Diagnosis of abnormal uterine bleeding using PALM COEIN classification and its management: An institutional experience

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ABSTRACT
Aims: Categorization and treatment of abnormal uterine bleeding based on FIGO - PALM COEIN classification system

Methods: A prospective cross-sectional observational study was conducted in the Department of Obstetrics and Gynaecology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru for a period of 1 year from January 2019 to December 2019. All cases with abnormal uterine bleeding in 20 - 50 years of age were taken. Clinical details and imaging tests recorded, and categorized by FIGO- PALM COEIN classification for diagnosis and treatment. Statistical Package for Social Sciences version 21 was used to analyse the data and presented as frequencies and percentages.

Results: Out of 300 women of AUB, 190 had structural (PALM) and 110 women had nonstructural (COEIN) aetiology; 138 women among 300 underwent hysterectomy and 20 patients underwent hysteroscopic polypectomy. Levonorgestrel intrauterine device inserted in 40 patients, 85 women were managed medically and 17 women lost to follow-up for further management.

Conclusion: FIGO PALM-COEIN classification system for the diagnosis and treatment of abnormal uterine bleeding was adopted for the uniform standard.

Keywords: Abnormal uterine bleeding, leiomyoma, ovulatory disorder, PALMCOEIN

INTRODUCTION
Abnormal uterine bleeding (AUB) is the most common problem encountered among the non-pregnant women in the reproductive age group. It has substantial effect on health-related quality of women’s life. AUB is caused by a variety of pelvic pathology, systemic diseases or by medication related. The investigation and management of AUB will not be uniform and systematic unless a standardised method is in practice.

PALM COEIN classification system (Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia) for structural causes and (Coagulopathy, Ovulatory disorders, Endometrial, Iatrogenic and Not otherwise classified) for non-structural causes of AUB was proposed by International Federation of Gynecology and Obstetrics (FIGO) in 2011. In the 2018 FIGO system, AUB secondary to anticoagulants was moved from the coagulopathy category to the iatrogenic. AUB not otherwise classified contains rare etiologies and include arteriovenous malformations (AVMs), myometrial hyperplasia, and endometritis. Across the globe many gynaecological societies have adopted PALM – COEIN system to revise new guidelines for diagnosis and management of AUB. There are very limited data available in Indian women with Abnormal Uterine Bleeding (AUB) using FIGO - PALM COEIN classification system for overall treatment, hence our study was conducted.

The study was done to categorize women with AUB according to...
FIGO - PALM COEIN etiological classification system for the purpose of respective management options.

METHODS
A prospective cross-sectional observational study was conducted in the Department of Obstetrics and Gynaecology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru for a period of 1 year from January to December 2019. Institutional ethical committee clearance was taken. A total of 300 non-pregnant women of reproductive age between 20-50 years with abnormal uterine bleeding were included in the study. The women with obvious local lesions on vagina and vulva were excluded from the study. The written informed consent was taken from patients participated in the study. All the women in the study were clinically evaluated. A pelvic ultrasound was done to assess structural causes followed by hysteroscopy or saline sonography for abnormal uterine cavity and MRI to rule out myometrial pathology. Office endometrial biopsy or hysteroscopy guided biopsy was taken in women above 40yrs and for the patients with risk factors for endometrial cancer. For the evaluation of non-structural causes bleeding time, clotting time, and thyroid function test were done for all cases; and prothrombin time and activated partial thromboplastin time wherever required.

Coagulopathy was labeled for all known cases of coagulation disorder. Ovulatory disorder was defined as untimely and variable amount of bleeding. Endometrial disorders were the cause of AUB when timely or cyclical pattern of bleeding was observed. If symptoms were seen following the use of hormonal steroids or contraceptive device in the preceding 3 months then the cause of AUB was labeled as iatrogenic. The rest were included in the not yet classified category. The causes of AUB were categorized according to PALM-COEIN classification system and specific treatment was provided.

Data were tabulated in Microsoft Excel and SPSS version 21.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The descriptive statistics were presented as frequencies and percentages.

RESULTS
Out of 300 cases with AUB, 177 (59%) were seen in the age group of 41-50yrs followed by 31-40 yrs (n=99, 33%) and 20-30 yrs (n=24, 8%). Among 300 women 73% were parous women. Majority (66%) of the patients suffered symptoms of abnormal uterine bleeding for a period of more than 6 months. The most common pattern found was heavy menstrual bleeding followed by metrorrhagia, polymenorrhoea, menometrorrhagia, and hypomenorrhoea. [Table-1]

Table-1: Abnormal bleeding pattern

| Bleeding pattern       | N  | %   |
|------------------------|----|-----|
| Heavy menstrual bleeding| 170| 56.6|
| Metrorrhagia           | 60 | 20  |
| Polymenorrhoea         | 35 | 11.6|
| Menometrorrhagia       | 30 | 10  |
| Hypomenorrhoea         | 5  | 1.6 |

More than 60% had structural causes of AUB predominantly with leiomyoma and Adenomyosis. Ovulatory disorder was the commonest finding in non-structural causes. In the polyp group out of 25 women (8.3%), 10 women had cervical polyp and 15 women had endometrial polyp. Around 68 (22.6%) women had adenomyosis diagnosed on ultrasound and among them 10 patients had fibroid as well. Among 95 women with fibroid uterus majority had intramural fibroid and 18 women had submucosal fibroid. In 194 women endometrial biopsy was done. In 18 women histopathology showed endometrial hyperplasia and 2 women had endometrial carcinoma. In COEIN group 3 women were diagnosed with coagulopathy they were diagnosed to have idiopathic thrombocytopenic purpura with low platelet counts. Ovulatory disorders were found in 65 women and majority of women in ovulatory group demonstrated proliferative endometrium in histopathology. In iatrogenic group among 18 women, 5 were using intrauterine contraceptive device and 11 women were taking hormones irregularly in the preceding 3 months (COCs, emergency contraceptive pills) and 2 women were on anticoagulation for medical condition. [Table-2]

Table-2: Distribution of causes of AUB according to PALM-COEIN classification

| PALM category | N (%)     |
|---------------|-----------|
| AUB-P (Polyp) | 2 (8.3%)  |
| AUB-A (Adenomyosis) | 68 (22.3%) |
| AUB-L (Leiomyoma) | 95 (31.6%)  |
| AUB-M (Malignancy and hperplasia) | 20 (6.6%)  |
| Total         | 190 (63.3%) |
64.7% (194/300) had endometrial biopsy and majority had physiological endometrial pattern (either secretory or proliferative). Only two had endometrial carcinoma. [Table-3]

Table-3: Histopathological pattern of endometrial biopsy (N=194)

| Histopathological pattern       | N  | %   |
|---------------------------------|----|-----|
| Secretory                       | 114| 58.4|
| Proliferative                   | 56 | 28.8|
| Simple hyperplasia              | 10 | 3.3 |
| Complex hyperplasia             | 8  | 2.6 |
| Disordered endometrium          | 4  | 1.3 |
| Malignancy                      | 2  | 1.0 |

Treatment was individualised based on presentation, need of fertility and contraception. Majority (138, 46%) underwent hysterectomy and 20 had hysteroscopic polypectomy. Levonorgestrel intrauterine device inserted in 40 women, 85 women were managed medically and 17 women lost to follow-up for further management. [Table-4]

Table-4: Treatment approach for women with AUB

| Diagnosis                      | N  | Investigation                        | Treatment                                                                 |
|--------------------------------|----|--------------------------------------|---------------------------------------------------------------------------|
| Polyp                          | 25 | TVS, Hysteroscopy, Sono-hysterogram  | Cervical polypectomy/Hysteroscopic endometrial polyp resection in 25, LNG-IUS insertion done in 4 cases after polypectomy Hysterectomy done in 46 cases Medical management in 11 cases Adenomyomectomy in 3 cases Lost to follow up in 3 cases Medical management in 23 cases Myomectomy by laparoscopic/hysteroscopic in 13 cases LNG -IUS insertion done in 6 cases Hysterectomy done in 45 Lost to follow up 8 cases |
| Adenomyosis                    | 68 | TVS, MRI pelvis                      | Medical management in 25 cases Adenomyomectomy in 3 cases Lost to follow up in 3 cases Medical management in 23 cases Myomectomy by laparoscopic/hysteroscopic in 13 cases LNG -IUS insertion done in 6 cases Hysterectomy done in 45 Lost to follow up 8 cases |
| Leiomyoma                      | 95 | TVS, Sono-hysterogram                | Medical management in 25 cases Adenomyomectomy in 3 cases Medical management in 23 cases Myomectomy by laparoscopic/hysteroscopic in 13 cases LNG -IUS insertion done in 6 cases Hysterectomy done in 45 Lost to follow up 8 cases |
| Malignancy and hyperplasia     | 20 | Endometrial biopsy                   | Medical management in 3 cases LNG -IUS insertion in 1 case Medical management in 3 cases LNG -IUS insertion done in 1 case Medical management in 3 cases Myomectomy by laparoscopic/hysteroscopic in 13 cases LNG -IUS insertion done in 6 cases Hysterectomy done in 45 Lost to follow up 8 cases |
| Coagulopathy                   | 3  | Platelet count, coagulation profile  | Medical management in 2 cases Coagulopathy in 3 cases Medical management in 3 cases |
| Ovulatory disorders            | 65 | Endometrial biopsy                   | Medical management in 25 cases Adenomyomectomy in 3 cases Medical management in 23 cases Myomectomy by laparoscopic/hysteroscopic in 13 cases LNG -IUS insertion done in 6 cases Hysterectomy done in 45 Lost to follow up 8 cases |
| Iatrogenic                     | 18 | History of hormonal intake/copper T insertion | Medical management in 25 cases Adenomyomectomy in 3 cases Medical management in 23 cases Myomectomy by laparoscopic/hysteroscopic in 13 cases LNG -IUS insertion done in 6 cases Hysterectomy done in 45 Lost to follow up 8 cases |
| Endometrial                    | 6  | Endometrial biopsy                   | Medical management in 25 cases Adenomyomectomy in 3 cases Medical management in 23 cases Myomectomy by laparoscopic/hysteroscopic in 13 cases LNG -IUS insertion done in 6 cases Hysterectomy done in 45 Lost to follow up 8 cases |

DISCUSSION

In the present study, most of the women were in the perimenopausal age group (41–50 years). The age distribution of AUB in our study revealed that 59% of cases belonged to 41-50 years and menorrhagia (56.6%) was the commonest presenting complaint. About 66% of women had symptoms for more than 6 months. These findings were similar to a study by Jaitly et al. and Shoba PS et al. This may be due to anovulation and increased resistance to gonadotrophic stimulation.

In our study the structural PALM component (63.3%) contributed more for the cause of AUB as compared to functional COEIN (36.6%) which is similar to study done by Betha K et al whereas in study done by Devanshi Mishra et al, both the components of PALM COEIN classification was equally contributing to the clinical causes of AUB. Leiomyma, AUB-L (31.6%) being the major cause of AUB in our present study similar to other studies which also showed leiomyoma as the predominant cause of AUB. Leiomyomas are the major contributor in structural cause for AUB. Heavy menstrual bleeding (HMB) was the commonest presenting complaint with leiomyoma. The symptoms of AUB are more related to the location and
size of the myoma. Submucous fibroids have high association with AUB, as increased endometrial surface area contributes to excessive bleeding. Polyps (AUB-P) were found in 25 (8.3%) women in the present study. Similar finding (11.2%) was seen in a study done by Doraiswamy et al. Women with endometrial polyps presented to us as intermenstrual bleeding, HMB and postmenopausal bleeding; and the diagnosis was made on the basis of increased endometrial thickening with a feeder blood vessel on a transvaginal pelvic ultrasound that was confirmed by visualization with sonohysterography or hysteroscopy. In our study 10 Cervical polyps were diagnosed on clinical examination, 15 women had endometrial polyps diagnosed either on ultrasound or hysteroscopy.

The cause of AUB due to adenomyosis AUB-A was seen in about 68 (22.6%) women in our study, similar to the studies done by Qureshi et al. It is one of the common causes of AUB between 35-50 years. Adenomyosis is the presence of ectopic endometrial tissue in the myometrium. The diagnosis of adenomyosis by ultrasound examination is sometimes practically difficult, MRI is the better one and diagnostic is the histopathology only. In a study by Taran et al, 70 to 80% of women undergoing hysterectomy for adenomyosis are in their fourth and fifth decade of life and are multiparous. Multiparous women had high incidence of adenomyosis. It was explained that during pregnancy adeno myotic foci to be included in the myometrium due to the invasive nature of the trophoblast leading development of Adenomyosis.

In the present study, AUB- M (Malignancy and hyperplasia) endometrial hyperplasia accounted for 9.2% and adenocarcinoma for 1% which was similar to the study done by Mishra et al and Singh et al. 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. Ovulatory disorders AUB-O seen in 65 patients (21.6%) being more important cause amongst functional causes in the present study which was similar to findings of Singh et al and Mishra. Coagulopathy (AUB-C) is found in 1% of women presenting with AUB, in the present study which is similar to Qureshi et al study (0.3%) and Mishra et al (0.8%). Von Willebrand disease is said to be the most common inherited bleeding abnormality. In our study, AUB-E contributed to 2% of patients and its aetiological diagnosis is limited by unavailability of tests in places.

In present study women with AUB-P, were managed with hysteroscopic polypectomy, and sent for histopathology to rule out any malignancy. In a women with Multiple polyps and fertility is not desired– LNG-IUS was inserted to avoid recurrence. Pereira et al stated hysteroscopic removal was the gold standard treatment for endometrial polyps. Fraser et al suggested that the use of LNG-IUS was useful to prevent the development of endometrial polyps.

In women with AUB-A the treatment was challenging. Hysterectomy remains the definitive treatment for women for whom fertility is not a concern. As suppressive hormonal treatments such as continuous use of oral contraceptive pills, progestogens, LNG-IUS, can temporally induce regression of adenomyosis but prevent pregnancy. So, adeno myomectomy was offered to women who were desirous to conceive. The procedure was technically challenging as there is no clear plane between adenomyoma and normal myometrium. However, new drugs, such as selective progesterone receptor modulators, aromatase inhibitors, and anti-platelet therapy, are under development for the treatment of Adenomyosis.

Treatment was individualized for fibroid like tranexamic acid, NSAIDS or combined oral contraceptives (COCs), mifepristone, progesterone receptor modulators such as ulipristal acetate, GnRH analogues were given. For failed medical treatment and eligible candidates surgery was performed. As reported by Taran et al preoperative GnRH analogues and ulipristal acetate treatment for 3-4 months was given to improve anemia, to reduce intraoperative blood loss and need for blood transfusion. NICE guideline recommends, in the absence of pressure symptoms, medical treatment may be more appropriate, particularly when fertility preservation is required. Tranexamic acid and NSAID remain the only fully non-contraceptive medical options.

The women with simple endometrial hyperplasia without atypia with low risk for progression to endometrial cancer were managed with progesterone therapy (Medroxy progesterone 10mg daily for 3-6 months). In our study Tranexamic acid and NSAID were considered the first-line therapy non-
structural causes of AUB. In women desiring effective contraception, LNG-IUS and COCs were recommended. Cyclic oral progestins (from day 5 to 25), are recommended if COCs are contraindicated; similar approach of management was recommended by Khrouf et al. NSAIDs are to be avoided in patients with bleeding disorders or platelet function abnormalities.

CONCLUSIONS
FIGO – PALM COEIN structured diagnostic classification of abnormal uterine bleeding and their respective management options have been applied.

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