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Original Article

Retrospective histopathology study and classification of endometrial biopsies and curetting.

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ABSTRACT

Introduction:

Abnormal Uterine Bleeding is one of the most common presenting complaints of the gynecology department. It can be due to various factors depending on the patient's age. The evaluation of Abnormal uterine bleeding requires adequate history, physical examination, and laboratory investigations, including imaging and endometrial sampling. Endometrial biopsy and subsequent histopathological study remain the gold standard for diagnosis of causes of abnormal uterine bleeding. Endometrial hyperplasia and carcinoma of the uterus are more common in postmenopausal age groups. This helps in the early detection of malignant lesions, thereby helping in the early appropriate treatment.

Aim:

To find out the pathological pattern in different cases of abnormal uterine bleeding, correlate the abnormal endometrial pathology pattern with age, hormonal treatment history, and to find out the incidence of endometrial hyperplasia with or without atypia and carcinoma.

Materials and methods: This is a retrospective study of endometrial sampling (endometrial curettage and biopsy) in cases presented with abnormal uterine bleeding for the past 3 years (2022 - 2025) in the Department of Pathology, Sree Narayana Institute of Medical Sciences. The total number of samples taken was 268.

Results:

Normal cyclical endometrium was the most commonly observed pattern in the study (proliferative 10.82% and secretory 39.92%). Endometrial biopsy also identified structural abnormalities such as a polyp (14.92%). Endometrial hyperplasia without atypia was seen in 3.73%, and atypical hyperplasia was noted in 1.86%. Endometrial carcinoma was found in 3 cases, all of them in the postmenopausal age group.

Conclusion:

Endometrial study helps to differentiate ovulatory from anovulatory dysfunctional uterine bleeding. Endometrial sampling and subsequent histopathological study can lead to early detection of endometrial hyperplasia and carcinoma and have a significant impact on the management of abnormal uterine bleeding.

Keywords: Abnormal uterine bleeding, Atrophic endometrium, Endometrial carcinoma, Endometrial hyperplasia, Endometritis.

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Introduction

Abnormal uterine bleeding (AUB) is defined as changes in frequency of menstruation, duration of flow, or amount of blood loss from a pattern observed during normal menstrual cycles or menopause. It is one of the most

common presenting complaints of the gynecology department.

Several terms are popularly used to describe patterns of AUB. Menorrhagia refers to bleeding occurring at normal intervals (21 to 35 days but with heavy flow (>80 ml) or duration (>7 days). Metrorrhagia is bleeding of any



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amount that is acyclical and occurs irregularly or continuously in between normal cycles. Bleeding occurring at irregular, noncyclic intervals and with heavy flow (>80 ml) or duration (>7 days) is called menometrorrhagia.

Polymenorrhoea is cyclical bleeding which is normal in amount but occurs at frequent intervals of less than 21 days. Oligomenorrhoea describes bleeding occurring at intervals greater than 35 days. Postmenopausal bleeding (PMB) is bleeding recurring in a menopausal woman at least one year after cessation of cycles. Dysfunctional uterine bleeding (DUB) is diagnosed after exclusion of pregnancy or pregnancy-related disorders, medications, iatrogenic causes, obvious genital tract pathology, and systemic conditions².

Approximately 30% of all gynaecological patients have complaints of AUB. In 8–50% cases of endometrial carcinoma, the most common presentation is AUB. Dysfunctional uterine bleeding (DUB) is present in 50% of the women with AUB, which includes abnormal bleeding due to non-organic causes⁷.

The cause of AUB varies according to the age, endometrial response to hormones and their variations, and other structural lesions³. The International Federation of Obstetrics and Gynaecology (FIGO) provided the most recent terminology update in 2018, which introduced an acronym to define bleeding patterns and included intermenstrual bleeding as a characteristic feature of AUB¹.

Various direct and indirect pathological entities related to the reproductive tract can contribute to AUB. To better categorize the potential causes of AUB, FIGO has developed a two-part system that distinguishes between structural (PALM) and non-structural (COEI) entities. The PALM group includes four structural conditions: polyps, adenomyosis, leiomyomas, and malignancies, such as atypical endometrial hyperplasia and epithelial intraepithelial neoplasia, which can be assessed through imaging and histopathological examination. The COEI group includes coagulopathies, ovulatory abnormalities, endometrial dysfunction, and iatrogenic causes from medications, such as gonadal steroids, certain antidepressants, coagulopathy, drugs, or intrauterine devices. Their diagnosis typically relies on laboratory tests. Additionally, the N category (not otherwise classified) involves rare causes of AUB, such as caesarean section, scar defects, and arteriovenous malformations, which may require histopathological analysis or imaging for detection. Notably, multiple AUB etiologies can co-exist in a single patient⁴.

It is of great importance as it is the most common sign of anemia in the pre-menopausal period and a suspicion of malignancy in the post-menopausal period. Endometrial

sampling, which is widely used for the diagnosis and treatment of endometrial pathologies, is performed using dilation curettage (D/C), aspiration (office biopsy)⁸.

Histopathological characterization of endometrial biopsies and curettings by the light microscope is considered the gold standard for diagnosis of the etiology of AUB, because of the relative ease and safety of obtaining samples, along with reasonable reporting time and diagnostic accuracy. Dilation and curettage (D&C) is a surgical procedure that scrapes the endometrial lining for diagnostic and therapeutic indications⁶. A biopsy is the removal of tissue from a living patient for the purpose of microscopic examination and diagnosis.

These exhibit a wide range of histopathological patterns due to normal and abnormal cyclical changes, drugs, hormones, infections, metabolic disease, and malignancies. So, management of AUB is not complete without tissue diagnosis, especially in perimenopause and post menopause⁷.

Unfortunately, nearly half of women with AUB and its associated complications do not seek medical care or receive appropriate treatment, often due to a lack of awareness. This oversight can lead to the diagnosis of malignancies at advanced stages, when prognoses are less favourable. This underscores the necessity for more research into AUB prevalence and risk factors across diverse populations, especially among women in developing regions with limited resources who face higher risks.⁴

Materials and Methods

The study was done in the Department of Pathology, Sree Narayana Institute of Medical Sciences. This is a retrospective cross-sectional study for a period from May 2024 to June 2025, after approval and clearance from the Institutional Ethical Committee. Clinical data were obtained from case sheets and histopathology request forms. Endometrial samples were collected either through endometrial biopsy or by dilatation and curettage performed under sedation as an office procedure. All samples were fixed in 10% formalin and submitted to the histopathology laboratory. The gross morphology of each specimen was recorded, and total submission of the endometrial samples was ensured. The tissue specimens were processed using an automatic tissue processor, and paraffin blocks were prepared. Sections of 4–6 μ m thickness were cut and stained with hematoxylin and eosin (H&E). The stained slides were examined by a pathologist and evaluated for various pathological findings. The collected data were analyzed using frequency distribution and presented in tables and charts.



The study sample was endometrial biopsies and curetting, and the total sample collected was 268.

The samples were calculated by the formula:

$$n = z^2pq/d^2$$

$$z = 1.96$$

$$p = 0.1947$$

$$q = 1 - p = 0.8053$$

$$d = 5\% = 0.05$$

$$n = (1.96)^2 \times 0.1947 \times 0.8053 / (0.05)^2 \\ = 240.93.$$

By adding a non-responsive rate of 5%. $241 \times 5/100 = 12.05 = 12$

$241 + 12 = 253$. So the total number of samples, $n = 253$

Statistical analysis

Data will be collected retrospectively from clinical records and histopathology reports. Each case will be anonymized and coded. Data cleaning and cross-verification will be done to ensure accuracy. Data will be analysed using SPSS. Analysis will include descriptive statistics (mean, frequency, percentages), chi-square test, and kappa statistics to assess clinicopathological agreement. A p -value < 0.05 will be considered statistically significant.

Result

Histopathologic examination of the 268 cases showed various patterns in AUB. Normal cyclical pattern showing proliferative and secretory phase in 147 patients (50.74%) was the most common finding. Hyperplasia was observed in 15 patients (5.59%), of which 5 patients presented with atypical endometrial hyperplasia. Chronic endometritis was seen in 2 patients.

A total of 52 /268 cases (19.40%) showed a disordered proliferative pattern, which was most commonly seen between 40 and 49 years of age. Atrophic endometrium was seen in 13 cases, and most of them were elderly patients. Carcinoma of the endometrium was seen in 3 cases (1.11%).

The spectrum of histopathological diagnoses we encountered in endometrial biopsy is given in Table 1.

The age of the patients ranged from 20 to 75 years. The age group with the maximum number of patients was 40-49 years (61.19%), followed by 50-59 years (22.01%).

Table 2 depicts the age-wise distribution of endometrial histopathological patterns.

Table 1: Histopathological diagnosis of endometrial biopsy.

Diagnosis	No. of patients	Percentage
Proliferative endometrium	29	10.82 %
Secretory endometrium	107	39.92 %
Simple hyperplasia without atypia	10	3.73%
Simple hyperplasia with atypia	5	1.86 %
Disordered proliferative endometrium	52	19.40 %
Atrophic endometrium	13	4.85 %
Endometrial polyp	40	14.92 %
Pill endometrium	4	1.49 %
Chronic endometritis	2	0.74 %



Carcinoma	3	1.11 %
Pseudodecidualization	3	1.11 %
Total	268	99.95 %

Table 2: Endometrial Histopathological diagnosis according to age group

Age Group	P	S	SHW	SH	DPE	A	EP	PI	CE	CA	PD
20-29		1					1				
30-39	3	10			5		6				
40-49	23	80	1	6	30	1	15	3	2		3
50-59	3	16	3	2	17	4	11	1		2	
60-69			1	2		5	5			1	
>70						3	2				
Total	29	107	5	10	52	13	40	4	2	3	3

P - proliferative endometrium. S- secretory endometrium.

SHW - simple hyperplasia with atypia; SH- simple hyperplasia without atypia. DPE - disordered proliferative endometrium. A - atrophic endometrium. EP - endometrial polyp. PI - pill. CE - chronic endometritis. CA - carcinoma. PD- pseudodecidualization.

Discussion

Abnormal uterine bleeding is one of the most frequently encountered clinical problems in the gynaecology department. Causes can vary depending on the age of the

patient. PALM - COEI system mentions the structural causes such as polyp, adenomyosis, leiomyoma, and malignant lesion, which require imaging studies and biopsy for clinical diagnosis. Non-structural causes such as coagulopathies, ovulatory abnormalities, endometrial dysfunction, and iatrogenic causes (COEI) require laboratory tests and biopsy if indicated.

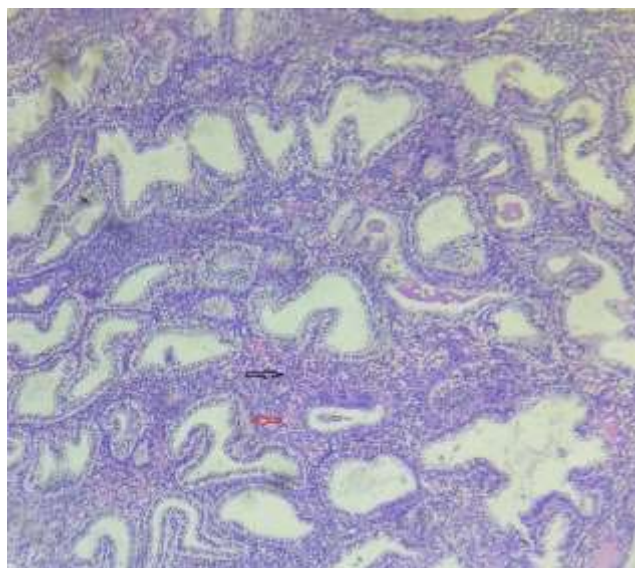


Figure 1: Histopathology of secretory endometrium(10x): Red arrow showing endometrial glands with vacuolation and black arrow showing endometrial stroma.

Endometrial biopsies help to differentiate between ovulatory and anovulatory causes of abnormal uterine bleeding. Anovulatory dysfunctional uterine bleeding is due to the disturbed function of the hypothalamic pituitary ovarian axis, leading to unopposed estrogen stimulation. Anovulatory dysfunction of uterine bleeding can be caused by polycystic ovarian syndrome, and during the perimenarchal and perimenopausal ages. Ovulatory dysfunctional bleeding can be due to a defect in the control of menstrual blood loss. Ovulatory dysfunction can occur in endocrinopathies or can be iatrogenic, caused by drugs such as gonadal steroids. The endometrium is usually in the proliferative phase during the anovulatory cycle, and in the secretory phase, ovulatory cycle, it is dysfunctional uterine bleeding. So endometrial biopsies help to distinguish between ovulatory and anovulatory causes. Endometrial hyperplasia and carcinoma of the

uterus are the common causes of abnormal uterine bleeding. Endometrial sampling and subsequent histopathological study can lead to early detection of Endometrial hyperplasia and carcinoma.

The most common pattern observed was normal cyclical endometrium ($\approx 51\%$) is concordant with study by Alshdaifat et al.⁶ (57.7%) and also aligns with many Indian studies, such as the study by Vijayaraghavan et al.¹ (56.9%) composed of the proliferative phase endometrium in 35%, secretory phase endometrium in 18.8% and menstrual endometrium in 3.1%. Secretory endometrium was seen 39.92%, suggesting the ovulatory nature of bleeding, aligning with a study by Albers et al.¹² As mentioned in the previous paragraph, proliferative endometrium occurs in anovulatory DUB and secretory endometrium in ovulatory DUB. So identifying the patterns helps in narrowing the cause of bleeding.

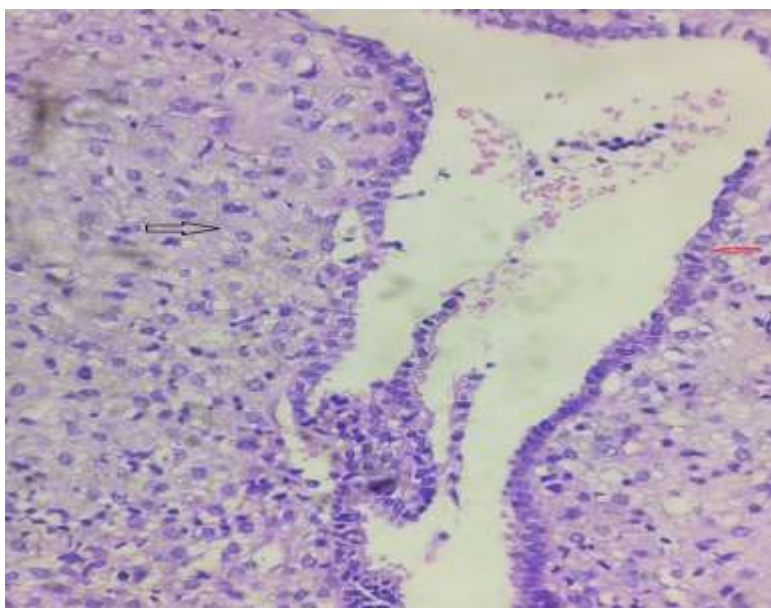


Figure 2: Histopathology of decidualized endometrium(40x): Red arrow showing endometrial glands and black arrow showing decidualized stroma

Disordered proliferative endometrium (DPE) was seen in 19.40%, aligning with studies by Doraiswami et al.⁹ (20.7%) and Khan et al.¹³ (16.6%). Disordered proliferative endometrium is common around perimenopausal years due to frequent anovulatory cycles and unopposed estrogen stimulation. It also occurs in

exogenous estrogen therapy. Histologically, they are characterised by a normal gland-to-stroma ratio, lining of pseudostratified, mitotically active proliferative epithelium, cystically dilated glands, with some showing budding.

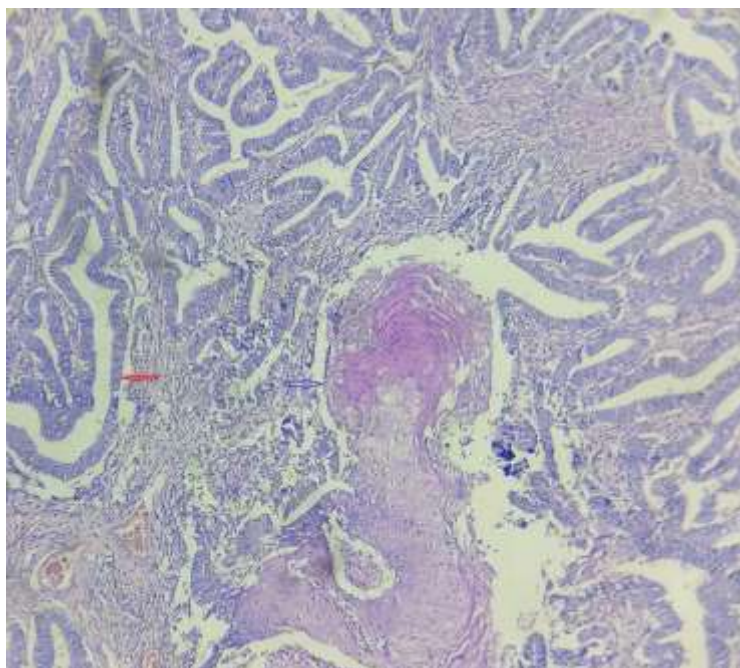


Figure 3: Histopathology of endometrial carcinoma(10x): Red arrow shows crowded atypical glands. The blue arrow shows squamous metaplasia.

Endometrial hyperplasia without atypia was noted in 3.73%, and atypical hyperplasia was observed in 1.86% in our study, aligning with observations of Saraswathi et al(6.1%). Endometrial hyperplasia is usually seen in the perimenopausal age group. Unopposed estrogen stimulation during this period can cause endometrial hyperplasia. An obese person also has increased availability of peripheral estrogen due to aromatization of

androgen to estrogen in adipose tissue. Endometrial hyperplasia with atypia is a precursor to endometrial carcinoma. So identifying endometrial hyperplasia with atypia in biopsies is helpful in the prevention of endometrial carcinoma. Endometrial hyperplasia with atypia is characterised by nuclear atypia in addition to an increased gland-to-stroma ratio.

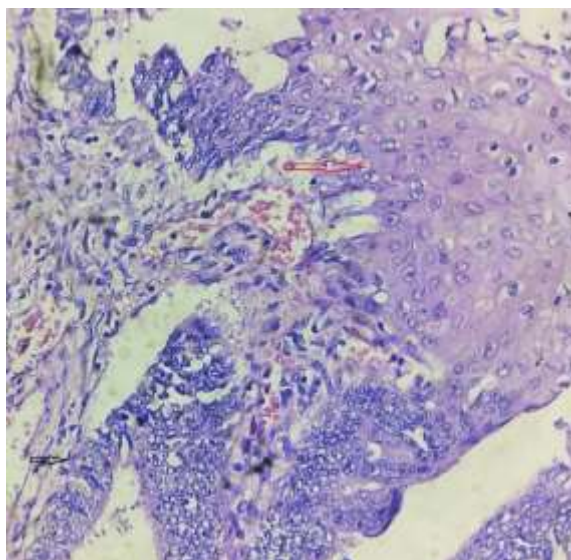


Figure 4: Histopathology of endometrial carcinoma(40x): Black arrow shows glandular atypia. The red arrow shows squamous metaplasia.

The age distribution pattern in our cohort—maximum cases in the 40–49 year group followed by 50–59 years—is also consistent with multiple studies (Saraswathi et al., Khan et al., and Vaidya R. et al.^{3,13, 14}), which identify perimenopausal age as the peak period for AUB

presentations due to fluctuating ovarian function. Overall, our findings align closely with published literature, supporting the global and regional trends of endometrial pathology contributing to AUB across reproductive and perimenopausal age.

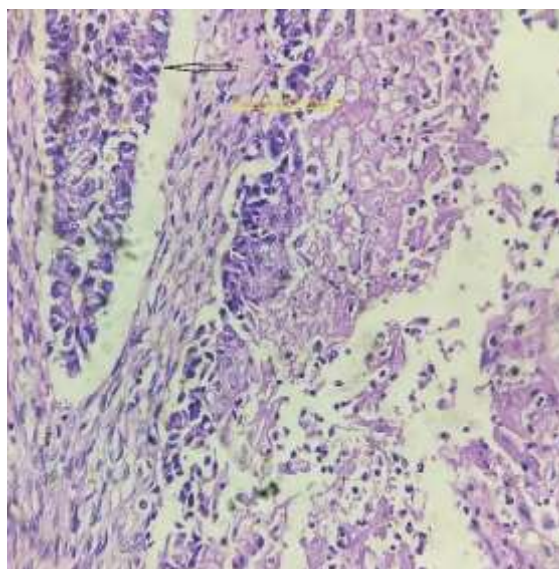


Figure 5: Histopathology of endometrial carcinoma(40x): Black arrow shows myometrial invasion. The yellow arrow shows squamous metaplasia.

The prevalence of endometrial carcinoma was 1.11%, comparable with a study by Sherwani et al. (¹³). Endometrial carcinoma can be of two types: one is type 1 endometrioid carcinoma, common between 40 and 60 years of age, and usually associated with a history of unopposed estrogen stimulation. They usually express estrogen and progesterone receptors and have a favourable prognosis. The second type, type 2 serous carcinoma, occurs in more elderly persons. They usually don't have a history of hyperestrogenism. They are ER, PR negative, and p53 mutant. Endometrial carcinoma is usually seen in the peri and post menopausal age group. Women on hormone therapy who present with postmenopausal bleeding need to be evaluated for carcinoma.

Atrophic endometrium was noted in (4.85%) cases, predominantly in postmenopausal women, above 50 years group, maximum cases between 60-69 years, which is due to deficiency of estrogen and aligns with studies by Doraiswami et al⁹ (2.4%) and less compared to study focused on postmenopausal age group, 11.5% in study by Anitha et al¹⁵. Studies by Vijayaraghavan et al¹, Alshdaifat et al⁶, and Tilva et al⁷ also noted atrophic endometrium mainly in women above 50 years of age. Glandular lining in atrophic endometrium appears to be mitotically inactive. The term cystic atrophy is applied when glands are cystically dilated and are lined by cuboidal or flattened epithelium. The exact etiology for bleeding in atrophic endometrium is not known, possibly due to thin-walled veins superficial to expanding cystic glands.

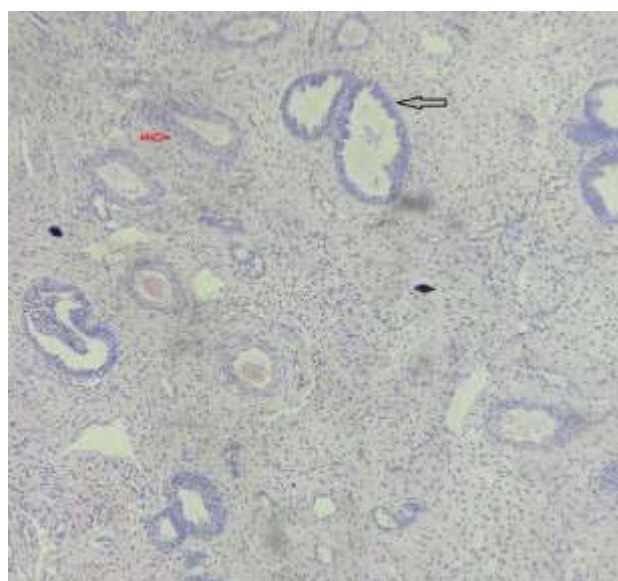


Figure 6: Histopathology of endometrial polyp (10x): Black arrow shows endometrial glands lined by stratified epithelium. The red arrow shows thick-walled vessels.

Endometrial polyps were seen in 14.92%, consistent with Indian and international studies (10–24%), reinforcing their recognized role in AUB pathophysiology. A study by Ghanbarzadeh *et al*¹¹ showed an endometrial polyp in 5.3% cases, lower compared to the study. A study by Vani BS *et al*³ showed Endometrial polyps in only 2.6% of cases, much lower compared to our study. Endometrial polyps are characterised by fibrous stroma with thick-walled vessels and cystically dilated glands with a lining of atrophic to weakly proliferative endometrium. Lower uterine segment endometrium can sometimes be confused with a

polyp, but they lack the thick-walled vessels. Chronic endometritis (0.74%), pill endometrium (1.49%) were some other rare findings observed. The presence of plasma cells more than usual is the most significant finding in chronic endometritis. They may be associated with pelvic inflammatory disease or retained products of conception. It is also important to diagnose specific types of chronic endometritis, such as granulomatous endometritis and xanthomatous endometritis, for specific treatment. Mild non-specific chronic endometritis can be associated with bacterial vaginosis. The present study shows a variation in endometrial histopathological



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patterns in abnormal uterine bleeding (AUB), according to various age groups, aligning with findings of previously published literature. Functional endometrial patterns were mainly seen in younger age groups, while organic and neoplastic lesions were seen more with advancing age. Proliferative and secretory endometrium were the most frequent findings observed in the reproductive age group (20–39 years), probably due to normal ovulatory cycles and functional causes of AUB. Similar findings have been observed in studies by Bhatta and Sinha. 2, which showed that in women under 30 years of age, proliferative endometrium was in 6/13 (46.15%) patients and secretory endometrium in 4/13 (30.76%) under 30 years of age. The vast majority of cases belonged to the perimenopausal age group (40–49 years) and showed pathological patterns such as disordered proliferative endometrium (DPE), endometrial polyps, and simple hyperplasia (with and without atypia), possibly due to anovulatory cycles and unopposed estrogen exposure.

Similar age-related increases in DPE and hyperplastic lesions have been reported by Doraiswami et al., Tilva et al., and Vani et al.^{3,7,9}. Alshdaifat et al⁶ also documented a predominance of proliferative and disordered patterns in this age group. A study by Tilva et al⁷ also showed the majority of disordered proliferative endometrium in the 41–50 year age group (~78 % of DPE cases). Endometrial polyps were more frequently found in women aged 40–59 years, aligning with findings by Inal et al⁸ and Vijayaraghavan et al¹, which showed a higher prevalence of polyps in perimenopausal women due to localized estrogenic stimulation.^{1,8} Atrophic endometrium was almost exclusively seen in postmenopausal age group due to prolonged absence of estrogenic stimulation and constituted a major cause of postmenopausal bleeding, correlates well with studies by Doraiswami et al⁹. and Inal et al⁸, which showed atrophic endometrium as the most frequent cause of postmenopausal AUB.^{8,9} Endometrial carcinoma was found in 3 cases, with 2 cases in 50–59 years and one in 60–69 years similar to study by Bhatta S et al² which showed statistically significant association between endometrial carcinoma and postmenopausal age group compared to premenopausal women (17.9% vs. 2.12%, p=0.002)

This finding highlights the relevance of endometrial sampling in postmenopausal women presenting with AUB. Hyperplasia with atypia also occurred in 40–69 years, again highlighting the importance of endometrial biopsy in this group. Atypical hyperplasia was observed in 1.86%, which is a precursor to malignancy, the early detection of which is significantly beneficial.

As a single-center study conducted in a tertiary care hospital, the findings may not be fully generalizable to the broader population. Uniform clinical, radiological, and

hormonal correlation was not available for all cases, limiting comprehensive clinicopathological assessment. Endometrial biopsy and curettage have limited access to tissue and may fail to detect focal lesions such as small polyps. Myometrial invasion may be difficult to diagnose because of limited tissue, leading to underdiagnosis. Long-term follow-up data regarding treatment response, progression of hyperplasia, or subsequent development of carcinoma were not available. Certain risk factors, such as body mass index, metabolic comorbidities, parity, and duration of hormonal therapy, could not be consistently assessed.

Conclusion(S)

Most common pattern observed in our study was normal cyclical endometrium (proliferative 10.82% and secretory 39.92%) . The proliferative phase occurs in anovulatory bleeding, and the secretory phase occurs in ovulatory bleeding. Endometrial study thus helps to distinguish between ovulatory and anovulatory bleeding, which have different etiologies. An endometrial biopsy could also identify structural abnormalities such as a polyp (14.92%). Atypical endometrial hyperplasia was observed in 1.86%, which is a precursor to carcinoma. Endometrial carcinoma was found in 3 cases, all of them in the postmenopausal age group, stressing the importance of endometrial biopsy in case of bleeding, especially in the peri and post menopausal age group.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Authors' Contribution

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

Funding

No source of funding.

Data Availability

All datasets analyzed in the study are included in the manuscript and presented as tables and figures.



Ethics Statement

Our study has been approved by the institutional ethics committee. IEC number is IEC/131/103

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