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A clinical study on abnormal uterine bleeding in premenopausal women

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Abstract

Background: Abnormal uterine bleeding is defined as any bleeding outside of normal menstrual cycle with excessive duration, frequency and amount of loss. AUB accounts about 70% in perimenopausal women in gynaecology OPD. Abnormal uterine bleeding is not a disease, it is a symptom. The aim of the study was to evaluate abnormal uterine bleeding in perimenopausal women and to study the various menstrual abnormalities and causes of AUB in perimenopausal women.

Study design: This study was a hospital based cross sectional study which included 95 women in perimenopausal age group (40-51 years) with abnormal uterine bleeding. The history, clinical examination, USG and histopathological findings was collected. Clinical findings were classified by PALM-COEIN classification. All women underwent endometrial sampling to rule out endometrial pathology.

Results: The mean age of the patients was 44.89(±2.93) years. Parity of more than 2 (46.3%) was most common. Menorrhagia (58.9%) was the most common bleeding pattern followed by menometrorrhagia (23.2%). Leiomyoma 37 (38.9%) was the most common clinical finding followed by adenomyosis 29 (30.5%). Ultrasonographically fibroid uterus (37.8%) was the most common USG findings followed by Adenomyosis (30.5%). The most common endometrial thickness was 9-12mm (43.1%). Histopathological examination revealed secretory phase endometrium (35.8%) was the most common finding followed by proliferative endometrium (20%).

Conclusion: Uterine fibroid was the leading cause of AUB. Clinical examination and ultrasound findings correlated well in the diagnosis of fibroids. Evaluation of the endometrium in perimenopausal women presenting with AUB is essential to rule out endometrial pathology.

Keywords: Clinical, abnormal uterine bleeding, premenopausal women

Introduction

Menstruation is a cyclic bleeding from the uterine endometrium in response to ovarian hormones which is under the control of hypothalomo-pituitary-ovarianaxis. Menstrual disorders are a common indication for medical visits among women of the reproductive age^[1].

Abnormal uterine bleeding (AUB) is defined as any bleeding outside of normal menstrual pattern with excessive duration, frequency and amount of loss. Abnormal uterine bleeding is not a disease, it is a symptom. AUB accounts for 70% of the complaints among premenopausal women in gynaecology OPD.² AUB is a general term and can have variable bleeding patterns such as menorrhagia, menometrorrhagia, oligomenorrhea, metrorrhagia, polymenorrhea, mid cycle spotting^[3].

An international expert consensus from the FIGO menstrual disorders working group has proposed a standardized classification system for AUB. This classification allows the characterization of more than one etiology in the same patient. There are 9 main categories within the classification system named for the acronym PALM-COEIN. The PALM side of the classification refers to structural causes that could be evaluated and diagnosed on imaging and or biopsy. The COEIN side allows consideration of underlying medical disturbances that could result in AUB^[4].

All premenopausal women with AUB will need thorough evaluation to rule out malignant causes of AUB. Literature, suggests using the age 45 years as a cut-off for sampling the endometrium in all women with AUB. However, irregular menstrual bleeding justifies investigating women regardless of their age^[5]. Evaluation involves clinical examination, transvaginal sonography and an endometrial sampling. TVS is a non invasive and simple

diagnostic procedure in studying the patterns of the endometrium by excluding the organic pathology in AUB cases. It is also used for visualizing the uterine structures. Endometrial sampling is thought to be a safe and effective method for histological assessment of the endometrium. It is used as an alternative to the more invasive method of D&C. Endometrial sampling is a valuable tool in the assessment of patients with AUB and that Pipelle is the best outpatient device available [6]. Dilatation and curettage (D&C) is a simple but invasive procedure for histopathological evaluation of the endometrium and the assessment of AUB. Early detection of precancerous lesion like endometrial hyperplasia with atypia can also be ruled out. Histopathological examination of endometrial samples remain still the gold standard procedure in detection of endometrial pathology [7].

TVS and D&C together remain as a practical, cost effective and dependable investigation for AUB.

The present study aims to evaluate the various menstrual abnormalities and causes of AUB in premenopausal women and to correlate clinical evaluation with ultrasonographic and histopathological examination.

Methodology

This hospital based cross sectional study was conducted in Mahatma Gandhi Medical College and Hospital between January 2017 and March 2019. All premenopausal women with abnormal uterine bleeding attending the OPD formed the study population. Sample size was calculated based on the National family health survey 3 in Pondicherry, which showed prevalence of premenopausal women of Pondicherry as 13.6%. The required sample size calculated was 95. After obtaining approval from the Institute Ethics committee, all premenopausal women (40-51 years) with abnormal uterine bleeding attending the OPD for the first time were enrolled in the study consecutively.

Written and informed consent was obtained from all patients before enrolling in the study. Participants were clinically evaluated by detailed history, clinical examination and a provisional diagnosis was made. They were all subjected to ultrasound examination (Transabdominal / Transvaginal). The presence of any lesions in the uterus, their morphological features and endometrial thickness was noted. Adnexal pathology were looked for and documented. They were all subjected to endometrial sampling. Clinical diagnosis was correlated with USG and HPE findings. They were managed conservatively, medically or surgically depending upon the cause. Data was collected in a Proforma sheet and analysed.

Results

The mean age of women with abnormal uterine bleeding in the

present study was 44.89 \pm 2.93 years. Among these women a parity of more than 2 was most commonly noted. Fifty women (52.6%) had a parity of more than 2.

The bleeding patterns of the patients were analysed. Of the 95 women, 56(58.9%) had menorrhagia, 22(23.2%) had menometrorrhagia, 8(8.4%) had polymenorrhea, 5 (5.3%) had oligomenorrhea and 4 (4.2%) had metrorrhagia. The pattern of menstrual disorders is shown in table 1.

Table 1: Patterns of Menstrual Disorders

Menstrual disorders	No. of patients	Percentage
Menometrorrhagia	22	23.2%
Menorrhagia	56	58.9%
Polymenorrhea	8	8.4%
Oligomenorrhea	5	5.3%
Metrorrhagia	4	4.2%
Total	95	100%

The history and clinical examination of the patients was used to classify them into the PALM-COEIN classification. Of all 95 women with AUB the most common clinical finding was AUB-L (Leiomyoma) in 37 (38.9%), followed by 29 (30.5%) with AUB - A (Adenomyosis), 12 (12.6%) women with AUB - P (Polyp), 12(12.6%) had AUB- E (Endometrial), 4(4.2%) had AUB- O (Ovulatory) and only 1(1.1%) had AUB-M (Malignancy). PALM and COEIN groups accounted for 83.2% and 16.8% respectively. The clinical classification of the patients is shown in the table 2.

Table 2: Clinical findings

Clinical findings	Number of patients	Percentage
AUB(P)	12	12.6%
AUB(A)	29	30.5%
AUB(L)	37	38.9%
AUB(M)	1	1.1%
AUB(O)	4	4.2%
AUB(E)	12	12.6%

Of all 95 women the most common abnormality detected on USG was fibroid uterus 36(37.8%), followed by adenomyosis with 29 (30.5%) patients. Twenty four (25.2%) women had no uterine abnormalities, 5(5.3%) had fibroid polyp and only 1(1.1%) had uterine collection.

In the present study, 41 women had an endometrial thickness of 9-12mm (43.1%), 23 women had 13-16mm (24.2%) thickness and 15 had less than 8mm (15.8%) thickness, 7 women had very thick endometrium of 21-24 mm (7.3%) and 9 had 17-20mm (9.4%). The endometrial thicknesses are as shown in table 3.

Table 3: Endometrial thickness

Endometrial Thickness	No. Of Patients	Percentage
\leq 8mm	15	15.8
9-12mm	41	43.1
13-16mm	23	24.2
17-20mm	9	9.4
21-24mm	7	7.3

All 95 underwent endometrial sampling by way of fractional curettage. Of the 95 premenopausal women, the histopathological study showed secretory phase endometrium in 34(35.8%) cases, proliferative phase endometrium in 19(20%) and disordered proliferative phase endometrium in 16(16.8%). Endometrial hyperplasia without atypia was seen in 10(10.5%),

5(5.3%) had inadequate tissue for sampling. Benign endometrial adenomatous polyp was the histopathological report in all 7 cases of cervical polyp (7.4%), 2(2.1%) had benign leiomyomatous polyp, 1(1.1%) had complex hyperplasia with atypia and 1 (1.1%) had complex hyperplasia without atypia. The histopathological study reports are shown in table 4.

Table 4: Histopathological examination (HPE)

Impression of Histopathological examination	No. of patients	Percentage
Secretory phase	34	35.8
Proliferative phase	19	20.0
Disordered Proliferative phase	16	16.8
Endometrial hyperplasia without atypia	10	10.5
Inadequate tissue for sampling	5	5.3
Benign Endometrial adenomatous polyp	7	7.4
Benign leiomyomatous polyp	2	2.1
Complex hyperplasia with atypia	1	1.1
Complex hyperplasia without atypia	1	1.1
Total	95	100.0

In the present study 37 women were clinically diagnosed to have fibroids and 29 women were diagnosed to have adenomyosis. 7 women had cervical polyps and 5 had fibroid polyps. The rest of the women had no significant clinical findings and were classified in to the COEIN part of the classification. The study tried to correlate clinical and USG findings. Ultrasonographically 36 women had fibroid and 29 had

Adenomyosis. 25 women did not show any abnormality on ultrasound. The clinical and USG findings correlated well for the women with fibroids and adenomyosis. The USG findings of those women who were classified into the COEIN group did not correlate therefore the overall correlation between clinical and ultrasonographic findings was not statistically significant. The findings are shown in table 5.

Table 5: Association between clinical finding and USG finding

Abnormalities	Clinical findings	In USG
Fibroid	37	36
Cervical & Fibroid polyp	12	5
Adenomyosis	29	29
Others	17	25
Total	95	95
$X^2 = 0.54, p = 0.91$		

The present study attempted to correlate endometrial thickness to the histopathological findings. It showed that secretory phase endometrium was the commonest finding in all thicknesses. In the present study proliferative endometrium was the next commonest histopathology despite varying thickness of

endometrium. Thicker endometrium did not always show hyperplasia and thinner endometrium did not show atrophy. Statistically HPE did not correlate with endometrial thickness. The findings are as shown in table 6.

Table 6: Correlation of HPE with Endometrial Thickness

Histopathological Examination	Endometrial Thickness				
	≤8mm	9-12mm	13-16mm	17-20mm	21-24mm
Secretory Phase Endometrium	5(33.3%)	13(31.7%)	10(43.4%)	2(22.2%)	4(57.1%)
Proliferative Phase Endometrium	4(26.6%)	6(14.6%)	5(21.7%)	2(22.2%)	2(28.5%)
Disordered Proliferative Phase Endometrium	3(20%)	8(19.5%)	3(13%)	2(22.2%)	0(0.0%)
Endometrial Hyperplasia Without Atypia	1(6.6%)	4(9.7%)	3(13%)	1(11.1%)	1(14.2%)
Inadequate Tissue For Sampling	0(0.0%)	4(9.7%)	1(4.3%)	0(0.0%)	0(0.0%)
benign endometrial adenomatous polyp	2(13.3%)	2(4.8%)	1(4.3%)	2(22.2%)	0(0.0%)
Benign leiomyomatous polyp	0(0.0%)	2(4.8%)	0(0.0%)	0(0.0%)	0(0.0%)
Complex hyperplasia with atypia	0(0.0%)	1(2.4%)	0(0.0%)	0(0.0%)	0(0.0%)
Complex hyperplasia without atypia	0(0.0%)	1(2.4%)	0(0.0%)	0(0.0%)	0(0.0%)
Total	15(15.8%)	41(43.1%)	23(24.2%)	9(9.4%)	7(7.4%)
$X^2 = 30.05, p = 0.874$					

Discussion

In the present study the mean age of women with abnormal uterine bleeding was 44.89 ± 2.93 years. Among these women a parity of more than 2 was most commonly noted. Fifty women (52.6%) had a parity of more than 2, followed by a parity of 1-2 in 44 (46.3%) women and only 1(1.1%) nulliparous woman. Many of the analysed literature showed similar age group and parity. Nullipara were few in most studies [2, 3, 6].

In the present study menorrhagia was the most common clinical presentation seen in 58.9% of cases followed by menometrorrhagia at 23.2%. Most of the analysed literature on

premenopausal bleeding suggest that menorrhagia is the most common symptom followed by menometrorrhagia [2, 3].

PALM COEIN classification was used for provisionally classifying patients who presented with abnormal uterine bleeding. In the present study 38.9% had AUB (L). Also, 30.5% of the women had AUB (A) and 12.6% had AUB(P). 4.2% were diagnosed to have AUB(O), 12.6% had AUB (E) and 1.1% had AUB(M). PALM and COEIN groups accounted for 83.2% and 16.8% respectively. Leiomyoma was the major components in the structural group and endometrial causes contributed maximum in the functional group.

In the study by Mishra *et al* the PALM and COEIN components accounted for 50.23% and 49.57% respectively. AUB (L) was the major etiological factor in the structural group and ovulatory disorder was the major component in the functional group.⁷ In the study by Archana Singh *et al* PALM and COEIN groups accounted for 60% and 39.9% respectively. Leiomyoma was the commonest cause of AUB 36.75% followed by Ovulatory disorder in 26%. In both the above mentioned studies subsequent histopathological examination accounted for approximately 70% of the cases to have PALM component as the cause of AUB. The clinical findings of the present study are similar to the studies done by Mishra *et al* and Archana Singh *et al*.^[8, 9] Most women with AUB will have a spectrum of hyper estrogenic features (eg): fibroids and adenomyosis will co-exist with anovulatory endometrial changes in women with AUB.

All women who presented with AUB underwent a pelvic ultrasound. Of all 95 women the most common abnormality detected was fibroid uterus 36(37.8%), followed by adenomyosis with 29 (30.5%) patients. Twenty four (25.2%) women had no uterine abnormalities, 5(5.3%) had fibroid polyp, and only 1(1.1%) had uterine collection. In the present study, clinical diagnosis of Leiomyoma and adenomyosis correlated well with the USG findings. However, there were a large percentage of women who had normal clinical findings but abnormal endometrial thickness. They were considered as normal uterus as there was no uterine or adnexal gross pathology. The study attempted to co-relate clinical findings with that of ultrasonography and found that it was not statistically significant (p=0.91).

In the study by Alakananda *et al*, clinical and ultrasonographic findings correlated well with the diagnosis of benign pathology^[10] They showed a 96% correlation between clinical and USG diagnosis of Leiomyoma and 61.5% correlation between clinical and ultrasonographic diagnosis of Adenomyosis. Their findings were similar to our study. The gold standard to make the final diagnosis of adenomyosis has always been histological examination of hysterectomy specimens. The advent of new imaging techniques such as TVUS and MRI have allowed the clinician to make non invasive diagnosis of adenomyosis. Currently TVUS is the first line imaging technique available to diagnose adenomyosis.

Fibroid polyps that occupy and distort the uterine cavity may cause symptoms such as abnormal uterine bleeding, subfertility and recurrent pregnancy loss. The best imaging technique for fibroid polyp is usually TVUS and saline infusion sonohysterography enhances the ability to detect intrauterine pathology compared to conventional TVUS alone.

All 95 premenopausal women who presented with abnormal uterine bleeding underwent ultrasonography and their endometrial thickness was measured transvaginally. The mean endometrial thickness was 12.9mm. The present study attempted to correlate endometrial thickness to the histopathological findings. It showed that secretory phase endometrium was the commonest finding in all thicknesses and proliferative endometrium was the next commonest histopathology despite varying thickness of endometrium. Thicker endometrium did not always show hyperplasia and thinner endometrium did not show atrophy. Statistically HPE did not correlate with transvaginally measured endometrial thickness. The study by Shobitha *et al* to correlated transvaginal sonography of the endometrium to histopathology suggested that a measured thickness of 8mm and above was an indication for diagnostic curettage. The sensitivity of detecting endometrial hyperplasia with TVS alone is poor. They did not suggest any cut off value below which no

pathology was found^[11].

All 95 women in the premenopausal age group who presented with abnormal uterine bleeding underwent a fractional curettage. Thirty four women (35.8%) had secretory phase endometrium and 19 women (20%) had proliferative phase endometrium. The findings of the present study correlated well with the study of Jetley *et al*. In the study by Jetley *et al* 32.4% of women had secretory phase endometrium, 30.5% had proliferative phase endometrium and 6.8% had disordered proliferative phase endometrium^[12, 13]. In the present study sixteen women (16.8%) had disordered proliferative phase endometrium. Endometrial hyperplasia was seen in 24(10.9%) cases, among that simple hyperplasia without atypia was seen in 19(8.6%), complex hyperplasia without atypia was seen in 4(1.8%) and complex hyperplasia with atypia was seen in 1(0.4%).

In the present study 5(5.3%) cases were reported as inadequate tissue sampling, 7(7.4%) had benign endometrial adenomatous polyp and 2(2.1%) turned out to be benign leiomyomatous polyp. After the histopathological examination 55.8% of the women were diagnosed to have AUB(E). By the clinical classification of PALM-COEIN only 12.6% had AUB(E). The increase in the number of women showing AUB (E) after histopathological examination (55.8%) is because of the combined presence of all hyper estrogenic conditions in the same women. Also it goes to prove that endometrial sampling and HPE are important investigations in premenopausal women presenting with AUB.

Summary and Conclusion

The present study was conducted on 95 premenopausal women with AUB, with the objective of studying various menstrual patterns and correlation of clinical findings with ultrasound findings and histopathology examination. The data collected and analysed showed that the most common age group was 45 years \pm 2.93 and the more common parity was two and above. The commonest menstrual pattern seen was menorrhagia and fibroid uterus was the most common uterine pathology. Also doing an endometrial sampling for premenopausal AUB adds more meaning to the management. This study would have been validated better if it was done on a larger population. Also future studies should include Pipelle sampling as that is an inexpensive, non-invasive method of endometrial sampling.

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