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Histopathological patterns of endometrial lesions in patients with abnormal uterine Bleeding in rural area of Western Maharashtra

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Abstract

Background: Abnormal uterine bleeding (AUB) is considered one of the most common and challenging problems presenting to the gynecologist. Histopathological examination of endometrial biopsy is gold standard diagnostic tool in evaluation of AUB. Our study is aimed at determining the spectrum of endometrial pathologies in different age group patients presenting with AUB at our hospital which caters largely to women living in rural area.

Methods: This was a retrospective study done on patients presenting with AUB over the period Jan 2013- Dec.2015, in Department of Pathology, Ashwini rural medical college and research centre, Kumbhari, Tq. South Solapur, in Western Maharashtra(India). The histopathological findings of AUB were categorized into functional and organic causes. A detailed histological study was carried out and the findings were noted. A statistical analysis between age of presentation and a specific endometrial cause was done using chi-square test.

Results: The most common age group presenting with AUB was 41- 50 yrs (42%). Mean age for women presented with AUB was 44.2 years. The commonest pattern in these patients was normal cyclical endometrium (33.9%): Proliferative and secretory phase. The commonest pathology was endometrial hyperplasia (22.2%). Other causes identified were disordered proliferative endometrium(13.7%), atrophic endometrium(13.2%), benign endometrial polyp(8%), deficient secretory phase(3.3%), chronic endometritis(2.4%), and endometrial carcinoma(2.3%). It has been observed that, there was highly significant association between age group and histopathological diagnosis ($p<0.01$).

Conclusions: Histopathological examination of endometrium is gold standard diagnostic tool in evaluation of AUB and there is an age specific association of endometrial lesions.

Keywords: Abnormal uterine bleeding (AUB); dysfunctional uterine bleeding (DUB); Endometrial hyperplasia

Introduction

AUB is defined as a bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle or after menopause[1]. It is considered one of the most common and challenging problems presenting to the gynecologist. It contributes to about one-third of all outpatients coming to gynaecolgy OPD[2,3]. Heavy bleeding may affect a woman's health both medically and socially, causing problems such as iron deficiency in the developed world and of chronic illness in the developing world[4]. AUB includes both dysfunctional uterine bleeding (DUB) and bleeding from structural causes like fibroids, polyps, pregnancy complications and endometrial carcinoma[5]. DUB is defined as AUB without a demonstrable organic cause[6]. In most instances DUB is due to the occurrence of an anovulatory cycle[7]. It can be diagnosed after exclusion of structural, iatrogenic, medications, pshycological and systemic disorders by various diagnostic techniques[8]. Histopathological examination of endometrial biopsies is gold standard diagnostic tool in evaluation of AUB and a specific diagnosis helps to plan the therapy for successful, resourceful management of AUB, where hysterectomy is not the answer, it is the interplay of hormones[9].

Our study is aimed at determining the spectrum of endometrial pathologies in patients of different age group presenting with AUB at our hospital which caters largely to women living in rural area.

Materials and Methods

Source of data: This was a retrospective study done on patients presenting with AUB over the period Jan 2013-Dec. 2015, in Department of Pathology, Ashwini rural medical college and research centre, Kumbhari, Tq. South Solapur, in Western Maharashtra (India).

Inclusion criteria: Women presented with AUB in all age group.

Exclusion criteria: Patients with bleeding due to leiomyomas, cervical pathology, pregnancy related complications, and hemostatic disorders were excluded from the study.

Methods of collection of data: Total number of cases studied was 212 cases by applying inclusion and exclusion criteria. Ethical clearance was taken by ethical committee for this study. Endometrial specimens were obtained by either endometrial curetting or hysterectomy and fixed in 10% formalin. The specimens were processed routinely and stained with Haematoxylin and Eosin (H&E) stain. The histopathological findings of AUB were categorized into functional and organic causes. The functional

causes of AUB included in this study were normal cyclical endometrium (proliferative and secretory phases) and other abnormal changes in the endometrium like atrophic endometrium, disordered proliferative endometrium, deficient secretory phase and irregular shedding. Organic intrauterine lesions which were the cause of AUB in this study include chronic endometritis, endometrial hyperplasia, benign endometrial polyp, endometrial carcinoma and endometrial stromal nodule. A detailed histological study was carried out and the findings were noted. Descriptive statistics such as mean, SD and percentage was used. A statistical analysis between age and specific endometrial causes was done using chi - square test and p value <0.05 were considered as statistically significant.

Results

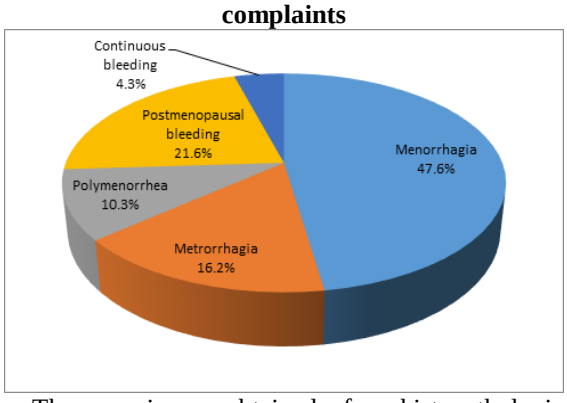
The age of patient ranged from 23-76 years. Mean age of women presented with AUB in our study was 44.2 years. Maximum number of patients 89 (42%) were in the age group 41-50 years, followed by 79 patients (37.2%) in age group of 31-40 years. Distribution of cases according to age group is shown in Table 1.

Table 1: Distribution of cases according to age group

Age group (Years)	No. of patients	Percentage
21-30	8	3.8
31-40	79	37.2
41-50	89	42
>50	36	17
Total	212	100

Data on the clinical presentation was not available for all cases. Out of 212 cases of AUB, the details of pattern of bleeding were available in only 185 patients. The predominant pattern of bleeding was menorrhagia 88 patients (47.6%) as shown in (Graph 1).

Graph 1: Distribution of cases according to complaints



The specimen obtained for histopathological examination, 119 samples (56.1%) obtained from hysterectomy specimen and rest 93 samples (43.9%) were obtained from endometrial curettage.

A total of 212 patients presented with AUB were analyzed. Out of 212 patients, 137 (64.6%) were due to functional causes as no organic pathology was found, while 75 (35.4%) cases showed definite endometrial pathology (Table 2). Out of 137 functional causes of AUB, proliferative endometrium 59 (43%) was most common pattern. Out of 75 organic causes, endometrial hyperplasia 47(62.7%) was most common.

Table 2: Distribution of cases of AUB according to cause

Cause of AUB	No. of patients (n=212)	Percentage
Functional Cause	137	64.6%
Organic cause	75	35.4%

Histopathological examination revealed various patterns in AUB as illustrated (Table 3). Normal cyclical pattern: proliferative and secretory phases (Fig. 1 & 2) were the most common and seen in 72 (33.9%) patients. Endometrial hyperplasia and disordered proliferative endometrium were the next common histological patterns seen in 47 (22.2%) and 29 (13.7%) cases, respectively. Out of the 47 cases of endometrial hyperplasia, 33 cases of simple hyperplasia without atypia (Fig. 3), 3 cases of simple hyperplasia with atypia, 10 cases of complex hyperplasia without atypia (Fig. 4) and a single case of complex hyperplasia with atypia (Fig. 5). Atrophic endometrium (Fig. 6) was seen in 28 (13.2%) cases, endometrial polyp (Fig. 7) 17 (8%) cases and endometrial carcinoma 5 (2.3%) cases. Out of 5 cases of endometrial carcinoma, 4 cases were well differentiated endometroid adenocarcinoma (Fig. 8) and one was moderately differentiated endometroid adenocarcinoma (Fig.9). One of the cases was of well differentiated endometroid adenocarcinoma showing squamous metaplasia (Fig. 10). In our study, only one case of endometrial stromal nodule (0.5%) (Fig. 11) was found.

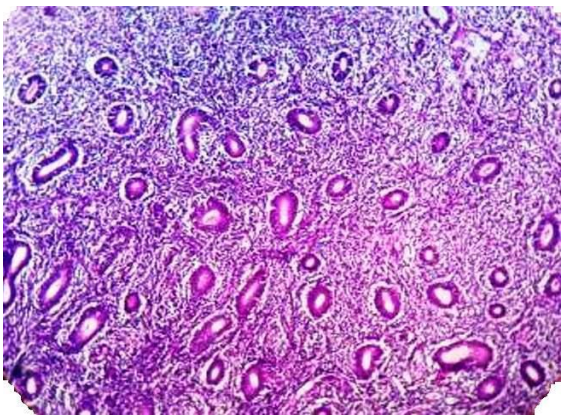


Fig. 1: Proliferative phase with round to tubular glands lined by low columnar epithelium surrounded by cellular stroma (H&E, 10X)

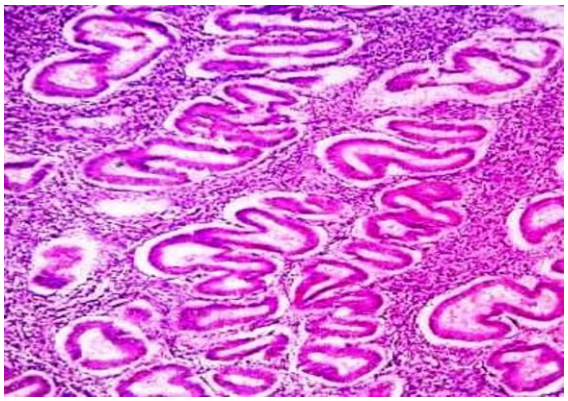


Fig. 2: Secretory phase with tortuous glands showing supranuclear vacuolations and secretions within glands (H&E, 10X)

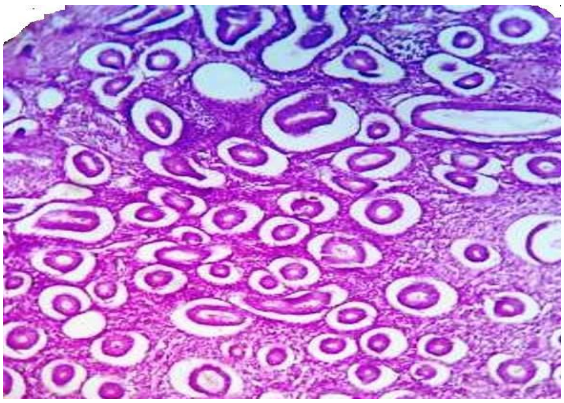


Fig. 3: Simple hyperplasia without atypia show glandular crowding and cystic glandular dilatation (H&E,10X)

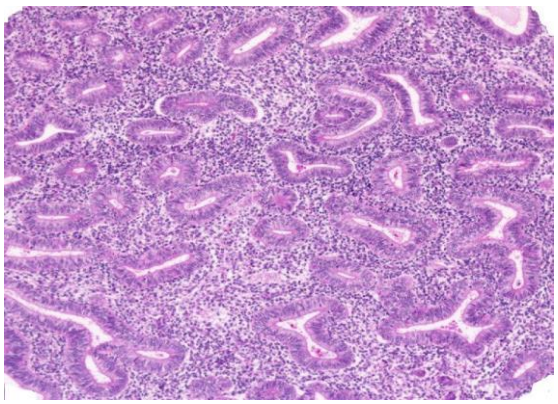


Fig. 4: Complex hyperplasia without atypia showing increase in the number and size of endometrial glands, branching and angulations of endometrial glands without nuclear atypia. (H&E,10X)

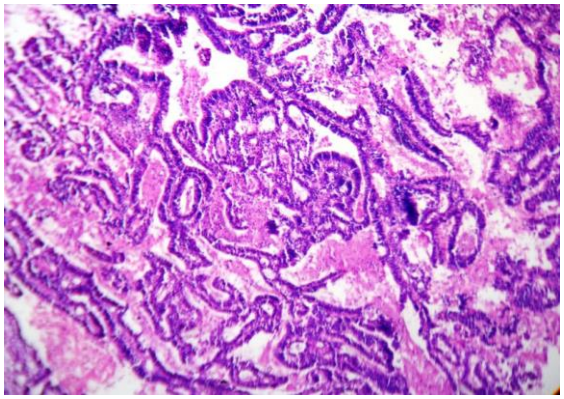


Fig. 5: Complex hyperplasia with atypia showing complex architecture with branching, angulations of endometrial glands with nuclear atypia (H&E,4X)

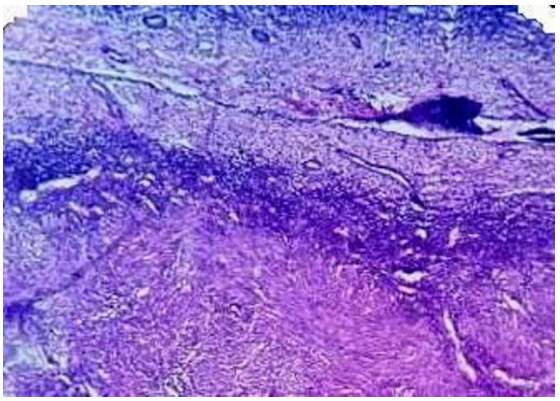


Fig. 6: Atrophic Endometrium showing very few glands against compact stroma (H&E,4X)

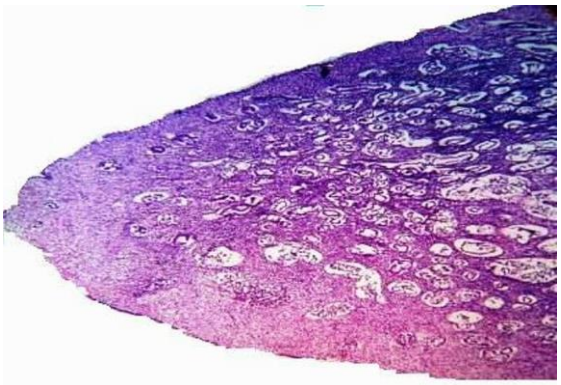


Fig. 7: Endometrial polyp with varying sizes glands with fibrovascular stroma (H & E, 4X)

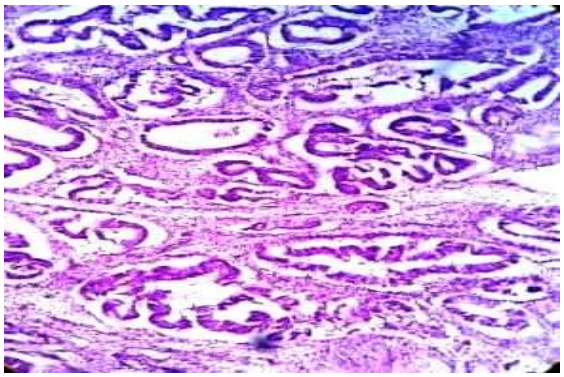


Fig. 8: Well differentiated endometroid adenocarcinoma, showing overcrowding of glands with nuclear atypia (H&E, 10X)

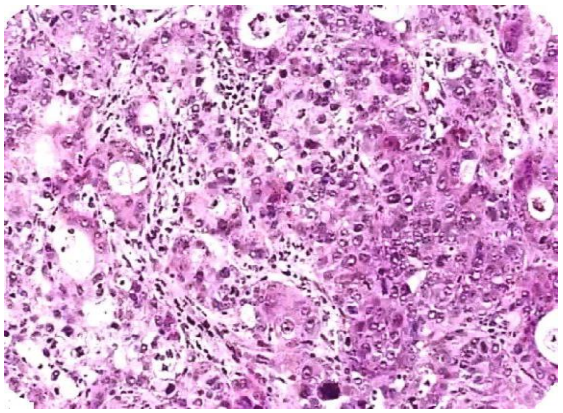


Fig. 9: Moderately differentiated endometroid adenocarcinoma, showing well-formed glands mixed with solid sheets of malignant cells with nuclear atypia (H&E, 40X)

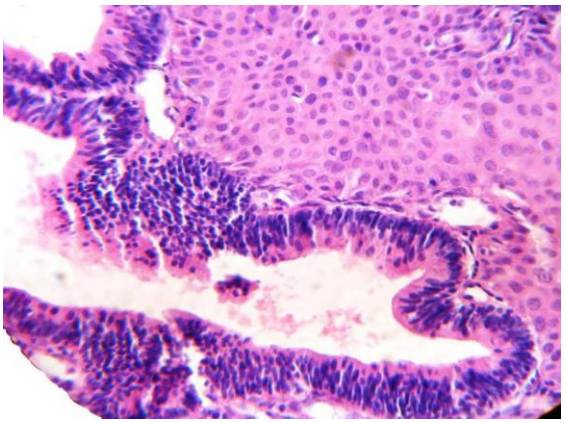


Fig. 10: Well differentiated endometroid adenocarcinoma with benign squamous metaplasia (H & E, 40X)

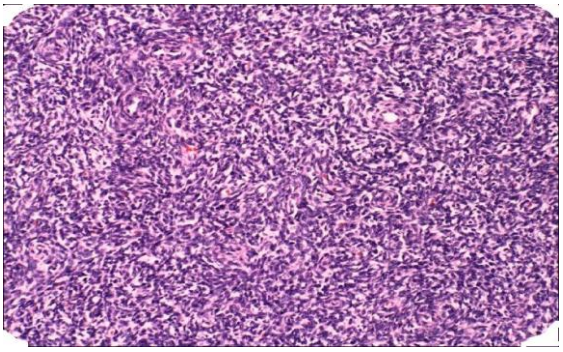


Fig. 11: Endometrial Stromal nodule with small, uniform cells with oval nuclei and scanty cytoplasm in sheets and focally arranged concentrically around spiral arterioles (H&E, 10X)

Table 3: Distribution of cases of AUB according to histological pattern

Histological diagnosis	Total no. of cases (n=212)	Percentage
Proliferative phase	59	27.8
Secretory phase	13	6.1
Atrophic	28	13.2
Disordered proliferative endometrium	29	13.7
Deficient secretory phase	7	3.3
Chronic Endometritis	5	2.4
Endometrial polyp	17	8
Simple hyperplasia without atypia	33	15.6
Simple hyperplasia with atypia	3	1.4
Complex hyperplasia without atypia	10	4.7
Complex hyperplasia with atypia	1	0.5
Endometrial carcinoma	5	2.3
Endometrial stromal nodule	1	0.5
Irregular shedding	1	0.5
Total	212	100

In this study, there was highly significant association between age group and histopathological diagnosis ($p<0.01$). Proliferative and secretory pattern was predominantly found in 35 (59.3%) and 13 (69.2%) patients respectively in age group of 31-40 years. Disordered proliferative endometrium 17 (58.6%), Endometrial hyperplasia 20 (42.5%), endometrial polyp 8 (47.1%) were common in 41-50 years age group. Atrophic endometrium and endometrial carcinoma were predominantly seen in >50 years age group.

Distribution of cases as per age group was illustrated in (Table 4).

Table 4: Histopathological patterns according to age group (n=212)

Histological diagnosis	Age group (years)				
	21-30	**31-40**	**41-50**	**>50**	**Total**
Proliferative Phase	6 (10.2%)	35(59.3%)	18(30.5%)	-	59
Secretory Phase	-	9 (69.2%)	4(30.8%)	-	13
Atrophic	-	1(3.6)	13 (46.4%)	14 (50%)	28
Disordered proliferative endometrium	-	6 (20.7%)	17 (58.6%)	6 (20.7%)	29
Deficient secretory phase	-	3 (42.9%)	4 (57.1%)	-	7
Chronic endometritis	-	1 (20%)	2 (40%)	2 (40%)	5
Endometrial polyp	1 (5.9%)	4 (23.5%)	8 (47.1%)	4 (23.5%)	17
Simple hyperplasia without atypia	1 (3%)	13(39.4%)	15 (45.5%)	4 (12.1%)	33
Simple hyperplasia with atypia	-	3 (100%)	-	-	3
Complex hyperplasia without atypia	-	3(30%)	5 (50%)	2 (20%)	10
Complex hyperplasia with atypia	-	-	-	1 (100%)	1
Endometrial carcinoma	-	-	2(40%)	3(60%)	5
Endometrial stromal nodule	-	-	1(100%)	-	1
Irregular shedding	-	1(100%)	-	-	1
Total	8	79	89	36	212

X^2 value= 90.76, df = 36, $p<0.01$

Discussion

Endometrium is mirror of hormonal status in women. Histological variation can be seen in endometrium according to age of women, phase of menstrual cycle and any another specific pathology[10]. In normal cycles, menstrual shedding is followed by endometrial proliferation under estrogenic stimulation. During this phase, the endometrial glands grow and become tortuous[11]. The secretory activity in the second half of the menstrual cycle is characterized by endothelial proliferation, thickening of the wall and coiling, forming the spiral arterioles on the ninth postovulatory day[11,12]. AUB is the most common & perplexing problem in women of all age groups.

In our study, the most common age group presenting with AUB was 41-50 years. Similar observations were also made by S. Vaidya et al[13], Agrawal et al[14], Doraiswami et al[15], Jairajpuri ZS et al[16]. An increased number of cases in this age group could be due to the fact that as menopause approaches, decreased number of ovarian follicles and their increased resistance to gonadotrophic stimulation, results in low level of oestrogen which cannot keep the normal endometrium growing[17]. The mean age of women presented with AUB in our study was 44.2years, which was comparable to 43 years by S. Vaidya et al[13] & 41 years by Agrawal et al[14].

Commonest bleeding pattern in our study were found to be menorrhagia 47.6%, followed by metrorrhagia 16.2%. Ara and Roohi[18], observed results comprising menorrhagia 49.06%, metrorrhagia 39.13%. Muzaffar et al[19] comprising menorrhagia 51.9% and metrorrhagia 35.4%.

Incidence of functional cause of AUB in our study was 64.6% which was comparable to Ara & Roohi[18] 62.1%, Muzaffar et al[19] 61%, Abdullah LS[20] 61.5%. Incidence of organic cause of AUB in our study was 35.4% which was higher than data published by S. Vaidya et al[13] 19%.

Histopathological evaluation of endometrial biopsies and curettage revealed various patterns ranging from physiological to pathological lesions of the

endometrium. In the present study, the most common pattern was normal cyclical endometrium: Proliferative (27.8%) and secretory (6.1%), total amounting to 33.9%. The incidence of 27.8% of proliferative endometrium compares with that of 26.23% by Bhatta S et al[21], 24.9% by Jairajpuri ZS et al[16], while higher incidence of 38.1% by Rupal Shah et al[22] and 33% by Riaz S et al[23]. Bleeding in proliferative phase is due to anovulatory cycle, due to progressive rise of estrogen to comparatively high level, which is followed by sudden fall in estrogen due to feedback inhibition of pituitary or of FSH secretion and bleeding results[24]. Proliferative pattern was predominantly found in 31-40 years of age group, similar to A. Khare et al[25].

In the present study secretory phase was found in 6.1% cases. The incidence was lower when compared with results of other study[16,24,26]. Bleeding in secretory phase is due to ovulatory dysfunctional uterine bleeding, is explained by inability of corpus luteum to synthesize adequate amount of progesterone, although it remains active throughout the entire period of 12-14 days[24].

Disordered proliferative endometrium which is an exaggeration of the normal proliferative phase without significant increase in the overall ratio of glands to stroma. It lies at one end of the spectrum of proliferative lesions of the endometrium and carcinoma at the other end with intervening stages of hyperplasias[15]. These are frequent findings on pathologic examination of endometrial biopsy samples in perimenopausal and postmenopausal women and indicate anovulatory cycles[27]. In this study, 29 (13.7%) cases were diagnosed, while in the literature, its incidence varies from 5.7% to 20.54%[15,16,20]. Similar to other studies[15,20], it was more common in the 41-50 years of age group.

Endometrial hyperplasia, an important cause of AUB, is defined as an increased proliferation of the endometrial glands relative to the stroma, resulting in an increased gland-to-stroma ratio. Endometrial hyperplasia deserves special attention because of its relationship with endometrial carcinoma. Endometrial Hyperplasia was classified according to World Health Organization (WHO), originally proposed by Kurman & Norris, into simple and complex on the basis of architecture and each was further subdivided into typical and atypical, based on cytology[28]. Only 1% of simple hyperplasia and 3% of complex hyperplasia without cytological atypia progresses to carcinoma where as 8% of simple hyperplasia and 29% of complex hyperplasia with cytological atypia do so. Hence reporting of endometrial hyperplasia into typical and atypical types has its prognostic and therapeutic implications with atypical type have increased incidence of progression to malignancy[29]. Complex hyperplasia with atypia has considerable morphologic overlap with well-differentiated endometrioid adenocarcinoma, and an accurate distinction between complex hyperplasia with atypia and cancer may not be possible. The mere presence of hyperplasia is not basis for hysterectomy. Most of cases of endometrial hyperplasia are treated by hormonal therapy and avoiding hysterectomy.

Unopposed exposure of the endometrium to esterogen leads to endometrial hyperplasia, which was second common cause of AUB in our study and observed in 22.2% of cases. Literature reports quite variable incidence of endometrial hyperplasia. Silander[30] found it to be 6.66%. Vaidya et al[13] and Khan et al[26] report it as 10.9% and 12.6% respectively in their studies. A rather high incidence of 25.5% was reported by Shilpa M.D[11]. Similar to other studies[13,16,21,27] observed that endometrial hyperplasia was the most frequent result in women aged 41-50 years, probably due to exposure to unopposed esterogen .

Prolonged oesterogen stimulation also results in formation of endometrial polyp[22]. The incidence of benign endometrial polyps was 8% in this study which was similar to Silander[30] 6.66%. The higher incidence was found in Parmar J et al[9] 10.78% & Doraswami S. et al[15] 11.2%. In our study, higher incidence of 47.1% was seen in 41–50 years age group; similar to other study[15,16]. Lower incidence of the endometrial polyps in the younger age group may be attributed to a possible spontaneous regression mechanism, which is characteristic of the cycling endometrium in reproductive age group[15].

Atrophic endometrium was observed in 28 (13.2%) cases of AUB, was comparable to 12% by Acharya et al[31]. Others report it as 1% by Khan et al[26] and 1.1% by Jairajpuri ZS et al[16]. Post-menopausal bleeding is frequently associated with an atrophic endometrium. The exact cause is not known. It is postulated that as a consequence of prolonged absence of any exogenous or endogenous estrogenic stimulation resulting in thin atrophic endometrium susceptible to minor injury and may be responsible for post-menopausal bleeding even in the absence of identifiable lesion[21].

In our study endometrial carcinoma was found in 5 (2.3%) patients, Riaz S et al**[23]** reported 1.0% & Abdullah LS et al**[20]** reported 1.8%. Lower incidences of 0.4% by Khan S, et al[26] and 0.47% by Jairajpuri ZS[16] had also been reported in the literature. Likewise, higher incidences of 4.4% and 5.71% have been reported by and Doraiswami et al[15] & Bhatta S et al[21] respectively. As reported in the literature[15,20,21,25], endometrial carcinoma was a commonly seen in more than 50 years of age group. Hence histopathological examination of endometrium should be done generously in women presenting with AUB after the age of 40 years to rule out malignant pathology.

In our study, only one case of Endometrial stromal nodule (0.5%) was found. In most of the cases it is impossible to differentiate between endometrial stromal nodule and low grade endometrial sarcoma on the basis of curettage specimens and thus distinction can only be

established on hysterectomy specimen on the basis of vascular and myometrial invasion[32]. In our case, the tumor is composed of small, uniform cells with oval nuclei and scanty cytoplasm in sheets and focally around arterioles without vascular and myometrial invasion, so it was categorized as endometrial stromal nodule.

Chronic endometritis, diagnosed in 2.4% of cases concurs with the reported incidence of 2.6% by Rupal shah et al[22]. Majority of them were >40years age group similar to study by Damale et al[24]. Chronic endometritis, characterized by irregular fibrotic stroma & infiltrate of lymphoplasmacytic cells has been known to follow pregnancy or abortion & may be the result of IUCD or accompanied by mucopurulent cervicitis & PID[23].

The other causes of AUB included in our study were cases of deficient secretory phase 7 (3.3%), while Rupal Shah et al[22] observed 5 (1.24%) patients. Irregular shedding was seen in only one case (0.5%) of AUB, while Gulia et al[27] reported 0.23%.

Histopathological examination of endometrial biopsies is gold standard diagnostic tool in evaluation of AUB and revealed various patterns ranging from normal endometrium to malignancy. Majority of the patients with AUB presented with normal cyclic endometrium, followed by endometrial hyperplasia and disordered proliferative endometrium. There was an age specific association of endometrial lesions. Normal cyclical proliferative endometrium was predominantly found in 31-40 years age group. Incidence of endometrial hyperplasia, disordered proliferative endometrium & endometrial polyp was high in 41-50 years of age group. The incidence of endometrial carcinoma was high after 50years of age group. These results clearly had shown that histopathological study is mandatory for all cases of AUB so as to rule out preneoplastic or malignant lesions. This simple study of endometrial curettage or biopsy can be of great help to gynecologists to plan therapy of a patient presented with AUB by close follow up of a patient who has precursor lesion or by timely surgical intervention in case of malignant lesions.

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