



# CLINICOPATHOLOGICAL STUDY OF ENDOMETRIUM IN PATIENTS WITH ABNORMAL UTERINE BLEEDING

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## ABSTRACT

**Objectives:** Abnormal Uterine Bleeding (AUB) is considered one of the most common and challenging problems presenting to the gynaecologist, regardless of the age the women. The present study was done with the aim of studying the histopathological pattern of the endometrium in women of various age groups presenting with abnormal uterine bleeding.

**Methods:** This was a prospective study conducted on endometrial curettings of 460 patients in the Department of Pathology, from January 2013 to August 2014.

**Results:** The age of patients ranged from 18 to 70 yrs. The patients were categorized in reproductive age group (<40yrs), perimenopausal >40yrs and post-menopausal group (>50yrs/clinical scenario). Maximum number of patients were in the perimenopausal group, 220 patients (47.8%), followed by 182 patients (39.6%) in the reproductive age group. Post-menopausal patients constituted 12.6 % ( 58) of total no of cases. Menorrhagia was the most common presenting symptom. Normal cyclic endometrium, 210 cases (45.65%), was the most common histopathological pattern seen in the reproductive and perimenopausal group, whereas in the postmenopausal group simple hyperplasia, 16 cases (27.6%), followed by complex hyperplasia, 8 cases (13.7%) was the commonest pattern seen. Malignancy was seen in 7 cases (1.52%)

**Conclusion:** Histopathological examination of endometrial curetting specimens in patients with Abnormal uterine bleeding showed a wide spectrum of histopathological changes ranging from normal endometrium on one hand to malignancy on another hand thus rendering endometrial curetting an important diagnostic procedure in evaluation of Abnormal uterine bleeding. Accurate analysis of endometrial samplings is the key to effective therapy and optimal outcome

**Key Words:** Abnormal uterine bleeding, Endometrial hyperplasia, Histopathology

## INTRODUCTION

Normal menstruation is defined as bleeding from secretory endometrium associated with ovulatory cycles, not exceeding a length of five days. Any bleeding not fulfilling these criteria is referred to as Abnormal Uterine Bleeding (AUB)<sup>1</sup>. It is one of the frequently encountered gynaecological problem and is responsible for about one third of patients visiting gynaecological OPD (Out Patient Department)<sup>2</sup>.

It can be caused by a wide variety of structural and functional causes. Common structural causes include fibroids, polyps, adenomyosis or neoplasia. The largest single group encompasses functional disturbances, referred to as Dysfunctional

Uterine Bleeding (DUB). DUB is defined as any excessive bleeding (excessively heavy, prolonged or frequent) of uterine origin which is not due to demonstrable organic disease, complications of pregnancy or systemic disease<sup>3</sup>.

Histopathological examination of endometrial biopsy, taken by dilatation and curettage, remain the standard diagnostic procedure for the diagnosis of endometrial pathology<sup>4</sup>. It should be considered in all women if AUB does not resolve with medical management and particularly in those above the age of 40 years, and in women who are at increased risk of endometrial cancer. An accurate histopathological diagnosis facilitates the implementation of optimal treatment strategies and unnecessary radical surgery may be avoided.

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The present study was undertaken to determine the histopathological pattern of the endometrium in women of various age groups presenting with Abnormal Uterine Bleeding

## MATERIAL AND METHODS

The Present study was conducted in the Department of Pathology, Government medical College, Srinagar. This was a prospective study conducted on 460 specimens of endometrial curetting's received from patients presenting with Abnormal Uterine Bleeding over a period of 20 months from January 2013 to August 2014.

Patients were divided into three groups; Reproductive age group : <40 yrs, Perimenopausal age group : >40 yrs and Postmenopausal age group : Patients who have had cessation of menstrual cycles for at least a period of twelve months with dating of postmenopausal period from the final menstrual period. Patients with bleeding due to pregnancy related complications such as abortions, gestational trophoblastic diseases or ectopic pregnancy were excluded from the study. Detailed clinical history was obtained.

Specimens were fixed in 10% formalin followed by routine processing. The paraffin block sections were cut at 4-5 $\mu$  and the sections were stained by routine Haematoxylin and Eosin (H&E) stains, and special stains were used when required. Data was analysed using the Statistical Package for Social Science (SPSS version 20) for windows.

## RESULTS

A total of 460 cases of endometrial curetting's presenting with Abnormal Uterine Bleeding were studied. Of these 51(11.08%) specimens were inadequate /inconclusive for opinion. The age of patients ranged from 18 to 70yrs. Maximum number of patients, 47.8 % ( 220), were in the perimenopausal group followed by 39.6 % ( 182) patients in the reproductive age group. Postmenopausal patients constituted 12.6% (58) of total number of cases.

The most common presenting symptom was menorrhagia (56.73%) followed by polymenorrhea (17.82%). (Table 1)

Functional causes accounted for majority of the diagnosis, 274 (59.56%). Of these secretory endometrium being the most common histological pattern (27.17% cases) followed by proliferative endometrium (18.69% cases). While secretory endometrium was the most common functional cause of AUB in reproductive and perimenopausal age groups respectively, atrophic endometrium predominated among postmenopausal patients. Among organic causes simple cystic hyperplasia accounted for majority of the diagnosis in all the

three age groups.

In the reproductive age group (table 2) secretory endometrium seen in 34.06% (62 cases) of cases, was the most common histopathological pattern observed followed by proliferative endometrium 24.72% (45 cases) and disordered proliferative endometrium 9.3% cases (17 cases). Among organic causes, most common histological finding was endometrial hyperplasia 10.98% cases (20 cases), out of which simple hyperplasia without atypia was seen in 16 cases , complex hyperplasia without atypia in 3 cases and complex hyperplasia with atypia in 1 case. One case of uterine malignancy (rhabdomyosarcoma) was also seen. In addition acute endometritis and endometrial polyp was also seen in 8 cases and 7 cases respectively

In the perimenopausal patients (Table 2) functional causes predominated and most common pattern seen was secretory endometrium in 30% cases (66 cases) followed by proliferative endometrium in 16.8% cases (37 cases), disordered proliferative endometrium in 12.3% cases (27 cases) and hormonal effect in 4.1% cases (9 cases). Simple hyperplasia seen in 14.5% cases (32 cases), followed by complex hyperplasia without atypia in 4.5% cases (10 cases), endometrial polyp in 2.7% cases (6 cases), chronic endometritis in 2.27% cases (5 cases), complex hyperplasia with atypia in 0.5% cases (1 case) and malignancy in 0.9% cases (2 cases) were the organic lesions seen. Among malignant lesions, one case each of endometrial carcinoma and malignant mixed mullerian tumour was diagnosed.

Among postmenopausal patients (Table 2) organic causes were more common than functional causes. Simple hyperplasia without atypia was seen in 27.6% cases (16 cases), complex hyperplasia without atypia in 10.3% cases (6 cases), complex hyperplasia with atypia in 3.4% cases (2 cases) and malignant lesions 6.9% in cases (4 cases). Malignant lesions in post-menopausal group included 2 cases of endometrial carcinoma and one case each of clear cell adenocarcinoma and endometrial stromal sarcoma. Endometrial polyps in 3.4 % cases (2 cases), acute endometritis in 3.4% cases (2 cases) and granulomatous endometritis in 1.7 % cases (1case) were other organic lesions diagnosed. Among functional causes most common was atrophic endometrium seen in 12.06 % cases (7 cases), followed by proliferative endometrium in 6.8% cases (4 cases), disordered proliferative endometrium in 3.4% cases (2 cases) and secretory endometrium in 3.4 % cases (2 cases).

## DISCUSSION

AUB is a common gynaecological complaint accounting for one third of patients visiting outpatient clinics<sup>5</sup>. It is caused by a wide variety of disorders represented by an aberrant

physiologic status at one hand to uterine malignancy at the other. The present study was done to evaluate the histopathology of endometrium in abnormal uterine bleeding.

In our study organic causes of AUB were seen in 29.34 % (135) and functional causes in 59.56 % (274) patients. Similar observations were made in the study done by Vaidya S et al<sup>6</sup>.

Most patients in our study were in the perimenopausal age group (47.8%). This could be due to the fact that as menopause approaches, decreased number of ovarian follicles and their increased resistance to gonadotrophic stimulation, results in a low level of estrogen, which cannot keep the normal endometrium growing<sup>7</sup>. Lesser number of patients were seen in the higher ages which may be due to earlier evaluation, detection as well as management of the disease. Menorrhagia was the most common presenting feature (56.73%) followed by polymenorrhea (17.82%). These findings were compatible with the study done by Muzaffar M et al<sup>8</sup>.

The two most common histopathological pattern were normal cyclic pattern (secretory and proliferative endometrium) in the perimenopausal and reproductive age group and atrophic endometrium in the post-menopausal age group. The abnormal bleeding in the proliferative phase could be due to anovulatory cycles and in the secretory phase due to ovulatory dysfunctional uterine bleeding. Similar results were reported by Doraiswami et al<sup>9</sup>.

Disordered proliferative serves as a bridge between normal proliferation and hyperplasia. It denotes an endometrial appearance that is hyperplastic but without an increase in endometrial volume. An essentially normal proliferative phase endometrium with a few widely scattered cystic glands would better be called "disordered proliferative" than simple hyperplasia<sup>10</sup>. Disordered proliferative endometrium was seen in 12.17% of patients in our study. Study of Vaidya et al<sup>6</sup> showed 13.4% cases. In our study disordered proliferative endometrium was more common in perimenopausal group similar to study of Doraiswami et al<sup>9</sup>.

Endometrial hyperplasia is a precursor of endometrial cancer. The incidence of endometrial hyperplasia without and with atypia peaks in the early fifties and early sixties respectively with symptoms of irregular or prolonged bleeding due to anovulatory cycles in majority of cases, secondary to sustained level of oestrogens<sup>11</sup>. The overgrowth not only affects glands and stroma but there is also abnormal vascularisation. In our study endometrial hyperplasia was found in 18.9% of cases, which is concordant to observations made by Sheetal G P<sup>12</sup> (20%) but higher than that observed by Doraiswami et al<sup>9</sup> (6.11%) and Abid et al<sup>13</sup> (5%). Most common type of hyperplasia encountered was simple hyperplasia without atypia (Fig 1) in 13.91% cases. Hyperplasia was found to be the most common cause of AUB in post-menopausal women

and most common organic cause of AUB in reproductive and peri-menopausal women. However, its frequency peaked in perimenopausal age group accounting for about 50% cases. Similar observations were made by Vaidya et al<sup>6</sup> and Muzaffar M et al<sup>8</sup>.

Endometrial cancer is the most common malignancy of the female genital tract with 80% patients being post menopausal<sup>14</sup>. In our study malignancy was observed in 1.52% cases (7cases). Of these there were 5 cases of endometrial carcinomas with 3 cases diagnosed as type1 (Fig 2) and 2 cases as type 2 endometrial carcinoma.

Other tumours included one case each of endometrial stromal sarcoma and rhabdomyosarcoma. Most of the patients belonged to post-menopausal age group. Similar observations are seen in literature from sub continent<sup>6, 12, 13, 15</sup> as compared to the west<sup>16,17</sup> where higher incidence is reported. This may be attributed to early child bearing and multiparity practised by women in our subcontinent.

Polyps such as endometrial polyps and submucosal leiomyomatous polyps are common source of AUB in all age groups<sup>18</sup>. In our study 15 polyps (3.26%) were seen of which 12(2.62%) were reported as endometrial polyps and 3(0.65%) as submucosal leiomyomatous polyps. Data from other studies shows variable trends ranging from 1.2% to 14.10%<sup>8, 9, 12, 13</sup>. None of the polyps in our study showed atypical changes.

Atrophic endometrium was seen predominantly in post-menopausal group accounting for 12.6% cause of AUB in this group. This is compatible to the observation made by Doraiswami et al<sup>9</sup> (9.5%) but lower than the results observed by Abid et al<sup>13</sup> and Gredmark et al<sup>19</sup>. Anovulatory cycles followed by ovarian failure leads to atrophic changes in the endometrium at menopause.<sup>14</sup>

Chronic endometritis was observed in 2.6% of endometrial curettings of which 2 were granulomatous endometritis (due to tuberculosis) positive for AFB (Fig 3).

Study by Vaidya et al<sup>6</sup> showed chronic endometritis in 3.23% cases. The diagnosis of chronic endometritis is made on the basis of presence of plasma cells. Chronic endometritis is often a result of intra uterine contraceptive devices (IUCD), pregnancy and incomplete abortions.

Hormonal effect (exogenous administration) was noted in 2.17% cases (10cases) out of which 9 cases were seen in perimenopausal group. Muzaffar et al<sup>8</sup> have reported 2.3% cases as pill effect similar to our observation however majority of their cases were in the 31-40 year age group were as in our study cases were in the 41-50 year age group

Specimens inadequate for reporting were 51, accounting

for 11.8% of the total cases. . In our study specimens were labelled unsatisfactory for reporting when there were scant glands and stroma, fragmented tissues and haemorrhage. A study by Harmanli et al<sup>20</sup> revealed that an inadequate endometrial sample has a high negative predictive value of ruling out endometrial neoplasm. Similar views were expressed by Bakour et al<sup>21</sup> in their study wherein they observed scant tissue in atrophic endometrium with no focal lesion on ultrasound scan has little chance of missing relevant pathology.

## CONCLUSION

Histopathological examination of endometrial curetting's in patients with AUB showed a wide spectrum of pathological changes ranging from normal endometrium on one hand to malignancy on other hand thus rendering endometrial curetting an important diagnostic procedure in evaluation of AUB. In the present study since most of the preneoplastic lesions were seen in the perimenopausal group and neoplastic in postmenopausal age group, therefore it is especially recommended in women above 40 years of age presenting with AUB, to rule out preneoplastic lesions and malignancy. Accurate analysis of endometrial samplings is the key to effective therapy and optimal outcome.

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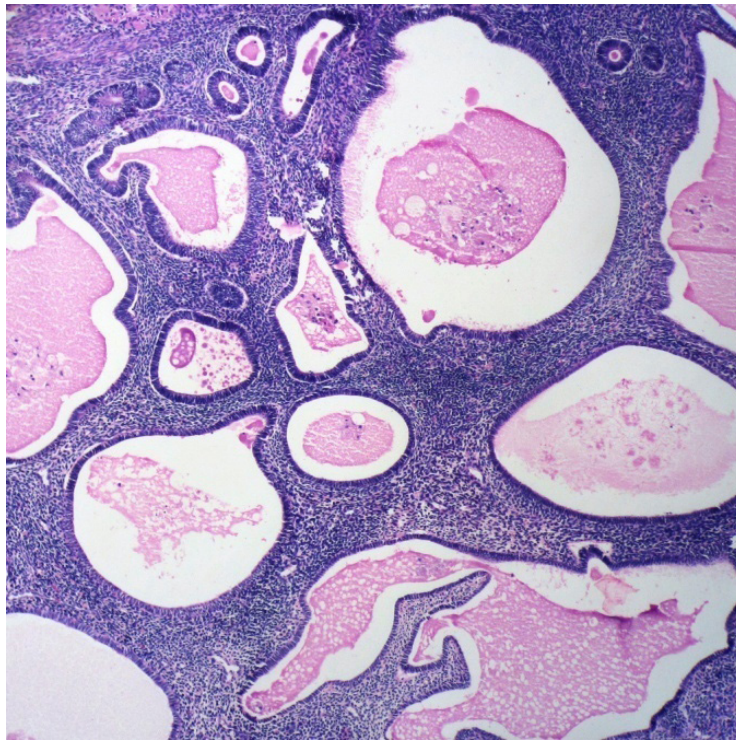
**Table 1: Pattern of bleeding in patients with abnormal uterine bleeding in different age groups**

Pattern of bleeding	Reproductive	Perimenopausal	Postmenopausal	TOTAL
Menorrhagia	120(65.93%)	141(64.09%)	0	261(56.73%)
Polymenorrhea	48(26.37%)	34(15.45%)	0	82(17.82%)
Metorrhagia	9(4.94%)	20(9.09%)	0	29(6.30%)
Menometrorrhagia	5(2.74%)	25(11.36%)	0	30(6.52%)
Postmenopausal bleeding	0	0	58(100%)	58(12.61%)
TOTAL	182	220	58	460

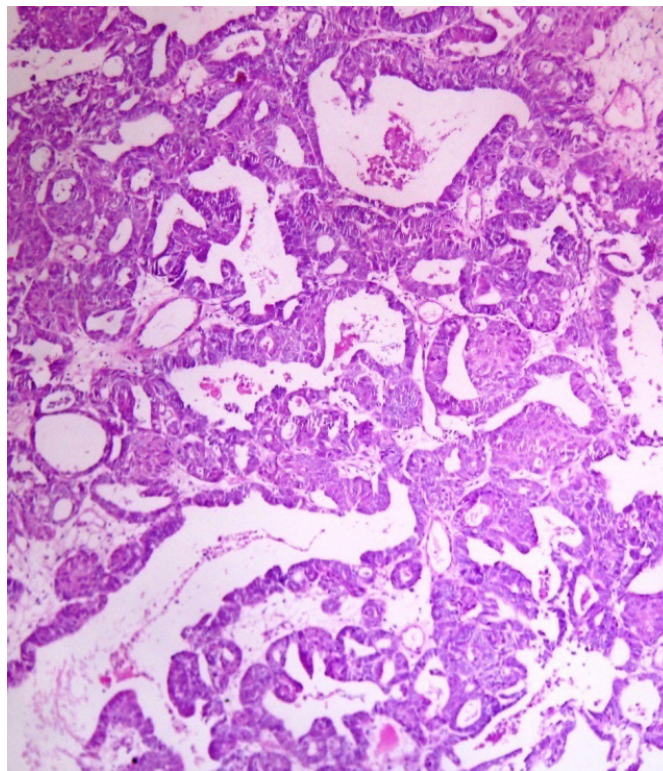
n = 460

**Table 2: Histopathological pattern seen in various age groups**

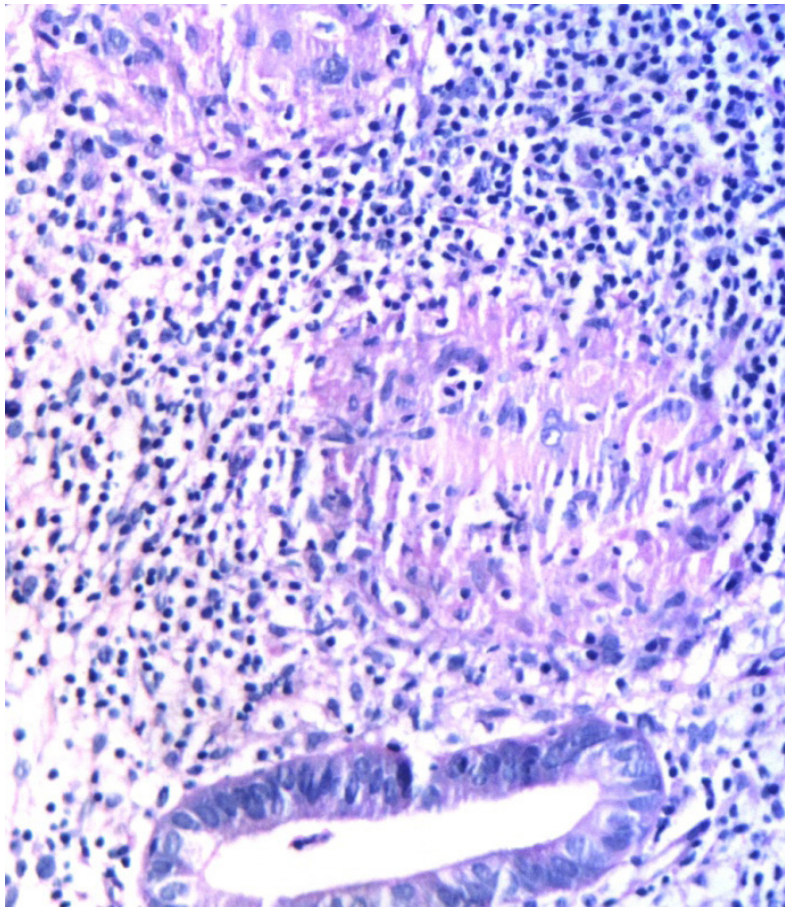
Histopathological diagnosis	Reproductive age group	Perimenopausal age group	Postmenopausal age group	Total
Secretory endometrium	62(34.1%)	66(30%)	2(3.4%)	130(27.17%)
Proliferative endometrium	45(24.7%)	37(16.8%)	4(6.8%)	86(18.69%)
Disordered proliferative endometrium	17(9.3%)	27(12.3%)	2(3.4%)	46(12.17%)
Hormonal effect	1(0.5%)	9(4.1%)	0	10(2.17%)
Dysmenorrhea membranacea	1(0.5%)	1(0.5%)	0	2(0.43%)
Atrophic endometrium	0(0.00%)	1(0.5%)	7(12.1%)	8(1.95%)
Acute endometritis	8(4.4%)	0(0.00%)	2(3.4%)	10(2.17%)
Chronic non-specific endometritis	1(0.5%)	5(2.27%)	0	6(1.30%)
Granulomatous endometritis	1(0.5%)	0(0.00%)	1(1.7%)	2(0.43%)
Endometrial polyp	7(3.84%)	6(2.7%)	2(3.4%)	15(3.26%)
Simple hyperplasia without atypia	16(8.8%)	32(14.5%)	16(27.6%)	64(13.91%)
Complex hyperplasia without atypia	3(1.6%)	10(4.5%)	6(10.3%)	19(4.13%)
Complex hyperplasia with atypia	1(0.5%)	1(0.5%)	2(3.4%)	4(0.86%)
Malignancy	1(0.5%)	2(0.9%)	4(6.9%)	7(1.52%)
Inconclusive	18(9.9%)	23(10.4%)	10(17.2%)	51(9.78%)
Total	182(100%)	220(100%)	58(100%)	460(100%)



**Figure 1:** Simple Hyperplasia without atypia. Mild increase in gland stroma ratio with cystic dilation of glands lined by proliferative epithelium (H&E, 100X)



**Figure 2:** Well differentiated Endometrioid carcinoma (type1). Crowded atypical glands with glandular confluence and without intervening stroma (H&E, 100X)



**Figure 3:** Chronic Granulomatous endometritis. Well-formed granulomas in the stroma of the endometrium. (H&E, 400X)