity and menstrual cyclicity. Ovulatory dysfunction during this time may result in prolonged unopposed oestrogen exposure and therefore abnormal proliferation and unpredictable shedding of the endometrium. So, women can present with a wide spectrum of bleeding patterns ranging from frequent or prolonged menstrual bleeding to heavy or irregular bleeding. Although most of these changes are benign and due to hormonal dysfunction, AUB in this period may also be associated with structural uterine lesions, endometrial hyperplasia, atypia and malignancy(2-4).

The International Federation of Gynaecology and Obstetrics (FIGO) has developed a classification system, PALM–COEIN, to standardise the description of causes of AUB. The PALM components are polyp (P), adenomyosis (A), leiomyoma (L) and malignancy and hyperplasia (M), which are structural or pathological causes. The COEIN components are coagulopathy (C), ovulatory dysfunction (O), endometrial causes (E), iatrogenic causes (I), and causes not otherwise classified (N). This classification has improved consistency in clinical assessment and research in women with AUB.(5,6)

Clinically, it is important to distinguish between physiological menstrual irregularity and pathological uterine bleeding in women during the menopausal transition. Anovulatory bleeding is common but structural abnormalities such as leiomyoma, endometrial polyps and adenomyosis can coexist. More importantly, endometrial hyperplasia and carcinoma need to be excluded, particularly in women with persistent, recurrent, or heavy bleeding and those with risk factors for endometrial pathology. Evaluation therefore necessitates careful clinical evaluation together with appropriate imaging and endometrial sampling if indicated.(7)

Histopathological evaluation of endometrial tissue still plays an important role in the evaluation of AUB, especially in cases of clinical suspicion of endometrial hyperplasia or malignancy. Histopathology can identify a wide spectrum of endometrial changes including proliferative and secretory patterns, disordered proliferative endometrium, endometrial hyperplasia and endometrial polyps and malignant lesions. Importantly, the clinical diagnosis based on symptoms and imaging may not always correlate with the final histopathological diagnosis. A study performed on 236 perimenopausal women shows that different percentages of structural and nonstructural aetiologies can be identified by clinical and histopathological assessment, demonstrating the complementary role of histopathology in the workup of AUB. (8)

With the introduction of transvaginal ultrasonography, endometrial sampling and hysteroscopy, the work-up of AUB has evolved considerably. Transvaginal ultrasonography is useful for assessing uterine morphology, endometrial thickness and structural lesions, and endometrial sampling provides a direct tissue-based assessment. Endometrial sampling is of particular importance in women at high risk for developing endometrial hyperplasia or cancer. The clinical assessment should therefore combine age of patient, bleeding pattern, risk factors, findings on examination and imaging studies with histopathological findings.(9-11)

The pattern and burden of AUB may differ according to demographic, socio-economic and geographical characteristics. Data from tertiary care hospitals are especially valuable since they provide a window into the spectrum of gynaecologic problems seen among women referred for specialist evaluation. However, there is still a need for region specific data on clinical presentation and histopathological spectrum of AUB among women undergoing menopausal transition in North Coastal Andhra Pradesh. Such information may assist clinicians in identifying clinically significant endometrial pathology and allow for timely diagnosis and appropriate management.(12)

Therefore, the present study was carried out to evaluate the clinical presentation and histopathological spectrum of abnormal uterine bleeding during menopausal transition and to find out the correlation between clinical findings and histopathological diagnoses among the women attending a tertiary care hospital in North Coastal Andhra Pradesh.

Materials and Methods

Study Design and Setting

This was a hospital based observational cross sectional study carried out in the Department of Obstetrics and Gynaecology in collaboration with Department of Pathology at Great Eastern Medical School and Hospital (GEMS & Hospital), Ragolu, Srikakulam, Andhra Pradesh. It is a tertiary care teaching hospital for North Coastal region of Andhra Pradesh.

Study Population

The study was conducted among women with abnormal uterine bleeding (AUB) presenting to Obstetrics and Gynaecology outpatient department or inpatient services during the menopausal transition who underwent sampling of endometrial or uterine tissue as part of their clinical evaluation.

The menopausal transition was defined as the period before the last menstrual period, with alterations in menstrual cycle regularity and hormone activity. AUB was defined as bleeding which was abnormal as to frequency, regularity, duration or volume compared to the individual's usual menstrual pattern.

Study Duration

The study was conducted over a period of **18 months**, from June 2016 to **November 2017**.

Sample Size

A total of **150 women** fulfilling the eligibility criteria were included in the study. A consecutive sampling method was used to recruit eligible participants during the study period.

Inclusion Criteria

Women were included if they fulfilled the following criteria:

1. Women in the menopausal transition presenting with abnormal uterine bleeding.
2. Women who underwent endometrial sampling, endometrial biopsy, dilatation and curettage, hysteroscopy-guided biopsy, or hysterectomy for evaluation of AUB.
3. Women who provided informed consent for participation in the study.
4. Availability of adequate clinical information and histopathological material for evaluation.

Exclusion Criteria

The following women were excluded:

1. Pregnant women and women with pregnancy-related bleeding.
2. Women with previously diagnosed endometrial or cervical malignancy undergoing treatment or follow-up.

3. Women receiving hormonal therapy that could significantly alter the endometrial histological pattern, where adequate clinical information was unavailable.
4. Women with inadequate or non-representative tissue samples.
5. Women who did not provide consent for participation.

Clinical Data Collection

Relevant demographic and clinical data were recorded by pre-designed proforma for data collection. Variables studied were age, age at menarche, parity, menstrual pattern, duration and nature of abnormal bleeding, associated symptoms, menopausal status, body mass index, relevant medical history, contraceptive or hormonal therapy and other risk factors for endometrial pathology.

Bleeding type and duration was recorded as reported by the patient. Clinical examination findings, including abdominal and pelvic examination, were recorded. Relevant laboratory investigations and imaging findings especially pelvic ultrasonography/transvaginal ultrasonography were recorded where available.

Histopathological Evaluation

Endometrial tissue samples obtained through various procedures—including endometrial biopsy, dilatation and curettage, hysteroscopy-guided biopsy, and hysterectomy—were submitted to the Department of Pathology. The specimens underwent standard histopathological processing, with tissue sections prepared and stained using hematoxylin and eosin (H&E). Experienced pathologists examined these under light microscopy. Histopathological findings were categorized into diagnostic groups: proliferative endometrium, secretory endometrium, disordered proliferative endometrium, atrophic endometrium, endometrial polyp, endometrial hyperplasia without atypia, atypical endometrial hyperplasia/endometrial intraepithelial neoplasia, endometrial carcinoma, chronic endometritis and other inflammatory lesions, as well as other pathological findings. In cases of hysterectomy specimens, additional uterine pathologies such as leiomyoma, adenomyosis, and structural abnormalities were also documented.

Clinical–Histopathological Correlation

In this study, the clinical presentation and imaging findings were integrated with the final histopathological diagnosis, focusing on the connections among age, bleeding patterns, clinical risk factors, endometrial thickness, and histopathological changes. The investigation evaluated the proportions of benign, premalignant, and malignant endometrial lesions, as well as how histopathological diagnoses varied across different age groups and clinical manifestations of abnormal uterine bleeding (AUB).

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using appropriate statistical software. Continuous variables were expressed as mean $\pm$ standard deviation (SD) or median with interquartile range, as appropriate. Categorical variables were presented as frequencies and percentages.

Associations between categorical variables, such as age group, bleeding pattern, clinical/imaging findings, and histopathological diagnosis, were assessed using the Chi-square test or Fisher's exact test, as appropriate. For continuous variables, the Student's t-test or Mann–Whitney U test was used depending on data distribution.

A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee of Great Eastern Medical School and Hospital, Srikakulam. Written informed consent was obtained from all participants before enrollment. Patient confidentiality was maintained throughout the study, and data were analyzed using study-specific identification numbers without revealing personal identifiers.

Results:

A total of 150 women presenting with abnormal uterine bleeding (AUB) during the menopausal transition were included in the study. All participants underwent clinical evaluation and histopathological assessment of endometrial or uterine tissue.

Demographic Characteristics

The age of the study participants ranged from 40 to 55 years, with a mean age of 47.8 ± 3.6 years. The majority of women belonged to the 46–50-year age group (42.0%), followed by the 41–45-year group (30.0%).

Age group (years)	Number	Percentage
40–45	45	30.0
46–50	63	42.0
51–55	42	28.0
Total	150	100

Most participants were multiparous. The predominant presenting complaint was heavy menstrual bleeding, followed by prolonged and irregular bleeding.

Clinical Pattern of Abnormal Uterine Bleeding

Heavy menstrual bleeding was observed in 58 (38.7%) women, while 34 (22.7%) presented with prolonged bleeding and 29 (19.3%) had irregular bleeding. Intermenstrual bleeding was reported by 17 (11.3%) women, while 12 (8.0%) presented with a combination of heavy and irregular bleeding.

Bleeding pattern	Number	Percentage
Heavy menstrual bleeding	58	38.7
Prolonged bleeding	34	22.7
Irregular bleeding	29	19.3
Intermenstrual bleeding	17	11.3
Heavy + irregular bleeding	12	8.0
Total	150	100

Clinical and Ultrasonographic Findings

Transvaginal ultrasonography was available for all participants. An increased endometrial thickness was observed in 72 (48.0%) women. Leiomyoma was identified in 38 (25.3%), endometrial polyp in 15 (10.0%), adenomyosis in 9 (6.0%), and other or nonspecific findings in 16 (10.7%) women.

Histopathological Findings

The histopathological examination demonstrated a broad spectrum of endometrial changes. Proliferative endometrium was the most common finding, observed in 38 (25.3%) cases, followed by endometrial hyperplasia without atypia in 31 (20.7%) cases.

Secretory endometrium was identified in 21 (14.0%) cases, while atrophic endometrium was observed in 18 (12.0%). Endometrial polyps were identified in 13 (8.7%) cases. Chronic endometritis was present in 8 (5.3%) cases.

Premalignant lesions, including atypical hyperplasia/endometrial intraepithelial neoplasia, were identified in 7 (4.7%) women, while endometrial carcinoma was detected in 5 (3.3%) women.

Histopathological diagnosis	Number	Percentage
Proliferative endometrium	38	25.3
Endometrial hyperplasia without atypia	31	20.7
Secretory endometrium	21	14.0
Atrophic endometrium	18	12.0
Endometrial polyp	13	8.7
Chronic endometritis	8	5.3
Atypical hyperplasia/EIN	7	4.7
Endometrial carcinoma	5	3.3
Other benign findings	9	6.0
Total	150	100

Overall, 136 (90.7%) women had benign histopathological findings, whereas 7 (4.7%) had premalignant lesions and 5 (3.3%) had malignant lesions. The remaining 2.0% had other pathological findings.

Histopathological Findings According to Age

Benign proliferative and hyperplastic changes were more frequently observed among women aged 40–50 years. Premalignant and malignant lesions were predominantly observed in women aged 51–55 years.

Histopathological category	40–45 years (n=45)	46–50 years (n=63)	51–55 years (n=42)	Total
Benign lesions	43	58	35	136
Atypical hyperplasia/EIN	1	3	3	7
Endometrial carcinoma	1	2	2	5
Other findings	0	0	2	2
Total	45	63	42	150

Correlation Between Bleeding Pattern and Histopathology

A clinically significant association was observed between the pattern of abnormal uterine bleeding and histopathological findings. Endometrial hyperplasia was particularly frequent among women presenting with heavy or prolonged bleeding. All five cases of endometrial carcinoma presented with either heavy, prolonged, or persistent irregular bleeding.

Among women with heavy menstrual bleeding, **15 (25.9%)** had endometrial hyperplasia without atypia, while 3 (5.2%) had atypical hyperplasia/EIN and 2 (3.4%) had endometrial carcinoma. The association between bleeding pattern and major histopathological categories was statistically significant ($p < 0.05$).

Correlation with Endometrial Thickness

Women with increased endometrial thickness on ultrasonography demonstrated a higher frequency of abnormal histopathological findings compared with women having relatively thin endometrium. Among the 72 women with increased endometrial thickness, 26 (36.1%) had endometrial hyperplasia without atypia, 6 (8.3%) had atypical hyperplasia/EIN, and 5 (6.9%) had endometrial carcinoma.

The association between increased endometrial thickness and significant endometrial pathology was statistically significant ($p < 0.001$).

Overall Clinical–Histopathological Correlation

The study demonstrated that although the majority of women with AUB during the menopausal transition had benign endometrial pathology, a clinically important proportion had premalignant or malignant lesions. Histopathological examination therefore provided additional diagnostic information beyond clinical presentation and ultrasonographic assessment.

The overall distribution showed that 90.7% had benign pathology, 4.7% had premalignant pathology, and 3.3% had malignant pathology. The occurrence of premalignant and malignant lesions was higher among older women and those presenting with persistent, heavy, or prolonged abnormal uterine bleeding.

Discussion

Abnormal uterine bleeding (AUB) is one of the most common complaints in gynaecology in the menopausal transition. The transition from normal ovulatory cycles to ovarian ageing is associated with increasing problems with ovulation and variable exposure of the endometrium to oestrogen and progesterone. Therefore women may develop a variety of bleeding patterns and underlying endometrial abnormalities. The FIGO PALM–COEIN system provides a standardised approach to understanding structural and non-structural causes of AUB and highlights the possibility of the presence of more than one aetiological factor in an individual patient.(1,6)

In the present study, 150 women with AUB during menopausal transition were evaluated. The age of the participants ranged from 40 to 55 years with a mean age of 47.8 ± 3.6 years. The highest percentage of women was in the 46-50 years age group (42.0%). This female preponderance in the later years of perimenopause is consistent with the rising incidence of menstrual disturbances with the gradual decline of ovarian function. Similarly, Damle et al. reported the majority of cases in the perimenopausal age group with proliferative endometrium as the predominant histopathological pattern in a study of 119 women with AUB.(13)

In our study, the commonest clinical presentation was heavy menstrual bleeding (38.7%), followed by prolonged bleeding (22.7%) and irregular bleeding (19.3%). This finding is comparable with previous Indian studies. Menorrhagia was reported in 48.86% women with AUB, Damle et al. Talukdar and Mahela also found menorrhagia as the most common presenting symptom among perimenopausal women being evaluated for AUB.(13,14) Heavy bleeding predominates, possibly in relation to the increasing prevalence of anovulatory cycles during the menopause transition, resulting in prolonged endometrial stimulation with subsequent irregular and sometimes excessive shedding.(6) In the present

study, histopathological examination showed broad spectrum of endometrial changes. The most frequent finding was proliferative endometrium (25.3%) followed by endometrial hyperplasia without atypia (20.7%). 14.0% cases showed secretory endometrium and 12.0% cases showed atrophic endometrium. These findings highlight that AUB during the menopausal transition is not a single pathological entity but rather both physiological/hormonal changes and structural or neoplastic abnormalities.

The most common histological pattern found by us was proliferative endometrium which is comparable to the observations of Damle et al. who found proliferative endometrium in 35.22% of perimenopausal women followed by endometrial hyperplasia in 23.86%.⁽¹³⁾ Similarly, the most common functional endometrial pattern was secretory endometrium in a study of 219 perimenopausal women by Doraiswami et al., followed by proliferative endometrium, indicating that the relative distribution of functional endometrial patterns may vary between populations.⁽¹⁵⁾ Such variation may be due to differences in age distribution, duration of AUB, timing of sampling during the menstrual cycle, and demographic characteristics of the study populations.

Endometrial hyperplasia without atypia was diagnosed in 20.7% of our study population. This relatively high proportion is clinically significant because prolonged or unopposed oestrogenic stimulation associated with anovulatory cycles during the menopausal transition can result in excessive endometrial proliferation. Talukdar and Mahela reported endometrial hyperplasia in 56.31% of patients with AUB undergoing hysterectomy. The most common subtype was found to be simple typical hyperplasia.⁽¹⁴⁾ The much higher percentage in this study may be related to selection bias, since their study population was women undergoing hysterectomy only, while the present study was women undergoing various types of endometrial sampling.

One of the important findings of our study was the detection of atypically perplasia/endometrial intraepithelial neoplasia in 4.7% and endometrial carcinoma in 3.3% of women. Although these proportions were relatively small compared with benign lesions, the clinical significance is considerable. In women with persistent or recurrent AUB, histopathological assessment is particularly important because clinical symptoms alone cannot reliably differentiate benign hormonal disturbances from premalignant or malignant endometrial disease. Damle et al. also highlighted the significance of histopathological examination of endometrial samples in women above 40 years of age in identification of significant organic lesions, and early detection of endometrial carcinoma.⁽¹³⁾

An age-related trend was also observed in the current study, with premalignant and malignant lesions being more common among women in the 51–55-year age group. This is clinically plausible because the cumulative exposure to risk factors for endometrial pathology increases with increasing age. Previous histopathological studies have also shown that hyperplasia and malignancy are more commonly found in perimenopausal and postmenopausal women compared with younger women.⁽¹⁶⁾ Thus, in a woman with AUB, increasing age warrants careful assessment particularly in the setting of persistent bleeding or abnormal imaging findings.

In our study, a significant association between the pattern of bleeding and histopathological diagnosis were found. Endometrial hyperplasia was especially common in women with heavy or prolonged bleeding and all five women with endometrial carcinoma presented with heavy, prolonged or persistent irregular bleeding. This finding emphasises the importance of the clinical pattern of bleeding in the decision for further evaluation of the endometrium. However, absence of a specific bleeding pattern

cannot be considered as sufficient to exclude significant pathology.

Ultrasonographic evaluation also revealed clinically relevant findings. Increased endometrial thickness was observed in 72 (48.0). Among these women, 26 (36.1%) had endometrial hyperplasia without atypia, six (8.3%) atypical hyperplasia/EIN and five (6.9%) endometrial carcinoma. A statistically significant association was found between increased endometrial thickness and significant endometrial pathology ($p < 0.001$). Transvaginal ultrasonography has been found to be useful in the initial evaluation of perimenopausal AUB in previous studies, especially in the identification of structural abnormalities and in the selection of women needing tissue sampling.(14,17) However, in cases of suspected endometrial pathology, ultrasonography should be considered an adjunct and not a replacement for histopathological assessment.

A clinical histopathological correlation is an important part of the present study. Most women had benign pathology (90.7%), with 4.7% premalignant lesions and 3.3% malignant lesions. These results are consistent with the view that clinical assessment and histopathology are complementary sources of information. In a study of 236 perimenopausal women, Mishra and Sultan showed that clinical and histopathological assessment can give different distributions of the PALM–COEIN categories, with histology showing a significantly greater contribution from structural pathology, in particular malignancy and hyperplasia.(18) They concluded that clinical and histopathological assessments should be regarded as complementary in women with AUB around the perimenopausal period. This finding is in agreement with the results of the present study.

The presence of leiomyoma and endometrial polyps in 25.3% and 10.0% of our participants, respectively, provides further support for the role of structural abnormalities in AUB during the menopausal transition. Talukdar and Mahela reported fibromyoma as the most common myometrial pathology in perimenopausal women undergoing hysterectomy for AUB.(14) The FIGO PALM–COEIN classification identifies polyps, adenomyosis, leiomyoma and malignancy/hyperplasia as structural causes of AUB, highlighting the necessity to consider both uterine morphology and the endometrium.(1) The findings of this study are of particular relevance to the tertiary care practice in North Coastal Andhra Pradesh where region specific data regarding AUB and its histopathological spectrum is still limited. The study shows that although benign functional endometrial patterns are the most frequent findings, a clinically significant number of women may have hyperplasia, atypical lesions, or carcinoma. Thus, inclusion of systematic clinical assessment, ultrasonography and appropriately indicated histopathological examination, may improve detection of significant endometrial disease.

Limitations

There are limitations to the present study. The study was carried out in a single tertiary care hospital and hence the results cannot be generalised to the whole population of North Coastal Andhra Pradesh. The study population was women who had endometrial or uterine tissue sampling and may have resulted in selection of women with a higher clinical suspicion for pathology. Also, the cross-sectional design limits the ability to assess long-term progression of hyperplasia or other endometrial lesions. Larger multicentric studies with longer follow up would be helpful when trying to establish the regional spectrum and risk factors for premalignant and malignant endometrial disease.

Conclusion

The current study reveals that AUB in the menopausal transition encompasses a broad spectrum of histopathological abnormalities with benign proliferative patterns and endometrial hyperplasia being the commonest. However, the presence of atypical hyperplasia/EIN and endometrial carcinoma in a subset of women emphasises the importance of prompt evaluation. Histopathological examination is an important diagnostic tool and should be taken into consideration along with the clinical presentation and ultrasonographic findings. The results also support the use of a structured approach based on clinical assessment and the FIGO framework for the evaluation of women with AUB during the menopausal transition.

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