

**ABNORMAL UTERINE BLEEDING IN REPRODUCTIVE WOMEN: DIAGNOSIS, MANAGEMENT AND TREATMENT****SANTHOSH KUMAR VENUGOPALAN\*, NITHYA SERMUGA PANDIAN, PAVANI M, SRINIVASA RAO T, RAJINI Y, KHADEER SK, RAVICHANDIRAN V**Department of Pharmacology, School of Pharmaceutical Sciences, Vels University (VISTAS), Chennai - 600 117, Tamil Nadu, India.  
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**ABSTRACT**

Abnormal uterine bleeding (AUB) is a common cause for concern among reproductive women and their families, as well as a frequent cause of visits to the Emergency Department and/or health care provider. In the pilot study, which was conducted in 50 patients, observed that the majority of patients were admitted due to menorrhagia, and most of them were peri-menopausal women. Fibroid uterus is the most common cause in the study population, other than cyst and adenomyosis. Among the 50 patients, 54% were managed with drugs, 32% with surgery and drugs and the remaining with surgery alone. Among the drugs used, tranexamic acid is an effective therapy for the management of aub. The adolescents were treated with oral progestins. Anemia that was assessed in 20% and was corrected with folic acid supplements, iron sucrose and blood transfusions if required. Hysterectomy was done in the majority of patients with cyst and fibroid excisions.

**Keywords:** Abnormal uterine bleeding, Menorrhagia, Fibroid uterus, Tranexamic acid, Progestins, Anemia, Hysterectomy.**INTRODUCTION**

Abnormal uterine bleeding (AUB) may be acute or chronic and is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency, or duration and occurs in the absence of pregnancy [1,2]. AUB refers to an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to prevent further blood loss. AUB occurs in the setting of ovulatory dysfunction because of the effects of chronic unopposed estrogen on the endometrium. Abnormalities at any level of the hypothalamic-pituitary-ovarian axis can result in the interruption of the ovulatory cycle.

In an effort to create a universally accepted system of nomenclature to describe uterine bleeding abnormalities in reproductive-aged women, an alternative classification system polyp, adenomyosis, leiomyoma, malignancy and hyperplasia, coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified, known by the acronym PALM-COEIN, was published in 2011 by the International Federation of Gynecology and Obstetrics and adopted by the American College of Obstetricians and Gynecologists [1]. The PALM-COEIN system classifies uterine bleeding abnormalities by bleeding pattern and etiology. The overarching term AUB is paired with descriptive terms to denote bleeding patterns associated with AUB, such as heavy menstrual bleeding (instead of menorrhagia) and intermenstrual bleeding (instead of metrorrhagia). AUB is further classified by one (or more) letter qualifiers that indicate its etiology. The term dysfunctional uterine bleeding - often used synonymously with AUB in the literature to indicate AUB for which there was no systemic or locally definable structural cause - is not part of the PALM-COEIN system, and discontinuation of its use is recommended [1].

**ESTABLISHING THE DIAGNOSIS**

The evaluation of women with AUB includes a thorough medical history and physical examination, appropriate laboratory and imaging tests, and consideration of age-related factors [2]. Recommended assessments include the following:

1. Age distribution
2. Reasons for admission in the study

3. Menopause status in the study population
4. Past medical history
5. Laboratory investigations
6. Etiologies
7. Diagnostic tests
8. Treatment.

**Age-based considerations***20-24 years*

AUB is the most common during adolescence. During the first 12-18 months after the onset of menstruation, the immaturity of the hypothalamic-pituitary-gonadal axis frequently is the cause of AUB. By the 3<sup>rd</sup> year after menarche, 60-80% of menstrual cycles are 21-34 days long, regardless of age at menarche [3-5]. Females with earlier menarche reach regularly ovulation sooner than those with delayed menstruation. Obesity is becoming an increasingly important contributor to anovulatory cycles in adolescents. Maintaining and achieving ideal body weight are laudable goals during adolescence and may decrease aberrations in menstruation in later life [6]. Anovulatory bleeding in teenagers can become excessive, prolonged, and require pharmacologic therapy. Rarely, incessant bleeding can become a medical emergency that requires hospitalization and more intense evaluation and treatment or surgical intervention.

The differential diagnosis of AUB in adolescents is quite similar to that of other age groups, except that the risk of endometrial hyperplasia and malignancy is extremely low. Patients with AUB can have a concomitant bleeding disorder. Von Willebrand disease is the most common bleeding disorder in women [7]. Adolescents who require hospitalization (i.e., those who present with a hemoglobin level of <10 g/dL) or require blood transfusion have a 20-30% risk of a coagulopathy [8,9].

*25-34 years*

Pregnancy, sexual trauma, and sexually transmitted infections must be ruled out initially, regardless of reported sexual history. Patients also should be evaluated for polycystic ovary syndrome (PCOS) by assessing for signs of hyperandrogenism, such as acne and hirsutism, on physical examination.

Laboratory testing in an adolescent should initially include a measurement of the serum  $\beta$ -human chorionic gonadotropin (hCG) level if the urine pregnancy test result is positive and a complete blood count with platelets. If the platelets are normal, further testing for a coagulopathy should be considered when significant bleeding or anemia is present [10]. The goals of therapy are to halt abnormal bleeding, prevent its recurrence, avert morbidity, and improve the quality of life. For many individuals, the establishment of regular menstruation with a predictable amount of blood flow, duration, and pattern is essential for preserving the quality of life. Patients with evidence of iron deficiency should be treated with oral iron therapy. When anemia does not resolve or improve significantly with oral iron therapy, consultation with a blood management team can determine if intravenous iron therapy is needed.

### 35-44 years

PCOS is one of the most common causes of AUB-O in women of reproductive age. Symptoms may include non-cyclic bleeding hyperandrogenic signs and the characteristic ovarian appearance on ultrasonography [11]. Obesity is a significant co-morbid condition. Premalignant or malignant endometrial pathology should be considered in these high-risk patients, especially if there is an inadequate response to medical therapy.

### Greater than 45 years

Although bleeding changes in women in this age group are largely related to normal menopausal transition, it is important to rule out endometrial hyperplasia and cancer. Perimenopause commences with the onset of cycle irregularity and finishes 1 year after the last menses [12]. The mean age of menopause in women in developed countries is 51.9 years, and smokers develop menopause earlier than nonsmokers [13]. In North America, the average duration of the menopausal transition is 4 years and is most often associated with menstrual irregularity.

In perimenopausal women, AUB-O is caused by naturally declining ovarian function. Intermittent anovulation during perimenopause causes recurrent bouts of AUB. Menstrual cycles during menopause can fluctuate between predictable ovulatory bleeding and erratic AUB-O, which can be especially frustrating for the patient.

Pregnancy must be excluded during the evaluation. Pregnancies, although rare, may still occur until 1 full year without menses. Therefore, for women without contraindications, hormonal contraception, rather than hormone therapy, should be used for pregnancy prevention, menstrual control, and alleviation of perimenopausal symptoms in women at risk. Premenopausal use of hormone therapy will not provide menstrual regularity or contraception.

### Menstrual history, physical examination and laboratory investigations

According to Vihko and Apter [14] the role of age at menarche is crucial. Specifically, the patient who is older at menarche is more likely to have a longer time of anovulatory, "irregular" cycles. The length of cycles and the length of bleeding in days, as determined by recording data on a calendar, should always be considered. It is also of great importance the number of pads or tampons used over a 24-hrs period, as well as for how many days they are used. According to Brown more than three soaked pads or six full regular-absorbency tampons per day for 3 or more days likely equates to >80 ml of blood loss. The number, if any, of "regular" periods experienced by the patient and the history of heavy bleeding, clots or leaking, especially overnight (because this may be associated with a clotting disorder) should always be mentioned. In addition questions should be made about the characteristics of the patient's very first period, because a "heavy" first period may conceal a bleeding disorder, most commonly von Willebrand disease [15]. Finally, patients past medical history and family history should always be taken into consideration. Clinical examination is always very helpful and in a patient with prolonged or heavy bleeding the evaluation should

always begin with vital signs. The physician should assess the patient hemodynamically and look for signs of tachycardia, hypotension or orthostatic changes. Then the physical examination should proceed to the genitourinary system and the physician should search for signs of anemia, as well as clues of other possible underlying causes, such as lacerations, vaginal discharge/inflammation or trauma. Furthermore, it is of great importance the verification that the bleeding is in fact from the vagina/cervical origin (in sexually active women), the absence of a foreign body (e.g., a retained tampon) and that the appearance of the cervix is normal. Finally, pain during bimanual palpation of the cervix, the adnexa or the uterus is indicative of possible pelvic inflammatory disease. In sexually active adolescents who cannot tolerate a speculum or bimanual examination, a pelvic examination under anesthesia may need to be done. In non-sexual active adolescents, recto-abdominal palpation should be carefully considered.

Initial laboratory investigations should include the following:

1. Urine pregnancy test and/or quantitative serum  $\beta$ -HCG
2. Complete blood cell count
3. Pelvic ultrasound may prove helpful to the diagnosis.

According to Brown [15], in case of severe bleeding or when an underlying bleeding disorder is suspected, the following lab tests should be added:

1. Prothrombin time
2. Partial thromboplastin time
3. Bleeding time and platelet aggregation
4. von Willebrand panel must be done prior to initiating hormonal therapy and coagulation factor levels/activity (depending on family history and ethnicity).

On the other hand, if an endocrine disorder is suspected laboratory investigations should include:

- Thyroid stimulating hormone, for thyroid disorders
- Prolactin levels >100 ng/ml suggest a possible pituitary adenoma
- Total and free testosterone (Testo, FTesto), usually elevated in polycystic ovarian syndrome
- Dehydroepiandrosterone sulfate (DHEA-S) to assess for adrenal tumors
- Luteinizing hormone and follicle-stimulating hormone, may aid in the evaluation of pituitary or ovarian function. Finally, for patients in whom an infectious etiology is suspected a swab culture of the discharge and a urethral meatus swab for gonorrhea and chlamydia testing should be taken.

## RESULTS

### Age distribution

The total number of patients included in the study from the study site based on their inclusion/exclusion criteria was found to be 50. In which the patient age group between 20 and 24 were 4% (2), 25-34 were 16% (8), 35-44 were 42% (21) and above 45 were 38% (19). The results indicated that the people aged between 35 and 44 was commonly getting affected by AUB (Table 1).

### Reasons for admission in the study population

The reason for patient's admission to the study site was also thoroughly screened. The results revealed that patients admitted to the study site with varying symptoms such as menorrhagia 56% (28), dysmenorrhea 40% (20), oligomenorrhea 12% (6), abdominal pain 88% (44) and burning micturition 38% (19) (Table 2). The other reasons for admission to the study site were categorized.

### Menopause status in the study population

The patient menstrual status of the study population was categorized as pre-menopause, peri-menopause, and menopause. The category of menopause was 4% (2) which include the patient whose menstruation was stopped (Table 3).

**Past medical history**

The study population was screened for the presence of various medical conditions. 20% (10) of the population suffered from anemia, 6% (3) with hypothyroidism and 6% (3) (Table 4) with suffering from diabetes mellitus.

**Laboratory investigations**

The study population was subjected to various laboratory investigations, which has helped inaccurate diagnosis of the disease state and selecting the choice of therapy. All patients were subjected for blood tests, which include haemoglobin (Hb) 100% (50), packed cell volume (PCV) 100% (50), bleeding time (BT) 96% (48), and clotting time (CT) 96% (48). It was known fact that the patients having abnormal bleeding will definitely reduce the Hb levels, which ultimately leads to anemia (Table 5). Other tests also performed, which include fasting blood sugar, thyroid function test.

**Etiologies**

The study population was thoroughly screened to identify the problems. The results revealed that 40% (20) of the study population had fibroid uterus, 34% (17) with ovarian cyst, 6% (3) with adenomyosis (Table 6).

**Table 1: Age distribution of study population**

Age group % (n)	Overall n=50 (%)
20-24	2 (4)
25-34	8 (16)
35-44	21 (42)
>45	19 (38)

**Table 2: Reason for admission in the study population**

Reason for admission	Patient n=50 (%)
Menorrhagia	28 (56)
Oligomenorrhoea	6 (12)
Dysmenorrhoea	20 (40)
Burning micturition	19 (38)
Abdominal pain	44 (88)

**Table 3: Menopause status in the study population**

Menopause	Overall n=50 (%)
Attained	2 (4)
Not attained	48 (96)

**Table 4: Past medical history in the study population.**

Medical conditions	Overall n=50 (%)
None	34 (68)
Diabetes mellitus	3 (6)
Hypothyroidism	3 (6)
Anemia	10 (20)

**Table 5: Laboratory investigations of the study population**

S.No	Investigations % (n)	Overall n=50 (%)
1.	Hb	50 (100)
2.	PCV	50 (100)
3.	BT	48 (96)
4.	CT	48 (96)
5.	FBS	36 (72)
6.	TSH	1 (2)
7.	T3	2 (4)
8.	T4	2 (4)

Hb: Haemoglobin, PCV: Packed cell volume, BT: Bleeding time, CT: Clotting time, FBS: Fasting blood sugar, TSH: Thyroid stimulating hormone

**Diagnostic tests**

The study population was thoroughly screened to identify the problems. The results revealed that 20% (10) of the study population performed ultrasonography (USG) pelvis, 20% (12) were performed dilatation and curettage (D and C), 56% (28) (Table 7) performed both.

**Treatment**

The treatment provided to the study population was characterized based on its modalities. 54% (27) of the population had undergone drug therapy alone, styptovit (S.V), trapic (T.A), regesteron (R.S), S.V + T.A, T.A + R.S and other drugs 32% (16) (Table 8.0) drug therapy + surgery (Table 8.1) and 14% (7) (Table 8.2) surgery alone.

**Table 6: Etiologies observed in the study population**

Age group % (n)	Overall n=50 (%)	Fibroid uterus (%)	Ovarian cyst (%)	Adenomyosis (%)	None (%)
20-24	2 (4)	0 (0)	0 (0)	0 (0)	2 (4)
25-34	8 (16)	2 (4)	4 (8)	0 (0)	2 (4)
35-44	21 (42)	8 (16)	7 (14)	2 (4)	4 (8)
>45	19 (38)	10 (20)	6 (12)	1 (2)	2 (4)
Total	100%	20 (40)	17 (34)	3 (6)	10 (20)

**Table 7: Diagnostic tests performed for the study population**

Age group % (n)	Overall n=50 (%)	USG pelvis (%)	D and C (%)	Both (%)
20-24	2 (4)	2 (4)	0 (0)	0 (0)
25-34	8 (16)	5 (10)	2 (4)	1 (2)
35-44	21 (42)	2 (4)	4 (8)	15 (30)
>45	19 (38)	1 (2)	6 (12)	12 (24)
Total	50 (100)	10 (20)	12 (20)	28 (56)

USG: Ultrasonography, D and C: Dilatation and curettage

**Table 8.0: Treatments provided for the study population**

Age group % (n)	Overall n=50 (%)	Drug therapy alone (%)	Drug therapy+ surgery (%)	Surgery alone (%)
20-24	2 (4)	2 (4)	0 (0)	0 (0)
25-34	8 (16)	4 (8)	4 (8)	0 (0)
35-44	21 (42)	11 (22)	7 (14)	3 (6)
>45	19 (38)	10 (20)	5 (10)	4 (8)
Total	50 (100)	27 (54)	16 (32)	7 (14)

**Table 8.1: Drug therapies provided for the study population**

Age group % (n)	Overall n=50 (%)	S.V (%)	T.A (%)	R.S (%)	S.V+T.A (%)	T.A+R.S (%)	Others (%)
20-24	2 (4)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)
25-34	8 (16)	1 (2)	5 (10)	0 (0)	0 (0)	2 (4)	0 (0)
35-44	21 (42)	4 (8)	8 (16)	1 (2)	2 (4)	0 (0)	6 (12)
>45	19 (38)	4 (8)	5 (10)	2 (4)	2 (4)	0 (0)	6 (12)
Total	50 (100)	9 (18)	18 (36)	4 (8)	4 (8)	3 (6)	12 (24)

S.V: Styptovit, T.A: Trapic, R.S: Regesteron

**Table 8.2: Surgery carried out in study population**

Age group % (n)	Overall n=50 (%)	Fibroid excision (%)	Cyst excision (%)	Hysterectomy (%)	None (%)
20-24	2 (4)	0 (0)	0 (0)	0 (0)	2 (4)
25-34	8 (16)	1 (2)	3 (6)	0 (0)	4 (8)
35-44	21 (42)	2 (4)	5 (10)	9 (18)	5 (10)
>45	19 (38)	1 (2)	4 (8)	10 (20)	4 (8)
Total	50 (100)	4 (8)	12 (24)	18 (36)	16 (32)

32% (16) of overall study population were treated with surgery and 14% (7) of the overall population were treated with surgery and supported by drug therapy. 8% (4) of overall study population undergone fibroid excision, 24% (12) undergone cyst excision, and 36% (18) undergone hysterectomy. The results revealed that the higher number of hysterectomy were carried out compared with fibroid excision.

## DISCUSSION AND CONCLUSION

The total number of study population included from the study site for the pilot study during the study period was 50. Among the study population, the age was ranging from 20 to 50 years. The total number of 4% (2) patients were between the ages 20 and 22, 16% (8) patients between the age 25 and 34, 42% (21) patients between the age 35-44, and 38% (19) patients were above 45 years (Table 1). Among them patients admitted to the study site with varying symptoms like menorrhagia 56% (28), dysmenorrhea 40% (20), oligomenorrhea 12% (6), abdominal pain 88% (44) and burning micturition 38% (19) (Table 2). Among them the patient menstrual status of the study population was categorized as pre-menopause, peri-menopause, and menopause. The category of menopause 4% (2) which includes the patient whose menstruation was stopped (Table 3).

Among the study population, 20% (10) of the population suffered from anemia, 6% (3) with hypothyroidism and 6% (3) with diabetes mellitus (Table 4). Among the study population, all patients were subjected for blood tests. 100% (50) of them were performed Hb, 100% (50) of them performed PCV, 96% (48) of them performed BT, and 96% (48) of them performed CT (Table 5) among the study population patients were thoroughly screened to identify the problems. The results revealed that 40% (20) of the study population had fibroid uterus, 34% (17) with ovarian cyst, 6 (3) with adenomyosis (Table 6). Among the study population, patients were thoroughly screened to identify the problems. The results revealed that 20% (10) of the study population performed USG pelvis, 24% (12) were performed D and C, 56% (28) performed both (Table 7). Among the study population, the treatment provided was characterized based on its modalities. 54% (27) of the population had undergone drug therapy alone, 32% (16) drug therapy + surgery and 14% (7) surgery alone (Table 8.0).

Among the study population 54% (27) of them were treated with drug therapy alone in which 18% (9) treated with S.V, 36% (18) treated with T.A, 8% (4) treated with regestrone, 8% (4) and 6% (3) treated with combination of S.V+T.A and T.A+regestrone, 24% (12) treated other drugs (Table 8.1). Among the study population, 32% (16) of them were treated with surgery and 14 % (7) of the overall population treated with surgery and supported by drug therapy. 8% (4) of overall study population undergone fibroid excision, 24% (12) undergone cyst excision and 36% (18) undergone hysterectomy (Table 8.2).

Thus from the results it can be concluded by the use of patient information from which revealed that some of the symptoms of the AUB were found to be improved. This reveals that the treatment given to the patient was efficient. The study states that the patient symptoms were improved with drug therapy. Totally 50 patients were included. AUB is a common and sometimes debilitating condition in women of reproductive age. Standardization of related terminology, a systematic approach to diagnosis and investigation, and a step-wise approach to intervention is necessary.

A thorough medical history followed by complete physical examination, and the appropriate laboratory investigations are of great importance. Endometrial biopsy should be obtained if possible in all women presenting with AUB, over 40 years of age. While D and C may have a diagnostic role, it is not effective therapy for women with heavy menstrual bleeding. The optimum therapy of AUB depends on understanding the mechanisms, pathogenesis, and possible factors

involved. Medical management should be the initial treatment for most patients. Anemia need to be assessed and treated in these patients. In patients with anovulatory bleeding, the goal of treatment is to regulate cycles, minimize blood loss, and prevent complications from chronic unopposed estrogen.

The management of AUB in patients with no other etiology will in part be directed by the amount of flow, the degree of associated anemia, as well as patient and family comfort with different treatment modalities, while the options for medical care of AUB generally include: Combined oral contraceptives, progestins, non-steroidal anti-inflammatory drugs, anti-fibrinolytics-tranexamic acid, GnRH analogs danazol and levonorgestrel intrauterine system. The need for the surgical treatment is based on the clinical stability of the patient, the severity of bleeding, contraindications to medical management, the patient's lack of response to medical management and the underlying medical condition of the patient. There are improved outcomes with vaginal hysterectomy surgical route of choice for hysterectomy. The choice of surgical modality is based on the fore mentioned factors plus the patient's desire for future fertility.

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