|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
PubMed (National Library of Medicine ID: 101738825)
Index Copernicus Value 2018: 75.71
Original Research Article Volume 4, Issue 1; January: 2020; Page No. 209-213

STUDY TO CORRELATE CLINICAL AND HISTOPATHOLOGICAL FINDINGS OF ABNORMAL UTERINE BLEEDING ACCORDING TO FIGO'S PALM-COEIN CLASSIFICATION

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Article Info: Received 18 December 2019; Accepted 22 January. 2020
DOI: https://doi.org/10.32553/ijmbs.v4i1.896
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Conflict of interest: No conflict of interest.

Abstract
Abnormal uterine bleeding (AUB) is a common and debilitating condition with high direct and indirect costs. AUB frequently co-exists with fibroids, but the relationship between the two remains incompletely understood and in many women the identification of fibroids may be incidental to a menstrual bleeding complaint. Abnormal uterine bleeding (AUB) is one of the common presenting complaints encountered by a Gynaecologist. The International Federation of Gynaecology and Obstetrics working group on menstrual disorders has recently developed a classification system (PALM–COEIN) for causes of the AUB in non-gravid women. The present study was conducted with the aim to study and analyse the structural (PALM) and the functional (COEIN) component of the PALM–COEIN system of AUB in perimenopausal age group. A total of 200 perimenopausal women (aged 40 years and above till 1 year beyond menopause) who were admitted with complaints of abnormal uterine bleeding comprised the study population. Clinical diagnosis and allocation to PALM–COEIN was done. Endometrial biopsy and hysterectomy specimens (wherever applicable) were obtained and sent for histopathology. As per the histopathological findings, possible underlying causes were categorized. Clinical diagnosis was then correlated with histopathology-based final diagnosis. PALM and COEIN components contributed almost equally for AUB when assessed clinically. The histological examination revealed significantly more cases of PALM (structural or anatomical) component of AUB. The PALM COEIN classification system helps us in understanding various etiological causes of AUB and can be used by clinicians and researchers for international comparisons.
Keywords: Abnormal uterine bleeding (AUB) , PALM–COEIN . Perimenopause

Introduction

Abnormal uterine bleeding (AUB) is a common and debilitating condition with high direct and indirect costs. AUB frequently co-exists with fibroids, but the relationship between the two remains incompletely understood and in many women the identification of fibroids may be incidental to a menstrual bleeding complaint. A structured approach for establishing the cause using the Fédération International de Gynécologie et d'Obstétrique (FIGO) PALM-COEIN (Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia), Coagulopathy, Ovulatory disorders, Endometrial, Iatrogenic and not otherwise classified classification system will facilitate accurate diagnosis and inform treatment options.[1] Abnormal uterine bleeding (AUB) is one of the common presenting complaints encountered by a Gynaecologist. It is a significant cause of hysterectomy and thus is a major health problem. AUB is also associated with significant social and physical morbidities in all societies and may be a reflection of serious underlying pathology[2]. AUB may be acute or chronic and is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency or duration and occurs in the absence of pregnancy[3,4]. AUB is the commonest menstrual problem during perimenopause which is defined as the period of 2–8 years preceding menopause and 1 year after the final menses[5]. The International Federation of Gynaecology and Obstetrics working group on menstrual disorders has recently developed a classification system (PALM–COEIN) for causes of the AUB in non-gravid women[6]. There are nine main categories, which are arranged according to the acronym PALM–COEIN: polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified. PALM side of the classification refers to structural causes that may be evaluated by imaging techniques and/or histopathology and the COEIN side by investigating the underlying medical disturbances. FIGO recommends endometrial tissue testing as a first-line management in women of perimenopausal age group who have AUB[7,8]. The present study was conducted with the aim to study and analyse the structural (PALM) and the functional (COEIN) component of the PALM–COEIN system of AUB in perimenopausal age group women of our region. This was followed by the histopathological studies and correlation of cases wherever applicable particularly for the structural (PALM) component and for categories of

AUB-E or AUB-O of the COEIN (functional) aspect. Aim is to study and analyse the structural (PALM) and functional (COEIN) component of PALM-COIEN system of AUB in perimenopausal women.

Material and Methods:

After approval from the Institutional Review Board (IRB no. 764/2018) and informed written consent from all the patients this prospective and interventional study was carried out in Department of Obstetrics and Gynaecology from March 2018 to July 2019 at, Govt. Medical College and Sir. T. General Hospital, Bhavnagar, Gujarat.

Inclusion criteria:-

- Perimenopausal women aged 40 years and above till 1 year beyond menopause who have complaints of abnormal uterine bleeding.

Exclusion criteria:-

- Patient refusal
- Women who are <40 years of age and those beyond 1-year menopause were excluded from the study
- Obstetrics cause of bleeding

The present study was conducted at the tertiary center, government medical college of Bhavnagar. A total of 200 perimenopausal women (aged 40 years and above till 1 year beyond menopause) who were admitted with complaints of abnormal uterine bleeding comprised the study population. Women who were 40 years of age and less than 40 year and those beyond 1 year of menopause were excluded from the 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. Clinical diagnosis and allocation to PALM–COEIN was done. 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. Endometrial biopsy and hysterectomy specimens (wherever applicable) were obtained and sent for histopathology. As per the histopathological findings, possible underlying causes were categorized. 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. 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 of AUB-O and AUB-E with the clinical assignments.

Statistical analysis:

Data were analysed by SPSS version 16, and descriptive statistics were presented as frequencies, percentages and bar charts. Chi-square applied to know the significance of the correlation

Results:

- The majority of this woman less than 50-year age group 80.5%. There were women age group between 51-55 year was 20% and 56-60 year is 0.5%.
- Most common presenting symptoms was heavy menses for 6 months to 1 year (58.5%) followed by frequent menses (15%), intermenstrual bleeding (5%) and irregular bleeding (20.5%).
- In total 35 (17.5%) women were obese, 27 (13.5%) were hypertensive, 12(6%) had thyroid abnormalities, 9 had (4.5%) had diabetes mellitus and 17(8.5%) had anaemia. Associated risk factor.
- Majority of these women were multipara (73.5%) followed by grand multipara (21%), primipara (4.5%) and nullipara (1%).

Table 1: Distribution of cases as per clinical based diagnosis palm.

DIAGNOSIS	TOTAL CASES N=102 (51%)	Percentage of PALM	Structural Percentage
AUB-P	10	5%	9.8%
AUB-A	22	11%	21.56%
AUB-L	67	33.5%	65.68%
AUB-M	03	1.5%	2.94%
AUB-A; L	00	00%	00%

Distribution of cases based on clinical PALM component was 51%. Leiomyoma most common cause in PALM 67/200(65.68%) in structural group. Leiomyoma was 2nd most common cause of AUB.Adenomyosis contribute 11% of cases to cause AUB followed by polyp which was 5% and malignancy contribute 1.5%. Clinically both adenomyosis and fibroid was not found.

Table 2: Distribution of cases as per clinical diagnosis of coein

DIAGNOSIS	TOTAL CASES N=98(49%)	PERCENTAGE OF COEIN	FUNCTIONAL PERCENTAGE
AUB-C	0	00%	00
AUB-O	80	40%	81.63%
AUB-E	18	09%	18.37%
AUB-I	00	00%	00
AUB-N	00	00%	00

Distribution of cases clinical basedCOEIN component contribute about 49%. Total 80 cases out of 200 due to ovulatory disorder and 18 cases due to endometrial disorder. Ovulatorycause was contributing about 40% and endometrial cause about 9%. adulatory cause is most common cause of AUB.

Table 3: Distribution of cases as per histopathological based diagnosis palm-coein

Diagnosis	Total cases N=118 (59%)	Percentage (59%)	Structural Percentage
AUB-P	09	4.5%	7.6%
AUB-A	27	13.5%	22.88%
AUB-L	66	33%	55.937%
AUB-M	13	6.5%	11.01%
AUB-A;L	03	1.5%	3.54%

Distribution of cases according Histopathological PALM. Total 118 cases were diagnosed in PALM category .16 cases were not diagnosed by clinical PALM. There were 3 cases diagnosed as a AUB-A; L.

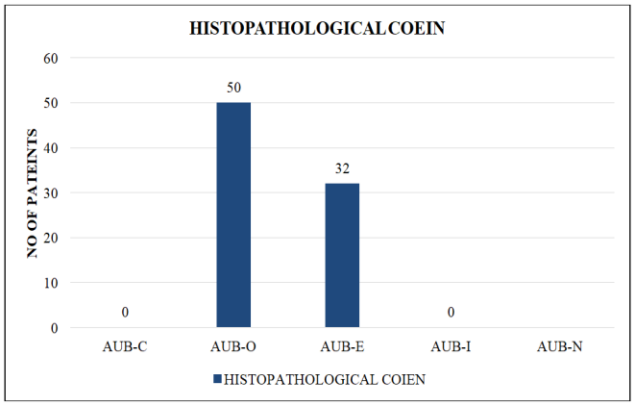

Figure 1:

Distribution of cases according Histopathological of COEIN category. Total 82 cases were diagnosed in COEIN category. Out of 82 cases 50 cases due to AUB-O and 32 due to AUB-E.

Table 4: Correlation of clinical and histopathological diagnosis

Category	Clinical PALM n=102	Histopathological PALM n=118
AUB-P	10	09
AUB-A	22	27
AUB-L	67	66
AUB-M	03	13
AUB-A;L	00	03

In clinical and histopathological correlation clinically polyp cases were 10 but in histopathological polyp cases were 9 which was almost similar. In leiomyoma also clinically diagnosed cases were 67 but in histopathological diagnosed cases were 66.In adenomyosis clinically diagnosed cases were 22 but histopathological diagnosed cases were 27.In malignancy histopathological diagnosed cases were significantly higher in number which was 13 but clinically diagnosed cases were only 3.In fibroid and adenomyosis clinically cases were not diagnosed but in histopathological diagnosed cases were 3

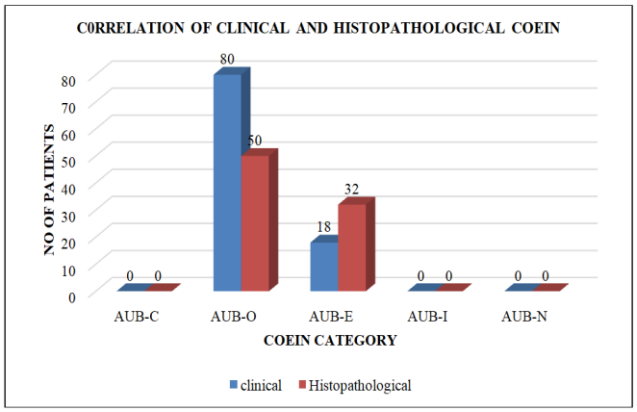

Figure 2

In COEIN category clinically ovulatory cases were 80 but histopathological diagnosed cases were 50. In endometrial cases clinically diagnosed cases were 18 but histopathological diagnosed cases were higher in number which was 32.

Table 5: Correlation of clinical and histopathological based diagnosis

Category	Clinical PALM N=102(51%)	Histopathological PALM N=118(59%)	p value
AUB-P	5%	4.5%	>0.05(NS)
AUB-A	11%	13.5%	>0.05(NS)
AUB-L	33.5%	33%	>0.05(NS)
AUB-M	1.5%	6.5%	<0.05(S)
AUB-A;L	00%	1.5%	<0.05(NS)

Table 6:

Category	Clinical COEIN N=98(49%)	Histopathological COEIN N=82(41%)	p value
AUB-O	40%	25%	>0.05(NS)
AUB-E	9%	16%	<.05(S)

For AUB-P, AUB-A, AUB-L, AUB-AUB-A; L and AUB-O P value is Not significant P value is >0.05. For AUB-M and AUB-E P value is significant P value is >0.05.

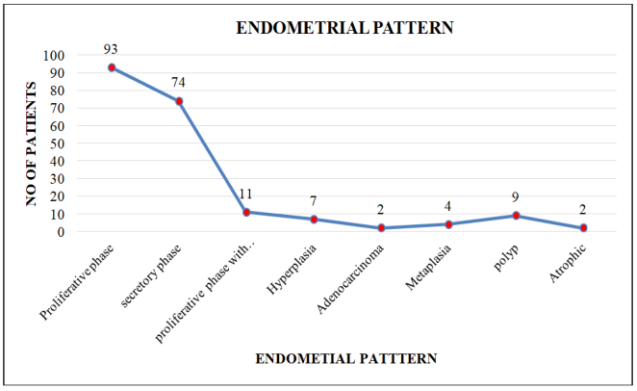

Figure 3:

The majority had proliferative phases changes in 93(46.5%) and secretory in 74(37%). This was followed by proliferative phase of dilation of gland 11(5.5%), polyp 9(4.5%), hyperplasia 7(3.5%), metaplasia,4(2%), adenocarcinoma 2(1%) and atrophic endometrium 2(1%) women.

Discussion:

PALM side of the classification refers to structural causes that may be evaluated by imaging techniquesor histopathology and the COEIN side by investigating the underlying medical disturbances. Perimenopausal women show a significant number of underlying organic pathology. The onus here in AUB management is to exclude complex endometrial hyperplasia and endometrial cancer. Evaluation of endometrium and/or organ histopathology have the dual advantage of finding an accurate reason causing the AUB and to rule outendometrial or other cancers or a potential for the cancer in future like endometrial hyperplasia with atypia. Office hysteroscopy and increasing sophisticated imaging will assist provision of robust evidence for the underlying cause.

On analysis of various categories, in AUB-P (polyp) the difference in clinical and histopathological diagnosis was not significant (P>.05). In the present study, 7.6% of cases of AUB was caused by polyps. Most of the cases were polyps in present study which could be diagnosed clinically by per speculum examination. This observation differs from others khan study et al[9] who found the difference to be highly significant in case of polyps but also similar to Devanshi Mishra et al and Kalpana Betha study et al[10]. In present study too, the clinically identified higher number of polyps although not to significant proportions. In present study no significant difference in adenomyosis same observation found in Betha study et al in which most of adenomyosis were diagnosed by USG. In Bhosle study et al[11] histopathological diagnosed cases were more ccompare to clinical cases[12]. In AUB-L (Leiomyoma) the difference in clinical and histopathological diagnosis was not significant (p>0.05). The explanation may be that most symptomatic fibroids can be easily diagnosed by history and clinical pelvic examination and by USG.similar observation in Bhosle et al Devanshi Mishra et al[13] and Bharati Mishra et al[14] studies. In AUB-M (malignancy and hyperplasia) the difference in clinical and histopathological diagnosis was significant (p<0.05). In AUB-O (ovulatory disorders) the difference in clinical and histopathological diagnosis was not significant (p>.05).In present study 40% cases of AUB due to ovulatory dysfunction. In AUB-E (endometrial disorders) the difference in clinical and histopathological diagnosis was significant (p<.05), with the clinically assigned cases less in number than those detected by histopathology. 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. In the present study there were significantly greater number of cases assigned to AUB-E on histopathological ground can be justified by this arbitrary approach. Similar observation found in Devanshi Mishra study et al.

Conclusion:

PALM and COEIN components contributed almost equally for AUB when assessed clinically. On the other hand, the histological examination revealed significantly more cases of PALM (structural or anatomical) component of AUB. The histological examination significantly more cases of PALM this is due to more cases of AUB-M. There is no significant difference in cases of AUB-P, AUB-A, AUB-L and AUB-O. Histopathological diagnosis also revealed structural causes to be the major contributor of AUB in perimenopausal women. All can cause heavy and irregular bleeding it is difficult to differentiate between pre malignant or malignant. For management part also clinical impression should be placed into proper perspective of this classification so that accurate diagnosis based on proper work up can help in optimizing the treatment protocol. The PALM COEIN classification system helps us in understanding various etiological causes of AUB and can be used by clinicians and researchers for international comparisons.

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