A retrospective study of clinicopathological correlation of abnormal uterine bleeding as per FIGO 2011 PALM- COEIN classification in women who underwent hysterectomy

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Abstract

Background: Abnormal uterine bleeding (AUB) is a common problem affecting the women of reproductive age group and may also have a significant impact on their physical, social, and emotional aspects directly affecting their quality of life. The International Federation of Gynecology and Obstetrics (FIGO) devised a universally acceptable system of nomenclature and classification, namely PALM–COEIN classification of AUB in the year 2011. The objective of the present study was to analyze the structural (PALM) and functional (COEIN) component of FIGO system in the Indian scenario. **Aim and objective:** To study the causes of AUB based on PALM-COIEN classification in women who have underwent hysterectomy at a tertiary care centre, MAPIMS 2. to establish a clinicopathological correlation. COEIN classification in women who underwent hysterectomy. **Methods:** Retrospective study Study setting: Obstetrics and gynaecology department of Tertiary care center. **Study duration:** from 2016 to 2022 **Study population:** All the females of the reproductive age group who presented with AUB to the gynecology clinics whose and underwent hysterectomy. **Sample size:** 300 **Results:** Leiomyoma (30%) was the most common cause of AUB closely followed by adenomyosis (29.66%) overall. The clinicopathological correlation in hysterectomy cases was good with concordance rate of 85.03%. The concordance between clinical and pathological diagnoses for AUB‑ L, AUB‑ A, AUB‑ M, and AUB‑ A, L was statistically significant with $P < 05$ in positive cases. However, additional finding of adenomyosis was diagnosed in 48.2% of the cases apart from primary clinical diagnosis. **Conclusions:** A good clinicopathological correlation was seen in the cases when classified according to PALM–COEIN classification. The system also provides for consideration of multiple etiologies contributing toward AUB both clinically and histopathologically. However, histopathology remains the cornerstone in establishing the accurate diagnosis as the cases without specific symptoms can be missed clinically.

Keywords: Abnormal uterine bleeding, FIGO, Hysterectomy, PALM–COEIN

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Introduction

Abnormal uterine bleeding (AUB) is a common problem affecting the women of reproductive age group and may also have a significant impact on their physical, social, and emotional aspects directly affecting their quality of life.[1] AUB is a bleeding pattern differing from normal menstrual pattern or after menopause in frequency, duration, and amount of blood flow.[2]

According to the International Federation of Gynecology and Obstetrics (FIGO), acute AUB could be classified as "an episode of bleeding in a woman of reproductiveage, who is not pregnant, that is of sufficient quantity to require immediate intervention to prevent further blood

loss." In addition, chronic AUB is "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] In the premenopausal period, it may cause anemia, and in the postmenopausal period, it may raise the suspicion of malignancy.[4]

AUB is the result of diverse structural and functional etiologies. Due to controversial and nonuniform nomenclature and a lack of standardized methods for investigation and etiological categorization, the investigation and management of AUB patients is greatly affected. To circumvent this, FIGO devised a universally acceptable system of nomenclature and classification, namely PALM–COEIN classification of AUB in 2011.[5]

PALM–COEIN classification includes nine main categories: polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified. PALM aspect of the classification refers to structural causes that may be evaluated by imaging techniques and/ or histopathology; however, COEIN group represents functional aspect.[5]

The definitive treatment of AUB is hysterectomy; however, the less invasive options are also available which include medical therapy and endometrial ablation.[5,6] Moreover, when planning a hormonal therapy, it is essential to rule out precancerous conditions such as hyperplasia or subclinical endometrial cancer.[7]

The PALM–COEIN system aids in classification of women with AUB in a systemic manner which in turn is useful for both the clinicians and researchers in providing reliable information for research like epidemiological and prevalence studies along with accurate diagnosis and treatment.

This system also helps in selecting appropriate treatment for the women with different patterns of menstrual bleeding as well.[3] Histological assessment remains the cornerstone in the current practice in patients of AUB as it clinches the diagnosis and guides the correct management plan.

Aim & Objective:

1. To study the causes of AUB based on PALM-COIEN classification in women who have underwent hysterectomy at a tertiary care centre, MAPIMS
2. To establish a clinicopathological correlation as per PALM COEIN classification in women who underwent hysterectomy

Material and Methods

Study design: Retrospective study, **Study setting:** Obstetrics and gynecology department of Tertiary care center. **Study duration:** from 2016 to 2022 **Study population:** All the females of the reproductive age group who presented with AUB to the gynecology clinics and underwent hysterectomy.

Sample Size: 300
Inclusion criteria:
1. All the females of the reproductive age group who presented with AUB to the gynecology clinics and underwent hysterectomy was performed were included in the study

Exclusion criteria
2. Women who underwent hysterectomy for uterovaginal prolapse
3. Women who underwent cesarean hysterectomy

Study procedure: The demographic and clinical details of the patients were recorded including history of previous and current menstrual history, obstetric history, history of contraceptive use, other comorbid conditions, and general as well as systemic examination. Detailed gynecological examination findings including cervix (position, any polyp, hypertrophy, growth, etc.,), uterus (size, position, consistency, and any lump), and adnexa (any mass, tenderness, and mobility) were observed.

After arriving at a clinical diagnosis, each case was allocated to a category according to PALM–COEIN classification. Wherever indicated, ultrasound or other special tests were done to aid the diagnosis. Endometrial biopsy/hysterectomy (whichever indicated) was performed. On histopathology, all the cases were categorized based on the PALM–COEIN classification.

A correlation between clinical and histopathological diagnoses was evaluated.

Data Analysis: Data were analyzed using SPSS software (IBM SPSS software version 21.0. IBM Corp., Armonk, NY, USA) and results expressed as percentages, bar diagrams, and pie charts. McNemar's test was applied for concordance between clinical and pathological findings. $P < 0.05$ was considered statistically significant.

Result And Observations
The study included 300 patients in the reproductive age group. Most of the patients were in the perimenopausal age group of 41–50 years (56%), with a mean age of 41 years, and menorrhagia was the most common complaint. Of the total 300 cases, there were 147 cases ofhysterectomy where a clinicopathological correlation for the structural causes was done.

The maximum number of AUB cases according to the PALM–COEIN classification belonged to the category AUB‑L (30%) closely followed by AUB‑A (29.66%) overall. Among the functional causes, ovulatory disorders (AUB‑O) were the most common (26.66%) followed by endometrial (AUB‑E) causes (15%) [Table 1].

Table 1: Distribution of cases according to PALM‑COEIN classification on histopathology

Category	Number of cases ($n=300$), n (%)
P (including P, A; P, A, L)	21 (7)
A (including A, L; P, A)	89 (29.66)
L (including A, L)	90 (30)
M	13 (5)
O	80 (26.66)
E	45 (15)
P, A	7 (2.33)
A, L	42 (14)
AUB‑ P, A, L	1 (0.33)
AUB‑ P, L	3 (1)
AUB: Abnormal uterine bleeding	

Most of the cases were reported as secretory endometrium (42%) followed by proliferative endometrium (40%) in histopathology. Disordered proliferative endometrium also contributed toward AUB with a percentage of 12%. Granulomatous and chronic endometritis was also reported in 1% of cases each [Figure 1]. AUB‑P accounted for 7% of the total 300 cases, and of these, 12 cases were diagnosed in hysterectomy specimen and the rest in the endometrial biopsy specimen.
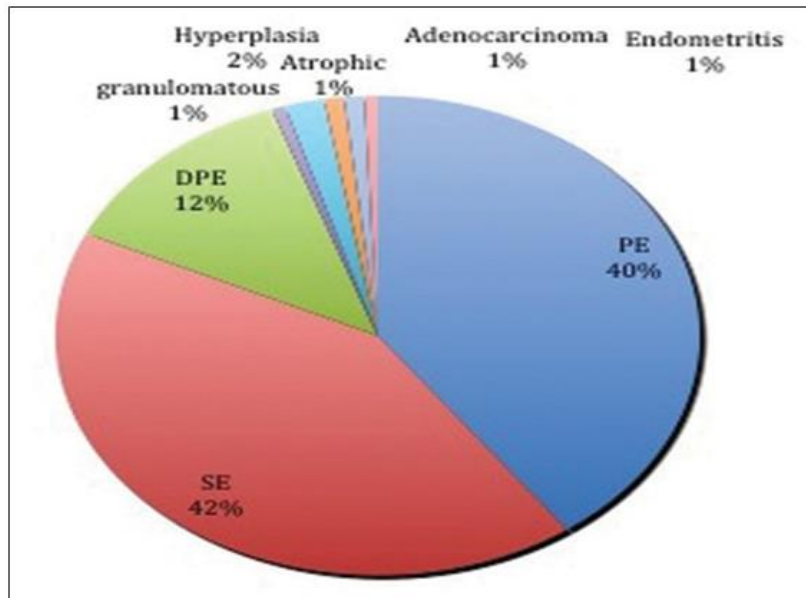

Figure 1: Distribution of cases according to endometrial findings

AUB‑M included 5% of the total cases with simple hyperplasia constituting the maximum number of cases (31% of cases in AUB‑M), and the endometrioid carcinoma was the most common malignancy reported (23% of cases in AUB‑M), with an incidence of 1.3% (4/300). Two cases of complex hyperplasia (15% of cases in AUB‑M) were reported which were not suspected clinically, and both the cases showed atypia on histopathology [Figure 2]. Dual pathology AUB‑A, L; AUB‑A, P; and AUB‑P, L were reported in 14%, 2.33%, and 1% of the cases, respectively. A single case was also reported as AUB‑P, A, L on histopathology of the hysterectomy specimen. The histopathological features of structural causes of AUB are depicted in Figures 3.
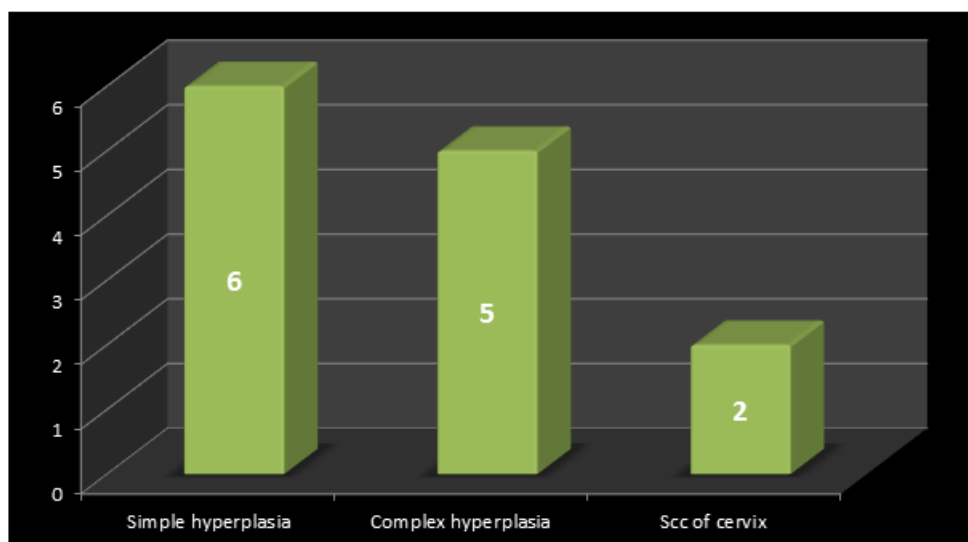
Figure 2: Distribution of cases in abnormal uterine bleeding‑ M category

Out of the 147 cases of hysterectomy, the clinical and pathological results were concordant in 85.03%. The concordance rates in the clinical and pathological diagnosis in the cases of AUB‑ P, AUB‑ A, and AUB‑ L were good with 90%, 90.9%, and 91%, respectively. However, the results were statistically significant in the case of AUB‑ A and AUB‑ L with $P < 0.05$ [Table 2].

Table 2: Correlation of clinical and histopathological diagnosis

Classification	Clinical diagnosis (total number of cases, $n=147$)	Histopathological diagnosis (total number of cases, $n=147$)	Concordance between clinical and histopathological diagnosis in positive cases (%)	P
AUB‑ P (including P, A; P, A, L; P, L)	9	12	90	0.63
AUB‑ A (including P, A; P, A, L; E, A)	30	85	90.9	<0.001
AUB‑ L (including A, L; P, A, L; P, L)	81	88	91	<0.001
AUB‑ M	18	10	55.6	0.008
AUB‑ P, A	1	7	0	0.125
AUB‑ A, L	11	42	73.3	<0.001
AUB‑ P, A, L	0	1	0	
AUB‑ P, L	3	3	75	1.0
AUB‑ E (including E, A)	0	7	0	0.18
AUB‑ E, A	0	3	0	
AUB: Abnormal uterine bleeding				

Supplementary findings on histopathology were detected in 65 cases which were missed clinically with AUB‑A being the most common entity. An additional diagnosis of adenomyosis (AUB‑A) was given on histopathology in 55 cases (48.2%) apart from the primary clinical diagnosis. The clinicopathological concordance rates were moderately fair in AUB‑P, L; AUB‑A, L; and AUB‑M with a percentage of 75%, 73.3%, and 55.6%, respectively.

In AUB‑M clinically, more number of cases were suspected (18 cases); however, only 10 cases were confirmed histopathologically. This might explain the lower concordance rate in AUB‑M [Table 2]. The clinicopathological concordance, however, was statistically significant in cases of AUB‑A, L and AUB‑M with $P < 0.001$ and 0.008, respectively. Clinicopathological correlation of PALM component in hysterectomy cases is depicted graphically in Figure 4.
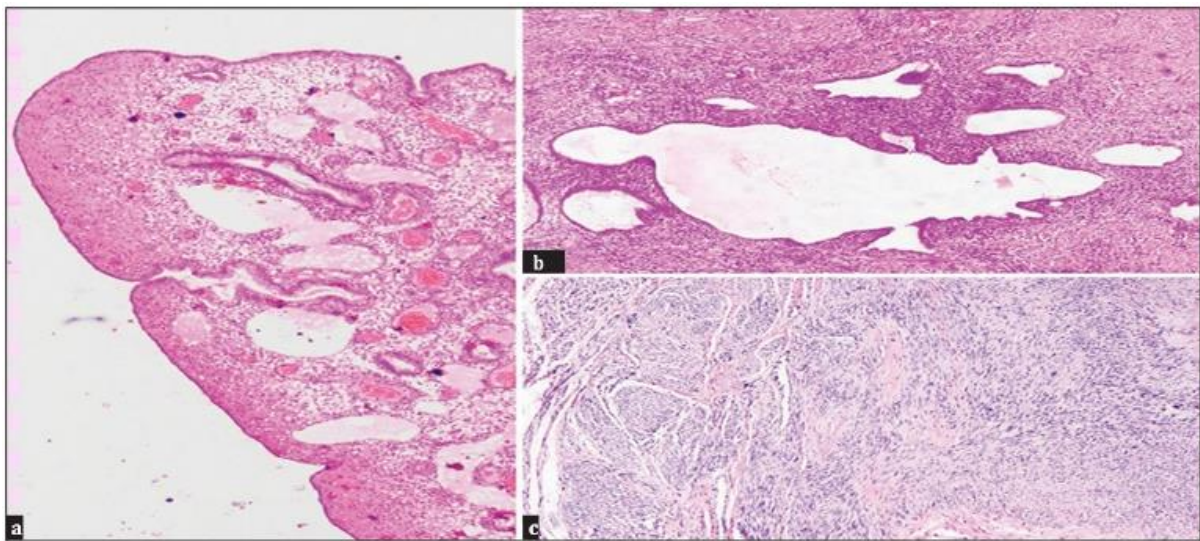

Figure 3: (a) A polyp lined on all sides by columnar epithelium and glands with dilated blood vessels in the stromal matrix (H and E, ×40), (b) adenomyosis with endometrial glands and stroma in the myometrium (H and E, ×40), (c) leiomyoma with a capsule.
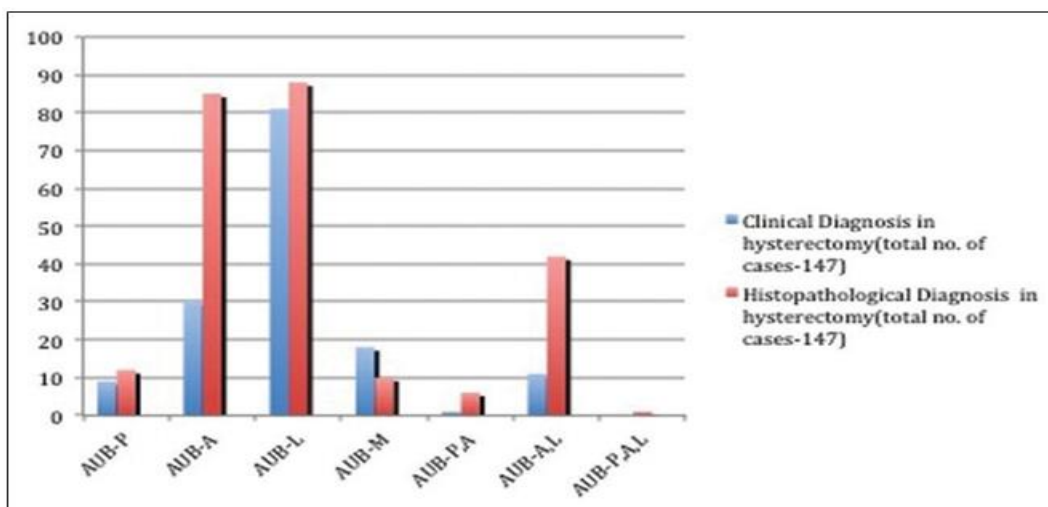**interlacing smooth muscle bundles (H and E, ×40)**

Figure 4: Graphic representation of clinicopathological correlation of PALM component in hysterectomy cases

Discussion

In the present study, most of the patients were in the perimenopausal age group (41–50 years), and the major complaint was menorrhagia which was in accordance with other researchers.[1,2,4,7] A total of 300 cases including 147 cases of hysterectomy were included in the study, and a clinicopathological correlation was done in the hysterectomy cases for structural component (PALM). We found that leiomyoma (AUB‑L 30%) was the most common cause of AUB closely followed by adenomyosis (AUB‑A, 29.66%) which was in accordance with studies by other authors.[7‑10]

Age is suggested to be an important risk factor with a lifetime risk more than 60% in women with age over 45 years.[7‑9] Ovulatory disorders with a share of 26.66% were the most common cause of AUB in the functional category (COEIN) in our study which was similar to findings of Mishra and Sultan.[7] In the later reproductive years, there may be unusual disturbed ovulations labeled as "luteal out‑of‑phase" events contributing toward AUB.[11]

In our study, AUB‑E has also contributed as a significant cause of AUB with 15% of the cases in histopathology. AUB‑E is a diagnosis of exclusion where AUB occurs with predictable and cyclic menstrual bleeding and without any definable cause. The deficiency in locally produced vasoconstrictors such as endothelin‑1 and prostaglandin F2a and increased vasodilators such as prostaglandin E2 and prostacyclin may lead to heavy menstrual bleeding. However, the tests are not yet available to clinicians for evaluating such abnormalities.[11]

The most common histopathological finding in the endometrium was secretory endometrium (42%) closely followed by proliferative endometrium (40%) which was similar to Mishra and Sultan.[7] (secretory – 41.52% and proliferative –‑ 37.28%) but differed with findings of Jetley et al.,[2] Deka et al.,[12] and Shukla et al.[8] where proliferative endometrium was most common. However, the percentage of cases of proliferative endometrium was similar with Deka et al.[12] (37%) but lower cases with secretory endometrium (18%). Mishra and Sultan.[7] also had reported similar percentages with atrophic endometrium as 2.1%.

A clinicopathological correlation for structural causes was done in 147 cases of hysterectomy. The correlation was good with consistent results in 80.95% of cases; however, histopathology aided in the diagnosis in16/147 (10.88%) cases where no diagnosis was offered by the clinician. Mishra and Sultan.[7] had also studied the two components of this system in clinical practice and clinicopathological correlation of AUB with context of PALM component in particular in 236 perimenopausal women. In their study, PALM and COEIN components contributed almost equally for AUB when assessed clinically; however, histopathology revealed significantly more cases of PALM (structural or anatomical) component of AUB similar to our study where we found more structural than functional causesin histopathology (175/300 vs. 125/300).

We found that major proportion of cases included AUB‑L and most of the cases diagnosed clinically were confirmed histopathologically which was statistically significant ($P < 0.05$) [Table 2]. This could be explained on the basis that leiomyoma can be easily diagnosed in clinical examination and radiological investigations. A similar finding was reported by Mishra and Sultan.[7]

In the category AUB‑A, the clinical diagnosis was confirmed histopathologically which was statistically highly significant ($P < 0.001$); however, additional 55 (48.2%) cases were diagnosed histopathologically which were missed clinically. Similar findings with more number of cases with adenomyosis detected on histopathology have also been reported by other researchers.[7,10] Adenomyosis may be easily missed clinically due to lack of specific signs and symptoms.[7,13]

All the 9 cases of AUB‑P diagnosed clinically were confirmed histopathologically with additional 3 cases reported in histopathology. Thus, the concordance rate in histopathological diagnosis was 90%; however, the number of cases was few; therefore, no statistical significance could be established. This was similar to a study by Mishra and Sultan.[7] where the clinical and histopathological findings were similar but differed with findings of Khan et al.[10] where they have reported a significant difference in the clinical and histopathologicalfindings in case of AUB‑P.

Coexistent cases of AUB‑A, L and AUB‑P, A were noted in 27.89% and 4.76% of hysterectomy cases, respectively, and almost all the cases were diagnosed on histopathology which were missed clinically. Our finding was in accordance with other studies where they found more number of cases in histopathology than clinically.[7,13]

Simple hyperplasia without atypia was the most common entity in AUB‑M with a percentage of 27%. Other authors have also reported similar findings with simple hyperplasia without atypia being most common.[14] The clinicopathological concordance was highly significant statistically with $P = 0.008$ as all the 10 cases had a positive clinicopathological correlation. However, Mishra and Sultan.[7] had reported a difference in the clinical and histopathological findings.

Both simple hyperplasia and complex hyperplasia with or without atypia are known to be precancerous lesion of endometrial carcinoma and are reported to be 1%–3% in hyperplasia without atypia and 8%–29% in hyperplasia with atypia.[15] Endometrial carcinoma was the most common type of malignancy reported in our study with an incidence of 1% which was similar to findings byother authors.[4,8,12]

Parulekar critically evaluated this new system and opined that dividing causes into two broad categories – PALM and COEIN – based on visually objective structural criteria and criteria unrelated to structural abnormalities did not serve any great purpose. According to him, such grouping does not change the process of diagnosis and treatment in any way. He further stated that malignancy and hyperplasia have not been subcategorized while functional ovarian tumors have not been included.[16]

The PALM–COEIN system, however, has certain advantages. PALM–COEIN being an easy pneumonic has made the causes of AUB easy to remember.[17] The system also provides for consideration of multiple etiologies simultaneously, and thus, further investigations are required to reach at a more accurate diagnosis.[7] This system is applicable globally, and thus, a standardized universal terminology provided by this system would help in easier communication among the clinicians and thus effective management as well as prognostication of the patients and also would help in multi‑institutional research and education in AUB.[17,18]

Conclusion

According to our study, we found that the clinicopathological correlation was good when the cases were classified under PALM–COEIN classification and leiomyoma was the most common etiology contributing toward AUB in the perimenopausal age group.

The consideration of multiple etiologies in this system also helped in reporting of dual pathology such as AUB‑A, L and AUB‑A, P in our study. Histopathology, however, helped in accurate diagnosis of few cases missed clinically including a handful of cases misdiagnosed as some different pathology. Thus, we found that PALM–COEIN classification is a useful system clinically and histopathologically as both are complementary to each other and allocating a proper category would help in optimization of the treatment of the patient.

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