

The Role of FIGO PALM-COEIN Classification of the Underlying Causes of Abnormal Uterine Bleeding and Clinicopathological Correlation of Patients Undergoing Hysterectomy in a Tertiary Care Referral Center of Western Rajasthan

*Meenakshi Gothwal¹, Arunima Saini¹, Pratibha Singh¹, Garima Yadav¹, Poonam Elhence², Shashank Shekhar¹, Nitesh Samriya³

¹Department of Obstetrics & Gynaecology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India. ²Department of pathology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India.

³Department of Pathology, Dr S N medical College, Jodhpur, Rajasthan, India.

Abstract

Background: The International Federation of Gynaecology and Obstetrics working group on menstrual disorders has 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 the two components of this system in clinical practice in general and establish a clinicopathological correlation of AUB with the context of the PALM component in particular.

Methodology: The data of 158 patients who underwent hysterectomy for abnormal uterine bleeding in 1 year at the tertiary care Centre of western Rajasthan was collected from old case records and analysed. The patients were initially worked up in the outpatient department with the history and clinical examination, followed by transabdominal or transvaginal ultrasonography depending on the uterine size and the pathology. The patients requiring more detailed pictures were advised computed tomography (CT) scan. All the patients were screened for common medical disorders like thyroid disorders, prolactin levels, and blood sugar levels. Thereafter an endometrial biopsy and liquid-based cytology were done for all the patients to rule out malignancy. The relative contribution of various causes of PALM (structural) and COEIN (functional) components and clinicopathological correlation was analysed.

Results: 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, i.e., 17.2% versus 82.8%. AUB-L was the commonest (41.1%) aetiology overall.

Conclusion: The PALM–COEIN classification system should consider both the clinical and histopathological diagnoses in women having AUB. It is concluded that the most common cause of AUB is leiomyoma and the most common age group undergoing hysterectomy is the 4th decade. Although the medical treatment options are there, patients of premenopausal age require hysterectomy who do not benefit from medical regimens.

Keywords: Hysterectomy; Abnormal Uterine Bleeding; PALM–COEIN; Histopathology.

Introduction

Abnormal uterine bleeding (AUB) refers to any departure from the normal menstrual pattern in terms of duration of cycle, regularity, flow and

Corresponding Author: *Meenakshi Gothwal

Department of Obstetrics & Gynaecology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India
meenakshigothwal@gmail.com

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frequency¹. The old term has been abandoned. In 2011, the new FIGO classification system came up known as PALM- COEIN^{2,3}, which abandoned the old terminology of “Dysfunctional uterine bleeding”. Thereafter, the use of AUB (Abnormal uterine bleeding) and HMB (Heavy menstrual bleeding) was done for menstrual disorders. PALM-COEIN classifies menstrual disorders into structural and non-structural causes. The structural causes include PALM that is Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia while the non-structural pentagon includes COEIN- Coagulopathy, and Ovulatory disorders, Endometrial cause, Iatrogenic and Not yet specified. The normal menstrual cycle frequency is 24-38 days, with flow lasting for 4.5-8 days and 20-80 ml flow⁴. The overall prevalence of AUB in India is 17.9 % although it varies in each country⁽³⁾. Therefore, our aim of the present study was to analyse the structural (PALM) and functional (COEIN) components of FIGO system in western Rajasthan.

Material and Method

Data were collected from old case sheets, discharge records, histopathology reports, and outpatient and inpatient ward records. The data of patients who underwent hysterectomy for abnormal uterine in 1 year at a tertiary care referral center in western Rajasthan was entered into an excel sheet and analyzed. Informed consent was taken for the same. The patients were initially worked up in the outpatient department with the history and clinical examination, followed by transabdominal or transvaginal ultrasonography depending on the uterine size and the pathology. The patients requiring more detailed pictures were advised Computed tomography (CT) scan. All the patients were screened for common medical disorders like thyroid disorders, prolactin levels, and blood sugar levels. Thereafter an endometrial biopsy and liquid-based cytology were done for all the patients to rule out malignancy.

Inclusion criteria were patients in reproductive and postmenopausal age groups and only the patients who underwent hysterectomy for AUB were analysed. Exclusion criteria were subjects with incomplete abortion and women with incomplete preoperative medical history data.

Inclusion Criteria:

- 1) Patients in reproductive and postmenopausal age group.
- 2) Only the patients who underwent hysterectomy for AUB were analysed.
- 3) Hysterectomy via any route either laparoscopic, abdominal or vaginal was included.

Exclusion Criteria:

- 1) Incomplete abortion
- 2) Lost to follow up patients.

Statistical analysis

The data were entered into spreadsheets. Descriptive data were analysed on the parameters of range, mean \pm SD, and frequencies analyzed using software SPSS version 21 (SPSS, Chicago, IL, USA).

Results

All the patients fulfilling the inclusion criteria were grouped according to the different age groups. A total of 158 patients underwent a hysterectomy. The maximum number of patients who underwent hysterectomy for abnormal uterine bleeding were in the 40-49 years age group comprising 50.7 % of the total (80/158). Out of one hundred and fifty-eight patients, 35 (21.9%) were in the age group 50-59 years; 28 (18%) patients were in the age group 30-39 years, 12(7.8%) patients were in 60-69 years age group and only 3(1.6%) above 70 years of age. (Table 1)

Table 1: Age distribution of patient

AGE GROUP	NO. OF PATIENTS (158)	PERCENTAGE (%)
30-39	28	18.0
40-49	80	50.7
50-59	35	21.9
60-69	12	7.8
70-79	3	1.6

Sixteen patients were found to be obese, 15 were hypothyroid, 1 was hyperthyroid, 18 were diabetic and 25 patients were anaemic.

The patients were divided according to the structural and nonstructural causes of abnormal uterine bleeding which is PALM-COEIN classification. One hundred and thirty-one patients (82.8%) had a structural cause while the remaining 27(17.2%)

had the non-structural cause of AUB. Eighty-eight (55.5%) patients had a leiomyoma (AUB-L) comprising a major fraction of the total hysterectomies conducted for AUB while 21 (13.4%) patients had malignancy and hyperplasia (AUB-M) constituting the second major cause. Sixteen patients (10.1%) had no specified cause (AUB-N) and adenomyotic uterus (AUB-A) each. Seven percent (11/158) of patients had ovulatory dysfunction (AUB-O), while only 3.9% (06/158) of patients had endometrial polyp (AUB-P). None of the patients had coagulopathy, endometrial or iatrogenic cause. (Table 2)

Table 2: Splitting of various patients as per the aetiology (PALM-COEIN classification)

CAUSE	NO. OF PATIENTS	Percentage (%)	Percentage (%)	BROAD CLASSIFICATION
Polyp	06	3.9	82.8%	STRUCTURAL CAUSES
Adenomyosis	16	10.1		
Leiomyoma	88	55.5		
Malignancy	21	13.4		
Coagulopathy	-	-	17.2%	NON-STRUCTURAL CAUSES
Ovulatory dysfunction	11	7.0		
Endometrial causes	-	-		
Iatrogenic	-	-		
Not specified	16	10.1		
TOTAL	158	100		

Among the total hysterectomy procedures, 57.8% (91/158) were total abdominal hysterectomy (TAH), 29.7% (47/158) were total laparoscopic hysterectomies (TLH), 9.4% (15/158) were Robotic hysterectomy (RH) while 3.1% (05/158) were non-descent vaginal hysterectomies (NDVH). 44.7% (21/47) of TLH cases were undertaken for AUB-L and 21.1% (10/47) for AUB-A and AUB-N each. 7.9% (04/47) TLH cases were done for AUB-P while the remaining 2.6% (01/47) were done for AUB-O and AUB-M each. More than half the total abdominal hysterectomies (TAH) i.e., 63.5% (58/91) were done for large fibroids while 21.6% (20/91) were done for AUB-M. 8.1% (07/91) TAH were done for AUB-O, 4.1% (04/91) for AUB-N and 2.7% (02/91) for AUB-A. Among the fifteen Robotic hysterectomies done for AUB, 40% (06/15) were done for AUB-L while 16.7% (03/15) for AUB-P, AUB-A and AUB-O each. Among the five non-descent vaginal hysterectomies (NDVH), 60% (03/05) were done for AUB-N and the remaining 20% (01/05) for AUB-A and AUB-L each. (Table 3).

Table 3: Surgery taken for each aetiology

CAUSE	TLH	%	TAH	%	RH	%	NDVH	%
Polyp	04	7.9	-	-	03	16.7	-	-
Adenomyosis	10	21.1	02	2.7	03	16.7	01	20
Leiomyoma	21	44.7	58	63.5	06	40.0	01	20
Malignancy	01	2.6	20	21.6	-	-	-	-
Coagulopathy	-	-	-	-	-	-	-	-
Ovulatory dysfunction	01	2.6	07	8.1	03	16.7	-	-
Endometrial causes	-	-	-	-	-	-	-	-
Iatrogenic	-	-	-	-	-	-	-	-
Not specified	10	21.1	04	4.1	-	-	03	60
TOTAL (158)	47	100	91	100	15	100	05	100
	(29.7%)		(57.8%)		(9.4%)		(3.1%)	

Amongst all the histopathological findings, the most common was chronic cervicitis which accounted for 72.75% (114/158) of the total patients. 59.3% (68/114) of patients with chronic cervicitis were in the 40-49-year age group followed by 20.4% (23/114) in the 30-39-year group, 18.3% (21/114) in the 50-59-year group and 1.1% (01/114) in 60-69 years and 70-79 years age group each.

The second most common histopathological entity in AUB patients was proliferative endometrium accounting for 34.4% (54/158) patients, with 68.2% (37/54) patients in the 40-49-year age group followed by 20.5% (11/54) in 50-59-year age group and 11.4% (06/54) patients in 30-39-year age group. 17.2% (27/158) patients had secretory pattern endometrium with a majority of 59.1% (16/27) patients in the 40-49-year age group followed by 31.8% (09/27) patients in the 30-39-year age group and 9.1% (02/27) patients in 50-59-year age group. A total of 12.5% (20/158) patients had non-secretory endometrium with the majority of patients i.e., 43.8% (09/20) in the 40-49-year age group followed by 25% (05/20) each in 30-39 year and 50-59-year age groups each. 6.3% (01/20) of patients were in the 70-79-year age group. 11.7% (19/158) patients had malignancy, among which 53.3% (10/19) patients were in the 60-69-year age group, followed by 26.7% (06/19) patients in the 50-59-year age group, 13.3% (02/19) patients in 40-49-year age group and 6.7% (01/19) patients in 70-79 year age group. 10.2% (16/158) of patients had disordered proliferative endometrium. 46.2% (07/16) patients were in 40-49-year age group, 30.8% (05/16) in 50-59-year age group, 15.4% (03/16) in 60-69-year age group and 7.7% (01/16) in 30-39-year age group. 5.5% (09/158) of patients had simple hyperplasia without atypia with 33.3%

(03/09) in each of the 30-39-year, 40-49-year age groups, 22.2% (02/09) in 50-59-year age group and remaining 11.1% (01/09) in 60-69-year age group. 3.9 % (06/158) of patients had polyp with 60% (04/06) in the 40-49-year age group followed by 20% (01/06) each in the 50-59 year and 60-69-year age group. Only 2.3% (04/158) patients had chronic endometritis, with 66.7% (03/04) patients in the 40-49-year age group and 33.3% (01/04) patients in the 30-39-year age group. 1.6 % (04/158) patients had atrophic endometrium with 50% (02/04) patients in the 30-39-year age group and another 50% (02/04) patients in the 50-59-year age group. 0.8% (01/158) patients in the 50-59-year age group had an unsatisfactory sample while another 0.8% (01/158) patients in the 40-49-year age group had simple hyperplasia with atypia. It must be noted that 73.4% (115/158) patients of AUB had overlapping histopathological findings and not just a single one. (Table 4)

Table 4: Histopathology of patients with AUB in various age groups

Histopathology diagnosis	30-39 years	40-49 years	50-59 years	60-69 years	70-79 years	Total	%
Proliferative	06 (11.4%)	37 (68.2%)	11 (20.5%)	-	-	54	34.4
Simple hyperplasia without atypia	03 (33.3%)	03 (33.3%)	02 (22.2%)	01 (11.1%)	-	09	5.5
Simple hyperplasia with atypia	-	01 (100%)	-	-	-	01	0.8
Secretory	09 (31.8%)	16 (59.1%)	02 (9.1%)	-	-	27	17.2
Non-secretory	05 (25%)	09 (43.8%)	05 (25%)	-	01 (6.3%)	20	12.5
Atrophic	02 (50%)	-	02 (50%)	-	-	04	1.6
Disordered proliferative	01 (7.7%)	07 (46.2%)	05 (30.8%)	03 (15.4%)	-	16	10.2
Carcinoma	-	02 (13.3%)	06 (26.7%)	10 (53.3%)	01 (6.7%)	19	11.7
Polyp	-	04 (60%)	01 (20%)	01 (20%)	-	06	3.9
Chronic cervicitis	23 (20.4%)	68 (59.3%)	21 (18.3%)	01 (1.1%)	01 (1.1%)	114	72.7
Unsatisfactory	-	-	01 (100%)	-	-	01	0.8
Chronic endometritis	01 (33.3%)	03 (66.7%)	-	-	-	4	2.3
Total	50	150	56	16	03		

On the basis of histopathology, The PALM component turned out to be 173 /187 (92.51%) cases of AUB, which was 42 cases more than those assigned by clinical criteria. In the case of COEIN,

only AUB-O and AUB-E classes could be evaluated histologically and constituted 14/187 (7.49 %) of overall AUB cases. The difference was significant statistically ($p < 0.05$) in clinical and diagnostic correlation (Table 5). Values did not differ significantly in cases of AUB-P and AUB-O. On the other hand, histopathology could diagnose more cases in comparison with clinical-based diagnosis in the categories of AUB A and cases having both adenomyosis and leiomyoma. The difference was significant statistically in all three.

Table 5: Clinico-pathological correlation

Category	Clinical Diagnosis PALM(n=131)	Histopathological diagnosis PALM (n=173)	P value <0.05
AUB P	6	8	$p > 0.067$ not significant
AUB A	16	36	$P < 0.04$ significant
AUB L	88	96	$P < 0.036$ significant
AUB M	21	25	$P < 0.01$ significant
AUB A, L	0	8	$P < 0.01$ significant
	COEIN(n=27)	COEIN (n= 14)	
AUB C	0	-	-
AUB O	11	13	> 0.05 Not significant
AUB E	0	1	-
AUB I	0	-	-
AUB N	16	-	-

Table 6: Comparing the etiologies of AUB in various studies.

Cause	Our study	Jain Uma et al	Sreeja Rani et al	Sinha A et al
Polyp	3.9	3	5	16.2
Adenomyosis	10.1	8	10	6.2
Leiomyoma	55.5	68	54	20.2
Malignancy	13.4	6.3	04	5.1
Coagulopathy	-	-	-	-
Ovulatory dysfunction	7.0	-	-	18.1
Endometrial causes	-	-	-	26.8
Iatrogenic	-	-	-	0.4
Not specified	10.1	-	04	0.4
Leiomyoma + Adenomyosis	-	15	20	-
Polyp + Adenomyosis	-	-	01	-
Polyp + Leiomyoma	-	-	04	1.1
Polyp+ Ovulatory	-	-	-	1.8
Leiomyoma + Ovulatory	-	-	-	2.2
Adenomyosis + Ovulatory	-	-	-	1.5

Discussion

Abnormal uterine bleeding is reported in 9-14% of women from menarche to menopause.² A diagnosis of AUB is important as the recommendations have undergone minor variations. The normal menstrual cycle frequency is 24-38 days(2,4). Cycles which are less than 24 days are labelled “frequent” while more than 38 days are labelled “infrequent”. The normal cycle-to-cycle variation over 12 months is 2-20 days(2,4). If the variation is more than 20 days, it is labelled “irregular”. The normal duration of flow

is 4.5-8 days^(2,4). Menstruation lasting more than 8 days is considered “prolonged” while less than 4.5 days is considered “shortened”. The normal blood flow varies from 20-80ml. Blood flow of less than 20 ml is termed “light” while more than 80ml is termed “heavy”⁽⁴⁾. A patient with AUB-P presents with prolonged bleeding, intermenstrual bleed, and irregular contact bleeding but vaginal examination mostly shows a normal uterine size. The patients can be infertile and the polyp is found during workup for AUB. Adenomyosis is also a very common entity in gynae patients. The patients have typically severe dysmenorrhea with heavy flow. Examination reveals a uniformly enlarged uterus up to 12 weeks in size. Leiomyoma is a common finding in 30% of patients and is mostly asymptomatic in 50% of patients. Submucosal fibroids are commonly associated with menstrual disturbances in form of heavy prolonged menses. Intramural fibroids can also present with a variable amount of bleeding disturbances⁽⁴⁾. Subserosal fibroids do not interfere with the menstrual patterns although the patient can have long-standing pain, and pressure symptoms in form of bladder and bowel complaints. Examination reveals an irregularly enlarged uterus. One of the other most commonly encountered entities in day-to-day gynaecology practice is AUB-M. It comprises patients in the perimenopausal group who have irregular, frequent menses and those with postmenopausal bleeding. Examination reveals either a normal or mildly enlarged uterus. The non-structural causes of AUB include COEIN⁽¹⁾. Coagulopathy is an entity which usually presents in pubertal age in form of menorrhagia. Usually, there is either a family history or the patient has abnormal bleeding episodes or easy bruise tendency in past. Examination reveals a normal size of the uterus with petechial spots on the body. Another entity which is very common in gynecology practice is Ovulation disorder in the form of the polycystic ovarian syndrome. Examination reveals an obese patient or thin patient with or without signs of insulin resistance and hirsutism. A vaginal examination shows a normal uterine size. AUB-E is a diagnosis of exclusion. Examination shows a normal uterine size. AUB-I includes the past use of any medication or Post-partum intrauterine copper device (PPIUCD). AUB-N is labelled when the cause of AUB is not yet identified. Examination of both reveals normal uterine size.

The first imaging modality used for diagnosing these structural causes of AUB is ultrasonography (USG). It can show a thickened endometrium in cases of AUB-P and AUB-M, both can be differentiated using Saline infusion sonography (SIS) in which a smooth intracavitary mass points towards a polyp. Moreover, there can be a loss of endomyometrial differentiation and heterogeneous echotexture. 3D USG or Magnetic Resonance Imaging (MRI) can help locate the site and extent of myoma, also differentiating it from adenomyosis. Especially for submucous fibroids, hysteroscopy can be done. Sometimes Doppler ultrasonography can be employed to diagnose arteriovenous malformations (AVM) and to differentiate myoma from adenomyosis. Endometrial aspiration is performed as an office procedure in AUB patients more than 40 years age, while in patients with high-risk factors like PCOS, irregular bleed despite medical treatment, tamoxifen use, history of breast or colon or endometrial cancer in the family, obesity, hypertension or Endometrial thickness >12mm on USG, it is performed in less than 40 years age group. Also, endometrial aspiration has been shown to be a highly useful, convenient, safe and effective means for detecting an endometrial histological pattern.⁵

The treatment of AUB -P is hysteroscopic polypectomy which can be followed by Levonorgestrel intrauterine device insertion (LNG-IUS-Mirena). Similarly, for AUB-A, LNG-IUS is the first line of treatment, followed by Gonadotropin-releasing hormone agonists (GnRH) in second place⁽³⁾. Those wishing to retain the uterus can undergo adeno-myomectomy while the others not relieved by either option can go for hysterectomy. AUB-M patients having endometrial hyperplasia without atypia, LNG IUS or progesterone therapy is the treatment while those with atypia require hysterectomy except those requiring fertility preservations can be given high dose progestins with a regular follow-up. AUB-C treatment includes tranexamic acid or combined oral contraceptive pills or LNG-IUS. Treatment options for AUB-O include COC, cyclic luteal phase progesterone (10-14days) or a 21-day progesterone course for 3 months, and LNG-IUS⁽⁴⁾. Those not relieved with medical management can undergo a hysterectomy as a last resort.

In our study, the most common age group of patients undergoing hysterectomy for AUB is 40-49 years comprising nearly half the total number of patients while the second most common age group is 50-59 years. This is in concordance with previous studies conducted by Muzaffar M et al (2005)⁶, Sreeja Rani Et al(2013)⁷, Sajeetha et al(2017)⁸, Jain Uma et al(2018)⁹ and Sinha A et al (2018)¹⁰

In our study, 55.5% of patients had leiomyoma which is in concordance with a study done by Sreeja et al⁽⁷⁾ and Jain Uma et al⁽⁹⁾ while discordant with that of Sinha et al⁽¹⁰⁾ where AUB-E was more common. (Table 7) A similar study from the United States on a large number of patients undergoing hysterectomy revealed leiomyoma as the major cause.¹¹ Histopathological pattern of endometrium in women with AUB is quite variable depending upon age, parity, and ethnicity. Endometrial hyperplasia was present in 6.3 % of our cases, out of which most were simple adenomatous hyperplasia without atypia (87.5 % cases of endometrial hyperplasia) this finding was almost similar to the study conducted by Mishra et al⁽³⁾ in 2016.

For AUB-L, the choice of treatment depends on the age of the patient, desire for fertility and the presenting symptoms. Those symptomatic patients aged 40 years and above, who declined LNG-IUS can undergo a hysterectomy. Those less than 40 years and requiring fertility preservation have medical management in the form of Nonsteroidal anti-inflammatory drugs (NSAIDs), hemostatic agents like Tranexamic acid, Antifibrinolytics like ethamsylate, and hormonal treatment (combined oral contraceptive pills). Other drugs used to decrease myoma size include antiprogesterone (Mifepristone), aromatase inhibitors (Anastrozole) and Gonadotropin hormone-releasing hormone (GnRH) analogues, selective progesterone receptor modulators (SPRM) ulipristal acetate. Hysteroscopic myomectomy is done for submucous myomas grade 0-1 measuring less than 4 cm while abdominal myomectomy is done for sizes more than 4cm. LNG-IUS is a good treatment option in patients with myoma grades 2-6 and those not planning to conceive in the next one year. As the patients were in more than 40-year age group, not willing for fertility preservation and those not responded to medical management, hysterectomy

was the only option. The total incidence of AUB–M is 13.4% in our study which is slightly higher than studies showing 5%, 1.8%, 0.4% incidence by Mirza et al¹², Sajeetha et al⁸, Muzaffar Met al⁶. (Table 6).

The incidence of AUB percentage in the present study is almost similar to Sreeja et al⁽⁷⁾ and Jian et al⁽⁹⁾ and for AUB-P and AUB-L while the percentage of AUB-O and AUB-N is higher as compared to Sreeja et al⁽⁷⁾ and Jain et al⁽⁹⁾. Moreover, there are more isolated structural abnormalities rather than a combination of a few.

As far as histopathology is concerned, proliferative endometrium is the most common finding, which is in concordance with the study done by Sajeetha et al⁸ while in discordance with a study done by Sinha et al¹⁰ where the secretory pattern was the commonest. Taking the undergraduate and postgraduate teaching in mind the PALM COEIN is an easy mnemonic to remember the various causes of AUB.

In the present study the difference in clinical and histological diagnosis in AUB-P (polyp), AUB-O (ovulatory disorders) and AUB-L (Leiomyoma) was not significant ($p > .05$) and this result is in concordance with a study conducted by Mishra et al⁽³⁾ and Jain et al⁽⁹⁾.

In our present study, the clinical and histopathological diagnosis of a combination of AUB-A;L (adenomyosis and leiomyoma) and AUB-M were highly significant ($p < .01$) which was similar to the finding of Mishra et al⁽³⁾.

There were no patients diagnosed clinically in AUB-E, or AUB-I group and no patient was diagnosed histopathologically in AUB-I and AUB-N groups so histopathological correlation can be made out.

Conclusion

In our study, we found good clinicopathological correlation when the cases were classified under PALM COEIN. The PALM component contributed more as compared to COEIN components for AUB when assessed clinically. It is concluded that the most common cause of AUB is leiomyoma and the most common age group undergoing hysterectomy is the 4th decade. The most common

histopathological finding was chronic cervicitis and proliferative phase endometrium. Although the medical treatment options are there, patients of premenopausal age require hysterectomy who do not benefit from medical regimens.

Strength and limitation

Based on the new classification, this observational study investigates the aetiology of AUB in women of Rajasthan. At the same time, age distribution and operation are carried out for each aetiology are also analysed. Limitation for this research: it has a small sample size and mainly the PALM group is taken into consideration based on collection of data from the records. Therefore, the sample size needs to be increased further and both the component need to study in detail in future studies to substantiate the results.

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