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A Histopathological Study of Endometrial Biopsies in Abnormal Uterine Bleeding

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Abstract

Background: Abnormal uterine bleeding (AUB) is a very common gynecological problem for which histopathological examination of the endometrium is the gold standard to confirm the exact nature of the lesion and to rule out malignancy.

Methods: A prospective study was done in the Department of Pathology from October 2019 to October 2021 on two hundred endometrial biopsy specimens received from clinically diagnosed cases of AUB.

Result: AUB was most commonly seen in the age group of 41- 50 years. Most of the cases clinically presented with heavy menstrual bleeding. The most common histopathological finding was proliferative endometrium seen in 29% cases followed by secretory endometrium in 17% cases, endometrial carcinoma in 15% of cases and endometrial hyperplasia in 14.5% of cases.

Conclusion: Endometrial biopsy is a valuable tool for assessment of endometrial status in cases of AUB due to relative ease, accessibility of procedure and rapid availability of results.

Keywords: Abnormal uterine bleeding; Proliferative endometrium; Secretory endometrium; Carcinoma; Hyperplasia

Abbreviations: AUB: Abnormal Uterine Bleeding; AEH: Atypical Endometrial Hyperplasia; EIN: Endometrial Intraepithelial Neoplasia

Introduction

Menstrual disorders among women of all age groups continue to be a challenging proposition for clinicians to manage, the most important of them being abnormal uterine bleeding (AUB) [1]. The endometrium undergoes dynamic physiological and morphologic changes by the complex interplay of endogenous sex steroids and other systemic as well as iatrogenic factors and when this gets disturbed it. manifests as AUB. [2].

AUB is defined as a bleeding pattern that differs in frequency, duration, and amount from a pattern observed during a normal menstrual cycle or after menopause [3]. In India, the reported prevalence of AUB is around 17.9% [1]. The FIGO Working Group on Menstrual Disorders has classified the various causes for AUB into structural /organic causes and non-structural causes and represented as an acronym PALM- COEIN: polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified [4,5].

Clinical bleeding patterns are determined by the heaviness, duration of flow, regularity, and frequency [6]. The terminologies menorrhagia, metrorrhagia, menometrorrhagia and dysfunctional uterine bleeding are poorly defined and confusing. FIGO Menstrual disorders Working Group in 2011 proposed to abandon the terminology dysfunctional uterine bleeding and use the terms AUB and heavy menstrual bleeding [5].

The causes of AUB vary with age. In the reproductive age group, it is most commonly due to hormonal imbalance while in the perimenopausal and menopausal women AUB is generally due to hyperplasia and malignancies [7]. Significant mortality or morbidity can occur if endometrial hyperplasia is untreated with progression to malignancy [2]. Endometrial biopsy is the gold standard method for distinguishing normal endometrium from pathological endometrium. Endometrial biopsy, dilation and curettage (D&C), and hysteroscopy are the most common

endometrial sampling methods [8]. The D & C is the gold standard in diagnosing AUB, however over years it has been replaced by Pipelle's endometrial biopsy as it is a safe and simple outpatient diagnostic procedure. Evaluation of endometrial biopsies helps not only to identify the cause of AUB but also to provide an appropriate treatment thereby reducing the need for complications associated with hysterectomies [9]. The aim of this study is to determine the spectrum of endometrial pathologies in patients of different age groups presenting with AUB.

Materials and Methods

This was a descriptive study conducted in the Department of Pathology, GSL Medical College and General Hospital, Rajahmundry from October 2019 to October 2021.Clinical history was collected from the patients .The study included a total of two hundred endometrial biopsies obtained from patients presenting with abnormal uterine bleeding of all age groups.

Inclusion Criteria

Endometrial biopsies in patients presenting with AUB

Exclusion Criteria

a) Patients presenting with bleeding due to primary or secondary bleeding disorders,

b) AUB secondary to cervical and vaginal lesions.

c) Unsatisfactory samples (Only blood clots and fibrin; no endometrial gland /stroma)

Endometrial biopsy specimens were obtained by either Pipelle's endometrial biopsy or by dilatation and curettage. The samples received were fixed in10% formal saline. All the gross findings were recorded. Paraffin blocks were made from these biopsies after subjecting to standard histopathology processing. Tissue sections were made as per standard protocol and stained by Hematoxylin and Eosin (H&E) stain. The slides were examined by a pathologist. Microscopic findings and histopathological diagnosis were noted (Figure 1-3).

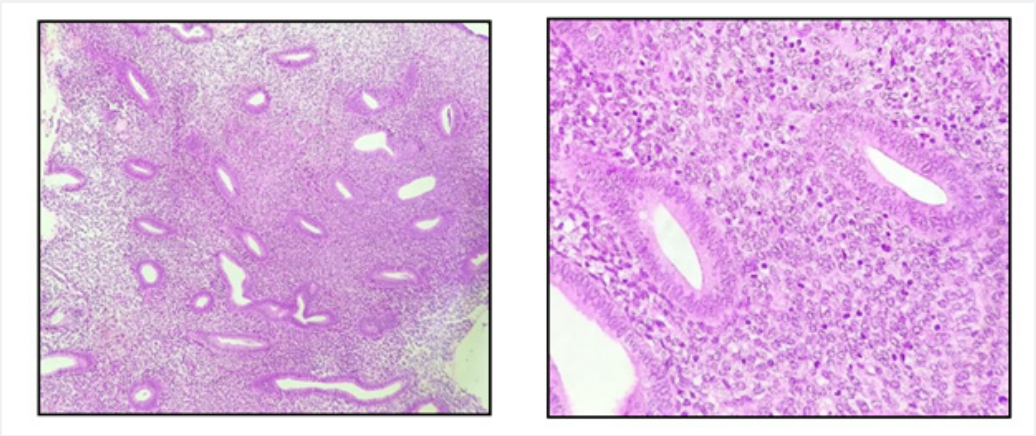

Figure 1: Proliferative endometrium:
Low power view(10X)showing evenly distributed tubular glands in compact stroma
High power view(40X) showing tubular glands lined by columnar cells with pseudostratification of nuclei

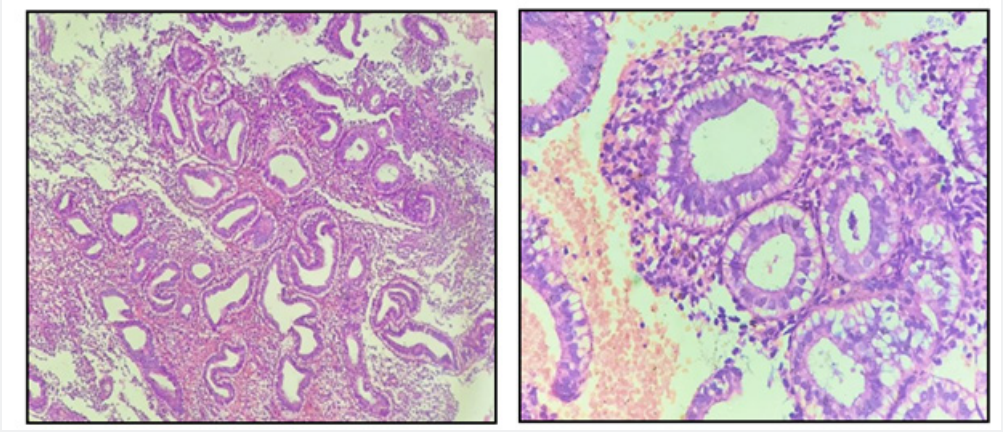

Figure 2: Secretory endometrium
Low power and high power view(10X,40X) showing tortous glands in edematous stroma

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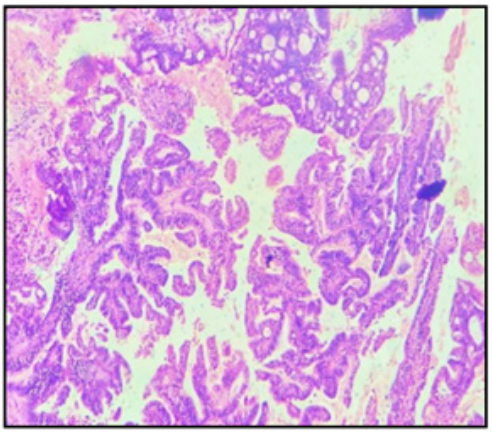

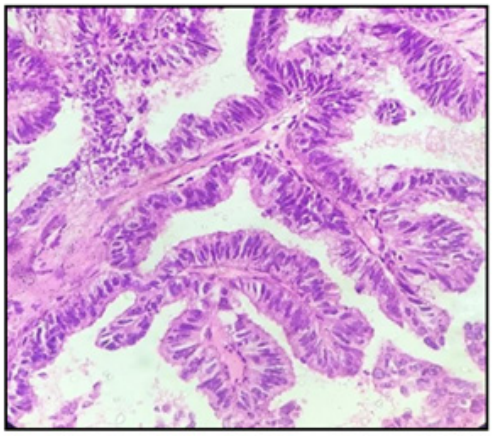

Figure 3: Well differentiated adenocarcinoma
Low power view(10X) showing tumour arranged in complex papillary and glandular patterns
High power view(40X) showing tumour in complex papillary pattern with nuclear pleomorphism and pseudo stratification.

Statistical Analysis

Statistical analysis was performed using MS excel 2010.

Result

The present study included patients aged 21 to 84 years. Majority of cases (36%) were seen in the age group of 41-50 years (Table 1). The incidence of AUB was found to be 89% in multiparous women, 5.5%in nulliparous women and 5.5% in grand multiparous women. The presenting symptoms in this study were heavy menstrual bleeding found in 39.5 % cases, postmenopausal bleeding in 29.5 % cases, heavy and prolonged menstrual bleeding in 16 % cases, intermenstrual bleeding in 6 % cases, frequent menstrual bleeding in 5% cases and infrequent menstrual bleeding in 4% cases (Table 2).

Table 1: Distribution of Cases According to Age Group.

Age Group(years)	Number of Cases	Percentage (%)
21-30	15	7.50%
31-40	56	28.00%
41-50	72	36.00%
51-60	33	16.50%
61-70	17	8.50%
>70	7	3.50%
Total	200	100%

Table 2: Distribution of Bleeding Patterns.

Bleeding Pattern	Number	Percentage(%)
Heavy menstrual bleeding (HMB)	79	39.50%
Heavy and prolonged menstrual bleeding (HPMB)	32	16.00%
Intermenstrual bleeding (IMB)	12	6.00%
Infrequent bleeding (InMB)	8	4.00%
Frequent menstrual bleeding (FMB)	10	5.00%
Postmenopausal bleeding (PMB)	59	29.50%
Total	200	100%

Proliferative phase endometrium was the most common etiology in 29% cases followed by secretory phase endometrium in 17% cases, endometrial carcinoma in 15% cases, endometrial hyperplasia in 14.5% cases, atrophic endometrium in 8% cases, disordered proliferative endometrium in 4.5% cases, endometrial polyp in 4% cases, non-specific/chronic endometritis in 3.5% cases, "Progesterone Pill" induced endometrium in 3.5% cases, shedding endometrium in 0.5% cases and products of conception in remaining 0.5% cases.

Normal endometrial pattern comprising of proliferative phase endometrium, secretory phase endometrium and shedding endometrium was predominantly found in 31-40and 41-50 year age group while endometrial carcinoma and endometrial hyperplasia were predominantly found in 51-60 year age group. Out of two hundred samples, one hundred and forty-one samples belonged to the pre-menopausal age group with proliferative endometrium and secretory endometrium being the most common etiology. Whereas in the post-menopausal age, endometrial carcinoma was the most common etiology followed by endometrial hyperplasia and atrophic endometrium (Table 3).

Endometrial hyperplasia constitutes 14.5% of cases, out of which 58.6% cases were hyperplasia without atypia and 41.4% cases were AEH/EIN. Among 30 endometrial carcinomas, 29 (96.7%) were of endometrioid type and 1 (3.3%) case of serous sub type.

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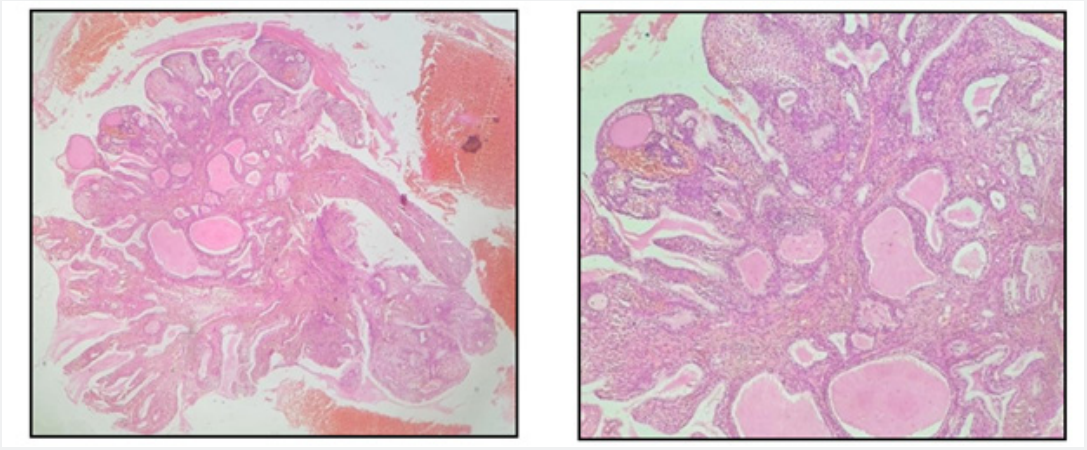

Figure 4: Endometrial polyp
Low power view(10X) showing a polypoid mass made up of benign endometrial glands scattered in fibrovascular stroma.
High power view(40X) showing glands of varying sizes scattered in fibrovascular stroma

Table 3: Histopathological Findings Among Various Age Groups.

Histological Pattern	Age groups						Total
	21-30	31-40	41-50	51-60	61-70	> 70	
Proliferative	07 (12.1%)	25 (43.1%)	26 (44.8%)	--	--	--	58 (100%)
Secretory	4 (11.7%)	16 (47.1%)	14 (41.2%)	--	--	--	34 (100%)
Shedding	--	--	1 (100%)	--	--	--	1 (100%)
Disordered proliferative	--	4 (44.4%)	5 (55.6%)		--	--	9 (100%)
"Progesterone Pill" induced	--	2 (28.5%)	5 (71.5%)	--	--	--	7 (100%)
Endometrial polyp	1 (12.5%)	2 (25%)	2 (25%)	2 (25%)	1 (12.5%)	--	8 (100%)
Atrophy	--	--	3(18.8%)	9(56.2%)	4(25%)	--	16(100%)
Endometritis	2 (28.6%)	--	3 (42.8%)	--	2 (28.6%)	--	07 (100%)
Hyperplasia	--	06 (20.7%)	07 (24.1%)	11 (38%)	04 (13.8%)	01 (3.4%)	29 (100%)
Endometrial carcinoma	1 (3.3%)	--	6 (20%)	11 (36.7%)	6 (20%)	6 (20%)	30 (100%)
Products of conception	--	1 (100%)	--	--	--	--	1 (100%)

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Discussion

AUB exhibits different presentations and varied causes leading to considerable social and physical morbidity in all societies, thus demanding appropriate evaluation and management [10]. Endometrial evaluation is performed to assess the hormonal influence of the endometrium and also to diagnose premalignant and malignant conditions [11].

The most common age group presenting with AUB in the present study is 41-50 years (36 %) followed by 31-40 years which is in concordance with the studies done by Jairajpuri ZS et al. [12] (35.89%) and Khurram N et al. [13] (37%). An increased number of cases in this age group, which is mostly the perimenopausal age, could be due to the fact that as women reach menopause, there is a decrease in the number of ovarian follicles along with increased resistance to gonadotrophic stimulation resulting in a low level of oestrogen which is an essential requirement for growth and maintenance of normal endometrium. [14]. The highest incidence of AUB is seen in multiparous women in the present study (89%) which is in concordance with the study done by Golecha N et al. [15] (82%)

Heavy menstrual bleeding (39.5%) is the most common type of bleeding pattern noted which correlates with the study done by Singh P et al. [16] (40%). The next common bleeding pattern observed is postmenopausal bleeding which correlates with the study done by Bindroo S et al. [17]. Histopathological examination of the endometrium showed patterns ranging from physiological to pathological lesions of the endometrium. The most predominant histopathological finding is the normal cyclical pattern (46.5%) which correlates with the studies done by Singh P et al. [13] Khurram N et al. [16] and Rachamallu L et al. [18]. The bleeding in the proliferative phase may be due to anovulatory cycles and bleeding in the secretory phase may be due to ovulatory dysfunctional uterine bleeding.

The high proportion of endometrial carcinoma (15%) in our study compared to other studies [19-22] is presumably because our hospital is a teaching hospital and a referral centre for oncology cases. Most of the endometrial hyperplasia cases presented in the postmenopausal age group. Endometrial hyperplasia is a precursor for endometrial cancer with an overall risk of progression to cancer being 5-10%. Hence, its identification is important in cases presenting with AUB. Atrophic endometrium constituted 8% of the total number of cases with most cases presenting in the postmenopausal age group similar to the study done by Bhatta S et al. [20]. Benign endometrial polyps constituted 4 % of the total number of cases in the present study which correlates with the study done by Khan et al. [11] Prolonged oestrogen stimulation leads to hyperplasia of basal endometrial layer resulting in polyp formation.

Chronic/non-specific endometritis was diagnosed in 3.5% of cases which correlates with the study done by Vaidya et al. [23] Endometritis is a contributing factor for AUB. Subepithelial capillary plexus and surface epithelium are rendered fragile by inflammatory mediators leading to breaks and micro erosions resulting in uterine bleeding.

Conclusion

AUB is one of the most common conditions affecting women of all ages. It is caused by various endometrial pathologies that can directly and indirectly lead to clinical problems causing impairment of physical and mental health of women. Endometrial sampling through both office endometrial biopsy and endometrial curettage after dilatation are equally useful in obtaining endometrial samples.

Histopathological evaluation of endometrial biopsies plays a crucial role in the evaluation of and diagnosis of various gynaecological conditions. AUB cases on assessment by histopathological examination in this study revealed varying patterns: endometrial hyperplasia, atrophic endometrium and endometrial carcinoma which can overtly be considered as the aetiology in many cases. However, in the remaining cases, the endometrial histology was within normal limits and was either in proliferative phase or in secretory phase indicating the possible existence of an eluding aetiology.

In postmenopausal women, endometrial carcinoma is the commonest cause for AUB. However, in this study, this ominous disease was detected in equal proportions to endometrial hyperplasia in women of reproductive age also and hence requires to be kept in mind while assessing AUB cases in this age group.

Hence, accurate identification of the causative factor of AUB by histopathological evaluation of endometrial biopsy samples still remains the gold standard for the diagnosis of endometrial pathology.

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