

**Abnormal Uterine Bleeding in Perimenopausal Age Group Women: Single Centre Experience**Patel MS<sup>1</sup>, Patel DM<sup>2</sup>, Antala KP<sup>3</sup>, Raza ZZ<sup>4</sup>, Thakkar UG<sup>5</sup><sup>1,3</sup>Department of Obstetrics and Gynecology, Smt. S.C.L. General Hospital, Ahmedabad, India<sup>2</sup>Department of Obstetrics and Gynecology, Jamnabai General Hospital, Vadodara, India<sup>4</sup>Department of Obstetrics and Gynecology, IKDRC-ITS, Ahmedabad, India<sup>5</sup>Department of Regenerative Medicine, IKDRC-ITS, Ahmedabad, India

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**Abstract:**

**Background:** Abnormal uterine bleeding (AUB) can be defined as any abnormality in normal menstrual cycle. It creates emotional, physical and social discomfort to menstruating female. AUB is the commonest menstrual problem observed in perimenopausal age group. PALM–COEIN classification given by International Federation of Gynecology and Obstetrics (FIGO) as well as American College of Obstetricians and Gynecologists (ACOG) suggested currently used AUB classification system. Various diagnostic and therapeutic approaches are available to treat AUB.

**Material and Methods:** Total 94 patients were enrolled in this study and compared their demography, different diagnostic methods used and results of medical as well as surgical treatment modalities.

**Results:** Transvaginal ultrasonography (TVS) is a method of diagnosis to rule out endometrial and intrauterine abnormalities. However, Ultrasound allows examining endometrium, and its hyperplasia, polyp/ fibroid. If it is abnormal or inconclusive then further investigations may be needed. Medical treatment is the preferred choice but Hysterectomy is the definitive surgical treatment for AUB.

**Conclusion:** TVS is the superior diagnostic method and hysterectomy is the definitive treatment for AUB.

**Keywords:** Menstrual Cycle, Menopause, Abnormal Uterine Bleeding, Transvaginal Ultrasonography, Hysterectomy.

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**Introduction**

Abnormal uterine bleeding is a symptom. Abnormal uterine bleeding (AUB) is defined as any variation from the normal menstrual cycle and includes changes in regularity and frequency of menses, in the duration of flow, or in the amount of blood loss [1]. It is a symptom. Abnormal uterine bleeding is associated with significant social and physical morbidities in all societies and may be a reflection of serious underlying pathology [2]. AUB is a common condition affecting women at all ages and the commonest menstrual problem during perimenopause.[3] It is important to reach correct clinical diagnosis and identify the causative factor.

Abnormal menstrual bleeding pattern have been traditionally expressed by terms like menorrhagia, metrorrhagia, polymenorrhea, and oligomenorrhea. In order to create an universally accepted nomenclature to describe abnormal uterine bleeding, International Federation of Gynecology and Obstetrics (FIGO) and American College of Obstetricians and Gynecologists (ACOG)

introduced newer system of terminology to describe AUB. The newer classification system is known by the acronym PALM–COEIN (FIGO–2011) [4]. It is used to classify the abnormal uterine bleeding on the basis of etiology. Polyp, adenomyosis, leiomyoma, malignancy and coagulopathy, hyperplasia, ovulatory dysfunction, endometrial, iatrogenic, and not yet classified are the different etiological factors expressed by one (or more) letters. FIGO recommends endometrial tissue testing as a first-line management in women of perimenopausal age group who have AUB [5][6]. Histology clinches the diagnosis and guides the management plan. Ultrasonography is usually a safe initial investigation as it is non-invasive and can give us an idea about any structural cause.

Hysteroscopy has been generally accepted as gold standard in evaluation of the uterine cavity [7]. It has high sensitivity and specificity in diagnosis due to the fact that the uterine cavity and intrauterine pathology are directly visualized. Histopathological evaluation of endometrial tissue by curetting or

aspiration is a safe & effective method for determining the cause of AUB after excluding systemic and structural causes [8].

### **Aim and objective of study**

This was a prospective single arm open-labeled clinical research study to evaluate the etiology of AUB, various histopathological changes in endometrium, diagnostic modalities as well as various medical/ surgical management approach to treat AUB in peri-menopausal women. This study was approved by the Institutional Review Board. We obtained informed consent for participation in research activities in accordance with the committee's standards from the individual described herein.

### **End points of study**

Study endpoints included appropriate diagnostic and therapeutic available options to treat AUB in perimenopausal females.

### **Inclusion and exclusion criteria**

Study included females with  $\geq 40$  years of age with structural and functional causes of AUB and complains of menorrhagia/ intermenstrual bleeding. Our study excluded females less than 40 years of age, malignancy, systemic illness, pelvic inflammatory diseases, thyroid dysfunction, coagulopathy, seropositive females and pregnant women.

### **Material and methods**

The authors enrolled 94 patients of AUB in the Department of Obstetrics and Gynecology at our institute between June' 2023 to June' 2024.

The accurate incidence of Abnormal Uterine Bleeding (AUB) is challenging to determine due to several factors. Many patients receive treatment on an outpatient basis, which makes it difficult to capture comprehensive data. Additionally, during the transition phase of the menstrual cycle, normal variations can sometimes be mistaken by patients as abnormal bleeding. This complexity underscores the need for careful assessment and accurate diagnosis in cases of AUB. However, in India, approximate incidence is 9% to 14%.

The maximum numbers (59) of the patients were seen in the age group of 40-45 which is perimenopausal age. In India average age of menopause is 47.5 years [10]. 30 patients were in the group of 46-50 years and, 5 in >50 years. (Table-1) Increased incidence of AUB in this age group due to the fact that these women are in their climacteric period approaching menopause, when cycles become intermittently anovulatory due to decline in the number of ovarian follicles and estradiol level [11] Patients of parity 4 and above were maximum 46.81%. Similar association was also found in Bha-

rat et al 2016.[12] (Table-2) Higher the parity and greater the age which leads to decreased ovarian function and AUB. In all patients, ultrasonography was done primarily. It gave primary diagnosis for 80 patients. Out of them, 30 females had fibroid in USG. (Figure-1) Adenomyosis was confirmed by histopathology examination in 12 patients post hysterectomy. (Table-3) Other diagnostic modalities were done in patients who needed further evaluation. Total 50 women underwent dilation and curettage (D & C) among them 12 women underwent therapeutic D & C and 38 underwent endometrial biopsy (EB). EB was taken between 15th- 20th day of menstrual cycle. Various endometrial patterns were observed.

Out of them, 58% of women had a proliferative endometrium suggested AUB in perimenopausal women was predominantly anovulatory. Endometrial hyperplasia was seen in 7 women indicating unopposed estrogen action in an anovulatory AUB. (Table-4) This is due to the fact that these women are in their peri- menopausal period, when cycles become intermittently anovulatory due to decline in the number of ovarian follicles and estradiol level [11].

Total 65 patients have taken medical therapy, out of them, 39 women received oral progesterone as an initial management, which if not effective, were switched to oral contraceptive pills or were given Tranexamic acid and mefenamic acid as an adjuvant. Danazol, GnRH agonists and SERM were used for reduction in size of large leiomyoma or resistant cases to Progesterone or oral contraceptive pills. Very few patients opted for danazol, GNRH agonists and SERMs as treatment options in our study due to higher cost and need of compliance. Treatment failure, by the end of 6 months, for progesterone was around 38.46%, whereas for combined pills, TXA+MF, Danazol, GNRH agonists was found to be 42.86%, 72.73%, 33.33% and 33.33% respectively. Failure of therapy with Progesterone and combines pills was mainly due to lack of compliance.

This led to intermittent menstrual bleeding. Majority of patients attending our hospital being uneducated, can be a reason behind medical treatment failure. Increased percentage of treatment failure in patients subjected to Danazol, GNRH agonist and SERMs as medical therapy due to higher costs, long treatment protocol and greater side effects. Two trials COOPER ET AL1997 and KUPPERMAN 2004 showed that 54% of the women on progesterone as the initial therapy needed surgery at the end of one year. (Table-5)

Therapeutic D & C was offered to 15 women with an acute bleeding episode who hadn't given consent for hysterectomy and continued with medical management for 6 months. D & C with hyster-

oscopy offered to 7 women with uterine polyp. (Figure-2) Hysterectomy was performed in 18 patients with advanced changes of adenomyosis and large fibroid. (Table-6) By the end of 6 months, 52.12% patients required hysterectomy due to persistent complaints with D & C or medical management and 47.88% were benefitted with medical therapy  $\pm$  D&C. According to Carlson KL et al 25% of patients initially treated non-surgically, subsequently underwent hysterectomy [13] which

when compared to this study is 52.12%. A total of 49 patients underwent hysterectomy out of which maximum (32.65%) were due to leiomyoma. 24.49% underwent hysterectomy due to adenomyosis. 10.20% of the patients undergoing Hysterectomy, as a definitive management, were because of ovulatory dysfunction. The percentage of hysterectomy due to endometrial hyperplasia was 16.32%. (Table-7)

**Table 1: Age distribution in abnormal uterine bleeding**

Age wise Distribution (In Years)	No. and (%) of cases N=94	Reneta Nicolae et al 2015[9] N=103
40-45	59 (62.76%)	67.97%
46-50	30 (31.92%)	23.03%
>50	05 (5.32%)	10%

**Table 2: Parity wise distribution of Abnormal uterine bleeding**

Parity	No. and (%) of cases N=94	Bharat et v al 2016 [12] N=103
0 (Nulliparous)	2 (2.12%)	3(2.91%)
1	8 (8.51%)	10(9.71%)
2	15 (15.96%)	19(18.45%)
3	25 (26.60%)	27(26.21%)
$\geq$ 4	44 (46.81%)	44(42.72%)

**Table 3: Ultrasonography findings in patients of abnormal uterine bleeding**

Findings	No. of Cases (N=94)	Percentage (%)
Polyp	7	7.45%
Adenomyosis	15	15.96%
Ovulatory dysfunction	12	12.76%
Normal	14	14.89%
Endometrial Hyperplasia	16	17.02%
Leiomyoma	30	31.91%

**Table 4: Histopathological data of dilatation and curettage/ endometrial biopsy material**

Endometrial Pattern	No. of Cases (N=50)	Percentage (%)
Proliferative	29	58%
Secretory	12	24%
Hyperplasia	7	14%
Atrophic	2	4%

**Table 5: Medical management of abnormal uterine bleeding and its failure**

Treatment	Total No. of patients underwent medical management (N= 65)	Patients Needing Hysterectomy	Percentage of patients required hysterectomy after medical management failure (%)
Progesterones	39 (41.49%)	15	38.46%
LNG-Mirena	1 (1.06%)	-	-
Tranexamic+ Mefenemic Acid	11 (11.70%)	8	72.73%
Danazol	3 (3.19%)	1	33.33%
Estrogen+ Progesterone	7 (7.45%)	3	42.86%
GnRH Agonist	3 (3.19%)	1	33.33%
SERM	1 (1.06%)	-	-

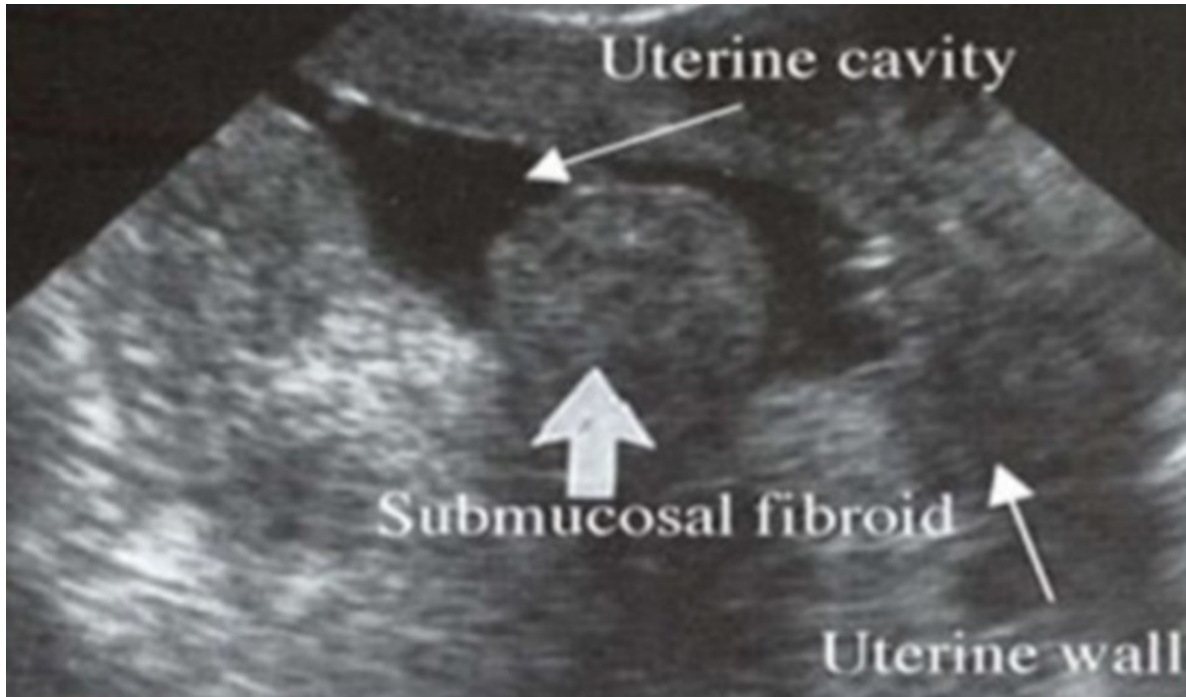
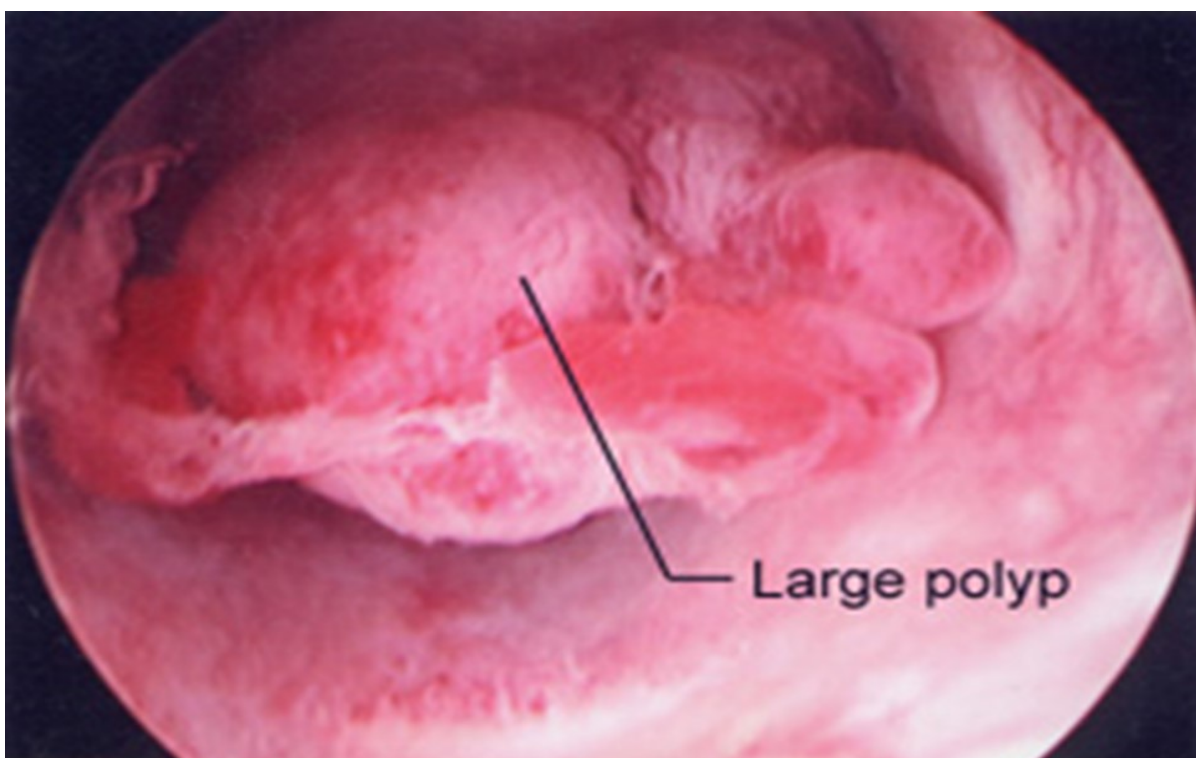
\*LNG- levonorgesterel, GnRH- Gonadotropin releasing hormone, SERM- selective estrogen receptor modulator

**Table 6: Primary surgical management of abnormal uterine bleeding**

Modality	No. and (%) of cases
Primary D & C	15 (15.96%)
Primary Hysterectomy	18 (18.75%)
D & C + Hysteroscopy	7 (7.45%)

**Table 7: Indications of hysterectomy in patients with abnormal uterine bleeding**

Histopathology in Hysterectomy	No. and (%) of Cases N=49	Chanderdeep et al 2014[14] (%)
Leiomyoma	16(32.65%)	27%
Adenomyosis	12(24.49%)	13%
Ovulatory Dysfunction	5(10.20%)	10.7%
Endometrial Hyperplasia	8(16.32%)	9.4%
Other	8(16.32%)	39.9%

**Figure 1: Ultrasound revealed submucosal fibroid in a patient with abnormal uterine bleeding****Figure 2: Hysteroscopy showed large polyp in a patient with abnormal uterine bleeding**

## Discussion

Throughout history, a normal menstrual cycle has been seen as a key marker of good reproductive health. Any changes in the volume, duration, or regularity of this cyclical shedding are therefore seen as signs of dysfunction and are typically not well-received, especially among women in the perimenopausal period.

Abnormal uterine bleeding is a term that is commonly used to refer to any bleeding that does not meet the criteria for normal menstrual bleeding. The causes of abnormal uterine bleeding can vary widely and include diseases of the reproductive system as well as non-gynecologic causes. Organic causes of abnormal uterine bleeding can be further categorized into reproductive tract diseases, iatrogenic causes, and systemic diseases. In cases where no organic cause for abnormal uterine bleeding can be identified, a diagnosis of dysfunctional uterine bleeding (DUB) is made based on the process of exclusion.

In cases of abnormal uterine bleeding, routine non-invasive tests typically include a complete blood count, platelet count, prothrombin time (PT), Activated partial thromboplastin time (APTT), and liver function test to rule out any coagulation and bleeding disorders. Women in the reproductive age group may undergo evaluation of serum and urine human chorionic gonadotropin (HCG) levels to exclude pregnancy. To investigate a potential endocrine cause, thyroid function test, follicle stimulating hormone (FSH), luteinizing hormone (LH), and prolactin levels are assessed. Following the exclusion of these factors, gynecologists may opt for imaging studies such as pelvic ultrasound (USG), transvaginal USG, and tissue sampling. Dilution and curettage can be utilized as both a diagnostic and therapeutic measure.

The sensitivity of endometrial biopsy for the detection of endometrial abnormalities has been reported to be as high as 96%. [15,16] Medical treatment tailored to the individual woman's therapeutic goals, underlying medical conditions, and tolerance of side effects will encourage compliance and maximize the likelihood of treatment success. For abnormal uterine bleeding, definitive treatment is provided by hysterectomy. Hysteroscopic myomectomy can be used as a treatment for abnormal uterine bleeding secondary to sub mucosal fibroids.

The results of the present study provide compelling evidence that the frequency of menstrual disorders rises significantly as individual's progress in age. Among the age groups investigated, individuals with age between 40 to 50 years were found to be the most common demographic presenting with excessive bleeding during menstruation. Present study like several others showed anovulatory

cycles, disordered proliferative pattern, hyperplasia and benign endometrial polyp occurring more commonly in the age group 41-50 years. [17]

Endometrial biopsy should be considered when the ET is >12mm. It should always be considered when long term estrogen exposure is present, but not necessary when the endometrial thickness is <4mm. Majority of patients presented with heavy menstrual bleeding as their abnormal pattern of bleeding. Ultrasonography was the most commonly used diagnostic modality. Women who had a proliferative endometrium in histopathological findings were 58%, which goes onto say that anovulation is a significant cause of AUB in perimenopausal age group.

Failure of treatment and subsequent requirement for surgery, by the end of 6 months, for progesterone was around 38.46%, whereas for combined pills, TXA+MF, danazol, GNRH agonists was found to be 42.86%, 72.73%, 33.33% and 33.33% respectively. Most common indication of hysterectomy was leiomyoma (32.65%). Most commonly used method of hysterectomy in the current study was abdominal hysterectomy

## Conclusion

AUB, or abnormal uterine bleeding, is more commonly observed in women over the age of 40 and above who have given birth multiple times. Among these patients, heavy menstrual bleeding is the most frequently reported symptom. The recommended approach for managing AUB in perimenopausal women involves diagnosing the condition, managing symptoms, and treating the underlying cause. This can be achieved through various medical and surgical treatment options that are currently available. To rule out any endometrial or intrauterine abnormalities, trans-vaginal ultrasonography is considered a superior diagnostic procedure. It is often used as the initial investigation for patients experiencing abnormal uterine bleeding. Ultrasonography allows for the examination of the endometrium, detection of endometrial hyperplasia, identification of endometrial polyps, and assessment of uterine fibroids. If the ultrasound report is inconclusive or abnormal, further investigations may be required.

In the cases of peri-menopausal AUB, medical therapy is an effective treatment options. Typically, hormonal therapy in the form of progesterone is administered during the luteal phase of the menstrual cycle. However, the success of such medical treatments is often hindered by issues with patient compliance and the need to switch to alternative therapies or add adjuvant medical treatments. Despite these challenges, medical treatment remains the preferred choice for many gynecologists and general practitioners. MIRENA

is a newer medical hormonal treatment option for AUB. However, its usage is limited in our healthcare setting due to its high cost. Hysterectomy is considered the definitive surgical treatment for AUB as it involves the removal of the diseased organ. However, since hysterectomy is a major surgical procedure, it carries the risk of complications.

Therefore, it is advisable to recommend minimally invasive procedures, medical management, and natural treatments whenever possible. Hysterectomy can still be a viable alternative for women from low socio-economic backgrounds and those who are illiterate. Involving patients in the decision-making process can enhance the success rate of treatment.

The choice of treatment depends on several factors and should be tailored to each individual case. Many patients continue to choose hysterectomy as their preferred treatment option, despite the current medical treatment being based on a rational approach that takes into account physical, socio-economic, and mental factors.

#### Abbreviations

- aPTT-activated partial thromboplastin time
- AUB- abnormal uterine bleeding
- D and C- dilation and curettage
- DUB-dysfunctional uterine bleeding
- EB- endometrial biopsy
- FSH-follicle stimulating hormone
- GnRH-gonadotropin releasing hormone
- HCG-human chorionic gonadotropin
- LH-luteinizing hormone
- MF-mefenamic acid
- PT-prothrombin time
- SERMs-selective estrogen receptor modulator
- TVS- transvaginal sonography
- TXA-tranexamic acid
- USG-ultrasound sonography

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