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Original Research Article

Histopathological Spectrum of Endometrium in Perimenopausal Women with Abnormal Uterine Bleeding

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Abstract:

Background: In perimenopausal women, abnormal uterine bleeding (AUB) is a common cause of affecting the quality of life in an otherwise healthy woman. AUB could be only clinical symptom of an underlying pathology such as carcinoma or premalignant endometrial hyperplasia. Proper therapy is only possible when underlying cause of AUB is accurately diagnosed. Endometrial biopsy has long been considered to be gold standard for diagnosis of AUB.

The objective of the study was to analyze different histopathological lesions of the endometrium responsible for AUB in perimenopausal women.

Methods: A two-year prospective study was conducted in a tertiary care hospital of Punjab, which included 264 cases of clinically diagnosed AUB in perimenopausal age group. Endometrial tissue collected by sampling procedures such as endometrial biopsy, dilatation and curettage (D &C), and fractional curettage was evaluated b histopathological examination and followed by clinical correlation.

Results: The most common clinical presentation was represented by menorrhagia (62%), followed by metrorrhagia (27%) and then polymenorrhoea (06%). Out of 264 cases of AUB, the commonest functional lesion observed in the study was secretory endometrium (35.6%), followed by proliferative endometrium (27.2%). Most common organic lesion responsible for AUB was endometrial polyp (6.4%), followed by chronic endometritis (4.5%). Endometrial hyperplasia was seen in 18 cases. Endometrial carcinoma was detected IN 06 cases in the study.

Conclusion: Our study revealed that atypical uterine bleeding in perimenopausal women is most commonly dysfunctional in origin. In addition, a significant number of cases of AUB have underlying organic lesions like hyperplasia and malignancy and thereby highlighting the need of endometrial histopathological workup in cases of AUB in perimenopausal women.

Keywords: Perimenopausal women, Atypical, Endometrium, Disordered proliferative, Menorrhagia.

Introduction

Perimenopause is an ill-defined period around the final years of reproductive life of women [1,2]. It starts with the first onset of menstrual irregularity and ends after First year of amenorrhea has occurred, thereby defining the final menstrual period (FMP)[3,4]. This is associated with profound hormonal changes, which in turn leads to concomitant symptoms.

Perimenopausal symptoms are highly prevalent with abnormal uterine bleeding being one of the major gynaeclolgical complaint; accounting for approximately 70% of gynaecological outpatient visits to gynaecological clinics in perimenopausal and postmenopausal women.1 The mosaic of appearance of perimenopausal / menopausal symptoms especially Abnormal uterine bleeding has become increasingly clear thanks to the conduct of various / several cohort studies. Abnormal uterine bleeding (AUB) is defined as menstrual bleeding which is abnormal in frequency, quantity, duration or regularity [3,4]. It can present as menorrhagia, metrorrahagia, polymenorrhoea and intermenstrual bleeding. Abnormal uterine bleeding (AUB) maybe an expression of hormonal milieu or it could be the clinical presentation of benign or malignant lesions of female genital tract in perimenopausal women.

AUB is a common reason for women of all ages to consult their gynaecologist. Endometrial biopsy or curettage could be safe and effective diagnostic

step in evaluation of AUB after ruling out medical causes. Based on the current recommendation of the American College of Obstetricians and Gynaecologists endometrial tissue sampling should be a first line procedure in the management of AUB in women over 45 years.

AUB affects nearly more than 50% of perimenopausal women [2]. Endometrial sampling could be effectively used as the first diagnostic step in AUB, although at times, its interpretation could be quite challenging to the practicing pathologists. The histopathology report contributes notably in the clinical management of AUB in perimenopausal women.

This present study was done to evaluate histopathology of endometrial causes of AUB, in perimenopausal age group and to document the spectrum of pathologies and their frequencies. Our hospital is a tertiary care centre in Northern India and our findings reflect the range of possible causes of AUB in this region.

We studied variation in the endometrial pathologies in perimenopausal age group. The main objective of our study is to focus on physiological (hormonal) changes associated with menstrual transition and also to find out frequencies of different organic lesions responsible for AUM in perimenopausal women.

Material and Methods

This prospective study was done on 264 patients in the perimenopausal age group who present with AUB ad underwent endometrial sampling from November 2021 to November 2023 in a tertiary care centre. Relevant and necessary data on age and clinical symptoms, duration of abnormal bleeding and menstrual history, HRT, and gynaecological examinations were obtained from accompanying laboratory request forms and Patient records.

Various sampling procedures such as endometrial biopsy, fractional curettage, and hysterectomy specimens were accepted as source of endometrial tissue. For endometrial biopsy, the pipelle or dilatation and curettage methods are minimally invasive methods and in certain case curettage itself can be therapeutic. The specimens were fixed in 10% formalin, paraffin blocks of the tissue were prepared and sections cut and stained with hematoxylin and eosin stain and examined under light microscope by the pathologist.

All the patients in this study were in the age group of 40-55 yrs. Cases having Pregnancy related bleeding were excluded from this study. Relevant and necessary data on age and clinical symptoms were taken from the accompanying laboratory request forms and patient records.

Results

A total of 264 endometrial biopsies from the patients with the clinical diagnosis of atypical uterine bleeding, were analyzed in the present study. All the patients were in the age group of 40-55yrs.

Data on the clinical presentation was retrieved from Laboratory forms. Out of 264 cases, the most common clinical presentation was menorrhagia (42.4) followed by metrorrhagia, polymenorrhoea and continuous bleeding. Most common clinical presentation was Menorrhagia (62%), followed by metrorrhagia (27%), polymenorrhoea (6%) and continuous bleeding (5%).

Table 1: Histopathological distribution of cases of AUB in perimenopausal women according to FIGO classification

S. No.	FIGO Classification (PALM-COEIN) for AUB	Lesion	No. of patients	Percentage
1	AUB-E	Proliferative	72	27.2%
2	AUB-E	Secretory	94	35.6%
3	AUB-E	Menstrual	05	1.8%
4	AUB-I	Effects of exogenous Hormone therapy	16	6.06%
5	AUB-E	Disordered Proliferative Endometrium	32	12.1%
6	AUB-E	Chronic Endometritis	04	1.5%
7	AUB-P	Endometrial polyp	17	6.4%
8	AUB-M	Simple hyperplasia without atypia	12	4.5%
9	AUB-M	Hyperplasia with atypia	06	2.2%
10	AUB-M	Malignancy	06	2.2%
		Total	264	100%

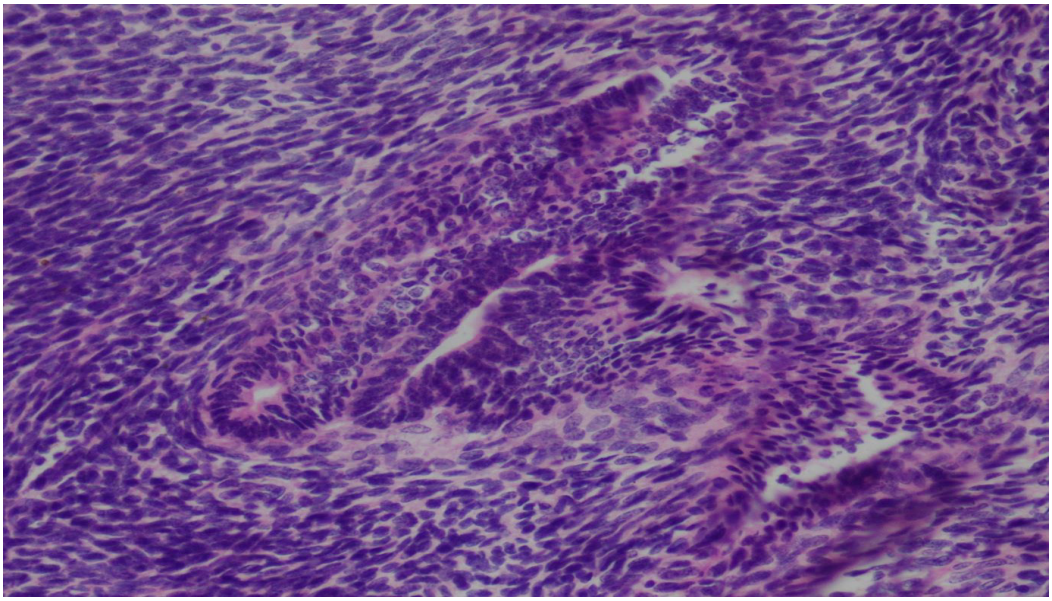

Figure 1: Microscopic examination showing proliferative endometrium (40x)

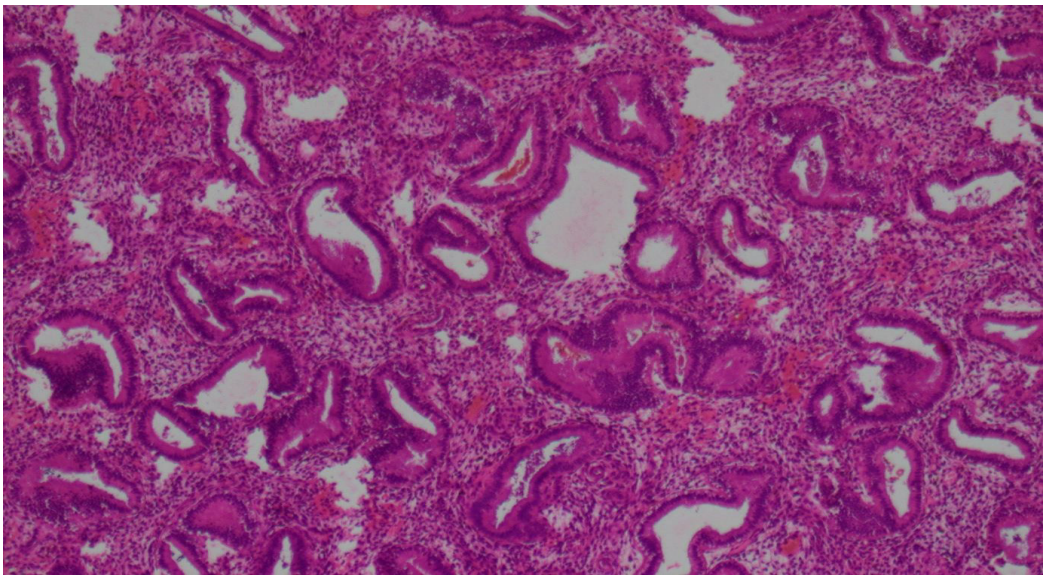

Figure 2: Microscopic examination showing secretory endometrium (40x)

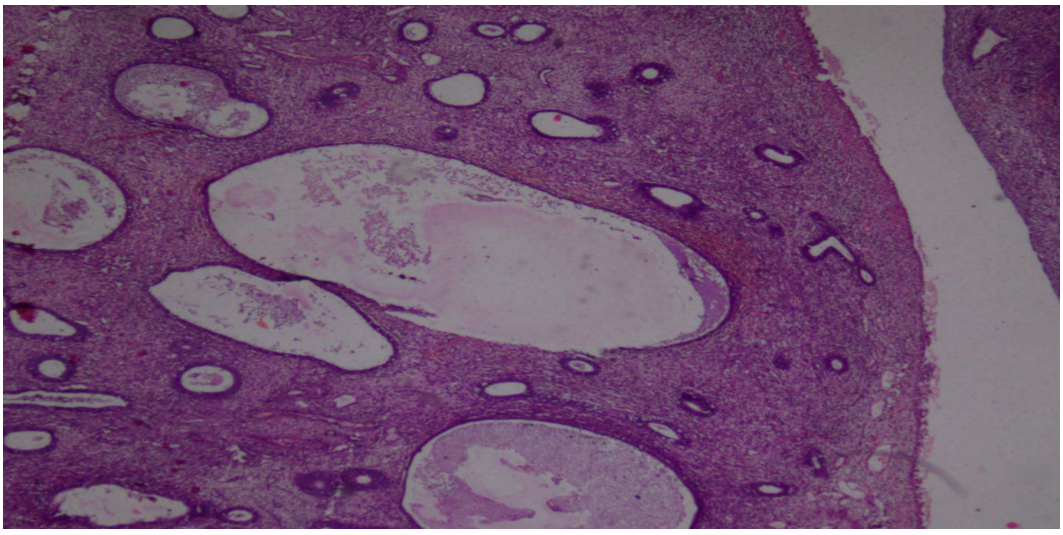

Figure 3: Microscopic examination showing Disordered Proliferative endometrium (10x)

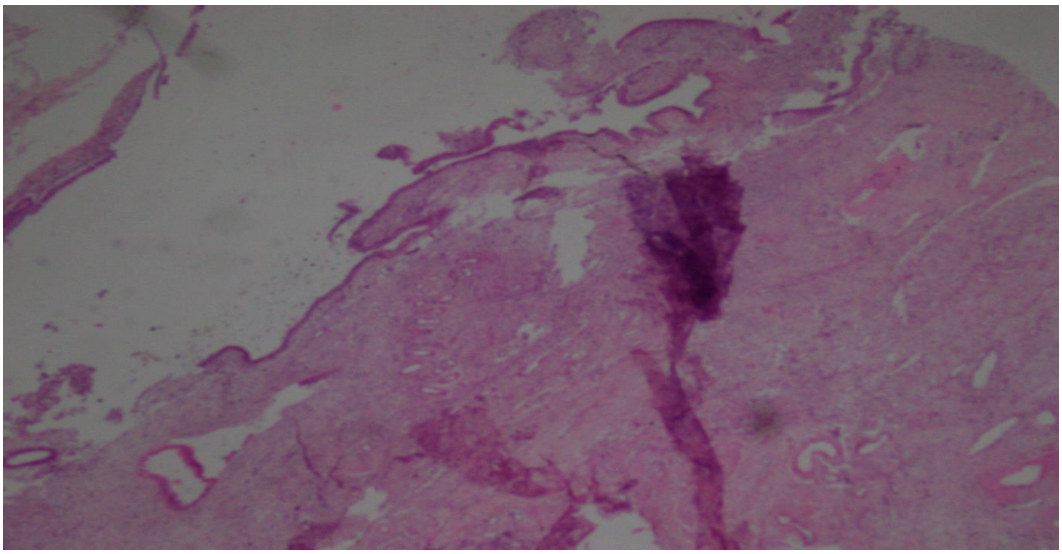

Figure 4: Microscopy showing endometrial polyp (10x)

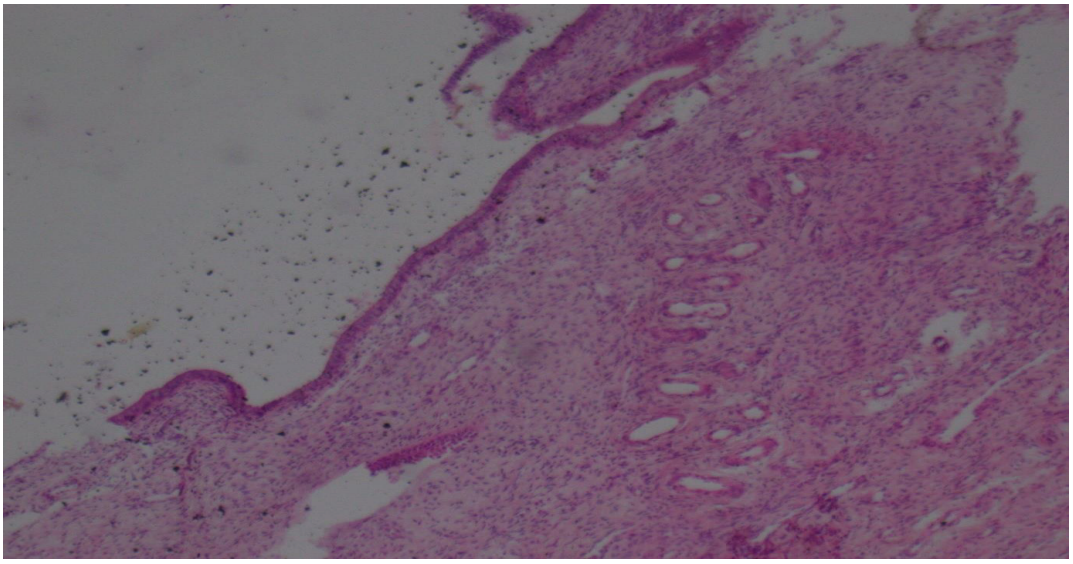

Figure 5: Microscopy showing Endometrial polyp (40x)

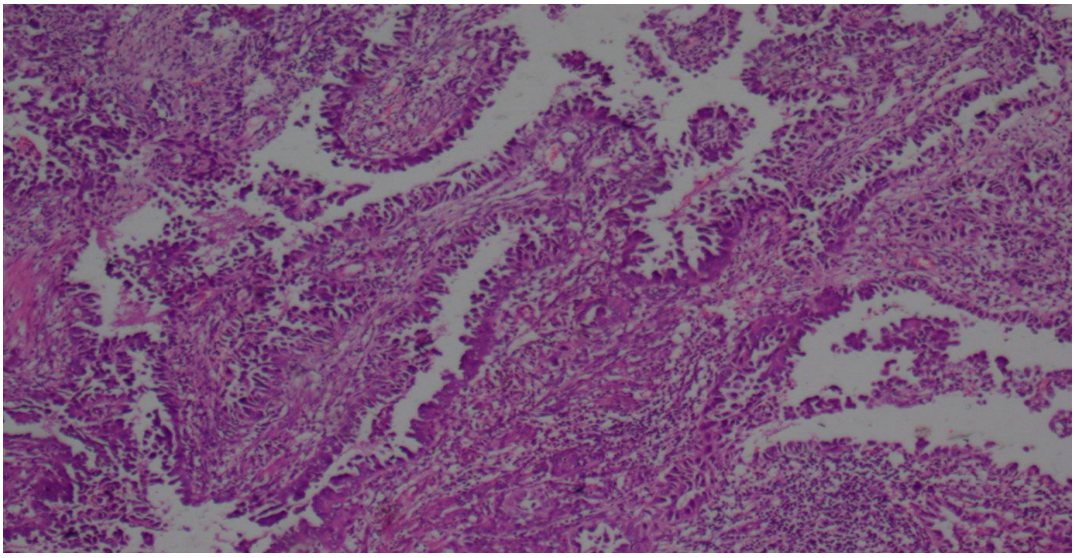

Figure 6: Microscopic examination showing endometrial carcinoma (40x)

The International Federation of Gynaecology and Obstetrics introduced a new classification system PALM-COEIN (polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic and not yet classified. This classification has been approved as a FIGO Classification system for AUB in order to homogenize terminology.

The PALM-COEIN classification system was developed to facilitate clinical care, research and communication among clinicians, investigators and even patients. Majority of the analyzed endometrial samples were reported to have functional causes of AUB (Table 1). Out of normal cyclical patterns (Proliferative, secretory and menstrual), secretory endometrium was reported in 94 Cases (35.6%), followed by proliferative type in 72cases (27.7%). Disordered proliferative endometrium was seen in 32 Samples (12.1%). Disordered proliferative endometrium was common cause of AUB, reported in 32 cases (12.2%). Among the endometrial pathologies, the hyperplasias constituted 6.8% % of all pathologies. In the entire study population, hyperplasias and malignancies collectively comprised (24) 9.09%%.

Discussion

Perimenopause or menopausal transition represents a period of time during changing hormonal levels manifest in varying symptoms in women who are progressing towards their final menstrual period (FMP). Duration of menopause is variable, the median of which is four years. Perimenopause has two stages: the early transition and the late transition, and are linked to specific hormonal events, which in turn are linked to symptoms.

For women in menstrual transition, the PALM-COEIN classification of AUB applies and utilized to establish a differential diagnosis of bleeding and to guide evaluation and management. [6,7]

Bleeding patterns among perimenopausal women vary, making it very difficult to distinguish between “normal” and “abnormal”. During the perimenopausal phase, women are more likely to experience an increased number of days of bleeding, with 77% reporting at least 3 episodes of 10+ days of bleeding. [5] Abnormal uterine bleeding has a noticeable impact on the physical as well as mental health and quality of life.

Abnormal uterine bleeding in perimenopausal women presents a tough challenge to the clinician, as physiological hormonal changes may mimic, or mask pathological conditions/diagnoses. Endometrial tissue sampling is the gold standard for a definitive diagnosis and also to differentiate endometrial hyperplasia from invasive carcinomas. [8] Analysis of endometrial tissue can be a diagnostic challenge to pathologists because of dynamic nature of endometrium which shows variable and overlapping histological findings depending upon age, phase of menstrual cycle and any specific pathology.

Our study attempts to analyze atypical uterine bleeding among women in the age group 40-55 yrs. The spectrum of causes of AUB in our study is wide and variable and is more common in perimenopausal women due to changes in hormonal milieu. Aberrations in ovarian follicle maturation, ovulation, or corpus luteum formation due to abnormalities of the hypothalamic-pituitary-ovarian axis; hence causing the hormonal imbalance and resulting in AUB.

In our study, a significant proportion of cases (64.7%) are due to physiological cyclical endometrium (secretory, proliferative or menstrual). Most common finding was secretory endometrium. In perimenopausal women during cyclical phase, AUB is usually due to anovulatory cycles. Many endocrine disorders like hypothyroidism, thyrotoxicosis, and diabetes can also cause abnormalities of hypothalamic- pituitary- ovarian axis, leading to ovulatory dysfunction which causes AUB [8].

Disordered proliferative endometrium (DPE) was the second most commonly found pathology. Chronis anovulation in perimenopausal women leads to relative increase in estrogen levels in comparison to progesterone levels as there is no corpus luteum formation. This unopposed estrogen stimulation leads to prolonged proliferative phase and the subsequent endometrium is prone to shedding thus resulting in irregular, painless bleeding [9]. Chronic non-specific endometritis is third most common endometrial pathology in our study (6.4%), followed by benign endometrial polyp (4.5%). Many previous studies suggested association of Chronic endometritis with AUB [10,11,12,13]. Excessive and unopposed estrogen is responsible for formation of endometrial polyp and is a common cause of AUB in perimenopausal women [14,15].

In our study, the endometrial hyperplasias and malignancy together constituted 9.09% of the total cases and is similar to various other reported studies [16,17,18]. In peri-menopausal women, AUB is the most common clinical presentation and primary risk factor is exposure to long term unopposed estrogen [19,20]. It is therefore recommended that all the peri-menopausal women with AUB should undergo endometrial biopsy examination for early detection of and treatment of premalignant and malignant conditions.

Conclusion

The histomorphological spectrum of causes of AUB in perimenopausal women is very wide and highly variable ranging from normal physiological

changes to endometrial hyperplasias and malignancies. Atypical uterine bleeding in perimenopausal women is most commonly dysfunction in origin. In addition to this, a significant number show underlying pathological lesions. Thus, significance of histopathological examination of endometrial biopsies in perimenopausal women with AUB cannot be overemphasized in the timely diagnosis of paraneoplastic and malignant conditions and to guide further management.

In conclusion, histopathological report of endometrial sampling is a crucial diagnostic modality used in the management of perimenopausal women with AUB and in improving quality of life.

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