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Original Research Article

Study of histopathology of endometrium in perimenopausal women with abnormal uterine bleeding

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ABSTRACT

Background: The objective was to evaluate the incidence and prevalence of different histopathological endometrial pattern in patients of abnormal uterine bleeding (AUB) in peri-menopausal women and analyse the type of various menstrual irregularities in AUB cases.

Methods: In this study, 164 perimenopausal women aged 41-48 years have been taken having considered appropriate within the inclusion criteria. Histopathological examination was done after obtaining the endometrial curetting's by Dilatation and curettage or office Pipelle's canula.

Results: Mean age group of subjects was found to be 44.05 years. Majority of subjects were of normal body mass index. Heavy menstrual bleeding was the chief complaint in majority of subjects. Ultrasound finding was leiomyoma in more than 73% subjects. Proliferative pattern of endometrium remained the finding in most of the individuals. Among AUB-M, hyperplasia without atypia occurred in 53.84% and hyperplasia with atypia occurred in 38.46% individuals.

Conclusions: Leiomyoma was the most common etiology contributing towards AUB in the perimenopausal age group. The difference between adenomyosis and leiomyoma may not be easily made clinically as signs and symptoms of adenomyosis and leiomyoma are very similar. Thus, it is important to use histopathological examination as a complementary diagnostic tool in classifying the structural causes of AUB.

Keywords: Abnormal uterine bleeding, AUB-M: Abnormal uterine bleeding- malignancy and hyperplasia

INTRODUCTION

The endometrium that lines the uterine cavity is one of the most dynamic tissues in the human body. Shedding of this endometrium results in the mechanism of normal menstruation.¹ Normal menstruation is defined as the visible manifestation of cyclic physiological uterine bleeding due to shedding of the endometrium following invisible interplay of hormones mainly through hypothalamo-pituitary-ovarian axis.² An estimated blood loss of 20-80ml with an average of 35 ml occurs during menstruation, any bleeding not fulfilling the condition of normal menstruation is termed as "abnormal uterine bleeding".³ AUB is defined as uterine bleeding that is

abnormal in volume, cycle, and/or timing, and should be present in the majority for the last 6 months.⁴ It is the commonest presenting symptom and major gynaecological problem affecting 20% of healthy perimenopausal women.⁵ It amounts to approximately 35% of gynaecology OPD visits and 25% of gynaecological surgeries. It includes both organic and non-organic causes of uterine bleeding. It can be caused by systemic diseases, endocrine disorders, pregnancy, drugs, fibroids, polyps, adenomyosis and endometrial causes.

Acute AUB could be classified as "an episode of bleeding in a non-gravid woman of reproductive age group, that is sufficient in quantity to require immediate intervention for

preventing further blood loss". Additionally, chronic AUB is "bleeding from the uterine corpus that is abnormal in duration, volume and/or frequency and has been present for the majority of the last 6 months". In the premenopausal period, it may cause anemia, and in the postmenopausal period, it may raise the suspicion of malignancy.⁶

Perimenopause, as defined by WHO is the period of 2-8 years preceding menopause and 1 year after complete cessation of menses. Thus, it is the period surrounding menopause which is characterized by decreasing ovarian function, manifesting in menstrual irregularities which include the various forms of abnormal uterine bleeding.⁷ The average age of menopause in Indian women is 46 years.⁸ The International Federation of Gynecology (FIGO) has recently developed a classification system for the causes of AUB in non-gravid women known as PALM-COEIN. PALM refers to the structural causes: polyp, adenomyosis, leiomyoma, malignancy and hyperplasia. COEIN refers to coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not yet classified.

The structural causes of AUB can be evaluated by imaging techniques and/or histopathology whereas functional causes are diagnosed by investigating the underlying medical disturbances.⁹ The modalities used to diagnose the structural causes of AUB include ultrasonography, hysteroscopy, endometrial sampling, sonosalpingography and dilatation and curettage. After excluding the organic causes of AUB the endometrial pattern obtained in the endometrial biopsy of patients help us in knowing the underlying pathology thus assisting us in further management. The evaluation of a patient with AUB in perimenopausal age begins only after thorough history, general physical examination and systemic evaluation. Apart from routine investigation PAP smear, endometrium sampling, pelvic ultrasound and hysteroscopy is done.¹⁰ The diagnosis of AUB can be quite challenging despite a detailed history, various blood tests, and a thorough pelvic examination often involving ultrasonography, the causes of the bleeding is established only in 50-60% of cases. A number of minimally invasive surgical options do exist now and are promising like endometrial ablation, thermal balloon therapy and uterine artery embolization but restricted availability, utility and cost factor limit them from being widely used.

The study was done to evaluate the histopathological findings of endometrium in perimenopausal age women presenting with abnormal uterine bleeding, to know the prevalence of AUB and their categorization into PALM-COEIN classification.

METHODS

The study was carried out in the department of obstetrics and gynaecology, Government Multispeciality Hospital, Chandigarh (from March 2021 to April 2022) after obtaining clearance from research and ethics committee

and informed consent from the patients. The women chosen belonged to age group 41-48 years women in perimenopausal age group with any of the abnormalities in menstrual cycle: heavy menstrual bleeding/infrequent menstrual bleeding/frequent menstrual bleeding/prolonged menstrual bleeding/irregular menstrual bleeding/light menstrual bleeding/intermenstrual bleeding, were included in the study after excluding as per exclusion criteria (pregnancy and its complications, acute pelvic inflammatory disease, abnormal cervical PAP smear, previous abnormal endometrial biopsy, hemostatic disorders, women on hormonal therapy, follow up cases of breast cancer or family history of ca-breast on anticancer drugs. The endometrial biopsy was taken only after complete work up which includes detailed history, general examination, per abdominal, per speculum and per vaginal examination and baseline investigations like hemogram, coagulogram, blood sugar, LFT, TSH, viral markers. Endometrial biopsy was done (using Pipelle's canula) on the patients in the pre-menstrual phase and the sample was sent for histopathological analysis. Routine histopathological processing of the samples was done and tissue sections will be studied under light microscopy. The results obtained were taken into consideration for the respective management of the condition.

Sample size

This utility calculates the sample size required to estimate a proportion (53%) with a specified level of confidence and precision. The sampling technique used in the study was convenient sampling.

$n = (Z^2 \times P(1-P)/E^2)$, $n = 164$ (approximately), where Z = value from standard normal distribution corresponding to desired confidence level (Z = 1.96 for 95% CI), P (0.53) is the expected true proportion, E (0.09) is the desired precision.

Total sample size = 164.

RESULTS

The study was conducted at Government Multispecialty Hospital, Chandigarh, focusing on women with abnormal uterine bleeding who visited the obstetrics and gynecology department from March 2021 to April 2022. Eligible subjects underwent USG and histopathological investigations, necessary interventions, and result analysis. In the participant demographic profile (Table 1), the average age was 44.05 years, with notable distribution in the 41-45 and 46-48 age groups. Most participants were Hindu housewives in the middle socioeconomic class with normal BMI. Chief complaints included heavy menstrual bleeding (68.9%) and intermenstrual bleeding (9.8%), persisting for 6-12 months (84.8%). Histopathology findings (Table 5) identified leiomyoma (66.50%) as most common, followed by polyps (8.50%) and adenomyosis (7.30%). Ultrasonographic results (Table 2) highlighted leiomyoma prevalence (73.17%), while provisional

diagnoses (Table 3) indicated leiomyoma-related AUB (73.2%) as prominent. Endometrial patterns (Table 4) were primarily proliferative (70.55%) and secretory (22.69%), with less frequent occurrences of hyperplasia without atypia (4.26%) and hyperplasia with atypia (3.96%).

Table 1: Demographic profile of participants.

Parameter	Number of subjects (n=164)	Percentage
Mean Age: 44.05 years		
Age (years)		
41-45	109	66.5
46-48	55	33.5
Religion		
Hindu	130	79.26
Sikh	28	17.07
Muslim	06	3.65
Occupation		
Housewife	162	98.78
Employed	02	1.21
Socioeconomic status		
Upper middle class	35	21.34
Middle class	129	78.65
BMI		
Normal	120	73.17
Overweight	29	17.68
Obese	15	9.14
Chief complaints		
Frequent cycle	05	3
Heavy menstrual bleeding	113	68.9
Heavy and prolonged menstrual bleeding	06	3.7
Intermenstrual bleeding	16	9.8
Light menstrual bleeding	07	4.3
Prolonged menstrual bleeding	12	7.3
Frequent and heavy menstrual bleeding	05	3
Duration of symptoms (months)		
1-<6	10	6.1
6-12	139	84.8
12.1-24	12	7.3
>24	03	1.8
Parity		
0	01	0.6
1	18	11
2	82	50
3	46	28
>3	17	10.4
PAP smear		
NILM	139	84.8
NILM+ inflammatory	25	15.2

BMI: body mass index, PAP: Papanicolaou test, NILM: negative for intraepithelial lesion or malignancy

Table 1 provides a comprehensive snapshot of the demographic characteristics of 164 research participants. It includes their mean age (44.05 years), age distribution, religious affiliations, occupations, socioeconomic statuses, body mass index (BMI) classifications, chief complaints related to menstrual bleeding, symptom durations, parity, and PAP smear results.

Table 2: Ultrasonographic finding in participants.

Parameter	Number of subjects (n=164)	Percentage
Leiomyoma	120	73.17
Adenomyosis	24	14.63
Endometrial hyperplasia	12	7.31
Endometrial polyp	19	11.58
Endocervical polyp	01	0.60

The Table 2 presents ultrasonographic findings in a group of 164 participants. It highlights the prevalence of various conditions such as leiomyoma (73.17%), adenomyosis (14.63%), endometrial hyperplasia (7.31%), endometrial polyps (11.58%), and endocervical polyps (0.60%).

Table 3: Provisional diagnosis in participants (on the basis of PALMCOEIN classification).

Parameters	Number of subjects (n=164)	Percentage
AUB-P	20	12.2
AUB-A	22	13.4
AUB-L	120	73.2
AUB-M	17	10.4
COEIN	0	0

PALMCOEIN: polyp, adenomyosis, leiomyoma, malignancy, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not-yet-classified AUB: Abnormal uterine bleeding in polyp, adenomyosis, leiomyoma, malignancy and hyperplasia.

Table 3 shows provisional diagnoses of abnormal uterine bleeding (AUB) in 164 participants using PALMCOEIN classification. Most cases are related to leiomyoma (73.2%), followed by adenomyosis (13.4%) and malignancy (10.4%). Polyp-related cases account for 12.2%, while no cases are classified under COEIN.

Table 4: Pattern of endometrium in participants.

Parameters	Number of subjects (n=164)	Percentage
Proliferative	115	70.55
Secretory	37	22.69
Hyperplasia without atypia	07	4.26
Hyperplasia with atypia	05	3.96
Endometrial carcinoma	01	0.6

Table 4 shows endometrial patterns in 164 participants. Most had proliferative patterns (70.55%), followed by secretory patterns (22.69%). Hyperplasia without atypia was in 4.26%, hyperplasia with atypia was in 3.96%, and endometrial carcinoma was in 0.6% of cases.

Table 5: Histopathology finding in participants.

Parameter	Number of subjects (n=164)	Percentage
Leiomyoma	110	66.50
Polyp	14	8.50
Adenomyosis	12	7.30
Endometrial hyperplasia without atypia	07	4.30
Endometrial hyperplasia with atypia	06	3.70
Leiomyoma + adenomyosis	06	3.70
Leiomyoma + adenomyosis + polyp	02	1.20
Adenomyosis + polyp	01	0.60
Endocervical polyp	01	0.60
Adenomyosis + endometrial hyperplasia without atypia	01	0.60
Leiomyoma + polyp	01	0.60
Polyp + endometrial hyperplasia without atypia	01	0.60

Table 5 show histopathology findings in 164 participants. The most common findings are leiomyoma (66.50%), followed by polyps (8.50%) and adenomyosis (7.30%). Various combinations of these conditions were also observed in smaller percentages.

Figures 1-4 depict the various histopathological findings of endometrium.

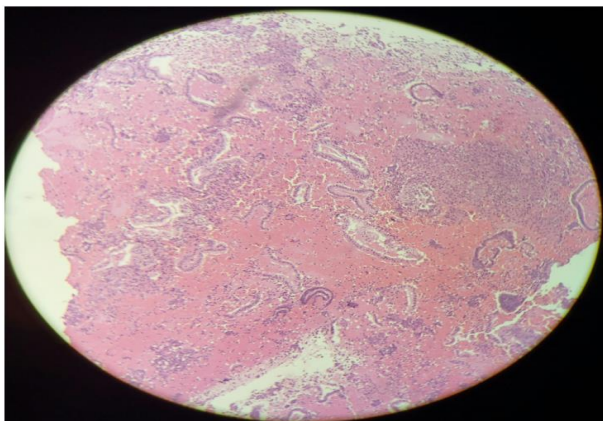


Figure 1: Shedding endometrium.

This figure portrays the endometrial tissue during the shedding phase of the menstrual cycle. The endometrial lining is being sloughed off, marking the beginning of the menstrual period.

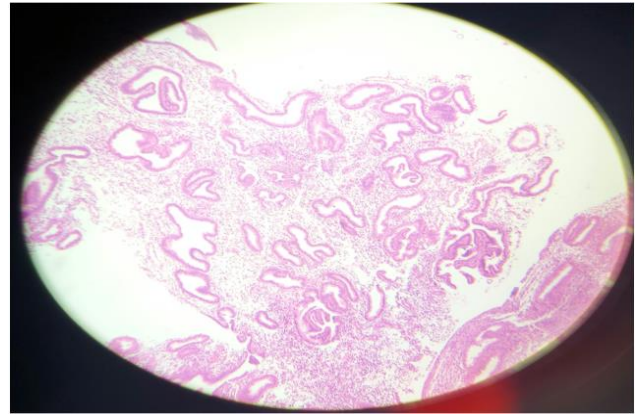


Figure 2: Secretory endometrium.

In this figure, the endometrial tissue is in the secretory phase, indicating the preparation for potential pregnancy. The glands within the tissue shows signs of increased secretion and development.

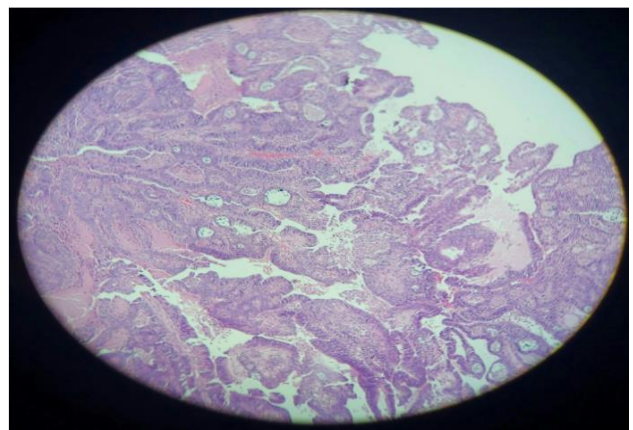


Figure 3: Villoglandular adenocarcinoma.

This figure displays villoglandular adenocarcinoma, a type of endometrial cancer. Characterized by glandular structures with finger-like projections, it highlights the malignant transformation of endometrial tissue.

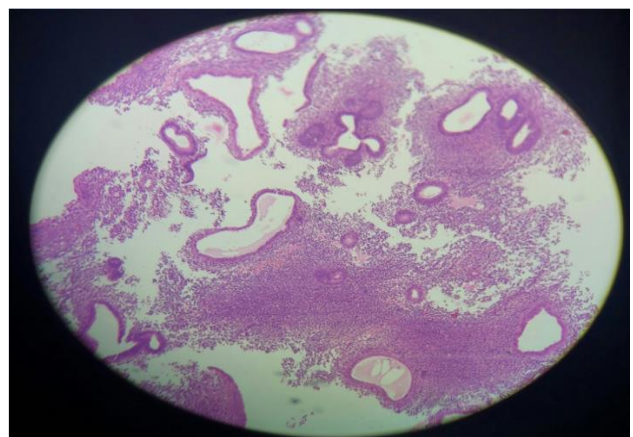


Figure 4: Disordered proliferative endometrium.

This figure depicts a disordered proliferative endometrium, indicating irregular growth and changes in the endometrial lining. This pattern might be associated with hormonal imbalances or other factors.

DISCUSSION

Abnormal uterine bleeding is defined as any bleeding from the genital tract which is a deviation from the normal in volume, duration, regularity or frequency. In present study, 164 women with AUB were examined in obstetrics and gynaecology department, GMSH, Chandigarh. A detailed history, clinical examination and routine investigations were done. USG was offered as initial non-invasive investigation. Further investigations were done by endometrial curettage, either by D and C or pipelle's biopsy. Further intervention was done as per the endometrial histopathology. Various parameters of our study were compared with the studies of different authors.

The mean age of women was calculated in various studies with varied results. Neena et al studied 288 subjects and observed that mean age of subjects was 37.66 years.¹¹ Khushnood et al studied 30 subjects and found 40.33 years as mean age.¹² The mean age was 41.26 years in the study by Bedary et al who studied 676 subjects.¹³ However, highest mean age was observed in the study by Suseela et al which was 45 years.¹⁴ The mean age of subjects in the present study (2021) was 44.05 years. Hence the mean age of subjects in our study was comparable to the study of Suseela et al (Table 1).¹⁴

The distribution of parity in the subjects was analysed by various studies. Suseela et al studied in 100 subjects were multiparous in both Mohammad et al and Snehkiran et al studies, while the study by Lotha et al had the highest number of multiparous women accounting to 87%.¹⁴⁻¹⁷ In our study, 88.41% women were multiparous. Hence, our study was comparable with the studies by Mohammad et al, Lotha et al and Snehkiran et al.¹⁵⁻¹⁷ BMI was studied by Sajitha et al.¹⁸ (2014) and Mishra D et al.¹⁹ (2017). Sajitha et al.¹⁸ studied 156 subjects and found 3.8% subjects as obese, whereas obesity was found in 9.35 women out of 236 subjects in Mishra D et al.¹⁹ study. In present study in 164 women, 9% were found to be obese (Table 1).

Heavy menstrual bleeding (HMB) was the commonest pattern of bleeding observed by Sajitha et al in 47% subjects, Lotha et al in 49%, Misra et al in 51.5%, Khan et al in 55.85%, Bashir et al in 56.73%, Khushnood et al in 60% and Suseela et al in 61% subjects.^{12,14,17-21} In present study, heavy menstrual bleeding was observed in 68.9% subjects. Hence, in our study HMB as chief complaint was comparable to studies of Suseela et al and Khushnood et al (Table 1).^{12,14} In present study, PAP smear was normal in 85% which is comparable to Mahapatra et al study in which it was normal in 96%.²² In studies done by Banale et al, Suneet et al and Maurya et al on 285, 50 and 156 subjects respectively, proliferative pattern was found to be the most common endometrial pattern in endometrial curetting's accounting to 32.63%, 36% and 30.6% subjects respectively.^{15,23,24} Also, in our study, proliferative pattern was maximum (70.55%) (Table 4). Comparison of single pathology and multiple pathologies causing AUB was studied by Arnold et al in which single pathology was

found in 48.9% subjects and multiple pathologies in 51.1% on HPE, unlike in present study single pathology was seen in 92% and multiple pathologies in 8% on HPE (Table 5 and Figures 1-4).²⁵

The mean age of study population was 44.05 years. Majority of the subjects were in the age group of 41-45 years (66.5%) COEIN cause of AUB was not detected in our study.

CONCLUSION

It was concluded that the histopathological correlation with the clinical symptoms of AUB was good as the classification of cases under PALM-COEIN was done. Leiomyoma was the most common etiology contributing towards AUB in the perimenopausal age group. Histopathology, however helped in accurate diagnosis of cases missed clinically. Thus, we found that PALM-COEIN classification is a useful system clinically and histopathologically as both are complementary to each other and allocating a proper category would help in optimization of the treatment of the patient. The difference between adenomyosis and leiomyoma may not be made easily clinically as signs and symptoms of adenomyosis and leiomyoma are very similar. So, histopathological analysis differentiates between the two. This emphasizes the importance of histopathological examination as a complementary diagnostic tool in classifying the structural causes of AUB.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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