

CLINICOPATHOLOGICAL EVALUATION OF ABNORMAL UTERINE BLEEDING IN PERIMENOPAUSAL WOMEN

VIVARNA GEDALA¹, SREE SAILAJA PIDUGU*¹, BALLA SUDHA RANI¹

Department of Obstetrics and Gynaecology, GITAM Institute of Medical Sciences and Research, Visakhapatnam, Andhra Pradesh, India.

*Corresponding author: Sree Sailaja Pidugu; Email: spidugu@gitam.edu

Received: 10 August 2023, Revised and Accepted: 20 November 2023

ABSTRACT

Objective: Abnormal uterine bleeding (AUB) is defined as any bleeding from the uterus that is deviated from normal in terms of regularity, duration, frequency, and amount of blood loss. It interferes with the woman's physical, emotional, social, and material quality of life. The prevalence of AUB ranges between 11% and 13% rising to 24% in perimenopausal women. The aim of this study is to analyze the demographic profile and risk factors of AUB in perimenopausal women, to classify the causes of AUB based on PALM-COEIN classification, and to correlate the clinical and sonological findings with post-operative histopathology findings.

Methods: A cross-sectional study was conducted in the Department of Obstetrics and Gynecology at GIMSR hospital, Visakhapatnam, for 1 year from September 2022 to September 2023. A total of 151 perimenopausal women with complaints of AUB in the age group of 41–50 years who underwent hysterectomy were included in the study.

Results: The most common clinical presentation was heavy menstrual bleeding (HMB) seen in 96 cases (63.5%). Clinically, the PALM component accounted for 61% of cases and the COEIN component accounted for 39% of cases. Ultrasonographically, the PALM component was detected in 76.8% of cases. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of ultrasound for detection of PALM lesions.

Conclusion: Leiomyoma was the most common cause clinically, sonologically, and pathologically. Correlation was good for leiomyoma. USG has good specificity for diagnosis of AUB-A and AUB-P but low sensitivity.

Keywords: Perimenopause, Abnormal uterine bleeding, Leiomyoma.

© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.22159/ajpcr.2023v16i12.50237>. Journal homepage: <https://innovareacademics.in/journals/index.php/ajpcr>

INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the most common gynecological complaints frequently encountered in adult women. AUB is defined as any bleeding from the uterus that is deviated from normal in terms of regularity, duration, frequency, and amount of blood loss [1]. It interferes with the woman's physical, emotional, social, and material quality of life [2]. The prevalence of AUB ranges between 11% and 13% rising to 24% in perimenopausal women [3]. In 2001, Stages of Reproductive Ageing Workshop defined "Perimenopause as the beginning with menopausal transition and ending 12 months after the last menstrual period." It typically occurs in women in their 40's to early 50's [4]. PALM-COEIN is the classification system for AUB given by the International Federation of Gynecology and Obstetrics (FIGO) in an attempt to standardize the terminology, investigations, diagnosis, and management of AUB [5]. PALM represents structural causes of AUB – Polyp, Adenomyosis, Leiomyoma, Malignancy, and Hyperplasia. COEIN represents non-structural causes such as Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not yet classified. The most common presentation of AUB is heavy menstrual bleeding (HMB), which is a major concern for many women, frequently resulting in referral for hysterectomy [6]. The treatment of AUB includes medical management, endometrial ablative procedures, polypectomy, myomectomy, and hysterectomy as the last resort. Hysterectomy is one of the most commonly performed surgeries worldwide [7].

The diagnosis of AUB can be done clinically, by imaging and by histopathology. There might be a variation between clinical, sonological, and histopathological diagnosis.

The aim of this study is to analyze the demographic profile, risk factors of AUB in perimenopausal women, to classify the causes of AUB based on PALM-COEIN classification, and to correlate the clinical and sonological findings with post-operative histopathology findings.

METHODS

A cross-sectional study was conducted in the Department of Obstetrics and Gynecology at GIMSR hospital, Visakhapatnam, for 1 year from September 2022 to September 2023. Approval from the Institutional Ethics Committee was taken before commencing the study.

A total of 151 perimenopausal women with complaints of AUB in the age group of 41–50 years were included in the study. Detailed history was taken from the case sheets with regard to age, parity, socioeconomic status, menstrual history, pattern of abnormal menstrual bleeding, duration of symptoms, contraception history, family history, obstetric history, and associated comorbidities such as hypertension, diabetes, thyroid disorder, and history of previous treatment.

General, systemic, and gynecological examinations were performed and a provisional diagnosis was made. Ultrasonography was performed and structural causes of AUB (PALM) were excluded from the study. The findings of laboratory investigations and ultrasonography were recorded. All structural causes (PALM) were excluded by clinical examination and sonology. COEIN group is suspected after excluding the PALM group. Endometrial biopsy was performed for all the patients above 45 years and some patients between 41 and 45 years with risk factors by endometrial sampling with pipelle's curette or Dilatation and curettage or under hysteroscopic guidance and the reports were collected. Hysterectomy was performed and operative findings were

noted in the study. Report of hysterectomy specimens was collected and the final diagnosis was made. Clinical findings, sonological findings, and histopathology reports were evaluated and correlated.

Inclusion criteria

Women in the age group 41–50 years with AUB who underwent hysterectomy.

Exclusion criteria

Women who did not require a hysterectomy, post-menopausal women, and women with cervical lesions, and adnexal tumors were excluded from the study.

Statistical analysis

Qualitative variables were represented with frequency and percentage. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

RESULTS

one hundred and fifty one perimenopausal AUB cases who underwent hysterectomy were included in this study. About 63% were in the age group 41–45 years and 37% were in the age group 46–50 years. A highest number of AUB cases were seen in para 2 (63%) as shown in Table 1.

27 patients were obese with body mass index >30 kg/m² (18%), 10 patients had diabetes mellitus (6.6%), 16 patients had hypertension (10.6%) and 18 were hypothyroid (12%).

The most common clinical presentation was HMB seen in 96 cases (63.5%) followed by heavy and prolonged menstrual bleeding in 15.3% (Table 2).

Table 1: Parity distribution

Parity	No. of cases	Percentage
Nulliparous	10	6.6
Para 1	22	14.5
Para 2	95	63
≥Para 3	24	15.9

Table 2: Distribution of cases based on menstrual pattern

Menstrual pattern	No. of cases	Percentage
Heavy menstrual bleeding	96	63.5
Heavy and prolonged menstrual bleeding	23	15.3
Inter menstrual bleeding	20	13.2
Frequent bleeding	12	8

Table 3: Distribution of cases as per clinical diagnosis

Diagnosis	No. of cases	Percentage
AUB-P	5	3.3
AUB-A	22	14.6
AUB-L	65	43
AUB-O	40	26.5
AUB-E	19	12.6

AUB: Abnormal uterine bleeding

Table 4: Distribution of cases as per ultrasound findings

Diagnosis	No. of cases	Percentage
AUB-P	8	5.3
AUB-A	27	17.9
AUB-L	72	47.6
AUB-M	9	6
Normal uterus	10	6.6
Bulky uterus	25	16.6

AUB: Abnormal uterine bleeding

Clinically PALM component accounted for 61% of cases and the COEIN component accounted for 39% of cases as shown in Table 3. Over all AUB-L accounted for the highest number of cases (43%), followed by AUB-O in 26.5% of cases. AUB-P accounted for the least number of cases (3.3%).

As shown in Table 4, Ultrasonographically, PALM component was detected in 76.8% of cases (Table 4). 72 (47.6%) cases were leiomyoma, 27 (17.9%) cases were Adenomyosis, eight (5.3%) cases were endometrial polyp, nine (6%) cases were endometrial hyperplasia and 25 (16.6%) cases were diagnosed as a bulky uterus. The uterus is normal in 10 cases (6.6%).

Endometrial biopsy was done in 60 cases and Table 5 shows the different endometrial patterns as per pre-operative endometrial biopsy report.

As shown in Table 6, Histopathological findings of hysterectomy specimens were as follows (Table 6): Leiomyoma 73 (48.3%), adenomyosis 33 (21.9%), and normal myometrium 45 (30%). Out of 72 ultrasonographically diagnosed leiomyoma, 68 were confirmed histopathologically, and four turned out to be adenomyosis. Hysterectomy for adenomyosis was done in 27 cases and 22 were confirmed by histopathological examination (HPE), one turned out as leiomyoma, and four turned out as normal myometrium. Out of 25 cases of the bulky uterus in USG, the HPE report revealed normal myometrium in 17 cases, leiomyoma in three cases, and adenomyosis in five cases. Out of 10 cases of the normal uterus, the HPE report revealed normal myometrium in seven cases, leiomyoma in one case, and adenomyosis in two cases. HPE of the endometrium showed proliferative endometrium in 83 cases (55%), secretory endometrium in 50 (33%), endometrial polyp in 12 cases (8%), and endometrial hyperplasia in six cases (4%). Two cases were endometrial hyperplasia with atypia. USG detected nine cases of thickened endometrium, out of which five cases were confirmed by HPE and two cases turned out as endometrial polyps. Relation between ultrasonography findings and histopathology findings is shown in Table 7.

Table 8 shows the sensitivity, specificity, PPV, and NPV of ultrasound for the detection of PALM lesions.

DISCUSSION

In this study, 151 peri-menopausal hysterectomized women were analyzed. Most of them are between 41 and 45 years of age (63%) which was coherent with the study conducted by Daga and Phatak [8]

Table 5: Distribution of cases as per endometrial biopsy (n=60)

Endometrial pattern	No. of cases	Percentage
Proliferative	33	55
Secretory	14	23.33
Disordered proliferative	2	3.33
Hyperplasia without atypia	3	5
Hyperplasia with atypia	2	3.33
Endometrial polyp	4	6.67
Inadequate sample	2	3.33

Table 6: Distribution of cases as per post-hysterectomy histopathology report

Diagnosis	No. of cases	Percentage
AUB-P	12	7.95
AUB-A	33	21.85
AUB-L	73	48.34
AUB-M	6	3.98
AUB-O	21	13.9
AUB-E	6	3.98

AUB: Abnormal uterine bleeding

Table 7: Histopathological findings in relation to ultrasonography diagnosis

USG diagnosis	HPE findings						
	Myometrium			Endometrium			
	Normal	Leiomyomatous changes	Adenomyomatous changes	Proliferative	Secretory	Endometrial polyp	Endometrial hyperplasia
1. AUB-P (n=8)	8	-	-	-	-	8	-
2. AUB-A (n=27)	4	1	22	18	9	-	-
3. AUB-L (n=72)	-	68	4	43	29	-	-
4. AUB-M (n=9)	9	-	-	1	1	2	5
5. Normal uterus (n=10)	7	1	2	6	3	1	-
6. Bulky uterus (n=25)	17	3	5	15	8	1	1
Total	45	73	33	83	50	12	6

HPE: Histopathological examination

Table 8: Sensitivity and specificity of ultrasonography diagnosis with HPE diagnosis

USG	HPE report						
	Present	Absent	Total	Sensitivity (%)	Specificity	PPV	NPV
Leiomyoma							
Present	68	4	72	93.15	94.9	94.44	93.7
Absent	5	74	79				
Adenomyosis							
Present	22	5	27	66.66	95.76	81.48	91.13
Absent	11	113	124				
Polyp							
Present	8	0	8	66.66	100	100	97.2
Absent	4	139	143				
Malignancy							
Present	5	4	9	83.33	97.2	55.55	99.3
Absent	1	139	140				

and the highest number of women were para 2 (63%). This finding was comparable to the study of Daga and Phatak [8] and Mohammed and Prejisha [9]. The most common bleeding pattern was HMB in 63.5% of women similar to the study done by Jain *et al.* (62%) [10] and Singh (67.8%) [11].

Clinically PALM component accounted for 61% of all the cases. AUB-L was the most common diagnosis in 43% of cases followed by ovulatory dysfunction (AUB-O) in 26.5% of cases and AUB-A in 14.6% of cases. Ovulatory disorders were the most common cause of AUB in the COEIN component which was similar to the study by Mishra and Sultan [12]. In perimenopause, ovulatory disorders are common as chronic anovulation due to derangement of hypothalamo-pituitary-ovarian axis causes heavy and irregular menstrual bleeding. AUB-E is considered diagnosis of exclusion where AUB presents as cyclical HMB without any identifiable cause. AUB-O is the second most common diagnosis clinically. However, less number of cases were diagnosed by histopathology as AUB-O and AUB-E similar to the study done by Singh *et al.* [13].

PALM component accounted for 76.8% of cases on ultrasound. Sonographically leiomyoma was seen in 72 cases (47.6%). Out of these, 68 were confirmed by histopathology and four turned out as adenomyosis. The sensitivity of ultrasound for the diagnosis of leiomyoma was 93.15% and specificity was 94.9% which is similar to the study done by Sharma *et al.* [14]. In this study, 33 cases were diagnosed as adenomyosis by histopathology. USG diagnosed 22 of them. Ultrasound was able to detect adenomyosis with a sensitivity of 66.6%, specificity of 95.76%, PPV of 81.48%, and NPV of 91.3%. The sensitivity and specificity are similar to the study conducted by Siedler *et al.* (sensitivity 63%, specificity 97%) [15]. Talukdar and Mahela in their study on perimenopausal women reported a lesser sensitivity of ultrasound for Adenomyosis (47.62%) [16].

Bulky uterus was the sole finding in 25 cases on ultrasound which were clinically diagnosed as AUB-O and AUB-E. Out of these, histopathology revealed normal myometrium in 17 cases, Adenomyosis in five cases, fibromyoma changes in three cases, endometrial hyperplasia in one case, and endometrial polyp in one case. HPE of endometrium showed proliferative endometrium in 83 cases (55%), secretory endometrium in 50 cases (33%), endometrial polyp in 12 cases, and endometrial hyperplasia in six cases. A higher incidence of proliferative endometrium was observed in our study which is compatible with the study of Khan *et al.* (46.6%) [17].

Hyperplasia without atypia was the dominant finding in four out of six cases and two were hyperplasia with atypia. Sonologically nine cases were identified as thickened endometrium out of which two turned out as endometrial polyp and five were confirmed by histopathology. All the eight cases of endometrial polyp on USG were confirmed histologically. USG was able to suggest endometrial polyp with a sensitivity of 66%, specificity of 100%, PPV of 100%, NPV of 97.2%, and AUB-M with a sensitivity of 83.3%, and specificity of 97.2%. Uhasai *et al.* reported a sensitivity of 66% for endometrial polyp which is similar to our study and a higher sensitivity for AUB-M (100%) [18].

CONCLUSION

In the present study, we classified the causes of AUB in perimenopausal women who underwent hysterectomy according to PALM COEIN classification and evaluated the causes clinically, sonologically, and pathologically. Leiomyoma was the most common cause clinically, sonologically, and pathologically. AUB-O was the second most common cause clinically, whereas AUB-A is the second most common cause by sonology and histopathology. We attempted to correlate the structural causes of AUB sonologically and pathologically. Correlation was good for leiomyoma. USG has good specificity for the diagnosis of AUB-A and AUB-P but low sensitivity. Hence, it is important not to rule them out based on ultrasound findings alone.

REFERENCES

- Fraser IS, Critchley HO, Broder M, Munro MG. The FIGO recommendations on terminologies and definitions for normal and abnormal uterine bleeding. *Semin Reprod Med* 2011;29:383-90.
- National Institute for Health and Clinical Excellence. Heavy Menstrual Bleeding. London: National Collaborating Centre for Women's and Children's Health, RCOG Press; 2007.
- Marret H, Fauconnier A, Chabbert-Buffet N, Cravello L, Golfier F, Gondry J, et al. Clinical practice guidelines on menorrhagia: Management of abnormal uterine bleeding before menopause. *Eur J Obstet Gynecol Reprod Biol* 2010;152:133-7.
- Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, et al. Stages of reproductive aging workshop (STRAW). *J Womens Health Gend Based Med* 2001;10:843-8.
- Munro MG, Critchley HO, Broder MS, Fraser IS, FIGO Working Group on Menstrual Disorders. FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in nongravid women of reproductive age. *Int J Gynaecol Obstet* 2011;113:3-13.
- National Health Committee. Guidelines for the Management of Heavy Menstrual Bleeding. Christchurch, New Zealand: National Health Committee; 1998.
- Graves EJ. National hospital discharge survey: Annual summary, 1992. *Vital Health Stat* 13 1994;119:1-63.
- Daga S, Phatak S. Sonography evaluation of abnormal uterine bleeding in perimenopausal women with pathological correlation. *J Datta Meghe Inst Med Sci Univ* 2019;14:288-92.
- Mohammed N, Prejisha B. A study of correlation of etiological and histopathological findings in females undergoing hysterectomy for abnormal uterine bleeding in accordance with PALMCOIEN classification. *Paripex. Indian J Rese* 2014;3:76-7.
- Jain P, Arya SB, Pant H, Sinha M, Sah S, Goel R. To study the clinico-pathological correlation in abnormal uterine bleeding. *Int J Clin ObstetGynaecol* 2021;5:111-4.
- Singh A. A study of PALM-COEIN classification of abnormal uterine bleeding (aub) in perimenopausal women at a tertiary care teaching hospital. *J Med Sci Clin Res* 2018;6:287-92.
- Mishra D, Sultan S. FIGO's PALM-COEIN classification of abnormal uterine bleeding: A clinico-histopathological correlation in Indian setting. *J Obstet Gynaecol India* 2017;67:119-25.
- Singh K, Agarwal C, Pujani M, Raychaudhuri S, Sharma N, Chauhan V, et al. A Clinicopathological correlation of international federation of gynecology and obstetrics's PALM-COEIN classification of abnormal uterine bleeding: Indian scenario. *J Midlife Health* 2019;10:147-52.
- Sharma K, Bora MK, Venkatesh BP, Barman P, Roy SK, Jayagurunathan U, et al. Role of 3D ultrasound and doppler in differentiating clinically suspected cases of leiomyoma and adenomyosis of uterus. *J Clin Diagn Res* 2015;9:C08-12.
- Siedler D, Laing FC, Jeffrey RB, Jr, Wing VW. Uterine adenomyosis. A difficult sonographic diagnosis. *J Ultrasound Med* 1987;6:345-9.
- Talukdar B, Mahela SS. Abnormal uterine bleeding in perimenopausal women: Correlation with sonographic findings and histopathological examination of hysterectomy specimens. *J Midlife Health* 2016;7:73-7.
- Khan S, Hameed S, Umber A. Histopathological pattern of endometrium on diagnostic D and C in patients with abnormal uterine bleeding. *Annals King Edward Medical Univ* 2011;17:166-70.
- Uhasai K, Naik D, Rathnamma P. Efficacy of MRI over ultrasound in evaluation of abnormal uterine bleeding with histopathological correlation. *Cureus* 2023;15:e38560.