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Original Research Article

Histopathological evaluation of endometrial sampling in perimenopausal women with abnormal uterine bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is one of the common symptoms in the gynaecology outpatient department. About one third of women are affected at some time in their lives. The perimenopausal women show significant number of underlying organic pathology. The evaluation of endometrium and/or organ histopathology has the dual advantage of finding the cause of AUB and to rule out endometrial cancer or the potential for cancer in future like endometrial hyperplasia with atypia. The aim of the study was to determine the histopathological pattern of endometrial sampling in perimenopausal women with AUB and to follow them up for a period of six months after the procedure.

Methods: The prospective observational study was conducted at the department of obstetrics and gynaecology at Sree Gokulam Medical College and Research Foundation, Venjaramood, Thiruvananthapuram, Kerala, for a period of one year from December 2019 to December 2020. The study was conducted on 116 perimenopausal women 41-52 years who presented with AUB and had undergone endometrial sampling. These ladies were subsequently followed up for six months post procedure to assess the response to medical treatment or the need for any surgical intervention like hysterectomy.

Results: A total 39.65% patients had heavy and prolonged menstrual bleeding and 18.16% patients had irregular bleeding. 14.65% patients had prolonged flow, 8.6% had heavy flow, 6.8% had infrequent with prolonged flow, 6% had prolonged, infrequent with heavy bleeding. Non-structural (COEIN) causes contributed to about 60.4% of AUB in perimenopausal women and 39.6% had structural (PALM) causes. 49% cases were secretory endometrium. 29.3% had disordered proliferative endometrium, 4.3% had proliferative endometrium, 5.2% each had polyp or hyperplasia without atypia. 18 (15.5%) cases underwent hysterectomy, 3 patients who had adenocarcinoma underwent staging laparotomy, 2 patients had LNG IUS insertion and 40 patients were on follow up requiring either no treatment and 53 (45.68%) patients were given antifibrinolytics or hormonal therapy.

Conclusions: Heavy and prolonged menstrual bleeding was the most common presenting symptom. COEIN contributed to about 60.4% of cases. Evaluation of the endometrium showed that, secretory endometrium was commonest (49%) followed by disordered proliferative endometrium (29.3%). On follow up for six months, 15.5% patients underwent hysterectomy, 2 patients had insertion of levonorgestrel IUD, 45.68% patients had medical management with antifibrinolytics or hormones and were on follow up. The responsibility of gynaecologist in the management of AUB in perimenopausal women is to exclude hyperplasia of endometrium and endometrial cancer.

Keywords: Perimenopausal AUB, Endometrial sampling, palm-coein

INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the common

symptoms in the gynaecology outpatient department. About one third of women are affected at sometime in their lives. It is estimated that approximately 30% of women

complain of menorrhagia. Excessive bleeding is the main presenting complaint in women referred to gynecologist and it accounts for 2/3rd of all hysterectomies.^{1,2}

Chronic non-gestational AUB in the reproductive years is defined as bleeding from uterine corpus that is abnormal in regularity, volume, frequency or duration and has been present for the majority of the preceding 6 months. Acute AUB is defined as an episode of heavy bleeding that, in the opinion of the clinician, is of sufficient quantity to require immediate intervention to minimise or prevent further blood loss.³

In the revised International Federation of Gynaecology and Obstetrics-Abnormal Uterine Bleeding (FIGO-AUB) system 1 in 2018, terms such as menorrhagia, metrorrhagia, oligomenorrhoea and dysfunctional uterine bleeding has been removed.

Definitions of the AUB symptoms are given in the Table 1.³ Heavy menstrual bleeding is defined by National Institute of Clinical Excellence as excessive menstrual blood loss, which interferes with a woman's physical, social, emotional and/or material quality of life.⁴

Table 1: FIGO AUB system-1 nomenclature and definitions of AUB symptoms.

Parameters	Normal	Abnormal
Frequency	>24-≤38 days	Frequent (<24 days)
		Infrequent (>38 days)
		Absent= amenorrhea
Duration	≤8 days	Prolonged (>8 days)
Regularity	Regular (shortest to longest cycle variation: ≤7-9 days)	Irregular (shortest to longest cycle variation ≥8-10 days)
Flow volume	Normal	Light Heavy
Intermenstrual bleeding	None	Random Cyclic-early cycle Mid cycle Late cycle
Unscheduled bleeding on progestin ± oestrogen gonadal steroids (birth control pills, rings, patches or injections)	Not applicable (not on gonadal steroid medication)	Present
	None (on gonadal steroid medication)	

FIGO working group on menstrual disorders has developed classification system (PALM COEIN) for causes of AUB in non-gravid women in 2011 and was revised in 2018. The acronym PALM COEIN facilitates classification, with PALM referring to structural etiologies that can be imaged and/or defined histopathologically (polyp, adenomyosis, leiomyoma, malignancy or atypical endometrial hyperplasia), and COEIN referring to non-structural etiologies that cannot be imaged, but clinical assessment with detailed history and appropriate physical examination, sometimes supported by laboratory testing, can largely imply or make a diagnosis of cause (coagulopathy, ovulatory disorders, primary endometrial disorders, iatrogenic, not otherwise classified).³

Perimenopause is defined as period of two to eight years preceding menopause and one year after the final menses.⁵ Follicular development at this period is found to be erratic with increased percentage of anovulatory cycles.⁶

The perimenopausal women show significant number of underlying organic pathology. The responsibility of gynaecologist in the management of AUB in perimenopausal women is to exclude hyperplasia of endometrium and endometrial cancer. The evaluation of endometrium and/or organ histopathology has the dual

advantage of finding the cause of AUB and to rule out endometrial cancer or the potential for cancer in future like endometrial hyperplasia with atypia.

Transvaginal ultrasonography (TVUS) is an appropriate and important screening tool and, in most instances, should be performed early in the course of the investigations.³ Transvaginal ultrasound is 80% sensitive and 69% specific for identifying submucous myomas and is superior to trans-abdominal ultrasound, 96% sensitivity and 86% specificity in diagnosis of intrauterine abnormality.⁷

FIGO recommends endometrial sampling as the first line management of perimenopausal women with AUB. Although some studies have indicated that age is not important as an independent variable, most suggest that endometrial sampling be considered for all women over a certain age, usually 45 years.^{8,9} Regardless of the clinical guideline, when AUB is persistent and either unexplained or inadequately treated, endometrial sampling is necessary- if possible- in association with hysteroscopic evaluation of the uterine cavity.⁴

Histology contributes to better understanding of mechanism of action that initiate, regulate and lead to AUB. Better insights may trigger the development of therapeutic procedures that would either prevent or control

vascular breakdown which results in unexpected uterine bleeding.²

A blind Dilatation and Curettage (D and C) is a procedure for all women with AUB in >40 years age group. In 10-25% of patients D and C may miss an existing endometrial pathology. Office endometrial biopsy results in adequate samples 87-97% time, and detects 67-96% of endometrial carcinomas.¹⁰

Hysteroscopy allows direct visualization of the endometrial cavity and is combined with endometrial biopsy. Saline sonohysterogram involves introducing 5-15 ml of saline solution into the uterine cavity followed by transvaginal ultrasound scan that might help diagnose an intrauterine mass.¹¹

The aim of the study was to determine the histopathological pattern of endometrial biopsies in perimenopausal women with AUB in a tertiary care hospital in Kerala and to evaluate their treatment outcomes.

Aim and objectives

The aim of the study were (a) to determine the histopathological pattern of endometrial currettings and/or endometrial biopsies in perimenopausal women with AUB; and (b) to evaluate their treatment outcomes.

METHODS

The prospective observational study was conducted at the department of obstetrics and gynaecology at Sree Gokulam Medical College and Research Foundation, Venjaramood, Trivandrum, Kerala for a period of one year from December 2019 to December 2020.

The study was conducted on 116 perimenopausal women 41-52 years who presented with AUB and had undergone endometrial sampling with either D and C or outpatient endometrial biopsy with EZE curette.

These ladies were subsequently followed up for six months post procedure to assess the response to medical treatment or need for any surgical intervention like hysterectomy.

Criteria

Patients with AUB between 41 to 52 years who presented to obstetrics and gynecology OPD were included in our study. Patients with inadequate sample were excluded.

RESULTS

A total of 116 perimenopausal women underwent D and C or endometrial biopsy in this study period and samples were submitted for histopathological examination.

From the Table 2 it was seen that about 39.65% patients

had heavy and prolonged menstrual bleeding and 18.16% patients had irregular bleeding. 14.65% patients had prolonged flow, 8.6% had heavy flow, 6.8% had infrequent with prolonged flow, 6% had prolonged, infrequent with heavy bleeding.

From the Table 3 it was seen that non-structural causes contributed to about 60.4% of AUB in perimenopausal women and 39.6% had structural causes.

From the Table 4 it was seen that 49% cases were secretory endometrium. 29.31% had disordered proliferative endometrium, 4.3% had proliferative endometrium, 5.2% each had polyp or hyperplasia without atypia, 2.58% each had well differentiated adenocarcinoma or atrophic endometrium.

From Table 5, it was seen that 18 (15.5%) cases underwent hysterectomy, 3 patients who had adenocarcinoma underwent staging laparotomy, 2 patients had LNG IUS (Levonorgestrel intrauterine system) insertion and 93 patients were on follow up with no treatment (40 patients) or given antifibrinolytics or hormonal therapy (53 patients).

Of the 18 hysterectomies, 6 patients had endometrial hyperplasia without atypia and opted for hysterectomy, 8 patients had failed medical therapy and 4 patients had associated leiomyoma.

Table 2: Patterns of menstrual bleeding.

Patterns of bleeding	Number of patients	Percentage (%)
Frequent bleeding (<24 days cycle)	4	3.5
Infrequent bleeding (>38 days)	2	1.72
Prolonged flow (>8 days)	17	14.65
Irregular bleeding	22	18.16
Heavy flow	10	8.62
Infrequent + prolonged bleeding	8	6.89
Infrequent + prolonged + heavy flow	7	6.03
Heavy + prolonged flow	46	39.65
Total	116	100

Table 3: Structural and non-structural causes.

Etiology of AUB	Number of patients	Percentage (%)
Structural causes (PALM)	46	39.6
Non-structural causes (COEIN)	70	60.4
Total	116	100

Table 4: Histopathological patterns of endometrium.

Histological patterns	Number of patients	Percentage (%)
Secretory endometrium	57	49
Disordered proliferative endometrium	34	29.31
Proliferative endometrium	5	4.31
Polyp	6	5.2
Atrophic	3	2.58
Well differentiated adeno carcinoma	3	2.58
Decidualised	2	1.72
Hyperplasia without atypia	6	5.2
Total	116	100

Table 5: Management outcomes.

Management outcomes	Number of patients	Percentage (%)
Hysterectomy	18	15.5
Staging laparotomy	3	2.5
LNG IUS	2	1.8
Medical management	53	45.68
No treatment	40	34.48
Total	116	100

DISCUSSION

Evaluation of AUB in perimenopausal age is an important step since excessive or continuous bleeding may severely compromise the quality of woman's life and daily activities leading to anaemia if left untreated. AUB may be the reflection of serious underlying pathologies. In perimenopausal women, AUB presents in different menstrual patterns like heavy menstrual bleeding, frequent menstrual cycles, intermenstrual bleeding and amenorrhea followed by continuous heavy bleeding.

In the present study 116 patients with AUB from 41-52 years were included and these women were subjected to either dilatation and curettage or office endometrial aspiration with Eze curette. These patients were followed up for six months post procedure.

D and C is a useful and cost-effective method of detecting intrauterine lesions. It is a diagnostic as well as a therapeutic procedure. The sensitivity of endometrial aspiration for detection of endometrial abnormalities has been reported to be as high as 96% with 2-6% false negative rates. Hysteroscopy guided biopsy is the gold standard method for screening as well as diagnostic purposes.¹² In this present study most of the women (39.6%) presented with heavy menstrual bleeding (HMB) followed by irregular bleeding (18.16%). In the study by

Kalambe et al 48.4% patients had HMB ,35.83% patients had irregular bleeding.¹³ In Gupta et al study, commonest symptoms were heavy menstrual bleeding (72%) followed by heavy and frequent bleeding.¹⁴ Sreelekshmi et al reported 83.7% heavy menstrual bleeding, frequent menstrual bleeding (26.6%) and intermenstrual bleeding (4%).¹² In the study done by Archana Singh et al, HMB contributed to 67.58% of cases.¹⁵ In all these studies and our study, HMB (heavy + prolonged menstrual flow) contributed to the highest percentage of cases.

In our study PALM structural causes contributed to 39.6% cases and COEIN functional causes 60.4% cases. In Tukaram et al study functional causes contributed to 41 (55%) of cases and organic lesions contributed to 33 (45%) of cases.¹⁶ In the study conducted by Singh et al PALM and COEIN accounted for 60% and 39.9% respectively unlike our study.¹⁵ In the study conducted by Kalambe et al PALM contributed to 57.5% and COEIN to 42.5% cases.¹³

The present study showed secretory endometrium in 49% of cases followed by disordered proliferative endometrium in 29.31%, polyp and non-atypical endometrial hyperplasia in 5.17%, proliferative endometrium 4.31%. In Sreelakshmi et al study proliferative endometrium contributed to 30.3%, secretory endometrium was 27.4% and disordered proliferative endometrium 6.6%.¹² In the study by Vani et al 30.3% cases were proliferative endometrium, 25.97% were secretory endometrium and 5.62% were disordered proliferative endometrium.¹⁷

Disordered proliferative endometrium

Abnormal proliferative endometrium with architectural changes due to persistent unopposed estrogen stimulation. Generally taken as benign, not precancerous. It is the continuum of the spectrum of changes seen with persistent, unopposed estrogen stimulation, which can lead to hyperplasia without atypia. There is presence of irregularly shaped or cystic dilated glands with relatively normal gland to stroma ratio. Common in patients with polycystic ovary syndrome, obesity and perimenopausal women and is associated with anovulation. It may be asymptomatic or presents with abnormal uterine bleeding. It is diagnosed with endometrial biopsy or curettage. Ultrasound may show irregularly thickened endometrium. Treatment is observation or progesterone if symptomatic AUB or elimination of the cause of estrogen excess (eg: weight loss in obesity). Endometrial hyperplasia without atypia is a continuum with disordered proliferative endometrium. Here, the gland to stroma ratio is >1 .¹⁸

Endometrial hyperplasia (EH)

Proliferation of endometrial glands with resulting increase in gland to stroma ratio. Current classification system includes: hyperplasia without atypia and atypical hyperplasia/endometrial intraepithelial neoplasia (AH/EIN). AH/EIN is considered a premalignant condition. It has increased risk of both progression to and

simultaneous endometrial endometrioid adenocarcinoma. Endometrial hyperplasia occurs due to unopposed estrogen. Treatment of EH without atypia includes progestin therapy oral or intrauterine device. Hysterectomy is an aggressive management as risk of progression to adenocarcinoma is low. Definitive treatment of AH includes hysterectomy with or without bilateral salpingo-oophorectomy. If patient desires fertility oral progestin can be given.¹⁹

In our study, 18 (15.5%) patients underwent hysterectomy, 45.68% (53) patients took medical management, 2 patients had LNG IUCD insertion. In the study by Sreelakshmi et al 69.6% underwent hysterectomy.

CONCLUSION

In our study, 116 perimenopausal women with AUB 41-52 years underwent endometrial sampling. Heavy menstrual bleeding was the most common presenting symptom. The functional cause COEIN contributed to about 60% of cases. On evaluating the endometrium, secretory endometrium was commonest (49%) followed by disordered proliferative endometrium (29.3%). On follow up for six months, 15.5% patients underwent hysterectomy, 2 patients had insertion of levonorgestrel IUD, 45.68% patients had medical management with antifibrinolytics or hormones and is on follow up. The responsibility of gynaecologist in the management of AUB in perimenopausal women is to exclude hyperplasia of endometrium and endometrial cancer.

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