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Histopathology

ROLE OF SMALL BIOPSY IN DIAGNOSIS OF SPECTRUM OF ENDOMETRIAL LESIONS: A STUDY FROM A TERTIARY CARE CENTRE IN GREATER NOIDA

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ABSTRACT **Introduction**: Histopathological characterization of endometrial biopsies and curettings constitute an important tool for diagnosis of endometrial pathology; whether benign, pre-malignant and malignant, and help the gynecologist to decide appropriate therapeutic strategy. The present study was carried out to document the histopathological appearances seen in endometrial biopsies, and their age–wise distribution in patients with infertility and abnormal uterine bleeding due to endometrial causes. **Materials and Methods:** A total of 75 specimens of endometrial curettings and biopsies from patients with abnormal uterine bleeding due to endometrial causes and inability to conceive, received in the Pathology department, Noida International Institute of Medical Science over a period of one year, were retrieved and analyzed retrospectively, and their findings were documented. The tissue had been received in 10% formalin, processed routinely, and the slides had been stained with Hematoxylin and Eosin. **Results**: The most common histopathological diagnosis was disordered proliferative endometrium, seen in 34.67% cases followed by proliferative endometrium in 14.67%, secretory phase endometrium (9.33%) and atropic endometrium(8%). 9.33% biopsies showed pill endometrium. Retained products of conception were confirmed histologically in 4% cases. Endometrial hyperplasias were seen in 10.67% cases The most common finding in patients of infertility was proliferative endometrium indicating anovulatory cycles. **Conclusion:** Endometrial biopsy is a valuable tool in assessment of endometrial status in infertility, as well as benign and malignant pathology in abnormal uterine bleeding due to relative ease and accessibility of procedure and rapid availability of results.

KEYWORDS :

INTRODUCTION:

In day -to-day surgical pathology practice endometrial samples are one of the most common specimens and pose unique challenge for the pathologist.[1] Endometrial biopsies are obtained for a number of reasons that include abnormal uterine bleeding in certain age groups, incomplete abortions, or suspected neoplasia and the endometrium may be sampled prior to certain procedures to treat infertility to determine the phase of the cycle to guide further tests or treatments.[2-3] Abnormal uterine bleeding (AUB) is the most common indication for endometrial sampling. Abnormal uterine bleeding (AUB) is a term used to describe any type of bleeding that doesn't fall within normal ranges for amount, volume, frequency ,duration or cyclicity.[4] In postmenopausal women, it is defined as any bleeding after 1 year of menstrual cessation.[5] Majority of the AUB patients belongs to perimenopausal and post menopausal age groups. However, this is most common complaints in all age groups.[6] AUB has both structural as well as functional causes. Menorrhagia, metrorrhagia, intermenstrual bleeding and post menopausal bleeding are various clinical presentation of the patient.[7] It is also one of the commonest cause of iron deficiency anemia and chronic malaise around the world.[8]

Based on these possible underlying etiologies, the International Federation of Gynaecology and Obstetrics (FIGO) in 2011 devised a classification named PALM-COEIN for the etiology of AUB. PALM accounts for structural features like polyps, adenomyosis, leiomyoma, and malignancy. COEIN addresses non-structural causes like coagulation defects, ovulatory dysfunction, endometrial causes, iatrogenic causes, and non-classified ones.[9] Endometrial biopsy is used as a diagnostic aid in AUB. It is done as a first-line test in women >45 years of age presenting with AUB. Endometrial biopsy is also done in patients <45 years of age with a history of unopposed estrogen exposure, failed medical management, and persistent AUB.[10] The prime idea is to rule out the precursor lesions like hyperplasia and aggressive endometrial carcinoma.[9]

For evaluation of patient for infertility endometrial biopsy is equally important . The dating of the endometrium by its histological appearance is helpful clinically to document ovulation, assess hormonal status and determine cause of endometrial bleeding and infertility.[11] We aim to document findings from cases of endometrial biopsies in woman of different age groups to confirm the exact nature of the lesion and to rule out malignancy.

MATERIALS AND METHODS:

This study was conducted in the Department of Pathology, Noida International Institute of Medical Science, Greater Noida. A total of 75 cases of endometrial curettings and biopsies obtained from patients presenting with abnormal uterine bleeding due to endometrial causes and failure to conceive, were included in the study.

The biopsy specimens had been obtained by conventional dilatation and curettage or biopsy performed as an inpatient procedure. The specimens had been received in 10% formalin and underwent routine histological processing followed by Hematoxylin and Eosin staining.

Criteria for exclusion :

1. Patients with organic lesions involving the genital tract like leiomyomas, adenomyosis, cervical and vaginal pathology.
2. Endometrial findings in TAH+BSO specimens were not included in this study.
3. Patients with systemic disease like haemostatic disorders etc.

Criteria for adequacy of specimen: In specimens where no endometrial tissue was seen or no conclusion could be arrived at, in spite of the presence of some tissue, a diagnosis of inadequate for evaluation was given.

RESULTS:

A total of 75 endometrial biopsies done in patients sent for histopathological examination and their findings were analyzed in this study. Based on the age of the patients who underwent endometrial sampling were categorized into three groups: reproductive, perimenopausal and postmenopausal. Chief complaints of all the

patients were also noted. It was observed that most patient presented with AUB. Menorrhagia was the commonest (n=48, 64%) clinical presentation followed by metrorrhagia (n=15, 20%) and post menopausal bleeding (n=7 , 9.33%). Five patients of reproductive age group presented with complaints of an inability to conceive (6.67%) [Table 1].

Table 1: Clinical presentation of patients who submitted sample of endometrial biopsy[n=75]:

S.no.	Clinical presentation	No. of cases
1	Menorrhagia	48
2	Metrorrhagia	15
3	Post menopausal bleeding	7
4	Infertility	5

Age specific analysis clearly revealed that maximum number of patients belong to the age group 41-50 years (40%), followed by 31-40 years (37.34%) [Table 2].

Table 2: Age wise distribution of endometrial samplings specimen [n=75]:

Age	No. of cases	Percentage
Less =20	01	1.33
21-30	05	6.67
31-40	28	37.34
41-50	30	40
51-60	07	9.33
>60	04	5.33
Total	**75**	**100**

Among the endometrial biospies of 75 cases, the commonest histological pattern among all age groups was Disordered proliferative endometrium (34.67%). The second most common pattern, proliferative phase endometrium (14.67%) followed by secretory phase endometrium and atropic endometrium accounted 9.33% and 8% respectively. Hyperplasia with atypia and without atypia were seen in 2(2.67%) and 6 (8%) cases respectively. There was one case each of endometritis and endometrial polyp (1.33%). The histological images of few cases are mentioned in Figure 1A-D & 2A-B.

However, out of 75 cases, 10 cases presented with dual histological findings. Among them endometritis was seen in 7 cases whereas, 1 case of disordered proliferative endometrium also had endometrial polyp. Retained product of conception and pregnancy related complication as ectopic pregnancy were confirmed in 3 and 2 cases respectively. A significant number of cases show pill induced endometrial changes characterised by atrophic glands, pseudodecidualization along with inflammatory infiltrate due to exogenous hormonal treatment containing progesterone. Seven cases of pill endometrium (9.33%) were reported in our study. 4% endometrial samples were designated as inadequate for evaluation [Table3].

Table 3: Distribution of different endometrial lesions on histopathological evaluation [n=75]:

Histomorphological Pattern	No. of cases	Percentage [%]
Disordered proliferative Endometrium	26	34.67
Pill Endometrium	7	9.33
Proliferative endometrium	11	14.67
Secretory phase endometrium	7	9.33
Ectopic pregnancy	2	2.67
Atropic endometrium	6	8
Endometrial Hyperplasia with Atypia	2	2.67
Endometrial Hyperplasia without Atypia	6	8
Endometritis	1	1.33
Endometrial Polyp	1	1.33
Retained product of conception (RPOC)	3	4
Inconclusive	3	4
TOTAL	**75**	**100**

Reproductive age group was most common among all the endometrium pattern (disordered proliferative endometrium, secretory phase endometrium and proliferative phase endometrium); whereas, atrophic endometrium cases were seen in peri-menopausal and post menopausal age groups. Cases of endometrial hyperplasia without atypia were also common in same age group. However, one case of endometrial hyperplasia with atypia was seen in reproductive age group [Table 4].

Table 4: Age wise distribution of different endometrial lesions on histopathological evaluation [n=75]

Histomorphological Pattern	Reproductive (18-40 Years)	Perimenopausal (41-50 Years)	Postmenopausal (>50 Years)
Proliferative Endometrium	8	3	
Secretory Endometrium	4	3	
Disordered Proliferative	13	9	4
Pill endometrium	4	3	
Atrophic Endometrium		4	2
Endometrial polyp	1		
Endometrial hyperplasia without atypia		3	3
Endometrial hyperplasia with atypia	1		1
Chronic endometritis		1	
Retained product of conception	3		
Ectopic pregnancy	2		
Osseous metaplasia	1		
Tubal metaplasia		1	
Inconclusive	1	2	
Tubal metaplasia		1	
Inconclusive	1	2	
Total	**39**	**32**	**10**

Other associated findings noted on histopathological evaluation [Figure 3A-B] in our study were osseous and tubal metaplasia [1 case each], arias-stella reaction [2cases], endocervical polyp [1case], chronic cervicitis with mild dysplasia [1case], calcified area [1 case] [Table 5].

Table 5: Other associated findings in endometrial biopsy sample [n=7]

S.no.	Associated findings	No. of cases
1.	Osseous metaplasia	1
2	Tubal metaplasia	1
3	Calcified area in endometrium	1
4	Endocervical polyp	1
5	Arias-stella reaction	2
6.	Chronic cervicitis with mild dysplasia	1

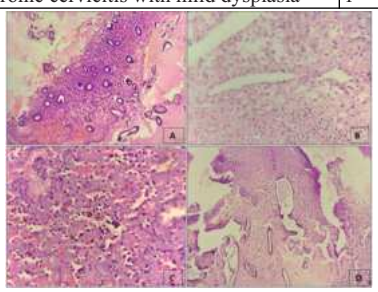

Figure 1 A-D: Sections examined show [A] Proliferative endometrium [H&E, 20X]; [B] Pill induced endometrium [H&E, 40X]; [C] Acute endometritis [H&E, 40X]; [D] Disordered proliferative endometrium [H&E, 20X]

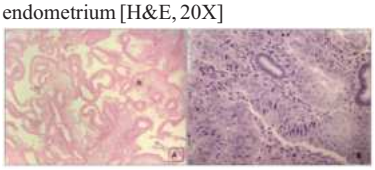

Figure 2 A-B: A- Endometrial hyperplasia without atypia [H&E, 20X]; B- Endometrial hyperplasia with atypia [H&E, 40X]

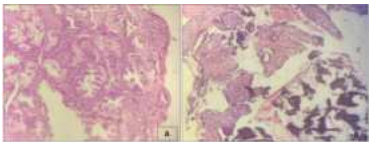

Figure 3 A-B: A- Arias stella reaction [H&E, 20X]; B- Osseous metaplasia surrounding endometrial glands [H&E, 20X]

DISCUSSION:

Abnormal uterine bleeding is one of the most common problems encountered in gynaecology outpatients and endometrial sampling

from these cases have been routinely received in histopathology. It can present in various patterns including menorrhagia, metrorrhagia and postmenopausal bleeding. Different causes of abnormal bleeding occur in varying frequencies in different age groups. Recent PALM-COEIN classification approved by FIGO categorises the causes of abnormal uterine bleeding into structural and non structural namely – polyp, adenomyosis, leiomyoma, malignancy and hyperplasia; coagulopathy;ovulatory dysfunction; endometrial; iatrogenic and not yet classified. The reporting of endometrial biopsy is of great challenge due to its dynamic cyclical changes and spectrum of histomorphological pattern in response to exogenous hormone. If the tissue obtained is scanty or devoid of stroma, it may be difficult to assess the biopsy. The pathologist plays an important role in early detection of endometrial prescursor lesions and exclusion of malignancy.

In this study age of the patients varied, ranging from 14 years to 74 years. The age distribution in our study revealed that most of the cases were seen in 41-50 years of age group which is in concordance with study done by Singh S et al., Shukla et al. and Saraswathi et al.[12-14] followed by 31-40 years (37.34%), 51-60 years (9.33%) and 21-30years (6.67%) which is also seen in Ashumi Gupta et al. Study[15]. Few cases presented at >60yrs age and in adolescent age group as seen in Ashumi et al[15] study were are also seen in our study .

Menorrhagia is one of the common presentations of AUB.[16] In our study patients presented with different types of bleeding pattern and the commonest pattern observed was menorrhagia (64%). In the study by Nayak et al and singh S et al.menorrhagia were seen in 49.1% and 36.8% of cases, which was a higher percentage compared to our study.[13] The second most common abnormal bleeding metrorrhagia (20%) followed by post menopausal bleeding (9.33%). Similar patterns of abnormal bleeding included menorrhagia (48.6%), followed by metrorrhagia (29.7%) and postmenopausal bleeding (5.8%) was reported in study of Ashumi et al study.[15]

A significant number of cases showed disordered proliferative which is charecterised by foci of dilated irregular shaped glands with focal outpouchings and branching as seen in 26 (34.67%) cases in present study.This finding was in concordance with the findings of Bhat et al.[6]

Endometrial hyperplasia has been classified by the WHO previously on the basis of architectural complexity and cytological atypia – namely simple and complex hyperplasia with or without atypia respectively.[17] The new WHO classification recognizes hyperplasia into two categories namely endometrial hyperplasia without atypia and atypical endometrial hyperplasia/endometrioid intraepithelial neoplasia.[18]

Endometrial hyperplasia accounted for 8 (10.67%) cases in which majority (6 cases) was without atypia and remaining 2 cases showed atypia. Only one case of this study occurred in reproductive age group, whereas, other cases were found in perimenopausal and postmenopausal age group as also seen in study done by Khare et al.[19]

There were three cases of retained bits of product of conception (POC) in this study. All the cases were presented with abnormal uterine bleed along with past history of abortion as seen in the study of Tiwari A. et al.[1]

Out of 75 specimens of endometrial biopsies studied, 5 patients presented with complaints of inability to conceive. This included patients with primary (4 cases) as well as secondary infertility (01 case). All the patients were in second and third decade of life. The histological patterns in all the cases were proliferative phase endometrium. One case of infertility was also associated with chronic endometritis. Similar study was seen in the study of Punnet Kaur et al.[11] Two cases with pregnancy related complication such as ectopic pregnancy were reported. Histomorphological findings in these patients were secretory phase endometrium with extensive decidualisation but no villi. Decidua but no villi was also seen 2% cases in the study of Puneet et al.[11]

Endometrial polyp is the benign outgrowth from the uterine cavity comprising of endometrial gland, stroma and thick walled blood vessels.[20]In our study, 1.33% shows benign endometrial polyp. Similar result were seen in the study of Baral et al (1.3%) and Tiwari et al (1%).[21, 1] However, two cases of our study also diagnosed endometrial polyp which was seen in association with endometrial hyperplasia with atypia and disordered proliferative endometrium, respectively.

Chronic endometritis as primary diagnosis was seen in only 1 case (1.33%) as seen in study of Ranjan et al. (2%) and Singh et al (1.6%).[8,14] However, 7 out of 75 cases were there in which endometritis was reported as secondary diagnosis. Chronic endometritis shows the presence of plasma cells, usually surrounding the superficial endometrial glands.[22] Neutrophilic infiltrate is seen normally in menstrual endometrium. However, in presence of mononuclear inflammatory cells including plasma cells and lymphocytes it may indicate endometritis. Acute endometritis may be seen in absence of plasma cells such as in abnormal bleeding related to complications of pregnancy.[23]

The incidence of atrophic pattern observed in our study was 8%. Similar pattern (11%) was seen in the study by Dwivedi et al.[24]Atrophic Endometrium is due to estrogen deprival in the menopausal period and the rupture of dilated venules beneath thin endometrium leads to abnormal uterine bleeding.[25]

Cases of pill endometrium due to exogenous hormonal treatment (progesterone) is characterized by atrophic glands, pseudo-decidualisation along with inflammatory infiltrates were also reported in this study. A total of 7 cases (9.33%) were reported mainly in reproductive and peri menopausal age groups. In the study by Sharma K et al.,12 cases (3.28%) of pill endometrium have been reported and highest is observed in reproductive age group which is comparable to our study.[26]

In our study 1 case each of osseous metaplasia, calcified area in endometrium,and tubal metaplasia and 2 cases of arias-stella reaction were reported. This is similar to report from a study by Ifeyinwa mary et al , Puneet et al.and Vjayaraghavan et al.[3,11,27]

CONCLUSION:

Endometrial sampling is an effective and reliable diagnostic tool. Its interpretation can be quite challenging and also may show inter-observer variability. Clinical information regarding age, menstrual history, parity and imaging studies are important prerequisites in the interpretation of endometrial samples and that can be helpful in providing the right treatment to the patient. AUB requires thorough and prompt evaluation as it can be a clinical manifestation of underlying premalignant or malignant conditons like endometrial carcinoma. It is a reliable yardstick to measure incidence of these conditions which lead to infertility or abnormal uterine bleeding in females. AUB significantly affects the quality life of women and results in anemia.

Endometrial sampling should be considered in perimenopausal and postmenopausal age group and in reproductive age group not responding to medical treatment. Hence, histopathological examination plays a critical role in early diagnosis of endometrial pathology and to provide appropriate gynaecological management.

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Conflicts of interest:
There are no conflicts of interest.

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