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A Prospective Observational Study of Abnormal Uterine Bleeding in Females of Reproductive Age Group at a Tertiary Care Hospital in Mumbai, India

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Abstract: <u>Background</u>: This study aimed to evaluate the epidemiological determinants, classification as per FIGO PALM COEIN and diagnostic and treatment modalities in 250 women of reproductive age (18-45 years) presenting with abnormal uterine bleeding. <u>Methods</u>: A prospective observational hospital based study was conducted for 250 women of reproductive age presenting with abnormal uterine bleeding in J. J. Hospital, Mumbai from July 2021 to December 2022 and their management was noted. <u>Results</u>: Majority were in the age group of 31 to 40 comprising of 147 (58.8%) women. Heavy menstrual bleeding was the most common symptom that 230 (92%) women presented with. AUB-L was noted in 102 (40.8%) women. Medical management was opted in 42% cases, surgical in 60% cases and chemoradiation was done 0.8% cases. <u>Conclusion</u>: Awareness on menstrual care and hygiene and easy accessibility of health care in society, among both male and female, is important to address any abnormality at the earliest so that adequate and appropriate management can be offered women have a better quality of life.

Keywords: Abnormal uterine bleeding, Heavy Menstrual Bleeding, Reproductive age, Fibroid, PALM COEIN

1. Introduction

Abnormal uterine bleeding is a common problem among women in the reproductive age group. Abnormal uterine bleeding may be accompanied by significant social embarrassment, and have a substantial effect on health-related quality of life. Abnormal uterine bleeding leads to loss of productivity and may result in surgical interventions including hysterectomy. The estimated worldwide prevalence of subjective, self-defined abnormal uterine bleeding varies greatly, from 4% to 52%. In India, abnormal uterine bleeding is reported to occur in 9% to 14% of women between menarche and menopause. India has a prevalence of abnormal uterine bleeding which is 17.9% approximately.

Regular cyclic menstruation indicates normal functioning hypothalamo-pituitary-ovarian axis and its target organs. Abnormal uterine bleeding is a common problem of adolescent girl & perimenopausal and postmenopausal women.

Abnormal uterine bleeding is the most common symptom of gynecological conditions, which is defined as any type of bleeding in which the duration, frequency, or amount is excessive for an individual patient. ⁴ Abnormal uterine bleeding is regarded as a sign of possible uterine disease, which includes acute and chronic abnormal uterine bleeding.

Chronic abnormal uterine bleeding is identified if the symptoms last for more than 6 months. Sometimes an acute episode of abnormal uterine bleeding can complicate chronic abnormal uterine bleeding. There is general inconsistency in the nomenclature used to describe abnormal uterine bleeding, in addition to a plethora of potential causes several of which may coexist in a given individual. There was a need for development of consistent and universally accepted nomenclature and development of a classification system, on several levels, for the causes of abnormal uterine bleeding, which can be used by clinicians, investigators, and even patients to facilitate communication, clinical care, and research. An international expert consensus from the FIGO Menstrual Disorders working group has proposed a standardized classification system for abnormal uterine bleeding to facilitate greater appreciation of the complexities of this clinical entity. It has put forward a system called "PALM COEIN" classification to help the clinician for stream lining the investigations and interpreting the results and also to provide evidence based clinical care. 5 Abnormal uterine bleeding can be due to causes which can be detected by clinical examination, imaging and histopathology and these comes under "PALM" group otherwise called structural lesions. The causes which cannot be detected by imaging but can be detected by clinical history supported by laboratory investigations belongs to the "COEIN" group otherwise called as non-structural lesions. Patients on anticoagulant

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drugs and on hormones when they develop Abnormal uterine bleeding, it should be considered as iatrogenic and N category is named as "not otherwise classified" because later on they may go to some unique group by further investigations like histopathological study or imaging techniques. Dysfunctional uterine bleeding is abnormal uterine bleeding that is exclusively due to HPO axis dysfunction.4

The classification system is stratified into nine basic categories that are arranged according to the acronym PALM-COEIN [pahm-koin]: Polyp, Adenomyosis, Leiomyoma, Malignancy and hyperplasia, Coagulopathy, Ovulatory disorders, Endometrium, Iatrogenic, and Not classified. In general, the components of the PALM group are discrete (structural) entities that are measurable visually, by use of imaging techniques, and/or by use of histopathology while the COEIN group is related to entities that are not defined by imaging or histopathology (non-structural). The categories were designed to facilitate the current or subsequent development of sub classification systems.

The system was constructed recognizing that any patient could have one or a spectrum of entities that could cause or contribute to the complaint of abnormal uterine bleeding and that definable entities such as adenomyosis, leiomyoma, and endocervical or endometrial polyps may frequently be asymptomatic and, therefore, not a contributor to the presenting symptoms. 6

In adolescent and perimenopausal age most of the menstrual cycles are anovulatory, irregular and prolonged. Pregnancy is not so common in adolescent and perimenopausal women, but can occur as infrequent ovulation is likely to continue in perimenopausal transitional period. So, the possibility of pregnancy related complications (threatened, incomplete abortion or ectopic gestation) should always be considered and excluded.

Abnormal uterine bleeding is a common gynecological complaint and it may involve females at any age group. 33% of women referred to gynecology clinics have abnormal uterine bleeding and the figure rises to 69% in premenopausal and postmenopausal women.7 Abnormal uterine bleeding accounts for two thirds of all hysterectomies.8 In this prospective observational study, an attempt is made to classify the abnormal uterine bleeding as per the etiology by clinical, laboratory, imaging, and histopathology and its management.

2. Methods

This observational prospective study was conducted in Department of Obstetrics and Gynaecology, Grant Government Medical College, Mumbai from July 2021 to December 2022, 250 women of reproductive age who presented with abnormal uterine bleeding in gynaecology OPD were selected, detailed history and clinical examination was conducted, investigations such as complete blood count, liver function test, renal function test, coagulation profile, thyroid profile, ultrasonography (abdomen and pelvis), hysteroscopy and histopathological report were noted and the probable cause of bleeding was identified according to PALM-COEIN classification and management was studied. Data compiled in excel sheet was analyzed statistically to calculate mean and standard deviation. Appropriate statistical test was applied whenever necessary.

3. Results

1) Distribution of cases according to age groups:

Table 1: Distribution of cases according to age groups:

Serial No.	Age group	No. of cases	Percentage (%)
1	< 20	17	6.8
2	21-30	23	9.2
3	31-40	147	58.8
4	41-45	63	25.2

We included 250 women in reproductive age group (18-45). Majority were in the middle age group of 31 to 40 comprising of 147 (58.8%) women, followed by perimenopausal age group of 41-45 which included 63 (25.2%) women followed by early reproductive age group of 18-20 which included 17 (6.8%) women, age group of 21 to 30 comprised of only 23(9.2%) women which is signified by ovulatory cycles and do not cause abnormal uterine bleeding.

2) Distribution of cases according to the presenting symptom:

Table 2: Distribution of cases according to the presenting

sympiom				
Serial	Presenting symptom	No. of	Percentage	
No.	1 resenting symptom	women	(%)	
1	Heavy menstrual bleeding	230	92.0	
2	Dysmenorrhea	9	3.6	
3	Intermenstrual bleeding	8	3.2	
4	Polymenorrhea	3	1.2	
		Serial No. Presenting symptom 1 Heavy menstrual bleeding 2 Dysmenorrhea 3 Intermenstrual bleeding	Serial No.Presenting symptomNo. of women1Heavy menstrual bleeding2302Dysmenorrhea93Intermenstrual bleeding8	

As per the distribution of presenting symptoms, heavy menstrual bleeding was the most common symptom that 230 (92%) women came with in the outpatient department while dysmenorrhea (3.6%), intermenstrual bleeding (3.2%), polymenorrhea (1.2%) were the main presenting symptoms in few women.

3) Distribution of cases according to associated symptoms:

Table 3: Distribution of cases according to associated

symptoms				
Serial	Associated	No. of	Percentage	
No.	symptoms	women	(%)	
1	Dysmenorrhea	37	14.8	
2	Infertility	3	1.2	
3	Polymenorrhea	72	28.8	
4	Pain in abdomen	93	37.2	
5	White discharge	4	1.6	
6	No symptom	41	16.4	

Out of 250 women 209 (83.6%) had associated symptoms. Pain in abdomen was the most common associated symptom which 93(37.2%) women complained of, polymenorrhea (frequent menses) was the next most common symptom experienced by 72 (28.8%) women, dysmenorrhea (pain during menses) was experienced by 37(14.8%) women,

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infertility by 3 (1.2%) women and white discharge by 4 (1.6%) women.

4) Comparative description between present abnormal menstrual cycle and past regular menstrual cycles

Table 4: Comparative description between present abnormal menstrual cycle and past regular menstrual cycles

	Serial no.	Variable	Mean \pm SD	Range
D	1	Duration	11.67 ± 6.40	3-60
Present abnormal Menstrual Cycle	2	Length	26.49 ± 5.03	15-60
Mensulai Cycle	3	No of pads	4.94 ± 0.73	2-8
D (D 1	1	Duration	4.34 ± 1.62	3-10
Past Regular	2	Length	29.76 ± 0.65	28-30
Menstrual Cycle	3	No of pads	2.74 ± 1.18	2-6

The difference between the past regular menstrual cycle and the present menstrual cycle has been described by duration of menses and the length of cycle and number of pads used per day (flow) in the above table. The duration of menses ranged between 3 days to 60 days with average of 11.67 days with a standard deviation of 6.4 days in present abnormal cycle while in past regular menstrual cycle duration was of 3 days to 10 days with an average of 4.34 days with a standard deviation of 1.62 days.

The length of cycle ranged between 15 to 60 days with an average of 26.49 days with standard deviation of 5.03 days which meant a wide variation in the cycle length as some women experienced polymenorrhea while other experienced amenorrhea followed by heavy menstrual bleeding as seen in metropathica hemorrhagica, while it was fairly consistent in past regular menstrual cycles ranging between 28 to 30 days with an average of 29.76 days with standard deviation of 0.65 days.

The number of pads soaked per day is significantly more in present abnormal menstrual cycles ranging between 2 to 8 pads with average being 4.94 pads while in past regular cycle the soakage of pads per day ranged between 2 to 6 pads with an average of 2.74 pads per day.

5) Distribution of cases according to anaemia:

Table 5: Distribution of cases according to anaemia:

Haamoglobin laval (g/dl)	No. of	Percentage
Haemoglobin level (g/di)	women	(%)
≤7 (Severe anaemia)	12	4.8
7.1 - 9.9 (Moderate anaemia)	108	43.2
10 – 10.9 (Mild anaemia)	84	33.6
≥11	46	18.4
	Haemoglobin level (g/dl) ≤7 (Severe anaemia) 7.1 – 9.9 (Moderate anaemia)	Haemoglobin level (g/dl) women ≤7 (Severe anaemia) 12 7.1 − 9.9 (Moderate anaemia) 108 10 − 10.9 (Mild anaemia) 84

Hemoglobin levels tested in blood examination informs us regarding the anemia in the women suffering from abnormal uterine bleeding. In above table, the hemoglobin levels have been categorized as per WHO classification of anemia, 12 (4.8%) women suffered from severe anemia (Hemoglobin level of 7 g/dl), 108 (43.2%) women had moderate anemia (7.1 to 9.9 g/dl), 84 (33.6%) women suffered from mild anemia (10 to 10.9 g/dl) while 46 (18.4%) women had normal hemoglobin concentration (more than 11 g/dl).

6) Distribution of cases according to USG findings:

Table 6: Distribution of cases according to USG findings

Serial	LICC findings	No. of	Percentage
No.	USG findings	women	(%)
1	Adenomyosis	48	19.2
2	Adenomyosis, thickened endometrium	3	1.2
3	Cervical growth	2	0.8
4	Fibroid	100	40
5	Fibroid, cyst	1	0.4
6	Fibroid, polyp	3	1.2
7	Fibroid, thickened endometrium	4	1.6
8	Polycystic ovary	17	6.8
9	Polyp	7	2.8
10	Thickened endometrium	43	17.2
11	Thickened endometrium, cyst	5	2
12	Normal	17	6.8
	Total	250	100

Ultrasonographic imaging is very important in the diagnosis of abnormal uterine bleeding as the organic cause can be noted through a small non-invasive out-patient procedure. Out of 250 women included in the study all were advised Ultrasonography of abdomen and pelvis, many of the women had multiple significant organic findings.

Fibroid was seen in 108 (43.5%) women, out of which 4 (1.6%) women also had thickened endometrium, polyp was seen in 3 (1.2%) women, cyst along with fibroid was noted in 1 (0.4%) woman. 52 (20.8%) women showed increased endometrial thickness, out of which 5 (2%) women also showed cyst and adenomyosis was seen in 3 (1.2%) women.

Adenomyosis was noted in 51 (20.4%) women, polycystic ovaries were noted in 17 (6.8%) women, polyp was noted in 7 (2.8%) women and cervical growth was noted in 2 (0.8%) women while 17 (6.8%) women showed normal ultrasonographic imaging.

7) Distribution of cases according to histopathological findings:

Table 7: Distribution of cases according to histopathological findings of dilatation and curettage with/without polypectomy/cervix biopsy

Serial No.	Histopathological Report	No. of cases	Percentage (%)
1	Carcinoma Cervix	7	2.8
2	Disordered Proliferative Endometrium with Chronic Cervicitis	23	9.2
3	Endometrial Hyperplasia Without Atypia	42	16.8
4	Endometrial Polyp with No Atypia	6	2.4
5	Proliferative Phase Endometrium with Chronic Cervicitis	29	11.6
6	Scanty Endometrium, Chronic Cervicitis	6	2.4
7	Secretory Phase Endometrium with Chronic Cervicitis	59	23.6
8	Submucosal Leiomyoma	9	3.6
9	Not done	69	27.6
	Total	250	100

From 250 cases, histopathological examination was conducted in 181 women as per requirement in the cases, the

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distribution according to its finding has been discussed in table 7.

Endometrial sampling was done and the results were distributed, secretory phase endometrium was seen in 59 (23.6%) cases, endometrial hyperplasia without atypia was noted in 42 (16.8%) cases, proliferative phase was noted in 29 cases (11.6%), disordered proliferative endometrium was noted in 23 (9.2%) cases, endometrial polyp was seen in 6 (2.4%) cases, scanty endometrium was received in 6 (2.4%) cases.

Cervical biopsy was conducted and chronic cervicitis was noted in 120 cases (48%) while 7 (2.8%) cases were of cervical carcinoma.

Polypectomy was done and submucosal fibroid was noted in 9 cases (3.6%), while endometrial polyp was seen in 6 cases

8) Distribution of cases according to Hysteroscopy findings

Table 8: Distribution of cases according to Hysteroscopy findings

Serial	Hysteroscopy	No. of	Percentage
No.		cases	(%)
1	ENDOMETRIAL FIBROID-POLYP	4	2.6
2	ENDOCERVICAL FIBROID-POLYP	9	6
3	IRREGULAR ENDOMETRIUM	42	27.4
4	POLYPOID ENDOMETRIUM	26	17
5	HYPERPLASTIC ENDOMETRIUM	26	17
6	ATROPHIC ENDOMETRIUM	46	30
	Total	153	100.0

Hysteroscopy was conducted in 153 (61.2%) women out of the 250 women included in our study. 46 (30%) women had atrophic endometrium, 42 (27.4%) women had irregular endometrium, 26 (17%) women had hyperplastic endometrium, 26 (17%) women had polypoidal growth. Endocervical pedunculated fibroid/polyp was seen in 9 (6%) women while endometrial polyp was noted in 4 (2.6%) women.

9) Distribution of cases according to management:

Table 9: Distribution of cases according to management

Serial No.	Primary management	No. of cases	Percentage (%)
1	Cervix Biopsy	6	2.4
2	Chemoradiotherapy	2	0.8
3	Dilatation and curettage	148	59.2
4	Emergency Dilatation and Curettage	8	3.2
5	Laparoscopy Assisted Vaginal Hysterectomy	5	2
6	Medical Management	46	18.4
7	Non-Descent Vaginal Hysterectomy	5	2
8	Polypectomy	9	3.6
9	Total Abdominal Hysterectomy	12	4.8
10	Total Laparoscopic Hysterectomy	9	3.6
	Total	250	100

In the above table, distribution as per the primary or initial management is done. In 46 (18.4%) women medical management was considered.

Dilatation and curettage with cervical biopsy were done in 148 (59.2%) women, emergency dilatation and curettage were done in 8 (3.2%) women, while only cervix biopsy was taken in 6 (2.4%) women.

Polypectomy was conducted in 9 (3.6%) women.

Hysterectomy as a primary management was done in 31 (12.4%) women, out of which total abdominal hysterectomy was done in 12 (4.8%) women, non-descent vaginal hysterectomy was conducted in 5 (2%) women, laparoscopy assisted vaginal hysterectomy was done in 5 (2%) women while total laparoscopic hysterectomy was done 9 (3.6%) women.

Chemoradiation was advised in 2 (0.8%) women.

10) Distribution of cases according to medical management:

Table 10: Distribution of cases according to medical

management			
Serial	Medical management	No. of	Percentage
No.	wiedicai management	cases	(%)
1	Leuprorelin	9	8.6
2	Levonorgestrel Intrauterine System	38	36.1
3	Mifepristone	3	2.9
4	Oral hormonal therapy	34	32.4
5	Tranexamic acid/Mefenamic acid	21	20.0
	Total	105	100

Medical management was done in 105 (42%) women out of the 250 women included in the study. 38 (36.1%) women were given levonorgestrel intrauterine system (LNG-IUS), oral hormonal therapy was used in 34 (32.4%) women for regularization of cycles. Tranexamic acid or Mefenamic acid were given to 21 (20%) women, mifepristone (antiprogestogen) was given to 3 (2.9%) women while leuprorelin (GnRH agonist) was used in 9 (8.6%) women.

11) Distribution of cases according to etiological classification (FIGO):

Table 11: Distribution of cases according to etiological classification (FIGO)

Serial No.	Classification	No. of cases	Percentage (%)
1	AUB-A	32	12.8
2	AUB-A, E	7	2.8
3	AUB-M (hyperplasia)	59	23.6
4	AUB-N	2	0.8
5	AUB-L	78	31.2
6	AUB-L, E	6	2.4
7	AUB-L, P	18	7.2
8	AUB-O	34	13.6
9	AUB-P	6	2.4
10	AUB-M (malignancy)	8	3.2
	Total	250	100

In the above table, classification of cases as per FIGO classification of abnormal uterine bleeding (PALM-COEIN) is done. Out of this, 33 (1.32%) women had multiple etiological factors.

AUB-P was diagnosed in 24 (9.6%) women, AUB-A was seen in 39 (1.56%) women, AUB-L was noted in 102 (40.8%)

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women while 8 (3.2%) women suffered from AUB-M (malignancy), AUB-M (endometrial hyperplasia) was noted in 59 (23.6%) women.

AUB-O was seen in 34 (13.6%) women, AUB-E was noted in 13(5.2%) women, 2 (0.8%) women were classified under AUB-N (not yet classified). There were no cases of AUB-C or AUB-I in our study.

4. Discussion

In present study, AUB-P was diagnosed in 24 (9.6%) women, AUB-A was seen in 39 (1.56%) women, AUB-L was noted in 102 (40.8%) women while 8 (3.2%) women suffered from AUB-M (malignancy), AUB-M (endometrial hyperplasia) was noted in 59 (23.6%) women. AUB-O was seen in 34 (13.6%) women, AUB-E was noted in 13 (5.2%) women, 2 (0.8%) women were classified under AUB-N (not yet classified). There were no cases of AUB-C or AUB-I in our study. Sinha K et al⁹ noted that in their study, AUB-P was 19.1%, AUB-A was 7.7%, AUB-L was 23.5%, AUB-M was 5.1%, AUB-O was 23.6%, AUB-E was 26.8%, AUB-I was 0.4%, AUB-N was 0.4%. Singh N et al¹⁰ noted that in their study, AUB-P was 7%, AUB-A was 29.6%, AUB-L was 30%, AUB-M was 5%, AUB-O was 26.6%, AUB-E was 15%. Ratnani et al11 noted that in their study, AUB-P was 13.3%, AUB-A was 20%, AUB-L was 35%, AUB-M was 21.6%, AUB-C was 0.6%, AUB-O was 20%, AUB-E was 0.4%, AUB-I was 1%, AUB-N was 1%. Kalambe et al¹² noted that in their study, AUB-P was 6.6%, AUB-A was 18.4%, AUB-L was 31.6%, AUB-M was 0.83%, AUB-C was 0.83%, AUB-O was 23.4%, AUB-E was 10.82%, AUB-I was 1.6%, AUB-N was 5.8%. Vasava et al¹³ noted that in their study, AUB-P was 2.5%, AUB-A was 8.5%, AUB-L was 25.7%, AUB-M was 8.1%, AUB-C was 0.3%, AUB-O was 28.2%, AUB-E was 14.5%, AUB-I was 2.2%, AUB-N was 9.7%. Sun et al¹⁴ noted that in their study, AUB-P was 16.24%, AUB-A was 4.94%, AUB-L was 12.35%, AUB-M was 1.9%, AUB-C was 1.04%, AUB-O was 57.74%, AUB-E was 2.66%, AUB-I was 2.18%, AUB-N was 0.95%. Jonathan et al¹⁵ noted that in their study, AUB-P was 15%, AUB-A was 53.4%, AUB-L was 47.1%, AUB-M was 15%, AUB-O was 17.2%, AUB-E was 1.1%.

In present study, management of the cases were as follows, dilatation and curettage was done in 59.2% cases, 39% underwent hysterectomy, 1.2% underwent myomectomy, 3.6% underwent polypectomy, medical management was opted in 42% cases, chemoradiation was done 0.8% cases. Sedhai et al¹⁶ noted that medical management was opted in 60% cases, 14% underwent hysterectomy, and 26% underwent dilatation and curettage. Shah JV et al¹⁷ noted that 44% opted for medical management and 66% cases underwent dilatation and curettage, 46.6% underwent hysterectomy.

In present study, LNG-IUS was used in 36.1% cases, Oral contraception pills were used in 32.4%, Tranexamic acid/ mefenamic acid was used in 20% cases, leuprorelin was given in 8.6% cases, mifepristone was used in 2.9% cases. Dhakane M et al¹⁸ noted that 40.3% cases were managed by Ormeloxifene, 21.7% by oral contraceptive pills, 14.7% by oral progestins, 3.3% by tranexamic acid/mefenamic acid. Shah JV et al¹⁷ noted that 46.6% cases were managed by oral progestins, 24% by tranexamic acid/mefenamic acid, 20% by oral contraceptive pills, 1% by LNG-IUS.

5. Conclusion

Abnormal uterine bleeding affects women in all stages of life and it is a major cause of morbidity and decreased quality of life in women. It is more common in perimenopausal age group female with an increased risk of surgical management. The prevalence has increased in recent times due to increase in the risk factors such as stress, hormonal imbalance, obesity, associated medical illnesses.

Women seeking medical help for menstrual problems has also increased due to awareness, education, easy accessibility of health care. But there is still a long way towards better health assistance in women suffering from abnormal uterine bleeding as it is still considered taboo to speak about menstrual problems and women do not seek health till there are physical signs of weakness associated with heavy menstrual bleeding or in cases of infertility. Failure of follow up is also very common in women with menstrual problems which in turn causes increased morbidity and increased incidence of surgical management.

Awareness on menstrual care and hygiene and easy accessibility of health care in society, among both male and female, is important to address any abnormality at the earliest so that adequate and appropriate management can be offered women have a better quality of life.

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Ethical Approval: The study was approved by the Institutional Ethical Committee of Grant Government Medical College, Mumbai.

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