WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 6, 374-384. Review Article ISSN 2277– 7105

CRITICAL STUDY ON ABNORMAL UTERINE BLEEDING: A REVIEW

[1]*Khushboo Jha, [2]Prof. Dr. K. Bharathi and [3]Dr. Sonu

[1]3rd Year PG Scholar, Department of Prasuti Tantra Evam Stri Roga, National Institute of Ayurveda, Jaipur.

[2]Head of Department, Department of Prasuti Tantra Evam Stri Roga, National Institute of Ayurveda, Jaipur.

[3]Lecturer, Department of Prasuti Tantra Evam Stri Roga, National Institute of Ayurveda, Jaipur.

Article Received on
28 March 2021,

Revised on 18 April 2021,
Accepted on 09 May 2021

DOI: 10.20959/wjpr20216-20483

***Corresponding Author**
Dr. Khushboo Jha
3rd Year PG Scholar, Department of Prasuti Tantra Evam Stri Roga, National Institute of Ayurveda, Jaipur.

ABSTRACT

Abnormal uterine bleeding is a broad term that describes irregularities in the menstrual cycle involving frequency, regularity, duration, and volume of flow outside of pregnancy. Up to one-third of women will experience abnormal uterine bleeding in their life, with irregularities most commonly occurring at menarche and perimenopause. A normal menstrual cycle has a frequency of 24 to 38 days, lasts 7 to 9 days, with 5 to 80 milliliters of blood loss. Variations in any of these 4 parameters constitute abnormal uterine bleeding. Older terms such as oligomenorrhea, menorrhagia, and dysfunctional uterine bleeding should be discarded in favor of using simple terms to describe the nature of the abnormal uterine bleeding. Revisions to the terminology were first published in 2007, followed by updates from the International Federation of Obstetrics and Gynecology (FIGO) in 2011 and 2018. In this Review, complete explanation has been described about the incidence, etiology, clinical features, differential diagnosis, management and complication.

KEYWORDS: Abnormal uterine bleeding, diagnosis, management.

INTRODUCTION

Abnormal uterine bleeding is a broad term that describes irregularities in the menstrual cycle involving frequency, regularity, duration, and volume of flow outside of pregnancy. Up to

one-third of women will experience abnormal uterine bleeding in their life, with irregularities most commonly occurring at menarche and perimenopause. A normal menstrual cycle has a frequency of 24 to 38 days, lasts 7 to 9 days, with 5 to 80 milliliters of blood loss. Variations in any of these 4 parameters constitute abnormal uterine bleeding. This activity reviews abnormal uterine bleeding diagnosis and treatment and explains the importance of an inter professional approach to evaluating and treating abnormal uterine bleeding.

Abnormal uterine bleeding (AUB) is a broad term that describes irregularities in the menstrual cycle involving frequency, regularity, duration, and volume of flow outside of pregnancy. Up to one-third of women will experience abnormal uterine bleeding in their life, with irregularities most commonly occurring at menarche and perimenopause. A normal menstrual cycle has a frequency of 24 to 38 days, lasts 7 to 9 days, with 5 to 80 milliliters of blood loss.[1] Variations in any of these 4 parameters constitute abnormal uterine bleeding. Older terms such as oligomenorrhea, menorrhagia, and dysfunctional uterine bleeding should be discarded in favor of using simple terms to describe the nature of the abnormal uterine bleeding. Revisions to the terminology were first published in 2007, followed by updates from the International Federation of Obstetrics and Gynecology (FIGO) in 2011 and 2018. The FIGO systems first define the abnormal uterine bleeding, then give an acronym for common etiologies. These descriptions apply to chronic, nongestational AUB. In 2018, the committee added intermenstrual bleeding and defined irregular bleeding as outside the 75th percentile.[2]

Abnormal uterine bleeding can also be divided into acute versus chronic. Acute AUB is excessive bleeding that requires immediate intervention to prevent further blood loss. Acute AUB can occur on its own or superimposed on chronic AUB, which refers to irregularities in menstrual bleeding for most of the previous 6 months.[3]

Normal menses in adolescents

To assess vaginal bleeding during adolescence, it is necessary to understand the range of normal menstrual cycles. During first 2 to 5 years after menarche, most cycles are anovulatory. Despite this, they are somewhat regular, within a range of approximately 21 to 45 days. In contrast to adult women, whose cycles typically range between 21 and 38 days[4] in more than one fourth of girls, a pattern of plus or minus 10 days and a cycle length of 21 to approximately 45 days are established within the first three cycles: in one half of girls, the

pattern is established by the seventh cycle; and in two third of girls, such a pattern is established within 2 years of menarche.[5]

Menstrual cycle frequency	21-45 days
Cycle variation from cycle to cycle	Less than in adults
Duration of flow	4-8 days
Volume of flow	4-80ml

The mean duration of menses is 4.7 days; 89% of cycles lasts 7 days. The average blood loss per cycle is 35ml, and the major component of menstrual discharge is endometrial tissue.[6] An 80ml\cycle is used as a definition of heavy menstrual bleeding and recurrent bleeding in excess of 80ml\cycle results in anaemia, although the clinical utility of the 80ml\cycle is questioned.

The common clinical practice of asking how many pads or tampons are soaked on a heavy day or per cycle can give a rough approximation of blood loss (three to five pads per day is typical). Individual variations in fastidiousness, lack of familiarity with the volume of blood loss other than ones own, and errors in estimation or recollection result in inaccuracies in estimations of menstrual volume. One study found that one-third of individuals who estimated their cycles to be moderate or light had bleeding in excess of 80ml\cycle, whereas nearly one half of those who described the bleeding as heavy had flow less than 80ml\cycle.[7] In addition, the amount of menstrual blood contained in each tampon or pad may vary both within brands as well as from one brand to another.[8] However changing pad hourly, clots size larger than “50 pence size” and requiring a change overnight are associated with a measured volume of greater than 80 ml.[9]

ETIOLOGY

PALM-COEIN is a useful acronym provided by the International Federation of Obstetrics and Gynecology (FIGO) to classify the underlying etiologies of abnormal uterine bleeding. The first portion, PALM, describes structural issues. The second portion, COEN, describes non-structural issues. The N stands for "not otherwise classified."

- P: Polyp
- A: Adenomyosis
- L: Leiomyoma
- M: Malignancy and hyperplasia
- C: Coagulopathy
- O: Ovulatory dysfunction

- E: Endometrial disorders
- I: Iatrogenic
- N: Not otherwise classified

One or more of the problems listed above can contribute to a patient's abnormal uterine bleeding. Some structural entities, such as endocervical polyps, endometrial polyps, or leiomyomas, may be asymptomatic and not the primary cause of a patient's AUB. In the 2018 FIGO system, AUB secondary to anticoagulants was moved from the coagulopathy category to the iatrogenic category. Conditions to be included in not otherwise classified include pelvic inflammatory disease, chronic liver disease, and cervicitis.

AUB not otherwise classified contains rare etiologies and includes arteriovenous malformations (AVMs), myometrial hyperplasia, and endometritis.[10]

EPIDEMIOLOGY

The prevalence of abnormal uterine bleeding among reproductive-aged women internationally is estimated to be between 3% to 30%, with a higher incidence occurring around menarche and perimenopause. Many studies are limited to heavy menstrual bleeding (HMB), but when irregular and intermenstrual bleeding are considered, the prevalence rises to 35% or greater. Many women do not seek treatment for their symptoms, and some components of diagnosis are objective while others are subjective, making exact prevalence difficult to determine.

PATHOPHYSIOLOGY

The uterine and ovarian arteries supply blood to the uterus. These arteries become the arcuate arteries; then the arcuate arteries send off radial branches which supply blood to the two layers of the endometrium, the functionalis and basalis layers. Progesterone levels fall at the end of the menstrual cycle, leading to enzymatic breakdown of the functionalis layer of the endometrium. This breakdown leads to blood loss and sloughing, which makes up menstruation. Functioning platelets, thrombin, and vasoconstriction of the arteries to the endometrium control blood loss. Any derangement in the structure of the uterus (such as leiomyoma, polyps, adenomyosis, malignancy, or hyperplasia), derangements to the clotting pathways (coagulopathies or iatrogenically), or disruption of the hypothalamic-pituitary-ovarian axis (through ovulatory/endocrine disorders or iatrogenically) can affect menstruation and lead to abnormal uterine bleeding.

HISTORY AND PHYSICAL

The clinician should obtain a detailed history from a patient who presented with complaints related to menstruation. Specific aspects of the history include:

- Menstrual history
  - Age at menarche
  - Last menstrual period
  - Menses frequency, regularity, duration, the volume of flow
    - Frequency can be described as frequent (less than 24 days), normal (24 to 38 days), or infrequent (greater than 38 days)
    - Regularity can be described as absent, regular (with a variation of +/- 2 to 7 days), or irregular (variation greater than 20 days)
    - The duration can be described as prolonged (greater than 8 days), normal (approximately 4 to 8 days), or shortened (less than 4 days)
    - The volume of flow can be described as heavy (greater than 80 mL), normal (5 to 80 mL), or light (less than 5 mL of blood loss)
    - Exact volume measurements are difficult to determine outside research settings; therefore, detailed questions regarding frequency of sanitary product changes during each day, passage and size of any clots, need to change sanitary products during the night, and a "flooding" sensation are important.
  - Intermenstrual and postcoital bleeding
- Sexual and reproductive history
  - Obstetrical history including the number of pregnancies and mode of delivery
  - Fertility desire and subfertility
  - Current contraception
  - History of sexually transmitted infections (STIs)
  - PAP smear history
- Associated symptoms/Systemic symptoms
  - Weight loss
  - Pain
  - Discharge
  - Bowel or bladder symptoms
  - Signs/symptoms of anemia
  - Signs/symptoms or history of a bleeding disorder
  - Signs/symptoms or history of endocrine disorders

- Current medications
- Family history, including questions concerning coagulopathies, malignancy, endocrine disorders
- Social history, including tobacco, alcohol, and drug uses; occupation; the impact of symptoms on quality of life
- Surgical history

The physical exam should include

- Vital signs, including blood pressure and body mass index (BMI)
- Signs of pallor, such as skin or mucosal pallor
- Signs of endocrine disorders
  - Examination of the thyroid for enlargement or tenderness
  - Excessive or abnormal hair growth patterns, clitoromegaly, acne, potentially indicating hyperandrogenism.
  - Moon facies, abnormal fat distribution, striae that could indicate Cushing's
- Signs of coagulopathies, such as bruising or petechiae
- Abdominal exam to palpate for any pelvic or abdominal masses
- Pelvic exam: Speculum and bimanual
  - Pap smear if indicated
  - STI screening (such as for gonorrhea and chlamydia) and wet prep if indicated
  - Endometrial biopsy, if indicated

Evaluation: Laboratory testing can include but is not limited to a urine pregnancy test, complete blood count, ferritin, coagulation panel, thyroid function tests, gonadotropins, prolactin. Imaging studies can include transvaginal ultrasound, MRI, hysteroscopy. Transvaginal ultrasound does not expose the patient to radiation and can show uterus size and shape, leiomyomas (fibroids), adenomyosis, endometrial thickness, and ovarian anomalies. It is an important tool and should be obtained early in the investigation of abnormal uterine bleeding. MRI provides detailed images that can prove useful in surgical planning, but it is costly and not the first-line choice for imaging in patients with AUB. Hysteroscopy and sonohysterography (transvaginal ultrasound with intrauterine contrast) are helpful in situations where endometrial polyps are noted, images from transvaginal ultrasound are inconclusive, or submucosal leiomyomas are seen. Hysteroscopy and sonohysterography are more invasive but can often be performed in office settings.

Endometrial tissue sampling may not be necessary for all women with AUB but should be performed on women at high risk for hyperplasia or malignancy. An endometrial biopsy is considered the first-line test in women with AUB who are 45 years or older. Endometrial sampling should also be performed in women younger than 45 with unopposed estrogen exposure, such as women with obesity and/or polycystic ovarian syndrome (PCOS), as well as a failure of treatment or persistent bleeding.

Treatment\Management

Treatment of abnormal uterine bleeding depends on multiple factors, such as the etiology of the AUB, fertility desire, the clinical stability of the patient, and other medical comorbidities. Treatment should be individualized based on these factors. In general, medical options are preferred as initial treatment for AUB.

For acute abnormal uterine bleeding, hormonal methods are the first-line in medical management. Intravenous (IV) conjugated equine estrogen, combined oral contraceptive pills (OCPs), and oral progestins are all options for treating acute AUB. Tranexamic acid prevents fibrin degradation and can be used to treated acute AUB. Tamponade of uterine bleeding with a Foley bulb is a mechanical option for the treatment of acute AUB. It is important to assess the patient's clinical stability and replace volume with intravenous fluids and blood products while attempting to stop the acute abnormal uterine bleeding. Desmopressin, administered intranasally, subcutaneously, or intravenously, can be given for acute AUB secondary to the coagulopathy von Willebrand disease. Some patients may require dilation and curettage.

Based on the PALM-COEIN acronym for etiologies of chronic AUB, specific treatment options for each category are listed below

Polyps are treated through surgical resection.

Adenomyosis is treated via hysterectomy. Less often, adenomyomectomy is performed. Leiomyomas (fibroids) can be treated through medical or surgical management depending on the patient's desire for fertility, medical comorbidities, pressure symptoms, and distortion of the uterine cavity. Surgical options include uterine artery embolization, endometrial ablation, or hysterectomy. Medical management options include a levonorgestrel-releasing intrauterine device (IUD), GnRH agonists, systemic progestins, and tranexamic acid with non-steroidal anti-inflammatory drugs (NSAIDs).

Malignancy or hyperplasia can be treated through surgery, +/- adjuvant treatment depending on the stage, progestins in high doses when surgery is not an option, or palliative therapy, such as radiotherapy.

Coagulopathies leading to AUB can be treated with tranexamic acid or desmopressin (DDAVP).

Ovulatory dysfunction can be treated through lifestyle modification in women with obesity, PCOS, or other conditions in which anovulatory cycles are suspected. Endocrine disorders should be corrected using appropriate medications, such as cabergoline for hyperprolactinemia and levothyroxine for hypothyroidism.

Endometrial disorders have no specific treatment as mechanisms are not clearly understood.

Iatrogenic causes of AUB should be managed based on the offending drug and/or drugs. If a certain contraception method is the suspected culprit for AUB, alternative methods can be considered, such as the levonorgestrel-releasing IUD, combined oral contraceptive pills (in monthly or extended cycles), or systemic progestins. If other medications are suspected and cannot be discontinued, the aforementioned methods can also help control AUB. Individual therapy should be tailored based on a patient's reproductive wishes and medical comorbidities. Not otherwise classified causes of AUB include entities such as endometritis and AVMs. Endometritis can be treated with antibiotics and AVMs with embolization[11]

Diffrential Diagnosis

Any bleeding from the genitourinary tract or gastrointestinal tract (GI tract) can mimic abnormal uterine bleeding. Therefore, bleeding from other sources fits into the differential diagnosis and must be ruled out.

The differential diagnosis for genital tract bleeding based on anatomic location or system

Vulva: Benign growths or malignancy

Vagina: Benign growths, sexually transmitted infections, vaginitis, malignancy, trauma, foreign bodies

Cervix: Benign growths, sexually transmitted infections, malignancy

Fallopian tubes and ovaries: Pelvic inflammatory disease, malignancy

Urinary tract: Infections, malignancy

Gastrointestinal tract: Inflammatory bowel disease, Behçet syndrome

Pregnancy complications: Spontaneous abortion, ectopic pregnancy, placenta previa

Uterus: Etiologies of bleeding arising from the uterine corpus are listed in the acronym PALM-COEIN.

PROGNOSIS

The prognosis for abnormal uterine bleeding is favorable but also depends on the etiology. The main goal of evaluating and treating chronic AUB is to rule out serious conditions such as malignancy and improve the patient's quality of life, keeping in mind current and future fertility goals and other comorbid medical conditions that may impact treatment or symptoms. Prognosis also differs based on medical versus surgical treatment. Non-hormonal treatment with anti-fibrinolytic and non-steroidal anti-inflammatory medications has been shown to reduce blood loss during menstruation by up to 50%.[6] Oral contraceptive pills can be effective, but there is a lack of data from randomized trials. For women with heavy menstrual bleeding as their primary symptom of AUB, the levonorgestrel-releasing IUD has been proven to be more effective than other[12] medical therapies and improves the patient's quality of life. Injectable progestogens and GnRH agonists can produce amenorrhea in up to 50% and 90% of women, respectively. However, injectable progestogens can produce the side effect of breakthrough bleeding, and GnRH agonists are usually only used for a 6-month course due to their side effects in producing a low estrogen state. With the surgical techniques, randomized clinical trials and reviews have shown that endometrial ablation controlled bleeding more effectively at 4 months postoperatively, but at 5 years, there was no difference compared to medical management. When trials have compared hysterectomy versus levonorgestrel-releasing IUD, the hysterectomy group had better results at 1 year. There was no difference in the quality of life seen at 5 and 10 years, but many women in the levonorgestrel-releasing IUD group had undergone a hysterectomy by 10 years.[13]

COMPLICATIONS

Complications of chronic abnormal uterine bleeding can include:

Anaemia
Infertility
Endometrial cancer
With acute abnormal uterine bleeding, severe anemia, hypotension, shock, and even death may result if prompt treatment and supportive care are not initiated.

CONCLUSIONS

Abnormal uterine bleeding is a common condition and is also debilitating condition with high direct and indirect costs. A structured approach to establishing the cause using the FIGO PALM –COEIN classification system will facilitate diagnosis and treatment options. As abnormal uterine plays important role in hampering the quality of life, thus treatment must remain individualized and encompasses the impact of pressure symptoms, desire for retention of fertility and contraceptive needs, as well as address the management of AUB in order to achieve improved quality of life.

REFERENCES

1. Fraser IS, Critchley HO, Munro MG, Broder M. Can we achieve international agreement on terminologies and definitions used to describe abnormalities of menstrual bleeding? Hum Reprod, Mar, 2007; 22(3): 635-43. [PubMed]
2. Munro MG, Critchley HOD, Fraser IS., FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. Int J Gynaecol Obstet, Dec, 2018; 143(3): 393-408. [PubMed]
3. ACOG committee opinion no. 557: Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Obstet Gynecol, Apr., 2013; 121(4): 891-896. [PubMed]
4. Treloar AE, Boynton RE, Behn B, et al. variation of the human menstrual cycle throughout reproductive life. Int J fertile, 1967; 156: 581-582.
5. Flug D, Largo RH, Prader A. menstrual patterns in adolescent swiss girl: a longitudinal study. Ann Hum Biol., 1984; 11: 495-508.
6. Fraser IS, McCarron G, Markham R.et al. blood and total fluid content of menstrual discharge. obstet gynecol, 198; 65: 194-198.
7. Fraser IS, McCarron G, Markham R. A preliminary study of factors influencing perception of menstrual blood loss volume. Am J obstet gynecol, 1984; 149: 788-793
8. Warner PE, Critchley HO, Lumsden, MA, et al. menorrhagia II: is the 80ml blood loss criterion useful in management of complaint of menorrhagia? Am J Obstet Gynecoi, 2004; 190: 1224-1229.
9. Warner PE, Critchley HO, Lumsden, MA, et al. menorrhagia I: measured blood loss, clinical features, and outcome in women with heavy periodes; a survey with follow up data. Am J obstet Gynecol, 2004; 190: 1216-1223.

10. Munro MG, Critchley HOD, Fraser IS., FIGO Menstrual Disorders Committee. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. Int J Gynaecol Obstet, Dec, 2018; 143(3): 393-408. [PubMed]
11. ACOG committee opinion no. 557: Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. Obstet Gynecol, Apr, 2013; 121(4): 891-896. [PubMed]
12. Cheong Y, Cameron IT, Critchley HOD. Abnormal uterine bleeding. Br Med Bull, Sep 01, 2017; 123(1): 103-114. [PubMed]
13. Emily Davis; Paul B. Sparzak Abnormal Uterine Bleeding https://www.ncbi.nlm.nih.gov/books/NBK532913/