Original Article

Histopathological Spectrum of the Endometrium in Patients with Abnormal Uterine Bleeding: A Prospective Observational Study

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Abstract

Background: Abnormal uterine bleeding (AUB) is a common gynaecological complaint that significantly impacts women's quality of life. It encompasses a wide spectrum of etiologies, from functional hormonal imbalances to structural lesions, including premalignant and malignant pathologies. Endometrial histopathological examination is crucial for accurate diagnosis and management. The aim is to analyse the histopathological spectrum of endometrial tissue in patients presenting with AUB and to correlate findings with clinical variables. **Material and Methods:** A prospective observational study was conducted over 24 months at a tertiary care hospital. A total of 228 women (≥18 years) presenting with AUB were enrolled. Endometrial sampling was performed using a Pipelle device. Tissues were processed for histopathological examination. Data on age, reproductive status, bleeding pattern, and comorbidities (diabetes, hypertension) were analysed. **Results:** The majority of patients were in the reproductive (43.0%) and perimenopausal (38.2%) age groups. Non-neoplastic/benign patterns predominated (81.1%), with proliferative (34.2%) and secretory (27.2%) endometrium being the most common. Hyperplasia was seen in 10.5% (atypical/EIN 3.5%), and carcinoma in 4.0%. A significant association was found between advancing age and malignancy ($p<0.001$). Postmenopausal bleeding was strongly correlated with hyperplasia and carcinoma ($p<0.001$). Diabetes ($p=0.008$) and hypertension ($p=0.012$) were significant risk correlates. Biopsy-hysterectomy concordance was 100% for carcinoma and hyperplasia without atypia. **Conclusion:** While benign functional endometrium is most common in AUB, a significant burden of hyperplasia and carcinoma exists, particularly in older, postmenopausal, and metabolically comorbid women. Endometrial biopsy is a reliable first-line diagnostic test, and its routine use enables early detection of serious pathology.

Keywords: Abnormal Uterine Bleeding; Endometrial Biopsy; Histopathology; Endometrial Carcinoma; Hyperplasia; Postmenopausal Bleeding.

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Introduction

Abnormal uterine bleeding (AUB) refers to any deviation from the normal menstrual cycle pattern in terms of frequency, duration, or volume of menstrual flow.[1] It is a prevalent gynaecological complaint affecting 10% to 30% of women of reproductive age and has a substantial impact on physical, emotional, and social well-being.[2] The International Federation of Gynaecology and Obstetrics (FIGO) PALM-COEIN classification system standardises the causes of AUB into structural (Polyp, Adenomyosis, Leiomyoma, Malignancy/Hyperplasia) and non-structural (Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, Not yet classified) categories, providing a framework for systematic evaluation and management.[3-5]

Endometrial tissue evaluation is pivotal in the diagnostic work-up of AUB, particularly to exclude premalignant and malignant pathology in peri- and postmenopausal women.[6] Office-based endometrial biopsy using a Pipelle device is a minimally invasive, cost-effective first-line diagnostic method.[7] The histopathological spectrum of endometrium in AUB ranges from normal cyclical patterns (proliferative and secretory) to benign lesions (polyps, atrophy), endometrial hyperplasia (with or without atypia), and endometrial carcinoma.[8-10] The risk of significant pathology increases with advancing age, obesity, chronic anovulation, and metabolic comorbidities such as diabetes and hypertension.[11,12]

Given the variability in AUB etiologies and the potential for serious underlying disease, continuous regional data on the histopathological spectrum are essential. This study was undertaken to analyse the histopathological patterns of endometrial tissue in patients presenting with AUB at a tertiary care centre in North India and to correlate these findings with key clinical variables, including age, reproductive status, bleeding pattern, and metabolic comorbidities.

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Materials and Methods

Study Design and Setting: This was a prospective observational study conducted in the Departments of Pathology and Gynaecology at K.M. Medical College & Hospital, Mathura, over 24 months.

Participants: A total of 228 women aged 18 years and older, presenting with symptoms of AUB, were enrolled after obtaining written informed consent. Exclusion criteria included: patients below 18 years, non-endometrial causes of bleeding (cervical/vaginal), coagulation disorders, intrauterine contraceptive device (IUCD) use, current hormonal therapy, gestational causes, and autolyzed or inadequate specimens.

Data Collection and Endometrial Sampling: Relevant demographic and clinical data (age, reproductive status, bleeding pattern, parity, comorbidities) were collected using a structured questionnaire. Endometrial biopsies were performed using a standard Pipelle device under sterile conditions in the outpatient department. The samples were fixed in 10% formalin and sent for histopathological examination.

Histopathological Examination: Fixed samples were embedded in paraffin, sectioned at 4 micrometers thickness, and stained with Hematoxylin and Eosin (H&E). Additional stains or immunohistochemistry (IHC) were performed as needed. Histopathological patterns were categorised as normal (proliferative, secretory), benign (polyp, atrophy), hyperplasia (without atypia, atypical/EIN), malignancy (endometrioid adenocarcinoma, serous carcinoma), or insufficient material.

Statistical Analysis: Data were analysed using SPSS version 26.0. Descriptive statistics were used to summarise findings. The association between clinical variables and histopathological outcomes was evaluated using Chi-square tests for categorical variables and ANOVA and t-tests for continuous variables. A p-value of <0.05 was considered statistically significant.

Results

Baseline Characteristics: The mean age of the 228 patients was 42.3 years (range 18–70). The majority belonged to the reproductive age group (18–40 years, 43.0%) and were premenopausal (49.1%), followed by perimenopausal (38.2%, 41–50 years) and postmenopausal women (18.8%, >50 years).

Histopathological Spectrum: The overall histopathological findings are summarised in Table 1. Non-neoplastic/benign patterns constituted the majority (81.1%), with proliferative endometrium being the most common single finding (34.2%). Hyperplasia was observed in 10.5% of cases, with atypical hyperplasia/endometrial intraepithelial neoplasia (EIN) accounting for 3.5%. Endometrial carcinoma was diagnosed in 4.0% of patients, predominantly of the endometrioid type.

Table 1: Distribution of Histopathological Patterns (n=228)

Histopathological Category	Specific Diagnosis	Number (n)	Percentage (%)
Non-Neoplastic / Benign		185	81.1
	Proliferative Endometrium	78	34.2
	Secretory Endometrium	62	27.2
	Atrophic Endometrium	19	8.3
	Benign Endometrial Polyp	26	11.4
Hyperplasia		24	10.5
	Hyperplasia without Atypia	16	7.0
	Atypical Hyperplasia / EIN	8	3.5
Malignancy		9	4.0
	Endometrioid Adenocarcinoma	7	3.1
	Serous Carcinoma	2	0.9
Insufficient Material		10	4.4

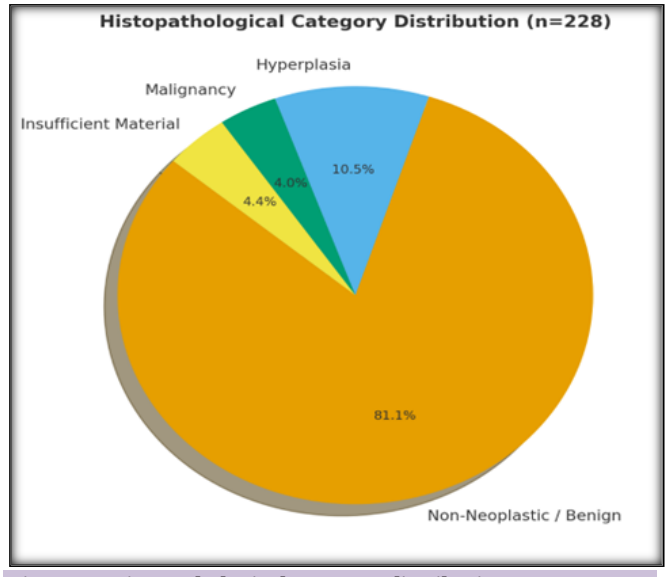

Figure 1: Histopathological category distribution

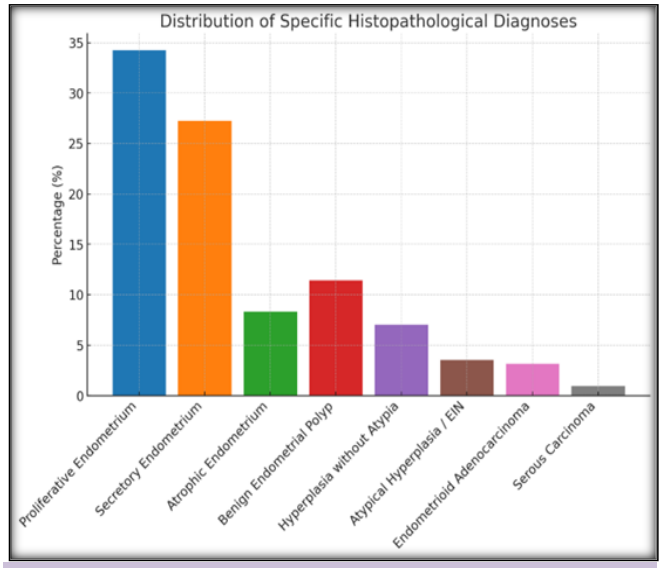

Figure 2: Distribution of specific Histopathological diagnoses

Association with Clinical Variables: A strong, statistically significant association was found between advancing age and histopathological category ($p<0.001$). Normal patterns declined with age, while hyperplasia (27.9%) and carcinoma (18.6%) peaked in the postmenopausal group [Table 2]. Similarly, reproductive status was significantly correlated with carcinoma ($p<0.001$); no carcinomas were found in premenopausal women, compared to 1.4% in perimenopausal and 18.6% in postmenopausal women [Table 3].

Table 2: Association between Age Groups and Histopathological Categories

Histopathological Category	18–40 yrs (n=98)	41–50 yrs (n=87)	>50 yrs (n=43)	p-value
Normal (Proliferative/Secretory)	85 (86.7%)	52 (59.8%)	3 (7.0%)	<0.001
Benign Pathology (Polyp, Atrophy)	12 (12.2%)	23 (26.4%)	10 (23.3%)	0.022
Pre-malignant (Hyperplasia)	1 (1.0%)	11 (12.6%)	12 (27.9%)	<0.001
Malignant (Carcinoma)	0 (0.0%)	1 (1.1%)	8 (18.6%)	<0.001

Table 3: Association between Reproductive Status and Endometrial Carcinoma

Reproductive Status	Endometrial Carcinoma Present	No Carcinoma	p-value
Premenopausal (n = 112)	0 (0.0%)	112 (100.0%)	< 0.001
Perimenopausal (n = 73)	1 (1.4%)	72 (98.6%)	
Postmenopausal (n = 43)	8 (18.6%)	35 (81.4%)	

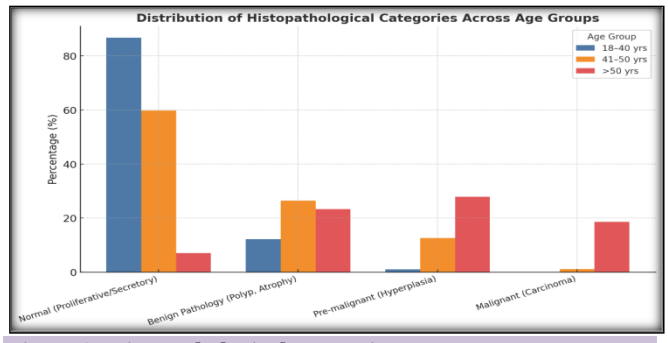

Figure 3: Histopathological categories across age groups

The Bleeding pattern was a significant predictor of pathology ($p<0.001$). Postmenopausal bleeding was associated with hyperplasia (20.9%) and carcinoma (18.6%), whereas menorrhagia was predominantly linked to benign proliferative endometrium (49.5%) [Table 4].

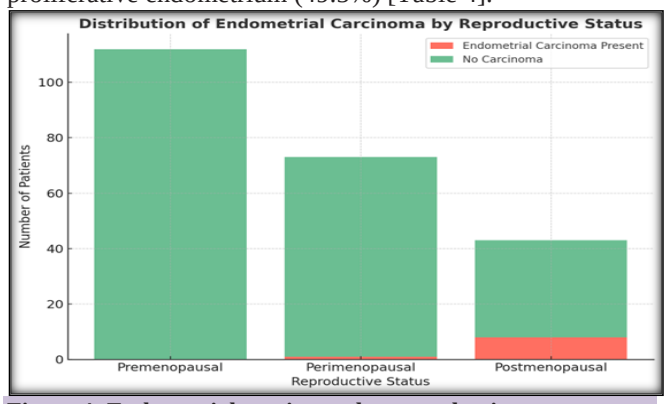

Figure 4: Endometrial carcinoma by reproductive status

Table 4: Clinical Presentation (Bleeding Pattern) vs. Common Histopathological Findings

Bleeding Pattern	Proliferative Endometrium (n = 78)	Benign Polyp (n = 26)	Hyperplasia (n = 24)	Carcinoma (n = 9)	p-value
Menorrhagia (n = 105)	52 (49.5%)	11 (10.5%)	5 (4.8%)	0 (0.0%)	< 0.001
Metrorrhagia (n = 68)	21 (30.9%)	12 (17.6%)	10 (14.7%)	1 (1.5%)	
Postmenopausal Bleeding (n = 43)	1 (2.3%)	3 (7.0%)	9 (20.9%)	8 (18.6%)	

Table 5: Comparison of Mean Age across Major Diagnostic Categories

Diagnostic Category	Number (n)	Mean Age ± SD (Years)	p-value
Normal Endometrium	140	38.2 ± 8.1	< 0.001
Benign Polyp	26	47.5 ± 9.3	
Hyperplasia	24	52.8 ± 7.5	
Carcinoma	9	60.7 ± 6.8	

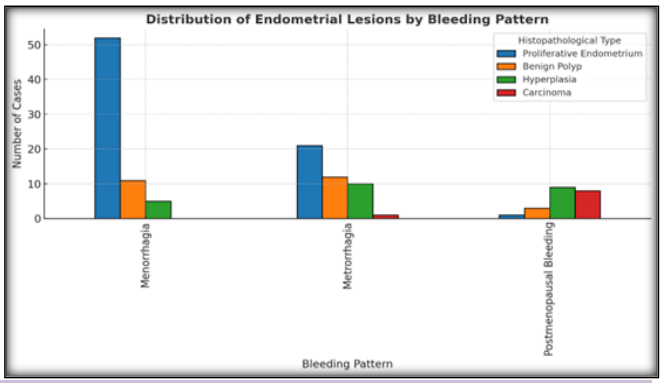

Figure 5: Endometrial lesion by bleeding pattern

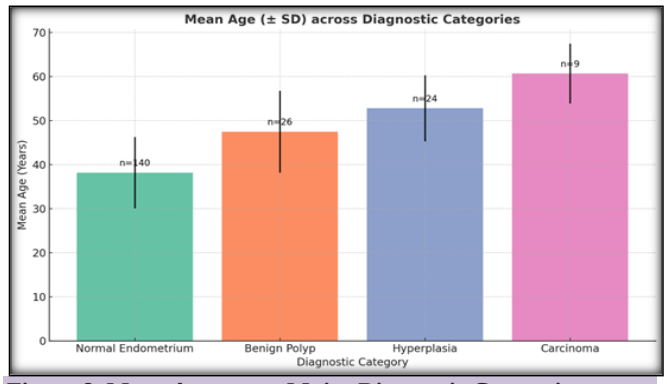

Figure 6: Mean Age across Major Diagnostic Categories

Table 6: Association between Diabetes Mellitus and Endometrial Pathology

Diabetic Status	Hyperplasia (n = 24)	Carcinoma (n = 9)	Normal/Benign (n = 195)	p-value
Diabetic (n = 51)	9 (17.6%)	5 (9.8%)	37 (72.5%)	0.008
Non-Diabetic (n = 177)	15 (8.5%)	4 (2.3%)	158 (89.3%)	

Table 7: Association between Hypertension and Endometrial Pathology

Hypertensive Status	Hyperplasia (n = 24)	Carcinoma (n = 9)	Normal/Benign (n = 195)	p-value
Hypertensive (n = 63)	11 (17.5%)	5 (7.9%)	47 (74.6%)	0.012
Normotensive (n = 165)	13 (7.9%)	4 (2.4%)	148 (89.7%)	

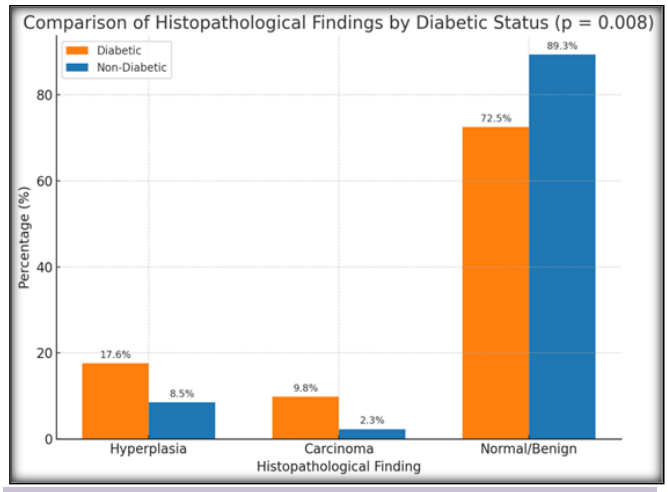

Figure 7: Association between Diabetes Mellitus and Endometrial Pathology

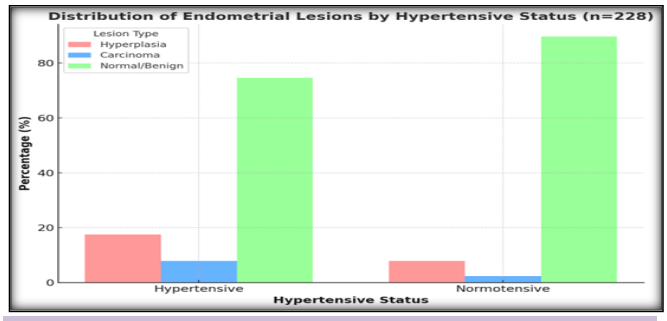

Figure 8: Association between Hypertension and Endometrial Pathology

Diabetes (p=0.008) and hypertension (p=0.012) were significantly associated with a higher prevalence of hyperplasia and carcinoma. The mean age increased progressively from normal endometrium (38.2±8.1 years) to hyperplasia (52.8±7.5 years) and carcinoma (60.7±6.8 years; p<0.001).

Table 8: Concordance between Endometrial Biopsy and Hysterectomy Diagnosis

Endometrial Biopsy Diagnosis	Total Biopsies	Cases with Hysterectomy	Concordant Diagnosis	Upstaged/Changed Diagnosis
Hyperplasia without Atypia	16	3	3 (100%)	0 (0%)
Atypical Hyperplasia / EIN	8	6	4 (66.7%)	2 (33.3%) *
Endometrial Carcinoma	9	8	8 (100%)	0 (0%)

Biopsy-hysterectomy concordance was high (100% for carcinoma and hyperplasia without atypia), but atypical/EIN showed a 33.3% upstaging rate to endometrioid carcinoma on final hysterectomy.

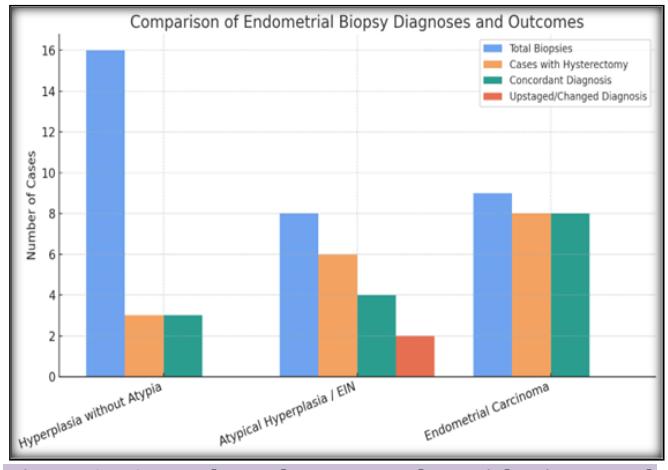

Figure 9: Concordance between Endometrial Biopsy and Hysterectomy Diagnosis

Discussion

This prospective study of 228 women with AUB provides a comprehensive analysis of the endometrial histopathological spectrum and its correlation with clinical parameters. Our findings align with the established understanding that AUB is predominantly a condition of the reproductive and perimenopausal years, largely due to functional hormonal disturbances. However, the study crucially demonstrates that clinically significant burdens of premalignant and malignant lesions cluster in older, postmenopausal women and those with metabolic comorbidities.

The age distribution in our study (43% reproductive, 38.2% perimenopausal) is consistent with previous research. Bindroo et al. (2018) reported a predominance of premenopausal cases (86.4%),[13] while Salvi et al. (2015) found a higher proportion of perimenopausal cases (52%),[14] reflecting variations in population demographics. The predominance of benign, functional endometrium (81.1%) in our study mirrors findings from Sharma et al,[15] (2018) and Bhat et al,[16] (2019) who reported proliferative endometrium as the most common pattern. This consistency across Indian studies reinforces that anovulatory cycles and hormonal imbalances are the leading mechanisms driving AUB in younger women.[17]

The prevalence of endometrial hyperplasia (10.5%) and carcinoma (4.0%) in our study falls within the range reported in

the literature (hyperplasia 10-26%, carcinoma 1-5%).[13-18] The marked increase in these lesions with age, particularly in the postmenopausal group (27.9% for hyperplasia, 18.6% for carcinoma), is a key finding. This age-dependent shift from benign to neoplastic pathology is a well-established phenomenon, driven by cumulative, unopposed estrogen exposure and the natural decline in ovarian function.[19]

A critical finding was the strong correlation between bleeding pattern and histopathology. Postmenopausal bleeding was significantly associated with hyperplasia and carcinoma ($p<0.001$), a finding that aligns with standard clinical guidelines that mandate prompt evaluation of this symptom to exclude malignancy.[20] Conversely, menorrhagia was most frequently associated with benign proliferative endometrium, supporting a more conservative initial approach in younger patients without risk factors.

The significant associations of diabetes ($p=0.008$) and hypertension ($p=0.012$) with endometrial hyperplasia and carcinoma are clinically important. These findings support the role of metabolic syndrome in the pathogenesis of endometrial cancer. Hyperinsulinemia, insulin-like growth factors, and chronic inflammation associated with these conditions promote endometrial proliferation and inhibit apoptosis, acting synergistically with unopposed estrogen.[21,22] The high mean BMI (30.5 kg/m²) in our carcinoma patients further strengthens the link between obesity and endometrial malignancy.[23]

The high diagnostic concordance between Pipelle biopsy and hysterectomy for carcinoma (100%) and hyperplasia without atypia (100%) validates the use of outpatient biopsy as a reliable first-line test.[24] However, the 33.3% upstaging rate for atypical hyperplasia/EIN to carcinoma is a crucial observation. This finding underscores the premalignant nature of EIN and supports current recommendations for definitive surgical management (hysterectomy) in women with atypical hyperplasia who have completed childbearing.[25] The 4.4% rate of insufficient tissue, mostly in postmenopausal women, highlights a limitation of blind biopsy in atrophic endometria and suggests a lower threshold for hysteroscopy in such cases.[26]

Our study has several limitations, including its single-centre design, potential sampling bias with the Pipelle device, lack of follow-up data, and the observational nature, which precludes establishing causality. Despite these, the strengths include its prospective design, adequate sample size, and comprehensive clinicopathological correlation.

Conclusion

In women presenting with abnormal uterine bleeding, benign functional endometrium is the most common histopathological finding. However, a clinically considerable proportion of patients harbor endometrial hyperplasia and carcinoma, particularly those who are older, postmenopausal, or have metabolic comorbidities such as diabetes and hypertension. Postmenopausal bleeding is a strong predictor of serious endometrial pathology. Endometrial biopsy using a Pipelle device is a reliable, first-line diagnostic tool with high concordance with hysterectomy specimens. The significant upstaging rate for atypical hyperplasia/EIN mandates timely definitive management. Routine histopathological evaluation of endometrial tissue in AUB, especially in high-risk groups, is essential for early detection of premalignant and malignant disease and for guiding appropriate, timely therapeutic intervention.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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