

Original Research Article

Histopathological Analysis of Abnormal Uterine Bleeding in Perimenopausal Women

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Abstract

Introduction: Atypical uterine bleeding (AUB) is the most common and frequent presenting complaint in gynaecology outpatient department in all age groups, especially in perimenopausal women accounting for more than 70%.

Methods: Prospective analytical study conducted from January 2017 to December 2017 in perimenopausal women (45-55 years). Other age groups with AUB, isolated cervical or vaginal pathology, leiomyoma of other types, bleeding diathesis, medications associated with AUB and pregnancy related causes of bleeding were excluded. Endometrial tissue collected by dilatation and curettage (D&C), endometrial biopsy and hysterectomy specimens subjected to histopathological examination were analysed.

Results: Total 150 specimens were analysed in which 83 were endometrial samples and 67 were hysterectomy specimens. Majority were multiparous women 45-50 years presented with heavy menstrual bleeding and showed proliferative endometrium as the predominant pattern (30%). Other endometrial patterns were simple hyperplasia without atypia (23.33%), complex hyperplasia without atypia (4%), secretory endometrium (15.33%), disordered proliferative endometrium (3.33%), irregular ripening (7.33%), irregular shedding (2%), atrophic (5.33%), endometritis (1.33%), endometrial polyp (4%) and carcinoma endometrium in 2% cases. Hysterectomy specimens revealed 51 cases of combined endometrial and myometrial pathologies. Myometrial pathologies included submucosal leiomyoma -44.77% and adenomyosis -31.34% as the causes of AUB.

Conclusion: AUB is one of the commonest reasons for women to seek medical help in all age groups, especially in perimenopausal age. Gynaecologists should pay attention towards these abnormal bleeding patterns along with the evaluation of endometrial tissue for histopathological findings which showed wide variety of abnormalities.

Keywords: Atypical Uterine Bleeding (AUB); Endometrium; Perimenopause.

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Introduction

Normal menstruation is defined as bleeding from secretory endometrium associated with ovulatory cycle and lasting for 5-7 days. The term Abnormal uterine bleeding (AUB) has been used to describe any bleeding not fulfilling the criteria of normal menstrual bleeding. It is defined as duration less than 2 or greater than 7 days, flow

greater than 80ml (or subjective impression of heavier than normal flow), cycle length less than 24 or greater than 35 days [1]. AUB in women of reproductive age is a manifestation of any number of disorders or pathologic entities².

It includes both organic and non organic causes of uterine bleeding [3]. It is the most common and frequent

presenting complaint in gynaecology outpatient department in all age groups, especially in perimenopausal women [4].

Perimenopause is defined as the period around the onset of menopause that is often marked by various physical signs such as hot flushes and menstrual irregularities. Perimenopause is the coming off from the reproductive years. Although the median age of menopause in North America is 51 years, the perimenopause is often highly variable in its age of onset, duration and bleeding patterns [5].

One-third of patient visits to the gynecologist are for AUB and it accounts for more than 70% of all gynecological consults in the perimenopausal and postmenopausal years. A thorough evaluation of patients is important for two main reasons: (1) to exclude serious pathology such as carcinoma or complex atypical hyperplasia, and (2) to identify the cause of bleeding so that proper therapy (which, in some cases, may be expectant management) can be embarked upon [5]. Although many women may be unsure of how often or how long they bleed, a careful history of bleeding patterns, frequency and heaviness is critical and will often assist with diagnosis. For instance, cyclic heavy menstrual bleeding without intermenstrual bleeding be unlikely to be carcinoma or even hyperplasia. The commonest cause of irregular bleeding is anovulatory uterine bleeding. Most often, anovulatory bleeding is not associated with anatomical abnormalities. One study of 443 women used transvaginal ultrasound and saline infusion sonohysterography (SIS) as the first step in triage and reported that 79% of women between 35 years old and menopause with AUB had no anatomic pathology [6]. Some women with AUB may have an enlarged cavity with increased surface area due to increasing parity, uterine hypertrophy secondary to leiomyoma with no submucosal component, or adenomyosis without endometrial abnormality [5]. A classification of causes of AUB is shown in Table 1 [2].

Further definitions of terminologies of AUB may be subdivided based on volume of menstruation, regularity, frequency, duration, chronicity and timing related to reproductive status. Table 2 provides the terminology and descriptions consistent with the FIGO Menstrual Disorders Working Group consensus statement [7,8].

Methods

The present study was a prospective analytical study conducted at Khaja Banda Nawaz Institute of Medical Sciences, Gulbarga in department of pathology from January 2017 to December 2017. Perimenopausal women in age group 45-55 years were included. Other age groups with abnormal uterine bleeding, isolated cervical or

vaginal pathology, leiomyoma of other types i.e, from type 3 to 8², bleeding diathesis, women on medications that can be associated with AUB (anticoagulants, antidepressants, hormonal contraceptives, tamoxifen, antipsychotics) and pregnancy related causes of bleeding were excluded from this study. After obtaining informed consent, detailed history was taken from all study participants such as age, parity, menstrual symptoms, detailed history regarding amount, duration and pattern of bleeding, use of exogenous hormones and other associated gynaecological problems were noted. Thorough physical and systemic examination was done; baseline investigations and pelvic ultrasound were done. Appropriate and relevant investigations were offered to all study participants. Endometrial tissue collected by sampling procedures such as dilatation and curettage (D&C), endometrial biopsy and hysterectomy specimens subjected to histopathological examination were analysed. All specimens were transported in 10% formalin to the pathology laboratory. The gross architecture was recorded with total submission of endometrial samples and representative bits were taken from the hysterectomy specimens. After fixation in 10% formalin for 12-24 hours, tissues were processed and embedded in paraffin. 3-4 μ sections were made, stained with haematoxylin and eosin stain. Microscopic examination was done by two pathologist.

Results

A total of 150 specimens were received in which 83 (55.33%) were endometrial samples – both endometrial biopsy and dilatation & curettage specimens, 67 (44.67%) were hysterectomy specimens. Of these 118 (78.67%) were in the age group of 45-50 years and 32 (21.33%) in 50-55 years. AUB was more commonly seen in multiparous women, 47.34% were para 2, 26.66% were para 3 and least common in nulligravida 2.66% only (Table 3).

Most commonest bleeding pattern had presented with history of heavy menstrual bleeding 62 (41.34%) followed by frequent menstrual bleeding 38(25.34%) and inter menstrual bleeding was the least common pattern seen in 4 (2.66%) cases only (Table 4).

Of the 67 hysterectomy specimens only 16 had isolated endometrial pathology and 51 had both endometrial and myometrial pathology. Myometrial pathology included 21 cases of pure adenomyosis , 30 cases of leiomyoma of submucosal types² in which 5 cases showed adenomyosis also. Leiomyoma of submucosal types² – type 0 (pedunculated intracavitary) – 7 cases, type 1 (<50% intramural)- 16 cases, type 2 (\geq 50% intramural)- 7 cases. Leiomyoma of other types² – type 3 (100% intramural, contacts endometrium), type 4 (intramural), type 5 (subserosal \geq 50% intramural), type 6 (subserosal<50%

Table 1: PALM-COEN classification of AUB²

Structural causes	Non-structural causes
Polyps	Coagulopathy
Adenomyosis	Ovulatory dysfunction
Lieomyomas - Submucosal	Endometrial
Others	Iatrogenic
Malignancy and Hyperplasia	Not yet specified

Table 2: Terminologies and definitions of terms of AUB^{7,8}

Characteristic	Terminology	Description
Volume	Heavy menstrual bleeding	Excessive menstrual blood loss which interferes with the woman’s physical, emotional, social and material quality of life and which can occur alone or in combination with other symptoms.
Regularity (Normal variation ± 2 to 20 days)	Irregular menstrual bleeding.	A range of varying lengths of bleeding free intervals exceeding 20 days within one 90 day reference period.
	Absent menstrual bleeding (amenorrhea)	No bleeding in a 90 day period.
Frequency (Normal every 24 to 38 days)	Infrequent menstrual bleeding.	Bleeding at intervals >38 days apart.
	Frequent menstrual bleeding.	Bleeding at intervals <24 days apart.
Duration (Normal 3 to 8 days)	Prolonged menstrual bleeding	Menstrual bleeding which exceeds 8 days in duration
Irregular, Non menstrual bleeding	Intermenstrual bleeding	Irregular episodes of bleeding, often light and short occurring in between normal cycles.
Acute or chronic AUB	Acute AUB.	An episode of bleeding in a woman of reproductive age, who is not pregnant, that is of sufficient quantity to require immediate intervention to prevent further blood loss.
	Chronic AUB.	Bleeding that is snot normal in duration, volume and frequency and is present for more than 6 months.

Table 3: Age and Parity of patients with AUB

Parity	Age- 45-50 years n*=118 (78.67%)	Age- 50-55 years n*=32(21.33%)	Number of cases (%) n*=150(100%)
Nulligravida	4	0	04 (2.66%)
Para 1	11	8	19 (12.66%)
Para 2	60	11	71 (47.34%)
Para 3	31	9	40 (26.66%)
Para 4	8	3	11 (7.34%)
Para 5	4	1	05 (3.34%)

*n= Number of cases.

Table 4: Bleeding patterns in AUB

Bleeding pattern	Number of cases (%)
Heavy menstrual bleeding	62 (41.34%)
Irregular menstrual bleeding	16 (10.66%)
Frequent menstrual bleeding	38 (25.34%)
Prolonged menstrual bleeding	30 (20%)
Inter menstrual bleeding	4 (2.66%)

Table 5: Endometrial patterns in AUB

Endometrial pattern	Endometrial samples (D&C and endometrial biopsy)	Hysterectomy specimens	Number of cases(%)
Proliferative phase	18	27	45 (30%)
Secretory phase	9	14	23 (15.33%)
Disordered proliferative	4	1	5 (3.33%)
Irregular ripening	7	4	11 (7.33%)
Irregular shedding	2	1	3 (2%)
Atrophic	4	4	8 (5.33%)
Endometritis	1	1	2 (1.33%)
Simple hyperplasia without atypia	25	10	35 (23.33%)
Complex hyperplasia without atypia	6	-	6 (4%)
Endometrial polyp	2	4	6 (4%)
Carcinoma endometrium	2	1	3 (2%)
Inconclusive	3	-	3 (2%)
Total	83	67	150 (100%)

intramural), type 7 (subserosal pedunculated), type 8 (other eg. cervical, parasitic) were excluded. Endometrial examination revealed various patterns in AUB (Table 5) consisting of normal cyclic pattern showing proliferative phase 45 (30%) cases- most predominant pattern, secretory phase 23 (15.33%) cases. Simple hyperplasia without atypia was seen in 35 (23.33%), complex hyperplasia without atypia in 6 (4%) cases. Hyperplasia with atypia was not seen. Other patterns were disordered proliferative phase 5 (3.33%), irregular ripening 11 (7.33%), irregular shedding 3 (2%), atrophic 8 (5.33%), endometritis 2 (1.33%), endometrial polyp 6 (4%) and carcinoma endometrium in 3 (2%) cases. While 3 (2%) cases were considered inconclusive because of inadequate fixation in formalin.

Discussion

Evaluation of AUB in perimenopausal age is a crucial step, since excessive or prolonged bleeding may cause disruption of women's daily activities, provoke serious medical consequences or exacerbate anaemia and in a certain percentage of cases may eventually be life threatening if left untreated [9]. AUB is the commonest problem in the perimenopausal age with highest incidence in many studies like Sreelakshmi U et al. [4], Gopalan U et al. [10], Doraiswami S et al. [11], Damle RP et al. [12] and Muzaffar M et al. [13]. This might be due to the fact that as women approach menopause, menstrual cycles shorten and often become intermittent anovulatory due to decline in the number of ovarian follicles and fluctuation in the estradiol level [14].

In present study majority of the cases 118 (78.67%) were between 45-50 years age group comparable with the study of Sreelakshmi U et al. [4] which had 127 (94.07%). The prevalence of AUB increased with parity and a fewer cases were seen in grand multiparous group as their relative frequency has decreased in recent years due to small

family norm. The most common symptoms were heavy menstrual bleeding 41.34% followed by frequent menstrual bleeding 25.34%. In Sreelakshmi U et al. [4] and Gupta A et al. [15] study commonest symptoms were heavy menstrual bleeding 83.7% and 72% followed by heavy and frequent menstrual bleeding 26.6% and 13% respectively.

In present study, out of 67 hysterectomy specimens 51 showed both endometrial and myometrial pathology. In which 21 cases of adenomyosis and 30 cases (44.77%) of submucosal leiomyoma were seen. 25 specimens were pure submucosal types of leiomyomas and 5 specimens had both leiomyoma and adenomyosis. Study by Saraswathi D et al. [3] showed 185 (87.26%) cases out of 212 hysterectomy specimens showing both leiomyoma and endometrial pathology. More number of cases showing leiomyoma in their study might be due to inclusion of all types of leiomyomas while our study included only submucosal types. While Juhi S et al. [16] showed 50 (25.64%) cases of leiomyoma and 19 (9.75%) cases of adenomyosis.

Among the endometrial patterns of AUB in perimenopausal group, Proliferative phase (30%) was the most predominant pattern followed by simple hyperplasia without atypia (23.33%). Proliferative endometrium was the predominant pattern in study by Sreelakshmi U et al. [4] (30.3%), Damle RP et al. [12] (35.09%). While, higher incidence was found in Khan S et al. [17] (46.6%) and Sheetal et al. [18] (42%). Endometrial hyperplasia (both simple and complex hyperplasia with or without atypia) comprised 25.54%, 18.5% and 36.2% in studies by Juhi S et al. [16], Sreelakshmi U [4] and Khare et al. [19]. While Doraiswami S et al. [3] showed higher incidence (68%).

Secretory endometrium was observed in 15.33% of cases in this study while Sreelakshmi U et al. [4] and Jain M [20] had slightly higher incidence as 27.4% and 28.9% respectively. But lowest incidence was reported by Damle

RP [12] (7.95%) and Juhi S et al. [16] (8.03%). Disordered proliferative endometrium was seen in 3.33% cases in the present study while Sreelakshmi U et al. [4] and Hoxhaj [21] observed 6.6% and 12.2% cases. Atrophic endometrium was observed in 5.33% cases in the present study while Sreelakshmi U et al. [4] observed 3.7% cases only. Chronic endometritis in the present study was found in 1.33% cases comparable with the study by Sreelakshmi U et al. [4] which showed 0.7% cases only, while it was seen with a higher incidence in a study by Damle RP et al. [12] (5.68%), Jain M [20] (6.1%) and Khare et al. [19] (6.4%). Endometrial polyp was found in 4% cases in present study while lower incidence was found by Gopalan U [10] (1.1%), Muzaffar M et al. [13] (1.2%) and Khan S et al. [17] (0.6%). Devi J [22] reported higher incidence of polyps (9.65%) in its study. Endometrial carcinoma was reported in 2% cases in present study which is similar to the studies by Devi J [22] (2.63%) and Khan S [17] (2%).

Conclusion

Abnormal uterine bleeding is one of the commonest reasons for women to seek medical help in all age groups, especially in perimenopausal age. Abnormal uterine bleeding with different menstrual patterns has significant effect on women's health and quality of life. The present study revealed heavy menstrual bleeding as the most commonest bleeding pattern in perimenopausal age with highest prevalence between the ages of 45-50 years. Heavy menstrual bleeding and frequent menstrual bleeding were mostly correlated with abnormal endometrial histopathological findings in this study. Cyclic proliferative endometrium followed by simple hyperplasia without atypia were the commonest endometrial patterns observed. Gynaecologists should pay attention towards these abnormal bleeding patterns along with the evaluation of endometrial tissue for histopathological findings which showed wide variety of abnormalities. Also submucosal type of leiomyoma and adenomyosis are the myometrial pathologies contributing for AUB.

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