



RESEARCH ARTICLE

ASSESSMENT AND CATEGORISATION OF ABNORMAL UTERINE BLEEDING ACCORDING TO
PALM-COEIN CLASSIFICATION

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is a common cause for concern among reproductive women, sometimes debilitating, for which patients seek advice in gynecology outpatient department. The aim of the study was: 1.To categorize women with AUB attending a rural teaching hospital according to new classification system PALM-COEIN by the International Federation of Gynecology and Obstetrics (FIGO). 2.To collect clinical and histopathologic data based on new terminology and definitions. 3.To correlate the clinical and pathologic features.

Materials and Methods: This study was a cross sectional descriptive study to categorize women with AUB according to PALM COEIN classification system by International Federation of Obstetrics and Gynecology (FIGO), conducted in MALLAREDDY INSTITUTE OF MEDICAL SCIENCES, Suraram, Hyderabad, Telangana from October 2015 to March 2017. The study carried out on 250 non-gravid women presenting with AUB attending gynecology OPD after considering inclusion and exclusion criteria. The variables were analyzed using frequencies, percentages and chi-square test. The data and graphical techniques were presented by latest version of statistical software (SPSS-6).

Results: In this study 250 nongravid women presented with AUB aged between 25-45years were included. Among women with 25-30 years Polyp was most common structural abnormality seen. Where as in women aged 31-45 years leiomyoma. Among women with 25-30 years iatrogenic cause was the most common and ovulatory dysfunction in 36-45 years age group among non-structural causes. 68.8% of women presented with chronic AUB, while only 31.2% presented with acute AUB. Among all causes of AUB, leiomyoma was the most common cause and coagulopathy was the least common cause accounting for 0.8% of all cases. On sub classifying polyps, 69.3% were arising from endometrium and 30.7% were from cervix. Of 26 cases of polyps, 16 cases (61.5%) were associated with proliferative phase of endometrium and 8 cases (30.7%) with secretory phase of endometrium. Most of the women with adenomyosis had secretory phase of endometrium (53.3%), where as leiomyoma were associated with (55.2%) secretory phase of endometrium, followed by proliferative phase of endometrium (38.15%). Most of the leiomyoma cases were from sub mucosal (68.5%) origin. Most of the cases of endometrial hyperplasia are of simple endometrial hyperplasia without atypia contributing to 64.2% of cases. In the category of malignancy and hyperplasia, endometrial hyperplasia contributed to 73.7% and malignancy contributed to 36.7%. Most of the cases with ovulatory dysfunction had endometrium in proliferative phase (52.9%), while atrophic were only 10% of endometrial causes of AUB.62% of the cases were having a history of using hormonal medications in the preceding three months, while 38% of women were using intra uterine contraceptive devices. 58% of women with AUB had single pathology and 42% of women were having multiple pathologies. This classification helps in denoting a patient with single or multifactorial etiology.

Conclusion: Confusion regarding the terminology, definitions and classification of AUB has been overcome by new standard terminology and universally accepted classification system, PALM-COEIN by the International Federation of Gynecology and Obstetrics (FIGO). Maximum number of patients with AUB were in 41-45 years age group and more common in multiparous women. Most common clinical presentation was HMB. In this study 42% of cases were identified to have multiple pathologies. This classification system helps in understanding various exact etiological causes of AUB and can be used by the clinicians to facilitate communication, clinical care and research. For this reason we strongly recommend adoption of this classification for AUB and HMB.

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INTRODUCTION

Abnormal uterine bleeding (AUB) is a common cause for concern among reproductive women, sometimes debilitating, for which patients seek advice in gynecology outpatient department. AUB affects 10 to 30 percent of reproductive age women and up to 50 percent of perimenopausal women (Williams Gynecology and Hoffman, 2012). It has significant

impact on quality of life (Fraser *et al.*, 2009). Review of current terminology in medical and historical literature of AUB reveals no universally accepted method for classifying AUB, the investigation and management of AUB among non gravid women of reproductive age has been hampered by confusing and inconsistently used nomenclature and also by the lack of standardized methods for investigation and categorization of the various potential causes (Woolcock *et al.*, 2008). A process

designed led to international agreement on terminologies and definitions of AUB. After a thorough 5-year review process beginning with workshops in 2005, a group of clinicians-investigators from 17 countries and 6 continents who had substantial experience in AUB research, developed and revised a draft system that was distributed for comments. In 2007, a publication proposed a method to reach a consensus under the title "process designed that leads to international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding" in *Fertil Steril* and *Hum Reprod* journals (2007). A consistent, universally accepted nomenclature and a new classification system called PALM-COEIN (Munro *et al.*, 2011) has been approved by International Federation of Gynecology and Obstetrics (FIGO), which can be used by clinicians, investigators and even patients to facilitate communication, clinical care and research. This new classification of AUB is chosen in this study as it has simple, intuitive, unambiguous and easily translated terms which aid in systematic approach to diagnosis, facilitating multi institutional investigation, and a step-wise approach to intervention. Indian studies on this classification system is sparse, as this is a new emergent topic and hence this study was undertaken. But it may require periodic modification and revision based upon further research.

Aims and Objectives

1. To categorize women with AUB attending a rural teaching hospital according to new classification system PALM-COEIN by the International Federation of Gynecology and Obstetrics (FIGO).
2. To collect clinical and histopathologic data based on new terminology and definitions.
3. To correlate the clinical and pathologic features.

MATERIALS AND METHODS

Study design: This study was a cross sectional descriptive study to categorize women with AUB according to PALM COEIN, the new classification system by International Federation of Obstetrics and Gynecology (FIGO). All non-gravid women presenting with AUB attending gynecology OPD of MALLAREDDY INSTITUTE OF MEDICAL SCIENCES, Suraram, Hyderabad, Telangana. Sample Size: 250 cases.

Eligibility criteria

A. Inclusion criteria: All non-gravid women of reproductive age group of 25-45 years attending gynecology OPD with AUB.

B. Exclusion criteria: 1. Pregnant women. 2. Obvious cervical cause for bleeding per vaginum. 3. Local lesions on vagina and vulva.

All non-gravid women of reproductive age group with AUB underwent structured questionnaire that included thorough medical and gynecologic history, physical examination, pelvic ultrasound etc. Endometrial biopsy and hysterectomy specimens were obtained for histopathology where required. The gross and microscopic findings of the hysterectomy samples were obtained. The causes were categorized according to PALMCOEIN classification system by FIGO.

RESULTS

This is a cross sectional study carried out on 250 non gravid women between 25-45 years who came to gynecology OPD with complaints of AUB. The data was analyzed considering the inclusion and exclusion criteria. The PALM-COEIN classification was used to classify causes of AUB.

Table 1. Age distribution in women with AUB

Age in years	Number	Percentage
25-30	44	17.6
31-35	33	13.2
36-40	68	27.2
41-45	105	42
Total	250	100

Of the 250 cases of women with AUB, 42% of cases were seen in the age group 41-45 years, 13% of cases were seen in 31-35 years age group.

Table 2. Age distribution of women in PALM –Structural group

Age in years	Polyp	Adenomyosis	Leiomyoma	Malignancy & Hyperplasia
25-30	10	1	4	1
31-35	3	5	10	1
36-40	4	9	25	1
41-45	9	15	37	16
Total	26	36	76	19

Table 2 shows the age distribution in PALM group, which contributes for structural causes of AUB. Among women with 25-30 years Polyp was most common structural abnormality seen. Where as in women aged 31-45 years leiomyoma.

Table 3. Age distribution of women in COEIN –Non structural group

Age in years	Coagulopathy	Ovulatory Dysfunction	Endometrial Causes	Iatrogenic	Not yet classified
25-30	2	6	3	17	0
31-35	0	5	8	1	0
36-40	0	11	9	7	2
Total	2	34	30	29	4

Table 3 shows the age distribution in COEIN group, which contributes for non structural causes of AUB. Among women with 25-30 years iatrogenic cause was the most common and ovulatory dysfunction is the predominant cause of AUB in 36-45 years age group.

Table 4. Distribution of women with AUB according to duration of symptoms

Chronicity of symptoms	Number	Percentage (%)
Acute	78	31.2
Chronic	172	68.8
Total	250	100

Table 4 shows most women (68.8%) presented with chronic AUB, while only 31.2% presented with acute AUB.

Among all causes of AUB, leiomyoma was the most common cause and coagulopathy was the least common cause accounting for 0.8% of all cases.

Table 5. PALM-COEIN classification of causes of AUB

Diagnosis	Number	Percentage (%)	Notation
Polyp	26	10.4	AUB-P
Adenomyosis	30	12	AUB-A
Leiomyoma	76	30.4	AUB-L
Malignancy & Hyperplasia	19	7.6	AUB-M
Coagulopathy	2	0.8	AUB-C
Ovulatory	34	13.6	AUB-O
Endometrial	30	12	AUB-E
Iatrogenic	29	11.6	AUB-I
Not yet classified	4	1.6	AUB-N

Table 6. Polyp sub-classification

Type	Number	Percentage (%)
Cervical polyp	8	30.7
Endometrial polyp	18	69.3
Total	26	100

On sub classifying polyps, 69.3% were arising from endometrium and 30.7% were from cervix. Of 26 cases of polyps, 16 cases (61.5%) were associated with proliferative phase of endometrium and 8 cases (30.7%) with secretory phase of endometrium.

Table 7. Adenomyosis Sub-Classification

Type	Number	Percentage (%)
Diffuse	18	60
Focal	12	40
Total	30	100

Table 7 shows sub classification of adenomyosis based on ultrasound or HPE report of the specimen. Most of them were diffuse in nature contributing to 60% of AUB cases. Most of the women with adenomyosis had secretory phase of endometrium (53.3%).

Table 8. Leiomyoma sub-classification

Type of Leiomyoma	Number	Percentage (%)
Submucosal (AUB-LSM)	24	31.5
Other types (AUB-LO)	52	68.5
Total	76	100

Table 8 shows most of the leiomyoma cases were from other than sub mucosal (68.5%) origin. Most of the leiomyoma cases were associated with secretory phase (55.2%) of endometrium, followed by proliferative phase of endometrium (38.15%).

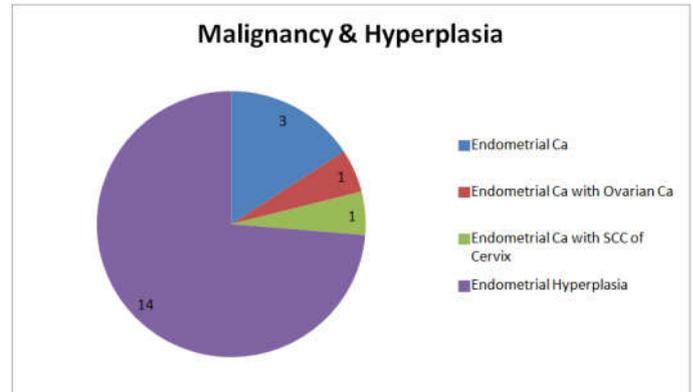
Table 9. Classification of Endometrial Hyperplasia

Type of Hyperplasia	Number	Percentage (%)
Simple Endometrial Hyperplasia without Atypia	9	64.2
Simple Endometrial Hyperplasia with Atypia	2	14.2
Complex Endometrial Hyperplasia without Atypia	2	14.2
Complex Endometrial Hyperplasia with Atypia	1	7.14
Total	14	100

Table 9 shows most of the cases of endometrial hyperplasia are of simple endometrial hyperplasia without atypia contributing to 64.2% of cases.

Most of the cases with ovulatory dysfunction had endometrium in proliferative phase (52.9%), most of the cases were in proliferative phase and contributed for 36.7%, while atrophic

were only 10% of endometrial causes of AUB. Around (62%) cases were having a history of using hormonal medications in the preceding three months, while 38% of women were using intra uterine contraceptive devices.



Graph shows in the category of malignancy and hyperplasia, endometrial hyperplasia contributed to 73.7% and malignancy contributed to 36.7%.

Table 10. Single / Multifactorial etiology in cases of AUB

AUB Cases	Number	Percentage (%)
Single Pathology	145	58
Multiple Pathology	105	42
Total	250	100

Table 10 shows 58% of women with AUB had single pathology and 42% of women were having multiple pathologies. This classification helps in denoting a patient with single or multifactorial etiology.

DISCUSSION

This study was undertaken to stratify the causes of abnormal uterine bleeding based on the PALM-COEIN classification which enables to correlate the clinical and pathological features and also to reach a precise underlying etiology for successful treatment of AUB. In the present study 250 non gravid women presented with AUB aged between 25-45 years were included. Majority (42%) of the patients with AUB were in the age group 41-45 years followed by 36-40 years (27.2%). A study by Arnold *et al.* (2015) also showed maximum number of cases in the age group 41-50 years (49%). Another study by Rizvi *et al.* (2013) 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 peri-menopausal 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 31-45 years 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.

AUB and duration of symptoms

The most common clinical presentation was chronic type (68.8%) of AUB, where the symptoms lasted for more than 6 months of duration. As in the present study, 60% of women with AUB had structural causes, these patients presented with chronic symptoms rather than acute onset of symptoms.

AUB and common causes

In the present study leiomyoma (30.4%) was the most common cause of AUB followed by ovulatory dysfunction (13.6%) and only less than 1% (0.8%) had AUB secondary to coagulopathy. In a similar study done by Qureshi *et al.* (2013) on AUB in the reproductive 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 al.* (2015) on 50 patients with AUB showed leiomyoma (20%) to be the most common cause noted followed by ovulatory causes. Where as in Arnold *et al.* (2015) study on women with AUB, adenomyosis (53.4%) was the most common structural lesion followed closely by leiomyoma (47.1%). Rizvi *et al.* (2013) in his study also had the most common structural abnormality as adenomyosis followed by leiomyoma and malignancy.

AUB - POLYP

The present study had 10.4% of polyps contributing to AUB. A similar outcome was found in Doraiswami *et al.* (2011) study where polyps account for 11.2%. Arnold *et al.* (2015) also had 15% of cases of polyp as the cause of AUB. While Qureshi *et al.* (2013) 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 in this study 38.5% of polyps were in 25-30 age group and 34.7% in 41-45 years age group. 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.

AUB - Adenomyosis

In the present study adenomyosis was seen in 12% of AUB cases and half of them were seen in 40-45 age group. This was almost similar to Qureshi *et al.* (Jonathan Arnold and Srivani Saravanan, 2015) 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%). According to Tarun *et al.* (2010), 70 to 80% of women undergoing hysterectomy for adenomyosis are in their fourth and fifth decade of life and are multiparous. In the present study TAH was done in 83.3% of cases 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 53.3% of cases.

AUB- Leiomyoma

Leiomyoma (30.4%) 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. 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.* (2015). 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 secretory phase.

AUB – Malignancy and hyperplasia

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 (7.6%) constitutes endometrial hyperplasia in 73.7% of cases and malignancy in 26.7% of cases. While Qureshi *et al.* (2013) had 6.6%. Arnold *et al.* (2015) had 15% in this category. As endometrial cancers are common in 50-60 age groups they were not frequently seen in this study. This was similar to Rather *et al.* (2013) study where 0.72% of cases had endometrial hyperplasia. 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 64.2% of cases which was similar to Arnold *et al* study (Jonathan Arnold and Srivani Saravanan, 2015) (65.4%).

AUB – Coagulopathies

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 0.8% accounted for coagulation defects where as 0.3% were seen in a study by Qureshi *et al.* (2013).

AUB-Ovulatory dysfunction

In our study ovulatory dysfunction (13.6%) was the most common cause in 35-45 years age group, while Arnold *et al.* (2015) had 17.2% of cases and Qureshi *et al.* (2013) had 24%

cases. Endometrial biopsy showed 52.9% 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.

AUB- Endometrial cause

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 12%, while Qureshi *et al.* (2013) 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 11.6% of AUB cases were seen while Qureshi *et al.* (2013) had 6% of cases. The endometrial biopsy showed most of the cases to be in proliferative phase.

AUB –Not yet classified

The category not yet classified is reserved for entities that are poorly defined and inadequately examined. Some of the rare entities like chronic endometritis, arterio venous malformations and myometrial hypertrophy were included, which contributed to 1.6% in this study. In future there is a need of further modifications in this category.

AUB -Etiology

In the present study of 250 women with AUB, 58% of cases had a single identified pathology and remaining 42% of cases had several different combination of pathologies. Which was similar to Arnold *et al.* (2015) study where 48.9% of cases had single pathology and 51.1% of cases had multiple pathologies.

Conclusion

Confusion regarding the terminology, definitions and classification of AUB has been overcome by new standard terminology and universally accepted classification system, PALM-COEIN by the International Federation of Gynecology and Obstetrics (FIGO). This is a cross sectional descriptive study done to classify non-gravid women of reproductive age with AUB with the new classification system PALM-COEIN.

- Maximum number of patients with AUB were in 41-45 years age group.
- AUB was found to be more common in multiparous women.
- Most of the patients presented with chronic symptoms of AUB.
- Most common clinical presentation was HMB.

- The most common cause of AUB was leiomyoma followed by ovulatory dysfunction.
- In this study 42% of cases were identified to have multiple pathologies.

This classification system helps in understanding various exact etiological causes of AUB and can be used by the clinicians, investigators and even patients themselves to facilitate communication, clinical care and research. For this reason we strongly recommend adoption of this classification for AUB and HMB.

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