Original Article

Frequency of Structural and Hormonal Causes of Abnormal Uterine Bleeding (AUB) in Perimenopausal Women

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Abstract

Objective: To evaluate the frequency of structural and hormonal causes of abnormal uterine bleeding (AUB) in perimenopausal women to support timely diagnosis, management, and prevention.

Methodology: This cross-sectional study was conducted in the Department of Obstetrics and Gynecology at Foundation University Islamabad, Fauji Foundation Hospital, from January to August 2024. It included all perimenopausal women aged 40–55 years presenting with AUB who had not yet attained menopause. A 5ml blood sample was collected from each case for laboratory investigations, including thyroid function tests (TSH and free T4), serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin levels, where clinically indicated, to assess hormonal abnormalities. Transvaginal ultrasonography (TVUS) was performed to evaluate the uterus, endometrium, and adnexal structures. Data were entered and analyzed using SPSS version 26.0.

Results: Leiomyoma 93(26.4%) was the most frequent abnormality, followed by cervical polyps (9.3%), endometrial hyperplasia without atypia (9.1%), adenomyosis (3.5%), endometrial polyps (3.2%), and malignant lesions including endometrioid carcinoma (0.3%) and cervical squamous cell carcinoma (0.3%). Hormonal and endometrial dysfunction-related abnormalities included disordered proliferative endometrium (24.6%) and chronic nonspecific endometritis (22.6%), with premalignant changes such as endometrial hyperplasia with atypia (0.8%). These findings varied significantly with age ($p < 0.05$).

Conclusion: Leiomyomas were the predominant structural pathology, while hormonal and endometrial abnormalities were also prevalent, especially in younger perimenopausal women.

Keywords: Perimenopause, Leiomyoma, Histopathology, Endometrial Hyperplasia, Abnormal uterine bleeding.

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Introduction

Abnormal uterine bleeding (AUB) is defined as any variation in the regular menstrual cycle in terms of flow rate, length, regularity, frequency, and volume. It includes heavy menstrual bleeding (HMB), intermenstrual bleeding (IMB) and post coital bleeding (PCB). Abnormal uterine bleeding reflects not just the volume of blood loss, but also the extent to which it disrupts a woman's everyday activities.[1]

Peri-menopause is the transitional phase leading up to menopause, marked by endocrine, biological, and clinical changes, beginning with the onset of menstrual irregularity and continuing until 12 months after the final menstrual period.[2] Various clinical signs, such as hot flushes and menstrual irregularities, significantly affect women's quality of life, marking the beginning of menopause. Perimenopause lasts around 5 years on average, but symptoms may begin as early as 8 years before the final menstrual period (FMP).[3] The average age of onset of perimenopause is 40 to 51 years but the symptoms may start to manifest as early as 40 years till as late as 55 years.[4] The onset age of perimenopause, how long it lasts, and the pattern of bleeding during this phase can all vary greatly from one woman to another.[3]

Up to one-third of women experience AUB at some point in their lives. It could be either particularly around

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the onset of menstruation (menarche) or during the perimenopause.[5] International Federation of Gynecology and Obstetrics recommends the use of PALM-COEIN classification to differentiate between structural and non-structural causes of AUB. It signifies 2 group where PALM associates itself with structural causes of AUB including Polyps (endometrial/cervical), Adenomyosis, Leiomyomas, Malignancy and hyperplasia and COEIN signifies AUB with nonstructural causes including Coagulopathy, Ovulatory problems, Endometrial abnormalities, Iatrogenic (hormonal contraceptive, anticoagulant or tamoxifen use, Asherman syndrome) and not discovered yet (chronic endometritis/arteriovenous malformation). [1,6]

In Pakistan previous studies suggest that 21% to 43% of perimenopausal women suffers HMB with structural causes being the primary contributors.[2] High prevalence of comorbidities such as, diabetes mellitus (DM), and obesity significantly contributes to the burden of AUB, particularly among reproductive-age and peri-menopausal women.[7] In advanced age women ovaries become less responsive to gonadotrophins (FSH/LH) leading to fluctuating release of estrogen and low progesterone causing AUB as well as mood changes and hot flashes. This makes it even more important to study this age group as it highlights the gap in literature where this population and their challenges seems to be underrepresented.

AUB in peri-menopausal women is a common yet often neglected health issue, particularly in our society where cultural taboos, lack of awareness, and limited access to healthcare services and timely medical treatment. The many women in this age group continue to suffer in silence, leading to delayed diagnosis and inadequate treatment. This neglect not only affects their physical and emotional well-being but also predisposes them to serious complications. However, there is a need to study the underlying structural and hormonal causes of AUB in this population so that early detection and appropriate management strategies can be developed. By addressing this gap, this study has been done to assess the structural and hormonal causes of AUB in peri-menopausal women the study may improve clinical outcomes, reduce preventable complications, and enhance the overall quality of life for peri-menopausal women.

Methodology

This cross-sectional study was conducted in the Department of Obstetrics and Gynecology (Unit II) at Foundation University Islamabad, Fauji Foundation Hospital (FFH) over an eight-month period from January 2024 to August 2024. Prior to the study conduction, an ethical institutional review committee approved this research (Ref No 533/RC/FFH/RWP Dated 02 March, 2022). Data was recorded using a specially designed proforma after obtaining informed consent from the participants. The sample size of 345 women calculated using the World Health Organization software taking the estimated prevalence of 34%[8] with 5% margin of errors and 95% confidence interval. This study employed nonprobability consecutive sampling technique. All the women aged 40–55 years presenting with AUB and not yet attained menopause (defined as 12 consecutive months without menstruation). All postmenopausal women; those on hormone replacement therapy, anticoagulants, or hormonal contraceptives within the past three months; women with known bleeding disorders, chronic liver disease, renal impairment, or thyroid dysfunction already under treatment; pregnant women or those with pregnancy-related complications; and women with a medical history of gynecologic malignancy were excluded. Written informed consent was obtained from each participant after explaining the study objectives, and the women were counseled that all their information would be kept confidential and that they had the right to withdraw from the study at any time. All the women underwent a detailed medical and clinical history including demographic details, parity, menstrual pattern, medical and surgical history, and associated systemic or endocrine symptoms. The careful pelvic examinations were performed to assess uterine size, tenderness, adnexal masses, or the pathology of cervix. A 5ml blood sample was obtained from each case for laboratory investigations including thyroid function tests (TSH and free T4), serum follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin levels where clinically indicated, to assess hormonal abnormalities. Furthermore, Transvaginal ultrasonography (TVUS) was performed in all cases to evaluate the uterus, endometrium, adnexa, and to detect structural lesions such as leiomyomas, polyps, adenomyosis, or thickness of endometrium. Additionally, among cases where TVUS was inconclusive, hysteroscopy was carried out for better evaluation of endometrial cavity. The patients with an

endometrial thickness ≥5 mm, persistent AUB, or clinical suspicion of hyperplasia or malignancy underwent endometrial sampling, and the biopsy specimens were examined histopathologically to detect hyperplasia, carcinoma, or benign the changes of endometrium. All the relevant information was collected via study proforma and entered in excel file which was further converted to SPSS version 26.0 for the purpose analysis.

Results

Total of 345 women were studied, with the most common age group of 45-49 years. The commonest complaint was HMB 172(49.9%) followed by IMB 105(30.4%) and PCB 68(19.7%). Women were mostly experiencing AUB for more than 6 months 187(54.2%). Only 26.1% of the sample lies within the normal range of BMI. In terms of parity, multiparous perimenopausal women were 325(72.8%). In Comorbidities, women with DM were 44.9% and 27.2% women were smoker. 62% women were not using any contraceptive method.98% of women had normal Pap smear during their initial diagnostic evaluations tabulated in Table I.

Based on histopathological evaluation, leiomyoma (26.4%), disordered proliferative endometrium (24.6%), and chronic nonspecific endometritis (22.6%) were the most common findings, followed by cervical polyps (9.3%) and endometrial hyperplasia without atypia (9.1%). Less frequent diagnoses included adenomyosis (3.5%), endometrial polyps (3.2%), and premalignant or malignant lesions such as endometrial hyperplasia with atypia (0.8%), endometrioid carcinoma of the endometrium (0.3%), and squamous cell carcinoma of the cervix (0.3%). According to age groups, disordered proliferative endometrium and chronic endometritis predominated in women aged 40–44 years, leiomyomas were most common in those aged 45–49 years, while hyperplastic and malignant lesions were more often seen in women aged 50–55 years. Most differences across age groups were statistically significant ($p < 0.05$), as shown in table II

Table I: Demographic and clinical characteristics of the AUB Patients. (n=345)

Variables		N(%)
Age Groups	40-44 years	103(29.9%)
	45-49 years	146(42.3%)
	50 -55 years	96(27.8%)
BMI	Normal	90(26.1%)
	Overweight	128(37.1%)
	Obese	127(36.8%)
Types of AUB	HMB	172(49.9%)
	IMB	105(30.4%)
	PCB	68(19.7%)
Comorbidity	DM	155(44.9%)
	Smoker	94(27.2%)
	PCOS	5(1.4%)
	Thyroid disorders	0(0%)
	Hyperprolactinemia	0(0%)
	Nil	91(26.3%)
Duration of AUB	1-6 months	158(45.8%)
	6-12 months	187(54.2%)
Parity	Nulliparous	20(47.2%)
	Multiparous	325(72.8%)
Pap smear	NILM	339(98.3%)
	NILM +inflammatory	6(1.7%)
Contraception	Not using	215(62%)
	Barrier method	100(28%)
	Permanent sterilization	30(8.6%)

Out of all perimenopausal women with abnormal uterine bleeding, structural pathologies were the most common, seen in 53% of cases, with the highest frequency in women aged 45–49 years. Hormone-dependent endometrial changes accounted for 24%, predominantly in women aged 40–44 years, while chronic endometritis was observed in 22%, mainly in the same age group. Most variations across age groups were statistically significant ($p < 0.05$) as shown in Table III.

Table II: Morphological patterns of AUB according to age group. (n=345)

Pathologies	40-44 years	45-49 years	50-55 Years	Total	P value
Leiomyoma	35	47	11	93(26.4%)	0.003
Disordered proliferative phase endometrium	56	24	3	83(24.6%)	0.006
Chronic nonspecific endometritis	50	28	0	78(22.6%)	0.008
Cervical polyps	19	13	0	32(9.3%)	0.01
Endometrial hyperplasia without atypia	8	10	12	30(9.1%)	0.01
Endometrial hyperplasia atypia	0	1	3	4(0.8%)	0.01
Adenomyosis	8	4	0	12(3.5%)	0.05
Endometrial polyps	6	4	1	11(3.2%)	0.06
Endometroid carcinoma of endometrium	0	0	1	1(0.3%)	0.7
Squamous cell carcinoma of cervix	0	0	1	1(0.3%)	0.7
Total	182	131	32	345(100%)	

Table III: Structural and hormonal abnormalities across age Groups. (n=345)					
Pathology	**40-44 years**	**45-49 years**	**50-55 years**	**Total (%)**	**P value**
Structural pathology	76	79	29	184(53%)	0.001
Hormones dependent endometrial pathology	56	24	3	83(24%)	0.006
Chronic inflammation of endometrium	50	28	0	78(22%)	0.008

Discussion

Mostly women in our study were of group B (42.3%) consistent with a multicenter European study where this age group was most affected by AUB.[9] HMB was the most common pattern (49.9%), similar to findings from Scandinavian data reporting 47% prevalence[10] and a Turkish study showing 50%.[11] Most participants were multiparous (72.8%) and not using contraception (62%), echoing trends reported in European cohorts.[9] Additionally, Pap smears were normal in 98.3%, aligning with a Canadian study where 95.6% of screened perimenopausal women had normal results.[12]

AUB in our study was predominantly contributed by structural causes (p=0.001), with leiomyomas significantly affecting perimenopausal women (p=0.003) specially in group B. The high prevalence of leiomyomas in our study is consistent with a study in India who reported a high prevalence of leiomyomas (85.3%) among perimenopausal women in South India.[13] Leiomyomas are estrogen-sensitive tumors that tend to grow rapidly during the perimenopausal period, as estrogen levels are not adequately opposed due to declining progesterone levels. Additionally, studies from Pakistan India and Denmark revealed leiomyomas as a key structural etiology of AUB in genetically predisposed population.[2,5,10]

In our study, cervical polyps were the second most common structural cause of AUB (p=0.01), mainly affecting women in group A. This is supported by EBCOG (2021) guidelines.[1] The higher frequency of cervical polyps in Group A is largely attributed to the fact that polyps often cause PCB and persistent vaginal discharge, prompting women to seek gynecological evaluation earlier rather than delaying consultation.

Endometrial hyperplasia, a precursor to endometrial cancer, was significantly associated with AUB in perimenopausal women in our study (p=0.01), particularly in group B and group C, consistent with a study in Brazil and India.[14,15] Its frequency in our study is significantly high (9.1%) when compared with Chinese study (1.3%).[16] High rates of obesity (36.8%) and DM (44.9%) in our sample align with two previous study from Pakistan who reported a threefold increased risk of hyperplasia in obese women.[17,18] These findings support the need for targeted lifestyle counseling on use of hormonal contraceptive methods to reduce risk in high-prevalence regions like Pakistan.

Another significant finding was frequency of adenomyosis (p=0.05) causing AUB. Adenomyosis is more commonly found in multiparous women or who have a history of uterine surgery. Women in our study were mostly multiparous increasing overall risk of adenomyosis. This pattern aligns with observations from studies in India,[13, 15] who reported a high incidence of adenomyosis in multiparous women with AUB. Further, a study from Denmark[10] confirmed that adenomyosis remains a major structural cause of AUB during the perimenopausal transition.

In our study, endometrial carcinoma was infrequent and not statistically significant (p=0.7). This aligns with global trends, as endometrial cancer primarily affects postmenopausal women, with a median age of 60 years, and is less common in perimenopause.[10, 13] Similarly, squamous cervical carcinoma was also rare (p=0.7), reflecting its peak incidence at around 55 years, likely due to the long latency of HPV-related progression.[17] Although these malignancies were not prominent in our cohort, they remain clinically significant and warrant separate investigation, especially in Pakistan where screening and early detection efforts need strengthening.[12]

Endometrial polyps in our study were not statistically significant contributors to AUB (p=0.06). Similar low prevalence and impact were reported by studies in India. [13, 15] as these lesions are more prevalent among postmenopausal women as compared to perimenopausal women supported by a study from Brazil.[14]

A significant finding in our study was the high frequency of disordered proliferative endometrium (p=0.006), mainly in Group A and B, likely due to hormonal imbalance and unopposed estrogen. During perimenopause, ovarian function becomes erratic. Follicular development is often incomplete leading to anovulation. Without luteal progesterone, endometrium remains under unopposed estrogen stimulation, leading to irregular, disorganized proliferation. Recent studies confirm that hormonal contraceptives, especially combined pills and LNG-IUS, can reduce the risk of

endometrial abnormalities by regulating endometrial proliferation.[19,20] However, a study in India suggest that response may vary, particularly in women with metabolic or endocrine conditions, highlighting the need for individualized management.[21]. Notably, 62% of women in our study were not using any contraception, which may reflect a lack of awareness about protective role of hormonal contraceptive methods.

A key finding in our study was the significantly high frequency of chronic nonspecific endometritis (p=0.008), particularly in Groups A and B. Infections like chlamydia and gonorrhea causes pelvic inflammatory disease (PID) which can lead to chronic nonspecific endometritis if remained untreated.[22] In developing countries, factors such as limited access to postpartum care, unsafe delivery practices, and antibiotic resistance contribute to persistent uterine infections.[23] Poor access to diagnostic tools like endometrial biopsy may delay diagnosis.[6] A previous study emphasizes the burden of unmanaged gynecologic conditions in Pakistan.[16] Additionally, cultural barriers to early care and limited sexual health education further exacerbate the risk.[24] Our finding is opposed by a study conducted in Nepal[25]. where the frequency was low (5%) This difference may be partly explained by the smaller study group size in Nepal. Moreover, legal access to safe abortion services and earlier treatment-seeking behavior among women contribute significantly to the lower frequency of chronic endometritis observed in Nepal compared to Pakistan.

Conclusion

Study revealed that the abnormal uterine bleeding in perimenopausal women is most commonly attributed to structural pathologies such as leiomyomas, along with significant contributions from endometrial changes including disordered proliferative patterns and chronic nonspecific endometritis, with less frequent, premalignant and malignant lesions, particularly among women aged 50–55 years. Overall findings emphasize the need for thorough evaluation, including hormonal assessment, imaging, and histopathological analysis, to ensure accurate diagnosis and timely management. Timely identification of structural and hormonal abnormalities is very important to prevent complications and malignancy, thereby improving the quality of life and long-term health outcomes for perimenopausal women.

STRENGTH AND LIMITATIONS: This study provides useful real-world data, including histopathological confirmation, and age-stratified analysis providing local evidence on AUB in perimenopausal women. However, as a single-center cross-sectional study, causal relationships could not be established and generalizability remains limited. Future multicenter and longitudinal studies are recommended to validate and expand these finding Future longitudinal research is needed to assess the progression and impact of these conditions over time.

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