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Original Research Article

Clinicopathological correlation of abnormal uterine bleeding according to PALM-COEIN classification in reproductive age group in a tertiary care center, North India

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ABSTRACT

Background: AUB is a common problem encountered by women of reproductive age group with increased risk during perimenopausal period. International Federation of Gynecology and Obstetrics (FIGO) has designed a new classification system PALM-COEIN in order to standardize the causes of AUB. Aims and Objectives were to stratify causes of AUB in women of reproductive age group in context to PALM-COEIN classification system. To establish a clinico-pathological correlation among causes of AUB taking aid of radiology wherever required.
Methods: All women of reproductive age group presenting with complaints of AUB in department of gynecology from January 2018 to December 2021 were included in the study. The cause were classified based on PALM-COEIN classification both clinically and histopathologically. Radiological investigation was carried out wherever required.
Results: Total 560 women of reproductive age group were registered. Majority 321 (57.32%) women were between 41-50 years of age and commonest complaint was heavy menstrual bleeding in 401 (71.60%). PALM and COEIN groups accounted for 40% and 60% respectively. Among structural causes, leiomyoma was the commonest cause 153 (27.32%) of AUB whereas among the functional causes most common was endometrial 188 (33.57%). The clinico-histopathological correlation was statistically significant in cases of AUB-P, AUB-A, AUB-O and AUB-E.
Conclusions: The PALM-COEIN classification system helps to understand the causes of AUB and gives simpler terminology, diagnosis and investigations of the causes of AUB and offers better patient management. It can provide better means of quality assurance and appropriateness of treatment.

Keywords: Abnormal uterine bleeding, FIGO, Menorrhagia, PALM-COEIN, Perimenopause

INTRODUCTION

AUB is a common problem encountered by females of reproductive age group which is known to significantly impact the physical, social, and emotional aspects and thus deteriorating the quality of life.[1] 20-30% of females in reproductive age group visiting to the out-patient department of gynecology present with complaint of AUB.[2] According to the International Federation of Gynecology and Obstetrics (FIGO), acute AUB is explained as "an episode of bleeding in a woman of reproductive age, who is not pregnant, that is of sufficient quantity to require immediate intervention to prevent further blood loss." In addition, chronic AUB is defined as "bleeding from the uterine corpus that is abnormal in duration, volume, and/ or frequency and has been present for the majority of the last 6 months".[3] Occurrence of AUB in premenopausal period may cause anemia, whereas in the postmenopausal period, it raises the suspicion of malignancy.[4] The most common clinical complaints of the patients are menorrhagia (heavy menstrual Bleeding), metrorrhagia (inter-menstrual bleeding),

menometrorrhagia (heavy and prolonged menstrual bleeding) and polymenorrhoea (frequent menstrual bleeding).[5] The FIGO working group on menstrual disorders has designed a classification system-PALM COEIN to address the causes of AUB in non-pregnant women of reproductive age. According to this classification the causes of AUB are divided into nine categories which are arranged according to the acronym PALM-COEIN: polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory disorders, endometrial, iatrogenic, and not classified.[5,6]

In initial stages, AUB can be medically managed. Cases which do not respond to medical management can be taken up for minimally invasive surgeries such as endometrial ablation, thermal balloon therapy and uterine artery embolization which provide a good alternative to hysterectomy.[7] However, in developing countries like India due to restricted availability and high-cost of the minimally invasive procedures, hysterectomy remains the most practiced surgical treatment. Histological assessment of the biopsies aids to determine the cause of AUB and guides the clinician to adopt best step towards patient management.[8]

The present study was conducted with the aim to classify the cases of AUB according to PALM-COEIN classification both clinically and histopathologically and to establish a clinicopathological correlation by this classification.

METHODS

The present study was a retrospective cross -sectional hospital-based study conducted in the department of Pathology in collaboration with the department of obstetrics and gynecology in a tertiary care hospital of North India. Detailed data of patients who presented with complaints of AUB over period of 5 years (January 2018 to December 2022) was collected following approval from the ethics committee. The study included 560 non-gravid females who presented with the complaints of AUB.

Inclusion criteria

All non-gravid females in reproductive age group presenting with complaints of AUB to the department of gynecology who underwent endometrial biopsy/hysterectomy.

Exclusion criteria

Women who did not give consent or who did not require endometrial biopsy/hysterectomy were excluded from the study.

The demographic and clinical details of the patients were recorded. Detailed gynecological examination findings including uterus (size, position, consistency, and any growth, cervix (position, polyp, hypertrophy, growth), and adnexa (any mass, tenderness, and mobility) were observed. After forming a clinical diagnosis, each case was clinically categorized according to PALM-COEIN classification. Radiological investigations like ultrasound or other special tests were done in required cases to aid the diagnosis. Endometrial biopsy/hysterectomy was performed as indicated. On histopathology, all the cases were categorized according on the PALM-COEIN classification. A correlation between clinical, radiological and histopathological diagnoses was evaluated.

Data collected was entered into Microsoft Excel worksheets and analysed by using SPSS Version 27. Qualitative data was expressed as frequencies and percentages and chi-square test was used to find association between the variables. The p value <0.05 (<0.01) was considered statistically significant.

RESULTS

The study included 560 females in reproductive age group. 321 (57.32%) of the patients were in perimenopausal age group of 41-50 years. The most common clinical presentation was heavy menstrual bleeding seen in 401 (71.60%) cases (Table 1).

Table 1: Distribution of cases based on symptoms.

Symptoms	No. of cases	%
Heavy menstrual bleeding	401	71.60
Inter-menstrual bleeding	147	26.21
Post-menopausal bleeding	12	2.14

All the cases were categorized clinically according to PALM-COEIN classification. PALM and COEIN groups accounted for AUB in 224 (40%) cases and 336 (60%) cases respectively. Endometrial pathology was found to be the commonest cause of AUB in 188 (33.57%) cases followed by ovulatory dysfunction in 148 (26.43%) cases, leiomyoma in 135 (24.11%) cases, polyp was seen in 58 (10.36%) cases and adenomyosis in 17 (3.04%) cases. AUB-M was seen in 14 (2.50%) cases. Carcinoma endometrium was commonest malignancy reported in 5 (35.71%) cases and carcinoma cervix in 2 (14.28%) cases.

All the cases were classified histopathologically based on PALM-COEIN classification. Among structural causes, most common was AUB-L in 153 (27.32%) cases followed by AUB-P in 70 (12.50%) cases. 26 (4.64%) cases were diagnosed as adenomyosis and 16 (2.86%) cases were categorized under in AUB-M. Out of the cases classified under AUB-M, 8 (50%) cases were reported as hyperplasia without atypia and 1 (6.25%) case was EIN. Most common malignancy was carcinoma endometrium in 5 (31.25%) cases followed by carcinoma cervix in 2 (12.50%) cases which was in complete concordance with clinical and radiological diagnosis. Among functional causes, AUB-E was the commonest seen in 250 (44.64%) cases followed by AUB-O in 45 (8.04%) cases.

Statistically significance result was seen in cases of AUB-P, AUB-A, AUB-O and AUB-E. However, categories AUB-L and AUB-M were statistically insignificant (Table 2).

Table 2: Correlation between clinical and histopathological correlation according to PALM-COEIN classification.

	Category	No. of cases of diagnosed clinically n (%)	No. of cases diagnosed histopathologically n (%)	P value
Structural	AUB-P	58 (10.36)	70 (12.50)	<0.05
	AUB-A	17 (3.04)	26 (4.64)	<0.05
	AUB-L	135 (24.11)	153 (27.32)	>0.05
	AUB-M	14 (2.50)	16 (2.86)	>0.05
Functional	AUB-C	-	-	-
	AUB-O	148 (26.43)	45 (8.04)	<0.05
	AUB-I	-	-	-
	AUB-E	188 (33.57)	250 (44.64)	<0.05
	AUB-N	-	-	-

Among cases classified under AUB-E, most common encountered pathology was secretory endometrium seen in 64 (24.24%) cases. The other endometrial lesions reported were proliferative endometrium in 55 (20.83%) cases, chronic endometritis in 5 (1.89%) cases, benign endometrium with diffuse stromal breakdown in 52 (19.70%) cases and exogenous hormone intake in 51 (19.32%) cases. Hyperplasia without atypia was seen in 8 (3.03%) cases, EIN was seen only in 1 (0.38) case and carcinoma endometrium was seen in 5 (1.89%) cases (Figure 1).

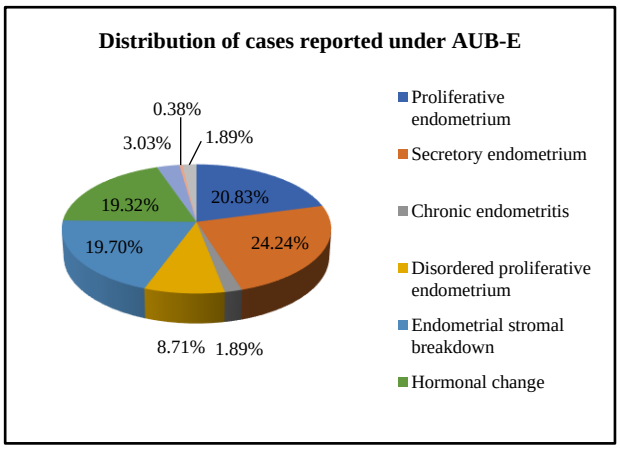

Figure 1: Distribution of cases reported under AUB-E.

A total of 403 (71.96%) cases were investigated radiologically by ultrasonography. Leiomyoma attributed towards the most common cause of AUB in 147 (36.47%) cases closely followed by ovulatory dysfunction in 139 (34.49%) cases. Polyp was reported in 61 (15.13%) cases, adenomyosis was reported in 26 (6.45%) cases Out of 12 (2.97%) cases in category AUB-M, hyperplasia in 5 (41.66%) cases. Carcinoma endometrium was reported in 5 (41.66%) cases and carcinoma cervix in 2 (16.66%) cases.

A strong positive correlation was established among clinical, radiological, and histopathological diagnosis where possible with concordance in cases of malignancy, polyp, and leiomyoma (Figure 2).

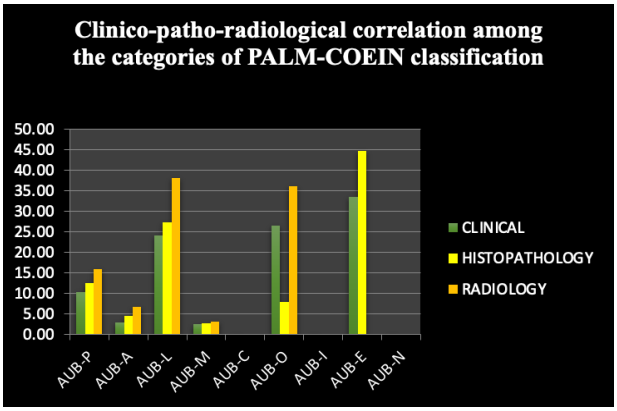

Figure 2: Clinico-patho-radiological correlation among the categories of PALM-COEIN classification.

DISCUSSION

AUB is the commonest condition causing altered quality of life in perimenopausal age group women. FIGO has framed a new classification system PALM-COEIN to standardize definition, nomenclature and causes of AUB.[6,9] Through the present study we have tried to categorize the patients based on PALM-COEIN classification and to correlate the various causes of AUB diagnosed clinically and pathologically. This will further aid in appropriate management of AUB in females.[10,11]

In the present study, most of the patients were in the perimenopausal age group with major complaint being heavy menstrual bleeding which was in concordance with other studies. Age is believed to be an important risk factor for AUB. The risk of occurrence increases over 60% in women aged 45 years.[4,9] The increased risk is attributed to

decline in ovarian function due to depletion of ovarian reserve thus causing anovulatory cycles. The endometrium is under the influence of unopposed estrogen causing proliferation and thus heavy menstrual bleeding. Estrogen excess promotes formation of fibroids, polyps, adenomyosis, endometrial hyperplasia etc that causes various menstrual abnormalities at this age.[12-14]

Perimenopausal period is defined as the period of menstrual transition which usually begins in the late 40s and may extend to late 50s. Bleeding irregularities may present as heavy menstrual bleeding, intermenstrual or post-menopausal bleeding. Leiomyoma was the most common cause of AUB among the PALM category and AUB-O was predominant cause in the COEIN category which was similar to the findings reported in other studies.[9,15,16]

Histopathological examination remains the gold standard which aids in accurate diagnosis of cause of AUB. It carries utmost legal, ethical, diagnostic, and therapeutic significance in these cases.[17]

Leiomyomas are commonly encountered in females with increased incidence with age. Patients present with HMB which may be due to their site, size, increase endometrial surface area, hyperoestrogenemia. AUB-L was predominant finding in our study among the structural causes, clinically as well as on radiology and histopathology which is similar to other studies.[6,9,16,17] Six cases of leiomyoma were missed on radiology which were seen as small intramural fibroids on histopathology.

Polyps were seen in women of all ages but the peak incidence was between 40 to 50 years. Majority of the polyps reported histopathologically in our study were endometrial which was in coherence with radiological diagnosis.[18,19] Most cases of adenomyosis were reported in age group of 40 to 50 years and were seen to be more common in multiparous women which could be due to oestrogen receptor mutations in the adenomyomatous areas and gene polymorphisms.[9,13,16,18]

During perimenopausal period, anovulatory cycles and unopposed estrogen causes endometrium to undergo hyperplasia and consequently into carcinoma endometrium. On histopathology we reported 8 (50%) cases of benign hyperplasia and 1 (6.25%) case of EIN. There were 5 (31.25%) cases of endometrial adenocarcinoma in AUB-M category and 2 (12.5%) cases of carcinoma cervix in this category. Thus, in our study benign hyperplasia was most common entity in category AUB-M which was similar to studies reported by other authors.[20] Both benign hyperplasia and EIN are known to be precancerous lesion of endometrial carcinoma and are reported to be 1-3% in benign hyperplasia and 8-29% in EIN.[16,18,21] All the cases of carcinoma were diagnosed on radiology. Endometrial carcinoma was the most common malignancy in our study which was similar to findings by other authors.[4,14]

In AUB-E we reported more cases based on histopathological diagnosis as compared to clinical. Endometrial pathology has significantly contributed towards cause of AUB histopathologically with occurrence rate of 44.64%. AUB E is considered as diagnosis of exclusion where AUB presents as heavy cyclical menstrual bleeding without any obvious classifiable cause. According to literature, decrease in vasoconstrictor such as endothelin 1 and prostaglandin F2a and increase in vasodilators such as prostaglandin E2 and prostacyclin may lead to menorrhagia.[22] At present there is no authenticated specific routine diagnostic methods available with the clinical to categorize the cases primarily as AUB-E. The most common histopathological finding in the endometrium was secretory endometrium (24.24%) closely followed by proliferative endometrium (20.83%) which was similar to study done by Mishra and Sultan but differed with findings of Jetley et al and Shukla et al where proliferative phase was more common.[9,13,14]

However, less cases were diagnosed under category AUB-O based on histopathology as compared to clinical diagnosis. AUB-O was the second most common cause after AUB-E which was in discordance to study done by Mishra and Sultan.[9] In later reproductive age group there may be unusual disturbed ovulation called 'luteal-out-of phase' (LOOP) events contributing towards AUB. The cases classified under this category included PCOD, hormonal dysfunction, and simple ovarian cysts.[23]

We did not report any cases under category AUB-C, AUB-I and AUB-N in our study, though it was reported by many authors.[24,25]

On analysis of various categories, the difference in clinical and histopathological diagnosis of the categories AUB-L and AUB-M were not statistically significant but was highly significant in categories AUB-P, AUB-A and AUB-O. Histopathologically more cases were categorized under AUB-E which made this category to be statistically significant.

Parulekar has evaluated this new classification system in detail and concluded that dividing the causes into two broad categories- PALM and COEIN- based on visually objective structural criteria and functional criteria does not serve any great purpose. According to him, such grouping shall not change the process of diagnosis and treatment in any significant manner. He also mentioned that malignancy and hyperplasia have not been subcategorized whereas functional ovarian tumors have not been included.[26]

However, the PALM-COEIN classification system has certain advantages. PALM-COEIN being an easy pneumonic has made it easy to recall the causes of AUB. This system also considers multiple etiologies simultaneously and therefore further investigations are required to reach at an accurate diagnosis.[9] This system is accepted worldwide and therefore provides

standardization of the terminologies which can further help in easy communication among the clinicians and thus improve the management as well as prognostication of the patients and shall aid in multi institutional research in AUB.[27]

CONCLUSION

It was concluded that clinico-radio-pathological correlation was good when the cases were classified according to PALM-COEIN classification. Leiomyoma was the commonest cause contributing toward AUB in the perimenopausal females. However, histopathology helped in making accurate diagnosis of the cases which were missed clinically or radiologically. Thus, we concluded that the PALM-COEIN classification is beneficial in categorizing the cases of AUB both clinically and histopathologically that would help in optimizing the patient management.

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