

Histopathological Insights into Endometrial Lesions Associated with Abnormal Uterine Bleeding

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Abstract:

Abnormal uterine bleeding produces a load of about 30% of all gynecological outpatient departments. It plays a major role in the rise in maternal morbidity and mortality. Thus it becomes important to make prompt and accurate diagnoses. Analysis of histopathological patterns in such cases can reveal many valuable insights.

In this observational study, 376 cases satisfying inclusion criteria were selected. Samples were received in 10% formalin solution, processed by routine process, and stained using H&E. Slides were then reported by a trained pathologist. Chi-Square, ROC, AUROC, and other appropriate statistical tools were applied to analyze the data. The most common age group was 41-50. Multipara with parity 3 or more was reported for 285 cases. Menopause was attained in 25 cases. The most prevalent histological finding was the proliferative phase, which was followed by the secretory phase. Cut-off was determined to be 44.5 using ROC. Menorrhagia (63.13%) was the most prevalent menstrual disease, followed by meno-metrorrhagia and metrorrhagia. In this study, functional factors are more prevalent than organic causes (84.04%). Menorrhagia (63.13%) is the most frequent presenting ailment in this study, followed by metrorrhagia. Using immunohistochemistry for confirmation of malignancies can increase the strength of the study in the future. The association between the benign and malignant lesions with menopausal status was not significant. Role of histo-morphological pattern of endometrium diagnosis plays a major role in early diagnosis and further management of AUB. Post-menopausal bleeding should be dealt with cautiously due to the higher incidence of malignancy in this age group.

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Introduction

Abnormal uterine bleeding (AUB) is defined as any uterine bleeding that deviates from the normal range in terms of volume, length, regularity, or frequency. AUB produces a load of about 30% of all gynecological outpatient departments. [1]

These illnesses affect people of all ages and have a major role in the rise in maternal morbidity and mortality. AUB is a common presenting symptom for the majority of female endometrial disease patients. [1, 2] Therefore, AUB supports the necessity of a prompt diagnosis.

The histological patterns of endometrial disorders vary widely. Simple endometrial hyperplasia to more complicated conditions like endometrial cancer is among these lesions. [2] Diagnosing most of these lesions requires taking an endometrial sample. The two most crucial sample techniques for the

conclusive identification of the lesions are curettage and endometrial biopsy. [3]

Research has indicated that the age of patients has an impact on the histological patterns of diagnosis. [4] The majority of young women who are fertile show signs of hormone imbalance more frequently. Nonetheless, endometrial hyperplasia and endometrial cancer are more common presentations in older women in the premenopausal and postmenopausal age groups. [4,5]

As per the available data, endometrial cancer is the most prevalent gynecological cancer in industrialized nations and the second most common in developing nations. It is just preceded by cervix cancer. According to US studies, endometrial cancer accounts for 6% of all gynecological cancer cases and ranks third in terms of gynecological cancer-

related deaths, after ovarian and cervical cancers. [6] Endometrial cancer is found in around 10% of perimenopausal and postmenopausal women with AUB worldwide. [7]

This study aims to study histopathological patterns of endometrial lesions in women of various age groups with AUB.

Material and Methods

This study descriptive prospective study was carried out for 1.5 years (between 1st August 2022 to 31st January 2024) in the Department of Pathology, Gandhi Medical College, Bhopal. Ethical clearance from the Institute Ethics Committee was obtained before conducting this study. Written consent was obtained from all the study participants.

Inclusion Criteria

All the patients with abnormal uterine bleeding older than 18 years reported at Gynaecology OPD.

Exclusion Criteria

The following patients were excluded from the study:

1. Incomplete History
2. Inadequate samples
3. IUCD in situ
4. Pregnancy complications such as ectopic pregnancy, molar pregnancy, and abortion
5. Bleeding, and coagulation defects
6. Antiplatelet medication users were not included.
7. Patients who were not willing to provide written consent.

Sample Size: The study comprised 376 cases in total that met the inclusion criteria.

Sample Collection: Endometrial samples were received in the pathology department. These consisted of endometrial biopsy and curettage samples. Also, endometrium of hysterectomy specimens of patients with AUB was included in the study. All the samples were received in 10% formalin.

Sample Processing: After grossing all samples, normal procedures were followed for processing. Following the steps for Haematoxylin and Eosin (H&E) staining, the tissue blocks made of wax were microtomed into sections of 4-5 micrometer thickness and then mounted on slides.

Sample Reporting: Slides were reported by a trained pathologist at Gandhi Medical College, Bhopal.

Data Collection and Statistical Analysis: Microsoft Excel was used to compile and analyze the data using Python (v3.9) and associated libraries, especially Matplotlib (v3.7), Seaborn (v0.11.2), and Pandas (v1.3.5). For quantitative variables, the results were shown as means and standard deviation, and for categorical variables as percentages. Descriptive analysis was performed to obtain the characteristics of the study population.

Appropriate statistical tests such as chi-square and ROC & AUROC were applied wherever required. The outcome was encoded appropriately and statistical comparisons were made with similar studies. A p-value of <0.05 was considered significant.

Results

Out of 376 cases reported in this study, the minimum age was 19 and the maximum was 77 with a distribution of 43.45 ± 6.46 . The age-wise distribution of cases is presented in Figure 1.

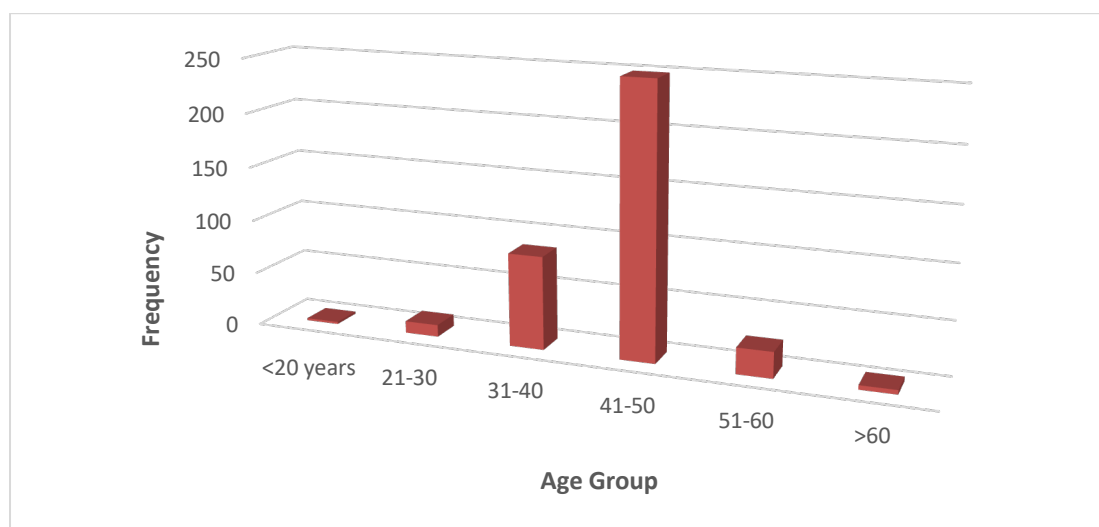


Figure 1: Distribution of study participants according to age groups

About 75.98% of the cases had multipara with a parity of 3 or more. Followed by 16.2% for Multipara with parity 2. LSCS history was reported for 6.65% of the cases. Menopause was achieved only for 6.65% of the reported cases. Distribution is presented in Table 1.

Table 1: Distribution of Clinical history of the patients

Characteristics	Frequency	Percentage (%)	Benign	Malignant	p-value
Parity					
Nulliparous	11	2.79	10	1	0.137
Multipara with parity 1	19	5.03	18	1	
Multipara with parity 2	61	16.2	61	0	
Multipara with parity 3 or more	285	75.98	280	5	
LSCS					
Yes	25	6.70	23	1	0.0245
No	351	93.30	346	6	
Menopause Attained					
Yes	25	6.65	23	2	0.0187
No	351	93.35	346	5	
Significant Medical/ Surgical History					
Yes	80	21.23	78	2	0.032
No	296	78.77	291	5	

The distribution of endometrial histopathological lesions among study subjects is presented in Table 2. The Proliferative Phase is the most common finding with approximately 59.04% of the cases, followed by the Secretory Phase for 27.93% of the cases.

Table 2: Distribution of Endometrium histopathological lesions

S. No.	Endometrial Histopathological Finding	Frequency	Percentage (%)
1	Atrophic endometrium	13	3.46
2	EH without atypia	12	3.19
3	EH atypia/ EIN	4	1.06
4	Secretory Phase	105	27.93
a	S/P with Endometrial Polyp	1	0.27
b	S/P with Adenomyosis	1	0.27
c	S/P with Uterine Prolapse	2	0.53
5	Proliferative Phase	222	59.04
a	P/P with Endometrial Polyp	11	2.93
b	P/P with Adenomyosis	24	6.38
c	P/P with Uterine Prolapse	7	1.86
d	P/P with Sub mucosal leiomyoma	2	0.53
6	Endometrial Adenocarcinoma	6	1.60
7	NKSCC	1	0.27
8	Pill Endometrium	12	3.19
9	Arias Stella Reaction	1	0.27
	Total	376	100

Distribution of benign and malignant cases based on Age group is presented in Figure 2. Most common age group for benign cases was 41-50 years followed by 31-40 years.

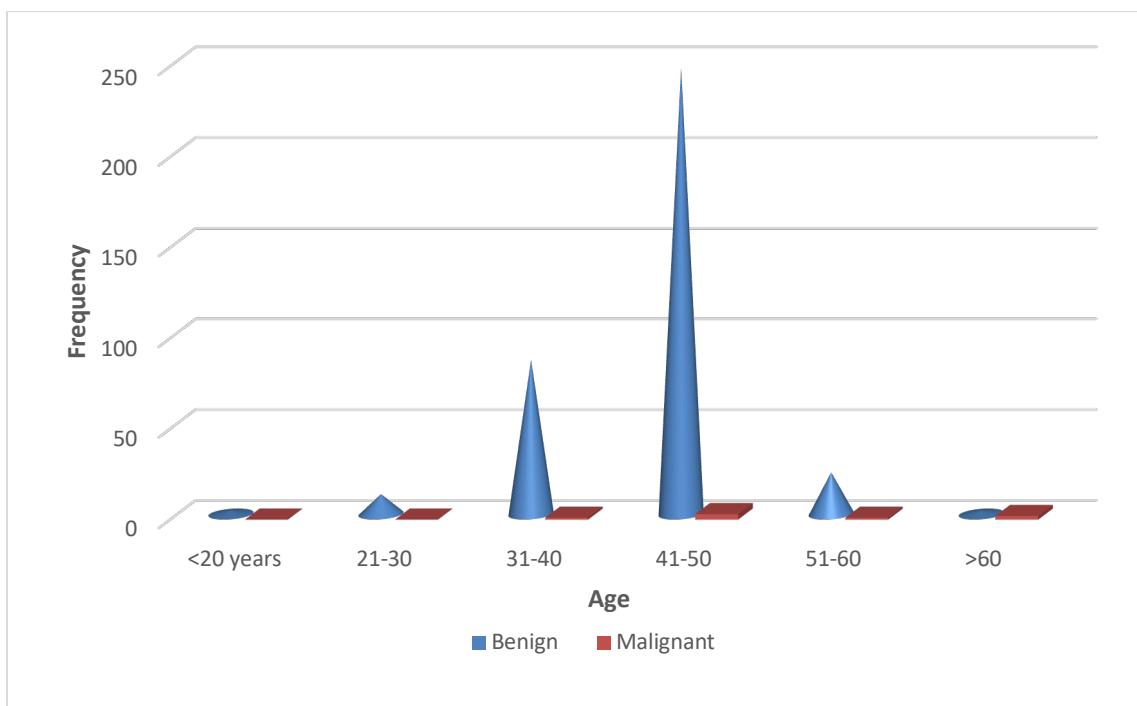


Figure 2: Comparison of Age group with the lesion benign or malignant

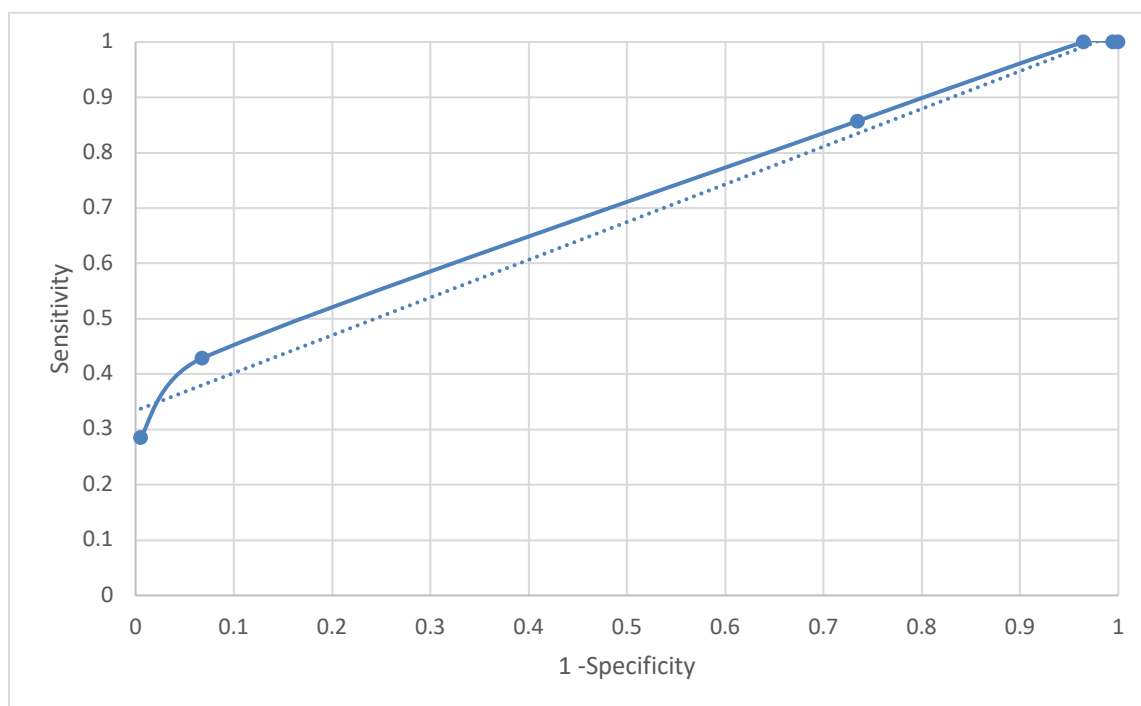


Figure 3: ROC curve for Age cut-off for the presence of malignancy

The Receiver Operating Characteristic (ROC) curve for determining the optimal age cut-off for predicting the presence of malignancy is present in Figure 3. The cut-off age is 44.5, the AUC is 0.6999, and sensitivity & specificity as 0.857 & 0.734 respectively.

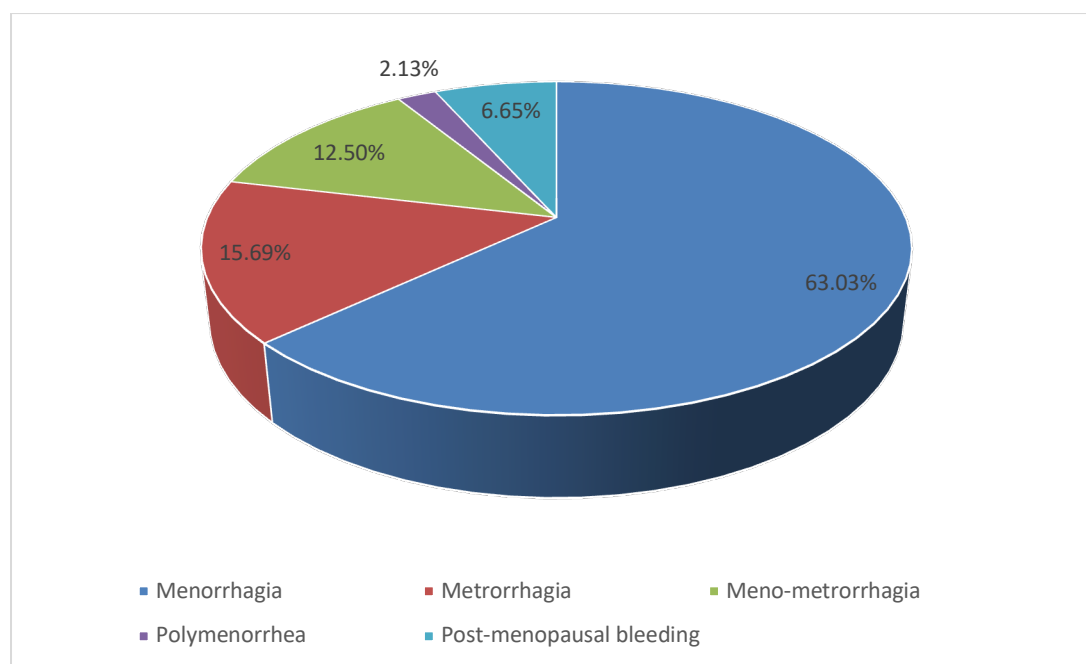


Figure 4: Bleeding Pattern in patients presenting with AUB

Menorrhagia accounted for 63.13% of all cases of menstrual disorders, with metrorrhagia and meno-metrorrhagia following closely behind (15.64%). Figure 4 represents the Bleeding pattern in patients presenting with AUB.

Discussion

Numerous illnesses of the reproductive system as well as non-gynecologic factors can result in abnormal uterine bleeding. AUB has both iatrogenic and systemic origins, as well as illnesses of the reproductive tract as organic etiologies. Once every organic cause of AUB has been ruled out, dysfunctional uterine bleeding can only be diagnosed. 376 AUB patients were included in the current study's sample.

Functional factors are more prevalent than organic ones in the majority of the research. In this study, functional factors also predominate (84.04%) over organic causes. The results of studies like Khan S et al. [8], Soleymani E et al. [9], and Vaidya S et al. [10] are similar to this. Organic reasons are more prevalent than functional causes in a few studies, including Ghani NA et al. [11], Forae GD et al. [12], and Abid M et al. [13].

In our study, the age group of 41–50 years had the highest incidence of AUB (66.22%), followed by the age group of 31–40 years (22.87%). In the majority of research, including Khan S et al. [8], Soleymani E et al. [9], Agrawal S et al. [14], and Jagadale K et al. [15], this age group is likewise the most frequently impacted. Menorrhagia (63.13%) is the most common presenting ailment in this study, followed by metrorrhagia (15.64%). According to numerous research, including Khan S et al. [8], Sajitha K et al. [16], Agrawal S et al. [14], and

Jagadale K et al. [15], menorrhagia is also the most common complaint. According to research like Bhatta S et al. [17] and Moghal N et al. [18], metrorrhagia is the most common complaint. In our study, polymenorrhoea is an uncommon complaint; nevertheless, Abid M et al. [13] found that it is the most common complaint.

In common histopathological diagnosis, the Proliferative phase (62.57%) is more than in Khan S et al. [8] – (PP-46.4%) while the Secretory phase constitutes (23.46%) as compared to 37.6% in Khan S et al. [8]. In our present study, the frequency of malignancy (2.79%) is higher than in all other studies except Sajitha K et al. [16] (4.5%).

Hyperplasias constitute 4.26% of cases of AUB in our study. A similar incidence of hyperplasia is found in studies like Abid M et al. [13], and Jairajpuri ZS et al. [19]. Incidence of the endometrial hyperplasia is slightly more than that found in the study of Soleymani E et al. [9] and less than in other studies.

Limitations:

The immunohistochemistry has not been used for confirmation of malignancies. The reasons for losing the patients during follow-up are lack of awareness regarding the significance of the collection of histopathology reports and then getting a repeat consultation.

Conclusion

As this study is centered in a hospital, it might not accurately reflect the disease's true occurrence in the general population. Because persistent anovulation is widespread in the peri-menopausal age group, the majority of patients (66.22%) are from

the 41–50-year age group. An erratic and unpredictable pattern of bleeding those changes in quantity, length, and character is linked to chronic anovulation. This study helped in evaluating the association between the age group and AUB i.e. predominant patients of AUB are in the age group of 41-50 years, parity and AUB i.e. multipara 3 or more patients, were the predominant group, predominant histopathological findings in cases of AUB which was a proliferative pattern of endometrium. The association of age group and malignancy was significant as the higher age group had more number of malignant lesion diagnoses with maximum malignant cases in the 41-50 year age group. The most common bleeding pattern was menorrhagia.

Though association between the benign and malignant lesions with menopausal status was not significant, as also the association between menopause and incidence of benign and malignant endometrial lesions. So this study helped in reiterating the fact that most cases of AUB if properly diagnosed are treatable medically, in the majority of cases, and by surgery in a few cases where organic causes are found.

Post-menopausal bleeding should be dealt with cautiously due to the higher incidence of malignancy in this age group. For the patients who presented with advanced age and diagnosis of endometrial carcinoma, the need for palliative treatment has increased, as because of advanced age, the mortality associated with surgery also increases. Role of histo-morphological pattern of endometrium diagnosis plays a major role in early diagnosis and further management of AUB.

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