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FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding

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Abstract:
Background:*Abnormal uterine bleeding (AUB) is a common gynecological problem in women, affecting their quality of life and making them seek treatment. AUB has many causes which makes it important to have a systematic approach that can lead to the correct diagnosis and guide management accordingly. The primary aim is to study the various causes of AUB and categorize the women presenting with the complaint as per the FIGO PALM-COEIN system after reaching a final diagnosis based of clinical, laboratory, imaging and histopathology findings. The study also enables to compare the different causes of AUB as per the frequency of occurrence.*
Materials & Methods: *An observational study was carried out on a 100 women in the reproductive age group, who presented with the complaint of abnormal uterine bleeding and were admitted to a tertiary care hospital for further evaluation. A clinical diagnosis was established first which guided further laboratory and imaging investigations. The final diagnosis was made from the available data and confirmed by histopathological correlation.*
Results: *The PALM and COEIN groups accounted for 72% and 28% respectively. Leiomyoma was the most common cause of AUB (32%) and adenomyosis was the 2nd most common cause of AUB (25%). This was followed by ovulatory dysfunction (15%), which was the most common cause in the COEIN group. The diagnosis obtained clinically often did not correlate with the imaging findings or histopathology report, especially for the PALM categories. Accurate classification of a case of AUB according to PALM-COEIN is only possible after studying all the aspects- clinical, laboratory, imaging and histopathology.*
Conclusion: *The PALM-COEIN system offers an easy and systematic way to approach a case of AUB. It was found that there were significantly higher number of cases in the PALM (structural causes) component than in the COEIN component (non-structural causes). Overall and amongst the PALM categories, leiomyoma was found to be the leading cause of AUB, while ovulatory dysfunction was the most common category in the COEIN group.*
Key Word: *Abnormal uterine bleeding, PALM-COEIN, leiomyoma*

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I. Introduction

Abnormal uterine bleeding (AUB) is bleeding from the uterus that is longer than usual or that occurs at an irregular time. Normal menstrual cycle typically lasts between 24 to 38 days and a normal menstrual period typically lasts up to 8 days. The average blood loss per cycle is 35 ml.[1]

Classification of abnormal uterine bleeding: FIGO 2011 publication presented two systems to which modifications were made in 2018.

- **FIGO AUB System 1**, Terminology and Definitions- defines the parameters of normal menstrual bleeding, establishes a mechanism for defining the various symptoms that comprise AUB. Terms such as menorrhagia, oligomenorrhea, metrorrhagia and dysfunctional uterine bleeding are eliminated.
- **FIGO AUB System 2**, Classification of causes of AUB in the reproductive years, the PALM- COEIN system- provides a structured infrastructure for research, education and clinical care by categorizing the various possible causes or contributors to the symptoms of non-gestational AUB in the reproductive years.

Suggested Normal limits for menstrual parameters- FIGO AUB System 1

Clinical Parameter	Descriptive term	Normal limits (5–95th percentiles)
Frequency of menses (days)	Absent Frequent Normal Infrequent	Amenorrhea <24 24-38 >38
Regularity of menses, cycle to cycle (Variation in days over 12 months)	Regular variation Irregular	Shortest to longest </= 7-9 days Shortest to longest > 8-10 days
Duration of flow (days)	Prolonged Normal	>8 days Up to 8 days
Volume of monthly blood loss (mL)	Heavy Normal Light	>80 5–80 <5
Heavy menstrual bleeding	Excessive menstrual blood loss which interferes with a woman's physical, social, emotional and/or material quality of life.[2]	
Inter-menstrual bleeding	Spontaneous bleeding occurring between menstrual periods, either cyclical or random.	

FIGO AUB System 2 is a stratification of causes into "structural" pathologies that can be "imaged" and/or defined histopathologically (PALM) and "non- structural", in that they cannot be imaged, but clinical assessment with detailed history and appropriate physical examination, sometimes supported by laboratory testing, can largely imply or make a diagnosis of cause (COEIN).[3]

Structural Causes	**PALM**
AUB-P	Polyp
AUB-A	Adenomyosis
AUB-L	Leiomyoma
AUB-M	Malignancy + Hyperplasia
Non-structural Causes	**COEIN**
AUB-C	Coagulopathy
AUB-O	Ovulatory dysfunction
AUB-E	Endometrial
AUB-I	Iatrogenic
AUB-N	Not otherwise classified

- **Polyps, AUB-P**

Most endometrial polyps are asymptomatic, but they can cause inter-menstrual bleeding, heavy menstrual bleeding, irregular bleeding and post-menopausal bleeding. Incidence of polyps increases with age.

- **Adenomyosis, AUB-A**

Frequently co-existing with fibroid, adenomyosis may be diagnosed on ultrasound or MRI or on **Leiomyoma, AUB-L**

- Uterine leiomyomas occur in as many as one-half of all women older than 35 years of age and are the most common tumors of the genital tract. [4]Abnormal bleeding is the most common symptom, however, most women remain asymptomatic, with submucosal fibroid being the most likely to cause bleeding.

- **Malignancy and Hyperplasia, AUB-M**

Includes cystic hyperplasia, adenomatous hyperplasia, hyperplasia with cytologic atypia, and invasive carcinoma, caused due to unopposed estrogen action. Abnormal bleeding is the most common presenting symptom in women with invasive cervical cancer. Uterine sarcoma is a rare cause of AUB.

- **Coagulopathy, AUB-C**

Hematologic causes, primarily von Willebrand disease, should be considered in women with heavy menstrual bleeding, particularly in those who have had heavy bleeding since menarche, family history of bleeding disorder, abnormal bleeding from other sites, failure to respond to conventional management.

- **Ovulatory Dysfunction, AUB-O**

Most anovulatory bleeding occurs due to estrogen breakthrough. Relatively low levels of estrogen stimulation results in irregular and prolonged bleeding while higher sustained levels cause episodes of amenorrhea followed by acute, heavy bleeding.

Many ovulatory disorders are related to endocrine disturbances- hypothyroidism, hyperthyroidism, hypothalamic dysfunction, hyperprolactinemia, premature ovarian insufficiency (POI), and primary pituitary disease.

- **Endometrial, AUB-E**

Endometrial factors can cause AUB/HMB in ovulatory cycles, either due to deficiency of local vasoconstrictors (endothelin-1, prostaglandin PGF2alpha) or excess of local vasodilators (prostacyclin I2, prostaglandin E2). Inflammation and infection including sexually transmitted infections leading to endometritis, cervicitis can also cause abnormal bleeding.

- **Iatrogenic, AUB-I**

Exogenous hormone therapy may lead to unscheduled endometrial bleeding. This is typically associated with use of hormonal contraceptive methods including oral contraception, contraceptive patch, vaginal ring, intramuscular regimens, levonorgestrel IUCD or those interventions that act on ovarian steroid release such as gonadotropin-releasing hormone (GnRH) agonists, aromatase inhibitors, selective estrogen receptor modulators (SERMs) and more rarely selective progesterone receptor modulators (SPRMs).

- **Not Otherwise Classified, AUB-N**

Includes pathologies that are either rare or poorly defined that do not easily fit within the other categories like arterio-venous malformations, endometrial pseudo-aneurysms, myometrial hypertrophy.

II. Material And Methods

This is an observational study carried out at a tertiary care hospital on 100 women who underwent treatment for abnormal uterine bleeding.

Study period:
May, 2019-April, 2020

Inclusion criteria:
Women in reproductive age group (15-49 years) presenting with complaint of abnormal uterine bleeding who were admitted for further investigation and management.

Exclusion criteria:
Women < 15 years or >49 years of age and those who were treated conservatively on out-patient basis are excluded from this study.
Cases with co-existing diagnosis like fibroid + adenomyosis, polyp + adenomyosis

Procedure methodology:

100 women were randomly selected from those who presented with the complaint of abnormal uterine bleeding and were admitted to the hospital for further work-up. Their history was thoroughly taken including past and present menstrual history, use of contraception, medical/ surgical co-morbidities. This was followed by general, systemic and gynecological examination of cervix (position, presence of any erythematous lesion, hypertrophy, mobility, presence of polyp), uterus (size, position, consistency, mobility) and adnexa (any palpable enlarged lump, tenderness and mobility). Routine blood investigations like complete blood count, renal function test, liver function test, blood sugar profile and other tests like thyroid function test, coagulation profile if needed were carried out. Based on the clinical findings, allocation to PALM-COEIN was done.

For further evaluation of PALM categories, a pelvic ultrasound to assess the uterus (uterine size, endometrial thickness, presence of endometrial polyp, adenomyosis or fibroids) and ovarian status (presence of any cyst, mass and its characteristics) was done. Wherever indicated, endometrial biopsy and hysterectomy specimens were obtained and sent for histopathology. Clinical diagnosis was then correlated with histopathology-based final diagnosis.

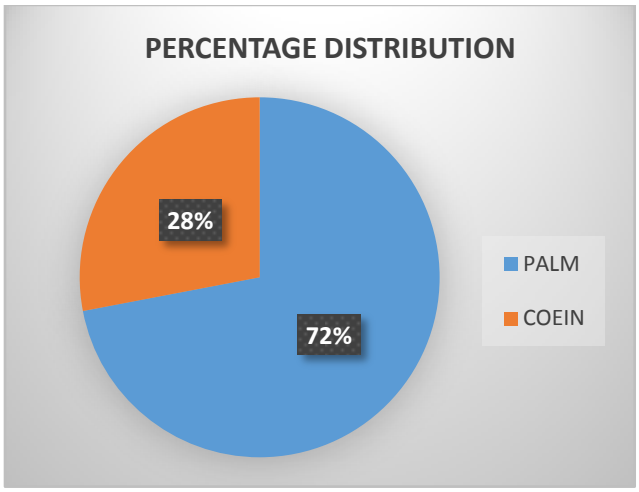
The COEIN aspect was evaluated based on clinical findings and lab investigations. Ovulatory dysfunction was defined as unpredictable timing and variable amount of bleeding, while AUB occurring in line with predictable/cyclic pattern were classified as endometrial disorder. Those with a history of hormone steroid intake during the preceding 3 months and/or onset of symptoms following contraceptive device or method were included in the iatrogenic category. Histopathology report of endometrial sampling/ D&C material aided in diagnosis of AUB-O and AUB-E.

III. Result

The study included 100 patients in the reproductive age group, randomly selected out of all gynecology admissions in 1 year period (May, 2019- April, 2020) out of which majority were in the peri-menopausal age group (41-49). Most patients presented with complaint of menorrhagia.

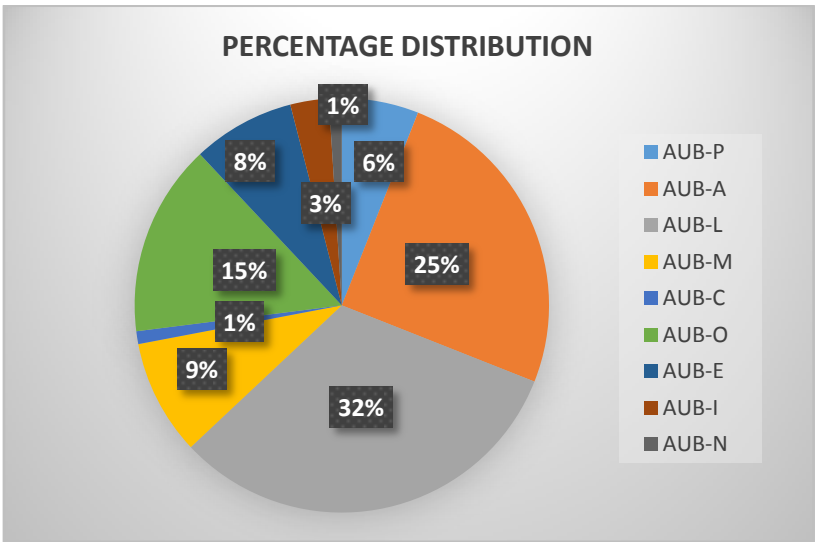
Distribution of cases as per clinical diagnosis:
The number of cases in each diagnosis was charted as percentage as total number of cases, n=100.

DIAGNOSIS	*PERCENTAGE OF CASES (%)*
PALM:	72
AUB-P (POLYP)	06
AUB-A (ADENOMYOSIS)	25
AUB-L (LEIOMYOMA)	32
AUB-M (MALIGNANCY & HYPERPLASIA)	09
COEIN:	28
AUB-C (COAGULOPATHY)	1
AUB-O (OVULATORY DYSFUNCTION)	15
AUB-E (ENDOMETRIAL)	8
AUB-I (IATROGENIC)	3
AUB-N (NOT OTHERWISE CLASSIFIED)	1



Out of the 100 patients studied, 72% belonged to PALM while 28% belonged to COEIN categories.

Amongst PALM, leiomyoma was the most common finding (32%) closely followed by adenomyosis (25%). In the COEIN category, ovulatory dysfunction (15%) was the most common cause followed by endometrial (8%).AUB due to coagulopathy, iatrogenic steroid/ contraception use or due to causes not otherwise classified like AV malformations were found to be the least common.



IV. Discussion

The worldwide impact of abnormal uterine bleeding in the reproductive years is substantial, with a prevalence of approximately 3-30%, among reproductive aged women. [5]It can cause a significant impact on the woman's physical, social and emotional aspects, directly affecting their quality of life.

This study classifies the causes of AUB based on frequency as observed in patients seeking treatment at a tertiary care hospital. The contribution of structural causes (PALM) was significantly higher than the non-structural causes (COEIN).

AUB-P could be due to cervical polyp usually diagnosed clinically by per-speculum examination and confirmed by D&C-polypectomy or endometrial polyp diagnosed on USG.

AUB-L was the overall leading category. Diagnosis was made by USG findings and correlated histopathologically whenever surgical approach was used in the management. Age is an important risk factor with majority cases occurring after 45 years of age.Higher association of AUB is seen with submucosal type, compared with intramural and subserous type.[6]This finding has been corroborated by other similar studies.[7][8]

Clinical diagnosis of AUB-A is often confused with AUB-L which requires further imaging to differentiate. However, reliable diagnosis can only be made after examining histopathological specimen.Co-existing cases of leiomyoma and adenomyosis are also often found.

Another important cause of AUB was AUB-M, i.e. malignancy and hyperplasia, diagnosed using USG and confirmed by endometrial sampling or D&C material sent for histopathology. Peri-menopausal women are predisposed to develop hyperplasia and eventually endometrial carcinoma, due to unopposed estrogenic action on the endometrium in the anovular cycles.Simple hyperplasia without atypia was the most common entity in AUB-M.

AUB-O should be suspected when the patient reports irregular & unpredictable menstrual bleeding that varies in amount, duration and character that is not accompanied by any visible or palpable genital tract abnormality.

AUB-E is difficult to diagnose as there is no routine test to identify such disorders. It may be suspected when the menstrual disturbance is predictable and fits within the regular cyclic pattern. However, it remains a diagnosis of exclusion.

On first contact with the patient, many are classified as AUB-O or AUB-E based on their menstrual history but a lot of these cases are later reclassified in one of the PALM categories following further imaging or tissue analysis.

AUB-C is a rare occurrence with early onset of menstrual disturbance, often with family history of similar problem.

AUB-I is diagnosed when the patient gives specific history of having undergone some form of hormone therapy including contraception, after ruling out any structural cause.

AUB-N is the category reserved for uncommon conditions like AV malformations diagnosed by specific imaging findings, which do not fit in any other category.

This study only compares the frequency of each component of the PALM-COEIN system in women in reproductive age group. Though majority women belonged to peri-menopausal age group, stratification of causes according to each age group has not been studied. Further study can be carried out comparing the clinical, imaging and histopathological findings to establish the degree of correlation amongst the different aspects of diagnosis.

V. Conclusion

FIGO PALM-COEIN classification is an easy and systematic approach to the differential diagnoses of abnormal uterine bleeding and guides further investigations and treatment.

Occurrence of AUB due to the PALM component (structural causes) is found to be significantly higher than that due to COEIN component (non-structural causes) in women of reproductive age group.
Overall, leiomyoma is the most common cause of AUB.

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