Original Research Article

Distribution of causes of abnormal uterine bleeding according to PALM COEIN classification in tertiary health centre and its histopathological correlation

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ABSTRACT

Background: AUB is a common problem among women of all ages, accounting for 20-30% of outpatient visits in the reproductive age group and 69 percent in the peri or postmenopausal age group. It has a major effect on women's personal, social, physical, and psychological well-being.

Methods: This prospective observational research was performed at J K Lone Mother and Child Hospital and Government Medical College, Kota, Rajasthan, from date January 2018 to July 2019, in the department of obstetrics and gynecology. The researchers looked at all women in the 40-year-old age group who had AUB and were not responding to nonsurgical care. Several causes of PALM and COEIN were investigated, and a histo-pathological association was calculated.

Results: Total 60 women with AUB not responding to medical management were taken. Majority (53.3%) women were between 40-50 years of age. Majority (63%) were para 2.Most common associated structural cause was leiomyoma (31%) followed by adenomyosis (25%) followed by ovulatory dysfunction (18%) followed by malignancy and polyp (10%).Most common histopathological finding was secretory phase (31.7%) followed by proliferative phase (28.3%) and then by hyperplasia (21.7%).ROC curve analysis showed that AUB-PALMCOEIN can predict diagnosis up to 95.8%. P value analysis for polyp, fibroid, ovulatory, endometrial was not significant showing that AUB-PALMCOEIN can predict diagnosis as much as histopathological examination. P value analysis for adenomyosis and malignancy was significant showing histopathology to be more accurate in giving diagnosis.

Conclusions: The PALM-COEIN classification aids in determining the cause of AUB and, as a result, efficiently adopting and planning for patient care. The structural cause of AUB played a larger role in the development of AUB. The major causes of AUB were divided into structural and non-structural causes in this research. The COEIN part of the classification needs to be improved further through in-depth analysis.

Keywords: Abnormal uterine bleeding, Histo-pathological, PALM-COEIN

INTRODUCTION

Abnormal uterine bleeding

Any change in the frequency of menstruation, the length of flow, or the amount of blood loss is known as AUB.[1] AUB is a common issue that affects women of all ages, accounting for 20-30% of outpatient visits in the reproductive age group and 69 percent in the peri or postmenopausal age group.[2]

PALM-COEIN classification

The PALMCOEIN classification scheme for causes of AUB in nonpregnant women of reproductive age group3 was established by the International Federation of

Gynecology and Obstetrics' working group on menstrual disorders. This classification scheme is divided into nine basic divisions, each of which is arranged alphabetically. AUB may cause pain and discomfort, as well as social humiliation and a reduction in health-related quality of life. The use of formal clinical practise guidelines is required for the management of such a common condition in a population with a broad variety of healthcare needs. In order to standardize clinical management practices, a unified set of practice guidelines based on scientific evidence is required. In 2011, FIGO introduced the PALMCOEIN classification. The FIGO nomenclature scheme can help to solve the problem of AUB management inconsistency.

PALM-COEIN stands for polyp, adenomyosis, leiomyoma, malignancy, hyperplasia, coagulopathy, ovulatory dysfunction, endometrial disorder, iatrogenic, and unclassified. Menorrhagia, polymenorrhoea, metrorrhagia, and intermenstrual bleeding are the most common clinical manifestations. The new terminologies approved by FIGO are:

Menorrhagia can be replaced with heavy menstrual bleeding (HMB) to explain excessive bleeding.

The term metrorrhagia should be replaced with intermenstrual bleeding (IMB), which occurs between specifically described cyclic and predictable menses.

Menometrorrhagia should be replaced by heavy and sustained bleeding (HPB).

Polymenorrhoea can be replaced by frequent menstrual bleeding.[4]

In our study detailed history was taken, investigation including CBC, UPT, coagulation profile, USG, colour doppler were done.

Histopathological correlations

Since there is always the risk of category reallocation, a detailed histopathological examination and clinical correlation is needed. Assessing a correlation can help decide how accurate clinical assignment to the category of AUB is and when a pathological correlation is required, particularly for the PALM aspect of PALM-COEIN, whereas the same can be done for the COEIN (functional) aspect using other investigations including haematological and endocrinological work up. FIGO suggests endometrial tissue examination as the first line of treatment for AUB in perimenopausal women. Histology confirms the diagnosis and directs the treatment strategy. When considering hormone therapy, a precancerous neoplasia such as suspected hyperplasia or subclinical endometrial cancer must be ruled out. As a result, a histological examination remains the cornerstone of current practice, as it accurately places the clinical diagnosis and allows for standard-inaction treatment.

The aim of this study was to investigate and analyze the structural (PALM) and functional (COEIN) components of the AUB PALM-COEIN system in perimenopausal women in our area. This was followed by histopathological studies and case correlations where applicable, especially for the structural (PALM) portion and the COEIN (functional) categories of AUB-E and AUB-O.

METHODS

The present study includes total 60 women (>40 years) with complaints of abnormal uterine bleeding and underwent surgery, admitted in the department of Obstetrics and Gynaecology at J K Lone Mother and Child hospital and Government Medical College located in Kota of Rajasthan state. The study period was one and half year. Patients aged above 40 years and patient who required abdominal hysterectomy for AUB and not responding to nonsurgical mode of treatment were included. Patients age below 40, gestational bleeding, genital prolapse, carcinoma cervix, bleeding diathesis, trauma induced bleeding were excluded. After approval from institutional ethical committee and obtaining written informed consent in local vernacular language, the patients who were fulfilling the inclusion criteria were included in the study. A systematic history of previous and current menstrual history, history of contraceptive usage, and medical/surgical history was collected, accompanied by a general, physical, structural, and gynecological review.

During the gynaecological test, the cervix (location, any erythematous lesion, hypertrophy, mobility, presence of polyp or ectopic), uterus (size, place, consistency, and mobility), and adnexa (tenderness and mobility) were all evaluated.

The clinical diagnosis and PALM-COEIN assignment were completed. A pelvic ultrasound was used to evaluate the uterus (uterine size, endometrial thickness, existence of endometrial polyp, adenomyosis, or fibroids) as well as the ovarian status (presence of any cyst, mass, and its characteristics). Wherever possible, endometrial biopsy and hysterectomy (with or without salpingoopherectomy) specimens were collected and submitted for histopathological analysis. When there was a question about malignancy, a Doppler USG was performed, followed by a biopsy. Possible underlying causes were classified based on histopathological findings. After that, the clinical diagnosis was compared to the histopathology-based final diagnosis. Wherever possible, a full blood count, coagulation profile, UPT (if pregnancy is suspected), and thyroid function test are performed.

The statistical package for social sciences (SPSS IBM) version 21.0 was used to analyses the data. The required univariate and bivariate analyses were completed. Quantitative variables are defined in terms of mean, median, range, and standard deviation, while qualitative variables are described in terms of proportions. Before

applying sufficient significance checks, the data was tested for normality. The Chi square test was used to measure the significance of the difference in means and the independent t test was used to calculate the difference in proportions. The significance of the p value was set to 0.05.

RESULTS

A total of 60 (100%) study participants were included in the study. Majority (53.3%) belong to age group 40-50 years. Majority were Para 2 (63.4%). Majority belong to rural area 38 (63.3%) and 22 (36.7%) reside in urban area.

Table 1: Clinical diagnosis of study participants with palm coein classification (n=60).

PALM COEIN classification	N (%)
Polyp	6 (10)
Adenomyosis	15 (25)
Leiomyoma	20 (31)
Malignancy or hyperplasia	6 (10)
Coagulopathy	0
Ovulatory dysfunction	11 (18)
Endometrial	2 (3.3)
Iatrogenic	1 (2)
Not yet classified	0

Table 2: Histopathological findings of study participants with AUB (n=60).

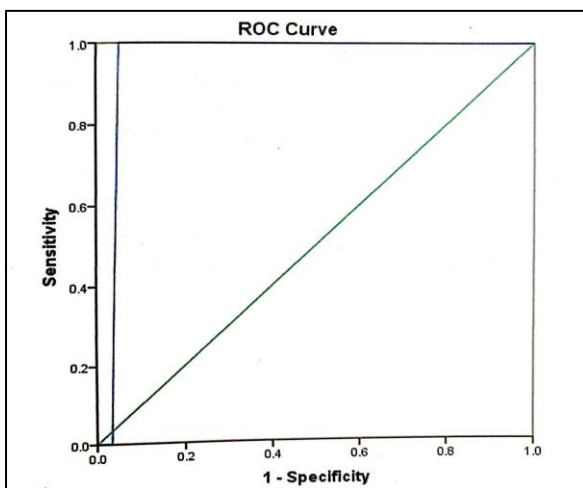| HPE findings	N (%)
Secretory phase	19 (31.7)
Proliferative phase	17 (28.3)
Hyperplasia	13 (21.7)
Adenocarcinoma	2 (3.3)
Tubercular	3 (5)
Inflammatory	2 (3.3)
Atrophic	4 (6.7)

Figure 1: Diagonal segments are produced by ties.

Table 3: Correlation of clinical and histopathological based diagnosis of AUB.

	PALM COEIN	HPE	P value
Polyp	6	8	0.2
Adenomyosis	15	13	0.02
Leiomyoma	20	21	0.2
Malignancy	6	13	0.03
Ovulatory	11	13	0.8
Endometrial	2	1	0.4
Adenomyosis and leiomyoma	0	2	0.01

Table 4: Test result variable(s) PALMCOEIN.

Area	Std. error	Asymptotic sig.	Asymptotic 95% confidence interval	
			Lower bound	Upper bound
0.958	0.027	0.119	0.905	1.000

Among the study participants, hypertension was found in 3 (5%) and diabetes mellitus was present in 2 (3.3%). Thyroid disorder was present in 3(5%). History of use of oral contraceptives was present in 7 (11.7%) study participants.

Only one participants (1.7%) reported family history of endometrial cancer. Majority (43.3%) patients were obese. History of PCOD was present in 3 (5%) study participants.

Leiomyoma (33%) was commonest cause of AUB followed by adenomyosis (25%) followed by ovulatory dysfunction (18%) then by Malignancy or polyp (10%). Most common histopathological findings was secretory phase (31.7%) followed by proliferative phase (28.3%) then by hyperplasia (21.7%).ROC curve analysis inferred that PALM COEIN classification was able to predict the histopathological examination up to 95.8%.Thus classification by palm coein etiological classification matches the histopathological examination. Benign lesions in the form of hyperplasia was found in 13 (21.7%) study participants and malignant lesion was found in 2 (3.3%).

DISCUSSION

The present study was done with objective to evaluate clinically the cause of AUB in perimenopausal and postmenopausal women according to AUB PALMCOEIN classification and to correlate clinically evaluate cause including ultrasonographic findings with histopathological finding after hysterectomy. The other objective was to calculate relative incidence of benign and malignant endometrial lesions. A total of 60 (100%) study participants were included in the study.

In present study majority of the patients were in the age 40-50 years (53.3%) followed by 51-60 years (41.7%)

which is corresponding to study done by Betha et al in which maximum patients were in the age group 41-45 years (42%).[5] Similar results were found in the study done by Anupma Suresh et al where maximum patients were in the age group 46-50 years (52.4%).[6]

In a study conducted by Mahapatra et al, it was discovered that AUB is more common in women in their fifth decade of life and in multiparous women.[7] The increased prevalence of AUB in this age group could be due to the fact that these women are approaching menopause, when their cycles become intermittently anovulatory as the number of ovarian follicles and estradiol levels decline.

In present study group women with parity 1 were (20.7%) and parity 2 were (55.38%) which is corresponding to study done by Byna et al where 16.9% were para 1 and 55.4% were para 2.[8] Similar results were found in the study done Betha et al where maximum patients were parity 2 (44%) followed by parity 3 (36%).[5] Adenomyosis was more common in multiparous women, with the diffuse subtype predominating. Pregnancy may facilitate the development of adenomyosis by enabling adenomyotic foci to be included in the myometrium due to the invasive presence of the trophoblast on the extension of myometrial fibres. Adenomyotic tissue may also have a higher oestrogen receptor ratio, and the hormonal environment of pregnancy may favour the formation of ectopic endometrium islands.

Hypertension was found in 3 (5%) patient and diabetes in 2 (3.3%) in whom endometrial hyperplasia was found in histopathological examinations. Hypothyroidism was present in 3 (5%) of patients out of which 2 had AUB-O. These findings are corresponding to study done by Suresh et al6 where significant p value correlation was found between hypertension and diabetes with endometrial hyperplasia. In her study, 18.9% patient with hypertension, 5% with diabetes mellitus and 5.3% with hypothyroidism had endometrial hyperplasia, difference in percentage could be explained due to large sample size of her study.

In present study AUB was found maximum in patients with BMI ≥25 with percentage of 44% which corresponded to study done by Betha et al5 where AUB was maximum in obese females (57%). Excess adipose tissue improves the peripheral aromatization of androstenedione to estrone in obesity. Elevated estrone levels in premenopausal women cause irregular feedback in the hypothalamopituitary axis, resulting in oligo or anovulation. The endometrium is constantly stimulated by estrogen in the absence of ovulation.

In our study 3 (5%) had PCOD, out of which two had AUB-M hyperplasia, in PCOS the thecal cells have generalized overactive steroidogenesis with increase in androgens and increased estrogen but decreased progesterone production. It leads to unopposed action of estrogens on endometrium which can lead to endometrial hyperplasia, atypical hyperplasia and endometrial cancers over years.

PALMCOEIN classification

In present study it was found that among the study participants, polyp (10%), adenomyosis (25%), leiomyoma (33%), malignancy or hyperplasia (10%), ovulatory dysfunction (13%), endometrial (3.3%), iatrogenic (2%), coagulopathy or not yet classified (0%).

Doraiswami et al found that the most common trend was natural cycling endometrium (28.4 percent).[9] The disordered proliferative pattern was the most common pathology, regardless of age group (20.5 percent). Other causes included pregnancy complications (22.7%), benign endometrial polyps (11.2%), endometrial hyperplasia (6.1%), carcinomas (4.4%), and recurrent endometritis (4.4%). (4.2 percent)

According to Guari et al, PALM-COEIN categorization was performed in 30 (37%) cases with 6 (2%) polyps, 38 (12.66%) adenomyosis, 74 (24.67%) leiomyoma, 15 (5%) malignancy and hyperplasia, 9 (3%) coagulopathy, 81 (27%) ovulatory dysfunction, 27 (9%) endometrial triggers, 24 (8%) About 7% (2.34%) of the cases fell into the mixed category.[10]

Sharda B et al conducted a study in which 350 women of reproductive age were given AUB for at least three months. Ovulatory dysfunction was the most common cause of AUB (n=99, 282.2%).[11] Endometrial causes (n=52,14.5 percent), adenomyosis (n=30, 8.5 percent), not yet identified (n=32, 9.7 percent), malignancy and hyperplasia (n=28, 8.1 percent), polyp (n=9, 2.5 percent), Iatrogenic (n=7, 2.2 percent), and coagulopathy (n=1, 0.3 percent) were the next most common causes (n=90, 25.7 percent).

Adenomyosis was found in 25 of our patient which corresponds to the study done by Palet al in which 21.9% patient had adenomyosis.[12]

Leiomyoma was found in 33% of the patients which corresponds to study done by Betha et al in which it was found in 30.4% of patient.[5] Fibroids become more common as people get older, with the majority of cases occurring between the ages of 41 and 45. Endometrial hyperplasia induced by hyper estrogenemia, the involvement of fragile and engorged vasculature in the perimyoma tissue, and the release of angiogenic factors such as VEGF and platelet-derived growth factor (PDGF), which impair local endometrial hemostasis, can all contribute to HMB.

Endometrial hyperplasia, which is marked by the proliferation of endometrial glands and the progression to endometrial carcinoma, is the cause of AUB. Obesity and chronic aovulation were discovered to be risk factors in this study of premenopausal women. As endometrial

cancers are common in the age group 50-60 years, the AUB-M was seen in 10%, similar to Qureshi et al study where AUB-M was seen in 10% of cases and AUB-O in 24% patients. A study done by Mishra D et al showed AUB-M in 3% and AUB-O in 37%. Difference in percentages could be because of different age groups of the study population.[13,14]

AUB-I was found in 2% of patients, it was due to IUCD leading to endometritis.

Correlation of PALMCOEIN with Histopathological diagnosis

In the present study on histopathological examination it was found that secretary phase endometrium was seen in 19 (31.7%), proliferative phase in 17 (28.3%), hyperplasia in 13 (21.7%), adenocarcinoma in 2 (3.3%), tubercular 3 (5%), inflammatory 2 (3.3%) and atopic 4 (6.7%).

According to Shukla et al, the most frequent histopathological finding was endometrial proliferative pattern, which was seen in 27 percent of patients, accompanied by endometrial hyperplasia (13.5 percent), secretory endometrium (12.7 percent), and disordered proliferative endometrium (10.9 percent).[15] In 1.7 percent of cases, malignancy was discovered.

Similarly in a study by Prassana et al out of 65perimenopausal women, 23 (35.38%) had proliferative type of endometrium, 20 (30.76%) women had secretory pattern, 9 (13.84%) had typical simple endometrial hyperplasia, 4 (6.15%) had atypical simple endometrial hyperplasia, 3 (4.61%) had adenomyomatous polyp and 6 (9.2%) women had irregular ripening.[8]

In a study by Layla A et al most common histopathological diagnosis found was secretory endometrium 571 (24.9%) 2nd most was proliferative endometrium 498 (21.7%), followed by endometrium polyp 227 (9.9%), disordered proliferative endometrium 200 (8.7%), Simple cystic hyperplasia 160 (7%), chronic endometritis 134 (5.8%), inactive endometrium 126 (5.5%), atrophic endometrium 70 (3.1%), Uterine malignancies 41 (1.8%), complex hyperplasia without atypia 33 (1.4%) and finally complex hyperplasia with atypia 15 (0.7%).[18]

In a study by Mohammed et al it was found that the most common histopathological diagnosis was of AUB-L in 43.7% cases and 2nd most being AUB-O.[17]

P>0.05 is not significant and <0.05 is taken as significant.

After examining various groups, the difference in clinical and histopathological diagnosis in AUB-P(polyp) was not significant (p>0.05). The majority of the cases in this study were cervical polyps, which were diagnosed clinically using a per speculum examination.

In AUB-A (adenomyosis), there was a significant difference in clinical and histopathological diagnosis (p0.05). This is due to the fact that the symptoms and signs of adenomyosis and leiomyoma can be so similar that clinically distinguishing between the two can be difficult. Due to the higher cost, we were also unable to use MRI as a diagnostic tool.

In AUB-L (Leiomyoma), there was no significant difference in clinical and histopathological diagnosis (p>0.05). It's likely that this is because most symptomatic fibroids can be detected with a combination of history, clinical pelvic examination, and ultrasonography.

The disparity in clinical and histopathological diagnosis in AUB-M (malignancy and hyperplasia) was highly important (p0.01).

Adenomyosis and leiomyoma (AUB-A;L) was a very important condition (p0.01). The results of AUB-M and AUB-A;L illustrate the importance of histological analysis as a complementary diagnostic method in the PALM portion of AUB.

The difference in clinical and histopathological diagnosis between AUB-O (ovulatory disorders) and AUB-E (abnormal uterine bleeding) was not important (p>0.05).

Benign lesions in form of hyperplasia was found in 13 (21.7%) study participants and malignant lesions in 2 (3.3%). Similar results were found in study done Layla A et al16where 20% in perimenopausal and post menopausal women had endometrial hyperplasia and 4% had malignancy. In a study by Shukla et al benign were 14% and endometrial carcinoma was found in 1.7%.

According to the PALM COEIN scheme, there aren't many studies that indicate the causes of AUB. This type of research will help us gain a deeper understanding of AUB's etiology and develop more successful management strategies. Because of the expense, MRI characterization of structural lesions of the uterus was not performed, and thus tertiary classification of leiomyoma was not performed in this study. In patients where malignancy was suspected colour doppler was done to demonstrate endometrial lesions and endometrial arteriovenous malformations as well as multiple irregular branching vessels in malignancy.

CONCLUSION

In women, the endometrium is a reflection of their hormonal status. Endometrial histological differences may be seen depending on the woman's era, menstrual cycle phase, and any other pathology. Pelvic ultrasound is the least invasive technique for visualizing the anatomy of the uterus and visualizing the thickness of the endometrium in the diagnosis of AUB. It can provide additional details that may help with diagnosis and treatment decisions in some cases.

Endometrial sampling, on the other hand, can be used as a first diagnostic phase in excessive uterine bleeding, but its understanding can be difficult for a practicing pathologist at times.

To successfully treat patients with AUB, it is important to determine the exact cause. The PALM-COEIN classification aids in determining the cause of AUB and, as a result, efficiently adopting and planning for patient-centered care.

AUB's systemic causes played a greater role in the disease's growth. Clinicians and researchers may use the PALM COEIN classification scheme to make global comparisons and better understand the various etiological causes of AUB.

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