http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v11i3.30

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Histopathological Spectrum of Endometrial Lesions in Women Presenting with Atypical Uterine Bleeding: Two Year Study

Authors
Jahnavi Marachapu[1]*, Swati Vij[2]
[1]*Specialist, Dept of Pathology, ESIC, Delhi
[2]Senior Resident, Department of Pathology, ESIC, Delhi

Abstract

Background: *Abnormal uterine bleeding (AUB) is a prevalent symptom experienced by patients of all ages in the O&G outpatient department, which can negatively impact the quality of life of an otherwise healthy woman. Proper treatment is challenging until an accurate diagnosis of the underlying pathology is made. AUB can be caused by a range of factors that differ across age groups. Conducting a histopathological examination of endometrial biopsy and curettage samples can effectively diagnose the cause of AUB at an early stage.*

Materials and Methods: *In this study, a retrospective analysis was performed on a cohort of patients who presented with abnormal uterine bleeding (AUB). The study was conducted between 2021 and 2022, and D&C material endometrial biopsy and curettage specimens were collected in the Pathology Department. All specimens were processed and stained with the H&E stain, and any changes in the endometrial samples were recorded. The patients were classified into three groups based on their age: reproductive age (17-40 years), perimenopausal (up to 50 years), and postmenopausal (above 50 years).*

Results: *A total of 200 specimens of endometrial biopsies and D&C materials, were collected of which 20 cases were excluded due to inadequate tissue sampling. The most common age group affected is the reproductive age group of patients presenting with complaints of AUB frequently observed in the age17- 40years, which constitute86 cases (47.78%), followed by perimenopausal age group with 72 cases (40.00%) and postmenopausal group with 22 cases (12.22%).The most common histopathological finding in this study was a normal menstrual pattern (45.56 %). The commonest finding observed in the study was secretory phase endometrium (25.00%), followed by proliferative phase endometrium (20.56%).Two cases of endometrial carcinomas were presented after the age 50 years. pregnancy related complications (PRC) were prevalent, In reproductive age and endometrial polyp was common in perimenopausal age groups after excluding functional causes. In post-menopausal age, atrophic endometrium was the commonest finding.*

Conclusion: *Pregnancy related complications are a common cause of abnormal uterine bleeding in women of reproductive age. However, it is important to perform a thorough histopathological workup and consider clinical factors to rule out endometrial hyperplasia or carcinoma, which are more common in perimenopausal and postmenopausal women. This study aimed to investigate the most common endometrial causes of AUB among different age groups, including reproductive, perimenopausal, and postmenopausal women, in our hospital.*

Introduction

The endometrium is a constantly changing tissue that is sensitive and responsive to hormones, particularly during active reproductive years. Among patients of all ages who are coming to gynaecology outpatient departments, excessive and irregular bleeding remains a common presenting symptom[1]. Abnormal uterine bleeding is characterized by a deviation in frequency, duration, or amount of bleeding from what is

typically observed during a normal menstrual cycle or after menopause[2].Abnormal uterine bleeding can result from various causes, including dysfunctional uterine bleeding (DUB), bleeding due to endocrine or psychological factors, and bleeding caused by structural abnormalities such as fibroids, polyps, endometrial hyperplasia, adenomyosis, ovulatory dysfunction, endometritis, pregnancy-related complications, and endometrial carcinoma. DUB refers to abnormal uterine bleeding that cannot be attributed to any identifiable organic pathology in the endometrium. This condition is caused by high levels of estrogen in the circulating blood[3-5] .Individuals with a medical history of anovulation, obesity, hypertension, diabetes, and exogenous estrogen use are at a higher risk of developing hyperplasia and adenocarcinoma. Endometrial biopsy and curettage are common methods of evaluating the causes of abnormal uterine bleeding (AUB). To ensure an accurate interpretation of endometrial samples, it is important to consider the patient's age, clinical history, menstrual history, and drug history, especially with regard to the use of exogenous hormones[6,7]. However, these procedures can pose a diagnostic challenge due to overlapping morphological features, sample inadequacy, and inter-observer variability[7].The objective of this study is to analyse the frequency and types of endometrial patterns in women with AUB across different age groups, including reproductive, perimenopausal, and postmenopausal women.

Materials and Method

A retrospective study was undertaken which included 200 endometrial samples with a clinical diagnosis of AUB. Out of which 20 samples were inadequate for proper diagnosis. The study was carried out in the Department of Pathology, ESIC Delhi, over a period of 2 years from January 2021 to December 2022. The study focused specifically on endometrial pathology and did not include patients with other conditions affecting the reproductive system or haemostasis. The information about patients' clinical history, including age, menstrual status, and hormone therapy, as well as their symptoms such as painful or heavy bleeding and menstrual cycle regularity, were obtained through clinical records. Endometrial samples were collected using various methods such as biopsy, curettage, and dilation and curettage. The processing of the endometrial samples involved fixation in 10% buffered formalin, which preserves the tissue structure. The tissue was then processed in an automated tissue processor, which involves dehydrating the tissue, clearing it in xylene, and embedding it in paraffin wax. Four-micron-thick sections were cut from the paraffin-embedded tissue blocks and stained with Haematoxylin and Eosin. A microscopic examination was then performed to study the tissue morphology and identify any abnormalities.

The patients were categorized into different age groups, namely reproductive (17 -40 years), peri-menopausal (up to 50 years), and postmenopausal (above 50 years). The histopathological findings were classified into functional causes, which include physiological cyclical changes, atrophic, secretory, proliferative endometrium, disordered proliferative endometrium, and nonspecific degenerative changes, and organic causes, which include endometrial polyp, chronic endometritis, endometrial hyperplasia, carcinomas, and pregnancy-related complications such as the retained product of conceptus and gestational trophoblastic diseases.

Results

The study has been conducted on endometrial specimens including endometrial curetting/biopsy and dilation and curettage which were received in the Department of Pathology, ESIC Delhi, for 2 year period with the clinical diagnosis of abnormal uterine bleeding.

During the study period, out of 180 patients, most patients belonged to the reproductive age group (17- 40 years) comprises of 86 cases (47.78%) followed by the perimenopausal age group (up to 50 years) comprises of 72 cases (40.00%) and

then the postmenopausal age group (above 50 years)comprises of 22 cases (12.22%).

Patients were distributed according to the pattern of bleeding. The maximum number of patients presented as menorrhagia was 100 cases (55.62%) followed by polymenorrhoea60 cases (33.33%). Postmenopausal bleeding was seen in 20 cases (11.11%).

The most common histopathological finding in this study was a typical menstrual pattern seen in 82 cases (45.56 %). Amongst these 82 cases, 45 cases (25.00%) were in the secretory phase and 37 cases (20.56%) were in the proliferative phase. The other histological patterns observed were hormonal imbalance and pill effect (14 cases, 7.78%), atrophic endometrium (14 cases, 7.78%), benign endometrial polyp (17 cases, 9.44%), products of gestation (9 cases, 5.00%), endometrial hyperplasia (12 cases, 6.67%), and endometrial carcinoma (2cases, 1.15%).chronic endometritis (12 cases, 6.67%) Among 12 cases of chronic endometritis, 2 cases were granulomatous endometritis and the other 10 cases were nonspecific endometritis. Among 12 cases of endometrial hyperplasia, 10 cases were simple hyperplasia without atypia, two cases were complex hyperplasia with atypia. Out of the two endometrial carcinoma cases, one was endometroid carcinoma, which was well-differentiated and the other was clear cell carcinoma. Thus 178 cases (98.15%) showed benign endometrial pathology while only 2 cases (1.15%) showed the presence of malignancy. (Table 1 and 3)

In the reproductive age group, the most common histological finding was the normal menstrual pattern (47 cases, 54.65%). The second most common pathological finding in this age group was pregnancy related complication such as products of gestation (9 cases, 10.47%), followed by disordered proliferative endometrium (8 cases, 9.30%) endometrial polyp (7 cases, 8.14%), and Hormonal imbalance and pill effect (6cases, 6.98%).

Similarly, In the perimenopausal age group, the most common histological finding was the normal menstrual pattern (33 cases, 45.83%). The most common pathological finding in this age group was disordered proliferative endometrium (9 cases, 12.50%) followed by endometrial polyp (8 cases, 11.11%), hormonal imbalance and pill effect (7 cases, 9.72%), followed by chronic endometritis (6 cases, 8.33%), endometrial hyperplasia which constitutes 5 cases of simple hyperplasia without atypia (5 cases,6.94%)and one case with complex hyperplasia with atypia (1 case,1.39%)

In the postmenopausal age group, the most common histological finding was atrophic endometrium (11 cases, 50.00%) followed by endometrial polyp (2 cases (9.09%), endometrial carcinoma (2 cases, 9.09%), hormonal imbalance and pill effect (1 case 4.55%), endometrial hyperplasia with atypia (1 case, 4.55%) and chronic endometritis (1 case, 4.55%).

Table 1: Histopathological diagnosis of endometrial biopsies, curettage

	17-40 years	Below 50 years	Above 50 years
Proliferative endometrium	21 (24.42%)	15 (20.83%)	1 (4.55%)
Secretory endometrium	26 (30.23%)	18 (25.00%)	1 (4.55%)
Simple hyperplasia	4 (4.65%)	5 (6.94%)	1 (4.55%)
Complex hyperplasia	0 (0.00%)	1 (1.39%)	1 (4.55%)
Atrophic endometrium	0 (0.00%)	3 (4.17%)	11 (50.00%)
Exogenous hormone/pill	6 (6.98%)	7 (9.72%)	1 (4.55%)
Endometritis	5 (5.81%)	6 (8.33%)	1 (4.55%)
Endometrial Polyp	7 (8.14%)	8 (11.11%)	2 (9.09%)
Carcinoma	0 (0.00%)	0 (0.00%)	2 (9.09%)
Disordered proliferative endometrium	8 (9.30%)	9 (12.50%)	1 (4.55%)
products of gestation	9 (10.47%)	0 (0.00%)	0 (0.00%)

Table-2: Categorisation in different age groups

Age	Group
Reproductive age	86 (47.78%)
Perimenopausal age	72 (40.00%)
Postmenopausal age	22 (12.22%)

Table-3: Endometrial lesions according to histopathology evaluation

	Histopathology finding	**Cases**	**Percentage %**
1	Proliferative Endometrium	37	20.56%
2	Secretory Endometrium	45	25.00%
3	Endometrial Hyperplasia	12	6.67%
4	Disordered Proliferative Endometrium	18	10.00%
5	Hormonal change/pill endometrium	14	7.78%
6	Inadequate sample	20	0.00%
7	Atrophic Endometrium	14	7.78%
8	Pregnancy related changes	9	5.00%
9	Endometritis	12	6.67%
10	Endometrial Polyp	17	9.44%
11	Endometrial Carcinoma	2	1.11%

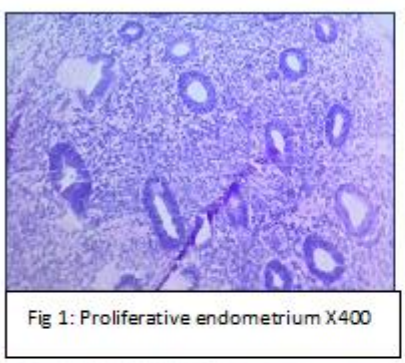
Fig 1: Proliferative endometrium X400

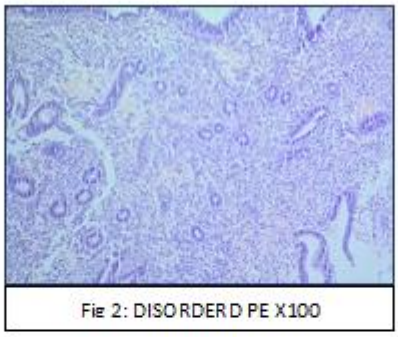
Fig 2: DISORDERD PE X100

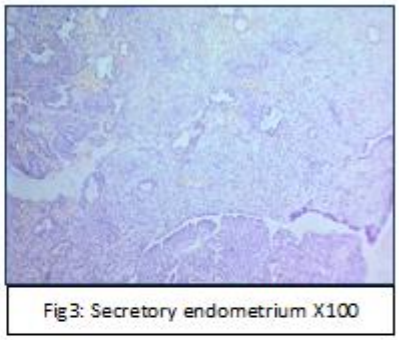
Fig3: Secretory endometrium X100

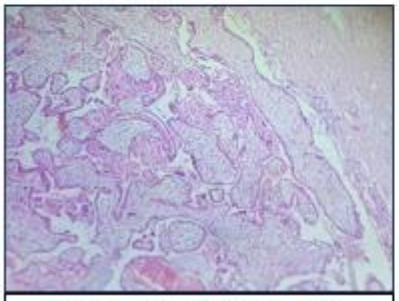
Fig 4:Products of Gestation X400

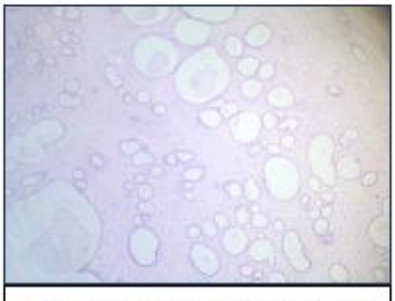
Fig 3:Benign Endometrial Polyp X100

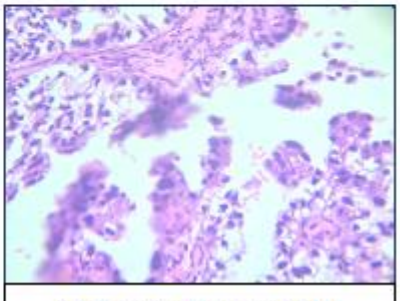
Fig 6: clear cell carcinoma X400

Discussion

The endometrium experiences regular changes during the ovulatory cycle due to hormonal fluctuations. Therefore, it's important to take endometrial samples at the appropriate time to ensure accuracy. Without sufficient clinical information, the diagnosis can be incorrect. Organic causes of abnormal uterine bleeding (AUB) may stem from reproductive diseases, iatrogenic factors, or systemic illnesses. When a specific cause of AUB cannot be identified, dysfunctional uterine bleeding (DUB) is presumed. AUB can manifest as heavy, prolonged or irregular flow during perimenopause, or as spotting or minimal bleeding post-menopause. It is essential to evaluate AUB properly to rule out malignancy. Abnormal uterine bleeding is a common health issue among women in India and

globally, which can lead to physical and mental health problems such as anaemia. Studies have shown that without treatment, endometrial hyperplasia can progress to malignancy in 10-20% of cases. Therefore, it is crucial for women aged over 35 years to undergo endometrial screening to detect and treat malignancies early[8]. In developing countries like India, it's necessary to develop simple and cost-effective diagnostic methods to identify the underlying causes of AUB for timely diagnosis and treatment. Among 200 cases of endometrial biopsy and curettage samples of AUB, patients that were received in the histopathology department, 20 cases were inadequate for definite diagnosis. During the 2 year study period, out of 180 patients, The incidence of abnormal uterine bleeding was more in reproductive age group than peri and postmenopausal age group which was 17- 40 years 86 cases (47.78%) followed by the perimenopausal age group up to 50 years (72 cases (40.00%) and then the postmenopausal age group above 50 years which constitute 22 cases (12.22%). Histopathological examination of the endometrial biopsies and curetting's revealed different phases of endometrium varying from physiological to pathological lesions. The majority of patients in the present study had normal endometrial findings, with secretory phase being most common than proliferative phase. The secretory phase is characterized by the presence of secretory glandular epithelium, increased glandular and stromal cellularity, and oedematous stroma. The proliferative phase is characterized by the presence of straight, long and narrow glands with prominent nuclei and mitotic figures. Secretory and Proliferative phase endometrium was observed in 30.23% and 24.42% patients. These patterns were observed in the reproductive age group more frequently. In our study, the majority of patients belonged to the age group 17-40 years. This finding is consistent with the studies conducted by Rajesh Patil et al [9] and Mitra K et al [10], which showed that AUB was predominantly observed in the age group below 40 years, with incidences of 45.2% and 62%, respectively. Doraiswami et al. [11] noted that the majority of cases of abnormal uterine bleeding (AUB) were found to be normal physiologic phases such as proliferative, secretory, and atrophic menstrual patterns. Anovulatory cycles may cause bleeding during the proliferative phase, while ovulatory dysfunctional uterine bleeding may lead to bleeding during the secretory phase. The main defect during ovulatory dysfunctional uterine bleeding is in the control of processes that regulate the volume of blood loss during the menstrual breakdown of the endometrium. This type of bleeding is characterized by regular episodes of heavy menstrual blood loss or menorrhagia. The findings of Vaidya et al[12] and Mariam A et al [13]are in agreement with the results of the present study. Vaidya et al reported a higher incidence of disordered proliferative endometrium (13.4%) and endometrial hyperplasia (10.92%) compared to the present study, but a similar incidence of endometrial cancer (2.48%). Mariam A et al observed that AUB was more common in the reproductive age group, and reported hormonal imbalance as the most frequent endometrial pathology, which is in line with the present study's findings. The incidence of endometrial carcinoma in Mariam A et al's study was also similar to the present study. Overall, these studies support the importance of accurate diagnosis and timely treatment of endometrial pathologies, especially in women with AUB.

Our study found that pregnancy-related complications were the most common finding in the reproductive age group, specifically in those below 30 years of age. In the 31-40 age group, cyclical endometrial changes were the predominant finding. These findings are consistent with the results of Doraiswami et al., Vaidya et al. reported the secretory phase as the predominant change in endometrial biopsy in the perimenopausal age group. Where as in our study, 18 cases (26.35%) showed a disordered proliferative pattern, which is consistent with the findings of Jetley S et al [14].

The term "disordered proliferative endometrium" refers to an endometrium that is hyperplastic but does not have an increase in endometrial volume. This condition is complex and may be mistaken for simple hyperplasia; however, the process is focal rather than diffuse. This study found hormonal changes in the endometrium in 14 (21.25%) cases, which is consistent with the findings of Sarika et al [15], who reported 13 cases (6.43%). However, Abid M et al [13]reported a higher incidence of hormonal changes at 27%.

Patients who have chronic endometritis may experience distressing symptoms such as abnormal uterine bleeding (AUB), pelvic pain, and infertility. It is important to diagnose this condition in a timely and accurate manner, as specific treatment can help the endometrium return to its normal functioning state.In contrast to our study, Jetley et al[14] reported a higher incidence of endometritis with 20 cases diagnosed. However, in our study, 12 cases were diagnosed with this condition. Out of these cases, ten showed chronic endometritis, and two cases showed necrotizing granulomatous endometritis.

Endometrial polyps are defined as fragments of endometrial tissue that are polypoidal in shape and lined with epithelium on three sides. These fragments are composed of fibrous stroma and thick-walled blood vessels. Our study found an incidence of endometrial polyps to be 28.34%, which is consistent with the results of Jetley S et al[14] and Doraiswami S et al[11]. Additionally, we found that 1.1% of cases were diagnosed with endometrial carcinoma, which is a common occurrence in the post-menopausal age group. This finding is comparable to the results reported by Sarika et al [15](1.98%). Our study found that 50.00% of cases in the above 50-year age group had atrophic endometrium. In the perimenopausal age group, there is a gradual loss of ovarian function, which eventually leads to the permanent thinning of the endometrium, known as atrophic or inactive endometrium. This thinning makes the endometrium more prone to bleeding on trauma due to anovulation. Our findings are consistent with the results of previous studies conducted by Anuradha et al,[16] and Abid M et al, [13]which reported a 20% and 33% prevalence of atrophic endometrium in post-menopausal age groups, respectively.

Conclusion

The examination of endometrial tissue in females with abnormal uterine bleeding across all age groups is crucial for identifying various histopathological patterns and underlying causes. Our study examined a broad range of histomorphological changes in endometrial biopsies taken from patients presenting with AUB, including cases with normal endometrium as well as malignancies. However, evaluating endometrial biopsies can be challenging for pathologists due to the frequent inadequacy of endometrial sampling, which requires careful screening to achieve accurate diagnoses. Our findings indicate that AUB is most commonly observed in the reproductive age group (17-40 years). Therefore, it is essential to conduct a thorough histopathological workup and clinical correlation in cases of abnormal uterine bleeding to ensure proper treatment and prevent further complications.

References

1. Tavassoli FA, Devilee P; Pathology and genetics of tumours of the breast and female genital organs. Tumors of the uterine corpus. In WHO classifications of tumours. IARC Press, Lyon France, 2003:221-232.
2. Ely JW, Kennedy CM, Clark EC, Bowdler NC. Abnormal Uterine Bleeding: A Management Algorithm. J Am Board Fam Med. 2006;19:590–602.
3. Aksel S, Jones GS. Etiology and treatment of DUB. Obstet Gynecol. 1974; 44:1-13.
4. Altchek A. Dysfunctional uterine bleeding in adolescence. Clin Obstet Gynecol. 1977;20:633–650.

5. Padubidri VG, Daftary SN. Howkins and Bourne Shaw's textbook of gynaecology. 16th ed. Elsevier;2015:321-22
6. Zuber TJ. Endometrial biopsy. Am Fam Physician. 2001;63(6):1131-5,1137-41
7. McCluggage WG. My approach to the interpretation of endometrial biopsies and curettings. J Clin Pathol. 2006;59(8):801-12.
8. Burbos N, Musonda P, Giarenis I, Shiner AM, Giamougiannis P, Morris EP, Nieto JJ. Predicting the risk of endometrial cancer in postmenopausal women presenting with vaginal bleeding: the Norwich DEFAB risk assessment tool. Br J Cancer. 2010;102(8):1201.
9. Patil R, Patil RK, Andola SK, Laheru V, Bhandar M. Histopathological spectrum of endometrium in dysfunctional uterine bleeding. Int J Biol Med Res 2013; 4(1):2798-801.
10. Mitra K, Chowdhury MK. Histological and histochemical study of endometrium in dysfunctional uterine haemorrhage. J Indian Med Assoc. 2003 Aug;101(8):484-5.
11. Doraiswami S, Johnson T, Rao S, Rajkumar A, Vijayaraghavan J, Panicker VK. Study of Endometrial Pathology in Abnormal Uterine Bleeding. J Obstet Gynaecol India. 2011 Aug;61(4):426-30.
12. Vaidya S, Lakhey M, Vaidya S, Sharma PK, Hirachand S, Lama S, et al. Histopathological pattern of abnormal uterine bleeding in endometrial biopsies. Nepal Med Coll J. 2013;15(1):74-7.
13. Abid M, Hashmi AA, Malik B, Haroon S, Faridi N, Edhi MM, et al. Clinical pattern and spectrum of endometrial pathologies in patients with abnormal uterine bleeding in Pakistan: need to adopt a more conservative approach to treatment. BMC women's Health. 2014;14(1):132.
14. Jetley S et al. Morphological spectrum of endometrial pathology in middle aged women with atypical uterine bleeding: A study of 219 cases. Journal of Mid-life Health Oct-Dec 2013 ; Vol 4 : Issue4.
15. Sarika More, et al. Histomorphological Spectrum of lesions in Endometrial Biopsy in Patients Presenting with Abnormal Uterine Bleeding- A study of 202 Cases.JCont Med A Dent May-Aug 2016 Vol 4 Issue 2
16. Anuradha, S. and Premlata, M. Spectrum of Endometrial Histopathology in Women Presenting with Abnormal Uterine Bleeding. Scholars Journal of Applied Medical Sciences. 2015;3(1):1-4.1