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Histomorphological Spectrum of Uterine Lesions in Patients Presenting with Abnormal Uterine Bleeding: Experience from a Tertiary Care Centre in Rural Haryana

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Abstract

Introduction: Abnormal uterine bleeding is the most common presenting complaint among women of all age groups attending the gynaecology out patient department. Abnormal uterine bleeding is a term used to describe any type of bleeding that does not fall within the normal ranges for amount, frequency, duration and cyclicity. Dysfunctional uterine bleeding is a clinical term used to describe abnormal uterine bleeding not attributable to any underlying organic lesions like Leiomyoma, Inflammation and Polyps. The causes of abnormal uterine bleeding vary with age. The present study was carried out to study the histomorphological spectrum of uterine lesions in women of all age groups presenting with abnormal uterine bleeding and to classify the lesions as Dysfunctional uterine bleeding or Organic causes. *Materials and Methods:* The retrospective study included a total of 163 specimens received either as endometrial curettings or hysterectomy specimens belonging to all the age groups (reproductive, perimenopausal and post menopausal), presenting with complaints of abnormal uterine bleeding was carried out in the Department of Pathology at a tertiary care centre in rural Haryana. *Results:* Maximum cases (39.26%) presenting with abnormal uterine bleeding were seen in the age group 31-40 years. Out of total 163 cases, there were 91 (55.82%) DUB cases, 69 (42.33%) were organic lesions and 3 (1.84%) cases were inadequate for opinion. Proliferative phase was seen in maximum cases of dysfunctional uterine bleeding (36/91 cases) and leiomyoma was the commonest pathology in organic lesions category (24/69 cases). *Conclusion:* Study of histomorphological pattern of the endometrium in patients of all the age groups presenting with abnormal uterine bleeding helps to diagnose and categorize the lesions as Dysfunctional uterine bleeding or Organic causes, to plan specific treatment modality, to assess therapeutic response and to rule out carcinoma.

Keywords: Abnormal Uterine Bleeding; Dysfunctional Uterine Bleeding; Hyperplasia; Leiomyoma; Normal Cyclical Endometrium.

Introduction

Abnormal uterine bleeding (AUB) is one of the frequently encountered, significant and at times alarming condition in women [1]. AUB is defined as a bleeding pattern that differs in frequency, duration and amount from a pattern observed during a normal menstrual cycle [2]. The International Federation of Gynaecology and Obstetrics working group on menstrual disorders has developed a classification system (PALM- COEIN) for causes of AUB in non gravid women of reproductive age. According to it, the nine main categories are Polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic and not yet classified [3]. AUB not associated with an organic cause is called Dysfunctional uterine bleeding (DUB) [4].

Histopathological categorization of endometrial biopsies and curettings by the light microscope is considered the gold standard for diagnosis of the etiology of AUB, because of the relative convenience

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and safety of obtaining samples along with reasonable reporting time and diagnostic accuracy [5]. In this study, we analyzed the different histomorphological patterns of endometrium and organic lesions among women of various age groups presenting with AUB.

Materials and Methods

The retrospective study included a total of 163 cases of all the age groups (reproductive, perimenopausal and postmenopausal) presenting with AUB in the Gynaecology Outpatient department (OPD) over a period of one year. The endometrial curettings or the hysterectomy specimens with/without salpingo oophorectomy for diagnostic and/or therapeutic purpose were received in the Department of Pathology at a tertiary care centre in rural Haryana.

The detailed clinical history, pattern of bleeding, use of oral contraceptive pills or other hormones, physical examination findings and results of all the relevant investigations were recorded. The pattern of bleeding was classified as menorrhagia, menometrorrhagia, polymenorrhea and postmenopausal bleeding.

Total 128 endometrial curettings and 35 hysterectomy specimens were received. If in a patient both endometrial curettings and subsequently hysterectomy was done, only hysterectomy specimen was included in the study. This way duplication of cases was ruled out and final diagnosis obtained by histopathological examination of hysterectomy specimen was considered for histomorphological spectrum of AUB. Total 128 endometrial curettings and 35 hysterectomy specimens received were fixed in 10% neutral buffered formalin. After gross examination of specimens, routine histopathological processing was done, followed by staining of sections with Hematoxylin and Eosin (H&E) stain. Histopathological examination of endometrial curettings and hysterectomy specimen was done and the findings were correlated with the clinical details and diagnosis.

The specimen in which no endometrial tissue was seen or no conclusion could be arrived at despite the presence of some tissue, were categorized as inadequate for evaluation.

Results

A total of 163 cases of AUB were studied. The patients' age ranged from 19 years to 67 years with mean age of 38.5 years. Patients were divided into three broad age groups

Table 1: Categorization and distribution of various lesions causing Abnormal Uterine Bleeding in reproductive, perimenopausal and postmenopausal age groups

S. No.	Category of Lesions	Age Group (In Years) Reproductive Age Group (≤ 40)	Perimenopausal Age Group (41-50)	Postmenopausal Age Group (>50)	Total
1.	Dysfunctional Uterine Bleeding	64	23	4	91
2.	Organic	35	29	4	69
3.	Inadequate For Opinion	-	1	2	3
	Total	99	54	10	163

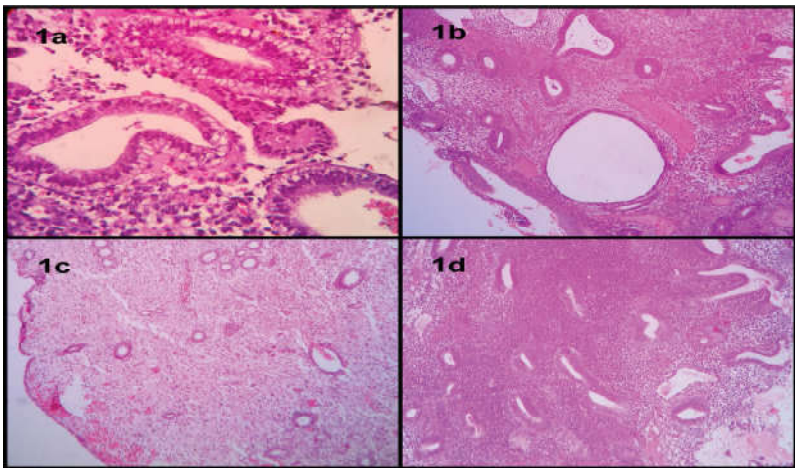

Fig. 1a: Secretory endometrium; Endometrial glands show subnuclear vacuolization and nuclear palisading. The stroma is edematous, (H& E; 400x). **b: Disordered proliferative phase;** Most of the endometrium is in proliferative phase but a few scattered glands are enlarged and irregularly shaped, (H& E; 100x). **c: Atrophic endometrium;** Scanty endometrial glands, round to cystically dilated, lined by flattened or cuboidal cells, (H& E; 100x). **d: Irregular ripening;** Glands show secretory changes but stroma appears compact, (H& E; 100x)

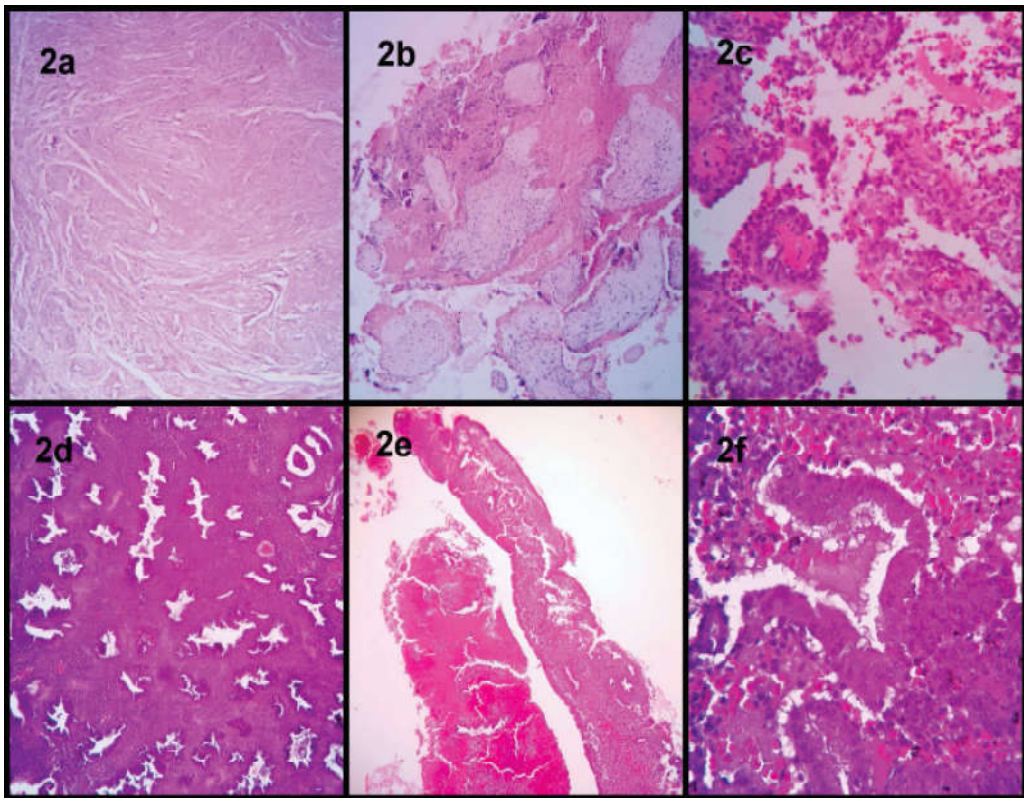

Fig. 2a: Leiomyoma; Whorled, anastomosing fascicles of uniform fusiform smooth muscle cells, (H& E; 100x). **b: Products of conception;** Chorionic villi, hyalinised at places showing dystrophic calcification focally (H& E; 100x). **c: Chronic Endometritis;** Aggregates of lymphocytes and plasma cells infiltrating the endometrial glands and stromal tissue (H& E; 400x). **d: Complex endometrial hyperplasia without atypia;** Glands show complex glandular outlines and are crowded. There is no cytologic atypia (H& E; 40x). **e: Endometrial polyp;** Secretory glands surrounded by dense stroma and dilated blood vessels. The tissue fragment is lined on three sides by endometrial lining (H& E; 40x). **f: Endometrial adenocarcinoma;** Well formed glands and masses of solid epithelium. The nuclei are enlarged with irregular, coarse nuclear chromatin and prominent nucleoli (H& E; 400x).

Table 2: Histomorphological spectrum of lesions in Abnormal Uterine Bleeding cases and their distribution in various age groups

S. No	Histopathological Diagnosis	Age (in years)						Total
		≤ 20	21-30	31-40	41-50	51-60	61-70	
1.	Proliferative phase	-	13	14	9	-	-	36
2.	Leiomyoma	-	-	6	16	2	-	24
3.	Secretory phase	1	2	15	6	-	-	24
4.	Products of conception	1	12	6	-	-	-	19
5.	Disordered proliferative phase	-	5	3	2	-	-	10
6.	Atrophic endometrium	-	-	-	3	2	2	7
7.	Endometritis	-	-	5	1	-	-	6
8.	Irregular shedding	-	-	5	1	-	-	6
9.	Simple hyperplasia without atypia	-	-	-	5	1	-	6
10.	Adenomyosis	-	-	3	1	1	-	5
11.	Irregular ripening	-	-	3	1	-	-	4
12.	Endometrial polyp	-	-	1	2	-	-	3
13.	Pill endometrium	-	1	2	-	-	-	3
14.	Complex hyperplasia without atypia	-	-	-	3	-	-	3
15.	Complex hyperplasia with atypia	-	-	-	1	-	-	1
16.	Endometrial adenocarcinoma	-	-	-	1	-	-	1
17.	Eosinophilic syncytial metaplasia	-	-	-	1	-	-	1
18.	Ovarian endometriosis	-	-	1	-	-	-	1
19.	Inadequate for opinion	-	-	-	1	2	-	3
	Total	2	33	64	54	8	2	163

Table 3: Histomorphological spectrum and frequency of various Dysfunctional Uterine Bleeding lesions

S. No.	Dysfunctional Uterine Bleeding Lesions	No. of Cases
1.	Proliferative phase	36
2.	Secretory phase	24
3.	Disordered proliferative phase	10
4.	Atrophic endometrium	7
5.	Irregular shedding	6
6.	Irregular ripening	4
7.	Pill endometrium	3
8.	Eosinophilic syncytial metaplasia	1
	Total	91

Table 4: Histomorphological spectrum and frequency of various Organic lesions

S. No.	Organic Lesions	No. of Cases
1.	Leiomyoma	24
2.	Products of conception	19
3.	Endometritis	6
4.	Simple hyperplasia without atypia	6
5.	Adenomyosis	5
6.	Complex hyperplasia without atypia	3
7.	Endometrial polyp	3
8.	Endometrial adenocarcinoma	1
9.	Complex hyperplasia with atypia	1
10.	Ovarian endometriosis	1
	Total	69

1. Reproductive age group (≤40 years; 99/163 cases)
2. Perimenopausal age group (40-50 years; 54/163 cases)
3. Post menopausal age group (>50 yrs; 10/163 cases).

Overall, the most common pattern of bleeding was menorrhagia. Total 128 endometrial curettings and 35 hysterectomy specimens were received. Out of total 163 cases of AUB, 91 cases were categorized as DUB, 69 cases were organic lesions and three cases were inadequate for opinion (Table 1). Majority of cases (64/163 cases) presented in the age group, 31-40 years. The histomorphological spectrum of lesions comprised 19 different histopathological diagnoses (Table 2), which were further grouped into three categories. The 91 DUB cases comprised 8 histopathological diagnoses (Table 3) and proliferative phase was seen in maximum cases (36/91 cases), followed by secretory phase (24/91 cases) (Figure 1a) and disordered proliferative phase (10/91 cases) (Figure 1b). Atrophic endometrium was seen in 7 cases (Figure 1c). Irregular shedding and irregular ripening (Figure 1d) were seen in 6 and 4 cases respectively. Pill endometrium was encountered in 3 cases; one case of eosinophilic syncytial metaplasia was also seen. Maximum numbers of DUB cases were seen in the reproductive age group, (64/100 cases) (Table 1). The organic causes of AUB were seen in 69 cases. Maximum organic causes were seen in the reproductive age group (35/69 cases). The number of organic lesions in the perimenopausal age group was slightly less; (29/69 cases). The most common organic lesion encountered was leiomyoma (Figure 2a), (24/69 cases); mainly seen in the perimenopausal age group, followed by retained products of conception (Figure 2b) (19/69 cases). Endometritis (Figure 2c) was seen in 6 cases. Endometrial hyperplasias were seen in total 10 cases, out of which 6 cases showed simple hyperplasia without atypia, 3 cases showed complex hyperplasia without atypia (Figure 2d) and in one case features of complex hyperplasia with atypia were seen. Adenomyosis as organic cause of AUB was seen in 5 cases. Three cases of endometrial polyp (Figure 2e) and one case each of endometrial adenocarcinoma (Figure 2f) and ovarian endometriosis were seen.

Discussion

For evaluation of endometrial curettings, complete clinical details, menstrual details along with history of exogenous hormones or drugs is required [6]. Aetiology of AUB relates to the patient's age as to whether the patient is premenopausal, perimenopausal or post menopausal [7].

In our study, maximum number of AUB cases were seen in 31- 40 years age group, where as 41- 50 years was the commonest age group for AUB in other studies [7,8,9,10]. This may be due to the presence of 19 cases

of retained products of conception in our study, which were obviously seen in reproductive age group patients. The perimenopausal age group comprised 33.13% cases in our study which is comparable to those reported by Saraswathi D *et al.*[11] (33.5%) and Mahapatra *et al.*[12] (37.9%)

In our study, the DUB as a cause of AUB was seen in 55.82% cases, organic lesions were seen in 42.33% cases and 1.84% cases were inadequate for evaluation.

The most common pattern in the present study was normal cyclical endometrium; proliferative phase (22.08%) and secretory phase (14.72%) total amounting to 36.8% AUB cases. This is comparable to the incidence of normal cyclical endometrium by Shah *et al.* [13] (47.3%) and Abdullah LS *et al.*[14] (46.6%).Our finding of proliferative phase in 22.08% cases is very much in alliance with the studies done by Saraswathi D *et al.*[11] (21.74%) and Jairajpuri ZS *et al.*[15] (24%) but contrasts with the higher incidences of 33% by Riaz S *et al.*[16], 38.1% by Shah *et al.*[13] and 42% by Patil SG *et al.*[17] The incidence of 14.72% of secretory pattern in our study is in alliance with that of 10.7% by Dangal G[18], 13.8% by Taib- Al Neaimy WM *et al.*[19] and 14% by Patil SG *et al* [17].

In the present study, out of total 35 hysterectomy specimens, 24 cases (68.57%) were leiomyomas, followed by 5 cases (14.28%) of adenomyosis. This is in contrast to study by Sawke NG *et al.*[20] who found maximum number of histopathologic diagnosis of adenomyosis (31%) followed by leiomyoma (25%). Gupta *et al.*[21] observed leiomyoma as cause of AUB in 53% of cases. Most other studies showed leiomyoma as most common lesion with a variable frequency [22,23,24] and as high as 78% [25]. Leiomyoma and adenomyosis are the leading causes of AUB in hysterectomy specimens [20].

Retained products of conception were seen in 11.65% cases and all belonged to the reproductive age group. Hence patients presenting in this age group with AUB should be investigated and evaluated for pregnancy by doing urine gravindex test.[26] Endometrial hyperplasia as a cause of AUB was seen in 6.13% cases. This is comparable to the incidence observed by Jetley *et al* [27]. However, in the perimenopausal age group, endometrial hyperplasia was seen in 16.98% cases, which is comparable to that observed by More S *et al.* [7] (19.75%) and less as compared to Slobada L *et al.*[28] (22.6%), Dangal G [18] (23%), Khare A [29] (36.2%). Doraiswami S [8] observed a high incidence (68%) of endometrial hyperplasia in the same age group. Nine out of 10 cases of endometrial hyperplasia were in the perimenopausal age group. High incidence of endometrial hyperplasia in perimenopausal age group may be due to persistent exposure of endometrium to the estrogenic stimulus in the setting of failure of ovulation during this period [7]. Identification of endometrial hyperplasia is important as it is thought to be the precursor of endometrial carcinoma [30]. Simple hyperplasia without atypia was the most common type of endometrial hyperplasia and was seen in 60% cases. Similar observation was made by Vakiani *et al.* [31] (71%), Pilli *et al.* [32] (73%) and Bolde *et al.* [4] (85%). In our study, there was only one case of complex hyperplasia with atypia which is in accordance to that observed by More *et al.*[7]. However, this is in contrast to the findings of Khare A[29] who observed a higher incidence of 33.3%.

Ten cases (6.13%) showed disordered proliferative pattern in our study which is in accordance with Jetley S *et al.*. [27] (6.8%), More S *et al.*[7] (7.42%) and Abdullah *et al.*[14] (8.5%). Due to chronic anovulation, there is widespread dilatation of glands, although the gland to stroma ratio remains normal[33]. It resembles simple hyperplasia, but the process is focal rather than diffuse [7].

Atrophic endometrium was seen in 4.29% of cases included in our study and the patients belonged to either perimenopausal or post menopausal age groups. The incidence in present study is comparable with the results seen by Abdullah *et al.*[14] (3.1%), Sajitha *et al.*[34] (4.7%), Mahapatra *et al.*[12] (5%) and Vaidya *et al.*[35] (5.1%). It is postulated that the thin walled veins superficial to the cystically dilated endometrial glands are made vulnerable to injury which leads to bleeding [36].

Luteal phase abnormalities; irregular shedding and irregular ripening were seen in 3.68% and 2.45% cases. In irregular shedding, a mixed pattern of proliferative and secretory phase is seen at least 5 days after the onset of bleeding. This occurs due to persistence of corpus luteum [33]. In irregular ripening, glands and stroma show discordant development due to insufficient progesterone secretion by the corpus luteum. [37]. Studies by Jaitley *et al.*[27] and Kaur *et al.*[33] show 1.3% and 8.5% cases with irregular ripening.

Chronic endometritis was seen in 3.68% cases and all except one case were seen in reproductive age group. It concurs with the reported incidence of 2% by Saadia A *et al.* [38] and 1.2% by Patil SG *et al.*[17] Higher incidences of endometritis were reported by Khare A [29] (6.4%) and Jetley *et al.* [27] (9.1%). One of our case revealed granulomatous endometritis compatible with tuberculous etiology. More S *et al.*[7] found tuberculous endometritis in 2 of the 6 chronic

endometritis cases. Chronic endometritis has been known to follow pregnancy or abortion and may be the result of IUCD or accompanied by Pelvic inflammatory disease [13].

Pill endometrium was seen in 3 cases (1.84%), all in reproductive age group. Kaur P *et al.* [33] found a higher incidence of 7% cases with progestin effect in their study. Khare A [29] found 4.3% cases with progestin effect in reproductive age group and 8.5% in perimenopausal age group.

The incidence of endometrial polyp was 1.84% in our study. More *et al.*[7], Jetley *et al.*[27], and Shah *et al.*[13] observed comparable incidences of 1.48%, 2.70%, and 2.63% respectively. Higher incidences of endometrial polyp were reported by Patil SG *et al.* [17] (5%), Doraiswami S [8] (11.2%). Polyps in endometrial curettage specimens can be identified as polypoidal fragments lined with epithelium on three sides, fibrous stroma and thick walled blood vessels [7].

Ovarian endometriosis was seen in one case. The chocolate cysts can enlarge so that the residual ovarian tissue fails to respond to hormonal stimulation resulting in ovulatory failure. This may lead to abnormal uterine bleeding. Brenner PF [39] has identified endometrosis as a cause of abnormal uterine bleeding.

One case (0.61%) of endometrial carcinoma was diagnosed on endometrial curettings in our study. Similar low incidences were seen by Mahapatra *et al.* [12] (0.7%), Kaur P *et al.* [33] (1%) and Baral *et al.* [36] (1%).

Three cases in this study were inadequate for opinion. It has been observed that an inadequate endometrial sample may be sufficient to rule out endometrial hyperplasia because of its high negative predictive value [7].

Conclusion

A wide spectrum of histomorphological patterns can be obtained in AUB cases ranging from normal cyclical endometrium, organic lesions, premalignant to malignant lesions. The various lesions seem to predominate in specific age groups. Study of histomorphological pattern of the endometrium in patients of all age group presenting with AUB helps to diagnose and categorize the lesions as DUB or Organic causes, to plan specific treatment modality, to assess therapeutic response and to rule out carcinoma. Endometrial biopsy and curettings is a valuable OPD procedure for assessing AUB cases due to relative ease, safety and accessibility of procedure and reasonable reporting time and diagnostic accuracy.

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