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Original Research Article

Spectrum of Endometrial Pathology in Abnormal Uterine Bleeding

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ABSTRACT

Background: Abnormal uterine bleeding (AUB) is defined as any alteration in the pattern or volume of menstrual blood flow. It is a very common gynecological condition and has a major impact on quality of life. In many instances it is related to the endometrial pathology. The study was done to evaluate the histopathology of endometrium for identifying endometrial causes of AUB and their incidence in different age groups.
Materials and methods: The study was done at a tertiary care institute over a period of one year from 1st January 2016 to 31th December 2016. Endometrial samples and hysterectomy specimen of patients with AUB, in whom non-endometrial pathology had been ruled out, were included in the study. The specimens were routinely processed and H&E stained slides were studied for endometrial pattern.
Results: Total of 248 cases were received, 150 endometrial tissue samples and 98 hysterectomy specimens. There were 49.2% women in perimenopausal (40-49 years), 26.2% in reproductive (<40 years) and 24.6% in post menopausal age group (>49 years). Well defined organic abnormality was present in 33.9%. Endometrial patterns included cyclic (36.7%), disordered proliferative (16.1%), atrophic (13.3%), chronic endometritis (2.4%), endometrial polyp (8.1%), endometrial hyperplasia (21%) and endometrial carcinoma (2.4%).
Conclusions: Patients with AUB show a varying spectrum of endometrial pattern, ranging from cyclic endometrium to carcinomas. It is therefore important to evaluate for endometrial pathology in all women presenting with AUB without a known cause.

Key words: Abnormal uterine bleeding, Endometrium

INTRODUCTION

Abnormal uterine bleeding refers to any non physiologic uterine bleeding. [1] It affects a great majority of women and is one of the most common indication for performing endometrial biopsies and curettage. The underlying pathology may be functional or organic. The present study was done to evaluate the spectrum of endometrial pathology that may result in abnormal uterine bleeding in women of different age groups.

MATERIALS AND METHODS

It was a cross sectional and descriptive study carried out at a tertiary care hospital, over a period of one year from 1st January 2016 to 31th December 2016. Endometrial tissue (endometrial curettage and biopsy) and hysterectomy specimen of patients presenting with abnormal uterine bleeding were included in the study. The relevant clinical details of the patients were noted. Cases having pathology other than endometrial, like leiomyoma, cervical, vaginal pathology etc. and inadequate

endometrial samples were excluded from the study. Pregnancy related complications were excluded from the study.

The samples were received in 10% formalin. Gross was noted, representative tissue was submitted. After processing in automated tissue processor, 4-5 micron thick paraffin embedded sections were made and stained by Hematoxylin and Eosin. Histopathological examination was done.

RESULTS

A total of 248 cases were received during this period, out of which there were 150 endometrial tissue samples and 98 hysterectomy specimens. The patient's age ranged from 23 years to 76 years. Maximum numbers of patients were in the age range 40-59 years (66.5%).

Table 1: Age distribution of patients presenting with AUB

Age range (in years)	Number of patients	Percentage (%)
20-29	3	1.2
30-39	62	25
40-49	122	49.2
50-59	43	17.3
60-69	13	5.3
70-79	5	2.0
Total	**248**	**100**

A total of 122 patients (49.2%) presenting with AUB were in the perimenopausal age group (40-49 years) followed by 65 patients (26.2%) in reproductive age group (<40 years) and 61 patients (24.6%) in the post menopausal age group (>49 years).

Table 2: Age group of women with AUB

Age group	No of cases	Percentage
Reproductive (<40)	65	26.2
Perimenopausal (40-49)	122	49.2
Postmenopausal (>49)	61	24.6

In 64 cases (33.9%) of AUB there was some well defined organic abnormality. In 164 cases (66.1%) it was due to some functional cause.

Table 3: Histopathological spectrum of endometrium in AUB

Histopathological diagnosis	No. of cases	Percentage (%)
Proliferative endometrium	71	28.6
Secretory endometrium	20	8.1
Disordered proliferative endometrium	40	16.1
Atrophic endometrium	33	13.3
Chronic endometritis	6	2.4
Endometrial polyp	20	8.1
Non-atypical hyperplasia	48	19.4
Atypical hyperplasia	4	1.6
Endometrial carcinoma	6	2.4
Total	**248**	**100**

Table 4: Age wise distribution of endometrial patterns in AUB

Histopathological diagnosis	20-29	30-39	40-49	50-59	60-69	70-79	Total
Proliferative endometrium	3	32	34	2	0	0	71
Secretory endometrium	0	6	13	1	0	0	20
Disordered proliferative endometrium	0	5	24	11	0	0	40
Atrophic endometrium	0	0	12	13	5	3	33
Chronic endometritis	0	0	4	1	1	0	6
Endometrial polyp	0	5	9	2	4	0	20
Non-atypical hyperplasia	0	13	22	11	1	1	48
Atypical hyperplasia	0	1	2	1	0	0	4
Endometrial carcinoma	0	0	2	1	2	1	6
Total	**3**	**62**	**122**	**43**	**13**	**5**	**248**

Histopathological examination of the endometrium showed various histological patterns in AUB (Table 3). Patterns of normal cyclical endometrium (proliferative and secretory phases) were the most common and seen in 91 (36.7 %) cases presenting with AUB.

Hyperplasia and disordered proliferative endometrium were the next common histological patterns which were seen in 52 (21.0%) and 40 (16.1%) cases respectively.

Atrophic endometrium and non atypical hyperplasia accounted for most cases (34 cases, 55.7%) of AUB in women over 49 years of age. In women between 40-49 years of age, normal cyclical endometrium (proliferative and secretory phases) was most common (47 cases, 38.5%). Disordered proliferative endometrium, hyperplasia and atrophy accounted for 24 (19.7%), 24 (19.7%) and 12 (9.8%) cases respectively, in women between 40-49 years. Similarly, in women less than 40 years of age normal cyclical endometrium (proliferative and secretory phases) was most common (41 cases, 63.1%) followed by hyperplasia in 14 cases (21.5%).

Endometrial polyp accounted for 20 cases (8.1%) presenting with AUB and was more common in women over 40 years of age. Chronic endometritis was also more common in women over 40 years of age and was found in 6 (2.4%) cases.

Malignancy as a cause of AUB was uncommon. There were 6 cases of carcinoma, all of which were in patients above 40 years of age.

DISCUSSION

Endometrial assessment is performed to diagnose malignancy or pre-malignant conditions and to evaluate the hormonal influences of the endometrium. The occurrence of menstrual disorders increases significantly with advancing age.

The commonest age group presenting with excessive bleeding in our study was 40–49 years (49.2%). Similar results were obtained in the study by Saraswathi D et al [2] with 33.5% of women between 41-50 years of age.

In most of the studies the cases of AUB were more in women more than 40 years of age.

Table 5: Percentage of women over 40 years of age presenting with AUB

Present study	More S et al [3]	Shah R et al [4]	Vaidya S et al [5]	Bhatta S et al [6]	Baral R et al [7]
73.8%	46.5%	62.9%	62.0%	76.2%	51.3%

The most likely etiology of AUB relates to the patient's age as to whether the patient is premenopausal, perimenopausal or postmenopausal. [8]

In many instances AUB is due to the occurrence of an anovulatory cycle in perimenopausal period. [9]

In most of the similar studies, more than 50% of women presenting with AUB were greater than 40 years of age.

Endometrium is a dynamic, hormonally sensitive and responsive tissue which constantly and rhythmically undergoes changes in the active reproductive life. [4]

In most of the cases of AUB there is no specific organic cause as is evident by various studies. In our study 66.1% of patients did not show any specific pathology for AUB. In other studies also majority of cases lacked a well defined organic cause.

In all the following studies including ours (table-6), cyclic endometrium was the most common finding. Proliferative or secretory varied according to the time of biopsy or hysterectomy.

Table 6: Endometrial patterns in AUB in different studies

Endometrial histopathology	Our study	More S et al [3]	Parmar J et al [10]	Vaidya S et al [5]	Bhatta S et al [6]	Baral R et al [7]
Cyclic endometrium	36.7	58.9	32.5	50.6	42.6	36.7
Disordered proliferative	16.1	7.4	33.3	13.4	6.6	26.7
Atrophic	13.3	2	-	4.7	7.4	-
Hyperplasia	21.0	15.3	10.8	10.9	18.0	18.3
Polyp	8.1	1.5	10.8	1.2	2.5	1.3
Inflammatory	2.4	2.97	3.9	3.2	6.6	2.7
Malignancy	2.4	1.98	0	2.5	5.7	1.0

To do away with the inconsistency in the nomenclature used to describe abnormal uterine bleeding (AUB) among non gravid women of reproductive age, the PALM-COEIN classification system has been approved by the International Federation of Gynecology and Obstetrics (FIGO) Executive Board as a FIGO classification system. [11-13]

There are 9 main categories, which are arranged according to the acronym PALM-COEIN: **P**olyp, **A**denomyosis, **L**eiomyoma, **M**alignancy (and hyperplasia), **C**oagulopathy, **O**vulatory disorders, **E**ndometrial, **I**atrogenic and **N**ot otherwise classified.

The term "DUB," which was previously used as a diagnosis when there was no systemic or locally definable structural cause for AUB, is not included in the system and should be abandoned. [14,15]

Amongst the endometrial causes also the classification system has been inconsistent and standardization is needed.

Baral R et al had divided endometrial changes as normal and abnormal physiologic changes. In normal they included proliferative, secretory and anovulatory changes while in abnormal they included pill endometrium, irregular shedding, disordered proliferative and decidualization. In the present study and in other studies it has been divided into cyclic endometrium (proliferative or secretory) and disordered proliferative endometrium.

Disordered proliferative endometrium is common in the perimenopausal age group and the same was found in present study (60%) and study by Vaidya S et al [5] in which 51.8% patients with disordered proliferative endometrium were in perimenopausal age group.

Postmenopausal bleeding is frequently associated with an atrophic endometrium. Atrophy of endometrium occurs as a consequence of the prolonged absence of any endogenous or exogenous estrogenic stimulation. The thin atrophic endometrium is susceptible to minor injury and may be responsible for postmenopausal bleeding even in the absence of an identifiable lesion. Superficial large, dilated vennules are situated under a thin endometrium which may rupture to cause excessive uterine bleeding. [16]

The incidence of atrophic endometrium was higher in our study (13.3%) than is other studies, including More S et al, Viadya S et al [5] and Bhatta S et al [6] in which the incidence was 2.0%, 4.7% and 7.4% respectively. The difference is probably due to a greater percentage of perimenopausal and postmenopausal women in our study compared to the other three studies (table 5).

The histologic criteria for endometritis in the literature has been somewhat variable with respect to the number of plasma cells present in the endometrial stroma as well as to secondary characteristics including neutrophils in the surface endometrium and gland lumina, increased lymphocytes, or lymphoid aggregates. [17-20]

The percentage of cases of AUB with endometritis was between 2-4% in most studies, including ours. The percentage was a bit higher in study by Bhatta S et al [6] (6.6%).

The frequency of endometrial polyp (8.1%) was more in our study as compared to other studies. As the prevalence of endometrial polyps increases with age [21,22] that as well was probably due to a greater percentage of perimenopausal and postmenopausal women in our study compared to the other studies (table 5).

Complex and atypical hyperplasia and endometrial carcinoma are infrequently reported in women with endometrial polyps. [23–25] However, we did not find any such case in our study.

In the study by More S et al, [3] Baral R et al [7] and Vaidya S et al [5] they had divided endometrial hyperplasia as simple and complex; typical and atypical. WHO in 1994 classified endometrial hyperplasias into 4 categories:

1. simple hyperplasia without atypia,
2. complex hyperplasia without atypia,
3. simple atypical hyperplasia,
4. complex atypical hyperplasia [26,27]

In the present study and in the study by Parmar J et al [10] hyperplasia was classified as hyperplasia without atypia and atypical hyperplasia, which is in accordance with the latest WHO classification [28] published in 2014 (Table)

The incidence of endometrial hyperplasia was comparable between different studies ranging from 15-21% (table 6) in our study we received only 4 cases (2.4%) of atypical hyperplasia and 48 cases (19.4%) of typical hyperplasia. In other studies also the cases of simple and typical hyperplasia were more common.

Table 7: New WHO classification of endometrial hyperplasias. [28]

New term	*Synonyms*	*Genetic changes*	*Coexistent invasive endometrial carcinoma*	*Progression to invasive carcinoma*
Hyperplasia *without* atypia	Benign endometrial hyperplasia; simple non-atypical endometrial hyperplasia; complex non-atypical endometrial hyperplasia; simple endometrial hyperplasia without atypia; complex endometrial hyperplasia without atypia	Low level of somatic mutations in scattered glands with morphology on HE staining showing no changes	< 1%	RR: 1.01–1.03
Atypical hyperplasia/ endometrioid intraepithelial neoplasia	Complex atypical endometrial hyperplasia; simple atypical endometrial hyperplasia; endometrial intraepithelial neoplasia (EIN)	Many of the genetic changes typical for endometrioid endometrial cancer are present, including: micro satellite instability; *PAX2* inactivation; mutation of *PTEN*, *KRAS* and *CTNNB1* (β-catenin)	25–33%	RR: 14–45

Endometrial carcinoma is one of the most common gynecologic malignancies and its incidence is increasing. 80% cases arise in postmenopausal women, and manifest with symptoms of bleeding. [29]

In our study, there were 6 cases (2.4%) of endometrial carcinoma, all in the perimenopausal and post menopausal women. The incidence was higher in the study by Bhatta S et al [6] (5.7%) with a sample size of 122 patients. However, the incidence was similar to our study in other studies by More S et al [3] (1.98%), Vaidya S et al [5] (2.5%) and Baral R et al [7] (1.0%).

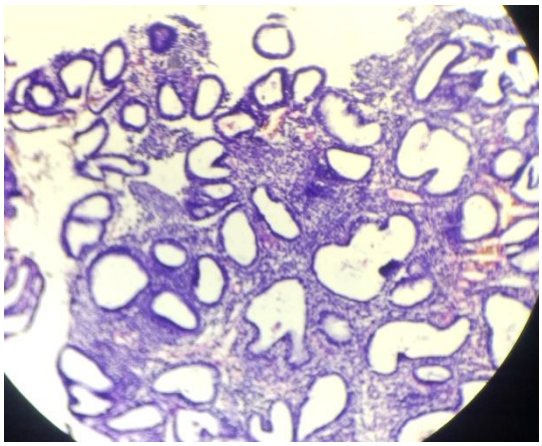

Figure 1

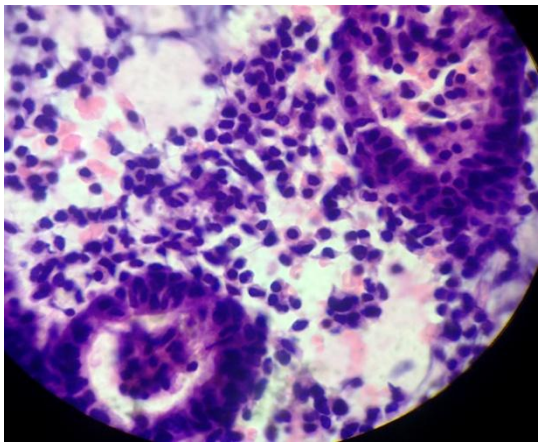

Figure 2

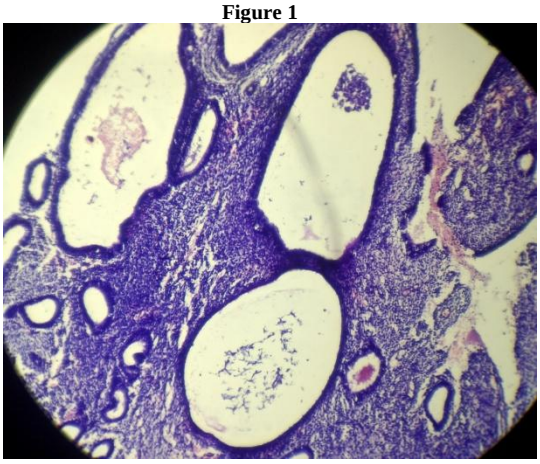

Figure 3

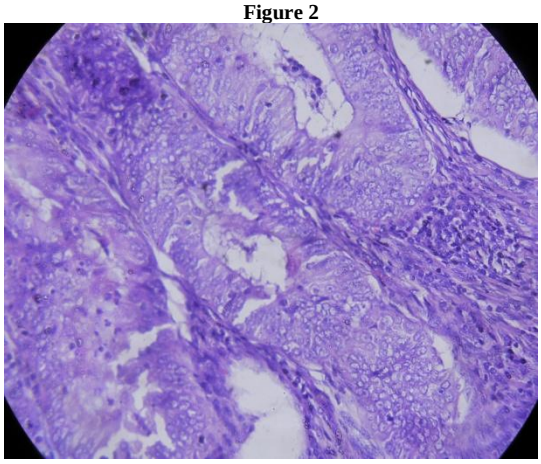

Figure 4

Figure 1: Photomicrograph of disordered proliferative endometrium showing disorganized proliferative phase glands with focal dilatation
Figure 2: Photomicrograph of chronic non specific endometritis. A dense chronic inflammatory infiltrate with many plasma cells surrounds the glands
Figure 3: Photomicrograph of simple cystic hyperplasia without atypia. Dilated endometrial glands with no or minimal outpunching
Figure 4: Photomicrograph of endometrial carcinoma. Glandular growth pattern with enlarged nuclei, loss of polarity and infiltration into myometrium

CONCLUSIONS

Abnormal uterine bleeding is a common cause of morbidity in women of all ages. Endometrial pathology plays an important role in the diagnosis of causes of AUB. The wide spectrum of endometrial lesions in case of AUB reflects the dynamic nature of the endometrium and therefore a lack of specific organic cause in most cases. A detailed clinical data including menstrual cycle, drug history etc. is a must before reporting a case of AUB. Specific pathologies like endometrial polyp, hyperplasia and carcinomas have an age dependent incidence and should be ruled out in patients presenting with AUB. While there is a wide range of possible endometrial patterns, there is a need for standardization of reporting to correlate with the treatment protocols so as to benefit the patient, which is the eventual aim of the reporting.

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