Original Article

Histopathological Patterns of Endometrial Biopsies in Abnormal Uterine Bleeding with Special Reference to Endometrial Carcinoma: A Study from North East India

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Abstract

Background: Abnormal uterine bleeding (AUB) is the most commonly presented gynecological symptom in women of all age groups. Endometrial sampling followed by its histopathological examination is an indispensable tool to investigate the cause of AUB.

Materials and Methods: The study was a hospital-based cross-sectional study that included 272 endometrial biopsies sent to the Pathology department for histopathological examination. The duration of the study was one year. Only endometrial biopsies for non-gestational AUB were included in the study. After processing the formalin-fixed tissue, paraffin blocks were made. Four-micron thick slides were prepared, stained with Hematoxylin & Eosin stain, and thoroughly examined under scanner, low, and high-power view. The samples were categorized by age groups and clinical presentation of uterine bleeding. The study was approved by the Institutional Ethics Committee.

Results: Out of 272 endometrial biopsies, 254 biopsies could be evaluated, as 18 were non-diagnostic due to cellular inadequacy. The majority of the patients (42.1%) were in the 41–50 years age group. Normal cyclical changes (35.8%) constituted the most common histopathological findings, followed by disordered proliferative endometrium (27.9%). Malignant lesions were detected in 1.2% of cases, while endometrial hyperplasia constituted 26.4% of cases, emphasizing the importance of endometrial biopsies in detecting precursor lesions and treating them in their early pre-invasive stages, thereby reducing morbidity and mortality (p-value 0.0001).

Conclusion: Endometrial sampling should be considered in all cases presenting with AUB. Histopathological examination of the endometrium should be regarded as the first-line investigative modality in peri- and post-menopausal age groups, where the incidence of endometrial hyperplasia and endometrial carcinoma is higher.

Keywords:

Abnormal uterine bleeding, Endometrial biopsy, Histopathological examination, Endometrial carcinoma, Endometrial hyperplasia, Precursor lesions of the endometrium

Introduction

Abnormal uterine bleeding (AUB) is the most common gynecological symptom seen in women of all age groups and is responsible for the majority of gynecological outpatient visits. It has a significant effect on a woman's physical, emotional, and social quality

of life.

Abnormal uterine bleeding (AUB) is defined as a bleeding pattern that differs in frequency, duration, and amount from the normal menstrual cycle [1]. It has varied presentations, including menorrhagia, metrorrhagia, metromenorrhagia, intermenstrual or irregular bleeding, polymenorrhea, oligomenorrhea, and postmenopausal bleeding [2].

Histopathological examination of the endometrium remains very relevant and should not be ignored in the modern era of molecular studies, as it is the first line of investigation in any non-pregnant woman presenting with abnormal uterine bleeding. It plays a vital role in differentiating non-neoplastic lesions from neoplastic ones, along with early detection of precursor lesions, follow-up, and prevention of malignancy. Careful study of endometrial biopsies can also identify subtle hormonal imbalances causing abnormal uterine bleeding.

This study also emphasizes the discrepancies in histopathological reporting of endometrial biopsies due to the dynamically variable spectrum of histomorphological patterns of the endometrium. As it is hormonally responsive, there is significant interobserver variation, making it challenging for pathologists. AUB has remained one of the most frequent indications for hysterectomy in developing countries, but 40% of cases are usually not associated with any definitive organic pathology. Surgical complications, mortality risks, various short-term morbidities, increased risk of intra-abdominal adhesions, postoperative infections, pelvic organ dysfunction, early onset of menopause, and thromboembolic events are associated with hysterectomy [3]. Hence, the non-negotiable role of histopathological examination of endometrial biopsies is emphasized. Since the endometrium is the most accessible tissue for histopathological evaluation of AUB, several methods are used for endometrial sampling, among which Dilatation and Curettage (D&C) is considered the gold standard [4].

Literature related to this topic from Northeast India is limited. The objectives of this study are: To evaluate the predominant histomorphological patterns of the endometrium in patients with varied presentations of AUB, and To determine the specific pathology in different age groups of patients presenting with AUB from Northeast India.

Materials and Methods

The present study is a hospital-based cross-sectional study conducted in the Department of Pathology over a period of one year, from January 2022 to December 2022.

Inclusion Criteria: Endometrial biopsies of all women in the age group of 20 to ≥60 years who underwent D&C for AUB were included in the study.

Exclusion Criteria: Patients with hemostatic disorders presenting with AUB were excluded from the study. Patients with isolated vaginal or cervical pathology, or leiomyoma, were excluded. Pregnant women presenting with AUB were excluded. Autolysed biopsy samples were excluded from the study.

Endometrial biopsies of 272 non-gestational patients who had undergone Dilatation & Curettage (D&C) in the Department of Obstetrics and Gynaecology were sent to the Department of Pathology for histopathological examination. Relevant clinical data were obtained from hospital records and laboratory reports. The samples were fixed in 10% neutral buffered formalin for 12-24 hours, and then the entire tissue was taken for processing and paraffin blocks were made. Four μm thick sections were made from paraffin blocks, and the labeled slides were stained with Hematoxylin and Eosin stains. The slides were thoroughly examined under a light microscope (scanner, low power view, and high power view) and categorized by age and clinical presentation. The

data collected were statistically analyzed in an MS Excel sheet using tables, charts, and bar diagrams. Variables were summarized using numbers and percentages. P < 0.05 was taken as statistically significant. The study was approved by the Institutional E thics Committee.

Results

Out of 272 cases, 254 abnormal uterine bleeding cases undergoing D&C for endometrial biopsy could be analyzed. Eighteen samples were labeled as inadequate and advised for rebiopsy. Abnormal uterine bleeding was most common in the 41-50 years age group. The most prevalent bleeding pattern was menorrhagia, which was most commonly seen in the 41-50 years age group (28.7%) (p < 0.0001, chi-square = 169.5755). Postmenopausal bleeding was commonly seen in the elderly age group of 51 to ≥60 years.

Most of the endometrial pathology, which constituted 107 cases (42.1%), was encountered in the 41-50 years age group. Normal cyclical endometrium (35.8%) constituted the predominant histopathological pattern noted in our study, followed by disordered proliferative/anovulatory endometrium (27.9%) and endometrial hyperplasia (26.4%).

Most cases of endometrial carcinoma were associated with postmenopausal bleeding (p < 0.0001, chi-square = 101.4477). Normal cyclical changes (35.8%) and chronic non-specific endometritis (3.9%) were common in the 31-40 years age group. Disordered proliferative endometrium/anovulatory endometrium (27.9%), endometrial hyperplasia (26.4%), and endometrial polyp (3.1%) were common in the 41-50 years age group. The risk of endometrial carcinoma increases from 31 years onwards, seen in 3 cases (1.2%) each in the 31-40, 41-50, and 51 to ≥60 years age groups (p < 0.0001, chi-square = 54.169).

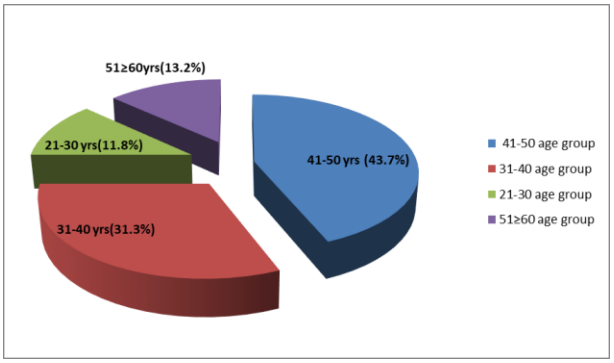

Figure 1: Age distribution of AUB presentation

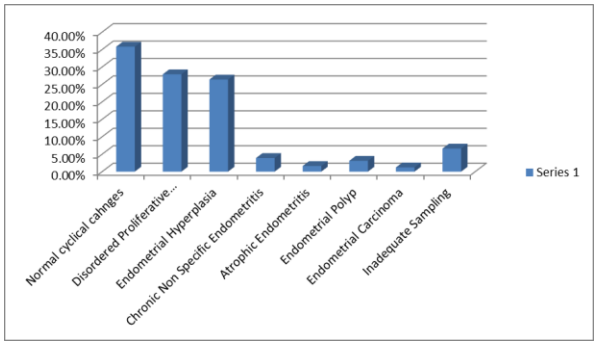

Figure 2: Histopathological patterns of AUB

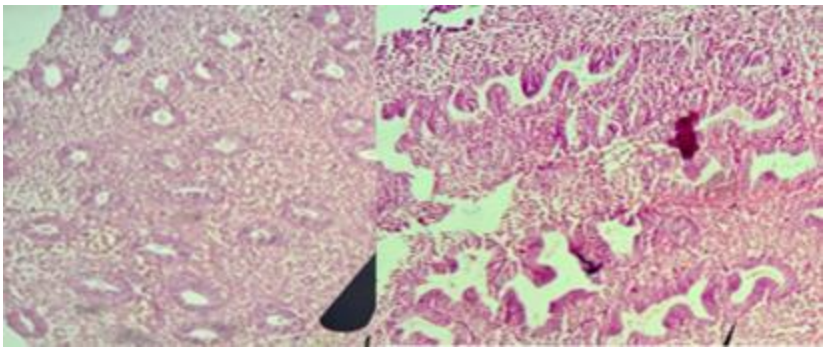

Figure 3: a:Microphotograph of Proliferative Endometrium(10x10 ,H&E) b: Microphotograph of Endometrial Hyperplasia without atypia (10x10,H&E)

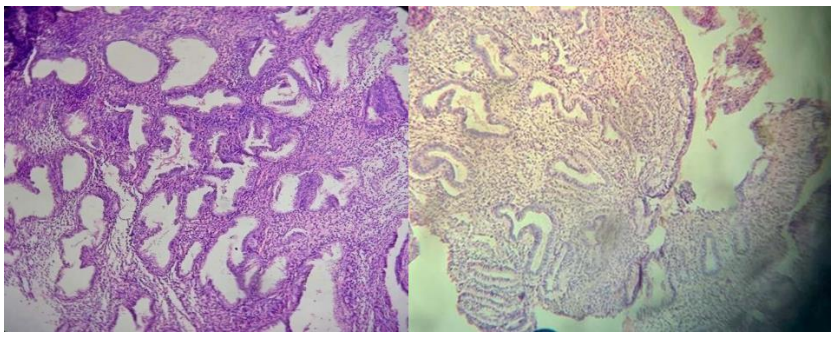

Figure 4: 4a :Microphotograph of Endometrial Hyperplasia without atypia (10x10,H&E) 4b :Microphotograph of Endometrial Polyp (10x10,H&E)

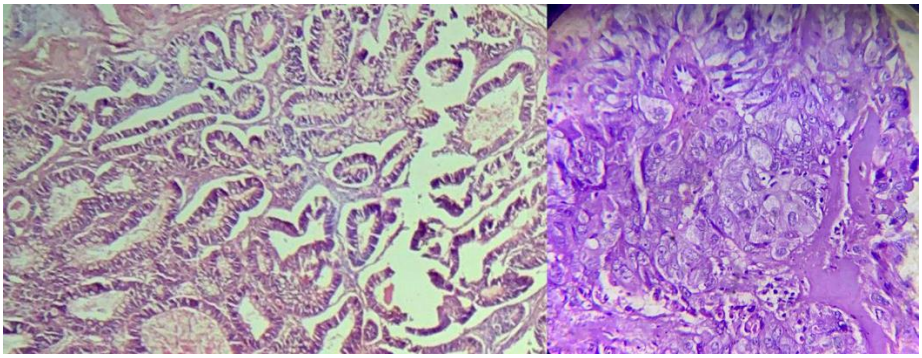

Figure 5: a : Microphotograph of Endometrioid Endometrial Carcinoma (10x10,H&E), b: Microphotograph of Endometrial Adenocarcinoma with squamous differentiation (10x10,H&E)

Discussion

Abnormal uterine bleeding is the most common complaint presented in the gynecological department and describes bleeding per vagina that does not meet the criteria of regular menstrual bleeding. AUB is one of the most important causes of iron deficiency anemia in females [5]. Most of the patients diagnosed with endometrial cancer initially presented with abnormal uterine bleeding [6]. Therefore, histopathologic study of endometrial samples is vital in diagnosing various conditions causing AUB, as the endometrium may show signs of a serious underlying condition, in which case aggressive treatment, including a major surgical

procedure, may be necessary [7]. The pathologist plays a significant role in the early detection of endometrial precursor lesions and the exclusion of malignancy [8].

Table 1: Distribution of clinical bleeding pattern according to age group

Bleeding Pattern	21-30 yrs	31-40 yrs	41-50 yrs	51≥60yrs	Total (Percentage)
Menorrhagia	21	47	78	5	151(55.5%)
Polymenorrhea	1	6	3	0	10 (3.6%)
Metrorrhagia	10	32	38	7	87 (31.9%)
Post menopausal	0	0	0	24	24 (8.8%)
Total (Percentage)	**32 (11.8%)**	**85 (31.3%)**	**119(43.7%)**	**36 (13.2%)**	**272 (100%)**

Table 2: Correlation between clinical bleeding pattern and Histopathological diagnosis

Histopathological Pattern	**Menorrhagia**	**Polymenorrhea**	**Metrorrhagia**	**Post menopausal bleeding**	**Total**
Normal cyclical endometrium	60	3	26	2	91 (35.8%)
Disordered Proliferative endometrium/Anovulatory endometrium	30	2	37	2	71 (27.9%)
Endometrial hyperplasia	48	1	12	6	67 (26.4%)
Chronic Non specificendometritis	1	1	5	3	10 (3.9%)
Atrophic endometrium	0	2	0	2	04 (1.6%)
Endometrial polyp	4	0	1	3	08 (3.1%)
Endometrial carcinoma	0	0	1	2	03 (1.2%)
Total (Percentage)	**143 (56.3%)**	**9(3.5%)**	**82 (32.28%)**	**20(7.87%)**	**254(100%)**

Table 3: Distribution of various Histological patterns of endometrium according to age group.

HISTOPATHOLOGIAL PATTERN		**Age Group(in years)**				**Total**
		21-30	**31-40**	**41-50**	**51≥60**	
Normal cyclical changes	Secretory	8	24	19	1	91(35.8%)
	proliferative	6	15	17	1	
Disordered Proliferative/anovulatory Endometrium		8	29	31	3	71(27.9%)
Endometrial hyperplasia	Without atypia	5	27	26	2	67(26.4%)
	With atypia	0	2	4	1	
Chronic non specificendometritis		0	5	3	2	10(3.9%)
Atrophic endometritis		0	0	1	3	4(1.6%)
Endometrial polyp		1	2	5	0	8(3.1%)
Endometrial Carcinoma		0	1	1	1	3(1.2%)
TOTAL(%)		**28 (11.0%)**	**105 (41.3%)**	**107 (42.1%)**	**14 (5.5%)**	**254 (100%)**

The incidence of AUB was highest among the age group 41-50 (43.7%), which was similar to studies by Vijayaraghavan A Sr. et al. and Sharma R et al. [2,9]. The youngest patient was 21 years old, and the oldest was 74 years old, which was similar to a study done by Gitika Hyanki et al. [10]. Pregnancy usually happens in the age group of 20-40 years; therefore, pregnancy-related complications are more common in these two decades rather than any organic abnormality. Hence, AUB was more prevalent in

the age group of 40-50 years than in other age groups.

The most common bleeding pattern was menorrhagia (56.3%), which, as a symptom, was a non-negotiable reason to immediately visit the gynecological OPD. The present study has shown menorrhagia as the most common bleeding pattern. Studies done by Vijayaraghavan et al. and Sharma R et al. have shown the same pattern of menorrhagia at 71.25% and 57.3%, respectively [2,9].

Normal cyclical patterns were the dominant histopathological findings in our study, comprising 91 cases (35.8%), with the secretory phase (57.1%) forming the majority, followed by the proliferative phase (42.8%). A study by Sanjita et al. also found the predominance of the secretory phase, while a study by Vijayaraghavan et al. showed the predominance of the proliferative phase of cyclical endometrium [1,2]. The majority were found in the 31-40 and 41-50 years age groups. These findings highlight the diagnostic role of endometrial biopsy over hysterectomy, as these conditions are absolutely medically treatable without any need for surgery. The variations in the cyclical patterns in these studies can be attributed to differences in hormonal levels among different patients.

There were 71 cases (27.95%) of disordered proliferative/anovulatory endometrium, comparable to the study by Gitika Hyanki et al., which had 20.3% of cases [10]. The incidence was highest in the 41-50 years age group. Disordered proliferation is common in perimenopausal age because of anovulatory cycles. Timely detection of this pattern can help in the proper management of these patients.

Endometrial hyperplasia comprised 67 cases (26.4%), which was comparable to the study by Prathipaa et al. (23.43%). It was most commonly found in the 41-50 years age group, closely followed by the 31-40 years age group, comprising 30 (44.8%) and 29 (43.2%) cases, respectively [8]. Out of 67 cases of endometrial hyperplasia, 60 cases (90%) showed no atypia, and 7 cases (10%) showed atypia, which is similar to the study reported by Sharma K et al. [11]. Early diagnosis of endometrial hyperplasia is necessary as it precedes malignancy and frequently presents with AUB [12]. Hence, endometrial study should be conducted even at a younger age, such as 30 years, to rule out the presence of precursor lesions of endometrial carcinoma and manage appropriately.

Only 3 cases of endometrial carcinoma were seen in this study (1.2%), which is comparable to the study by Dwivedi S. S. et al. (1.85%). One case each was seen in the age groups 31-40, 41-50, and 51≥60 [15]. Hence, it has been observed that the risk of endometrial carcinoma increases from 30 years onwards, so for prevention and early detection, histopathological examination of endometrial biopsy in patients with AUB is mandatory.

Chronic nonspecific endometritis was seen in 10 cases (3.9%), and the study was comparable to that done by Rupal Shah et al. (2.6%) [13]. Endometrial polyp is the benign outgrowth from the uterine cavity composed of glands, stroma, and blood vessels. In our study, 8 cases (3.1%) showed endometrial polyps, with the majority in the 41-50 years age group, which is comparable to the study by Zothansangi et al., which had 9 cases (1.35%) predominantly seen in the 41-50 years age group [14]. Atrophic endometrium is due to estrogen deprivation in the peri- and postmenopausal period, and the rupture of dilated venules beneath the thin endometrium leads to abnormal uterine bleeding. In the present study, 4 cases (1.6%) of atrophic endometrium were seen, where 3 of them were in the older age group 51≥60 and 1 in the 41-50 years age group. Our findings were similar to the studies by Vijayaraghavan et al. and Prathipaa et al., which also documented atrophic endometrium as a cause of AUB in elderly females [2,8]. Inadequate sampling was relatively common, occurring in 6.61% (18/272) of cases, where an opinion could not be formed. A study by Pratibha Singh et al. reported similar findings, where 16 out of 115 cases were inadequate for reporting [16]. This could be attributed to atrophic endometrium, where the cellularity is considerably low, or mostly due to technical error, inefficient

handling of the specimen, and inappropriate use of fixatives. Repeat biopsy was advised in such cases. Care should be taken to avoid such situations so that patients do not have to undergo the harassment of repeated procedures.

Conclusion

Endometrial sampling and its histopathological examination have helped classify the histopathological patterns in varying presentations of AUB in different age groups, which has aided in the early detection of precursor lesions and thereby decreased the incidence of endometrial carcinoma. Endometrial hyperplasia is common in the age group of 30-50 years, and endometrial carcinomas were found as early as 30 years of age. Early detection of endometrial hyperplasia and endometrial carcinoma will undoubtedly contribute to the appropriate management of patients, leading to improved outcomes. Increased awareness, better accessibility to healthcare facilities, and cost-effective health programs by the government will contribute to the prevention and early diagnosis of endometrial carcinoma in patients presenting with AUB.

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Competing interests: None declared.

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