Original Article

Spectrum of Endometrial Lesions in Patients with Abnormal Uterine Bleeding: A Histopathological Study

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is the most common menstrual problem in women of developing countries. Endometrial curettage followed by histopathological examination can be used for definitive diagnosis of AUB. This study was conducted to assess endometrial causes of AUB on histopathological examination and its association with different age groups presenting with AUB.

Methods: This study was conducted at Department of Pathology, Narayana medical college and hospital, Nellore, India on 264 women presenting with AUB over a period of 1 year from January to December 2015. A statistical analysis between endometrial histopathology and age of presentation was done using chi square test.

Result: Most of the patients with AUB presented in 30 -40 years age group (37.5%) with menorrhagia as the commonest bleeding pattern. The cause of AUB was determined 261 out of 264 endometrial samples as 3 specimens were inadequate for evaluation. Out of the remaining 261 cases, 223 (84.47%) cases were due to functional causes while the remaining 38 cases (14.39%) showed definite endometrial pathology (organic AUB). Endometrial causes of AUB and age of presentation showed positive association with p value <0.05.

Conclusion: Endometrial curettage is recommended in women of perimenopausal and menopausal age group presenting with AUB to rule out pre-neoplastic conditions and malignancy.

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Introduction

Abnormal uterine bleeding (AUB) is one of the most challenging and common problem for women of all ages consulting a gynecologist. [1] Abnormal uterine bleeding denotes bleeding pattern that does not fall within normal ranges for amount, frequency, duration and cyclicity.[2] It has led to many hysterectomy procedures without definitive diagnosis. Also, early diagnosis and timely treatment of AUB is important to rule out malignancy and to confirm the exact nature of lesion. Various diagnostic techniques like transabdominal/ transvaginal ultrasonography, hysteroscopy & dilatation and curettage are available for evaluation of AUB.[3] Out of these endometrial curettage is considered most cost effective method and also can pick small lesions. With limited resources, in developing countries like India, it is the most commonly used method of assessing AUB .[4] This study was done to evaluate the endometrial causes of AUB and to determine various histopathological patterns associated with AUB in different age groups.

Materials and Methods

This study was conducted by Department of Pathology, Narayana medical college and hospital, Nellore, Andhra Pradesh, India in 264 women presenting with AUB over a period of 1 year from January to December 2015.

Inclusion criteria- All endometrial curettage specimens received for AUB in reproductive and postmenopausal women were included in the study.

Exclusion criteria- Endometrial curettage done for evaluation of pregnancy related complications (threatened, incomplete or missed abortion, gestational trophoblastic disease, ectopic pregnancy, etc). AUB due to cervical or vaginal pathology. Systemic diseases that may cause abnormal uterine bleeding (hypothyroidism, cirrhosis, and coagulation disorders) were excluded from the study.

The endometrial tissue obtained by dilatation and curettage, were preserved in 10% buffered formalin and clinical details of the patient was obtained from the requisition forms and case sheets. Thereafter the specimen was processed by paraffin embedding and hematoxylin and eosin (H&E) staining. Microscopic evaluation and histopathology reporting were done by two pathologists, individually to reduce observer bias.

Data was compiled and analyzed using the statistical package SPSS version 19 for MS- Windows (SPSS Inc., Chicago, IL). Pearson chi square test is used to analyze the data and p-value is calculated wherever required. P-value of 0.05 or less was considered statistically significant.

Result

A total of 264 endometrial curetting from patients with AUB were analyzed for histopathology, age of presentation and cause of bleeding.

In our study, age of patients presenting with AUB ranged from 21-62 years. These 264 cases of AUB were categorized into five age groups with most of them present in 30 -40 years (37.5%) and perimenopausal age group (40-50 years, 36%). Most common pattern of bleeding was menorrhagia (62.5%) followed by metorrhagia (14%), post- menopausal bleeding (12%), menometorrhagia (6.1%) and polymenorrhea (5.3%) as depicted in figure 1.

The cause of AUB was determined in 261 out of 264 endometrial samples as 3 specimens were inadequate for evaluation. Out of the remaining 261 cases, 223 (84.47%) cases were due to functional causes as no organic pathology was found, while the remaining 38 cases (14.39%) showed definite endometrial pathology (organic AUB).

Out of 261 cases of functional AUB (table 1), proliferative pattern (49.62%) was most predominant followed by secretory pattern (23.48%), atrophic pattern (6.81%), irregular ripening (1.13%), irregular shedding (1.13%), luteal phase defect (2.26%).

Out of 38 cases of organic AUB (table1), Disordered proliferative endometrium (figure 2) was present in 10 patients. Twenty one cases of hyperplasia were diagnosed with 16 cases without atypia (Figure 3) and five cases showing atypia (Figure 4). Three cases presented with endometritis with one case possessing features of granulomatous endometritis. Two cases were of endometrial polyp with one showing features of hyperplastic polyp and other showing features of functional polyp. Adenocarcinoma endometrium was diagnosed in 2 cases of organic causes of AUB with one case of endometrioid carcinoma and one case of serous carcinoma (Figure 5).

Cyclic pattern of endometrium was mostly seen in 31-40 years of age i.e. reproductive age group, disordered proliferative pattern, hyperplasia and carcinoma were observed in perimenopausal and menopausal age group. This association is statistically significant with p value - 0.001

Discussion

AUB is the most commonly encountered symptom that confronts the gynecologist, thus posing a considerable health risk. It includes bleeding from structural/ organic causes and dysfunctional uterine bleeding (DUB). Structural causes include fibroids, polyps, hyperplasia, endometritis, endometrial carcinoma, pregnancy complications, etc.

Table 1: Age wise distribution of cases of AUB with histopathological pattern of endometrium.

Histopathology of endometrium	Age Group (in years)					Total
	20 -30	31-40	41-50	51-60	61-70	
Proliferative	4(3.1%)	56(42.7%)	46(35.1%)	23(17.6%)	2 (1.5%)	131(49.62%)
Secretory	3(4.8%)	27(43.5%)	22(35.5%)	10(16.1%)	0	62(23.48%)
Atrophic	0	0	3(16.7%)	11(61.1%)	4(22.2%)	18(6.81%)
Irregular ripening	0	1 (33.3%)	0	2 (66.7%)	0	3 (1.13%)
Irregular shedding	0	1 (33.3%)	1(33.3%)	1 (33.3%)	0	3 (1.13%)
Luteal phase defect	0	3 (50.0%)	3(50.0%)	0	0	6 (2.27%)
Disordered proliferative	1(10%)	2(20%)	7 (70%)	0	0	10(3.79%)
Hyperplasia without atypia	0	7 (43.7%)	4 (25.0%)	4 (25%)	1 (6.2%)	16 (6.06%)
Hyperplasia with atypia	0	1 (20.0%)	2 (40.0%)	2 (40.0%)	0	5 (1.89%)
Non specific Endometritis	0	0	2 (100%)	0	0	2 (0.76%)
Granulomatous endometritis	0	0	1 (100%)	0	0	1 (0.38%)
Endometrial polyp	0	1 (50.0%)	0	1 (50.0%)	0	2 (0.76%)
Adenocarcinoma	0	0	1(50.0%)	1 (50.0%)	0	2 (0.76%)
Inconclusive	0	0	3 (100%)	0	0	3 (1.13%)
Total	**8 (3.03%)**	**99 (37.50%)**	**95 (35.98%)**	**55 (20.83%)**	**7 (2.65%)**	**264**
p- value						**0.001**

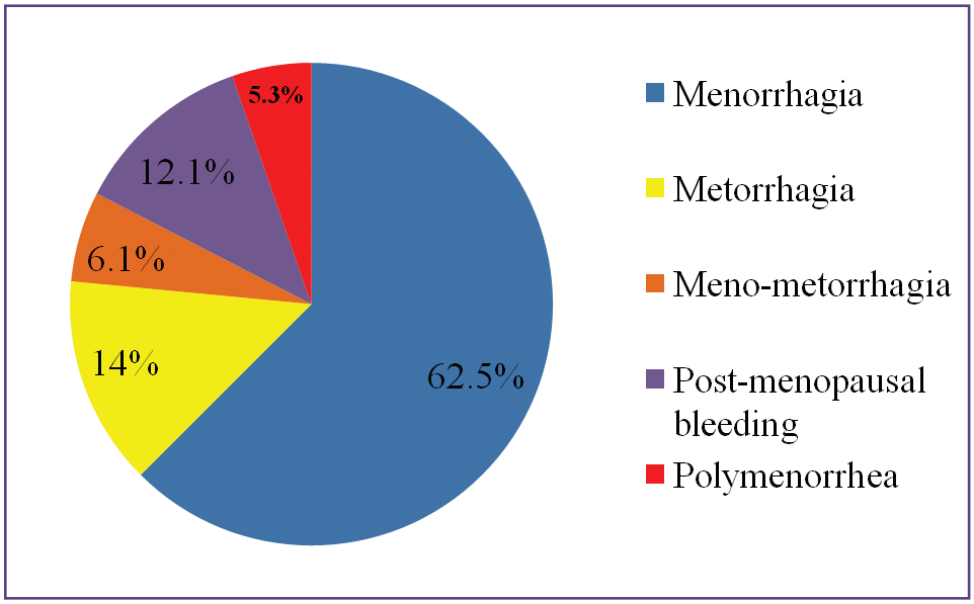

Fig. 1: Bleeding pattern of abnormal uterine bleeding.

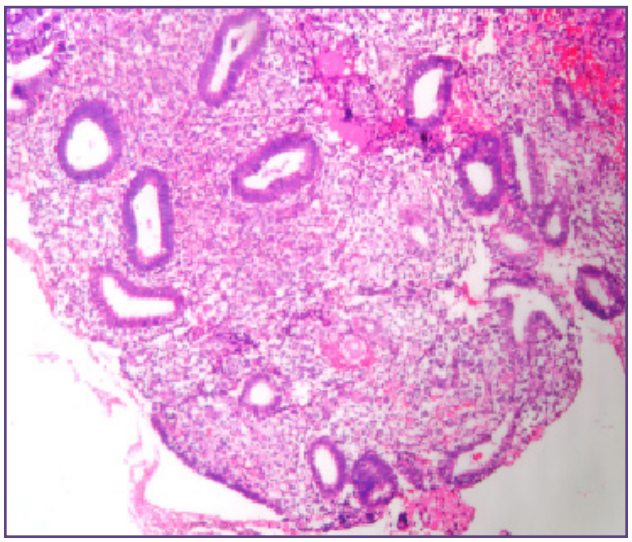

Fig. 2: Disordered proliferative endometrium, showing focal glandular dilatation of proliferative phase glands. (H&E, x100) .

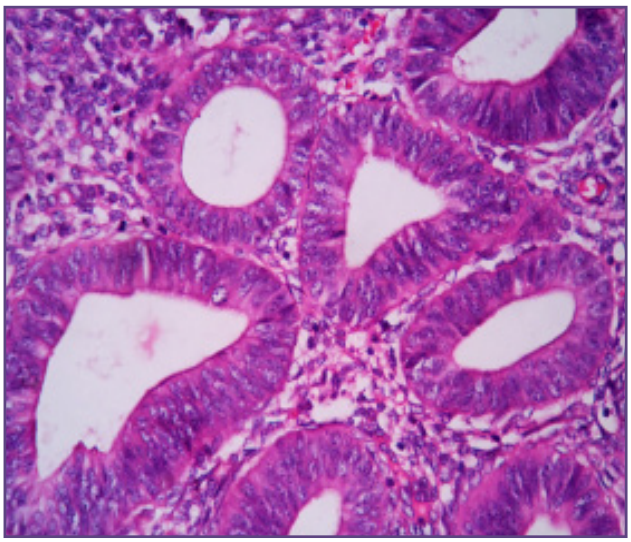

Fig. 3: Endometrial hyperplasia without atypia showing crowding of endometrial glands with compact stroma (H&E, x400).

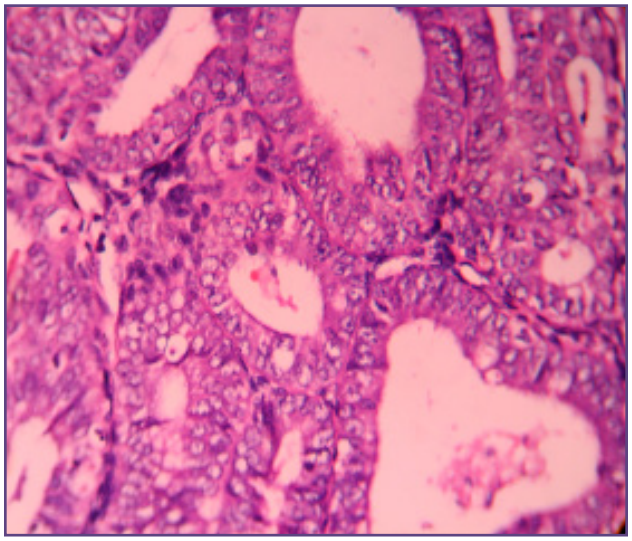

Fig. 4: Endometrial hyperplasia with atypia showing closely packed endometrial glands with sparse intervening stroma. Lining epithelial cells show cytological atypia, high nucleo-cytoplasmic ratio and irregular clumping of chromatin. (H&E, x400)

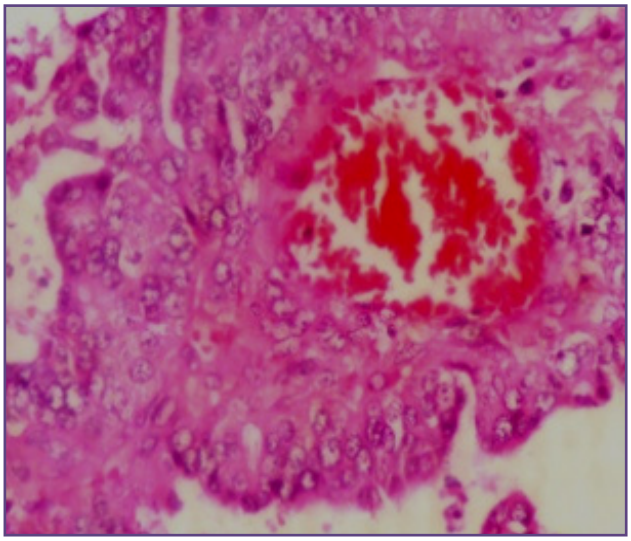

Fig. 5: Serous carcinoma endometrium showing broad papillae lined by atypical cells with irregular nuclei and vesicular nuclei with prominent nucleoli (H&E, x400).

[5] DUB is an abnormal uterine bleeding without any demonstrable organic cause and is diagnosed only after exclusion of structural, iatrogenic and systemic disorders by various diagnostic techniques. DUB, in most occasions, is due to the occurrence of an anovulatory cycle. [6, 7]

The etiology of AUB is different for various age groups – adolescent (12-18 years), reproductive (19-40 years), perimenopausal (41-50 years) and post menopausal age group (>50 years).[8] The youngest patient in this study was 21 year old female (reproductive age group) and eldest was 67 year old post menopausal women. No case was encountered in adolescent girls. This may be because abnormal bleeding in adolescent girls resolves spontaneously and also invasive procedures are avoided in this age group.

Maximum incidence of AUB in our study was observed in reproductive age group, followed by perimenopausal and post- menopausal. We also observed that increasing age was

significantly associated with aggressiveness of the lesion. Cyclic endometrium (90/193; 46.63%) was more common in reproductive age where as disordered proliferative endometrium (7/10; 70%) and hyperplasia (13/21; 61.9%) was commonly encountered in perimenopausal and menopausal women. All cases of endometrial carcinoma were noticed in age group of more than forty years. Similar distribution of cases was observed by Abid et al.[8] Increased prevalence of lesions in higher age group could be due to the fact that endometrium is exposed to estrogen for a longer period of time as compared to patients with younger age group.

The most common pattern of bleeding noticed was menorrhagia, followed by metorrhagia. These results are consistent with the studies conducted by Jyotsna et al [9] and Bhosle et al. [10]

We evaluated that predominant number of cases showed normal menstrual pattern (73.11%) with proliferative phase in 49.62% patients, secretory phase in 23.48% cases. Similar observations were made by Abdullah [11] et al. Abnormal bleeding in proliferative phase can be due to hormonal imbalance leading to anovulatory cycles and AUB in secretory phase can be due to ovulatory dysfunction like loss of LH surge.[12]

Atrophic endometrium was noticed in 6.8% cases. Studies conducted by Ara S [13] et al reported a similar incidence of 7%. The cause of AUB in atrophic phase is not clear. It can be due to diminished number and quality of ovarian follicles, abnormal local hemostatic mechanism or thin walled veins superficial to expanding cystic glands making vessels vulnerable to injury .[12]

In 25% patients with AUB, a well-defined structural/ organic abnormality is noticed.[14] While in our study, organic abnormality was found in only 14.39%. Large number of patients with lower age group might be the reason for this lower prevalence.

Disordered proliferative pattern of endometrium is seen in 3.79% cases. Similar incidence of 4.8% was seen by Jairajpuri et al [15]. It is thought to be an exaggeration of normal proliferative endometrium without significant increase in gland to stroma ratio. It is due to persistent estrogen stimulation. It differs from proliferative phase of endometrium by presence of non- uniform glands. Pathologically, disordered proliferative pattern simulates a simple hyperplasia but the process is focal in former whereas diffuse in later. [12] In this study disordered proliferative pattern was most commonly seen in perimenopausal women which is similar to the study of Doraiswami et al.[12] Also, in the spectrum of proliferative lesions of endometrium, it lies at one end with intervening stages of hyperplasia and carcinoma at other end. Hence, early diagnosis of patients at this stage of spectrum will definitely help gynecologists to prevent disease progression.[12] But pathologists must have clear cut rule for interpretation of disordered proliferative pattern and this should emerge as a waste paper basket diagnosis.

In our study, endometrial hyperplasia (21/264; 7.95%) was the most frequent structural cause observed for AUB. Diagnosis of endometrial hyperplasia is important as they are precursors of endometrial carcinoma. The calculated risk of progression of hyperplasia to cancer is 5-10%.[18] We classified hyperplasia into hyperplasia without atypia (16/21) and hyperplasia with atypia (5/21) according to the new WHO classification.[16] Incidence is lower as compared to studies by Abdullah et al [11] (9.1%) and Gredmark et al[17] (10%). The possible reason could be that most of the patients in this study belong to younger age group as compared to other studies.

Endometritis was diagnosed in 1.14% cases including 0.38% cases of granulomatous endometritis suggestive of tuberculosis. All cases were observed in 40- 50 years age i.e. peri-menopausal age group. The endometritis was diagnosed on the basis of presence of plasma cells and granulomatous endometritis contained epithelioid cells alongwith plasma cells and lymphocytes. Chronic endometritis is often a result of intra uterine contraceptive devices (IUCD), pregnancy and incomplete abortions. [15] This pathology needs to be diagnosed and kept in mind while dealing with a case of AUB because with specific treatment, endometrium can be reverted back to normal state.

Endometrial polyps (2/264; 0.76%) were seen in reproductive age group and peri- menopausal age group in equal amount. Polyp in reproductive age group was benign functional polyp and in perimenopausal age group was benign hyperplastic polyp. Functional polyp is peculiar to the cyclic nature of endometrium in reproductive age group. There is compelling difference between endometrial polyp and normal endometrium in receptor expression, cell proliferation and apoptosis regulation suggesting that polyp may provide a suitable background for the advancement of malignancy. [12]

Other benign lesions noted were irregular shedding (1.14%) and luteal phase defect (2.27%).

According to our study, the incidence of carcinoma endometrium is 0.8% including one case of endometrioid carcinoma and one case of serous carcinoma. Lower incidences of endometrial carcinoma 0.4% & 0.47% have

also been observed by Jairajpuri[15] et al & Khan[19] et al. This lower incidence of endometrial carcinoma in our patients can be due to early child bearing and multiparity as progesterone decreases the proliferative activity of endometrium during pregnancy.

The endometrial specimens were inadequate for evaluation in 3/264 (1.14%) cases. The specimen which showed scanty fragmented endometrial glands, stromal tissue and large areas of hemorrhage were labeled as unsatisfactory/ inadequate for reporting.

Conclusion

Histopathological examination of endometrial curetting is an important diagnostic procedure in evaluation of AUB, thus providing specific diagnosis to physician for affluent management of abnormal bleeding. Functional causes of AUB are much more common in reproductive age group whereas in perimenopausal and menopausal age group organic lesion were responsible for AUB. Thus endometrial curettage is recommended in women of perimenopausal and menopausal age group presenting with AUB to rule out pre-neoplastic conditions and malignancy.

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Competing Interests

None Declared

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