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Evaluation of Clinical, Radiological and Histopathological Spectrum of Abnormal Uterine Bleeding and Its Clinico-Pathological Correlation as Per International Federation of Gynaecology and Obstetrics (FIGO) PALM-COEIN Classification – A Descriptive Study in Tertiary Care Centre in Rural Area

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A B S T R A C T

Introduction*:** The most prevalent menstruation problem during the perimenopause is abnormal uterine bleeding (AUB). A method of categorization (PALM–COEIN) for the etiology of the AUB in non-gravid women has been created by the International Federation of Gynecology and Obstetrics working group on menstrual disorders. The current study's objectives were to investigate the two parts of this system in clinical practice generally and, in particular, to demonstrate a clinico-pathological association between the AUB and the PALM component. ***Materials and Method*:** This study was conducted on 100 perimenopausal women with symptoms of abnormal uterine bleeding. The subjects were aged 40 years and above and till one year after menopause. A clinical diagnosis was established using the PALM–COEIN classification following a comprehensive history and examination, followed by pelvic ultrasound.Analysis was done on the relative contributions of the different causes of the structural (PALM) and functional (COEIN) components. Histology evaluated the hysterectomy specimen and endometrial sample following all recommended investigations. A statistical analysis was performed on a clinicopathological connection. ***Results*:** When evaluated clinically, the contributions of the COEIN and PALM components to AUB were almost identical. Conversely, the histological analysis demonstrated a notably higher number of instances of the PALM (structural) component of AUB, namely 63%versus 48% ($p < 0.05$). AUB-L was the most prevalent (43%) aetiology overall. The discrepancy was primarily explained by the discovery of more instances of AUB-M (malignancy and hyperplasia) in highly significant proportions ($p \leq .01$) and coexisting cases of AUB-A;L.Conclusion*:** Since the two diagnostic modalities are complementary, the PALM–COEIN classification system should consider both the clinical and histological diagnoses in women with AUB around perimenopause. This will optimize the outcome by placing the clinical impression in the appropriate context of the classification.

Keywords: AUB, PALM COEIN, perimenopause.

INTRODUCTION

Abnormal uterine bleeding (AUB) refers to irregularities in the menstrual cycle, including issues with frequency, regularity, duration, or volume of flow, excluding pregnancy [1]. AUB is a common reason for women, particularly those of reproductive or peri-/postmenopausal age, to seek gynecological care [2-4]. It affects up to 30% of women at some point, potentially leading to anemia in premenopausal women and concerns about malignancy in

postmenopausal women. AUB impacts various aspects of a woman's life, including physical, emotional, and social well-being, and contributes significantly to absenteeism from work and healthcare costs.

The causes of AUB are categorized into structural (e.g., polyps, fibroids, adenomyosis, endometrial hyperplasia, malignancy) and nonstructural (e.g., coagulopathy, ovulatory dysfunction, iatrogenic factors) under the "PALM-COEIN" classification by FIGO. Diagnosis often involves a combination of medical history, physical examination, imaging, and endometrial sampling. Transvaginal sonography (TVS) is a key non-invasive diagnostic tool, helping to assess uterine pathology and endometrial thickness, with further tests required when abnormalities are detected.

Recent advancements include the use of color Doppler and hysteroscopy, which improve diagnostic accuracy and treatment planning. Hysteroscopy, in particular, allows direct visualization of the uterine cavity and can replace traditional diagnostic procedures like D&C. This study aims to assess the prevalence of AUB causes in perimenopausal women using FIGO's PALM-COEIN classification, integrating clinical, ultrasound, and histopathological findings to enhance diagnosis and management.

Review of Literature

Abnormal uterine bleeding (AUB) is a common clinical issue with a variety of potential causes. A thorough understanding of menstrual physiology and a careful history and evaluation are crucial in diagnosing and managing AUB.

Menstrual Physiology:

The menstrual cycle consists of two main phases:

Proliferative Phase (Days 5–14):

The endometrium becomes thick and shows a trilaminar (three-layered) pattern, with a thickness of 12–13 mm during ovulation.

Secretory Phase (Days 15–28):

The endometrium reaches a maximum thickness of 16–18 mm in response to estrogen and progesterone, preparing for potential implantation of a conceptus.

If pregnancy does not occur, the corpus luteum degenerates, leading to a decrease in estrogen and progesterone, which causes the endometrium to shed—initiating menstruation.

Hormonal Influence:

The sequence and timing of hormone levels—estrogen followed by estrogen and progesterone, and then their withdrawal—play a critical role in regulating the menstrual cycle. This process ensures the development of a stable and predictable endometrium, which results in a regular menstrual pattern. Even slight deviations in this sequence can cause menstrual irregularities, which are concerning for AUB.

Normal Menstrual Characteristics:

Cycle length: 24–38 days
Duration of flow: 4–8 days
Blood loss: 5–80 mL per cycle

Types of Abnormal Uterine Bleeding:

AUB can be categorized into different patterns:

Menorrhagia: Heavy or prolonged periods (>7 days or >80 mL of blood loss).
Metrorrhagia: Bleeding between expected menstrual periods, occurring over several cycles.
Menometrorrhagia: Excessive bleeding at irregular intervals.
Polymenorrhea: Frequent periods with intervals <24 days.
Oligomenorrhea: Infrequent periods with intervals >35 days.
Amenorrhea: Absence of periods for 90 days or more in women of reproductive age.
Intermenstrual Bleeding: Bleeding between regular cycles.
Postmenopausal Bleeding: Bleeding more than 12 months after the last menstrual period.

New Terminology for AUB:

The **International Federation of Gynecology and Obstetrics (FIGO)** proposed a revised classification of AUB in 2018. This update introduced standardized terminology to better define various menstrual patterns and AUB categories.

Parameter	Normal	Abnormal	☑
Frequency	Absent (no bleeding) = amenorrhea		☐
	Infrequent (>38 days)		☐
	Normal (≥24 to ≤38 days)		☐
	Frequent (<24 days)		☐
Duration	Normal (≤8 days)		☐
	Prolonged (>8 days)		☐
Regularity	Normal or "Regular" (shortest to longest cycle variation: ≤7-9 days)*		☐
	Irregular (shortest to longest cycle variation: ≥8-10 days)*		☐
Flow Volume (patient determined)	Light		☐
	Normal		☐
	Heavy		☐

Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses	None		☐
	Random		☐
	Cyclic (Predictable)	Early Cycle	☐
		Mid Cycle	☐
		Late Cycle	☐

Unscheduled Bleeding on Progestin ± Estrogen Gonadal Steroids (birth control pills, rings, patches or injections)	Not Applicable (not on gonadal steroid medication)	☐
	None (on gonadal steroid medication)	☐
	Present	☐

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In summary, a thorough understanding of normal menstrual physiology and the accurate categorization of AUB types are essential for diagnosing and managing abnormal uterine bleeding effectively.

The etiology of abnormal uterine bleeding (AUB) is multifactorial, and to address this complexity, the Menstrual Disorders Working Group of the International Federation of Gynecology and Obstetrics (FIGO) developed the **PALM-COEIN** classification system for AUB. This system, supported by the American College of Obstetricians and Gynecologists, categorizes the causes of AUB into two main groups:

Uterine Structural Abnormalities (PALM):
- **P**: Polyps
- **A**: Adenomyosis
- **L**: Leiomyoma (fibroids)
- **M**: Malignancy and Hyperplasia

Non-Structural Abnormalities (COEIN):
- **C**: Coagulopathy
- **O**: Ovulatory dysfunction
- **E**: Endometrial
- **I**: Iatrogenic (caused by medical treatment)
- **N**: Not classified (causes that don't fit into other categories)

This classification helps in identifying the specific underlying cause of AUB, which can range from structural issues, like polyps or fibroids, to non-structural causes, such as hormonal imbalances or blood clotting disorders. The classification streamlines diagnosis and management by offering a clear framework for understanding and categorizing the various factors that contribute to abnormal uterine bleeding.

In 2017, Singh K *et al*., studied 300 women with abnormal uterine bleeding (AUB) at a hospital in Faridabad, using the PALM-COEIN classification. The study found **leiomyoma** (30%) and **adenomyosis** (29.66%) as the most common causes of AUB. The clinicopathological correlation in hysterectomy cases was high, with an **85.03%**

concordance rate. Statistically significant concordance was found for diagnoses of AUB L, AUB A, and AUB A, L (**P < 0.05**). Additionally, **adenomyosis** was identified in **48.2%** of cases not initially diagnosed. The study concluded that PALM-COEIN offers a reliable classification system and underscores the importance of histopathology in accurately diagnosing AUB.

Mishra D *et al*., conducted a study in 2016 on 236 perimenopausal women with abnormal uterine bleeding (AUB) to assess the clinical and histopathological application of the PALM-COEIN system. Their findings showed that both PALM and COEIN components contributed equally to the clinical diagnosis of AUB, but histopathology revealed a higher proportion of PALM (structural) causes (50.23% clinically vs. 63.98% histologically, **p ≤ 0.05**). Notably, **AUB-M** (malignancy and hyperplasia) was more frequently detected, along with coexistent **AUB-A** and **AUB-L**. **AUB-L** was the most common cause (41.1%). The study concluded that both clinical and histopathological assessments are essential for accurate diagnosis of AUB, especially in perimenopausal women, as they complement each other.

Kitahara *et al.,* (2023) reported a nationwide study in Japan that included a total of 8081 AUB patients of whom, "39.9% had abnormal menstrual cycles and 56.9% had abnormal menstrual bleeding. In the survey, PALM had the highest percentage of AUB-L and COEIN had the highest percentage of AUB-O. Correspondence analysis showed that COEIN was strongly associated with abnormal menstrual cycles and PALM with abnormal menstrual bleeding"

Material and Method

It was a prospective descriptive study conducted at Department of Obstetrics and Gynecology, Dr KNS Memorial Institute of Medical Sciences, Barabanki for a period of 18months after approval from institutional ethics committee. The study group included patients presenting in Gynecological OPD with the chief complain of abnormal uterine bleeding.

Inclusion Criteria

1. Women attended Gynecology OPD with complain of Abnormal uterine bleeding and willing to participate in the study
2. Age more than 40 years and till one year after the menopause.

Exclusion Criteria: Women less than 40 years of age and those beyond 1 year of menopause

Method of Data Collection

The study collected socio-demographic and medical details, including menstrual, obstetric, contraceptive, and surgical history. A general and gynecological examination was performed, followed by a pelvic ultrasound to assess the uterus and adnexa. Relevant blood tests, including a complete blood count, thyroid function, and coagulation profile, were conducted. Endometrial biopsy, diagnostic curettage, or hysterectomy was done as necessary. The findings were classified according to the PALM-COEIN system, and a clinicopathological correlation was made between clinical diagnosis and histopathology.

Statistical Analysis

The data collected was tabulated in Microsoft Excel Worksheet and computer-based analysis was performed using the Statistical Product and Service Solutions (SPSS) 20.0 software (SPSS, Chicago, Illinois, USA) and Microsoft Excel 2010. The categorical variables were summarized as proportions and percentages.

RESULTS

The study primarily involved women aged 39-47 years, with an average age of 44.7 years. Most participants (66%) lived in rural areas, and 89% had a normal BMI. The majority were housewives (66%) and literate (82%). Socio-economically, 82% belonged to lower income groups. Obstetrically, 58% were multiparous, with a majority having a 10-20-year gap since their last childbirth. The most common symptoms were heavy menstrual bleeding (31%) and frequent menstrual bleeding (26%). Dysmenorrhea with heavy menstrual bleeding occurred in 19% of cases, while 81% had no such symptoms.

In the study, 48% of women had symptoms for 6-12 months, 29% for 1-6 months, and 23% for over 12 months. Regarding risk factors, 11% were obese, 7% hypertensive, 4% had thyroid issues, 2% had diabetes, 1% had a history of PCOS, and 78% had no risk factors. Clinical diagnosis using the PALM classification showed that structural causes (PALM) accounted for 48%, with Leiomyoma (AUB-L) as the primary etiology in 38% of cases. The COEIN components accounted for 52%, with ovulatory disorders (AUB-O) being the most common in 38% of cases. Ultrasound-based diagnosis showed PALM components at 57%, with Leiomyoma (AUB-L) as the major cause in 31%. In terms of

procedures, 48% of women underwent hysterectomy, 33% had endometrial aspiration, and 19% underwent hysteroscope-guided D&C.

It also showed that 39% of women had secretory alterations and 34% had proliferative changes on histopathology. Endometrial hyperplasia with or without atypia was found in 1% of women. Histopathology revealed that structural (PALM) causes accounted for 63% of AUB cases, which was 15% higher than clinical diagnoses. For non-structural (COEIN) causes, AUB-O and AUB-E were evaluated histologically, contributing to 31% of overall AUB cases. Clinical diagnoses were significantly higher than histopathology for AUB-E (13% vs. 4%). However, histopathology diagnosed more cases of AUB-A, AUB-M, and combined adenomyosis and leiomyoma. In comparison with ultrasound (USG) findings, histopathology identified more cases of AUB-O and AUB-E. No significant difference was found for other categories (AUB-P, AUB-A, AUB-L, AUB-M, AUB-C, AUB-I, and AUB-N).

Table 1: Sociodemographic details

Age Group *(in years)*	**Number *(n)***	**Percentage *(%)***
39–43	42	42.00
44–47	31	31.00
48–51	27	27.00
TOTAL	100	100.00
Mean ± S.D.	44.81	3.57
Locality (Residence)		
Urban	34	34.00
Rural	66	66.00
BMI (Kg/m^2)		
Underweight (<18.50)	0	0.00
Normal (18.50–24.99)	89	89.00
Overweight (25.00–29.99)	9	9.00
Obese (≥ 30.00)	2	2.00
Occupational Status		
House Wife	66	66.00
Teacher	14	14.00
Office Job	11	11.00
ASHA Worker	3	3.00
Daily Wage Earner	6	6.00
Educational Status		
Illiterate	18	18.00
Class 1 to 5/Primary School	1	1.00
Class 6 to 10/High School	43	43.00
Class 12/Higher Secondary	12	12.00
Graduate	20	20.00
Postgraduate	6	6.00
Socioeconomic Status		
Upper	3	3.00
Upper Middle	15	15.00
Lower Middle	19	19.00
Upper Lower	27	27.00
Lower	36	36.00
Parity		
0	1	1.00
1	4	4.00
2	13	13.00
3	24	24.00
4 or more	58	58.00
LCB *(in years)*		
<10	7	7.00
10–20	88	88.00
>20	5	5.00
Living issue		

0	1	1.00
1	4	4.00
2	40	40.00
3	34	34.00
4 or more	21	21.00
Abortion		
0	72	72.00
1	16	16.00
2 or more	12	12.00
Presenting Symptoms		
Frequent Menstrual Bleeding	26	26.00
Heavy Menstrual Bleeding	31	31.00
Intermenstrual Bleeding	10	10.00
Heavy Prolonged Menstrual Bleeding	21	21.00
Prolonged Menstrual Bleeding	11	11.00
Dysmenorrhoea		
Dysmenorrhoea with HMB	19	19.00
Dysmenorrhoea without HMB	81	81.00

Table 2: Distribution of Study Subjects According to PALM-COEIN as Per Clinical Diagnosis

Clinical Diagnosis	**Number *(n* = 100*)***	**Percentage *(%)***
PALM:		
▪ AUB-P (polyp)	4	4.00
▪ AUB-A (adenomyosis)	4	4.00
▪ AUB-A;L (adenomyosis and leiomyoma)	0	0.00
▪ AUB-L (leiomyoma)	38	38.00
▪ AUB-M (malignancy and hyperplasia)	2	2.00
COEIN:		
▪ AUB-C (coagulopathy)	0	0.00
▪ AUB-O (ovulatory disorders)	38	38.00
▪ AUB-I (iatrogenic)	1	1.00
▪ AUB-E (endometrial)	13	13.00
▪ AUB-N (not yet classified)	0	0.00

Table 3: Distribution of Study Subjects According to PALM-COEIN as Per Usg-Based Diagnosis

USG-based Diagnosis	**Number *(n* = 100*)***	**Percentage *(%)***
PALM:		
▪ AUB-P (polyp)	3	3.00
▪ AUB-A (adenomyosis)	6	6.00
▪ AUB-A;L (adenomyosis and leiomyoma)	4	4.00
▪ AUB-L (leiomyoma)	31	31.00
▪ AUB-M (malignancy and hyperplasia)	13	13.00
COEIN:		
▪ AUB-C (coagulopathy)	0	0.00
▪ AUB-O (ovulatory disorders)	0	0.00
▪ AUB-I (iatrogenic)	0	0.00
▪ AUB-E (endometrial)	0	0.00
▪ AUB-N (not yet classified)	0	0.00

Table 4: Distribution Of Study Subjects According to PALM-COEIN as Per Histopathology Based Diagnosis

Histopathology-based Diagnosis	**Number *(n* = 100*)***	**Percentage *(%)***
PALM:		
▪ AUB-P (polyp)	3	3.00
▪ AUB-A (adenomyosis)	8	8.00
▪ AUB-A;L (adenomyosis and leiomyoma)	3	3.00
▪ AUB-L (leiomyoma)	43	43.00
▪ AUB-M (malignancy and hyperplasia)	6	6.00

COEIN:		
▪ AUB-C (coagulopathy)	0	0.00
▪ AUB-O (ovulatory disorders)	27	27.00
▪ AUB-I (iatrogenic)	0	0.00
▪ AUB-E (endometrial)	4	4.00
▪ AUB-N (not yet classified)	0	0.00

Table 5: Correlation of Clinical and Histopathology-based Diagnosis

Diagnosis	**Clinical-based Diagnosis**		**Histopathology-based Diagnosis**		***p value****
	n	***%***	***n***	***%***	
PALM:					
▪ AUB-P (polyp)	4	4.00	3	3.00	0.680
▪ AUB-A (adenomyosis)	4	4.00	8	8.00	0.248
▪ AUB-A;L (adenomyosis and leiomyoma)	0	0.00	3	3.00	0.081
▪ AUB-L (leiomyoma)	38	38.00	43	43.00	0.471
▪ AUB-M (malignancy and hyperplasia)	2	2.00	6	6.00	0.149
COEIN:					
▪ AUB-C (coagulopathy)	0	0.00	0	0.00	–
▪ AUB-O (ovulatory disorders)	38	38.00	27	27.00	0.097
▪ AUB-I (iatrogenic)	1	1.00	0	0.00	0.219
▪ AUB-E (endometrial)	13	13.00	4	4.00	0.022*
▪ AUB-N (not yet classified)	0	0.00	0	0.00	–
**p value* < 0.05*; *Fisher Exact Test; The p-value is significant at* 5% *level of significance*					

Table 6: Correlation of Radiology (USG) and Histopathology-based Diagnosis

Diagnosis	**USG-based Diagnosis**		**Histopathology-based Diagnosis**		***p value****
	n	***%***	***n***	***%***	
PALM:					
▪ AUB-P (polyp)	3	3.00	3	3.00	1.000
▪ AUB-A (adenomyosis)	6	6.00	8	8.00	0.579
▪ AUB-A;L (adenomyosis and leiomyoma)	4	4.00	3	3.00	0.680
▪ AUB-L (leiomyoma)	31	31.00	43	43.00	0.078
▪ AUB-M (malignancy and hyperplasia)	13	13.00	6	6.00	0.091
COEIN:					
▪ AUB-C (coagulopathy)	0	0.00	0	0.00	–
▪ AUB-O (ovulatory disorders)	0	0.00	27	27.00	<0.001*
▪ AUB-I (iatrogenic)	0	0.00	0	0.00	–
▪ AUB-E (endometrial)	0	0.00	4	4.00	0.043*
▪ AUB-N (not yet classified)	0	0.00	0	0.00	–
**p value* < 0.05*; *Fisher Exact Test; The p-value is significant at* 5% *level of significance*					

DISCUSSION

The study emphasized the utility of the PALM-COEIN system in categorizing structural and functional components of AUB, providing a standardized tool for clinicians globally. The findings revealed that the majority of cases occurred in the 40-50 years age group, which is consistent with previous studies. High parity was also noted in this age group, although variations in age groups were observed across studies. The increase in AUB with advancing age, particularly around menopause, is linked to anovulatory cycles and hormonal changes, making AUB-O a common cause after AUB-L.

The most common complaint in the study was heavy menstrual bleeding (HMB), followed by frequent menstrual bleeding, with a higher association to COEIN components. Clinical diagnoses of PALM and COEIN were equally distributed, with AUB-L being the most common structural cause. Risk factors such as age and obesity were identified, with obesity linked to increased estrogen exposure leading to conditions like fibroids and endometrial malignancy.

Histopathological examination confirmed that the majority of AUB cases were structural (PALM), particularly AUB-L (fibroids), followed by AUB-A (adenomyosis) and AUB-M (endometrial malignancy). Histopathology remains the gold standard for diagnosing AUB, though ultrasonography is effective for diagnosing AUB-L and polyps. There was a notable clinicopathological difference in AUB-A and AUB-M, which could be attributed to the nonspecific nature of their symptoms.

A significant clinicopathological correlation was found for AUB-L, but less so for functional causes like AUB-O and AUB-E, which often require exclusion of other conditions. The study advocated for a bimodal or multimodal approach to diagnosis, combining clinical, radiological, and histopathological methods for accurate management, minimizing resource use, and reducing morbidity.

LIMITATIONS

Included sample size, questionnaire-based data collection, and inclusion of both rural and urban populations.

CONCLUSION

The study found that most cases of abnormal uterine bleeding (AUB) occurred in women aged 39–47 years, with a mean age of 44.72 years. The most common menstrual symptoms were heavy menstrual bleeding (31%) and frequent menstrual bleeding (26%). Regarding comorbidities, 11% were obese, 7% hypertensive, 4% had thyroid issues, and 2% had diabetes. Clinically, the contributions of the COEIN (52%) and PALM (48%) components were nearly equal, but histological analysis showed a higher prevalence of structural causes (PALM) at 63%, mainly due to AUB-M (malignancy and hyperplasia). The study highlights the importance of accurate diagnosis and treatment through a comprehensive clinical and histological work-up, especially since AUB-P, AUB-L, and AUB-O can present similarly, often around menopause.

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