VOLUME-9, ISSUE-6, JUNE-2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pathology

IMPORTANCE OF HISTOPATHOLOGICAL STUDY OF ENDOMETRIAL BIOPSY IN MANAGEMENT OF ABNORMAL UTERINE BLEEDING

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ABSTRACT **Background:** Abnormal uterine bleeding (AUB) is one of the most common gynaecological problem that Gynaecologist and Pathologist face worldwide. Endometrial biopsy reporting is a challenge to Histopathologist due to a wide spectrum of morphological patterns. **Aims:** To study wide spectrum of histopathological lesions in endometrial biopsies. **Methods:** This was a retrospective cross sectional study conducted over period of 2 years at a tertiary care centre. **Results:** In the present study, out of 226 cases of endometrial biopsies presenting with AUB, major bulk 86 cases (38.05%) showed normal histology of endometrium. Simple and complex endometrial hyperplasia was seen in 55 cases(24.33%). Endometrial carcinoma was seen in 22 cases (9.73%). Endometritis was seen in 20 cases (8.84%) **Conclusion:** The sensitivity of endometrial biopsy for detection of endometrial abnormalities is very high 96%. Correct histopathological diagnosis whether benign, premalignant and malignant, helps the treating Gynaecologist to decide appropriate therapeutic strategy. Endometrial biopsy is also a very useful screening modality for high risk patients of carcinoma endometrium.

KEYWORDS : Endometrial Biopsy, Abnormal Uterine Bleeding, Histopathology, Premalignant, Carcinoma.

INTRODUCTION:

Menstruation is a very complex process involving estrogen and progesterone receptors, endometrial vasculature with vasoactive substances by a process of tissue breakdown, remodelling, regeneration and repair [1]. Abnormal uterine bleeding refers to a symptom of excessive, scanty, prolonged, cyclic, unexpected or acyclic bleeding regardless of diagnosis or cause. It is one of the most common gynaecological problems that Gynaecologist and Pathologist face, accounting for 15-20% of gynaec OPD visits and 25% of gynaecological operations [2,3]. In India, women attending gynecological OPD, abnormal uterine bleeding constitute 30-50% [4]. AUB is the commonest gynaecological complaint leading to endometrial aspiration by biopsy or curettage. Endometrial biopsy reporting is a challenge to Histopathologist due to a wide spectrum of morphological patterns resulting from normal menstrual phase, excess role of hormones, exogenous hormones, a wide variety of intrauterine infections and tumours. It interferes significantly with quality of life in an apparently healthy female. AUB may be due to structural or functional reasons, common structural causes are fibroids, polyps, endometrial hyperplasia and carcinoma and complications of pregnancy. The functional disorders are called Dysfunctional uterine bleeding (DUB) and can be diagnosed only after exclusion of structural, iatrogenic, medication, psychological and systemic disorders[5].

Endometrial biopsy is a procedure in which a tissue sample is taken from the endometrium and is examined under the microscope by Histopathologist to detect hormonal imbalance or any specific pathology. Endometrial tissue sampling should be performed in patients with AUB older than 45 years as a first-line diagnosis. It should also be performed in patients younger than 45 with history of unopposed estrogen exposure as seen in obesity and PCOS, failed medical management, and persistent AUB. [6]. DUB occurs most commonly at the beginning or end of reproductive life. Anovulatory DUB is due to disturbance of hypothalamic pituitary ovarian axis [5] Management of Abnormal Uterine Bleeding (AUB) is complete only with tissue diagnosis especially in perimenopausal and postmenopausal state as they are at higher risk for endometrial hyperplasia and carcinoma [7 8] . Histopathology is the gold standard diagnostic modality to classify AUB which guides its treatment protocol for the Gynaecologist.

MATERIAL AND METHODS:

The present study was a retrospective cross sectional study carried out on 226 cases out of total 7836 histopathological specimens. It was conducted in the Histopathology section of Pathology Department of GMC Akola which is a tertiary care centre of Vidharbha region, Maharashtra, India.

Endometrial biopsies received from Department of OBGY over two years from Jan 2018- Jan 2020 were included in the present study. All patients had complaint of AUB in the form of menorrhagia, metrorrhagia, polymenorrhoea and post-menopausal bleeding. Detailed clinical history was taken, physical examination and pelvic examination findings were noted from records. The patients were subdivided into 5 groups according to the pattern of AUB into menorrhagia, metrorrhagia, polymenorrhoea, oligomenorrhoea and post-menopausal bleeding. Patients were also categorized into the following three age groups: reproductive (18-45 years), Perimenopausal (>45-till menopause) and

postmenopausal.

Inclusion Criteria:

1. All women with AUB > 45 years of age.
2. Women with <45 years with failed medical management.
3. Women with endometrial thickness >16mm in reproductive and perimenopausal age group on ultrasonography.
4. Women with endometrial thickness >5mm in postmenopausal age group on ultrasonography.
5. Women with postmenopausal bleeding and postcoital bleeding.

Exclusion Criteria

1. Pregnancy and vesicular moles.
2. Platelet and Coagulation abnormalities.
3. Intra-uterine Contraceptive Devices (IUCD) in situ

RESULTS

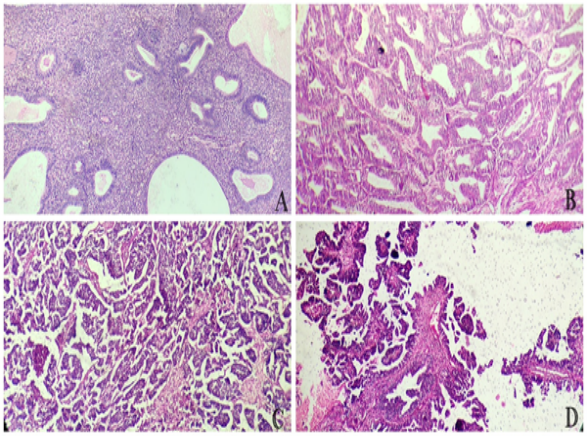
Histopathological findings of endometrial biopsies were studied in detail and following results were tabulated.

Table 1: Distribution of Endometrial findings (n=226)

Biopsy Findings	Frequency	Percentage (%)
Secretory Phase	36	15.92
Proliferation Phase	22	9.73
Disordered Proliferative Phase	18	7.9
Atrophic Endometrium	28	12.38
Pill Endometrium	5	2.21
Simple hyperplasia with atypia	10	4.42
Simple hyper plasia without atypia	12	5.30
Complex Hyperplasia with Atypia	17	7.52
Complex hyperplasia without atypia	16	7.07
Arias Stella Reaction	14	6.19
Acute Endometritis	6	2.65
Chronic Endometritis	9	3.98
Tuberculous Endometritis	5	2.21
Endometrial Polyp	6	2.65
Carcinoma Endometrium	22	9.73
Total	**226**	**100**

In the present study, out of 226 cases of endometrial biopsies presenting with AUB, major bulk 36 cases (15.92%) showed normal histology of endometrium in secretory phase, followed by 22 cases(9.73%)showing endometrium in proliferative phase. Simple hyperplasia was seen in 22 cases(9.82%) and complex hyperplasia in 33 cases (14.59%)

Endometrial carcinoma was seen in 22 cases (9.73%). Least common cases were of Tuberculous endometritis and pill endometrium with 05 cases (2.21%) each. (Table 1)



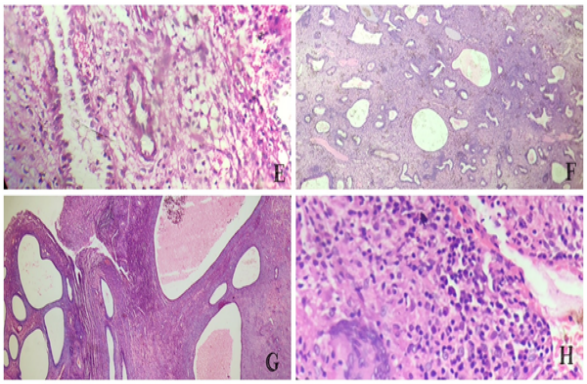
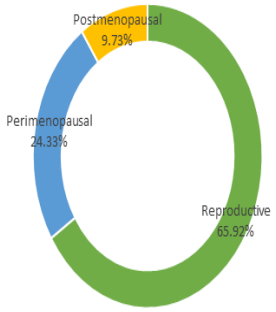


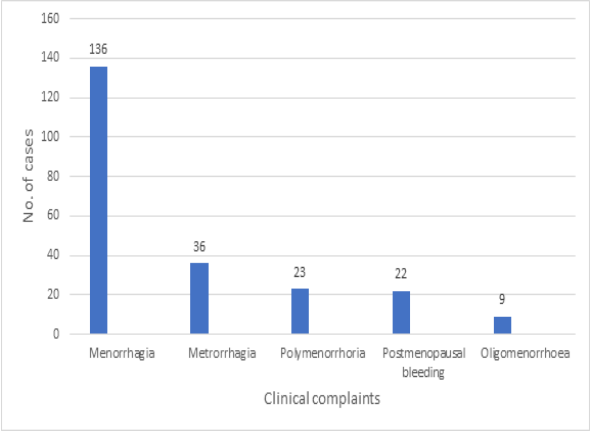
Figure A. Simple cystic hyperplasia(H&E,200x)
Figure B. Complex atypical hyperplasia(H&E,200x)
Figure C. Carcinoma endometrium (Moderately differentiated) (H&E,200x)
Figure D. Carcinoma endometrium (Well differentiated) (H&E, 200x)
Figure E. Aria Stella Reaction(H&E,400x)
Figure F. Atrophic endometrium(H&E,200x)
Figure G. Endometrial polyp(H&E,200x)
Figure H. Tuberculous endometritis(H&E,200x)

Figure 1: Distribution of age group. (n=226)



Out of 226 females, maximum i.e. 159 cases (65.92%) were found to be in reproductive age group (18-45 years), followed by 55 cases (24.33%) in peri-menopausal age group (more than 45 years till menopause). Whereas minimum of 22 cases (9.73%) were found to be in post-menopausal age group. (Figure 1). Minimum age found was 18 years with endometrium in secretory phase and maximum age was 65 years with carcinoma endometrium.

Figure 2: Distribution according to clinical complaints (n=226)



Out of 226 cases, maximum i.e. 136 females (60.17%) were having complaint of menorrhagia, followed by 36 females

(15.92%) having metrorrhagia. Whereas minimum i.e. 09 females (3.98%) were having oligomenorrhoea. (Figure 2)

DISCUSSION:

Abnormal uterine bleeding is one of the most frequently encountered gynecological problem world over. AUB is of concern as it can have serious medical and social consequences by causing anaemia, disruption of women's daily activities and sexual life[1]. Abnormal uterine bleeding is a diagnosis of exclusion in which no specific organic cause can be attributed to as the reason for the bleeding. The diagnosis is mostly based on patient's symptoms and clinical findings. In most of the cases, a pelvic ultrasonography is done to correlate the clinical findings[9]. Dilatation and curettage is said to be a diagnostic as well as a therapeutic procedure for these patients. The sensitivity of endometrial biopsy for detection of endometrial abnormalities is very high 96%[10,11]. Endometrial cancer, the most frequent gynaecologic malignancy in the developing world, which develops through preliminary stages of endometrial hyperplasia, which can be very well picked up even in small endometrial biopsies. Thus, correct histopathological diagnosis whether benign, premalignant and malignant, helps the treating Gynaecologist to decide appropriate therapeutic strategy.[12,13]

Table 2: Comparision Between Different Parameters Of Present Study And Other Studies In The Literature

Parameters	SajeethaKR[1]	SinghP[14]	SajithaK[15]	Anita[16]	BhatR[17]	Presentstudy
Totalcases	217	115	156	214	200	226
Maxi.Casesage group	41-50(52.99%)	46-50(40%)	46-55(42.95%)	Lessthan45years (58.41%)	40-50(76.5%)	Lessthan45years (65.92%)
Mostcommon complaints	Menorrhagia (43.78%), Metrorrhagia (18.43%)	Menorrhagia (40%)	Menorrhagia (47%)	Menorrhagia (52.3%), Menometrorrhagia(17.29%)	Menorrhagia	Menorrhagia (60.17%), Metrorrhagia (15.92%)
Mostcommon diagnosis	Proliferative phase(29.03%), Disordered proliferative (22.12%)	Proliferative phase(23.5%), Secretoryphase (18.2%)	Endometrial hyperplasia (25%), Secretoryphase (16.7%)	Disordered proliferative (10.28%), Pillendometrium (7.01%)	Proliferative phase(42.4%), Disordered proliferative (30%)	Secretoryphase (15.92%), Atrophic endometrium (12.38%)

In this present study, maximum cases were found to be less than 45 years of age (65.92%), which was in concordance with that done by Anita et al. Other found 41-50 years as most common age group.[1,17]We also found that, occurrence of menstrual disorders increases with advancing age. It may be due to the fact that these patients are in their climacteric period, as women approach menopause, cycles shorten and often become intermittently anovulatory due to a decline in the number of ovarian follicles and the estradiol level.[9]

Maximum females presentated with the complaint of excessive bleeding i.e. menorrhagia (60.17%), followed by metrorrhagia (15.92%) which was found to be similar with the studies done by Sanjeetha KR, Sigh P, Sajitha K, Anita and Bhat R. (Table 2)

We found endometrium in secretory phase to be the most common (15.92%) histopathological diagnosis, followed by atrophic endometrium (12.38%). While many other studies in the literature revealed proliferative phase endometrium most common.[1,14,17] (Table 1 & 2)

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. We found simple as well as complex hyperplasia with/ without atypia in peri-menopausal females (Fig A & B). This was comparable to other studies done in literature.[1,11,13]

Malignancy was seen in 22 cases (9.73%) in our study (Fig C & D). All were post-menopausal females. Sajitha K (6.4%), Singh P (2.6%) and Bhat R (3%) also found endometrial malignancy in their respective studies. (Table 1 & 2).Incidence of malignancy is pretty high in the present study as ours is a Tertiary Health Care Centre providing the best medical services.

We observed 28 cases (12.38%) of atrophic endometrium (Fig F) and all patients were in the peri- and postmenopausal age group. Anovulation in these women manifest as atrophic or inactive endometrium. Mechanism of bleeding due to atrophic endometrium in old age is stated in different studies as sclerotic degeneration of vessel wall or local abnormal haemostatic mechanism. This was similar to the findings of Zeeba et al.[18]

Arias stella reaction was seen in 14 cases(6.19%) with exaggerated progesterone effect from hormonal therapy. (Fig E)

Endometritis is seldom the direct cause of AUB, but is often a contributing factor. Subepithelial capillary plexus and surface epithelium are rendered fragile by inflammatory mediators leading to breaks and micro erosions. In our study,acute endometritis was seen in 6 cases (2.65%) with history of incomplete abortion.Chronic endometritis was seen in 9 cases (3.98%) with history of IUCD use.Anita etal [16] also had 0.93% of endometritis.

Endometrial polyp was seen in 6 cases (2.65%) (Fig G).
Histological pattern of women receiving hormonal pills show combination of inactive glands, abortive secretion, decidual reaction, and thin blood vessels is characteristic.We found pill endometritis in 5 cases(2.21%) with unopposed estrogen action.This was comparable with study done by Anita etal[16]. Tuberculous endometritis was seen in 5 cases(2.21%) of primary infertility. (Fig H)

CONCLUSION:

Endometrial lesions vary according to patient's age. Clinical information regarding age, menstrual history, parity and imaging studies are important prerequisites in interpretation of endometrial samples. Histopathological examination of endometrial biopsy is gold standard tool to diagnose gynaecological conditions, showing wide spectrum of changes ranging from normal endometrium to malignancy .Accurate analysis of endometrial biopsy is a key to effective therapy and optimal outcome.This would help in individualizing management of abnormal uterine bleeding with a view to conserve the uterus.Also endometrial biopsy acts as an important screening procedure for carcinoma endometrium in high risk pateints with simple and complex endometrial hyperplasia.

ACKNOWLEGMENT

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