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A GAMUT OF HISTOPATHOLOGICAL PATTERNS OF ENDOMETRIUM IN ABNORMAL UTERINE BLEEDING IN PERIMENOPAUSAL AND POSTMENOPAUSAL WOMEN

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ABSTRACT **BACKGROUND -** Abnormal uterine bleeding is most common gynecological problem associated with considerable morbidity and significantly affects the patient's family, personal, and social life. The main aim of the study was to analyze the histopathological patterns of endometrium in patients presenting with AUB.

AIMS AND OBJECTIVES

1) To assess the relationship of abnormal uterine bleeding in perimenopausal and postmenopausal group with age and parity.
2) To study various bleeding pattern in AUB.
3) To study the various risk factors associated with endometrial carcinoma
4) Assessment of endometrial histopathology in non-structural causes of AUB as per latest FIGO PALM COEIN classification in perimenopausal and postmenopausal age groups.

RESULT: A total 116 cases were analyzed. Perimenopausal and post-menopausal patients were taken from age 41-65 years of age. AUB was most prevalent in the perimenopausal age group. The most common bleeding pattern was menorrhagia 49.38%. Most common histopathological pattern in perimenopausal women Proliferative, Disordered proliferative, Secretory, Endometrial Hyperplasia without atypia, Endometrial Hyperplasia with atypia, Benign endometrial polyp, Endometrial carcinoma were 45.68%, 13.58%, 19.75%, 13.58%, 2.47%, 3.70% and 1.23%, respectively and in post-menopausal women Atrophic endometrium, Hyperplasia without atypia, Hyperplasia with atypia, Proliferative, Benign endometrial polyp, Secretory, Endometrial carcinoma, and Disordered proliferative were 37.14%, 20.00%, 11.43%, 8.57%, 2.86%, 2.86%, 5.71%, and 11.43%, respectively.

CONCLUSION: Histopathological evaluation of endometrial sample is indicated in women with AUB to rule out malignancy and preneoplasia. Endometrial biopsy is a major diagnostic tool in evaluation of AUB and specific diagnosis could help in management of AUB.

KEYWORDS :

INTRODUCTION

Abnormal uterine bleeding is defined as "a bleeding pattern that differs in frequency, duration and amount from a bleeding pattern observed during a normal menstrual cycle or menopause."[1]

Majority of females with endometrial diseases present with abnormal uterine bleeding.[2,3] Abnormal uterine bleeding describes all abnormal patterns of bleeding that may result from a wide variety of causes including non-structural causes like ovulatory dysfunction, coagulopathies etc and structural causes like polyps, endometrial hyperplasia, chronic endometritis, leiomyomas etc. AUB itself is not a disease but it denotes underlying pathology responsible for it. AUB may be the only presenting complaint in patients with pre-malignant or malignant endometrial lesions.

CLASSIFICATION OF AUB

The **PALM COEIN classification system** has been recently approved as a **FIGO** system for etiological classification of AUB in 2011.

PALM- Visually defined structural causes
COEIN- Unrelated to any structural causes
P-Polyp (AUB-P)
A-Adenomyosis (AUB-A)
L-Leiomyomas (AUB-L)
M-Malignancy (AUB-M)
C-Coagulopathy (AUB-C)
O-Ovulatory disorders (AUB-O)
E-Endometrial (AUB-E)
I-Iatrogenic (AUB-I)
N- Not classified

Maximum number of patients presented with abnormal uterine bleeding have underlying uterine pathologies and ranked as the most common gynaecological disorders worldwide affecting perimenopausal and postmenopausal age groups[2]. It has negative impact on women's health and wellbeing including anaemia, absenteeism, social embarrassment, impacting their quality of life and imposing financial burden[4,5].

Endometrium is the most dynamic tissue which lines the uterine cavity and a tissue for histopathological study, it undergoes cyclical proliferation, differentiation and shedding in response to ovarian steroids.

Endometrium is the best accessible tissue for histopathological evaluation of abnormal uterine bleeding. Endometrial sampling can be done by several methods like endometrial biopsy, dilatation& curettage, hysteroscopy. Various pathologies can be detected by analysing histopathological changes in endometrium ranging from simple hormonal imbalance (disorderly proliferative endometrium, non-secretory endometrium with stromal and glandular breakdown, luteal phase defect and pill effect) atrophic endometrium, endometritis, polyp, endometrial hyperplasia andcarcinoma.

Senstivity of endometrial biopsy for detection of endometrial pathology has been reported to be as high as 96%[6,7]. It is very useful tool for assessing patients of abnormal uterine bleeding mostly in developing countries with limited resources. Endometrial carcinoma is currently the most common gynaecological malignancy in developed countries. It has incidence of 7 new cases per 100000 women per year [8] Adenocarcinoma of endometrium is often preceded by proliferative precursor lesions "endometrial hyperplasia ".Thus early accurate diagnosis and proper treatment of endometrial hyperplastic lesions are essential to prevent progression to endometrial carcinoma and preclude unwarranted hysterectomy without definitive diagnosis[9]. Study of varieties in the normal morphological appearance of endometrium gives an essential background for evaluation of endometrial pathology[10]. As bleeding in perimenopausal and postmenopausal period may be the only manifestation pointing towards endometrial carcinoma it needs prompt and thorough evaluation.

This study done to evaluate the endometrial causes of AUB and to determine the specific pathology in perimenopausal and postmenopausal age groups.

In this study we will analyse different histological patterns of endometrium by taking endometrial biopsy and also observe the incidence of premalignant and malignant changes in histopathology of endometrial tissue.

MATERIALAND METHOD

STUDY DESIGN -Prospective observational study

Setting-The study were undertaken in department of obstetrics and gynaecology Swaroop Rani Nehru Hospital, Motilal Nehru Medical College, Prayagraj.

Study period-1 year

Patient selection-patients above 40 years of age presenting to gynaecology OPD and admitted in the department of obstetrics and gynaecology, Swaroop Rani Nehru Hospital, Motilal Nehru Medical College with history of abnormal uterine bleeding will be selected for study.

SAMPLE SIZE- Total 116 patient with abnormal uterine bleeding were taken to study histopathological patterns.

METHODOLOGY

The study includes all perimenopausal and postmenopausal women with complain of abnormal uterine bleeding.

INCLUSION CRITERIA

- Patients of age 40 to 50 years (Perimenopausal bleeding) presenting with complaint of abnormal uterine bleeding.
- Patients presenting with abnormal uterine bleeding after one year of cessation of menstruation (Postmenopausal bleeding).

EXCLUSION CRITERIA

1) Pregnancy Related complication
2) Intra Uterine devices
3) Genital tuberculosis
4) Bleeding and coagulation defects
5) Anti Platelet drugs
6) Cervical and vaginal pathology
7) Leiomyoma and Adenomyosis
8) Ovarian cyst and tumours
9) Hormone replacement therapy
10) Iatrogenic causes

METHODOLOGY

The study includes all perimenopausal and postmenopausal women with complain of abnormal uterine bleeding**.**

All the study participants were planned for endometrial sampling.
Time of sampling-It was performed in premenstrual period in perimenopausal patients and any time in postmenopausal patients.

Collection of sample-All specimen were transported in 10% formalin to pathology laboratory. Tissue sections(4-6micron) was cut and stain with hematoxylin and eosin(H&E).

RESULTS

In this study, total 116 patients were enrolled. Total 70.0% patients were enrolled in Perimenopausal group and 30.0% in Post-Menopausal group as shown in Table 1 and Figure 1.

Table 1: Distribution of patients in both group

	n	%
Perimenopausal	81	70.00
Post-Menopausal	35	30.00

Table 2 show the distribution of patients according to age (years) in between Perimenopausal and Post-Menopausal group. The distribution of patients on the basis of different 41-45 yrs, 46-50 yrs, 51-55yrs, 56-60yrs and 61-65 yrs of age range were 65.43%, 34.57%, 0.00%, 0.00% and 0.00% patients in perimenopausal group and 0.00%, 22.86%, 57.14%, 17.14% and 2.86% patients in Post-Menopausal group, respectively. On the basis of different age range both groups were significantly different ($p < 0.01$). The mean age was significantly higher in Post-Menopausal group (44.72±280) as compared to Perimenopausal group (53.60±3.47).

Table 2: Distribution of patients according to age (years) in both age groups

Age	Perimenopausal (n=81)		Post-Menopausal (n=35)		Chi-sq.	[1]p-Value
	n	%	n	%		
41-45 yrs	53	65.43	0	0.00		
46-50 yrs	28	34.57	8	22.86		
51-55 yrs	0	0.00	20	57.14	86.47	<0.001*
56-60 yrs	0	0.00	6	17.14		
61-65 yrs	0	0.00	1	2.86		
Mean±SD	44.72±280		53.60±3.47		p<0.001*	

=Chi-square test, * =Significant ($p<0.05$)

Table 3 show the distribution of perimenopausal patients according to histopathological endometrial patterns. The percentage of Proliferative, Disordered proliferative, Secretory, Endometrial Hyperplasia without atypia, Endometrial Hyperplasia with atypia, Benign endometrial polyp, Endometrial carcinoma were 45.68%, 13.58%, 19.75%, 13.58%, 2.47%, 3.70% and 1.23% in Perimenopausal group, respectively.

Table 3: Distribution of perimenopausal patients according to histopathological endometrial patterns

Histopathological endometrial patterns	Perimenopausal (n=81)	
	n	%
Proliferative	37	45.68
Disordered proliferative	11	13.58
Secretory	16	19.75
Endometrial Hyperplasia without atypia	11	13.58
Endometrial Hyperplasia with atypia	2	2.47
Benign endometrial polyp	3	3.70
Endometrial carcinoma	1	1.23

Table 4 show the distribution of Post-Menopausal patients according to histopathological endometrial patterns. The percentage of Atrophic endometrium, Hyperplasia without atypia, Hyperplasia with atypia, Proliferative, Benign endometrial polyp, Secretory, Endometrial carcinoma, and Disordered proliferative were 37.14%, 20.00%, 11.43%, 8.57%, 2.86%, 2.86%, 5.71%, and 11.43% in Post-menopausal group, respectively.

Table 4: Distribution of Post-Menopausal patients according to histopathological endometrial patterns

Histopathological endometrial patterns	Post-Menopausal (n=35)	
	n	%
Atrophic endometrium	13	37.14
Hyperplasia without atypia	7	20.00
Hyperplasia with atypia	4	11.43
Proliferative	3	8.57
Benign endometrial polyp	1	2.86
Secretory	1	2.86
Endometrial carcinoma	2	5.71
Disordered proliferative	4	11.43

DISCUSSION

In our study, age of patients ranged from 41-65 years.
The most common age group having complaint of abnormal uterine bleeding in perimenopausal group was 41-45 years (65.43%) with mean age of 44.72± 2.80 years.

This is due to the fact that these patients are in their climacteric period, as women approach the menopause, cycle shorten and become anovulatory due to decrease in number of graffian follicle and increased resistance to gonadotrophic stimulation results in low level of oestrogen which can not keep the normal endometrium growing.

The findings correlate with studies conducted by **Swati Bapurao Mune et al[2013]**

conducted study in age group 23-76 years and most common age of presentation were 41-45 years of age with mean age 44.2, **Roopmala M et al[2019]** conducted a retrospective study in age group 15-65 years and the maximum number of AUB cases were in 41-50 years, **Anitha S et al[2018]** conducted study in age group 20-60 years and most common age of presentation were 41-50 years of age, **Neha G Jagdale et al[2018]** conducted study in age group 21-55 years of age and most common age of presentation were 41-45 years of age, **Archana Tiwari et al[2016]** conducted study in age group 17-75 years of age and most common mean age group of presentation was 45.

In postmenopausal group postmenopausal bleeding was found in 51-55 years (57.14%) with mean age of 53.60± 3.47 years.

In postmenopausal patients findings of this study correlate with **Bhatta S et al[2005]**

found postmenopausal bleeding in 23.0%, **Indu Kaul et al[2012]** found postmenopausal bleeding with mean age 54.06± 6.64, **Sonali Rathi et al[2012]**

conducted study in 41-60 years with postmenopausal bleeding and found mean age of presentation was 55.75, **Arati Mallick et al[2013]** mean age of postmenopausal bleeding 57.12± 9.13 years, **Bharani et al[2008]** in which study were done in 52-65 years of age group and most common mean age of presentation was 55.2± 3.84, **Desai et al[2014]** conducted study in age group 45-68 years of age group and most common mean age of presentation 55±s 6.10.

ENDOMETRIAL HISTOPATHOLOGICAL PATTERNS PERIMENOPAUSAL PATIENTS

In present study maximum patient had proliferative pattern in 37(45.68%) cases followed by secretory in 16(19.75%), disordered proliferative endometrium in 11(13.58%), hyperplasia without atypia in 11(13.58%), benign endometrial polyp in 3(3.70%), hyperplasia with atypia 2(2.47%), endometrial carcinoma 1(1.23%).

Bleeding in proliferative phase due to anovulatory cycle, due to progressive rise of oestrogen, followed by sudden fall in oestrogen due to feedback inhibition of pitutary hormone and bleeding occurs.

Bleeding in secretory phase is due ovulatory dysfunction, inability of corpus luteum to synthesize adequate amount of progesterone. In perimenopausal patients endometrium responds to excessive or unopposed oestrogen stimulation due to absence of ovulation and production of progesterone and this induce hyperplastic response in proliferating endometrium.

Disordered proliferative endometrium is an exaggeration of normal proliferative phase without significant increase in overall glands stroma ratio and is due to persistant oestrogen stimulation. Endometrial hyperplasia is a precursor of endometrial cancer. An earlier stage of presentation due to increase health awareness could explain high incidence in our study.

Similar results were seen with the study conducted by **Neha G Jagdale[2018]** in which they found proliferative pattern 32.96%, secretory pattern 16.48%, hyperplasia without atypia 7.68%, hyperplasia with atypia 1.1%**, Swati Bapurao Mune et al[2015]** found proliferative pattern 27.8%, secretory pattern 6.1%, hyperplasia without atypia 20.28%, benign endometrial polyp 8%, hyperplasia with atypia 1.88%, atrophic endometrium 13.2%, endometrial carcinoma 2.3%, **K Sajitha et al[2011]** observed 12.2% proliferative pattern, 16.1% secretory pattern, hyperplasia without atypia 25%, benign endometrial polyp 5.12%, atrophic endometrium 5.12%,endometrial carcinoma 4.5%, **Kiran Rawat et al[2017]** found proliferative endometrium 29%, secretory endometrium 19.9%, disordered proliferative pattern 9.4%, simple hyperplasia 5.8%, complex hyperplasia 0.326%, atrophic endometrium 4.2%, **Humaira B et al[2015]** observed proliferative pattern 16.8%,secretory pattern30%, hyperplasia without atypia 19%, benign endometrial polyp 2.7%, hyperplasia with atypia 0.5%, endometrial carcinoma 0.9%, **Desai N et al[2015]**

found proliferative pattern 39%, secretory pattern 23%, hyperplasia without atypia 28%, hyperplasia with atypia 9%, atrophic endometrium 1%, **Bharat Talukdar et al[2015]** observed proliferative pattern 20.56%, secretory pattern16.11%, hyperplasia without atypia 46.11%, benign endometrial polyp 2.22%, endometrial carcinoma 1.11%, **Kafle N et al[2020]** found proliferative pattern 42.77%, secretory pattern 14.46%, chronic endometritis 13.26%, disordered proliferative pattern 5.42%, endometrial polyp 2.41%, endometrial hyperplasia without atypia 7.23%, endometrial hyperplasia with atypia 3.01%, endometrial carcinoma 2.41%, **Simridhi Bindroo et al[2018]** found proliferative pattern 37.2%, secretory endometrium 34%, endometrial hyperplasia 16%, disordered proliferative endometrium 2.4%, endometrial carcinoma 1.6%

ENDOMETRIAL HISTOPATHOLLOGICAL PATTERNS POSTMENOPAUSAL PATIENTS

In present study, histopathological examination of endometrium in postmenopausal women showed atrophic endometrium in 13 cases(37.14%) followed by hyperplasia without atypia in 7 cases(20), benign endometrial polyp in 1 cases(2.86%), hyperplasia with atypia in 4 cases(11.43%), endometrial carcinoma in 2 cases(5.71%), proliferative in 3 cases(8.57%), secretory in 1 case(2.86), disordered proliferative endometrium 4 cases(11.43%).

In postmenopausal women atrophic endometrium was most common findings due to decrease in estrogen level which leads to atrophy or thinning of endometrium results in bleeding. Thin walled veins superficial to the expanding cystic glands, make the vessels vulnerable to injury and leads to bleedingLimitation of my study is a small sample size.

Correlation with other studies **Arati Mallick et al[2013]** seen atrophic endometrium in 40.74%, endometrial carcinoma 12.96%, **Farhat Deeba et al[2016]** observed atrophic endometrium in 24.5%, hyperplasia without atypia 54.5%, benign endometrial polyp 3.6%, hyperplasia with atypia 4.5%, endometrial carcinoma 12.7%, **Sonali Rathi et al[2013]** seen atrophic endometrium 48.85% followed by endometrial carcinoma 10.34%, benign endometrial polyp 9.77%, proliferative pattern 8.05%, secretory pattern 3.44%, simple hyperplasia 5.75%, complex hyperplasia without atypia 8.05%, complex hyperplasia with atypia 5.75%, **Rekha B et al[2016]** observed atrophic endometrium 31%, proliferative pattern 21%, secretory pattern 5%, hyperplasia without atypia 27%, benign endometrial polyp 4%, hyperplasia with atypia 4%, endometrial carcinoma 6%, chronic endometritis 1%, **Desai K et al[2014]**

atrophic endometrium 24%, proliferative pattern 12%, secretory pattern 6%, hyperplasia without atypia 41%, hyperplasia with atypia 6%, endometrial carcinoma 12%, **RP Damle et al[2013]** observed atrophic endometrium 25.80%, proliferative pattern 19.35%, secretory pattern 12.90%, hyperplasia without atypia 19.35%, endometrial carcinoma 9.67%, chronic endometritis 6.45%.

CONCLUSION

Histopathological patterns of endometrial biopsy and curettage of women presenting with Abnormal uterine bleeding is one of the most common problem in women of all age groups in reproductive period. It is challenging gynecological problem caused by various endometrial pathologies. Endometrium is the mirror of hormonal status in women. Histological variations can be seen in the endometrium according to age of women and phase of her menstrual cycle and any other specific pathology.

Endometrial sampling could be effectively used as one of the diagnostic tool in abnormal utrerine bleeding although at times its interpretation could be quite challenging. It is a simple, cost-effective and appropriate method that provides accurate diagnostic yield. The present study highlights the importance of endometrial biopsy and its interpretation which plays a pivotal role in the management of AUB.

Histopathological examination of endometrial biopsies in patients of AUB in perimenopausal and postmenopausal bleeding shows a wide spectrum of changes ranging from normal endometrium in various hormonal cycles to malignancy.

AUB without structural pathology occurs in reproductive women of all ages but more common in adolescent and perimenopausal women. In perimenopausal years anovulatory cycle is most frequent which in turn causes changes in endometrium, which results in irregular bleeding. In absence of ovulation due to low progesterone, no secretory changes in endometrium. Unopposed oestrogen give rise to persistent proliferative or hyperplastic endometrium.

Risk factors which are associated with endometrial cancer like obesity, diabetes mellitus, hypertension. They are associated with chronic elevation of endogenous oestrogen or increased oestrogen action at the level of endometrium. These risk factors are modifiable, prevention and treatment and creating awareness regarding these modifiable risk factors will help in reducing the incidence of AUB.

Histological examination of endometrial biopsies is gold standard tool in evaluation of AUB and great help to gynaecologists to plan therapy of a patients presented with AUB by follow up of patients who has precursor lesion or timely surgical intervention in case of malignant lesion.

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