

Pattern of Abnormal Uterine Bleeding and Spectrum of Endometrial Pathology Among Perimenopausal Women

Uterine Bleeding
and Spectrum of
Endometrial
Pathology Among
Perimenopausal

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ABSTRACT

Objective: To determine the clinical pattern and endometrial pathology of abnormal uterine bleeding among perimenopausal women.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Hamdard University Hospital, Karachi from July 2019 to December 2020.

Materials and Methods: 105 perimenopausal women between 40-50 years of age who presented with abnormal uterine bleeding (AUB), and underwent dilatation and curettage for endometrial sampling were enrolled in this study after informed consent. A detailed clinical assessment of patients performed in the outpatient department; included history and clinical examination. Patients' medical records were evaluated for parameters including age, parity, clinical presentation and ultrasound findings. Histopathology evaluation was done by histopathologists.

Results: 57.1% participants were of age between 40-45 years, and 58.1% women were Multiparous. Pattern of uterine bleeding in perimenopausal women about 66.7%, women had frequent menstrual cycle and prolonged duration of bleeding 78.1%, history of heavy bleeding with clots, in 22.9%, 5.7% and 14.3% women had complaint of inter-menstrual, premenstrual and breakthrough bleeding respectively. 59% patients had more than 18 mm endometrial thickness. Proliferative endometrium was the most prevalent diagnosis 39% followed by secretory endometrium 31.4%, hyperplasia without atypia 11.4%, polyp 10.5%, endometritis 2.9%, hyperplasia with atypia 2.9% and 1.9% patients diagnosed with cancer. Factors like parity, pattern of bleeding, US findings and endometrial thickness had significant impact on different types of histopathology (P-value<0.05).

Conclusion: This study emphasises the need of endometrial sampling as an important diagnostic tool that would help in individualising the management of abnormal uterine bleeding with a view to reduce unnecessary benign hysterectomy procedures.

Key Words: Abnormal uterine bleeding (AUB), Perimenopausal women, Ultrasound (U/S), endometrial histopathology, Dilatation and curettage.

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INTRODUCTION

The World Health Organization (WHO) defines the Perimenopause period as the 2–8 years period preceding menopause and one year following the last menstrual period.

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Following an increase in follicle stimulating hormone (FSH), the hormonal level (estrogen) is displaying an overall increase, which is distinguished by insufficiency of progesterone secretion¹. Abnormal uterine bleeding (AUB) is defined as any variation from the normal menstrual cycle, including alterations in its regularity, frequency, heaviness of flow, duration of flow and the amount of blood loss. It is a very common gynaecological condition and one third of patients attending gynaecology OPD with this complaint.² AUB is an umbrella term which includes heavy menstrual bleeding, intermenstrual bleeding and ovulatory disorders which has replaced previously used inconsistent and confusing terminologies like menorrhagia, metrorrhagia and dysfunctional uterine bleeding³⁻⁴. International prevalence of AUB among women aged 15 to 49 years is believed to be between 3% and 30%, with a higher rate of occurrence around menarche and Perimenopause, and when irregular and intermenstrual bleeding are taken into consideration, the prevalence climbs to 35 percent or higher⁵. Atrophic

endometrium, chronic endometritis, endometrial polyp, hyperplasia, and cancer are among the AUB pathologies that can be studied by histological evaluation of endometrial specimens obtained after dilatation and curettage in AUB cases⁶. There may be several structural or functional aetiologies for the AUB. The “International Federation of Gynaecology and Obstetrics” working group on menstrual disorders has developed a classification system (PALM–COEIN) for causes of the AUB. There are 9 main categories, which are arranged according to the acronym PALM–COEIN “polyp, adenomyosis, leiomyoma, malignancy, and hyperplasia – coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified”. PALM side of the classification refers to structural causes that may be evaluated by imaging techniques and/or histopathology and the COEIN side by investigating the underlying medical disturbances⁷. Clinical bleeding patterns are determined by the heaviness, duration of flow, regularity, and frequency. The causes of AUB can either be structural (PALM) or non-structural (COEIN)⁸.

MATERIALS AND METHODS

A cross sectional study was conducted in Hamdard University Hospital, Karachi from July 2019 to December 2020. This study was approved by ethics review committee of department of Obstetrics and Gynaecology. A Non-probability consecutive sampling technique was used. Sample size was obtained by using “Open Epi” sample size calculator taking statistics of Endometrial polyp in perimenopausal patients with AUB 10.4%⁴, at margin of error 6% and confidence interval 95%. One hundred and five (n=105) perimenopausal women between 40-50 years of age who were presented with AUB which was defined as abnormal pattern of bleeding⁴ in term of, volume of bleeding (heavy / normal/ light), regularity (Irregular/ regular/ absent), frequency (frequent/normal/ infrequent), duration (prolonged/ normal/shortened) and other such as “inter-menstrual, pre/post menstrual, breakthrough”. All the women who were eligible on the basis of selection criteria enrolled. All the patients underwent dilatation and curettage (D & C) for endometrial sampling. Informed consents were also obtained prior to the procedure from all the participation. Patients below 40 years of age, postmenopausal women and women with other causes of abnormal uterine bleeding, coagulation disorders (thrombocytopenia, von willebrand’s disease), Hypothyroidism, Liver diseases and those on Hormone therapy, and inadequate endometrial sample were excluded from the study. A detailed clinical assessment of patients performed in the outpatient department included history and gynaecological examination. Assessment of blood loss was done by passage of blood clots and number of pads used per day. Patients’

medical records were reviewed to collect parameters including age, parity and clinical presentation. Ultrasound pelvis was done for the evaluation of endometrial thickness and for other structural causes of AUB. Endometrium was considered thickened or hyperplastic when endometrial thickness was ≥ 12 mm. Endometrial biopsies were performed in all the women and specimen saved in formalin. Microscopic evaluation was done by histopathologists. The spectrum of endometrial histopathology and structural causes as per the PALM component of FIGO classification system was studied.

Data was entered and analysed into SPSS version 22. Study variables like age, parity, pattern of bleeding, ultrasound findings and histopathology diagnosis were taken as a consideration. They were presented as frequency and percentages. Stratification for histopathology diagnosis was done with respect to all associated factors like parity, pattern of bleeding and ultrasound findings. Chi-square test was use for comparison and find out the association between study variables. Significance level kept 0.05.

RESULTS

In this study a total of 105 perimenopausal women were studied. Pattern of abnormal uterine bleeding and endometrial pathological spectrums were evaluated. The table 1 shows distribution of baseline characteristics and evaluation of the pattern of uterine bleeding. Majority 60(57.1%) of the participants were having age between 40-45 years with more than half 61(58.1%) of the women were Multiparous, 35(33.3%) women were grand Multiparous. Evaluation of the pattern of uterine bleeding in perimenopausal women revealed that 70(66.7%) women had frequent, 27(25.7%) had normal and only 8(7.6%) had history of infrequent menstrual cycle. Prolonged duration of bleeding was found in 70(66.7%) women, 31(29.5%) had normal and only 4(3.8%) women had shortened duration.82(78.1%) women had history of heavy bleeding with clots and 40(38.1%) women had irregular period.

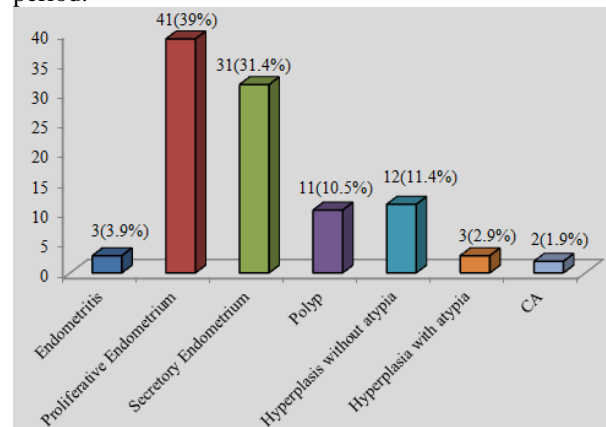


Figure No.1: Histopathological Diagnosis

Figure 1, presented the histopathology diagnosis distribution, Proliferative endometrium was observed among 39% of the perimenopausal women followed by secretory endometrium 31.4%, hyperplasia without atypia 11.4%, polyp 10.5%, endometritis 2.9%, hyperplasia diagnosed with atypia 2.9 and patients diagnosed with cancer 1.9%. We found that malignancy was least prevalent diagnosis.

Out of 105 study participants, 24(22.9%), 6(5.7%) and 15(14.3%) women had complaint of inter-menstrual, premenstrual and breakthrough bleeding respectively. Ultrasound findings showed that 18(17.1%) patients had adenomyosis, 16(15.2%) had fibroid, and polyp detect in 7(6.7%) patients. Among these women endometrial thickness was also assessed on Ultrasound findings showed that 62(59%) women had endometrial thickness more than 18 mm.

Table No.1: Patient’s Baseline characteristics and Pattern of bleeding

Patient’s Characteristics		n (%)
Age groups	40-45 years	60 (57.1%)
	46-50 years	45 (42.9%)
Parity	Nulliparous	9 (8.6%)
	Multipara 1-4	61 (58.1%)
	Grand multipara >4	35 (33.3%)
Characteristics of menstrual cycle		
Frequency	Frequent (<24 days)	70 (66.7%)
	Normal (24-38 days)	27 (25.7%)
	Infrequent(>38 days)	8 (7.6%)
Duration	Prolonged >8 days	70 (66.7%)
	Normal 4-8 days	31 (29.5%)
	Shortened <4 days	4 (3.8%)
Volume	Normal	23 (21.9%)
	Heavy with clots	82 (78.1%)
Regularity	Regular (2-20 days)	65 (61.9%)
	Irregular (>20 days)	40 (38.1%)
Inter-menstrual bleeding / spotting		24 (22.9%)
Premenstrual bleeding		6 (5.7%)
Breakthrough bleeding		15 (14.3%)
Endometrial thickness on ultrasound	Less than 18mm	43 (41%)
	18mm or more	62 (59%)
Ultrasound findings	Adenomyosis	18 (17.1%)
	Fibroid	16 (15.2%)
	Polyp	7 (6.7%)
	None	64(61%)

Comparisons of all histopathology diagnosis were done with the associated factors such as age of patients, parity, patterns of bleeding, ultrasound findings and endometrial thickness. Endometritis showed significant association with the duration of menstrual cycle (P= 0.019), Premenstrual bleeding (P= 0.037), and endometrial thickness (P= 0.035). Proliferative Endometrium showed significant association with the frequency of menstrual cycle (P= 0.000), Intermenstrual bleeding/spotting (P= 0.002), Postmenstrual bleeding (P= 0.047), and Ultrasound findings (P= 0.008). Secretory Endometrium showed significant association with the Parity (P= 0.000), Regularity of menstrual cycle (P= 0.048), Duration of

menstrual cycle (P= 0.009), Intermenstrual bleeding/spotting (P= 0.005), Breakthrough bleeding (P= 0.033), and Ultrasound findings (P= 0.000), and endometrial thickness (P= 0.006). Polyp showed significant association with the Duration of menstrual cycle (P= 0.046), Intermenstrual bleeding/spotting (P= 0.000), Premenstrual bleeding/spotting (P= 0.001), Breakthrough bleeding (P= 0.002), Ultrasound findings (P= 0.000), and endometrial thickness (P= 0.003). Hyperplasia without atypia showed significant association with the parity (P= 0.042), and endometrial thickness (P= 0.025). Hyperplasia with atypia showed significant association with the regularity of menstrual cycle (P= 0.025) (Table-2)

Table No.2: Comparison of Histopathology findings with associated factors

Study variables		Common Histopathological Diagnosis						
		Endometritis	Proliferative endometrium	Secretory endometrium	Polyp	Hyperplasia without atypia	Hyperplasia with atypia	Carcinoma
Parity	Nulliparous	0(0%)	1(11.1%)	8(88.9%)	0(0%)	0(0%)	0(0%)	0(0%)
	Multipara 1-4	3(4.9%)	25(41%)	12(19.7%)	9(14.8%)	11(18%)	1(1.6%)	0(0%)
	Grandpara > 4	0(0%)	15(42.9%)	13(37.1%)	2(5.7%)	1(2.9%)	2(5.7%)	2(5.7%)
P-values		0.328**	0.196**	0.000*	0.213**	0.042*	0.445**	0.130**
Frequency of menstrual cycle	<24 days	1(1.4%)	33(47.1%)	20(28.6%)	7(10%)	6(8.6%)	3(4.3%)	0(0%)
	24-38 days	2(7.4%)	2(7.4%)	12(44.4%)	4(14.8%)	6(22.2%)	0(0%)	1(3.7%)
	>38 days	0(0%)	6(75%)	1(12.5%)	0(0%)	0(0%)	0(0%)	1(12.5%)
P-values		0.251**	0.000*	0.156**	0.474**	0.095**	0.462**	0.036*
Duration of menstrual cycle	Prolonged	2(2.9%)	29(41.4%)	17(24.3%)	11(15.7%)	8(11.4%)	1(1.4%)	2(2.9%)
	Normal	0(0%)	10(32.3%)	16(51.6%)	0(0%)	3(7.9%)	2(6.5%)	0(0%)
	Shortened	1(25%)	2(50%)	0(0%)	0(0%)	1(25%)	0(0%)	0(0%)
P-values		0.019*	0.616**	0.009*	0.046*	0.663**	0.354**	0.601**
Regularity of menstrual cycle	Regular	2(3.1%)	23(35.4%)	25(38.5%)	6(9.2%)	8(12.3%)	0(0%)	1(1.5%)
	Irregular	1(2.5%)	18(45%)	8(20%)	5(12.5%)	4(10%)	3(7.5%)	1(2.5%)
P-values		0.863**	0.327**	0.048*	0.745**	0.718**	0.025*	0.726**
Intermenstrual bleeding/spotting	Yes	0(0%)	3(12.5%)	2(8.3%)	11(45.8%)	4(16.7%)	2(8.3%)	2(8.3%)
	No	3(3.7%)	38(46.9%)	31(38.3%)	0(0%)	8(9.9%)	1(1.2%)	0(0%)
P-values		0.339**	0.002*	0.005*	0.000*	0.358**	0.130**	0.051**
Premenstrual bleeding	Yes	1(16.7%)	0(0%)	0(0%)	3(50%)	1(16.7%)	0(0%)	1(16.7%)
	No	2(2%)	41(41.4%)	33(33.3%)	8(8.1%)	11(11.1%)	3(3%)	1(1%)

DISCUSSION

AUB is a variation from normal menstruation which consists of abnormal frequency, lasting excessively long, irregular, and heavier than normal is potentially a serious condition as excessive bleeding causes anaemia and affect quality of life leading to unnecessary hysterectomy.

Our study recruited one hundred and five endometrial samples of perimenopausal women with abnormal uterine bleeding. We observed that the age of the majority of the participants (57.1%) ranged between 40-45 years. Most prevalent bleeding pattern was heavy bleeding with clots (78%), frequent cycle and prolonged duration of bleeding (66.7%). Among our samples, we observed that majority of the women were multiparous (58.1%). In accordance with the observation of the following studies that AUB was common 32%⁴, 31%⁹, 33.5%¹⁰ and 37%¹¹ in age group 41-50years respectively. The difference in percentages is due to various age groups studied whereas in the present study women of age 41-50 years were included¹², whereas Indrani M et al observed 57.4% women presented with AUB in 40-44 years age group^{1,9,13}.

The pattern of uterine bleeding in our study showed that 66.7% women had frequent menstrual cycle, 66.7% had prolonged duration, 78.1% had heavy flow with clot, 22.9% women had complaint of inter-menstrual bleeding, and other showed that prolonged bleeding was the most prevalent AUB found in 42% patients, followed by heavy 35%, frequent 20% and 19% had intermenstrual bleeding⁸.

AUB in perimenopausal and postmenopausal patients is alarming and needs meticulous evaluation because it

could be the only clinical symptom of endometrial carcinoma and pre-neoplastic conditions in these patients. We assessed patterns in ultrasound and histopathological findings. In this series we observed that most of the women (59%) presented with more than 18mm thickened endometrium and 41% women had less than 18 mm in ultrasound, while another showed 23% fibroid, 7.7% adenomyosis, 4.7% polyp, thickened endometrium 4% and 58% normal scan findings¹². The study conducted in Kenya⁸ demonstrated 31% fibroid, 7% adenomyosis, 6% polyp and thickened endometrium 10%.

In our study proliferative endometrium was found as the most prevalent histopathological finding observed among 39% women followed by secretory endometrium which was found in 31.4% subjects whereas malignancy (1.9%), endometritis (3.9%) and hyperplasia with atypia (2.9%) were least prevalent findings of endometrial histopathology and others^{9,14} that showed proliferative endometrium as most common finding. A study conducted in 2020 in Pakistan, a endometrial polyps were identified in 15% of patients, endometrial hyperplasia in 12.5%, aberrant proliferative of endometrium in 8.3% of cases and cancer in 2.5% was discovered¹¹. Moreover, proliferative phase endometrium was the most common histopathological pattern, found in almost 1/3rd of cases, followed by endometrial hyperplasia 24.8%, chronic endometritis 16.8%, secretory phase 16.8%, and endometrial polyps 4.2%¹⁵. The results of present study also correspond with another study from Pakistan, where on analysing the histopathology results of the samples 34% were showing proliferative endometrium¹⁶. Similarly in another study the most

common histological pattern of endometrium includes proliferative endometrium (22.8%) followed by endometrial hyperplasia (19.40%)¹⁷. On the contrary, secretory endometrium revealed in 38.88% cases, proliferative endometrium in 34.92%, endometritis 7%, atypical hyperplasia 3.1% and carcinoma endometrium in 5.55% cases^{18,19}. In a study done in Nigeria, endometritis prevailed 25% followed by atypical hyperplasia 50% while typical Hyperplasia 31.7%, endometrial polyps 43.8% respectively²⁰. Our study finding with regards to histopathology is variable. This could be because of difference in sample size, and study design. Break through, Intermenstrual and premenstrual bleeding had significant association with polyp, and endometritis. Ultrasound findings had significant association with polyp, Proliferative and secretory endometrium, and endometrium thickness had significant association with endometritis, secretory endometrium, polyp, hyperplasia without atypia.

CONCLUSION

Dilatation and curettage is a cost-effective procedure in the evaluation of abnormal uterine bleeding. Accurate analysis of endometrial sampling is the key to effective therapy and optimal outcome. This would help in individualising the management of abnormal uterine bleeding with a view to reduce unnecessary benign hysterectomy.

Author's Contribution:

Concept & Design of Study:	Seema Ghani, Zubaida Masood
Drafting:	Humaira Tahir, Fauzia Ali
Data Analysis:	Shabnam Hassan, Saira Saeed
Revisiting Critically:	Seema Ghani, Zubaida Masood
Final Approval of version:	Seema Ghani, Zubaida Masood, Saira Saeed

Conflict of Interest: The study has no conflict of interest to declare by any author.

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