

Prevalence of Abnormal Uterine Bleeding and its Associated Risk Factors in Women of Perimenopausal Age Group- A Retrospective Study

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ABSTRACT

Introduction: Abnormal Uterine Bleeding (AUB) is defined as any deviation from the normal menstrual cycle that is abnormal in regularity, duration, volume and frequency. AUB may be accompanied by pain and discomfort which presents a substantial burden on patient's health, quality of life, society and healthcare system. There is also an increased incidence of associated co-morbidities like thyroid disease, diabetes and hypertension in AUB cases.

Aim: To estimate the prevalence of AUB according to the PALM-COEIN classification and its associated risk factors in the perimenopausal age group.

Materials and Methods: This retrospective study was conducted in the Gynaecology Department of Malabar Medical College, Kozhikode, Kerala, India. The data was collected from the medical records and computerised system of the hospital for a period of one year from January 2021 to December 2021. A total of 225 patients in the perimenopausal age group (40 years and above) attending Gynaecology Outpatient Department (OPD)

and admitted with complaints of AUB was included. Patient's information such as age, menstrual history, obstetric history, medical and surgical history, laboratory tests, imaging findings, endometrial biopsy results was obtained and analysed. Data was entered in Microsoft excel and analysed by using Statistical Package for the Social Science (SPSS) version 24.0.

Results: The total number of patients attending the Gynaecology OPD during the study period was 11765. The total number of AUB cases during the study period were 2154, so the prevalence for AUB was 18.3%. For the associated risk factors, 255 patients were considered, where maximum number of patients 103 (45.3%) were in the age group of 45-49 years. Structural causes accounts for 175 (77.6%) cases. Hypertension was the most common risk factor associated with AUB 68 (30.2%), followed by diabetes 32 (14.2%) and thyroid disorders 15 (6.6%).

Conclusion: The prevalence of AUB was 18.3% in present study. Abnormal Uterine Bleeding-Ovulatory dysfunction and Abnormal Uterine Bleeding- Endometrial had statistically significant association with thyroid disease.

Keywords: Co-morbidities, Endometrial biopsy, Heavy menstrual bleeding, Thyroid disease

INTRODUCTION

Abnormal Uterine Bleeding (AUB) is a common condition in the perimenopausal age group women [1]. AUB leads to loss of productivity and may result in surgical interventions including hysterectomy. More than one third of the patients present with AUB to the OPD [1]. The management of such a common ailment in a population with wide healthcare diversity like India, requires uniform clinical practice guidelines. The main goal of AUB management is to identify the patients with potential risk of developing malignancy and to rule out the underlying endometrial hyperplasia with atypia or endometrial cancer by subjecting to histopathological examination [1]. The International Federation of Gynaecology and Obstetrics (FIGO) and the American College of Obstetricians and Gynaecologists (ACOG) have recommended that a systematised nomenclature, the PALM-COEIN acronym, [Polyp, Pdenomyosis, Leiomyoma, Malignancy, and Hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and not yet classified] be used to describe abnormal menses and to abandon the terminologies like menorrhagia and menometrorrhagia. [1,2] A standard menstrual pattern index has been incorporated in the classification based on frequency, duration, regularity, volume and intermenstrual bleeding [2,3].

The PALM-COEIN classification is aetiopathogenesis based where PALM describes the structural (organic) causes like polyp, adenomyosis, leiomyoma, malignancy and COEIN denoting the

non structural (Non organic) causes like coagulopathy, ovulatory dysfunction and other causes of AUB [1,2] The reported prevalence of AUB in India is about 17.9% [4]. Previous studies have shown that prevalence varies between different regions and it ranges between 10-30% [4-6]. AUB and Heavy Menstrual Bleeding (HMB) are not synonymous. HMB is defined as excessive menstrual blood loss which interferes with a woman's physical, emotional and social quality of life. [1] The diagnosis of AUB depends on comprehensive assessment of the medical history and examination combined with blood tests, imaging modalities and histopathology. Different bleeding patterns also helps in the clinical diagnosis of various causes of AUB. The bleeding patterns, according to the new nomenclature is based on frequency, regularity, duration and volume of blood flow during menses. Based on this, it is categorised into frequent/infrequent cycles, regular/irregular cycles, prolonged/shortened cycles, heavy/light flow [1].

Diabetes and hypertension are known risk factors associated in the people at risk of developing endometrial malignancy and premalignant conditions [1]. The management options for women with AUB is either medical or surgical interventions. Medical management is the first line therapeutic option once malignancy has been ruled out. Surgical management includes both minimally invasive and open techniques such as hysterectomy and myomectomy [1]. There are only few studies comparing the association of AUB in perimenopausal age group with medical disorders [4-6]. In this study,

we have analysed the perimenopausal age group and associated co-morbidities compared to the other studies where reproductive age group population was considered.

Hence, present study was conducted to find the association and prevalence of medical co-morbidities in the people with AUB and to analyse the prevalence of AUB according to the PALM COEIN classification in perimenopausal age group and the risk factors associated with it.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Obstetrics and Gynaecology (OBG), Malabar Medical College, Kozhikode, Kerala, India. The data of January 2021 to December 2021 was collected retrospectively and data were analysed during March 2022 to July 2022. Ethical Committee clearance was obtained before collecting the data [IEC no-MMCHRC &IEC/2022]. As it is a retrospective observational study, data was collected from the medical records, verbal telephonic consent was taken and confidentiality was maintained.

Inclusion criteria: The patients in the perimenopausal age group (40 years and above) attending OBG, OPD and admitted with complaints of AUB were included.

Exclusion criteria: Patients with pregnancy and pregnancy related conditions, postmenopausal women, vaginal bleeding caused by vaginal and cervical causes were excluded.

Sample size calculation: Sample size was calculated using the formula:

$$n=Z^2 \frac{P(100-P)}{d^2}$$

Where n=sample size,

Z=standard normal deviate (for 95% confidence interval, the value is taken as 1.96)

P=prevalence or proportion of interest (from previous similar studies)

d=precision (allowable error)

$$N=(1.96)^2 * 30 * 70 / (6)^2$$

$$=224.09$$

For an estimated prevalence of 30% AUB, with 6% absolute precision, 95% confidence interval, a minimum sample size of 225 was calculated [1,4].

Study Procedure

- **Data collection:** The data was collected retrospectively from the medical records and computerised system of the hospital. Patient's information such as age, parity, menstrual history (Bleeding patterns according to FIGO classification [1], obstetric history, medical [associated co-morbidities] and surgical history, laboratory tests {Complete Blood Count (CBC), Coagulation tests, Thyroid Stimulating Hormone (TSH), Prolactin, Random Blood Sugar (RBS)}, imaging findings (transabdominal/transvaginal ultrasound), endometrial biopsy results were obtained. The data was collected through a structured proforma. For prevalence of AUB, total number of AUB cases among the total number of patients attending the Gynaecology OPD was taken.
- As per the **PALM-COEIN classification system** [2], the potential causes of AUB were established and then categorised accordingly. The diagnosis was done, according to the FIGO classification system by one or more of these assessments like history, physical examination, imaging studies, blood investigations. Histopathological examination by endometrial sampling was employed in the OPD whenever required for diagnosis.

P-Polyps categorised as present or absent based on the history, per speculum examination, ultrasound/histopathological examination.

A-Adenomyosis diagnosis was made based on history, ultrasound features (asymmetrical myometrial appearance and enlarged uterus).

L-Leiomyoma identified by clinical examination and ultrasound.

M-If malignancy or premalignancy was suspected, endometrial biopsy will be obtained.

C-Coagulopathy was identified by medical history and diagnosed by coagulation tests.

O-Ovulatory dysfunction included AUB cases due to anovulation, attributable to endocrinopathies, polycystic ovarian syndrome, hypo/hyperthyroidism, hyperprolactinaemia and weight changes.

E-Endometrial causes include those AUB cases who have predictable and cyclical bleeding typical to ovulatory cycles. The cause may be endometrial in origin. It is a diagnosis of exclusion.

I-Iatrogenic group includes intrauterine contraceptives, gonadal steroids, antibiotics, anticoagulants.

N-Not yet classified, rare pathologies or poorly defined causes which do not fit in the above categories.

- **Bleeding pattern was defined by following FIGO 2018 criteria [1].**

1. Frequency-amenorrhoea for duration of 90 days, cycle length >38 days (infrequent) or <24 days (frequent).
2. Duration-normal duration is ≤8 days; prolonged duration >8 days.
3. Regularity-normal or regular (shortest to longest variation ≤7-9 days); irregular (≥8-10 days).
4. Volume-only patient determined-light, normal and heavy; heavy (HMB)-bleeding volume sufficient to interfere with the woman's quality of life.
5. Intermenstrual bleeding-bleeding between cyclically regular onset of menses, either random or cyclic.

STATISTICAL ANALYSIS

Data was entered in MS excel and analysed by using SPSS version 24.0. Descriptive statistical measure like percentage and inferential statistical test like Chi-square and Fisher's exact probability test was applied. Association was interpreted statistically significant at p-value <0.05. Categorical variables were summarised as percentages. The statistical analysis was done on the basis of percentage distribution of the total number of patients. The results are expressed in terms of percentages and proportions.

RESULTS

The total number of patients attending the Gynaecology OPD during the study period was 11765. To know the prevalence, total AUB cases encountered OBG OPD during the study duration was considered. The total number of AUB cases during the study period was 2154. The prevalence of AUB was 18.3% [2154/11765]. Among these AUB cases, the data of 225 patients was collected through random sampling, to study the associated factors.

Structural (polyp+adenomyosis+leiomyoma+malignancy) causes accounts for 175 (77.6%) cases as per the PALM-COEIN classification, leiomyoma (AUB-L) was the most prevalent cause of AUB in the study. Next common cause of abnormal uterine bleeding was adenomyosis (AUB-A) followed by AUB-P [Table/Fig-1].

Maximum number of patients, 102 (45.3%) were in the age group of 45-49 years followed by 90 (40%) patients aged between 40-44 years and 33 (14.6%) aged 50 years and above.

Majority of patients, 88 (39.1%), complained of HMB as chief complaint. The other menstrual irregularities found were prolonged bleeding 52 (23.1%), frequent bleeding 35 (15.5%) and intermenstrual

AUB classification	Number	%
AUB-P	30	13.3
AUB-A	49	21.7
AUB-L	88	39.10
AUB-M	8	3.5
AUB-C	3	1.3
AUB-O	22	9.7
AUB-E	20	8.8
AUB-I	5	2.2
Total	225	100

[Table/Fig-1]: Distribution of AUB cases according to PALM COEIN classification.

bleeding 24 (10.6%). Around 68 (30.2%) women had associated hypertension with AUB, followed by diabetes and thyroid disorders [Table/Fig-2]. Hypertension was the most common risk factor associated with AUB. Hypertension was seen in 23 (26.1%) AUB-L patients, 13 (26.5%) AUB-A cases and 11 (50%) AUB-O cases. Among 88 AUB-L patients, 23 patients had associated hypertension. However, the association between hypertension and none of the types of AUB was statistically significant [Table/Fig-3].

Parameters	Number	%
Age (in years)		
40-44	90	40
45-49	102	45.3
50 and above	33	14.6
Types of co-morbidities		
Hypertension	68	30.2
Thyroid disease	15	6.6
Diabetes	32	14.2
Presenting complaint		
Heavy menstrual bleeding	88	39.1
Heavy and prolonged bleeding	52	23.1
Intermenstrual bleeding	24	10.6
Frequent bleeding	35	15.5
Infrequent/Scanty bleeding	26	11.5

[Table/Fig-2]: Demographic and clinical details of the study population (N=225).

AUB types	Hypertension		Total	χ^2	p-value
	Present	Absent			
AUB-P	7	23	30	1.109	0.292
AUB-A	13	36	49	0.762	0.382
AUB-L	23	65	88	2.077	0.149
AUB-M	3	5	8	0.132	0.715
AUB-C	1	2	3	0.004	0.948
AUB-O	11	11	22	3.825	0.050
AUB-E	8	12	20	0.714	0.397
AUB-I	2	3	5	0.165	0.683

[Table/Fig-3]: Association between hypertension and different types of AUB. Chi-square/Fisher's exact test were applied to calculate the p-values

Diabetes mellitus was also seen more commonly in AUB-L, AUB-O, AUB-A. Out of total 88 patients with AUB-L, 8 had diabetes and there was a significant association found between diabetes and AUB-L. However, the association between hypertension and none of the types of AUB other than AUB-L was statistically significant [Table/Fig-4].

Thyroid diseases was seen more commonly in AUB-O, AUB-E. Out of 22 AUB-O cases, 5 (22.7%) patients had associated thyroid disease. Among 20 AUB-E cases, 4 (25%) patients had a history of thyroid disease. AUB-O and AUB-E had statistically significant association with thyroid diseases [Table/Fig-5].

AUB types	Diabetes		Total	χ^2	p-value
	Present	Absent			
AUB-P	2	28	30	1.599	0.206
AUB-A	5	44	49	0.913	0.339
AUB-L	8	80	88	3.934	0.047
AUB-M	3	5	8	3.717	0.053
AUB-C	2	1	3	3.167	0.075
AUB-O	6	16	22	3.446	0.063
AUB-E	4	16	20	0.615	0.432
AUB-I	2	3	5	1.055	0.304

[Table/Fig-4]: Association between AUB and diabetes mellitus. p-value <0.05 was considered to be significant

AUB types	Thyroid disease		Total	χ^2	p-value
	Present	Absent			
AUB-P	1	29	30	0.154	0.694
AUB-A	2	47	49	0.246	0.619
AUB-L	2	86	88	3.399	0.065
AUB-M	1	7	8	0.002	0.961
AUB-C	0	3	3	0.181	0.669
AUB-O	5	17	22	7.45	0.006
AUB-E	4	16	20	4.140	0.041
AUB-I	0	5	5	0.234	0.658

[Table/Fig-5]: Association between AUB and thyroid diseases. p-value <0.05 was considered to be significant

DISCUSSION

Prevalence of AUB among the patients attending Gynaecology OPD during the study period was 18.3%. Kotagasti T in their study, found prevalence of AUB as 18.23% which is similar to present study [6]. The prevalence of AUB varies between 9-14% among menarche and menopause women [7]. In India, prevalence of AUB is reported to be 17.9% [4]. AUB was found to be more common in 45-49 years (45.3%) of age group followed by 40-44 years (40%) of age group. The comparison of findings of present study with contrast studies [8-10] are shown in [Table/Fig-6].

Previous studies	Place and year of the study	Sample size	40-44 years	45-49 years
Present study	MMC, Kerala, 2021	225	40%	45.3%
Nair R and Mallikarjuna M, [8]	Kerala Medical College, Mangod, 2015	50	58%	24%
Kumari A and Kumari R [9]	NMCH, Patna	180	65.55%	27.77%
Sinha K et al., [10]	AIIMS Patna 2014-2016	272	58.8%	-

[Table/Fig-6]: Comparison of previous studies with present study [8-10].

The incidence of menstrual disorders increases with increase in age [10]. In this study, HMB was the most common complaint found in 39.1% women. Similar findings were reported by Nair R and Mallikarjuna M, [8], which found heavy menstrual bleeding in 64% followed by intermenstrual bleeding in 18% of cases. The most common cause of AUB in the present study is leiomyoma with a prevalence of 39.10%, followed by adenomyosis (21.7%) and polyp (13.3%), ovulatory, unlike studies by Gouri SR et al., [11] and Goel P and Rathore SB, [12] where most common was AUB-O but disorders were comparable to Qureshi FU and Yusuf AW, [13] and Ratnani R and Meena NA, [14], where the common cause of AUB was leiomyoma. The comparison of findings of present study with contrast studies [11-14] are shown in [Table/Fig-7].

AUB is one of the common menstrual problems faced by women during their perimenopausal period, which is defined as the period of 2-8 years preceding menopause and one year after the final menses [15]. Follicular development during perimenopause is very

Number of patients (%)

Causes		Present study	Gouri SR et al., [11] Tirupathi 2014-15	Goel P and Rathore SB, [12] Jaipur 2016	Qureshi FU and Yusuf AW [13] Lahore 2010-11	Ratnani R and Meena NA, [14] Chhatisgarh 2015
Polyp	P	30 (13.3%)	06 (02.0%)	08 (02.7%)	30 (03.0%)	40 (13.3%)
Adenomyosis	A	49 (21.7%)	38 (12.7%)	28 (09.3%)	150 (15%)	60 (20.0%)
Leiomyoma	L	88 (39.1%)	74 (24.7%)	68 (22.7%)	250 (25%)	105 (35%)
Malignancy or Hyperplasia	M	8 (3.5%)	15 (05.0%)	08 (02.7%)	66 (06.7%)	65 (21.6%)
Coagulopathy	C	3 (1.3%)	09 (03.0%)	03 (01.0%)	03 (03.0%)	02 (00.6%)
Ovulatory dysfunction	O	22 (9.7%)	81 (27.0%)	85 (28.3%)	236 (24%)	60 (20.0%)
Endometrial	E	20 (8.8%)	27 (09.0%)	62 (20.7%)	48 (05.0%)	12 (04.0%)
Iatrogenic	I	5 (2.2%)	24 (08.0%)	13 (04.3%)	53 (06.0%)	03 (01.0%)
Not Yet Classified	N	-	19 (6.3%)	25 (08.3%)	155 (15%)	03 (01.0%)

[Table/Fig-7]: Comparison of distribution of causes in present study with contrast studies [11-14].

unpredictable which leads to variable estrogen levels. This results in anovulatory cycles which causes irregular abnormal uterine bleeding. [15]

The prevalence of AUB-L from previous studies varies between 9-30% [16]. Prevalence of AUB-L is more with advancing age, 35.1% in 40-49 years age group when compared to young people i.e. (24.3%) in age group of 30-39 years [16]. AUB-M accounts for 1.9-5% of AUB cases [16]. The prevalence of AUB -M in the present study was 3.5%.

The prevalence of adenomyosis is different among different subset of population. Prevalence of adenomyosis in women undergoing assisted reproductive technology is 20-25% [17], with associated endometriosis in 20-80% [18], and 20.9% in the general population undergoing ultrasound [19]. Uterine polyps are hyperplastic overgrowths of endometrial glands with prevalence of 7.8-34.9% [20]. Hypertension is the most common co-morbidity which was associated with AUB in the present study (30.8%), followed by diabetes and thyroid disease. Both hypertension and fibroid are highly prevalent diseases that are associated with significant subsequent morbidity [21,22]. Both these conditions involve alterations of smooth muscle cells; in case of fibroids, there are alterations seen in the myometrium and vascular smooth muscle, whereas in hypertension, only the vascular smooth muscle is altered. Hypertension is a consistently identified risk factor for uterine fibroids [23].

In the study conducted by Subedi S et al., thyroid disorders were seen in 10.6% patients with AUB. Thus, there is an association among causes of AUB and medical disorders [24]. The perimenopausal age is also associated with development of medical comorbidities like diabetes, hypertension [25]. Significant association was found between thyroid disease and AUB-O and AUB-E which explains the hormonal imbalance and causes of AUB. In the study done by Mitra N et al., hypertension was found in 18% patients, followed by diabetes in 12% patients of AUB, followed by hypothyroidism in 6% patients [26].

Limitation(s)

Because of the limitations in data collection and small sample size, the association between hypertension and diabetes could not be established adequately in the present study. The association of medical co-morbidities with AUB was also limited only to hypertension, diabetes, thyroid disease.

CONCLUSION(S)

The prevalence of AUB was 18.3% in the study population. AUB-O and AUB-E had statistically significant association with thyroid diseases. Clinicians should emphasise in the assessment and treatment of co-existent risk factors. Structural causes were the most common cause of AUB, among which AUB-L accounted for the majority of cases. A detailed history with special importance on age and type of bleeding pattern with gynaecologic examination

helps in reaching a proper diagnosis in the OPD. PALM-COEIN classification helps in reaching the proper diagnosis and to decide the management options for different causes. This study serves as a pilot analysis to assess the association between the different AUB types and chronic medical conditions.

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