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Histological Pattern of Endometrial Biopsies in Patients with Abnormal Uterine Bleeding- A Retrospective Study.

Dr Sakshi Chaurasia[1], Dr Nikita Singh[2], Dr U. R. Singh[3]
([1]Tutor, [2]Post graduate student, [3]Professor and Head of Department,
Department of Pathology, Shyam Shah medical college, Rewa, M.P., India)
**Corresponding Author: Dr Sakshi Chaurasia[1]*

ABSTRACT
Background: Abnormal uterine bleeding (AUB) is one of the most common presentation amongst the women of all age groups attending the Gynecology Out Patient Department. Abnormal uterine bleeding is defined as changes in frequency of menstruation, duration of flow or amount of blood loss. Endometrial sampling could be effectively used as a first diagnostic step in AUB. The aim of the present study was to determine the clinical spectrum and frequency of pathologies in endometrial biopsy of patients with AUB in our population.
Material & Method:
The retrospective study was conducted in the Department of Pathology, Shyam Shah Medical College, Rewa, (M.P.) over a period of two year from March 2018 to March 2020. This study was done on 210 patients presenting with abnormal uterine bleeding who underwent endometrial sampling in our hospital. The pattern of endometrial changes was studied and classified.
Results: The most common age group presenting with AUB was 41-50 years (42%). The commonest pattern in these patients was proliferative phase (32%), and secretory phase (21%). The commonest pathology was endometrial hyperplasia (16%) and endometrial carcinoma was seen in 0.95 % cases.
Conclusion: Patients with AUB show variable pathology on endometrial biopsy ranging from normal endometrium to malignancy thus emphasizing the importance of endometrial sampling as an important diagnostic tool in the management of abnormal uterine bleeding. Hence, the pathologist should be careful while reporting endometrial biopsy which is the key to effective therapy and optimal outcome

Keywords: Abnormal uterine bleeding, Endometrial Biopsy

I. INTRODUCTION

Endometrium is continuously under the effect of hormones throughout the life span of women[1] Abnormal Uterine Bleeding (AUB) is defined as any bleeding that does not correspond with the frequency, duration or amount of blood flow of a normal menstrual cycle and could be a sign of simple hormonal imbalance or a serious underlying condition necessitating aggressive treatment including a major surgical procedure. It affects 10-30% of reproductive aged women and upto 50% of perimenopausal women.[2]

The International Federation of Gynecology and Obstetrics working group on menstrual disorders has developed a classification system (PALM-COEIN) for causes of the AUB in non-gravid women of reproductive age. There are nine main categories, which are arranged according to the acronym PALM-COEIN: Polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified.

According to the proposed classification system, non-specific term like dysfunctional uterine bleeding should be abandoned to favor a more specific etiology like ovulatory dysfunction[3].
Endometrial atrophy manifests as abnormal bleeding and endometritis causes irregular shedding and thus evaluation is mandatory.
Since endometrium is the best accessible tissue for histopathological evaluation of uterine bleeding, several methods are used for endometrial sampling among which Dilatation and Curettage is used as standard practice in our hospital.

The most common presentations are menorrhagia, polymenorrhoea, metrorrhagia and intermenstrual bleeding. The aim of the present study was to determine the clinical spectrum and frequency of pathologies in endometrial biopsy of patients with AUB in our population.

II. MATERIALS AND METHODS

This was a retrospective study carried out in the Department of Pathology, Shyam Shah Medical College, Rewa, M.P. from March 2018 to March 2020 for a period of 2 year. This study included 210 endometrial samples with a clinical diagnosis of AUB.

Patients with isolated endometrial causes of abnormal uterine bleeding were included for study and those with retained product of conception, cervical, vaginal pathology and haemostatic disorders were excluded from the study.

Endometrial samples were obtained from dilatation and curettage or endometrial biopsy.
Specimens were received in 10% formalin. These were studied grossly; entire tissue was sent for processing and were processed in automated tissue processor. Four to five micron thick paraffin embedded serial sections were taken and stained by Haematoxylin and Eosin. Histopathological evaluation was done under light microscope.

Various endometrial patterns were classified as follows: Proliferative, Secretory, Unsatisfactory, Chronic Endometritis, Polyp, Hyperplasia and Carcinoma. Endometrial Hyperplasia was classified according to World Health Organization (WHO) into simple and complex on the basis of architecture and each was further subdivided into typical and atypical, based on cytology.
Data were collected in Microsoft Excel and analyzed.

III. RESULT

The present study has been conducted on 210 specimens of the endometrium (endometrial curetting/biopsy specimens) received in the Pathology Department of a tertiary care institution, with the clinical diagnosis of abnormal uterine bleeding during the period of 2 year from March 2018 to March 2020.
Patients' age ranged from 22-62 years and most of them were seen in the age group of 41-50 years (42%), followed by 31-40 years (37%). (Table 1)

Table 1 Distribution of patients with abnormal uterine bleeding in different age group

AGE IN YEARS	NUMBER OF PATIENT	PERCENTAGE
21-31	28	13.3
31-40	78	37
41-50	89	42
51-60	14	6.7
61-70	1	0.47
TOTAL	210	100

The cases studied were categorized into seven groups depending upon the histomorphological diagnosis (Table 2).

Table 2 Distribution of endometrial pattern in abnormal uterine bleeding

ENDOMETRIAL PATTERN	NUMBER OF PATIENT	PERCENTAGE
PROLIFERATIVE PHASE	67	32
SECRETORY PHASE	44	21
DISORDERED PROLIFERATIVE ENDOMETRIUM	40	19
INADEQUATE	4	1.9
ENDOMETRIAL POLYP	12	5.8
ENDOMETRIAL HYPERPLASIA	35	16
CHRONIC ENDOMETRITIS	6	2.8
ENDOMETRIAL CARCINOMA	2	0.95
TOTAL	210	100

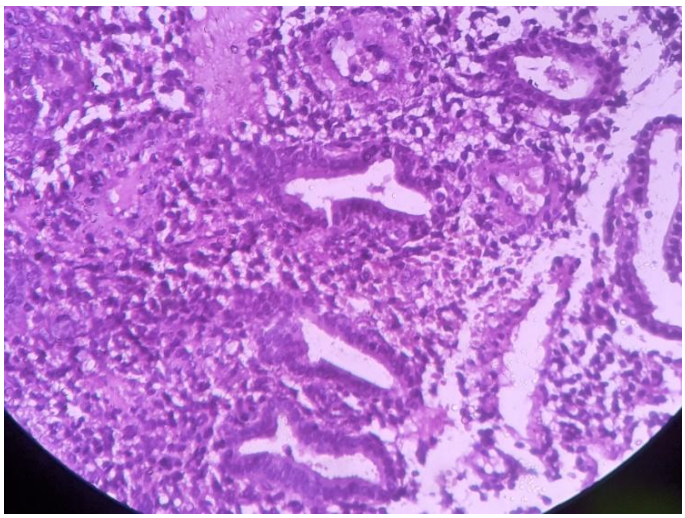

Fig 1 Simple endometrial hyperplasia. Endometrial biopsy of a 60yr old female presenting with AUB. (10x; H&E)

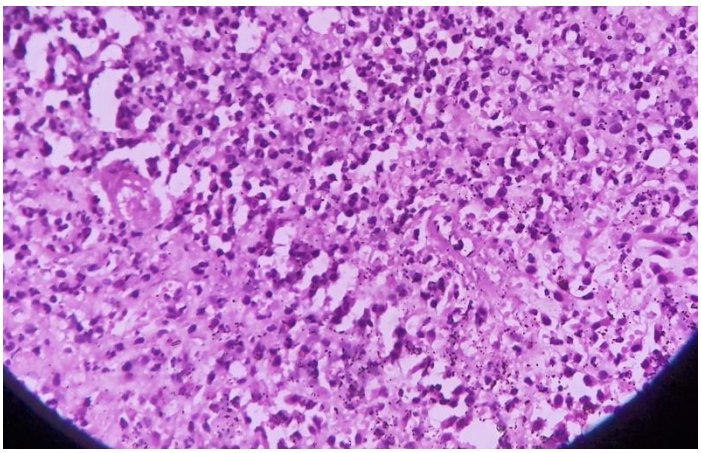

Fig 2 Chronic Endometritis. Endometrial biopsy of a 34yr old female presenting with AUB. (40x; H&E)

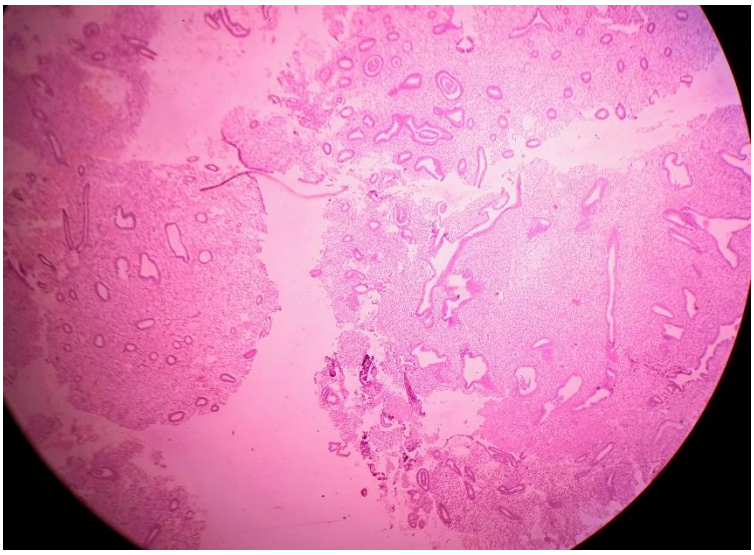

Fig 3. Disordered Proliferative Endometrium. Endometrial Biopsy of a 42yr old female presenting with AUB. (10x; H&E)

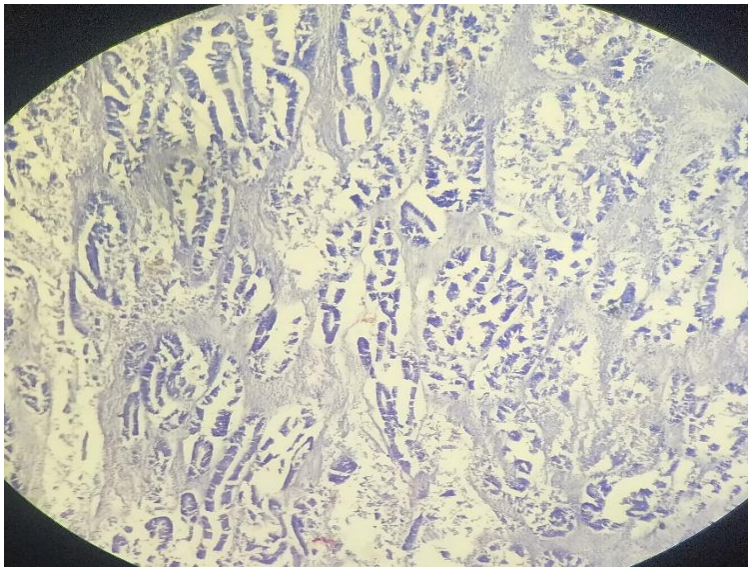

Fig 4. Endometrial carcinoma. Endometrial Biopsy of a 50yr old female (40x; H&E)

Amongst these, on microscopic examination of endometrial samples, proliferative phase was seen in maximum number of cases i.e. 67 (32%), followed by 44 cases of secretory phase (21%), disordered proliferation of endometrium was observed in 40 cases (19%).

Hyperplasia (Fig 1) was seen in 35 cases (16%) out of which 31 cases showed simple hyperplasia without atypia and whereas 4 cases showed simple atypical hyperplasia while no case of complex hyperplasia with or without atypia.

Chronic Endometritis (Fig 2) was seen in 6 case (2.8%) and Endometrial polyps were seen in 12 cases (5.8%). Endometrial carcinoma was encountered in 2 case (0.95%) in which one was Endometroid carcinoma (Fig 4) and other was carcinosarcoma (malignant mixed Mullerian tumor). Endometrial carcinoma is known to be common in post menopausal women, was observed in our study in 5^{th} and 6^{th} decades of life.
Finally, in 4 cases (1.9%), the sample was scanty and inadequate for opinion.

Table 3 Comparison of histological pattern in different age group

ENDOMETRIAL PATTERN	21-30	31-40	41-50	51-60	61-70	Total
Proliferative phase	17	28	20	2	-	67
Secretory phase	1	21	22	-	-	44
Disordered proliferative endometrium	6	11	20	3	-	40
Inadequate	1	3	-	-	-	4
Endometrial polyp	-	6	6	-	-	12
Chronic Endometritis	3	2	1	-	-	6
Endometrial Hyperplasia	-	7	19	8	1	35
Endometrial carcinoma	-	-	1	1	-	2
TOTAL	28	78	89	14	1	210

Between 41-50 years, the secretory pattern was the most common (22 cases) followed by proliferative phase (20 cases) and 20 cases of disordered proliferative endometrium. Endometrial hyperplasia was seen mostly in the age group 41-50 years (19 cases). In the 51-60 age group, endometrial hyperplasia was the most common pattern. One case of endometrial carcinomas was presented at age 50 years and one case of carcinosarcoma was seen at the age of 60 years. (Table 3)

IV. DISCUSSION

Endometrial biopsy has been a continuous source of frustration for the pathologist because of minimal clinical information and biopsy taken at an inappropriate moment of menstrual cycle; one is unable to recognize the abnormality [4]

The endometrium undergoes regular cyclical changes under recurrent hormonal changes of the ovulatory cycles [1].

Abnormal uterine bleeding is one of the most frequently encountered conditions in Gynecology. AUB is of concern as it can have serious medical and social consequences by causing anemia, disruption of women's daily activities and sexual life [5].

In normal cycles, the menstrual shedding is followed by endometrial proliferation under estrogenic stimulation. During this phase the endometrial glands grow and become tortuous. The secretory activity in the second half of the menstrual cycle is characterized by endothelial proliferation, thickening of the wall, and coiling of the spiral arterioles [5].

AUB with organic cause can be due to reproductive disease, iatrogenic causes and systemic diseases. When no specific organic cause of AUB is found, then by exclusion, a diagnosis of dysfunctional uterine bleeding (DUB) / abnormal uterine bleeding (AUB) is assumed. However, well defined organic abnormality is seen only in 25 % cases of abnormal uterine bleeding [6].

The etiology of AUB relates to the patient's age as to whether the patient is premenopausal, perimenopausal or post-menopausal[7].

In present study it was found that the incidence of menstrual disorders increases with advancing age. The commonest age group of 41-50 years presented with excessive bleeding. Similar finding was reported by Doraiswami S et al and Sarika et al[8,9].

Normal physiological phases of endometrium, such as proliferative and secretory pattern were encountered in maximum number of cases. Proliferative endometrium comprised of total 67 cases (32%) in our study, this finding is same with the studies done by Doraiswami S et al and Kumari sr et al[8,10].

The bleeding in the proliferative phase may be due to anovulatory cycles and because of ovulatory dysfunctional uterine bleeding in the secretory phase. Our study showed secretory phase in 44 cases (21 %), similar to the study done by sarika et al and Scommenga A et al [9,11].

A significant number of cases showed disordered proliferative endometrium in present study – 41 cases (19%). This was slightly more when compared with the findings of Bashir H et al and Vaidya et al which showed 12.17% and 13.4% respectively [12,13]. Disordered proliferative endometrium was commonly seen in perimenopausal age group similar to study of Doraiswami et al and kumar sr et al[8,10]. It denotes an endometrial appearance that is hyperplastic but without an increase in endometrial volume.There is no significant increase in the overall ratio of glands to stroma [14]. It resembles a simple hyperplasia, but the process is focal rather than diffuse. Diagnosing the patients at the earliest stage of this spectrum will be of definitive help to the practicing gynaecologists to prevent the disease progression, because on the other end of the spectrum is the endometrial carcinoma[15].

In present study, the most common pathological cause for abnormal bleeding was endometrial hyperplasia (16%). This is in consistent with the studies of sarika et al and kumari et al [9,10]. Endometrial hyperplasia is a precursor of malignancy. It is a common diagnosis in perimenopausal women often causing symptoms of irregular or prolonged bleeding. This is due to increased oestrogen levels. The overgrowth affects not only glands and stroma but there is also abnormal vascularisation [12]. Majority of the cases of hyperplasia were simple hyperplasia and women were in the perimenopausal age group. Many studies have showed a similar increased incidence in perimenopausal age group [8,17].

Patients with chronic endometritis may present with AUB, pelvic pain and infertility. It should be diagnosed because with specific treatment endometrium starts functioning normally. The diagnosis of chronic endometritis is made on the basis of the presence of plasma cells. In our study this condition was seen in few patients (6 cases), which is similar to the study done by Sarika et al [9].

The incidence of endometrial polyp was 5.8% in our study. Sajitha et al found endometrial polyp in 5.12% cases and Doraiswami S et al in 11.2% cases [8,18]. Polyps are difficult to be recognized on curettage specimen.

Incidence of endometrial carcinoma in our study was 0.95 % which was seen at 41-50 years of age group. This finding is comparable to the finding in Prajapati et al (0.99%) and Sandeepa et al (1.1%) [19,20]. On the contrary, this finding is lower than the incidence recorded by Doraiswami et al (4.4%) and Khare et al (3.7%) [8,16]. This dissimilarity may be explained by the majority of the population in our study which was mainly

from reproductive age group and only endometrial cause of AUB was considered in our study. Most of the studies found majority of cases of carcinoma in postmenopusal age [9,19]. The risk factors for endometrial carcinoma are generally known, the most common is endogenous or exogenous hyperestrogenism and the most common precursor lesion is the endometrial hyperplasia [21].

Finally, in four cases (1.9%) the endometrial biopsies were scanty and were inadequate for opinion. A study was done in Philadelphia to evaluate the negative predictive value of endometrial samples in 2004, where it was observed that an inadequate endometrial sample may be sufficient to rule out endometrial neoplasia because of its high negative predictive value [22].

V. CONCLUSION

Present study showed a wide spectrum of histomorphological changes in endometrial biopsies of patients presenting with AUB ranging from normal endometrium to malignancy thus necessitating endometrial sampling as an important diagnostic tool in the management of abnormal uterine bleeding. Most of these are age related pathologies. Hence, accurate histopathological screening of endometrial samples should be done, since it plays a cornerstone role in making the specific diagnosis which can help the clinicians for successful management of AUB and optimal outcome. This would also help in individualizing the management of abnormal uterine bleeding with a view to conserve the uterus.

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Corresponding Author: Dr Sakshi Chaurasia[1]
([1]Tutor, Department of Pathology, Shyam Shah medical college, Rewa, M.P., India)