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Research Article

A study on correlation between bleeding pattern and histopathological findings of endometrium among perimenopausal women

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ABSTRACT

Background: During climacteric, ovarian activity declines. Initially, ovulation fails, no corpus luteum forms, and no progesterone are secreted by the ovary. Therefore the premenopausal menstrual cycles are shortened, often anovulatory and irregular. The irregularity in menstrual cycle during perimenopause can be due to anovulation or to irregular maturation of follicles.

Methods: The endometrial samples (endometrial curettage/ biopsy and hysterectomy specimens) sent to pathology laboratory were analyzed. These specimens are fixed in 10% formalin and gross morphology was recorded. Endometrial samples were totally embedded and representative bits are taken from hysterectomy specimens. These bits were placed in cassettes and kept in fixative and processed in the automatic tissue processor. Paraffin tissue blocks were prepared and 3-4 micrometer thick sections were cut and stained with routine haematoxylin and eosin. A detailed histological study was carried out and the findings were noted.

Results: Among total study subjects, 62% of patient's endometrium was in proliferative phase, 26% of patient's endometrium was in secretory phase, 6% of patient's endometrium was in cystoglandular hyperplasia. Dysplasia with atypical changes was found in 2% of patients. Adenomatous polyp was found in 2% of patients. Simple hyperplasia was found in 2% of patients.

Conclusions: Patients with abnormal uterine bleeding should always be subjected to histopathological investigation.

Keywords: Abnormal uterine bleeding, Perimenopausal, Histopathological examination

INTRODUCTION

The endometrium is uniquely endowed throughout the female reproductive lifespan with complex regular cycle of periodic proliferation, differentiation, breakdown and regeneration.¹ Menstruation is the cyclic uterine bleeding experienced by almost all women of reproductive age.

Normal menstruation is defined as "the bleeding from secretory endometrium associated with an ovulatory cycle, not exceeding a length of five days". Any bleeding not fulfilling these criteria is referred to as abnormal uterine bleeding.² Abnormal uterine bleeding is a very common gynecological condition that affects all age

groups. One third of patients attending gynaecology OPD present with complaints of abnormal uterine bleeding.³ Bleeding is said to be abnormal when the pattern is irregular, abnormal duration (>7 days), or menorrhagia or abnormal amount (>80 ml/menses).⁴

During climacteric, ovarian activity declines. Initially, ovulation fails, no corpus luteum forms, and no progesterone are secreted by the ovary. Therefore the premenopausal menstrual cycles are shortened, often anovulatory and irregular. The irregularity in menstrual cycle during perimenopause can be due to anovulation or to irregular maturation of follicles.⁵ The increased risk of endometrial hyperplasia and endometrial carcinoma is

more evident in peri-menopausal and post-menopausal women with abnormal uterine bleeding.⁶ The varied pattern of endometrial changes attracted our attention in peri-menopausal and post-menopausal age so to study them in detail with the help of available clinical data.

The endometrial sampling is chosen to evaluate abnormal uterine bleeding because it has several advantages over other diagnostic methods. The hormonal assay is very expensive and laboratories with hormonal assay are not available in rural areas.

Ultrasonography clearly depicts the uterine contour and the status of the ovary, but fails to provide adequate information regarding the endometrium, except in atrophy and hyperplasia. Other investigations like hysteroscopy and hysterosalpingography are mainly helpful in diagnosing organic pathology.⁷ Endometrial curettage is relatively inexpensive and accurate as an outpatient procedure. The only disadvantage of endometrial biopsy is that, it is an invasive procedure.

An understanding of the varieties in the normal morphological appearance of the endometrium provides an essential background for the evaluation of endometrial pathology.

METHODS

The study population consisted of patients in the perimenopausal age group (45±5 years) presenting with abnormal uterine bleeding.

Sample size

All patients in the perimenopausal age group (45±5 years) with symptoms of abnormal uterine bleeding presenting at department of OBG, Tertiary care centre during the study period were included in the study

Sample size is based on level of precision; precision consists of significance level and allowable error. In this study 5% significance and 20% allowable error is considered. Totally 50 study subjects were included in the study as this number of patients attended hospital during the study period

Method of sampling

No sampling method adopted as all the study subject fitting to inclusion criteria were considered

Method of collection of data

Study tool

Pre tested semi structured Questionnaire. The Questionnaire was presented in the Department for critical review, following which necessary changes were made in the Questionnaire.

Data was collected using Pre tested semi structured Questionnaire which was filed by the investigator. The endometrial samples (endometrial curettage/ biopsy and hysterectomy specimens) sent to pathology laboratory were analysed.

These specimens are fixed in 10% formalin and gross morphology was recorded. Endometrial samples were hysterectomy specimens. These bits were placed in cassettes and kept in fixative and processed in the totally embedded and representative bits are taken from automatic tissue processor.

Paraffin tissue blocks were prepared and 3-4 micrometre thick sections were cut and stained with routine haematoxylin and eosin. A detailed histological study was carried out and the findings were noted. Statistical analysis was done.

Statistical tests used

1. Proportion
2. Mean
3. Standard deviation
4. Chi square test

Data entry and analysis

Using Micro soft excel and Statistical package for social sciences

Ethical consideration

The protocol designed for the present study was submitted to the Ethical committee, after getting clearance from Research committee. Verbal consent was also taken and Confidentiality of the data is maintained.

RESULTS

Table 1: Distribution based on findings on histopathological examination.

HPE findings	Frequency	%
Proliferative phase	31	62.0
Secretory phase	13	26.0
Cystoglandular hyperplasia	03	06.0
Dysplasia with atypical changes	01	02.0
Adenomatous polyp	01	02.0
Simple hyperplasia	01	02.0
Total	50	100.0

Among total study subjects, 62% of patient's endometrium was in proliferative phase, 26% of patient's endometrium was in secretory phase, 6% of patient's endometrium was in Cystoglandular hyperplasia. Dysplasia with atypical changes was found in 2% of patients, adenomatous polyp was found in 2% of patients, simple hyperplasia was found in 2% of patients.

Table 2: Relation between menorrhagia and findings on histopathological examination.

HPE findings	Menorrhagia		Total
	Yes	No	
Proliferative phase	21 (65.6%)	10 (55.5%)	31 (62%)
Secretory phase	09 (28.1%)	04 (22.2%)	13 (26%)
Cystoglandular hyperplasia	01 (03.1%)	02 (11.1%)	03 (06%)
Dysplasia with atypical changes	00	01 (05.5%)	01 (02%)
Adenomatous polyp	00	01 (05.5%)	01 (02%)
Simple hyperplasia	01 (03.1%)	00	01 (02%)
Total	32 (100%)	18 (100%)	50 (100%)

P value: 0.001

Among patients without history of menorrhagia, the more common endometrium finding was proliferative phase (55.5%) followed by secretory phases (22.2%). Cystoglandular hyperplasia was found in 11.1% of patients and adenomatous polyp was found in 5.5% of patients. This relation is found to be statistically significant.

Table 3: Relation between metrorrhagia and findings on histopathological examination.

HPE findings	Metrorrhagia		Total
	Yes	No	
Proliferative phase	05 (55.5%)	26 (63.4%)	31 (62%)
Secretory phase	03 (33.3%)	10 (24.3%)	13 (26%)
Cystoglandular hyperplasia	01 (11.1%)	02 (04.8%)	03 (06%)
Dysplasia with atypical changes	00	01 (02.4%)	01 (02%)
Adenomatous polyp	00	01 (02.4%)	01 (02%)
Simple hyperplasia	00	01 (02.4%)	01 (02%)
Total	09 (100%)	41 (100%)	50 (100%)

P value: 0.003

Proliferative phase was more commonly found in patients without h/o metrorrhagia (63.4%) compared to patients with h/o metrorrhagia (55.5%).

Secretory phase was more commonly found in patients with h/o metrorrhagia (33.3%) compared to patients without h/o metrorrhagia (24.3%).

Adenomatous polyp, simple hyperplasia and dysplasia were found in patients without h/o metrorrhagia. The relation between metrorrhagia and histopathological findings in this study is found to be statistically significant.

Table 4: Relation between menometrorrhagia and findings on histopathological examination.

HPE findings	Menometrorrhagia		Total
	Yes	No	
Proliferative phase	01 (25%)	30 (65.2%)	31 (62%)
Secretory phase	00	13 (28.2%)	13 (26%)
Cystoglandular hyperplasia	01 (25%)	02 (04.3%)	03 (06%)
Dysplasia with atypical changes	01 (25%)	00	01 (02%)
Adenomatous polyp	01 (25%)	00	01 (02%)
Simple hyperplasia	00	01 (02.2%)	01 (02%)
Total	04 (100%)	46 (100%)	50 (100%)

P value: 0.01

Table 5: Relation between polymenorrhoea and findings on histopathological examination.

HPE findings	Polymenorrhoea		Total
	Yes	No	
Proliferative phase	08 (57.1%)	23 (63.8%)	31 (62%)
Secretory phase	03 (21.4%)	10 (27.7%)	13 (26%)
Cystoglandular hyperplasia	01 (07.1%)	02 (05.5%)	03 (06%)
Dysplasia with atypical changes	00	01 (02.7%)	01 (02%)
Adenomatous polyp	01 (07.1%)	00	01 (02%)
Simple hyperplasia	01 (07.1%)	00	01 (02%)
Total	14 (100%)	36 (100%)	50 (100%)

P value: 0.01

Proliferative phase was more commonly found in patients without h/o menometrorrhagia (65.2%) compared to patients with h/o menometrorrhagia (25%).

Secretary phase was more commonly found in patients without h/o menometrorrhagia (28.2%) compared to patients without h/o menometrorrhagia (0%).

Adenomatous polyp and dysplasia were found in patients with h/o menometrorrhagia. The relation between menometrorrhagia and histopathological findings in this study is found to be statistically significant.

Proliferative phase was more commonly found in patients without h/o polymenorrhoea (63.8%) compared to patients with h/o polymenorrhoea (57.1%). Secretary phase was more commonly found in patients without h/o polymenorrhoea (27.7%) compared to patients without h/o polymenorrhoea (21.4%). Adenomatous polyp, Simple hyperplasia was found in patients with h/o polymenorrhoea. Dysplasia was found in patients without h/o polymenorrhoea. The relation between polymenorrhoea and histopathological findings in this study is found to be statistically significant.

Table 6: Relation between present cycles and findings on histopathological examination.

HPE findings	Present cycles		Total
	Regular	Irregular	
Proliferative phase	26 (68.4%)	05 (41.6%)	31 (62%)
Secretary phase	10 (26.3%)	03 (25.0%)	13 (26%)
Cystoglandular hyperplasia	01 (02.6%)	02 (16.6%)	03 (06%)
Dysplasia with atypical changes	00	01 (08.3%)	01 (02%)
Adenomatous polyp	00	01 (08.3%)	01 (02%)
Simple hyperplasia	01 (02.6%)	00	01 (02%)
Total	38 (100%)	12 (100%)	50 (100%)

P value: 0.34

Among patient with irregular cycles, 41.6% of patients were in proliferative phase, 25% were in secretary phase, 16.6% of patients had cystoglandular hyperplasia, and 8.3% of patients had adenomatous polyp and simple hyperplasia.

DISCUSSION

In the present study proliferative phase (35%) was found to be most common histologic pattern followed by secretary phase (26.5%), simple hyperplasia without atypia (24%), atrophic endometrium (3.5%), disordered proliferative (3%), mixed endometrium (3%), endometrial polyp (2%), endometrial adenocarcinoma (1%) and endometrial stromal sarcoma (0.5%). In the study done by Sadia Khan proliferative phase was most

common histological pattern followed by secretary phase, simple hyperplasia without atypia, complex hyperplasia without atypia, atrophic endometrium, endometrial polyp, endometritis and endometrial adenocarcinoma in that order.⁸

Table 7: Comparative study of incidence of disordered proliferative endometrium in AUB.

Authors	Year	Number	Percentage
Azim P ¹⁰	2011	128	5.4%
Mirza T ¹¹	2012	1000	23%
Bhatta S ¹²	2012	122	6.56%
Present study	2013	200	8%

Majority of the studies including the present study indicate that, the incidence of hyperplasia in AUB ranges from 19.4% to 31.25% whereas, a few other studies reported a higher incidence at 52% to 62% range while the lowest incidence 7% was reported by Sanyal.⁹

In the present study, the two important observations were made regarding endometrial hyperplasia in AUB and they are:

1. Endometrial hyperplasia was highest in the age group of 41-50 years.
2. It was highest in patients with history of heavy menstrual bleeding.

Mirza T noted maximum number of disordered proliferative endometrium accounting for the 23%. In the present study, the incidence of disordered proliferative endometrium was 8% which was close to the findings observed by Azim P.^{10,11}

CONCLUSION

There is positive correlation between presenting bleeding pattern and abnormal findings of endometrium in patients with abnormal uterine bleeding.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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