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Original Research Article

Clinical bleeding patterns and management of abnormal uterine bleeding in non-pregnant women: a cross-sectional study

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ABSTRACT

Background: Around 10 to 15 percent of women go through instances of unusual bleeding from their uterus at some point during their reproductive years. Additionally, up to one-third of women may come across irregular menstrual cycles. These irregularities often occur during two crucial phases in a woman's life: firstly, at the beginning of menstruation, which is known as menarche, and secondly, during the transition leading up to menopause, referred to as perimenopause. Aim of study was to determine the clinical bleeding patterns in nonpregnant women and its management.

Methods: During the study period spanning from November 2021 to December 2022, a cross-sectional study examined non-pregnant females aged 15 to 55 experiencing abnormal vaginal bleeding (AUB) who provided consent. However, certain exclusion criteria were established to ensure that the study's findings remained pertinent to the target population. Females exhibiting vaginal bleeding attributed to pregnancy or pregnancy-related factors were excluded from the study, as were those with vaginal bleeding stemming from vaginitis, cervical benign, premalignant, or malignant conditions, or traumatic causes. Descriptive statistics were employed in the study.

Results: Structural causes [PALM] accounts for 71 (61%) of cases whereas non-structural causes of chronic AUB account for 44 (39%) of cases. AUB-L, 45 (39.2%) was the most frequent finding in females with AUB. The second most common causes are AUB-O 23 (20%) followed by AUB-A 14 (12.2%), AUB-C 08(7%), AUB-M 07 (6.1%), AUB-E 06 (5.2%), AUB-P and AUB-I in 05 (4.3%) each and AUB-N 02 (1.7%).

Conclusions: Focusing on Abnormal Uterine Bleeding (AUB), it was observed that AUB-L, attributed to leiomyomas, emerged as the most prevalent cause among affected females. Subsequently, AUB-O, arising from ovulatory dysfunction, and aub-a, linked to adenomyosis, ranked as the second and third most common causes, respectively. Among the clinical manifestations of AUB, prolonged bleeding was identified as the most frequent symptom, followed closely by heavy bleeding.

Keywords: Abnormal uterine bleeding, AUB management, PALM-COIEN

INTRODUCTION

Abnormal uterine bleeding encompasses a wide spectrum of deviations within the menstrual cycle, encompassing anomalies in terms of frequency, duration, and volume of flow, all while excluding occurrences related to pregnancy. Menstrual blood itself is comprised of a

suspension of blood and tissue-derived solids, intermixed with a fusion of serum and cervicovaginal fluid. In the context of a standard menstrual cycle, a normal frequency typically falls within a range spanning 24 to 38 days. The duration of this cycle generally extends over a period of 4 to 9 days, accompanied by a recorded blood loss volume that falls within the range of 10 to 80 millilitres. It's

noteworthy that any divergence from these aforementioned parameters, whether in frequency, duration, or volume, signifies the presence of abnormal uterine bleeding.¹

The uterus and ovarian arteries play a vital role in supplying blood to the uterus. As they progress, these arteries transform into arcuate arteries. Subsequently, these arcuate arteries emit radial branches, intricately providing blood to both layers of the endometrium—the functionalise and basalis layers. Towards the culmination of the menstrual cycle, a decline in progesterone levels triggers the enzymatic breakdown of the functionalise layer within the endometrium. This natural breakdown sets into motion a process involving blood loss and shedding, collectively constituting what we identify as menstruation. This intricate process hinges on the orchestrated interplay of functioning platelets, thrombin, and vasoconstriction of the arteries that serve the endometrial region, culminating in the regulation of blood loss. However, deviations from this meticulously balanced process can arise from a range of factors. Anomalies in uterine structure, encompassing conditions such as leiomyoma, polyps, adenomyosis, malignancies, or hyperplasia, can exert significant influence. Moreover, disruptions to the intricate clotting pathways—referred to as coagulopathies or those inadvertently induced by medical interventions can also perturb the natural course of menstruation. Additionally, any disturbances to the delicate equilibrium of the hypothalamic-pituitary-ovarian axis, whether originating from ovulatory or endocrine disorders or induced through medical interventions, possess the potential to intricately impact the process of menstruation, thereby contributing to the occurrence of abnormal uterine bleeding.^{2,3}

The PALM-COEIN acronym, devised by the International Federation of Obstetrics and Gynaecology (FIGO), serves as an invaluable tool for categorizing the underlying causes of Abnormal Uterine Bleeding (AUB).⁴ Within this framework, PALM signifies structural factors, while COEI encapsulates non-structural factors. Notably, anatomic origins are more prevalent in women of reproductive age compared to other age groups. Consequently, the possibility of pregnancy must always be considered and ruled out when evaluating reproductive-age women experiencing unusual bleeding. Under PALM, the following structural factors are identified: P: Polyps, A: Adenomyosis, L: Leiomyoma, M: Malignancy and hyperplasia. Meanwhile, COEI encompasses the non-structural factors as C: Coagulopathy, O: Ovulatory dysfunction, E: Endometrial disorders, I: Iatrogenic, N: Not otherwise classified.

By employing this comprehensive classification, healthcare practitioners can systematically diagnose and address the myriad causes of AUB, enabling more effective and tailored interventions for patients.

Approximately 10 to 15% of women experience episodes of abnormal uterine bleeding at some point during their

reproductive years. Up to one-third of women encounter irregular menstrual cycles, with these irregularities commonly manifesting during the onset of menstruation (known as menarche) and the transitional phase leading to menopause (referred to as perimenopause). Approximately 55% of adolescents undergo abnormal uterine bleeding within the first year following the commencement of menarche. This phenomenon arises due to the immaturity of the hypothalamic-pituitary-ovarian axis, resulting in cycles without ovulation, also known as anovulatory cycles. It's worth noting that premenopausal women frequently experience menorrhagia, a condition characterized by heavy menstrual bleeding. In about 80% of these cases, anovulatory cycles are the underlying cause. While many studies tend to focus on instances of substantial menstrual bleeding, the inclusion of irregular and intermenstrual bleeding brings the prevalence to 35% or higher, as indicated by various research sources. A notable observation is that a significant number of women do not seek medical treatment for their symptoms. Moreover, the diagnostic process is composed of both objective and subjective components, rendering the determination of precise prevalence challenging.^{5,6}

Aim of study was to determine the clinical bleeding patterns in nonpregnant women and its management.

METHODS

Study setting

All patients of Nehru Chikitsalay BRDMC, Gorakhpur attending the outpatient department and admitted to the hospital, were included in the study.

Study design

This was cross-sectional study conducted from November 2021 to December 2022.

Study population

All Non-pregnant females of reproductive age group with AUB.

Sample size

The prevalence of the AUB in non-pregnant females is 15%.⁷ The following formula was used to calculate the sample size, $N = 4pq/L^2$

After putting the values= $4 \times 15 \times 85 / 7 \times 7 = 104$. After considering 10% non-response rate, sample size= $104 + 10\% \text{ non-response} = 115$

Inclusion criteria

Outdoor or admitted non-pregnant females in the reproductive age group (15 to 55 years) with abnormal

bleeding per vaginum giving informed consent for participation in this study.

Exclusion criteria

Vaginal bleeding caused by pregnancy and pregnancy-related factors, vaginal bleeding caused by vaginitis, vaginal bleeding caused by cervical benign, premalignant or malignant condition, traumatic vaginal bleeding, vaginal bleeding due to leech/ worm infestation were excluded from this study.

Methodology

This study focused on non-pregnant women experiencing abnormal uterine bleeding, who visited the Gynecology Outpatient Department (Gynae. OPD). These participants were carefully selected based on predefined inclusion and exclusion criteria and subsequently enrolled for the research. Detailed information regarding patients' medical history and clinical details was extracted from their medical records. Various diagnostic tests were administered, contributing to the establishment of a final diagnosis. Furthermore, pertinent clinical examinations were conducted as part of the assessment process. In accordance with the PALM-COEIN classification system, participants were categorized into either structural or non-structural causes, based on their diagnostic findings. The subsequent step involved devising individualized management plans for each participant. The study also aimed to explore any potential connections between the participants' clinical, sociodemographic profiles, the PALM-COEIN categories they fell into, and the management techniques employed.

Statistical analysis

For the purpose of analysis, descriptive statistics were employed to summarize categorical variables such as educational level and marital status. Meanwhile, continuous variables, including age and duration of bleeding among others, were summarized using the mean value along with the corresponding standard deviation. This comprehensive approach enabled the research team to gain valuable insights into the relationships between various factors, diagnostic categories, and management strategies, ultimately contributing to a more comprehensive understanding of abnormal uterine bleeding in non-pregnant women.

RESULTS

The patients' age ranged from 15-55y, majority of the participants belonged to 36-45y, 51 (44.3%) age group followed by 46-55y 36-45y age group then 26-35y and the least in the 15-25 y age group, 28(24%), 23 (20%) and 13 (11.4%) respectively. Only 07 (6.1%) of cases were unmarried, and the rest 108 (93.9%) were married. Most of the participants belonged to lower middle, upper middle, and lower class of socioeconomic status, 31

(26.9%), 33 (28.7%) and 27 (23.4%) respectively. Parity in the study ranged from para 1 to para ≥ 4 . 31 (26.9%) of them were para 2 followed by nullipara 21 (18.2%), 20 (17.4%) were para 1 while 18 (15.6%) were para 3 and para ≥ 4 each (Table 1).

Table 1: Distribution of the study participants according to their socio-demographic profile (N=115).

Variables	Frequency	(%)	
Age (years)	15-25	13	11.4
	26-35	23	20
	36-45	51	44.3
	46-55	28	24
Marital status	Unmarried	7	6.1
	Married	108	93.9
Socio-economic status	Upper class	10	8.70
	Upper middle	14	12.17
	Lower middle	31	26.96
	Upper lower	33	28.70
	Lower	27	23.47
Parity (N=108)	Nulliparous	21	18.2
	1	20	17.4
	2	31	26.9
	3	18	15.6
	≥ 4	18	15.6

Comorbidities associated with AUB were obesity 22 (19.1%), hypertension 20 [17.4%], diabetes 18 (15.7%), hypothyroidism 15 (13.1%), and TB 05 (4.3%). Majority of patients 68 (59.1%), presented with a history of prolonged bleeding followed by heavy bleeding. Both prolonged and heavy bleeding were present together in 39 (33.9%) of cases. The second most common presentation was polymenorrhea in 47 (40.8%). Intermenstrual bleeding was seen in 21 (18.2%), oligomenorrhea in 17 (14.7%), hypomenorrhea in 11 (9.6%) and Amenorrhea in 09 (7.8%). 32 (27.8%) of cases presented with dysmenorrhea and 30 (26.2%) of cases presented with the passage of clots. Structural causes [PALM] accounts for 71 (61%) of cases whereas non-structural causes of chronic AUB account for 44 (39%) of cases. AUB-L, 45 (39.2%) was the most frequent finding in females with AUB. The second most common causes are AUB-O 23 (20%) followed by AUB-A 14 (12.2%), AUB-C 08 (7%), AUB-M 07 (6.1%), AUB-E 06 (5.2%), AUB-P and AUB-I in 05 (4.3%) each and AUB-N 02 (1.7%) (Table 2).

All study participants had a pregnancy test and CBC level done. Most frequent lab test conducted was a pregnancy test at 115 (100%), CBC 115 (100%), and coagulation profile 45 (39.1)%. Hysteroscopy was done in only 06 (5.2%) of the participants. Among hormonal profile serum TSH was the most commonly done 50 (54.3%), followed by LH and FSH in 38 (41.3%) each. Estradiol and Prolactin in 16 (17.4%) each and testosterone in 09 (9.8%).

The most common histological pattern observed in the study was proliferative endometrium 14 (31%) followed by secretary 08 (17.8%) and endometrial hyperplasia 06 (13.3%). Atrophic endometrium is found in 02 (4.5%) of cases. Disordered proliferation, endometrial carcinoma,

and benign polyps were seen in 03(6.7%) of cases each. Out of 71 cases that had USG done, the most common finding was leiomyoma in 42(59.1%) of cases followed by adenomyosis in 13(18.3%) of cases (Table 3).

Table 2: Distribution of participants according to their clinical profile (N=115).

Variable		Frequency	(%)	
Co-morbidity	Hypertension	20	17.4	
	Hypothyroidism	15	13.1	
	Diabetes	18	15.7	
	Tuberculosis	5	4.3	
	Obesity	22	19.1	
Bleeding pattern	Menorrhagia	Prolonged bleeding	68	59.1
		Heavy bleeding	50	43.4
		Prolonged +Heavy	39	33.9
	Polymenorrhea	47	40.8	
	Inter menstrual	21	18.2	
	Oligomenorrhea	17	14.7	
	Hypomenorrhea	11	9.6	
	Amenorrhea	9	7.8	
	Dysmenorrhea	32	27.8	
	Passage of clots	30	26.2	
AUB as per PALM-COEIN	P	5	4.3	
	A	14	12.2	
	L	45	39.2	
	M	7	6.1	
	C	8	7.0	
	O	23	20	
	E	6	5.2	
	I	5	4.3	
N	2	1.7		

Table 3: Distribution of the participants according to investigations done (N=115).

Variables		Frequency	(%)
Pregnancy test		115	100
Complete blood count (CBC)		115	100
Coagulation profile		45	39.1
Hysteroscopy		6	5.2
Hormonal profile (n=92)	Thyroid stimulating hormone (TSH)	50	54.3
	Luteinizing hormone (LH)	38	41.3
	Follicle stimulating hormone (FSH)	38	41.3
	Estradiol	16	17.4
	Testosterone	9	9.8
	Prolactin	16	17.4
USG findings	Polyp	5	7
	Adenomyosis	13	18.3
	Leiomyoma	42	59.1
	Malignancy/hyperplasia	2	2.8
	Ovulation dysfunction	4	5.7
	Normal	5	7.1
Endometrial biopsy (n=45)	Proliferative endometrium	14	31.1
	Secretory endometrium	8	17.8
	Menstrual endometrium	1	2.2
	Disordered proliferation	3	6.7

Continued.

Variables	Frequency	(%)
Endometrial hyperplasia	6	13.3
Endometritis	4	8.9
Atrophic endometrium	2	4.5
Endometrial carcinoma	3	6.7
Benign polyp	3	6.7
Insufficient	1	2.2

Table 4: Distribution of the participants according to their management as per the PALM-COEIN criteria (N=115).

PALM-COEIN criteria	Mode of treatment		Outcome of treatment	
			Relieved	Not relieved (%)
P (5)	Surgery	Polypectomy (3)	3	-
		D and C (2)	1	1
A (14)	Medicine (3) Medicine f/b surgery [AH] (3) Surgery [AH] (8)		-	3 (100)
			3	-
			8	-
L (45)	Medicine (22) Medicine f/b surgery Surgery	Myomectomy (2)	1	1
		AH (5)	5	-
		Myomectomy (6)	4	2
		AH (10)	10	-
M (7)	Surgery (AH) (7)		6	1 (14.2)
C (8)	Medicine (8)		5	3 (37.5)
O (23)	Medicine (23)		17	6 (26.1)
E (6)	Medicine (6)		4	2 (33.3)
I (5)	Medicine (5)		3	2 (40)
N (2)	Medicine (2)		1	1 (50)

Polyps were treated surgically either by polypectomy or D&C. Four patients were relieved and one patient's symptoms reoccurred after 2 months of D&C. In the case of adenomyosis all 3 patients that were treated medically did not get relief after treatment while there were still 3 other cases in which after not getting relief from medicine, surgery was done after 2 months of medical treatment. In leiomyoma 6 out of 22 (27.3%) patients did not get relief after medical treatment. Surgical interventions including abdominal hysterectomy (AH) and myomectomy were offered either directly or after discontinuing medical treatment; except 3 cases of myomectomy, all were relieved. In malignancy 1 out of 7 cases of AH did not get relief from symptoms. In this study, all structural causes [COEI (Coagulopathy, Ovulatory dysfunction, Endometrial, and Iatrogenic)] were given medical treatment only. 25 to 40% of cases did not get relief after medical treatment for structural causes (Table 4).

DISCUSSION

In our study, patients' age ranged from 15-55y. The majority of AUB [44.3%] was in the 46-55y age group followed by the 36-45y age group then 26-35y and the least in the 15-25 y age group. Our study has found the maximum incidence of AUB in the perimenopausal group. As women approach menopause, cycles shorten and often

become intermittently anovulatory due to decline in the number of ovarian follicles and fluctuation in estradiol level leading to various patterns of abnormal bleeding. In Sajitha et al study, most of them were seen in the age group of 46-55y followed by 36-45y.⁸ Nepal et al also concluded that the most common age group of women with AUB was 40-44y.⁹ In Gubbal et al study, 39.4% of cases belong to 41-50y and 33.5% to 31-40y.¹⁰ In Rizwi et al, Muzaffar et al, and Jairajpur et al study, the majority of cases belonged to the fifth decade.¹¹⁻¹³

Only 6.1% of cases were unmarried, the rest were married and the majority of them belonged to low socioeconomic status. Therefore, their ignorance regarding the standard of health and nutrition and lack of knowledge contributed largely to not taking medical care. Sreelakshmi U et al¹⁴ also showed the same finding.

Parity in this study ranged from para 1 to para 6. 26.9% were Para 2 followed by nullipara, 17.4% were para 2 and 15.6% were para 3 and para \geq 4 (Table 1). Sajitha et al study found that most patients were in the low parity group followed by para 3-4.⁸ Other studies like Rambabu et al, and Afghan et al reported a higher incidence of AUB with the increase in parity.^{15,16} As per these studies, AUB was much more common in multiparous women than in nulliparous. In our study, the majority of patients [59.1%],

presented with a history of prolonged bleeding followed by heavy bleeding. Both prolonged and heavy bleeding were present together in 33.9% of cases. The second most common presentation was polymenorrhea in 40.8%. The majority of participants had more than one abnormal menstrual pattern. Intermenstrual bleeding seen in 18.2%, oligomenorrhea in 14.7%, hypomenorrhea in 9.6%, and Amenorrhea in 7.8%. 27.8% cases presented with dysmenorrhea and 26.2% of cases presented with the passage of clots. Sreelakshmi et al study showed that the majority of patients presented with a history of heavy menstrual bleeding in 83% and frequent menstrual bleeding in 26.6%, dysmenorrhea in 8.8%, and intermenstrual bleeding in 4%.^{14,13} In Gupta et al study, the most common symptom was heavy menstrual bleeding followed by heavy and frequent bleeding.¹⁷ Rambabu et al, Radhika et al, Rizwi et al, and Nayar et al, also concluded that HMB is the most common presentation of AUB in non-pregnant women.^{11,18-20} HPE of endometrial biopsy in patients presenting with AUB showed a wide spectrum of changes ranging from normal endometrium to malignancy. Endometrial biopsy was done in those patients where endometrial thickness was found to be ≥ 5 mm in pelvic USG. The most common histological pattern observed in the study was proliferative endometrium [31%] followed by secretory [17.8%] and endometrial hyperplasia [13.3%] as varied from Sajitha et al study where most common pattern was endometrial hyperplasia and secretory endometrium was next common pattern followed by proliferative endometrium.⁸ Identification of endometrial hyperplasia is important as they are thought to be precursors of endometrial carcinoma. Endometrial evaluation is especially recommended in women of perimenopausal age group presenting with AUB to rule out the possibility of any preneoplastic condition or malignancy. In Radhika et al study, proliferative phase and hyperplastic changes together were seen in 44.44% of cases; secretory endometrial in 28.8% of cases comparable to the study by Jairajpuri et al which showed secretory endometrium as the most common HPE finding followed by proliferative endometrium.^{19,21} Atrophic endometrium is found in 4.5% of cases in our study which is comparable to the study by Deligdisch et al, Chetna et al, and Purendar et al which showed in 5% of cases.²²⁻²⁴ In our study disordered proliferation, endometrial carcinoma, and benign polyps were seen in 6.7% of cases each. Vaidya et al study found normal cyclical endometrium in 40.9% of cases followed by disordered proliferative endometrium [13.4%] and [10%] cases of hyperplasia.²⁵ Out of 71 cases that had USG done, the most common finding was leiomyoma in 59.1% of cases, followed by adenomyosis in 18.3% of cases. Radhika et al study 48.3% had fibroid and 13.3% had adenomyosis.¹⁹ Structural causes [PALM] accounts for 61% of cases whereas non-structural causes of chronic AUB account for 39% of cases. AUB -L was the most frequent finding in females with AUB. This finding is comparable to Godfrey et al study's finding of nearly half [44.4%] of all study participants presenting with leiomyoma as the most common cause of AUB.²⁶ The second most common cause is AUB-O [20%] followed by

AUB-A [12.2%], AUB-C 7%, AUB-M [6.1%], AUB-E [5.2%], AUB-P and AUB-I in 4.3% each and AUB-N [1.7%]. As per Yu Sun et al study, AUB-O was the most frequent finding in AUB accounting for 57% of cases followed by AUB-P [16%] then AUB-L in 12%, AUB-A in 4.9%, AUB-E and AUB -I in 2% each and AUB-N in 0.9%.²⁷

The strengths of the study, the study was done under the supervision of experienced and skilled clinicians. The study was conducted in a real-world clinical setting, enhancing the external validity of the findings. This increases the generalizability of the results to broader populations and diverse healthcare settings.

The study's limitation lies in its cross-sectional design, which precludes establishing the temporal relationship between the cause and the outcome. To address this limitation in future research, a multicentric prospective study could be undertaken to better establish temporality.

CONCLUSION

This study reveals a diverse demographic and clinical profile of patients with abnormal uterine bleeding (AUB). The majority were in the 36-45 age group, married, and from various socioeconomic backgrounds. AUB presentations varied, with PALM structural causes predominating, particularly AUB-L. Comorbidities included obesity, hypertension, diabetes, hypothyroidism, and tuberculosis. Diagnostic tests, such as pregnancy tests, CBC, and hormonal profiles, were comprehensive. Treatment approaches were tailored to specific causes, with surgical interventions for polyps, varied responses in adenomyosis and leiomyoma, and medical management for structural causes. These insights underscore the complexity of AUB, guiding future research and treatment strategies.

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