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Histopathological Spectrum of Endometrial Changes in Abnormal Uterine Bleeding

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Abstract:
Background: *Abnormal Uterine Bleeding (AUB) is defined as any bleeding that does not correspond with the frequency, duration or amount of blood flow of a normal menstrual cycle. It is a very common gynaecological condition and is caused by a variety of endometrial lesions. This study aims to evaluate the histomorphological spectrum of endometrial lesions resulting in AUB in various age groups.*
Materials and Methods*: The present study was conducted at the SK diagnostics, Hyderabad, Telangana, India in 146 women presenting with AUB over 1 year from January to December 2019. The histopathological findings of endometrium in AUB were studied and categorized into functional and organic causes. Statistical analysis between the age of presentation and a specific endometrial cause was done using the chi-square test.*
Results: *The most common age group presenting with AUB was 31- 40 yrs (38.35%). The commonest pattern in these patients was Disordered proliferative endometrium (33.9%) followed by Proliferative (23.97%), pill endometrium (14.38%), secretory phase (13.01%), Nonatypical Hyperplasia (6.84%), Atypical Hyperplasia,polyp and atrophic endometrium (3.42% each). Endometrial carcinoma was reported in 2.05% of cases. It has been observed that there was a highly significant association between age group and histopathological diagnosis ($p<0.01$).*
Conclusion: *Histopathological examination of endometrial curettage samples helps in evaluating the functional and organic causes AUB in women of different age groups and also serves to identify malignancy and its precursors at an early stage.*
Keywords:*Abnormal Uterine bleeding, Biopsy, Endometrium, Menorrhagia*

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I. Introduction

Abnormal uterine bleeding (AUB) is one of the commonest complaints leading to endometrial sampling by endometrial curettage. It affects 10-30% of reproductive-aged women and up to 50% of perimenopausal women(1). Abnormal uterine bleeding may be defined as a bleeding pattern that differs in frequency, duration and amount from a bleeding pattern observed during a normal menstrual cycle or after menopause (2). Abnormal uterine bleeding can present as menorrhagia, metrorrhagia, polymenorrhea, metro menorrhagia, perimenopausal and postmenopausal bleeding(3)and has led to many hysterectomy procedures without a definitive diagnosis. Early diagnosis and timely treatment of AUB is important to rule out malignancy and to confirm the exact nature of the lesion.Diagnosis of AUB by endometrial curettage is considered as the most cost-effective and most widely employed method of assessing AUB in India (4,5) .Its management entirely depends upon the morphological type of endometrium found histopathologically. This study was done to evaluate the endometrial causes of AUB and to determine various histopathological patterns associated with AUB in different age groups.

II. Materials and Methods

The present study was conducted at theSK diagnostics, Hyderabad, Telangana, India in 146 women presenting with AUB over 1 year from January to December 2019.

Inclusion criteria

Endometrial samples(biopsy or dilatation & curettage) obtained from patients clinically diagnosed as DUB.

Exclusion criteria

Patients presenting with DUB due to pregnancy-related complications, systemic causes, iatrogenic causes like intrauterinecontraceptive device,cervical or vaginal pathology, inadequate endometrial samples, and Hysterectomy specimens.

The endometrial samples were fixed in 10% formalin for 12-24 hours and clinical details of the patient were obtained from the requisition forms and case sheets. Entire tissue was taken for routine processing. 5µ thickness sections taken from paraffin blocks were stained with Haematoxylin and Eosin (H&E) and studied under light microscopy. The age of the patients was categorized as reproductive (18-40 years), peri-menopausal (41-50years) and postmenopausal (>50 years) age groups.

The histopathological findings of AUB were categorized into functional and organic causes. The functional causes of AUB included in this study were normal cyclical phases (proliferative and secretory) of the endometrium and other abnormal physiological changes in the endometrium (atrophic endometrium,disordered proliferative endometrium, and pill endometrium).Organic intrauterine lesions which were the cause of AUB in this study includeendometrial hyperplasia with and without atypia, polyp, and endometrial carcinoma.

III. Results

The age of patients ranged from 22-63 years in this study. The most common pattern of bleeding was menorrhagia (65%) followed by metrorrhagia (13%), post-menopausal bleeding (10%), menometrorrhagia (8%) and polymenorrhea (4%) as shown in figure 1. These 146 cases of AUB were categorized into five age groups with most of them present in 31-40 years (56 cases, 38.35%) and 41-50 years age group (41-50 years, 53 cases, 36.30%). (Table 1).

Table 1: Distribution of cases according to age group

Age group	No. of patients	Percentage
20-30	14	9.58%
31-40	56	38.35%
41-50	53	36.30%
51-60	19	13.01%
61-70	4	2.73%
Total	146	

Table 2: Cases in different age groups:

Age group	Cases
Reproductive	70 (47.94%)
Perimenopausal	53 (36.30%)
Postmenopausal	23 (15.75%)

Table 3: Distribution of cases of AUB according to cause

Cause of AUB	No. of patients	Percentage
Functional causes	123	84.24%
Organic causes	23	15.75%

Table 4: Distribution of cases of AUB according to histological pattern

Histological diagnosis	No.of patients	Percentage
Proliferative phase	35	23.97%
Secretory phase	19	13.01%
Atrophic	5	3.42%
Disordered proliferative endometrium	43	29.45%
Pill endometrium	21	14.38%
Endometrial polyp	5	3.42%
NonatypicalHyperplasia	10	6.84%
Atypical Hyperplasia	5	3.42%
Endometrial carcinoma	3	2.05%

Table 5: Histopathological patterns according to age group (n=146)

Histological diagnosis	Age group (years)					
	21-30	31-40	41-50	51-60	61-70	Total
Proliferative phase	6	20	7	2	0	35
Secretory phase	4	12	2	1	0	19
Atrophic	0	0	1	2	2	5
Disordered proliferative endometrium	3	11	22	7	0	43
Pill endometrium	1	8	10	2	0	21
Endometrial polyp	0	1	3	1	0	5
Nonatypical Hyperplasia	0	4	5	1	0	10
Atypical Hyperplasia	0	0	3	2	0	5
Endometrial carcinoma	0	0	0	1	2	3
Total	14	56	53	19	4	146

Out of 146 patients, 123 (84.24%) were due to functional causes as no organic pathology was found, while 23 (15.75%) cases showed definite endometrial pathology (Table 3). Out of 123 functional causes of AUB, Disordered proliferative endometrium – 43 cases (29.45%) was the most common pattern. Out of 23 organic causes, endometrial hyperplasia without atypia -10 cases (6.84%) was the most common entity. Histopathological examination revealed various patterns in AUB as illustrated in tables 4 & 5. Statistical analysis between the age and endometrial lesion was done using the chi-square test and p- value 0.000 (<0.05) was considered as highly significant. We noticed that the comparison between functional and organic causes of AUB with age groups yielded a p value of 0.03 (<0.05) which is considered to be statistically significant.

Figure 1- Bleeding pattern of AUB

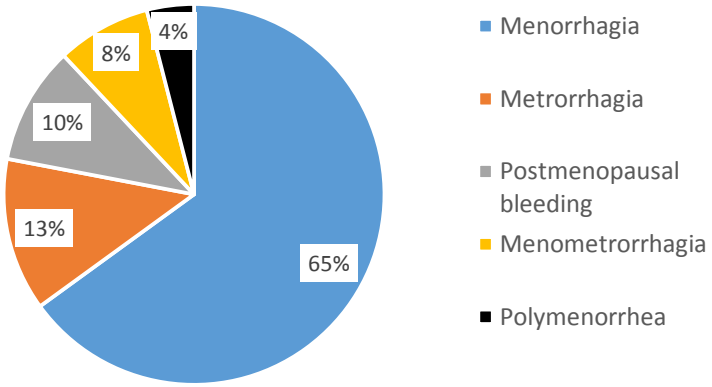
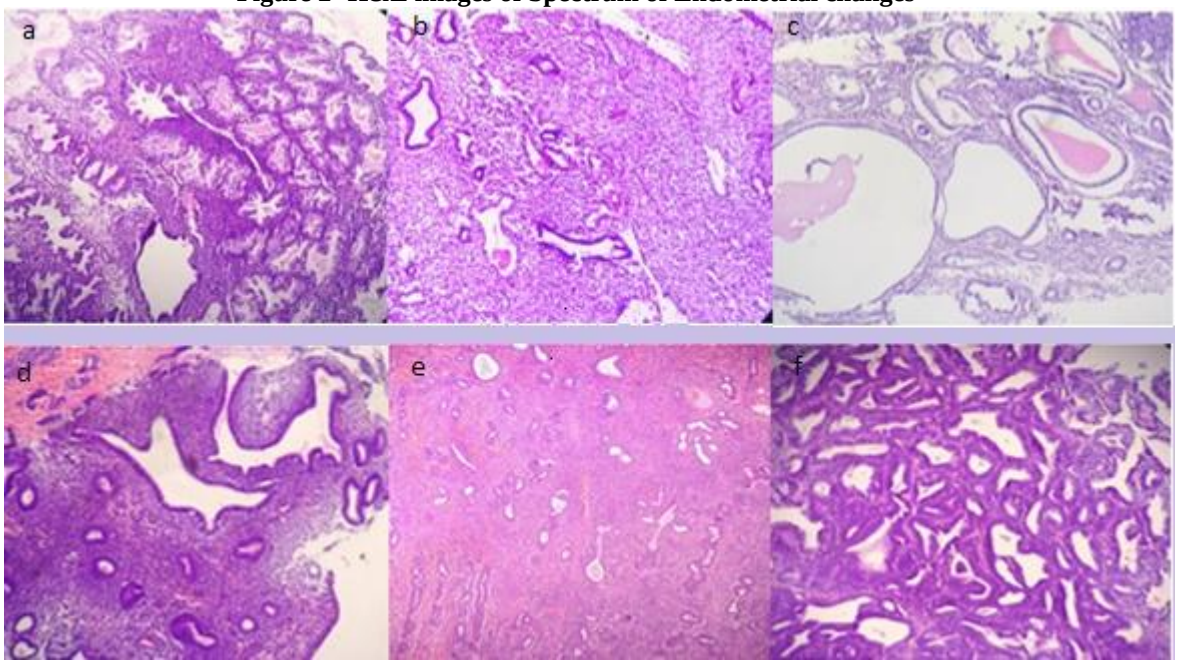


Figure 2- H&E images of Spectrum of Endometrial changes



a- Secretory endometrium, b- Pill endometrium, c- Atrophic endometrium, d- Disordered proliferative endometrium, e- Polyp, f- Endometrial carcinoma

IV. Discussion

In normal cycles, menstrual shedding is followed by a proliferative phase in which endometrial glands become tortuous associated with compact stroma under the influence of estrogen [(6)]. This is followed by the secretory phase.Histological variation can be seen in endometrium according to the age of the woman, phase of the menstrual cycle and any other specific pathology [(7)].AUB is the most commonly encountered symptom in Gynaecology and is usually associated with hormonal disturbance or intrauterine pathology. In many instances, AUB is due to the occurrence of an anovulatory cycle in the perimenopausal period[(8)].It is a significant cause of hysterectomy and thus is a major health problem[(9)].

The aetiology of AUB is different for various age groups – reproductive (19-40 years), perimenopausal (41-50 years) and postmenopausal age group (>50 years).Our study received the maximum number of cases from the reproductive age group (47.94%) (Table 2) which is comparable to the Study by Riju Rani et al who reported 51.6% and by Swatiet al who reported 41% cases from reproductive age group[10, 11]. In this study, the maximum incidence of DUB was found in the age group 31-40 years (38.35%) followed by 41-50 years (36.30%). However, majority cases of AUB were observed in the perimenopausal age group in the literature. [12, 13].

A large number of cases revealed a disordered proliferative pattern in this study with a maximum incidence in 41-50 years age group (51.1%) which was similar to the study by Vaidya S et al (51.8%) [14].The histological feature of the disordered proliferative phase resembles features of simple hyperplasia, but the process is more focal than diffuse. The reason for an increased incidence of dysfunctional uterine bleeding in this age group (41–50years) maybe because these patients are in their climacteric period characterized by decreased ovarian reserve, intermittent anovulatory cycles and decreased estrogen levels.

Proliferative endometrium was the next commonest type of endometrial pattern seen in 35 patients (23.97%) similar to Rajesh Patil et al (22.1%) and BhoomikaDadhania et al (21.33%). The secretory endometrial pattern is observed in 13% of cases which is in concordance with those of Pilli et al (13%). Abnormal bleeding in the proliferative phase can be due to hormonal imbalance leading to anovulatory cycles while AUB in secretory phase can be a result ofovulatory dysfunction like loss of LH surge [15].

The histological patterns observed in women who received hormonal pills showed a combination of inactive glands with abortive secretions, decidualisedstroma, and thin vessels. These changes were found in 21 cases (14.38%) with the majority in the perimenopausal age group. This is in contrast to Baral et al who reported pill endometrium in 10 cases (3%).

Endometrial hyperplasia is defined as an increased proliferation of the endometrial glands relative to the stroma, resulting in an increased gland-to-stroma ratio. Recent WHO classification divides endometrial hyperplasia into Nonatypical and atypical types which emphasizes the prognostic implications of this system of classification as atypical hyperplasia has increased risk of progression to malignancy. The diagnosis of endometrial hyperplasia is important as it is the precursor of endometrial carcinoma. Unopposed exposure of the endometrium to estrogen leads to endometrial hyperplasia. In this study, it is observed in 10.27% of cases. Vaidya et al [14] and Khan et al[16] reported it as 10.9% and 12.6% respectively in their studies.

Atrophic endometrium was observed in 5 cases of AUB (3.42%) and is more commonly seen in 51-60 and 61-70 years age group in this study. This is in concordance with More S et al (2%) and Vaidya et al (4.7%). Post-menopausal bleeding is frequently associated with an atrophic endometrium. The exact cause of bleeding from the atrophic endometrium is not known. It is postulated to be due to sclerotic degeneration of vessel wall or local abnormal haemostatic mechanisms.

Prolonged estrogen stimulation also results in the formation of endometrial polyp [17]. The incidence of benign endometrial polyps was 3.42% in this study similar to Silander[18] 6.66%. In our study, a higher incidence of 47.1% was seen in 41–50 years of age group; similar to another study [19]. The prevalence of polyps increases with age. However, this study observed a low frequency of polyps as there is a lesser percentage of postmenopausal women in this study.

Endometrial carcinoma can occur as a result of excess estrogenic stimulation and develops against a background of endometrial hyperplasia or de novo. It most commonly occurs in postmenopausal women and manifests with bleeding. In our study, there were 3 cases (2.05%) of endometrial carcinoma, all in the postmenopausal women. The incidence is similar to that of other studies by More S et al (1.98%), Vaidya S et al (2.5%) and Baral R et al (1.0%). [20, 21]

V. Conclusion

Histopathological evaluation of endometrial samples can be used as the first step for the diagnosis of abnormal uterine bleeding. Endometrial patterns varied in cases of DUB. Functional causes of AUB are much more common in the reproductive age group whereas in perimenopausal and Postmenopausal age group organic lesions are responsible for AUB. Thus studying the histomorphology of endometrium in curettage and biopsy samples help in the evaluation and further planning the treatment in AUB.

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