

**Original article**

**Abnormal Uterine Bleeding in Perimenopausal Age: Different causes and its relation with histopathology.**

*Nargis N<sup>1</sup>, Karim P, Sarwar KB<sup>3</sup>*

**Abstract:**

**Background:** Abnormal uterine bleeding (AUB) is the most common reason for gynecological visits for perimenopausal bleeding and may account for more than 25% of all hysterectomies. **Objective:** This study was aimed to review the causes of abnormal uterine bleeding in perimenopausal women establishing the correlation with ultrasonographic and histopathological examinations. **Study Method:** This descriptive study was conducted in the department of gynecology and obstetrics, Ibn Sina Medical College, Dhaka during January to December 2012. Two hundred and eleven women were selected for this study, who admitted into the hospital with abnormal uterine bleeding in perimenopausal age. The clinical, ultrasonographic and histopathological findings of these women were evaluated in this study. **Results:** Menorrhagia was the major symptom (52.6%) irrespective of age and parity. All these women underwent D&C followed by either medical management or hysterectomy depending upon the diagnosis. The histopathological findings of endometrium were analyzed and confirmed as fibroid uterus (58.28%) and DUB (17.58%) correlated well with transvaginal sonography (TVS) and histopathological examination. Hysterectomy conferred other uterine lesions as adenomyosis (18.71%), endometrial polyp (4.81%) and malignancy (1.06%). **Conclusion:** Abnormal uterine bleeding in perimenopausal age group is a common but ill-defined entity which needs proper evaluation. Accurate diagnosis of the causative factors of AUB in this age group is of utmost importance so that appropriate management can be established early that leads the minimization of the patients' sufferings.

**Key Words:** Abnormal uterine bleeding, Transvaginal sonography, Dilatation and curettage, Histopathological examination, perimenopause

DOI: <http://dx.doi.org/10.3329/bjms.v13i2.18295>

Bangladesh Journal of Medical Science Vol.13(2) 2014 p.135-139

**Introduction:**

Abnormal uterine bleeding (AUB) is a common gynaecological problem and the principal reason for gynaecological consultation<sup>1-4</sup>, accounting for up to (20%) of office visits to gynecologists<sup>4,5</sup>. AUB is defined as any bleeding that does not correspond with the frequency, duration or amount of blood flow of a normal menstrual cycle<sup>6-10</sup>. It is a symptom and not a disease that occurs in different patterns<sup>11,12</sup>. The terminology of abnormal uterine bleeding includes the following clinical entities<sup>13-15</sup>: oligomenorrhoea, polymenorrhoea, menorrhagia, menometrorrhagia, metrorrhagia, midcycle spot-

ting, dysfunctional uterine bleeding, abnormal acute uterine bleeding.

Perimenopause is the period 2-8 years preceding menopause and 1 year after the final menses (WHO). Menstrual irregularity occurs in more than one half of all women during the menopausal transition. Menorrhagia is cyclical bleeding at regular interval which is excessive in amount (80 ml) or duration. Menorrhagia is thought to be associated with uterine fibroid, DUB, adenomyosis, pelvic infections, endometrial polyp, clotting defects. Polymenorrhagia, intermenstrual bleeding and metrorrhagia are other common disorders at

1. Dr. Nazlima Nargis, Associate Professor, Gynecology and Obstetrics. Ibn Sina Medical College
2. Dr. Iqbal Karim, Armed Forces Medical College, Dhaka
3. Khondaker Bulbul Sarwar, Associate Professor, Dept of Community Medicine, ISMC, Dhaka.

**Corresponds to:** Dr. Nazlima Nargis, Associate Professor, Gynecology and Obstetrics. Ibn Sina Medical College, 1/1-B Kallyanpur, Dhaka-1216. E-mail: nazlimanargis@gmail.com

Perimenopause. There are so many studies on these issues in abroad but few in Bangladesh. To establish evidence based treatment guidelines study on AUB in Bangladeshi perimenopausal women is very important. Moreover endometrial sampling should be considered in all women with abnormal uterine bleeding particularly in those above the age of (40) years and in women who are at increased risk of endometrial cancer<sup>16</sup>.

**Patients and Methods:**

This study was carried out over a period of 12 months extended from the 1<sup>st</sup> January, 2012 till 31<sup>st</sup>December, 2012. Two hundred eleven women with different patterns of abnormal uterine bleeding admitted were included in this study. All obstetric causes of AUB (including abortion and pregnancy related causes) were excluded. We analyzed these women by recording age, parity, menstrual symptoms and associated symptoms for clinical evaluation. Transvaginal sonography was performed using vaginal transducer of 6.5 MHZ frequency on Logic Pro 100-GE USA. Endometrial thickness was measured in postmenstrual period ( 7-10 day) at the thickest part of endometrium 1cm from the endometrial myometrial interface at the interface at the fundus in the longitudinal plane as described<sup>17,18</sup>. Clinical impression and TVS reports were correlated. These women underwent D&C for endometrial sampling and specimen sent for histopathological examination (HPE). The HPE reports were analyzed. These women were managed either conservatively depending upon the or surgically response. Histopathological reports of endometrial pattern as well as that of the hysterectomy specimens were correlated with clinical diagnosis and ultrasonographic findings. This study was approved by local ethical Committee.

**Results**

A number of 211 women of different ages presented with AUB are included in this study. However the number of AUB is high in increased parity such as 3 or more (table -1). In the age group 40-45 years, we found 67 (46.2%) AUB among high multipara (>3 parity), followed by parity -3 (39; 26.8%) and so on. The total number of AUB in this group was 145 (68.7% of total). The patient came to hospital mostly with the complaints of menorrhagia (111; 52.6%), followed by polymenorrhagia (57; 24.6%), intermenstrual bleeding (32; 15.6%) and metrorrhagia alone (11; 5.2%). Clinical diagnosis were mostly fibroid (124; 58.7%), followed by DUB (66; 31.2%),

adenomyosis (14; 6.6%) and polyp (5;2.3%). TVS diagnosed (121; 57.34%) fibroid uterus, 62 (29.38%) women had endometrial thickness (>8mm) strong suspicious of DUB, 19 (9%) were adenomyosis and 9 were polyp (4.2%) (table 3). These women were managed by surgical approaches – D&C alone or D& C followed by hysterectomy. Histopathological findings of endometrium revealed that endometrium was proliferative in 116 (62.03%) cases, simple hyperplasia 27 (14.43%), secretory endometrium 38 (20.32%), endometrial polyp 4 (2.13%) and malignancy 2 (1.06%). Women who underwent hysterectomy were 182 (86.25%), polypectomy 5 (2.3%) and 24 were managed conservatively (11.37%). Histopathological reports of hysterectomy specimen were as follows: fibroid uterus 109 (58.28%), adenomyosis 35 (18.71%), DUD 32 (17.58%), leiomyosarcoma 2 (1.06%) and polypectomy was 5 (4.81%). Thus out of 124 suspected fibroid uterus 109 (58.28%) were confirmed by HPE, 13 (10.48%) women with small fibroids received medical management and were asymptomatic at the end of 3 months. Out of 66 suspected cases of DUB, 32 (48%) were confirmed by HPE, 23 (34.84%) turned out adenomyosis by HPE and 11 (16.66%) got conservative management. Hysterectomies done for adenomyosis were 14 and confirmed by HPE as well. The clinical, TVS and histopathological correlation is revealed on (table3).

**Table 1: Distribution of subjects on the basis of age group and parity**

Parity	40-45 yrs	46-50 yrs	> 50 yrs	Total
0	5(2.36%)	1 (0.47%)	0	6(2.84%)
1	6 (2.84 %)	2 (0.97%)	0	8
2	28 (13.27%)	22(10.42%)	1(0.47%)	50(23.69%)
3	39 (18.48%)	26(12.32%)	4 (1.89%)	69(32.70%)
High multiparity	67(31.75%)	8(3.79%)	3(1.41%)	78(39.96%)
Total	145(68.7%)	58(27.48%)	8(3.79%)	211(100%)

**Table 2: Distribution of subjects according to patterns of bleeding**

Parity	40-45 yrs	46-50 yrs	> 50 yrs	Total
0	5(2.36%)	1 (0.47%)	0	6(2.84%)
1	6 (2.84 %)	2 (0.97%)	0	8
2	28 (13.27%)	22(10.42%)	1(0.47%)	50(23.69%)
3	39 (18.48%)	26(12.32%)	4 (1.89%)	69(32.70%)
High multiparity	67(31.75%)	8(3.79%)	3(1.41%)	78(39.96%)
Total	145(68.7%)	58(27.48%)	8(3.79%)	211(100%)

**Table-3: Causes of AUB through Clinical, TVS and HPE**

Disease	Clinical	TVS	HPE
Fibroid	124 (58.76%)	121(57.39%)	109 (58.28%)
DUB	66 (31.27%)	62 (29.38%)	32 (17.58%)
Adenomyosis	14 (6.6%)	19 (9%)	35 (18.71%)
Polyp	5 (2.3%)	9(4.2%)	9 (4.81%)
Fibromyosarcoma			2 (1.06%)
Total	211	211	187

**Table-4 Different histopathological findings of endometrium by D&C or hysterectomy**

Histopathological findings	No. of cases	Percentage
Proliferative phase	116	62.03%
Secretory phase	38	20.32%
Simple hyperplasia	27	14.43%
Polyp	4	2.13%
Malignancy	2	1.06%
Total	187	88.62%

**Discussion:**

Abnormal uterine bleeding is one of the commonest gynaecological problems encountered in gynaecology OPD. Abnormal perimenopausal bleeding is associated with endometrial carcinoma in approximately 10% of cases<sup>20</sup>. So evaluation of women's risk factors for endometrial hyperplasia or carcinoma is recommended. Evaluation of patients with abnormal uterine bleeding involve ultrasonography, hysteroscopy and endometrial biopsy as majore modalities. Though endometrial sampling can be done by D&C, endometrial aspiration and hysteroscopy, hysteroscopy directed biopsy is considered Gold standard. Though hysteroscopes are not available, D&C is also an effective way to control uterine bleeding in absence of uterine pathology and systemic cause. We compared endometrial patterns with Jordan university, LTMMC and Sion Hospital and G.Michail et al study. In our study, proliferative endometrium was revealed in 116 cases (62%) compared with the Bhosle A and Fonseca M study which revealed that dysfunctional uterine bleeding represented by proliferative endometrium was found in 66.1% of cases, with the Jordan University study – 53% of cases, the Sion Hospital and the LTMMC study – 66.1% of cases and the study of G Michail et al – 9.8%.

Transvaginal sonography is an excellent diagnostic

tool for detection of gynaecological diseases. In general an endometrial thickness of more than 8mm is considered suspicious of endometrial pathology in perimenopausal women with AUB and further investigation is recommended<sup>18,19</sup>. Studies using transvaginal sonography has shown tat endometrial thickness neasured correlated well with results obtained on histopathology.

Women included in the present study were complaining of different patterns of AUB and the majority of them presented clinically with menorrhagia (52%). Similar findings were reported by others. Fibroids are common finding in women with menorrhagia. Menorrhagia in fibroids is due to increased in size of the uterine cavity thereby increasing the surface area of the endometrium, hyperestrogenemia causing endometrial hyperplasia , vascular alteration of the endometrium and obstetric effect of fibroid on uterine vasculature leading to endometrial venule ectasia which causes proximal congestion in the myometrium and the endometrium. Majority of women with uterine fibroid associated with menorrhagia are treated by hysterectomy (58%). In our study , Fibroid uterus was responsible for abnormal uterine bleeding (AUB) in 58% of women and the data concurs with the results from the studies performed in DHQ Hospital and Nishtar Hospital Multan –54.8% and Bombay Hospital –54%<sup>23</sup>.

Adenomyosis is a lesion characterized by the presence within the myometrium of foci consisting of glands and endometrial stroma, located at distance of the junction between the endometrium and the myometrium. it occurs more frequently during perimenopause, being a lesion detected in 20% of surgically treated gynaecological cases. Diagnosis of adenomyosis on clinical findings is usually different<sup>24</sup>. Transabdominal sonography (TAS) does not allow reliable diagnosis of adenomyosis or consistent differentiation from leiomyomas, even transvaginal sonography (TVS) has limitation in tissue characterization. MRI is more helpful to diagnose adenomyosis but expensive. In our study clinically only 6.6% were diagnosed as adenomyosis, USG diagnosed 9% and HPE diagnosed 18%. The reported prevalence of adenomyosis in hysterectomy specimens varies from 5% to70%. Menorrhagia associated with cycles can be treated with or without hormone. The anti-inflammatory medication mefenamic acid can reduce bleeding by 225 to 46%. We used it for menorrhagia associated wih small fibroids as

well in some cases of DUB in this study successfully. The LNG-IUS is a relatively new treatment that remains effective for 5 years. It has been found to reduce menstrual blood loss by 74 %-- 97%.

A number of minimally invasive surgical options for hysterectomy now exist and are promising like endometrial ablation, thermal ballon therapy and uterine artery embolization but restricted availability and cost factor limit their use.

Malignancy found in this study was found in 2 (1.06%) of cases and it is Leiomyosarcoma. The rate of diagnosis of endometrial neoplasia in this study did not reflect the real prevalence of these lesions.

### **Conclusions:**

The diagnosis of perimenopausal bleeding and prognostic evaluation is based on the histopathological

examination of the endometrium after biopsy. In our study fibroid uterus was the most common cause of abnormal uterine bleeding. Second common cause was DUB. Histopathology revealed majority of endometrium in proliferative phase. Histopathology also revealed malignancy in two out of two hundred and eleven cases which signifies importance of routine histopathology in such cases. Clinical, radiological and pathological evaluation correlated very well to diagnose fibroids. However clinically as well as USG proved of little help to diagnose adenomyosis.

As abnormal uterine bleeding (AUB) in perimenopausal age is a common findings so it needs proper evaluation. Accurate diagnosis for the cause of AUB and appropriate management at early stage can minimize patients sufferings.

### **References:**

1. Feng L, Li D. Evaluation of intrauterine disorders by hysteroscopy and transvaginal sonography. *Gynaecol Endoscopy* 2002;**11**:401-4. <http://dx.doi.org/10.1111/j.1365-2508.2002.00561.x>
2. Hunter DC, McClure N. Abnormal uterine bleeding: an evaluation endometrial biopsy, vaginal ultrasound and out patient ysteroscopy. *Ulster Med j* 2001;**70**:25-30.
3. Mihm LM, Quick VA, Brumfield BRJA et al. The accuracy of endometrial biopsy and saline sonohysterography in the determination of the cause of abnormal uterine bleeding . *Am J Obstet Gynaecol* 2002;**186**:858-60. <http://dx.doi.org/10.1067/mob.2002.123056>
4. Madan SM, AL-Jufairi AZ. Abnormal uterine bleeding: diagnostic value of hysteroscopy. *Saudi Med J* 2001;**22**:153-56.
5. Shwayder JM. Pathophysiology of abnormal uterine bleeding. *Obstet & Gynaecol Clin of North America* 2000;**27**:153-56.
6. Campbell S, Monga A. Gynaecology by Ten Teachers. 17th ed. *Arnold*, 2000:41-54.
7. Fraser NH. Abnormal uterine bleeding. *Obstet / Gynaecol Nurse Forum* 2000;**12**:1-6.
8. Lane ME, Dacalos E, Sobrero AJ et al . Squamous metaplasia of the endometrium in women with an intrauterine contraceptive device: a follow –up study. *Am J Obstet Gynaecol* 1974; **119**:693-97.
9. Quddus MR, Sung CJ, Zheng W et al. P53 immunoreactivity in endometrial metaplasia with dysfunctional uterine bleeding. *Histopathol* 1999;**35**:44-49. <http://dx.doi.org/10.1046/j.1365-2559.1999.00684.x>
10. Williams PL, Laifer-Narin SL, Ragavendra N. US of abnormal uterine bleeding. *Radiographics* 2003;**23**:703-18. <http://dx.doi.org/10.1148/rg.233025150>
11. Bhatla N. Jeffcoate,s Principles of Gynaecology. *International ed. Arnold*, 2001:560-570.
12. Razzak AH, Abdulmajeed AM. Endometrial findings in patients with abnormal uterine bleeding. *JUD* 1999;**2**:339-45.
13. Goodman A, Abnormal genital tract bleeding, *Clin Corner - stone* , 2 0 0 0 ; **3 ( 1 ) : 2 5 - 3 5 .** [http://dx.doi.org/10.1016/S1098-3597\(00\)90019-X](http://dx.doi.org/10.1016/S1098-3597(00)90019-X)
14. Oriel KA, Schragar S, Abnormal uterine bleeding, *Am*

- Fam Physician*, 1990;**60**(5):1371-1380; discussion 1381-1382.
15. Speroff L, Glass RH, Kase NG, Clinical gynecologic endocrinology and infertility, 6th edition, *Lippincott Williams & Wilkins, Baltimore*, 1999, 201-238, 499, 575-579.
  16. Oehler MK, Rees MCP. Menorrhagia: an update. *Acta Obstet et Gynaecol Scand* 2003;**82**: 405-22. <http://dx.doi.org/10.1034/j.1600-0412.2003.00097.x>
  17. Saha TK, Amer SA, Biss J, Thakare H, Williams S, Farreell CT, Calvert J. The validity of transvaginal ultrasound measurement of endometrial thickness: a comparison of ultrasound measurement with direct anatomical measurement. *BJOG* 2004;**111**:1419-24. <http://dx.doi.org/10.1111/j.1471-0528.2004.00177.x>
  18. Gvanberg S, Wikland M, Karlsson B, Norstrom A, Friberg LG. Endometrial thickness as measurement by endometrial ultrasonography for identifying endometrial abnormality. *Am J Obstet Gynaecol* 1991;**164**:47-52. [http://dx.doi.org/10.1016/0002-9378\(91\)90622-X](http://dx.doi.org/10.1016/0002-9378(91)90622-X)
  19. Spandorfer SD, Arrendondo-Soberon F, Loret de Mola JR, Feringbang RF. Reliability of intraobserver and intraobserver sonographic endometrial stripe thickness measurements. *Fertil Steril* 1998;**70**:152-4.
  20. Deanna E Telner, Difat Jakubovicz. Approach to diagnose and management of abnormal uterine bleeding.
  21. Debdas AK, Bahol A. Histological profile of diagnostic endometrial curettage and its significance. *J of the Indian Med Assoc* 1984;**82**:309-12.
  22. Mahmood MF. Irregular uterine bleeding over the age of (40) years 1988.
  23. Bhosle A, Fonseca M, Evaluation and histopathological correlation of abnormal uterine bleeding in perimenopausal women, *Bombay Hospital Journal*, 2010;**52**(1):69-72.
  24. Ken Tamai, Kaori Togashi. Department of Radiology, National Hospital Organization Kyoto Medical Center, Kyoto, Japan (K. Tamai, T.I)
-