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Original Research Article

Endometrial pathology in abnormal uterine bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is a common gynaecological complaint requiring histopathological evaluation for accurate diagnosis. Histopathological examination remains essential for diagnosing AUB and detecting premalignant and malignant lesions.
Methods: This prospective observational study was conducted in the Department of Pathology, Terna Medical College and Hospital, Navi Mumbai, over a period of two years from August 2022 to August 2024. The study was undertaken to evaluate the histopathological spectrum of endometrial lesions in patients presenting with AUB and to assess their age-wise distribution
Results: A total of 293 endometrial biopsies and hysterectomy specimens from patients presenting with AUB were studied. The majority of patients belonged to the 40-49 years age group (151cases, 51.7%). Non-organic (functional) causes constituted the majority of cases, accounting for 209 cases (71.6%), organic lesions were 83 cases (28.8%). Endometrial polyp was the most common organic lesion, observed in 36 cases (12.3%). Among the non-organic lesions, proliferative phase endometrium was the most common finding, accounting for 64 cases (21.9%). Disordered proliferative endometrium demonstrated a statistically significant association with age distribution (p=0.034), with maximum prevalence in women aged 40-49 years. Endometrial carcinoma showed a significant association with advancing age
Conclusions: The present study demonstrated that non-organic endometrial lesions with the highest incidence observed in the perimenopausal age group (40-49 years). Early detection of premalignant lesions, malignant lesions and helps in guiding appropriate patient management.

Keywords: Abnormal uterine bleeding, Endometrium, Histopathology, Endometrial hyperplasia, Endometrial polyp, Endometrial carcinoma

INTRODUCTION

Abnormal uterine bleeding (AUB) is a frequent gynaecological problem affecting women across the reproductive, perimenopausal, and postmenopausal age groups. It constitutes a significant proportion of gynaecological outpatient consultations and may substantially interfere with a woman's physical, psychological, and social well-being. AUB refers to bleeding originating from the uterine corpus that differs from normal menstruation with respect to its volume, frequency, duration, regularity, or timing, in the absence of pregnancy. Persistent or excessive bleeding may result in iron-deficiency anaemia, fatigue, physical discomfort, psychological stress, and impaired quality of life, thereby contributing to a considerable socioeconomic burden.[1,2]

The underlying causes of AUB are diverse and include both structural lesions of the uterus and non-structural disorders. The International Federation of Gynaecology and Obstetrics (FIGO) developed the PALM-COEIN classification system to provide a standardized framework for categorizing the causes of AUB. The structural causes are represented by PALM, comprising Polyp,

Adenomyosis, Leiomyoma, and Malignancy and Hyperplasia, whereas COEIN denotes the non-structural causes, namely Coagulopathy, Ovulatory dysfunction, Endometrial disorders, Iatrogenic causes, and causes Not otherwise classified.[3] The use of this standardized classification facilitates uniform terminology and assists clinicians in systematic evaluation and management of women presenting with AUB.

The endometrium undergoes characteristic morphological and functional alterations throughout the menstrual cycle in response to changes in ovarian hormones. Alterations in hormonal balance and endometrial response may produce a range of histological patterns, including proliferative, secretory, disordered proliferative, and other hormonally influenced changes. In addition to these physiological or functional alterations, a variety of pathological lesions may involve the endometrium. These include endometrial polyps, endometrial hyperplasia, endometrial intraepithelial neoplasia, and endometrial carcinoma, all of which may present clinically with AUB. Such lesions are of particular clinical significance in perimenopausal and postmenopausal women, in whom the possibility of premalignant or malignant endometrial pathology requires careful evaluation.[4,5]

Histopathological examination plays an important role in the evaluation of endometrial abnormalities and in distinguishing benign, premalignant, and malignant lesions. The pathologist contributes significantly to the recognition of endometrial precursor lesions and the accurate diagnosis and classification of endometrial malignancies.[15] Endometrial sampling provides tissue for microscopic assessment and is a relatively simple, minimally invasive, and cost-effective diagnostic approach. Histopathological examination of the obtained tissue can demonstrate a broad spectrum of findings, ranging from physiological and hormonally related changes to inflammatory conditions, hyperplastic lesions, and malignant neoplasms.[6,7] Recognition of premalignant lesions, particularly endometrial hyperplasia and endometrial intraepithelial neoplasia, is clinically important because appropriate and timely management may reduce the risk of progression to endometrial carcinoma.

Endometrial carcinoma is one of the important malignant neoplasms of the female genital tract, and its incidence has shown an increasing trend in several parts of the world. This rise has been associated with increasing prevalence of risk factors such as obesity, diabetes mellitus, hypertension, delayed menopause, and prolonged exposure to unopposed estrogen.[12,13] The occurrence of these risk factors, together with increasing life expectancy, highlights the importance of evaluating abnormal endometrial bleeding, particularly in women belonging to older age groups.

The histopathological spectrum of endometrial lesions may vary considerably with age because of differences in hormonal status, reproductive history, and the prevalence of specific risk factors across different stages of life. Assessment of the age-wise distribution of endometrial lesions can therefore provide useful information regarding the pattern of benign, premalignant, and malignant conditions encountered in clinical practice. Such information may assist clinicians in selecting appropriate diagnostic investigations and identifying patients who require further evaluation for significant endometrial pathology.

In view of the varied histopathological spectrum associated with AUB, the present study was undertaken to evaluate the different endometrial lesions identified on histopathological examination in patients presenting with AUB and to assess their distribution across various age groups in a tertiary care teaching hospital.

METHODS

This prospective observational study was conducted in the Department of Pathology, Terna Medical College and Hospital, Navi Mumbai, over a period of two years from August 2022 to August 2024. The study was undertaken to evaluate the histopathological spectrum of endometrial lesions in patients presenting with AUB and to assess their age-wise distribution. All endometrial biopsies and hysterectomy specimens received in the Department of Pathology during the study period with a clinical diagnosis of AUB were included in the study.

The inclusion criteria comprised all cases presenting with abnormal uterine bleeding in whom histopathological examination revealed either non-organic or organic endometrial lesions non organic lesions included proliferative phase endometrium, secretory phase endometrium, menstrual endometrium, disordered proliferative endometrium, hormonal endometrium, and atrophic endometrium. Organic lesions included endometrial polyps, endometrial hyperplasia without atypia, endometrial hyperplasia with atypia/endometrial intraepithelial neoplasia (EIN), and endometrial carcinoma. Cases with non-uterine causes of bleeding, pregnancy-related lesions, leiomyoma, adenomyosis, endometriosis, cervical lesions, and specimens with inadequate clinical or histopathological data were excluded from the study.

Relevant demographic and clinical details, including age, presenting complaints, and clinical diagnosis, were obtained from pathology requisition forms and hospital records. Patients were categorized into five age groups: <30 years, 30-39 years, 40-49 years, 50-59 years, and >60 years for age-wise analysis of histopathological findings.

All specimens were fixed in 10% neutral buffered formalin for adequate fixation. Gross examination was performed systematically, and relevant macroscopic findings including specimen type, dimensions, and presence of focal lesions were documented. Representative tissue

sections were processed using standard paraffin-embedding techniques. Sections of 4-5 µm thickness were prepared and stained routinely with Hematoxylin and Eosin (H and E). Histopathological examination was carried out under light microscopy by experienced pathologists.

The endometrial lesions were classified according to the World Health Organization (WHO) classification of female genital tumours and endometrial precancerous lesions. Histopathological diagnoses were categorized as non-organic (functional) and organic lesions.[6,14]

Data obtained from the histopathological records were entered into Microsoft excel and analyzed statistically. Descriptive statistics were expressed as frequencies and percentages. The association between age groups and various histopathological patterns was assessed using the Chi-square test. A p value of less than 0.05 was considered statistically significant. The results were presented in the form of tables and charts wherever appropriate.

RESULTS

A total of 293 endometrial biopsies and hysterectomy specimens from patients presenting with AUB were studied during the period from August 2022 to August 2024. The majority of patients belonged to the 40-49 years age group (151cases, 51.7%), followed by 30-39 years (60 cases, 20.6%), 50-59 years (60 cases, 20.7%), >60 years (15 cases, 5.1%) and <30 years (7 cases, 2.3%%).

Non-organic (functional) endometrial lesions constituted the majority of cases, accounting for 209 cases (71.4%), whereas organic lesions accounted for 84 cases (28.8%) (Table 1).

Among the organic lesions, endometrial polyp was the most common lesion, observed in 36 cases (12.3%), followed by endometrial hyperplasia without atypia in 35 cases (12.0%). Endometrial hyperplasia with atypia was identified in 6 cases (2.1%), while endometrial carcinoma was diagnosed in 7 cases (2.4%).

The majority of endometrial polyps (41.7%) and endometrial hyperplasia without atypia (60.0%) occurred in women aged 40-49 years. Endometrial carcinoma demonstrated a statistically significant association with advancing age (p=0.003), with the highest frequency observed in the 50–59 years age group.

Among the non-organic lesions, proliferative phase endometrium was the most common histopathological finding, accounting for 64 cases (21.9%), followed by disordered proliferative endometrium in 53 cases (18.1%), secretory phase endometrium in 48 cases (16.4%), menstrual phase endometrium in 20 cases (6.8%), progestinilised endometrium in 17 cases (5.8%) and atrophic endometrium in 7 cases (2.4%).

Most non-organic lesions were concentrated in the 40-49 years age group.

Disordered proliferative endometrium demonstrated a statistically significant association with age distribution (p=0.034), with maximum prevalence in women aged 40-49 years. Progestinilised endometrium also showed a significant age association (p=0.029), predominantly affecting women in the 40-49 years age group. Atrophic endometrium showed a highly significant association with advancing age (p<0.001), with the majority of cases occurring in women aged more than 60 years.

Overall, the present study demonstrated that non-organic endometrial lesions were more common than organic lesions in patients presenting with AUB. The peak incidence was observed in the perimenopausal age group (40-49 years). Endometrial carcinoma, disordered proliferative endometrium, progestinilised endometrium and atrophic endometrium showed statistically significant age-wise associations, whereas other lesions did not demonstrate significant variation across age group.

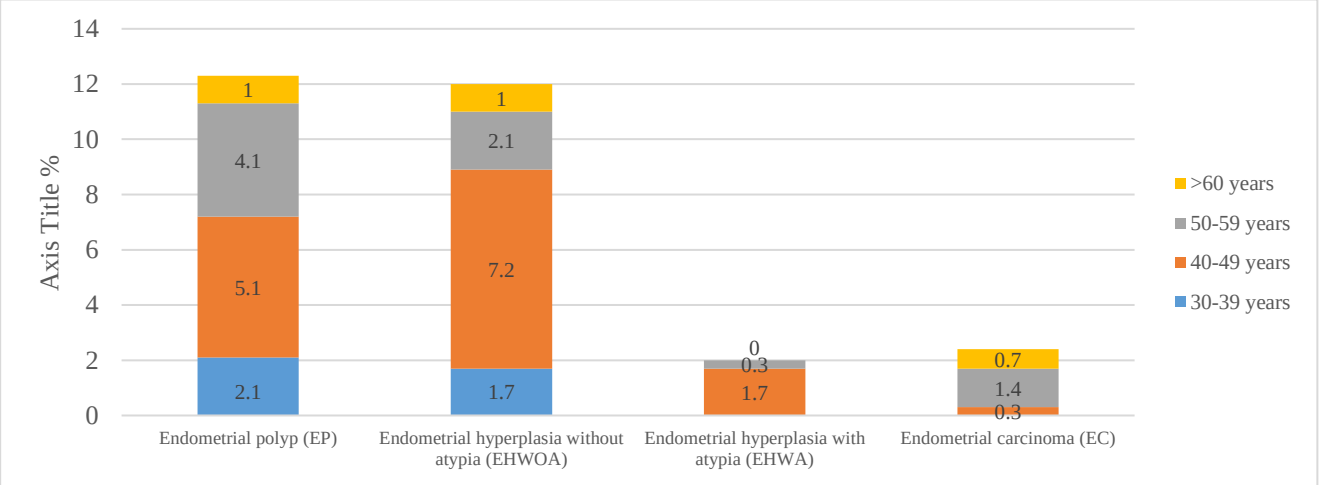


Figure 1: Age-wise distribution of organic endometrial lesions in patients with AUB (%).

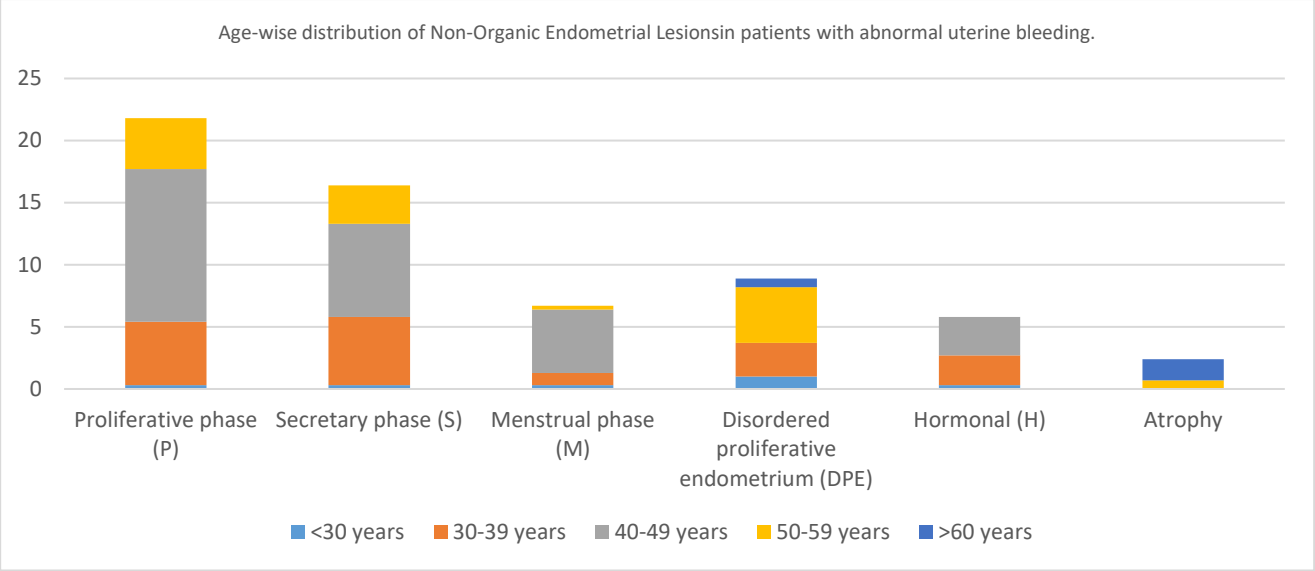


Figure 2: Age-wise distribution of non-organic endometrial lesions in patients with AUB.

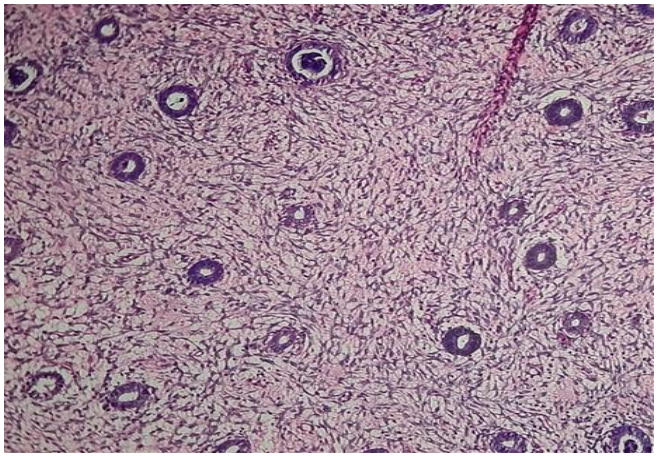


Figure 3: Proliferative phase endometrium.

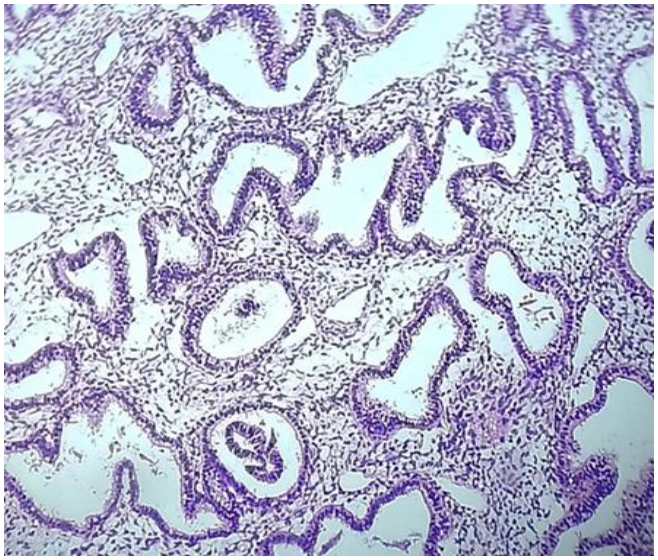


Figure 4: Secretory phase endometrium.

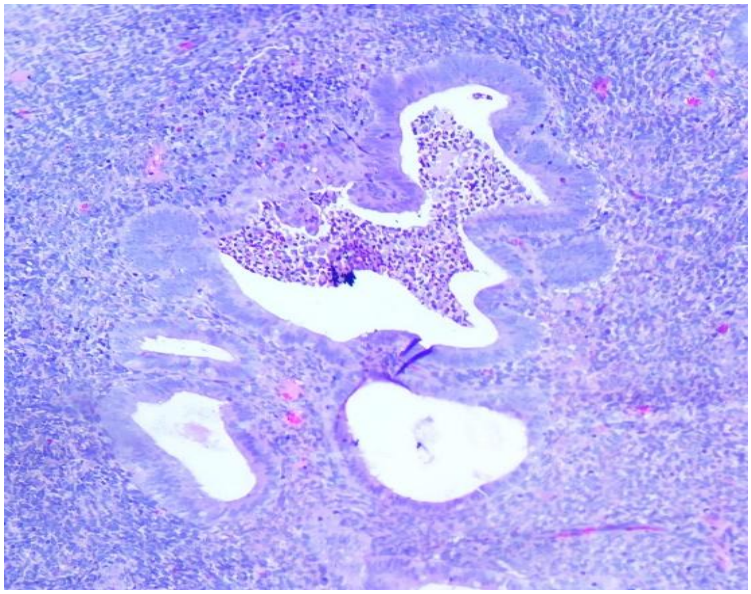


Figure 5: Disordered proliferative phase.

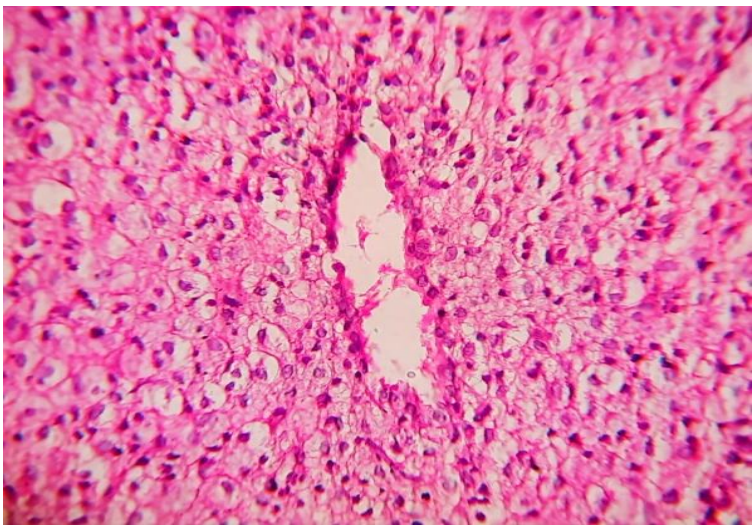


Figure 5: Progestinilised endometrium.

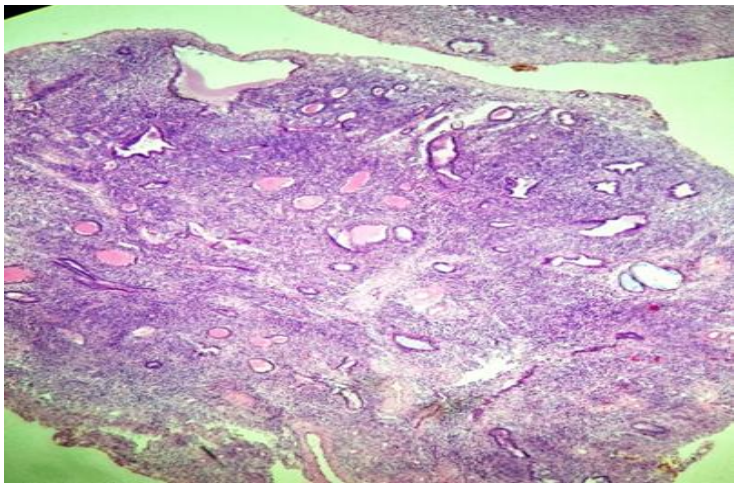


Figure 6: Endometrial polyp.

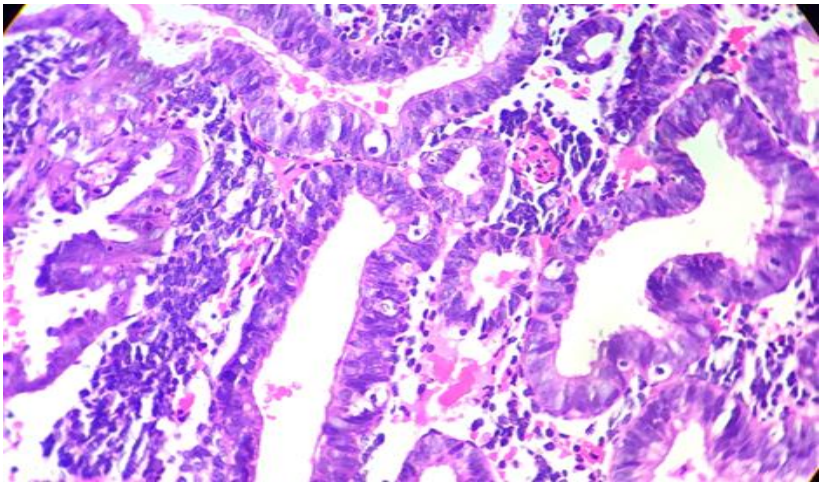


Figure 7: Endometrial hyperplasia with atypia.

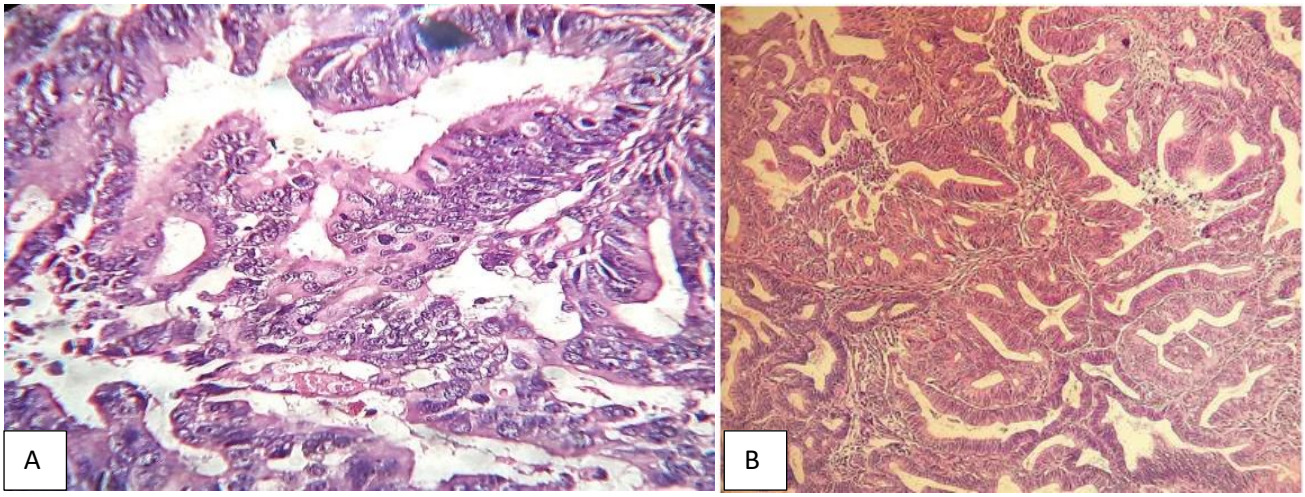


Figure 8 (A and B): A-Endometrial carcinoma (40×). B-Endometrial carcinoma (10×).

Table 1: Age-wise distribution of organic and non-organic endometrial lesions in patients with AUB.

Type of lesions	<30 years, (n=7)	30-39 years, (n=60)	40-49 years, (n=151)	50-59 years, (n=60)	>60 years, (n=15)	Total	Chi-square test for comparison (P value)
Organic							
Endometrial polyp (EP)	0 (0.0%)	6 (2.1%)	15 (5.1%)	12 (4.1%)	3 (1.0%)	36 (12.3%)	0.227
Endometrial hyperplasia without atypia (EHWOA)	0 (0.0%)	5 (1.7%)	21 (7.2%)	6 (2.1%)	3 (1.0%)	35 (12.0%)	0.540
Endometrial hyperplasia with atypia (EHWA)	0 (0.0%)	0 (0.0%)	5 (1.7%)	1 (0.3%)	0 (0.0%)	6 (2.1%)	0.567
Endometrial carcinoma (EC)	0 (0.0%)	0 (0.0%)	1 (0.3%)	4 (1.4%)	2 (0.7%)	7 (2.4%)	0.003
Total	0 (0.0%)	11 (3.8%)	42 (14.4%)	23 (8.0%)	8 (2.7%)	84 (28.8%)	
Non organic							
Proliferative phase (P)	1 (0.3%)	15 (5.1%)	36 (12.3%)	12 (4.1%)	0 (0.0%)	64 (21.9%)	0.286
Secretary phase (S)	1 (0.3%)	16 (5.5%)	22 (7.5%)	9 (3.1%)	0 (0.0%)	48 (16.4%)	0.101
Menstrual phase (M)	1 (0.3%)	3 (1.0%)	15 (5.1%)	1 (0.3%)	0 (0.0%)	20 (6.8%)	0.078
Disordered proliferative endometrium (DPE)	3 (1.0%)	8 (2.7%)	27 (9.2%)	13 (4.5%)	2 (0.7%)	53 (18.1%)	0.034
Progestinilised endometrium	1 (0.3%)	7 (2.4%)	9 (3.1%)	0 (0.0%)	0 (0.0%)	17 (5.8%)	0.029
Atrophy (A)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.7%)	5 (1.7%)	7 (2.4%)	<0.001
Total	7 (2.3%)	49 (16.8%)	109 (37.3%)	37 (12.7%)	7 (2.4%)	209 (71.4%)	

DISCUSSION

AUB is a frequent clinical presentation across different stages of a woman's reproductive life and is an important indication for endometrial sampling. Histopathological examination provides valuable information for characterizing endometrial changes and distinguishing physiological or hormonally related alterations from premalignant and malignant lesions. The present study was undertaken to assess the histopathological spectrum of endometrial lesions in women presenting with AUB and to evaluate their distribution across different age groups.

In the present study, the highest proportion of patients belonged to the 40-49 years age group, accounting for 51.7% of cases. Comparable findings have been reported by Doraiswami et al, Jetley et al and Khare et al who observed a greater frequency of AUB among women in the perimenopausal age group.[1-3] The increased occurrence of AUB during this period may be related to progressive alterations in ovarian function, hormonal fluctuations, and an increased frequency of anovulatory cycles. These changes can result in irregular endometrial stimulation and consequently produce abnormal patterns of uterine bleeding.

Non-organic endometrial changes constituted the majority of cases in the present study (71.4%), whereas organic lesions accounted for 28.8%. This distribution is comparable with observations from previous studies in which functional endometrial patterns predominated among women evaluated for AUB. Functional endometrial alterations are commonly associated with disturbances in the hypothalamic-pituitary-ovarian axis, particularly ovulatory dysfunction and variations in ovarian steroid secretion. Such hormonal disturbances are especially relevant during the reproductive and perimenopausal periods and may result in abnormal endometrial proliferation or maturation.

Among the functional endometrial patterns, proliferative-phase endometrium was the most frequently encountered finding, comprising 21.9% of cases. This was followed by disordered proliferative endometrium (18.1%) and secretory-phase endometrium (16.4%). Similar observations have been documented by Abdullah et al, Baral et al and Doraiswami et al who reported proliferative endometrium as the predominant histopathological pattern in patients with AUB.[4-6] The predominance of proliferative endometrium may be related to anovulatory cycles, particularly during the perimenopausal period, in which estrogenic stimulation may occur without the regular cyclical progesterone-mediated secretory transformation.

Disordered proliferative endometrium showed a statistically significant association with age (p=0.034), with the highest frequency observed among women aged 40-49 years. This pattern may reflect the hormonal alterations associated with the perimenopausal transition, during which irregular ovulation and relatively unopposed estrogenic stimulation can produce architectural and proliferative changes in the endometrium.[7] Although disordered proliferative endometrium is generally regarded as a benign pattern, its recognition is clinically relevant because persistent estrogenic stimulation may coexist with or contribute to the development of endometrial hyperplastic changes in susceptible women.

Among the organic lesions, endometrial polyp was the most frequently identified lesion, accounting for 12.3% of cases, followed closely by endometrial hyperplasia without atypia, which constituted 12.0% of cases. Similar findings have been reported by Jetley et al and Khare et al who identified endometrial polyps and hyperplastic lesions among the important structural causes of AUB.[1,2] Endometrial polyps are localized proliferations of endometrial glands and stroma and may present clinically with irregular or excessive uterine bleeding. Their detection has also increased with the wider use of imaging and endometrial sampling techniques.

Endometrial hyperplasia without atypia was identified in 12.0% of cases, whereas hyperplasia with atypia accounted for 2.1%. The hyperplastic lesions were predominantly observed in women aged 40-49 years. This finding is comparable with observations reported by Reed et al and Mutter et al. Hyperplastic changes are commonly associated with prolonged or unopposed estrogenic stimulation and may occur more frequently in the presence of risk factors such as obesity, diabetes mellitus, and anovulatory cycles.[8,12] The identification of atypical hyperplasia is of particular clinical significance because of its association with an increased risk of concurrent or subsequent endometrial carcinoma. Early recognition through endometrial sampling therefore allows appropriate clinical assessment and management.

Endometrial carcinoma was diagnosed in 2.4% of the cases in the present study and demonstrated a statistically significant association with age (p=0.003). Most cases were observed among women aged 50-59 years and older. This finding is consistent with observations reported by Lacey and Chia and with the WHO Classification of Female Genital Tumours, which describes endometrial carcinoma as a malignancy occurring predominantly in older and postmenopausal women.[9,11] The relatively low proportion of carcinoma observed in the present study may be related to the composition of the study population, which included a substantial number of reproductive and perimenopausal women.

Atrophic endometrium accounted for 2.4% of cases and demonstrated a highly significant association with age (p<0.001). Most cases occurred in women older than 60 years. Similar observations have been reported in previous studies, in which endometrial atrophy was recognized as an important cause of postmenopausal bleeding.[4,11] Following menopause, the reduction in ovarian estrogen production results in marked thinning of the endometrial glands and stroma. The resultant atrophic endometrium

may be susceptible to bleeding because of tissue fragility and vascular changes.

Overall, the present study demonstrates that non organic endometrial patterns constituted the predominant histopathological findings among women presenting with AUB, with the greatest proportion of patients belonging to the perimenopausal age group. Nevertheless, the detection of endometrial hyperplasia, atypical hyperplasia, and carcinoma emphasizes the importance of tissue diagnosis in the evaluation of AUB. The significant age associations observed for selected lesions further indicate that the histopathological spectrum varies across different stages of life. Endometrial sampling, therefore, remains an important diagnostic tool for identifying significant endometrial pathology and facilitating timely clinical management, particularly in women with persistent AUB and those in the older age groups.

CONCLUSION

The present study demonstrated that non-organic endometrial lesions were more common than organic lesions in patients presenting with AUB, with the highest incidence observed in the perimenopausal age group (40–49 years).

Proliferative phase endometrium was the most frequent histopathological finding, while endometrial polyp was the predominant organic lesion. Endometrial carcinoma showed a significant association with advancing age. Histopathological evaluation of endometrial samples remains an essential and reliable diagnostic tool for identifying the underlying cause of AUB, facilitating early detection of premalignant and malignant lesions, and guiding appropriate patient management.

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

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