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Correlation of the Various Clinical Findings and Chief Complains with Histopathological Pattern of Endometrium Biopsies: A Study of 300 Cases.

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ABSTRACT

Abnormal uterine bleeding and infertility are among the commonest conditions for which patients seek advice in the gynecological outpatient department. Endometrial biopsy is currently the most commonly used technique for histological evaluation of endometrial pathology. The study was aimed to find the incidence of various pathological lesions of endometrium i.e non-neoplastic as well as neoplastic and to correlate various clinical findings like age, chief complaints, and duration of these complaints with histopathological features. The present study included 300 endometrial biopsies with clinical diagnosis of Dysfunctional uterine bleeding or infertility, received in the Department of Pathology, Government Medical College, Patiala. The biopsies were processed and sections stained with H and E stain. Special stain (ZiehlNeelsen) was done wherever necessary. Primary infertility (75%) is more common than secondary infertility (25%). Most common presenting age group for DUB cases was 41-50 years (40.91%) and for infertile cases, 26-30 years (47.5%). The most common type of bleeding in DUB cases was menorrhagia (47.73%). Proliferative endometrium (30.45%) was the most common endometrial pattern in DUB cases and secretory endometrium (35%) in infertility cases. Benign neoplasms (endometrial polyp) constituted 3.64% of DUB cases and premalignant conditions (hyperplastic endometrium)-16.36% of DUB cases. Malignant neoplasms (endometrial carcinoma) were found in 3.64% of DUB cases, being most common in 6th decade of life (50%) and postmenopausal bleeding (62.5%) was the most common clinical presentation.

INTRODUCTION

Oral radiography was first performed within weeks of the discovery of Roentgens magical rays (x-rays) "Endometrium is the mirror of hormonal status in females"^[1]. Of all the target organs for ovarian hormones, endometrium is most sensitive. The endometrium is a dynamic tissue that undergoes physiologic and characteristic morphologic changes during the menstrual cycle as a result of sex steroid hormones coordinately produced in the ovary. The ovary, in turn, is influenced by the hormones produced by pituitary. Together, the hypothalamic, pituitary and ovarian factors and their interactions regulate maturation of ovarian follicles, ovulation and menstruation ^[2].

Abnormal uterine bleeding and infertility are among the commonest conditions for which patients seek advice in the gynecological outpatient department ^[3]. With medical advancements combined with increasing awareness about gynecological problems, women gain access to most of the diagnostic and therapeutic modalities. The endometrial biopsy is one of the various investigations chosen to evaluate the endometrial pathologies 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.

Endometrial Biopsy

Endometrial biopsy is currently the most commonly used technique for histological evaluation of endometrial pathology [4].

Endometrial biopsy is a procedure in which a tissue sample is taken from the inner lining of the uterus (endometrium), and is examined under the microscope for knowing the hormonal status or any pathology [5].

A normal endometrial cycle is associated with changes in both endometrial glands and stroma that allow the pathologist to diagnose microscopically the phase of menstrual cycle [6].

Results of endometrial biopsy

Normal results: Most biopsies are done to rule out endometrial cancer or endometrial hyperplasia. A normal result shows no cancerous or precancerous cells. Normal result indicates that the uterine lining is changing at the proper rate and the biopsy is said to be "in-phase" because the tissue looks appropriate and has developed normally for that phase of the menstrual cycle.

Abnormal results: If the endometrium is not developing at the appropriate rate, the results are said to be "out-of-phase" or abnormal. The endometrium that has not developed appropriately cannot support a pregnancy. This condition is called luteal phase defect and may need to be treated with progesterone. Endometrial cells showing hyperchromatism, pleomorphism and increased nucleo-cytoplasmic ratio suggest endometrial carcinoma.

Indications for Endometrial Biopsy

- Abnormal uterine bleeding
- Postmenopausal bleeding
- Detection of precancerous hyperplasia and atypia
- Endometrial dating
- Follow-up of previously diagnosed endometrial hyperplasia
- Evaluation of endometrial response to hormonal therapy
- Evaluation of infertility
- Abnormal Papanicolaou smear with atypical cells favoring endometrial origin
- Cancer screening (e.g. hereditary nonpolyposis colorectal cancer)

Contraindications

- Pregnancy
- Acute pelvic inflammatory disease
- Clotting disorders (coagulopathy)
- Acute cervical or vaginal infections
- Severe cervical stenosis

MATERIALS AND METHODS

The present study is a prospective analysis of 300 endometrial biopsies received in our department from obstetrics and gynaecology department and other adjacent hospital. The clinical diagnosis in all the cases was dysfunctional uterine bleeding or infertility. Supportive data like age, chief complaints and duration of complaints was obtained from the histopathological requisition forms accompanying the specimens, was noted and compiled. The biopsy tissue was fixed in 10% formalin solution for 6-24 hours and was grossly examined for any abnormalities. After processing, 1-2 paraffin blocks were prepared and sections of 4-5 microns thickness were cut, stained with routine Haematoxylin and Eosin and were examined under the microscope. Deep cuts and serial sections were taken wherever necessary. Special stain (Ziehl Neelsen stain) for acid fast bacilli was done in cases of granulomatous endometritis. The histopathological findings were recorded.

OBSERVATIONS

The present study was conducted on 300 cases received in the Department of Pathology our institution with clinical diagnosis of DUB or infertility. The clinical data was analyzed and histopathological pattern of endometrium was studied.

In the present study, out of 300 cases, 220 (73.33%) were with the clinical diagnosis of DUB and 80 (26.67%) of infertility.

The maximum cases of DUB were in the age group of 41-50 years (40.91%) i.e. 5th decade of life (Table-1).

Out of 80 cases of infertility, maximum infertile patients belonged to the age group of 26-30 years (47.5%) of both primary and secondary infertility. The youngest patient was of the age of 20 years and the oldest one was 40 years (Table-2).

The (Table-3) depicts the different patterns of bleeding in DUB. Maximum (47.72%) patients had complaint of menorrhagia followed by metrorrhagia (33.64%).

Of the 220 cases, maximum cases (40.45%) had duration of bleeding being upto 1 year

Of the 80 cases of infertility, maximum cases of primary infertility had same duration of infertility, however, in secondary infertility the patient remain infertile for 4-6 years. The maximum duration of infertility was 13 years (Table-4)

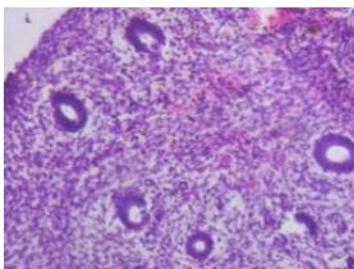
Various types of endometrial patterns seen on histopathological examination of 300 endometrial biopsies show 79 (26.33%) proliferative endometrium. Among these, 25 (31.65%) were in early proliferative phase (Figure-1) and 54 (68.35%) in late proliferative phase. 76 (25.33%) biopsies showed features of secretory endometrium. Among these, 36 (47.37%) showed in early secretory phase, 10 (13.16%) in mid secretory phase and 30 (39.47%) late secretory phase (Figure-2).

Out of the 300 biopsies, 38 (12.67%) biopsy sections simple hyperplasia without atypia (Figure-3). 16 (5.33%) biopsy sections showed features of luteal phase defect. Among these, 9 (56.25%) with delay of 3-4 days beyond the actual day of menstrual cycle, 5 (31.25%) with delay of 4-5 days and 2 (12.50%) endometrium biopsies showed delay of more than 5 days.

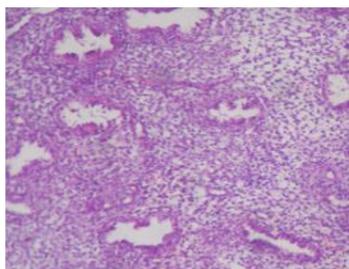
Endometritis were seen in 15 (5%) biopsy sections. Out of these 15 cases, 11 (73.33%) sections showed features of chronic non-specific endometritis, 4 (26.67%) granulomatous endometritis (possibly tubercular (Figure-4) and special stain (Ziehl-Neelsen stain) was positive in one section (25%) out of these 4 biopsy sections.

16 (12.67%) showed neoplastic lesion on histopathological examination, of which 50% were benign and 50% were malignant. 8 (2.67%) biopsy sections showed endometrial polyp (Figure-5). 7 out of 8 malignant neoplasm were endometrioid carcinoma (Figure-6) and 1 serous carcinoma of endometrium diagnosed (Figure-7).

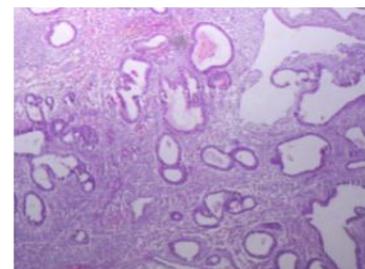
Anovulatory cycle was observed in 37 (12.33%) biopsy sections, 13 (4.33%) with features of disordered proliferative phase (Figure-8), 7 (2.33%) showed features of atrophic endometrium (Figure-9) and 3 (1%) irregular shedding of endometrium (Bar Diagram).



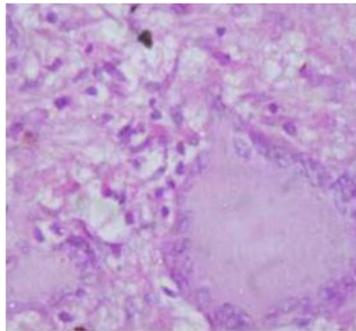
(Figure-1): Proliferative endometrium (H and E X100)



(Figure-2): Secretory endometrium (H and E X 100)



(Figure-3): Simple hyperplasia without atypia (H and E X100)



(Figure-4): Granulomatous endometritis (H and E X400)

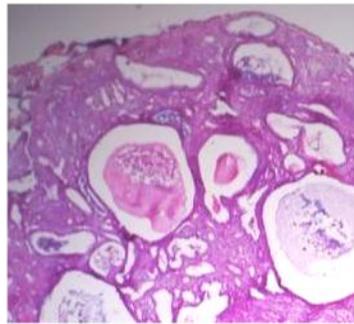
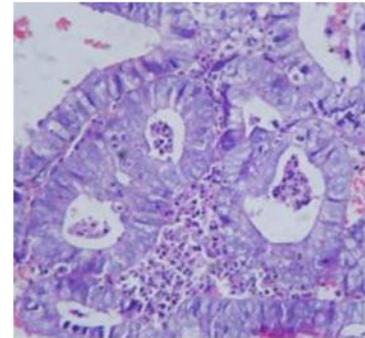
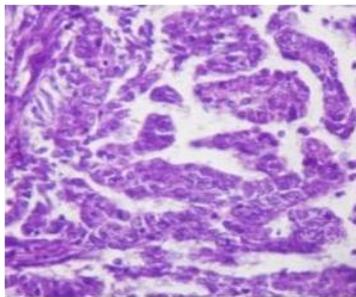


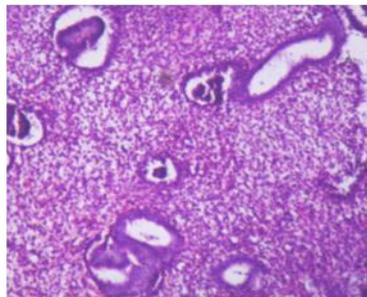
Figure-5): Endometrial polyp (H and E X400)



(Figure-6): Serous carcinoma endometritis (H and E X400)



(Figure-7): Serous carcinoma endometritis (H and E X400)



(Figure-8): Disordered proliferative endometrium (H and E X100)

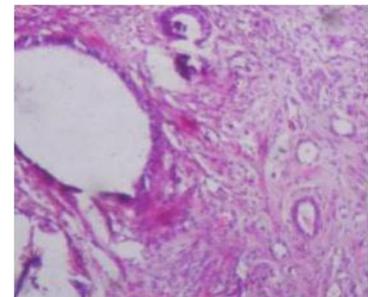


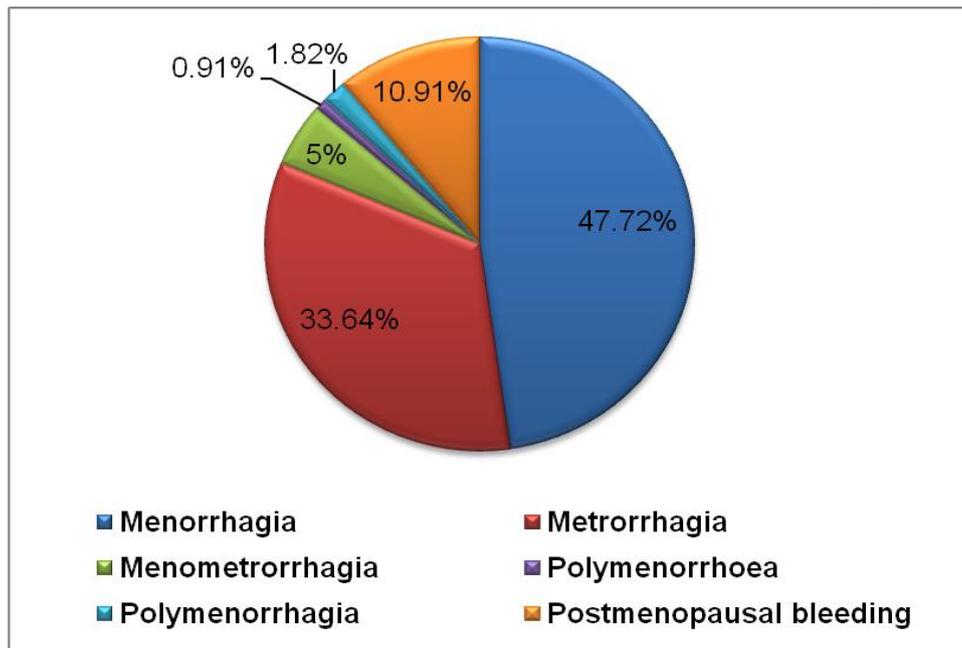
Figure-9): Atrophic endometrium (H and E X400)

Table 1: Age Wise Distribution of Cases of DUB (n=220)

Age Group (in years)	No. of cases	%age
< 20	-	-
21- 30	37	16.82
31- 40	70	31.82
41- 50	90	40.91
51- 60	17	07.72
61- 70	04	01.82
> 70	02	00.91

Table 2: Age Wise Distribution of Cases of Infertility (n=80)

Age group (in years)	Primary infertility (n=60)		Secondary infertility (n=20)		Total (n=80)	
	No. of cases	%age	No. of cases	%age	No. of cases	%age
< 20	01	100.00	-	-	01	01.25
21- 25	18	94.74	01	05.26	19	23.75
26- 30	27	71.05	11	28.95	38	47.50
31- 35	12	66.67	06	33.33	18	22.50
36- 40	02	50.00	02	50.00	04	05.00



Pie diagram showing type of bleeding in DUB cases

Table 3: Distribution of Cases of DUB According To Type Of Bleeding (n=220)

Type of bleeding	No. of cases	%age
Menorrhagia	105	47.72
Metrorrhagia	074	33.64
Menometrorrhagia	011	05.00
Polymenorrhoea	002	00.91
Polymenorrhagia	004	01.82
Postmenopausal bleeding	024	10.91
Total	220	100.00

Table 4: Distribution of Cases of Infertility According To Duration of Infertility (n=80)

Duration of infertility (in years)	Primary infertility (n=60)		Secondary infertility (n=20)		Total (n=80)	
	No. of cases	%age	No. of cases	%age	No. of cases	%age
2- 4	27	93.10	02	06.90	29	36.25
4- 6	18	66.67	09	33.33	27	33.75
6- 8	10	66.67	05	33.33	15	18.75
8- 10	04	80.00	01	20.00	05	06.25
> 10	01	25.00	03	75.00	04	05.00

DISCUSSION

The present study comprised of 300 cases of endometrial biopsies received in our.220 cases were of clinical diagnosis of DUB and 80 cases were of infertility.

Age of presentation

The age of the patient with DUB has been taken as a criterion for study in attempt to establish age incidence in DUB. Various workers came out with results which showed different age group distribution. In the present study of 220 cases of DUB, maximum cases were in 5th decade of life. The present study is in concordance with studies of Moghal [7], Doroswami et al [8], Anvikar et al [9] and Jairajpuri et al [10]. All of these studies concluded that the most common age group of patients presenting with DUB is 41-50 years.

Pattern of bleeding in DUB

The pattern of bleeding has been taken as a criterion for study in attempt to establish its incidence in DUB. In the present study, the most common pattern of bleeding was menorrhagia (47.73%) followed by metrorrhagia (33.64%). The finding is consistent with the studies of Anvikar et al [9] and Jairajpuri et al [10]. These studies concluded that the most common pattern of bleeding in DUB is menorrhagia. Metrorrhagia followed by menorrhagia was the most common bleeding pattern in the study of Moghal [7].

Endometrial pattern in DUB

Endometrial pattern has been taken as a criterion for study in attempt to establish its incidence in DUB. In the present study, most common pattern was proliferative, second most common secretory and third most common pattern being hyperplastic endometrium. This endometrial finding is consistent with the studies of Sanyal et al [11], Lidor et al [11], Purandare and Jhalam [12], Khan et al [13] and Deshmukh et al [14].

However, the studies of Moghal [7] and Gazozai et al [15] concluded that secretory endometrium was most common pattern, followed by proliferative endometrium, followed by hyperplastic endometrium. There was very small difference between incidence of first two patterns, 25.76% and 25.32% respectively in the study of Moghal. According to the study of Singhal et al [16], hyperplastic endometrium was the most common pattern followed by proliferative endometrium, followed by proliferative secretory endometrium.

Type of infertility

The type of infertility has been taken as a criterion for study in attempt to establish its incidence in infertility. In the present study of 80 cases of infertility, 75% were of primary infertility and 25% were of secondary infertility. So the incidence of primary infertility is found to be more than secondary infertility. This finding is in concordance with the study of Sahmay et al [17]. However, study of Ojo et al [18] showed greater incidence of secondary infertility than primary.

Age of presentation of infertility

In the present study of 80 cases of infertility, the most common age group was 26-30 years. The present study is in concordance with studies of Sahmay et al [17] and Ojo et al [18].

Endometrial pattern in infertility

In the present study, histopathological examination of endometrial biopsies revealed various endometrial patterns like secretory endometrium (35%), proliferative endometrium (15%), anovulatory endometrium (22.5%), LPD (20%), hyperplastic endometrium (2.5%) and tuberculous endometritis (5%). The most common pattern endometrial pattern being secretory is in concordance with the studies of Sahmay et al [17], Zavar et al [19] and Ojo et al [18]. However, the second most common pattern is different in various studies.

CONCLUSIONS

To conclude, a significant number of endometrial samples on histopathology revealed changes, rendering endometrial curetting and biopsy an important diagnostic procedure in evaluation of abnormal uterine bleeding in perimenopausal and infertile female. The accurate analysis of endometrial samplings is the key to effective therapy and optimal outcome.

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