Clinical Pattern and Spectrum of Endometrial Pathologies in Abnormal Uterine Bleeding in Perimenopausal and Postmenopausal Women: Experience in a Tertiary Care Institute

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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 the common presenting complaint in gynecology outpatient department (OPD) in all age groups. It is due to the anovulatory cycles which are commonly seen in extremes of age reproductive age groups in adolescent and perimenopausal women. Abnormal uterine bleeding is caused by wide variety of organic or nonorganic causes. Histopathological evaluation of the endometrial samples plays a significant role in the diagnosis of abnormal uterine bleeding.

Aim: To assess the clinical picture and endometrial pattern of abnormal uterine bleeding in perimenopausal and postmenopausal age groups.

Materials and methods: The study included analysis of 127 cases of endometrial samples obtained from patients of abnormal uterine bleeding above 40 years of age. The specimens were routinely processed and hematoxylin and eosin (H&E) stained slides were studied. Patients were categorized in two age groups perimenopausal (41–50 years) and postmenopausal (>50 years).

Results: The predominant age of presentation in AUB was perimenopausal age group 95 (74.8%). It was seen more frequently in grandmultiparous women. Most common presentation was menorrhagia (62.1%) of cases in the perimenopausal age group, whereas other group presented as postmenopausal bleeding. A total of 127 specimens of endometrium were analyzed. In perimenopausal age group predominant histopathological pattern was proliferative endometrium (34.7%) followed by disordered proliferative (15.8%). Atrophic endometrium (28.3%) was the most frequent finding followed by endometrial hyperplasia (25%) in postmenopausal age group. Two cases (6.2%) of endometrial carcinoma were reported in postmenopausal age group and one case (1%) in perimenopausal age group.

Conclusion: Histopathological evaluation with clinical correlation of endometrium is especially indicated in women over the age of 40 years to rule out preneoplastic lesions and malignancies. Careful screening can detect early cancer of endometrium which has excellent prognosis and improve quality of life.

Keywords: Abnormal uterine bleeding, Endometrium, Perimenopause.

INTRODUCTION

Abnormal uterine bleeding (AUB) is any alteration in the volume or pattern of menstrual blood flow. Two main categories of AUB are heavy menstrual bleeding and irregular menstrual bleeding, and many patients experience the combination of these symptoms.1 Menstrual disorders are the most frequent gynecologic condition in the general population and have a major impact on quality of life.2 Abnormal uterine bleeding is a very common gynecological condition that affects all age groups. One-third of patients attending gynecology outpatient department (OPD) present with complaints of abnormal uterine bleeding.3

As menopause approaches, the ovarian activity declines. Initially, ovulation fails leading to no corpus luteum formation and no progesterone is secreted by the ovary. The irregularity in menstrual cycle during perimenopause can be due to anovulation or to irregular maturation of follicles.4

Histopathological evaluation of the endometrial samples plays a significant role in the diagnosis of abnormal uterine bleeding. Dilatation and curettage (D&C) is
the mainstay of endometrial sampling since a long time. It also allows for a fractional curettage with separate sampling of both the endometrial and endocervical tissue. The underlying disease can be detected by histological variations of endometrium taking into account the age of the woman, the phase of her menstrual cycle, and use of any exogenous hormones.

Peri- and postmenopausal bleeding, with or without the use of hormone replacement therapy, is a common clinical problem. The exclusion of endometrial hyperplasia and carcinoma is the key issue in the evaluation of patients with abnormal uterine bleeding.5

The target of our study was proper evaluation of this age group women to help improve their quality of life and remove the worry of dreaded cancer risk from their minds.

MATERIALS AND METHODS

The prospective clinicopathological study of 127 cases of endometrium in abnormal uterine bleeding was carried out in the department of obstetrics and gynecology, Chhattisgarh Institute of Medical Sciences, Bilaspur, Chhattisgarh, India, over a period of 3 years from July 2011 to June 2014.

The age of patients with abnormal uterine bleeding ranged from 41 to 60 years. A history about her parity status was taken. Detailed menstrual history, like duration, pattern, flow, regularity and associated symptoms was recorded and evaluated.

Evaluation of the endometrium as a cause of AUB is done by cellular assessment by microscopic evaluation of endometrial samples obtained from dilatation and curettage or endometrial biopsy. Specimens were received in 10% formalin. These were studied grossly and multiple sections were taken from each taken and stained by hematoxylin and eosin (H&E). Histopathological endometrial patterns were studied. The subsequent reports collected and later analyzed along with keeping in mind the patient's clinical profile.

Inadequate endometrial samples and hysterectomy specimens were excluded from our study.

RESULTS

A total of 136 endometrial biopsies and curettings from patients with AUB were analyzed. The cause of AUB could be determined in only 127 out of 136 endometrial biopsies as nine biopsy specimens were inadequate for evaluation and excluded from our study.

Patients according to age at presentation divided further into perimenopausal (41–50 years) and postmenopausal (>50 years) age groups. Out of 127 cases, maximum numbers of patients were in the age group of perimenopausal (41–50 years) age group 95 (74.8%) and 32 (25.2%) cases were postmenopausal (>50 years) age group (Graph 1). It was more commonly observed in grandmultiparous women (40.2%) (Table 1). The most common presentation in perimenopausal age group was menorrhagia 59 (62.1%), polymenorrhagia 11 (11.6%) followed by menometrorrhagia nine (9.5%) (Table 2). The other group, however, presented as postmenopausal bleeding.

The histopathological picture of the perimenopausal age group showed the proliferative endometrium (Fig. 1) was the most common finding observed in 33 cases (34.7%) followed by disordered proliferative (Fig. 2) in 15 (15.8%), whereas endometrial hyperplasia in 19 cases (19.8%). Out of 19 cases of endometrial hyperplasia, simple hyperplasia constitute 17 cases and one case each of complex hyperplasia without atypia (Fig. 5)/with atypia were observed. In this age group, endometrial carcinoma was found in one case (1%) only (Table 3).

The endometrial samplings of the postmenopausal age group had atrophic endometrium (Fig. 3) as predominant picture in nine cases (28.2%), whereas endometrial...

Graph 1: Age-wise distribution of subjects of AUB

Table 1: Parity of patients observed in AUB patients (N = 127)

<table>
<thead>
<tr>
<th>Parity</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4</td>
<td>3.1</td>
</tr>
<tr>
<td>1</td>
<td>8</td>
<td>6.3</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>20.5</td>
</tr>
<tr>
<td>3</td>
<td>38</td>
<td>29.9</td>
</tr>
<tr>
<td>Grand multipara</td>
<td>51</td>
<td>40.2</td>
</tr>
</tbody>
</table>

Table 2: Symptoms at the time of presentation in perimenopausal AUB (N = 95)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menorrhagia</td>
<td>59</td>
<td>62.1</td>
</tr>
<tr>
<td>Polymenorrhagia</td>
<td>5</td>
<td>5.3</td>
</tr>
<tr>
<td>Polymenorrhea</td>
<td>11</td>
<td>11.6</td>
</tr>
<tr>
<td>Metrorrhagia</td>
<td>7</td>
<td>7.3</td>
</tr>
<tr>
<td>Menometrorrhagia</td>
<td>9</td>
<td>9.5</td>
</tr>
<tr>
<td>Metropathica</td>
<td>4</td>
<td>4.2</td>
</tr>
</tbody>
</table>
**Fig. 1:** Proliferative endometrium glands are tubular and regularly spaced in abundant stroma

**Fig. 2:** Disordered proliferative endometrium showing disorganized proliferative phase glands with focal glandular dilatation

**Fig. 3:** Atrophic endometrium, thin endometrium with only a few residual glands surrounded by an atrophic, somewhat fibrotic stroma. The junction between endometrium and myometrium is not sharply defined, and the underlying myometrium also appears atrophic

**Fig. 4:** Simple hyperplasia without atypia showing mildly irregular, variably sized glands in abundant stroma with squamous metaplasia

**Fig. 5:** Complex hyperplasia without atypia, highly irregular glands with scant stroma showing regular, uniform nuclei

**Fig. 6:** Endometrial carcinoma, enlarged nuclei, irregular to rounded, vesicular with prominent nucleoli
hyperplasia in nine cases (28.2%) of which simple hyperplasia without atypia (Fig. 4) in six cases (18.8%). Two cases (6.2%) of endometrial carcinoma (Fig. 6) was observed in this age group (Table 4).

According to World Health Organization (WHO), the endometrial hyperplasia is classified as simple or complex based on the absence or presence of architectural abnormalities, such as glandular complexity and crowding. Hyperplasia are further designated as atypical if they show nuclear atypia.

**DISCUSSION**

Abnormal uterine bleeding occurring as heavy, prolonged or acyclic flow at menopausal transition or as spotting or minimal bleeding at postmenopausal period may be alarming and needs thorough evaluation to rule out malignancy.\(^6\) Abnormal and excessive endometrial bleeding occurs in reproductive women of all age groups but is more common in adolescent and peri-menopausal women.\(^7\) Many studies have revealed that occurrence of menstrual disorders increases with advancing age.\(^8,9\)

In our study, 127 patients of abnormal uterine bleeding were evaluated to find out incidence, clinical and pathological picture. The incidence was more in perimenopausal age group than postmenopausal age group. The reason for this finding may be due to the fact that the patients were evaluated much earlier and treated appropriately, thereby decreasing the incidence in later age group.

In our study, majority of patients were between 41 and 50 years (74.8%) age group. Similar observations were also made by Doraiswami et al.\(^10\) and Jairajpuri et al.\(^10\) 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 estrogen which cannot keep the normal endometrium growing.\(^11\)

The incidence of AUB was high as the parity increases in our study. Similar results were seen in study conducted by Bhosle et al.\(^12\) and Usha et al.\(^13\)

The most common symptom was menorrhagia (62.1%) comparable to other studies 69.6% Yusuf et al.\(^14\) and 53.3%.\(^12\) The incidence of polymenorrhoea was (11.6%), comparable to figures quoted by Muzaffar et al 13%.\(^9\)

Incidence of menometrorrhagia (9.5%) and metrorrhagia in 7.3% similar to 6.5% by Bhosle et al and 5% by Patil et al in the perimenopausal age group, whereas the other group presented as post-menopausal bleeding. Similar findings were also noted by Usha et al and Katke et al.\(^13,16\)

In our study of perimenopausal age group, 34.7% of proliferative endometrium was observed which is similar to study done by Patil et al (34%),\(^15\) Dangal G (38.5%).\(^17\) Muzaffar et al also observed proliferative endometrium in perimenopausal age which are slightly lower than our study (25.8%).\(^8\) Bleeding in the proliferative phase may be due to anovulatory cycle in such cases shows progressive rise of estrogen to comparatively high levels, which is then followed by a sudden fall in estrogen due to feedback inhibition of pituitary or of FSH secretion and bleeding results.

In postmenopausal age group, we observed four cases (12.6%) of proliferative endometrium similar to other studies results.\(^8\)

In present study, 7.4% of secretory endometrium observed in 41 to 50 years of age. The incidence was lower than studies by (16.7%) Sajitha et al.\(^18\) 16.6%, Bhosle et al.\(^12\) The bleeding in secretory phase is due to ovulatory dysfunctional uterine bleeding and is characterized by regular episodes of heavy menstrual blood loss. The main defect is in the control of processes regulating the volume of blood lost during the menstrual breakdown of endometrium. This ovulatory bleeding is explained by the inability of the corpus luteum to synthesize adequate amount of progesterone.
Fifteen cases (15.8%) showed disordered proliferative pattern in our study which is similar to Abdullah LS. Disordered proliferative pattern lies at one end of the spectrum of proliferative lesions of the endometrium that includes carcinoma at the other end with intervening stages of hyperplasias. The term ‘disordered proliferative endometrium’ has been used in a number of ways and is somewhat difficult to define. It denotes an endometrial appearance that is hyperplastic but without an increase in endometrial volume. A higher incidence of disordered proliferative pattern was found in our study as compared to Nam-Hoon C et al, whereas the incidence in postmenopausal showed 6.2%.

Atrophic endometrium was the predominant finding 28.2% in postmenopausal age group due to absence of estrogenic stimulation leading to thin atrophic endometrium. Grendmark (50%) studied that atrophic endometrium was the most common cause of postmenopausal bleeding. The causes of bleeding in these women are most likely due to superficial petechial hemorrhages and mucosal ulceration arising from the fragile vasculature support provided by a thin underlying stroma.

Chronic endometritis was seen in (5.3%) in perimenopausal group which is similar with the findings of Khare et al, affecting 6.4% and Wahda et al (77%), Abdullah LS, and 3.1% in postmenopausal group which is in comparable with Bhatta S. Diagnosis of endometritis depends upon findings of neutrophils in the stroma of a nonmenstruating endometrium in acute endometritis and presence of plasma cells in the stroma in chronic endometritis. Patient with chronic endometritis can present with AUB, pelvic pain and infertility. This condition needs to be diagnosed because with specific treatment, endometrium starts functioning normally.

The incidence of endometrial polyp in our study 6.3% in perimenopausal and 6.2% in post-menopausal was less as compared to Bhatta S. These are small growths in the uterine cavity, which were soft, oval, pedunculated with a smooth surface. There is significant difference between the endometrial polyp and normal endometrium in receptor expression, cell proliferation and apoptosis regulation. These differences combined with nonrandom chromosomal aberrations and monoclonality suggests that polyp may provide a suitable microenvironment for the development of malignancy.

Endometrial hyperplasia was the commonest structural pathological change between the organic causes was detected in (19.8 %) with maximum age incidence in the age group of 41 to 50 years which is in concordance with and Slobada L (22.6%), Dangal G (23%), Muzaffar et al (25%) observed high incidence of endometrial hyperplasia in 41 to 50 years of age group. The incidence of simple endometrial hyperplasia was more common in the 41 to 50 years age group.

The endometrial hyperplasia in postmenopausal group showed 28.2%. In postmenopausal women only, we observed only complex hyperplasia with atypia.

The endometrial hyperplasia is commonly seen in perimenopausal age due to failure of ovulation. Persistent unripe follicles expose the endometrium to an abnormally excessive and prolonged estrogenic action. The results agree with their finding regarding the age distribution for cases with endometrial hyperplasia as the most of the cases in our study was in the age group of 41 to 50 years, therefore, the importance of histopathological evaluation of the endometrium in women of this age group cannot be underestimated as abnormal uterine bleeding in these women could be due to an underlying hyperplasia. Endometrial hyperplasia is a precursor of endometrial cancer. The incidence of endometrial hyperplasia without and with atypia peaks in early 50s and early 60s respectively.

We encountered one case (1%) of endometrial carcinoma in age group of 41 to 50 years similar to incidence reported by Yusuf et al (0.6%), whereas two cases (6.2%) in postmenopausal age group. In the present study, incidence of carcinoma endometrium was more common in the 51 to 60 years age group. The result of this study was almost similar to data mentioned by Yusuf et al. Malignant neoplasm are generally accepted to be relatively uncommon causes of PMB with endometrial carcinoma being involved in seven to 17.7% patient.

CONCLUSION

Abnormal uterine bleeding predominantly affects women of perimenopausal age group which is alarming and needs thorough evaluation including histological patterns and etiopathological factors. In a tertiary referral center, it is hereby the duty of the treating doctor to screen these patients. It gives a golden opportunity to not only find out cases in which organic lesions, like polyps, hyperplasia can be detected but also helps detect early atypical hyperplasia and cancer of endometrium which has excellent prognosis if detected early. Histopathological examination of endometrial biopsy is a major diagnostic tool in evaluation of AUB and a specific diagnosis could help the physician to plan therapy for successful management of AUB. Abnormal uterine bleeding is a major health problem that adversely affects the lives of women of this age group, therefore, the sole target is to improve the patient’s symptoms and the quality of life.
ACKNOWLEDGMENT

We sincerely thank Lt Col (Prof) Dr SK Mohanty, Dean and Professor Dr R Murthy, Medical Superintendent, CIMS, for granting permission. We also thank all interns for collecting the records.

REFERENCES