

Pattern of Bleeding with Histopathological Correlation in Patients Presenting with Abnormal Uterine Bleeding

Ranjan Agrawal¹, Gaurav Jaiswal², Muhammad Ekram², Mayank Agrawal³

ABSTRACT

Background: Abnormal uterine bleeding (AUB) is one of the most common presenting health issues amongst females. It is defined as any bleeding that varies in frequency, duration, and volume of blood flow. Endometrial biopsy followed by histopathology constitutes an important mode of investigation in patients presenting with AUB. The aim of this study was to analyze the histopathological patterns of endometrium in females who present with AUB and to assess the patterns in age various groups. **Methods:** The study was conducted in a tertiary care hospital of Western Uttar Pradesh, during one year duration. Endometrial biopsies of patients presenting with AUB, in whom all causes of pregnancy were ruled out, have been included in the present study. **Results:** Out of the 130 cases studied, the majority of biopsies were in the age group of 41-50 years (55.4%). Most of the patients presented with complaints of menorrhagia (70%). The most common histological pattern observed were endometrium in proliferative (35.4%) followed by secretory phase (19.2%). Endometrial hyperplasia was another important histopathological finding observed. Only two cases of endometrial carcinoma were reported during the present study period. **Conclusion:** Although a regular cyclical pattern of menstruation is observed commonly noted, endometrial biopsy should be done in the peri- and post-menopausal age groups wherein the incidence of endometrial hyperplasia and endometrial carcinoma is more commonly observed.

KEY WORDS: AUB, Endometrium, Polyp, Biopsy.

Introduction

The most prevalent medical condition affecting women across all age groups is abnormal uterine bleeding (AUB). Any bleeding pattern that differs from a pattern seen during regular menstrual cycles or even menopause in terms of frequency, length, and amount is referred to as AUB. When bleeding is irregular, lasts longer than seven days, or is excessive (more than 80 milliliters each menstruation), it is classified as abnormal. One of the most significant gynecological complaints, AUB accounts for roughly 30–35% of outpatient visits. It can manifest in a

variety of ways, including heavy menstrual bleeding, irregular or frequent cycles, post-coital bleeding, or post-menopausal hemorrhage. It affects women throughout all age ranges. It is a reflection of the underlying illness, which might be anything from cancer to hormonal imbalance. Women's quality of life is greatly impacted by AUB^[1]. The International Federation of Gynecology and Obstetrics (FIGO) developed the PALM-COEIN classification for the etiology of AUB in 2011 based on these probable underlying etiologies. Structural identities like polyps, adenomyosis, leiomyoma, and cancer are explained by PALM. Coagulation abnormalities, ovulatory dysfunction, endometrial, iatrogenic, and unclassified causes are among the non-structural causes of COEIN^[2]. AUB is diagnosed by endometrial biopsy as a diagnostic technique. It is typically used as the initial diagnostic method in females under the age of 45. In younger females with a history of unopposed estrogen exposure, unsatisfactory medical care, and persistence of AUB,

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Quick Response Code:



Website: www.jmsh.ac.in

Doi: 10.46347/jmsh.v11.i1.24.230

¹Professor & Head, Pathology, Rajshree Medical Research Institute, Bareilly, Uttar Pradesh, India, ²PG Resident, Department of Pathology, Rajshree Medical Research Institute, Bareilly, Uttar Pradesh, India, ³Senior Resident, Pathology, Shri Atal Bihari Vajpayee Government Medical College, Chhainsa, Faridabad, Haryana, India

Address for correspondence:

Ranjan Agrawal, Professor & Head, Pathology, Rajshree Medical Research Institute, Bareilly, Uttar Pradesh, India. E-mail: drranjan68@gmail.com

endometrial biopsy is especially critical^[3]. The most crucial step is ruling out precursor lesions including cancer and endometrial hyperplasia^[2]. The goal of the current investigation was to ascertain the endometrium's histological spectrum in women who presented with abnormal uterine hemorrhage.

Materials and Methods

With prior approval from the Institute Ethical Committee (Human Studies), the current study was a hospital-based observational study carried out in the Department of Pathology at Rajshree Medical Research Institute, Bareilly, in association with the Department of Obstetrics and Gynecology, over the course of a year, from June 2023 to May 2024.

Endometrial samples from 130 patients with AUB were included in the study. The current study did not include endometrial biopsies or curetting performed on patients with gestational reasons, such as incomplete or missed abortions, or retained products of conception. Important clinical information was gathered from the patients, such as age, presenting problems, menstrual details, particularly last menstrual period (LMP), periodicity, and regularity. The slides stained with hematoxylin and eosin were carefully inspected, and the histopathological observations were recorded. As required, slices stained with Ziehl-Neelsen were also evaluated.

With the use of SPSS software version 25, statistical analysis was performed on the observations pertaining to age, noteworthy clinical findings, and histological diagnosis. The categorical variables were analyzed using the Chi-square test. Fisher's exact test was used to examine whether these factors were related. A p-value of less than 0.05 was deemed statistically significant.

Results

AUB was found in 130 endometrial samples that were included in the current investigation. Three sets of observations were made based on the age range of the individuals who underwent endometrial sampling. The majority of the females (55.4%) fell in the age range of 41–50 years. It was observed that the reproductive age group of 18 to 40 years accounted for 24.6% of the AUB patients.

Menorrhagia was the most prevalent complaint among perimenopausal and reproductive age patients, according to age-specific analysis, which also demonstrated that it was statistically significant

($p=0.01$). Metrorrhagia was the second most common presentation in the perimenopausal and reproductive age groups. Fifteen individuals in all complained of bleeding after menopause (Table 1). With only four patients (3.08%), hypomenorrhea was the least frequent presentation.

Table 1: Showing age-wise distribution of pattern of bleeding

S. No.	Pattern of bleeding	Age 18-40	Age 41-50	Age >50	Total (%)
1	Menorrhagia	21	60	10	91 (70%)
2	Metrorrhagia	9	9	2	20 (15.38%)
3	Hypomenorrhea	2	1	1	4 (3.08%)
4	Post-menopausal bleeding	0	2	13	15 (11.54%)
Total		32	72	26	130

Proliferative phase endometrium (35.4%) was the histological pattern seen in the endometrial biopsies of 130 women with AUB across all age groups. Endometrium in secretory phase, followed by endometrial hyperplasia without atypia, was observed in 19 individuals (14.6%), making it the second most prevalent pattern. Together with menstrual endometrium, endometrial polyp, and adenomyosis, other patterns that were seen in decreasing order of frequency included disordered endometrium and leiomyoma.

Females less than 50 years were found to have granulomatous endometritis, adenomyosis, chronic non-specific endometritis and, Arias-Stella reaction. One case of endometrial carcinoma was recorded in each of the age groups of patients: perimenopausal and menopausal (Table 2).

Comparing the functional aetiology of uterine bleeding to the organic lesions (35%) of AUB, the former was much greater (65%). When compared to organic pathology, the aetiology of AUB was more functional in the reproductive and perimenopausal age group; however, in the post-menopausal age group, AUB was caused by both functional as well as the organic lesions. There was no significant correlation found between the age groups and either the functional or organic etiology of AUB ($p=0.65$ and $p=0.97$, respectively).

Table 2: Distribution of Abnormal Uterine Bleeding as per the age and various causes

Endometrial histopathology	Age Group (Years)			Total %	
	18-40	41-50	>50		
Proliferative phase	8	29	9	46	35.4
Secretory phase	5	16	4	25	19.2
Disordered endometrium	4	1	3	8	6.16
Menstruating endometrium	1	3	0	4	3.07
Atrophic endometrium	0	0	1	1	0.8
Chronic nonspecific endometritis	1	2	0	3	2.31
Granulomatous endometritis	1	0	0	1	0.8
Arias-Stella reaction	0	1	0	1	0.8
Adenomyosis	2	2	0	4	3.07
Leiomyoma	3	4	1	8	6.16
Endometrial polyp	2	1	1	4	3.07
Endometrial hyperplasia without atypia	4	11	4	19	14.6
Atypical endometrial hyperplasia	1	1	2	4	3.07
Endometrial carcinoma	0	1	1	2	1.54
Total	32	72	26	130	100

The most prevalent histological finding observed in patients with organic reasons was endometrial hyperplasia without atypia identified in 19 instances (14.6%) (Figure 1). This was followed in sequence by granulomatous endometritis, endometrial carcinoma (1.54%), atypical endometrial hyperplasia (3.07%), endometrial polyps (3.07%), and Arias-Stella reaction (0.8% each) (Table 2, with Figures 1 and 2).

Endometrium in proliferative phase was the most frequently observed histological pattern in patients presenting with menorrhagia, metrorrhagia, and post-menopausal bleeding. Menorrhagia and post-menopausal bleeding were the symptoms of atypical endometrial hyperplasia and endometrial polyp, respectively, in the reproductive and post-menopausal age groups. In women of reproductive age, endometrial hyperplasia without atypia most frequently manifested as menorrhagia. Metrorrhagia was observed together with granulomatous endometritis and Arias-Stella response. Metrorrhagia

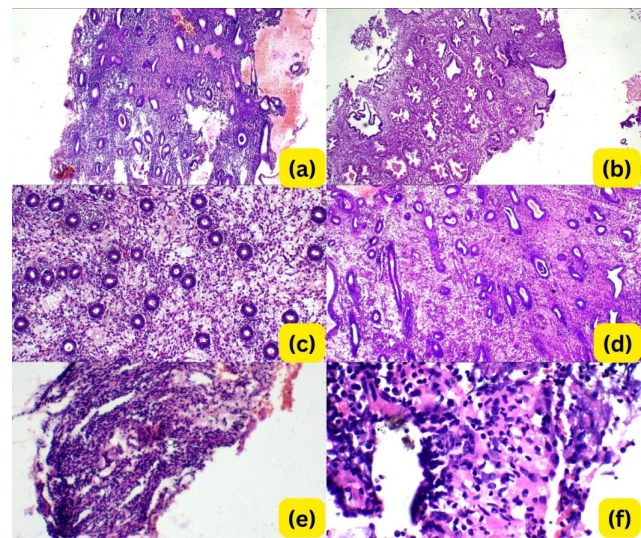


Figure 1: Histopathology Showing: (a) Endometrium in proliferative phase (H & E x 100); (b) Endometrium in secretory phase (H & E x 100); (c) Disordered Endometrium (H & E x 100); (d) Menstruating endometrium (H & E x 100); (e) Atrophic endometrium (H & E x 100); (f) Granulomatous endometritis (H & E x 400)

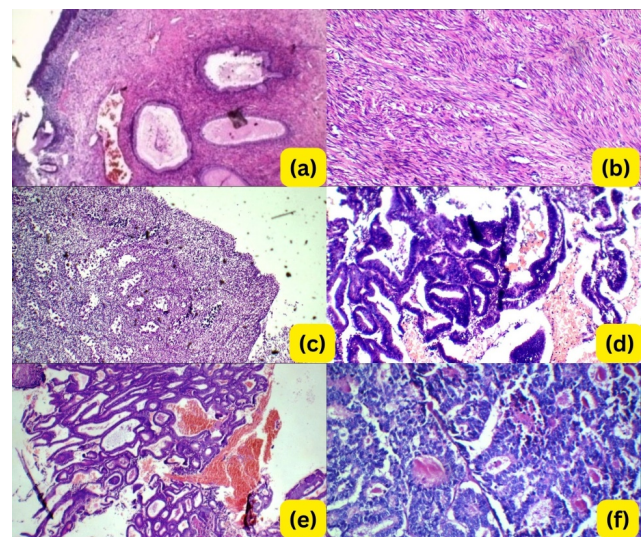


Figure 2: Histopathology showing: (a) Adenomyosis (H & E x 400); (b) Leiomyoma (H & E x 100); (c) Endometrial polyp (H & E x 100); (d) Endometrial hyperplasia without atypia (H & E x 400); (e) Atypical endometrial hyperplasia (H & E x 100); (f) Endometrial carcinoma (H & E x 400)

or menorrhagia were the symptoms of chronic endometritis (Table 3).

Discussion

Bleeding per vaginum that does not meet the requirements for regular menstrual bleeding is included in AUB. Numerous aetiologies, such as functional, organic, or pharmaceutical ones, may be to blame. The patient's age also has an impact on the etiology. A safe technique that aids in diagnosing endometrial disease is endometrial biopsy.

A comprehensive examination of the various patterns of endometrial biopsies was conducted, taking into account variables including age, the date of the last menstrual cycle, the length of the menstrual cycle, and the use of any medications. In the perimenopausal age group (41–50 years; 55.4%), females had the highest incidence of AUB. The women in this age range were in their climacteric, a time when the number of developed ovarian follicles and estradiol levels often decrease, leading to anovulatory cycles. According to research conducted by Khanam et al, Doraiswami et al, and Sharma et al. [3–5], the same age group was shown to be most affected. The post-menopausal age group had the lowest incidence of 20.0%, which may have been caused by early patient care and research, which also resulted in lower incidence in the older age groups.

Menorrhagia was found in 70% of the participants in the current investigation. In the age ranges of both perimenopausal and reproductive patients, this was the most often reported presenting ailment. The next frequently reported symptom was metrorrhagia. According to past research, menorrhagia was the most typical presentation among AUB patients [5–8].

The current investigation demonstrated that just one-third of AUB cases were caused by organic causes, with approximately two-thirds of cases resulting from functional aetiologies. This is similar to what Dwivedi et al. and Sharma et al. found. [7,8]

In 57.7% of the cases, the normal cyclical endometrium—which consists of proliferative phase endometrium (35.4%), secretory phase endometrium (19.2%), and disordered endometrium (3.1%)—was found. This result is similar to research by Vani et al. (56.27%) and Sharma et al. (55.1%). The most frequently seen histological pattern, according to Behera et al. and Mukhopadhyay et al., is the typical cyclical endometrium [7,9–11]. With the exception of

Table 3: Correlation between the bleeding pattern and histopathological diagnosis

Bleeding pattern	Histopathological diagnosis	No. of cases	%
Menorrhagia	Proliferative phase	33	36.3
	Secretory phase	22	24.1
	Menstrual endometrium	4	4.4
	Disordered endometrium	6	6.6
	Chronic non-specific endometritis	1	1.1
	Adenomyosis	2	2.2
	Leiomyoma	3	3.3
	Endometrial polyp	3	3.3
	Endometrial hyperplasia without atypia	14	15.3
	Atypical endometrial hyperplasia	1	1.1
	Endometrial carcinoma	2	2.2
	Total	91	100%
Metrorrhagia	Proliferative phase	4	20.0
	Secretory phase	2	10.0
	Disordered endometrium	2	10.0
	Granulomatous endometrium	1	5.0
	Chronic non-specific endometritis	2	10.0
	Adenomyosis	1	5.0
	Leiomyoma	3	15.0
	Arias-Stella reaction	1	5.0
	Endometrial hyperplasia without atypia	3	25.0
	Atypical endometrial hyperplasia	1	5.0
	Total	20	100%
Hypomenorrhea	Proliferative phase	2	50.0
	Secretory phase	1	25.0
	Leiomyoma	1	25.0
	Total	4	100%
Post-menopausal bleeding	Proliferative phase	7	46.7
	Atrophic endometrium	1	6.7
	Adenomyosis	1	6.7
	Leiomyoma	1	6.7
	Endometrial polyp	1	6.7
	Endometrial hyperplasia without atypia	2	13.4
	Atypical endometrial hyperplasia	2	13.4
	Total	15	100%
Total cases		130	

a study by Sajitha et al., where the secretory phase endometrium was the most frequently observed feature among the normal cyclical patterns, the proliferative phase endometrium was reported as the most common finding in most of the studies^[6]. Bleeding in the secretory phase is linked to ovulatory failure, while bleeding during the proliferative phase is caused by anovulatory cycles. One significant and distinctive aspect of our study was the finding of normal menstrual phase endometrium, which accounted for 3.07% of all the cases.

In the current study, 6.16% of the patients had disordered proliferative endometrium; patients in the 18–40 age range had the highest prevalence, closely followed by those in the over 50 age group. This result was similar to the previous Sharma et al. research^[7]. The incidence of disordered proliferative endometrium was found to be greater in findings by Doraiswami et al. and Chhatrasal et al. (20.5% and 19.5%, respectively)^[5,9]. Finding this pattern, which is the first stage of a spectrum of proliferative endometrial lesions, with stages of hyperplasia in between and endometrial carcinoma at the other end, aids in stopping the disease's progression. The age group of over 50 years old was the primary one in which atrophic endometrium was observed. Compared to earlier research, our study's atrophic pattern occurrence was significantly lower. According to the publication report by Doraiswami et al., the incidence is 2.4%^[5]. The bulk of the patients in this pattern's age group are over 50, with the highest occurrence of this pattern (11%) recorded in the Dwivedi et al. publication^[8]. Although the precise origin of bleeding in patients with atrophic endometrium is yet unknown, local hemostatic mechanisms are thought to be responsible. The surrounding thin-walled blood arteries are vulnerable due to the growing cystic glands.

Endometrial hyperplasia was shown to have the highest incidence among the organic lesions that cause AUB, accounting for 17.67% of all cases. 3.07% of the patients exhibited atypical hyperplasia, while 14.6% of the patients had hyperplasia without atypia. In those between the ages of 41 and 50, endometrial hyperplasia was found with the highest prevalence (52.17%). As in the majority of the prior investigations, this was the second most prevalent pattern in AUB as seen in the current investigation. Because these individuals were not recognized or looked into in the early phases of disordered proliferative endometrium, the frequency is higher.

Early and accurate detection of this pattern is crucial since endometrial hyperplasia is thought to be a precursor to endometrial cancer.

Pregnancy-related problems have been identified as a frequent cause of irregular uterine bleeding in a number of previous investigations conducted by Sharma et al., Vani et al., Chhatrasal et al., and Sharma et al., particularly in the reproductive age range^[1–7,7–14]. Therefore, information regarding the pregnancy test should always be recorded when assessing the endometrial biopsy of patients in this age group who present with AUB. Unlike the study conducted by previous authors^[9,14], endometrial biopsies performed for pregnancy-related problems were not included in this investigation.

It was observed that the third most frequent organic pathology causing AUB was endometrial polyps. All three age groups—reproductive, perimenopausal, and post-menopausal—saw an identical prevalence of polyps. According to the study by Doraiswami et al.'s, which included a majority of patients aged between 41 to 50, the highest prevalence of 11.2% was reported^[5]. According to the results of this investigation, the incidence of endometritis was 3.11%. Granulomatous endometritis was identified in one of the four cases, whereas chronic non-specific endometritis was found in the other three. Report by Doraiswami et al. revealed the highest incidence of endometritis, with 1 out of 17 cases classified as tuberculous endometritis^[4–6].

In cases of AUB, endometrial biopsy and its histological evaluation are mostly performed to rule out malignancy. The incidence of endometrial cancer was 1.54% in this study. In both the post-menopausal age group of females over 50 and the 41–50 age range, there was one instance each. According to reports by Samal et al., Sajitha et al., and Doraisami et al., there was a greater incidence of malignancy^[5,6,14]. Doraiswami in his publication documented eighteen occurrences of endometrial carcinoma, one of which was a malignant mixed Müllerian tumor. Eight cases of endometrial malignancy were reported by Sajitha^[5], of which seven were endometrial carcinoma and one was endometrial stromal sarcoma^[6]. Samal also reported 13 cases, of which 2 were classified as carcinosarcoma and 11 as endometrial adenocarcinoma^[14]. Despite the fact that histopathological remarks on the invasiveness and size of the tumor cannot be made, diagnosis of endometrial carcinoma can definitely be made.

Vanishing carcinoma is defined as endometrial biopsy-proven carcinoma that does not show the presence of tumor in the hysterectomy material that is obtained later. The prognosis is good in these situations, and adjuvant therapy is typically not required^[15].

Endometrial biopsy is often a simple outpatient procedure used to rule out any malignancy; however, the histological diagnosis may be challenging if there is bleeding or sparse endometrial tissue. Being a simple, safe and, of high diagnostic accuracy, endometrial biopsy carries a great significance in diagnosing the exact aetiology behind the presentation of AUB, the most common menstrual problem in females after puberty.

Conclusions

In the gynecology outpatient department, the most prevalent complaint made by patients is AUB. The frequency of cases presenting with AUB is also on the rise, which can be attributed to improved access and increased awareness of the healthcare facilities. AUB needs to be thoroughly and promptly evaluated in order to rule out any serious underlying disease that could be lethal, like endometrial cancer. Although it can be difficult to interpret endometrial biopsies, an accurate diagnosis can be achieved by comparing the patient's medical history with the radiological results. Females in the perimenopausal age group were reported to present with AUB more frequently than any other age group. Majority of the histopathological findings that were described showed typical cyclical endometrium, which included proliferative and secretory phases. The most prevalent pattern among the organic diseases was endometrial hyperplasia, with atypical hyperplasia accounting for a smaller proportion of cases. An additional common pathology was endometrial polyp. Thus, endometrial biopsy has shown to be a useful diagnostic technique and ought to be performed in all the patients presenting with AUB, regardless of their age group.

Disclosure

Conflict of Interest: Nil

Funding: Nil

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How to cite this article: Agrawal R, Jaiswal G, Ekram M, Agrawal M. Pattern of Bleeding with Histopathological Correlation in Patients Presenting with Abnormal Uterine Bleeding. *J Med Sci Health* 2025; 11(1):1-7

Date of submission: 21.07.2024

Date of review: 06.08.2024

Date of acceptance: 30.08.2024

Date of publication: 23.01.2025