

Evaluation of Abnormal Uterine Bleeding Based on Palm-Coein Classification

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Abstract

Background: Any deviation from the typical menstrual cycle that affects the regularity and frequency of menses, as well as the length of the flow or the volume of blood lost, is known as abnormal uterine bleeding (AUB). The goal of this study was to examine the various etiopathological causes of abnormal uterine bleeding in women between the ages of 20 and 55, as well as to assess the contributing aetiologies, frequent manifestations, diagnosis, assessment, and treatment of AUB using the PALMCOEIN approach.

Methods: This prospective study was carried out at Department of Obstetrics and Gynaecology in a tertiary care hospital, within two years. 100 hundred patients in reproductive age group who presented with abnormal uterine bleeding were enrolled. The demographic information was documented, and then a general, physical, systemic, and gynaecological examination was followed by a structured history of the patient's past and present menstrual history, history of using contraception, and medical/surgical history. Ovulatory dysfunction was characterized as unpredictable timing and a variable amount of bleeding for the sake of evaluating the COEIN component, whereas endometrial diseases referred to situations where AUB occurred in accordance with predictable/cyclical patterns.

Results: Twenty-one percent of the 100 cases in the research group had obesity as a risk factor, as did twelve percent of cases with thyroid problems, seven percent with hypertension, five percent with diabetes mellitus, and two percent of cases with a history of PCOS or a family history of endometrial cancer. In 61% of cases, there was heavy menstrual bleeding, and in 11% of cases, there was dysmenorrhea with menorrhagia. Intermenstrual haemorrhage occurred in 10% of the cases, while AUB occurred in the remaining instances. For instance, abdominal masses occurred in 7% of cases, vaginal masses in 4%, and urine retention in 4%. Proliferative phase was the most frequent pathology seen in 58 (58%) of the individuals.

Conclusion: The diagnosis and management of abnormal uterine bleeding are significantly easier and more objective when done with the PALM-COEIN technique. Additionally, it facilitates diagnosis.

Keywords: PALM-COEIN, abnormal uterine bleeding, manifestations, Ovulatory dysfunction, predictable/cyclical patterns.

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Introduction

Abnormal uterine bleeding (AUB) may be defined as any variation from the normal menstrual cycle that includes changes in both regularity and frequency of menses either in duration of flow or in amount of blood loss. Under the category of AUB, further definitions may be subdivided based on volume of menstruation, regularity, frequency, duration, chronicity, and timing related to reproductive status.

Review of current terminology in medical and historical literature reveals confusing and inconsistent definitions referring to menstrual bleeding [1]. As a result, the FIGO menstrual disorders working group (an international expert consensus committee) has developed new guidelines for terminology related to this topic [2].

This classification allows the characterization of more than one etiology in the same patient. The PALM side of the classification refers to structural causes that could be evaluated and diagnosed on imaging and /or biopsy. The COEIN side allows consideration of underlying medical disturbances that could result in AUB [3]. AUB occurs in 9 to 14 percent of women between menarche and menopause, significantly impacting quality of life and imposing financial burden [4].

The international federation of gynaecology and obstetrics (FIGO) adopted and published PALM-COEIN classification in 2011 [5], and the American college of obstetricians and gynaecologists (ACOG) adopted it in 2012 [6]. The new classification system - Polyps, Adenomyosis, Leiomyoma, Malignancy and hyperplasia-Coagulopathy, Ovulatory Disorders, Endometrial Causes, Iatrogenic,

Not Classified [PALMCOEIN] describes the causes of AUB in non-gravid women of reproductive age.

The new system which is published in the June issue of the international journal of gynaecology and obstetrics, facilitate basic sciences and critical research, as well as the practical, rational and consistent application of medical and surgical treatments.

Beginning with workshops in 2005, contributors from more than 17 countries on 6 continents developed the PALMCOEIN (pronounced as "pamkoin") classification system for causes of AUB in the reproductive years.

The basic system comprised of 9 categories: the first 4 are defined by visually objective structural criteria PALM; a second 4 that are unrelated to structural anomalies COEI, and a final category reserved for entities that are not yet classified(N).

The PALMCOEIN defines acute AUB as an episode of heavy bleeding, which demands immediate intervention in order to prevent copious blood loss. After the immediate intervention, a thorough examination that follows will reveal the underlying cause of the acute episode of AUB.

In contrast, chronic AUB is characterized by bleeding that lasted for the bulk of the past six months. Bleeding is also so unexpected and abnormal in volume and frequency. Chronic AUB, in a clinician's opinion does not require immediate intervention [7]

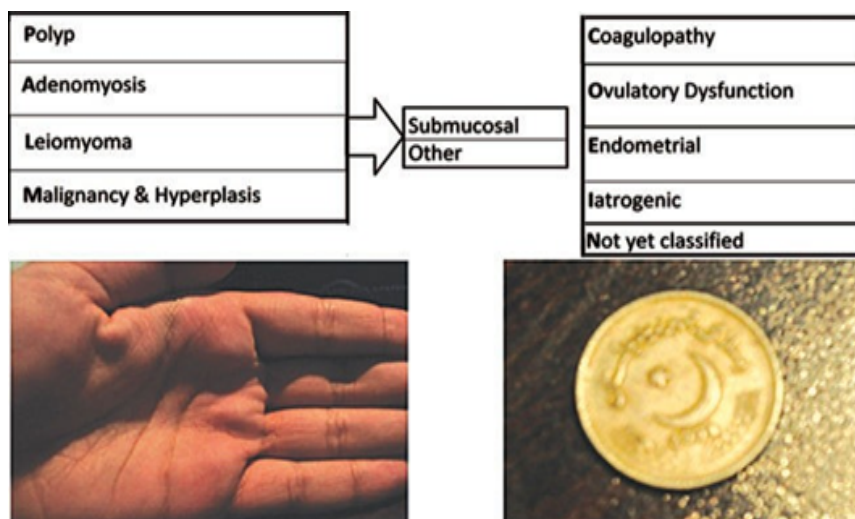


Figure-1: Adopted from Munro et al.[5] FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding in non-gravid women of reproductive age.

Figure-1 Palm-coein classification

Table 1: Suggested normal limits for menstrual parameters. Adapted from Fraser et al [8]

Clinical parameter	Descriptive term	Normal limits (5-95 th percentiles)
Frequency of menses (days)	Frequent Normal Infrequent	<24 24-38 >38
Regularity of menses, cycle to cycle (variation in days over 12months)	Absent Regular Irregular	No bleeding Variation ±2-20 days Variation >20 days
Duration of flow (days)	Prolonged Normal Shortened	>8.0 4.5-8.0 <4.5
Volume of monthly blood loss(ml)	Heavy Normal Light	>80 5-80 <5

Objectives:

To study the various etiopathological factors responsible for abnormal uterine bleeding in women ages 20-55 years and to evaluate the contributing aetiologies, common presentations, diagnosis, evaluation and management of abnormal uterine bleeding (AUB) on PALMCOEIN approach.

Materials and Methods

A prospective observational study of one hundred patients in reproductive age group who presented with abnormal uterine bleeding to the Department of Obstetrics

and Gynaecology in a tertiary care hospital. The study period was two years. All cases of abnormal uterine bleeding with complaints of menorrhagia, metrorrhagia, polymenorrhoea and menometrorrhagia in the age group 20-55 were included. Pregnant women and patients below 20 years and above 55 years were excluded from study.

The demographic details were noted, and a structured history of previous and current menstrual history, history of contraception use and medical/surgical history was followed by general, physical, systemic and gynaecological examination.

On gynaecological examination, cervix (position of cervix, any erythematous lesion, hypertrophy, mobility, presence of polyp or ectopy), uterus

(size position, consistency, mobility) and adnexae (any palpable enlarged lump, tenderness, and mobility) were assessed. Clinical diagnosis and allocation to PALMCOEIN was done. A pelvic ultrasound to assess the uterus (uterine size, endometrial thickness, presence of endometrial polyp, adenomyosis and fibroids) and ovarian status (presence of any cyst, mass) was done. Endometrial biopsy and hysterectomy specimens were obtained and sent for histopathology. As per histopathological findings, possible underlying causes were categorised. Clinical diagnosis was then correlated with histopathology-based final diagnosis.

For evaluation of the COEIN aspect ovulatory dysfunction was defined as unpredictable timing and variable amount of bleeding, while endometrial disorders referred to cases when AUB occurred in line with predictable/cyclic pattern. Iatrogenic category was categorized by the identification of hormone steroid intake during the preceding 3 months and/or onset of symptoms following contraceptive device or method. Following a thorough history and complete clinical examination, investigations including complete blood count, coagulation profile when applicable (for all previously known cases of defects of coagulation from younger age and AUB dating back from menarche), thyroid function test and blood sugar level estimations were done, and the results were

correlated with the clinical allocation. Endometrial histology was correlated in cases AUB-O and AUB-E with the clinical assignments.

Observations and Results

Of the 100 patients, the maximum number of patients 32% were noted in the age group of 36-40 years, followed by 20% in the age group of 41-45 years. 17% of the study subjects were in the age group of 46-50 years of age and 13% in the age group of 26-30 years followed by 11% in the age group of 31-35 years. 4 % of the study group were in the age group of 51-55 years and 3 % were in the age group of 20-25 years.

Out of the 100 cases of study group, 21% cases were associated with the obesity risk factor, 12% cases were associated with thyroid disorders, 7% cases had hypertension, 5% cases were associated with diabetes mellitus while 2% cases had history of PCOS and 2% cases had family history of endometrial carcinoma.

Of the study group, 61% of the cases presented with heavy menstrual bleeding followed by 11% of the cases with dysmenorrhoea along with menorrhagia. Intermenstrual bleeding is seen in 10% of the cases and the remaining cases were presented in association with AUB such as 7% of the cases presented with mass per abdomen while 4% of the cases presented with mass per vagina and urinary retention respectively. 2% of the patients presented with white discharge and HMB while 1% of the cases presented with white discharge and dysmenorrhoea.

Table 2: Duration of abnormal uterine bleeding in the subjects studied

Duration of AUB (in months)	Number of patients (n = 100)	Percent
1 – 6 months	58	58
6 –12 months	29	29
>12 months	13	13

Of the study group 58% presented with acute AUB, while only 42% presented with chronic AUB

Table 3: Distribution of cases as per clinical diagnosis

Diagnosis	Total cases (n = 100)	Percent
PALM		
AUB – P (polyp)	10	10
AUB – A (adenomyosis)	8	8
AUB – L (Leiomyoma)	55	55
AUB — M (Malignancy and hyperplasia)	9	9
COEIN		
AUB – C (coagulopathy)	1	1
AUB - 0 (Ovulatory disorders)	15	15
AUB – I (iatrogenic)	1	1
AUB – E (endometrial)	1	1
AUB – N (not yet classified)	0	0

Of the study group, 55% of the cases were contributed by leiomyomas followed by 15% of the cases due to ovulatory causes. 10% of the cases were contributed by polyps and 9% were due to malignancy and

hyperplasia. 8% were due to adenomyosis followed by 1 % due to coagulopathy and 1% due to iatrogenic causes and 1% due to endometrial causes.

Table 4: Distribution of cases based on endometrial pattern on histopathology

Endometrial pattern	No. of cases	Percent
Secretary phase	26	26%
Proliferative phase	58	58%
Cystoglandular hyperplasia	1	1%
Disordered proliferative endometrium	8	8%
Simple endometrial hyperplasia	1	1%
Complex endometrial hyperplasia without atypia	1	1%
Complex endometrial hyperplasia with atypia	1	1%
Pill induced endometrial changes	1	1%
Endometrial carcinoma	2	2%

The commonest pathology observed in the study was proliferative phase in 58 (58%) patients.

Majority of the cases presented with abnormal uterine bleeding were treated by surgical methods. Of the study group 60 (60%) cases were treated by total abdominal hysterectomy 21 (21%) cases were treated by medroxyprogesterone, 6 (6%) cases were treated by oral contraceptives pills, 4 (4%) cases treated by polypectomy. 2(2%) cases were treated with tranexamic acid, non-descent vaginal hysterectomy, radical with hysterectomy each. 1 (1%) case treated with laparoscopic assisted vaginal hysterectomy, cystectomy, laparoscopy with adhesiolysis each.

Discussion

The new FIGO classification system was developed because of the longstanding confusion about terminology and definitions related to AUB. It was not clear whether terms such as menorrhagia, metrorrhagia, menometrorrhagia, and dysfunctional uterine bleeding referred to symptoms or diagnosis. This confusion caused difficulties in the management of patients and in the designing of clinical studies about AUB. A consistent and universally accepted classification system should be used by clinicians, investigators, and even patients to facilitate communication, clinical care, and research. The basic system comprises nine

categories; the first four are defined as visually objective structural criteria (PALM); the second four are unrelated to structural anomalies (COEI); and the final one is reserved for entities that are not yet classified(N).

In the present study 100 non gravid women presented with AUB aged between 20-55years were included. Majority (32%) of the patients with AUB were in the age group 36-40 years followed by 41-45 years (20%) followed by 46-50 years(17%).A study by Arnold et al.⁹ also showed maximum number of cases in the age group 41-50 years (49%). Another study by Rizvi et al.¹⁰ also had 44.6% of cases in the age group 41-50. So it is imperative that the incidence of AUB is more prevalent in perimenopausal age group. According to age

wise prevalence of the structural causes of AUB (PALM group), polyps were predominantly seen in the age group 25-30 years and leiomyoma was most commonly seen in 40 -45years age group. Among the non- structural causes of AUB (COEIN group), iatrogenic causes were common in 25-30 age groups, while ovulatory dysfunction was common in 36-45 age groups.

The most common clinical presentation was acute type (58%) of AUB, where the symptoms lasted for less than 6months of duration. As in the present study, 70% of women with AUB had structural causes, these patients presented with acute symptoms rather than chronic onset of symptoms.

Table 5: comparative analysis of common causes of AUB

	Present study (n=100)	Qureshi et al. [11]	Venugopalan et al [12]	Arnold et al⁹	Rizvi et al¹⁰
Most common cause	Leiomyoma (55%)	Leiomyoma (25%)	Leiomyoma (20%)	Adenomyosis (53.4%)	Adenomyosis

In the present study leiomyoma (55%) was the most common cause of AUB followed by ovulatory dysfunction (15%) and only 1% had AUB secondary to coagulopathy. In a similar study done by Qureshi et al [11] on AUB in there productive age group (25-45yrs), leiomyoma (25%) was the most common structural lesion and ovulatory cause (24%) was the most common non structural lesion. Another study done by Venugopalan et al¹² on 50 patients with AUB showed leiomyoma (20%) to be the most common cause noted followed by ovulatory causes. Whereas in Arnold et al [9] study on women with AUB, adenomyosis (53.4%) was the most common structural lesion followed closely by leiomyoma (47.1%). Rizvi et al [10] in his study also had the most common structural abnormality as adenomyosis followed by leiomyoma and malignancy. In Oruc NI et al., [15] cases were classified

into two groups as structural causes (PALM) and non-structural causes (COEIN). There were 199 cases (49.4%) in the PALM group and 204 cases (50.6%) in the COEIN group. In the PALM group, polyp was found as the most common cause of abnormal uterine bleeding in 79 cases (19.6%). The most common cause in COEIN group iatrogenic was with 80 cases (19.9%).

The present study had 10% of polyps contributing to AUB.A similar outcome was found in Doraiswami [13] et al. (2011) study where polyps account for 11.2%. Arnold et al. [9] (2015) also had 15% of cases of polyp as the cause of AUB. While Qureshi et al. [11] had only 3% of cases of polyp as the cause of AUB. Literatures state that some but not all polyps present with AUB (39% of premenopausal women) (Abnormal Uterine Bleeding, 2014) and the

incidence of polyp increases between 40-50 years. While the increased incidence found in 25- 30 age group may be because of increase in hormonal therapy with estrogen. The histopathology of endometrium shows most of them in proliferative phase, which shows their growth is estrogen regulated.

In the present study adenomyosis was seen in 8% of AUB cases and half of them were seen in 40-45 age group. This was almost similar to Qureshi et al. [11] study where 15% of AUB cases had adenomyosis. While in Arnold et al study 53.4% of AUB cases were due to adenomyosis. In all these studies adenomyosis was the common cause of AUB in 40-50 years age group. Adenomyosis were predominantly seen in multiparous women in this study with diffuse subtype (60%). In the present study TAH was done in 50% of cases of adenomyosis because of severe dysmenorrhea, pelvic pain and failed medical management. There are no evidence based guidelines to treat adenomyosis using medical or minimally invasive methods. HPE of endometrium of adenomyosis showed secretory phase in 37.5% of cases.

Leiomyoma (55%) is the common cause of AUB in this study. Though fibroids are common in nulliparous women, the correlation of parity is not seen in this study. There is increase in incidence of fibroids with increasing age, majority of them presented in 41-45 years age group. In our study fibroid uterus was responsible for abnormal uterine bleeding in 55% of women comparable with a study of LTMMC hospital Mumbai and DHQ hospital Multan in which abnormal uterine bleeding evaluation revealed fibroid in 54% and 54.8% respectively. As most of the fibroids are asymptomatic and slow growing, patients presented late with AUB as they became symptomatic. Leiomyoma's are sub classified based on the site as submucosal (L-SM), and others (L-O). In this study majority of cases were having intramural and subserosal types (60.5%)

which was similar to Arnold et al [9]. It is usually the submucosal type that causes AUB, but in our study majority of AUB cases presented with intramural type. HMB seen in intramural type may be due to increased surface area of endometrium, hyperestrogenemia causing endometrial hyperplasia, presence of fragile and vascular perimyoma tissue and release of antigenic and growth factors like VEGF, BFGF, TGF- β which impairs local endometrial hemostasis. Bulky intramural tumours are thought to exert pressure and impinge on uterine venous system which causes venous dilatation with in myometrium and endometrium.

This explains why the intramural and subserosal tumours cause heavy menstrual bleeding. Management strategies are usually individualized and dependent on the patients age, severity of symptoms, size and location of fibroid. As the patients presenting in this area are from rural background, they usually present when they are symptomatic, approaching menopause with no desire for future fertility and not affordable to long term or costly conservative methods of management and wish to have a permanent remedy. These reasons unfortunately lead to an increase in the demand for TAH. The HPE of endometrium in most of the cases with leiomyoma were in proliferative phase.

Endometrial hyperplasia involves the proliferation of endometrial glands that results in a greater than normal gland to stroma ratio. AUB is noted in 80- 90% of women with endometrial carcinoma. Premenopausal women with increased BMI and chronic anovulation are the risk factors observed in this study. ACOG recommends endometrial assessment in any women >35 years with AUB and also younger than 35 years suspected of noncyclical uterine bleeding refractory to medical management. In the present study AUB-M category (9%) constitutes endometrial hyperplasia in 7% of cases and malignancy in 2% of cases. While Qureshi³⁹ et al.

(2013) had 6.6%. Arnold et al. [9] had 15% in this category. As endometrial cancers are common in 50-60 age groups they were not frequently seen in this study.

Endometrial biopsy was done in all cases of endometrial hypertrophy on ultrasound examination, especially when the endometrial image is non-homogenous and irregular of which simple type without atypia was seen in 50% of cases which was similar to Arnold et al study (65.4%).

Although there exists a spectrum of systemic disorders of hemostasis (coagulopathies) the most common of these is von Willebrand disease, approximately 13% of women with HMB. Approximately 90% of patients with these abnormalities can be identified by a structured history, testing for von Willebrand factor, ristocetin cofactor and coagulation assays. In our study basic coagulation profile was done for all the cases. Only 1% accounted for coagulation defects whereas 0.3% were seen in a study by Qureshi et al. [11]

In our study ovulatory dysfunction (15%) was the most common cause in 35-45 years age group, while Arnold et al. [9] had 17.2% of cases and Qureshi et al. [11] had 24% cases. Endometrial biopsy showed 50% cases in proliferative phase, which explains anovulation and progesterone deficiency. In this study most of the ovulatory dysfunction cases were having hypothyroid status, which might be leading to disturbance in ovulation. In perimenopausal years, ovulatory disorders are common due to derangements in the hypothalamo-pituitary-ovarian axis resulting in derangements of follicular maturation, ovulation, or corpus luteum formation, and anovulatory cycles are most frequent, and chronic anovulation is associated with an irregular and unpredictable pattern of bleeding. This explains why ovulatory disorders were found to be the second most common cause of AUB in this study and most other studies.

Endometrial cause of AUB is a diagnosis of

exclusion. The patients will have predictable and cyclic bleeding typical of ovulatory bleeding. A primary disorder of the endometrium is due to disturbances of metabolic molecular pathways like tissue fibrinolytic activity,

prostaglandins, inflammatory and vasoactive mediators. In the present study endometrial causes contributed to 1%, while Qureshi et al study had only 5% of cases of AUB. Many episodes of unscheduled bleeding are related to reduced circulating gonadal steroids

secondary to the patients compliance issues such as missed, delayed or erratic use of pills, transdermal patches and vaginal rings. This results in reduced suppression of FSH production and subsequent development of follicles that produce additional endogenous estradiol and irregular stimulation of endometrium may result in break through bleeding. Medications like anticonvulsants, hormonal steroids, antibiotics may have direct impact on endometrium by interfering with coagulation or influence on ovulation. IUCD at cellular level causes unbalanced ratios of prostaglandins and thromboxanes which leads to HMB, while at tissue level increases endometrial vascularity, congestion and degeneration which causes IMB. In our study 1% of AUB cases were seen while Qureshi et al. [11] had 6% of cases. The endometrial biopsy showed proliferative phase. The specific routine tissue assays which are not available at present may lead to negative histopathology in some cases. If available, these sophisticated tests may have a potential in order to establish a clearer diagnosis in the future. So far no such validated tests are available for clinical use, to attribute AUB-E as the primary cause of a woman's symptoms, so one has to rule out all other causes of AUB in clinical examination followed by a histological confirmation.

Among the study population, the treatment provided was characterized based on its modalities. 71% of the population had

undergone surgery along with drug therapy while 29% of the population were treated by drug therapy alone. venugopalan et al., [12] 2014 observed that 54%(27) of the population had undergone drug therapy alone, 32% (16) drug therapy + surgery and 14%(7) surgery alone. [16]

Since this classification was released, some countries have revised their guidelines for the diagnosis and management of what was formerly called “dysfunctional uterine bleeding” in favour of the new FIGO classification. ACOG recommended the use of the PALM-COEIN classification for both acute and chronic AUB in non-pregnant reproductive age women.¹⁴

This classification system assists in identifying the many exact etiological causes of AUB and can be utilised by clinicians, investigators, and even patients themselves to ease communication, clinical care, and research. In addition, when the explanation for abnormal bleeding could be recognised, it was simpler to treat the pathology. This classification offers a step-by-step approach to the AUB patient, which is helpful given that we discovered the majority of patients had more than one probable etiologic cause.

Conclusion

New standard terminology and a classification system that is universally accepted have eliminated the confusion that existed regarding the terminology, definitions, and classification of AUB. PALM-COEIN is the classification that was developed by the International Federation of Gynecology and Obstetrics (FIGO). Using the PALM-COEIN method makes the diagnosis and management of abnormal uterine bleeding much simpler and more objective. It also makes the diagnosis easier.

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