Histopathological Study of Endometrium in Abnormal Uterine Bleeding

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ABSTRACT
Background:
To evaluate the endometrial causes of abnormal uterine bleeding and to study the frequency of various histopathological patterns of endometrium among different age groups.

Materials and Methods:
The retrospective observational study was done on 150 patients with abnormal uterine bleeding in the age group of 20 to 74 years. This study was carried out in the department of pathology at MMCHR&I, Kanchipuram from November 2017 to December 2018. Histopathological examinations were done on the received endometrial specimens and various histopathological patterns of endometrium were noted.

Results:
The Abnormal uterine bleeding (AUB) was more common in the age group of 41 to 50 years. Majority of them were multipara. The most common complaint was menorrhagia 75(50%) followed by metrorrhagia 55(36.67%) and postmenopausal bleeding was noted in 20 cases (13.33%). The most common histopathological patterns were proliferative endometrium 65(43.33%) followed by disordered proliferative endometrium 26(17.33%) and then hyperplasia with atypia 6(4%). Endometrial carcinoma was found in 3 (2%) cases.

Conclusion:
It is very important to rule out premalignant conditions and malignancy in patients with abnormal uterine bleeding among different age groups especially in perimenopausal and postmenopausal age groups.

Keywords: Abnormal uterine bleeding, Disordered proliferative endometrium, Menorrhagia.

INTRODUCTION
The hormonally sensitive and responsive endometrial tissue constantly undergoes changes throughout the reproductive life [1]. Abnormal uterine bleeding (AUB) is defined as changes in the frequency of menstruation, amount of blood loss or duration of flow [2]. AUB is the commonest presenting symptom and perplexing condition in adult women leading to endometrial sampling [3]. Menorrhagia refers to increased blood flow(>80ml) or duration (>7 days) at normal intervals (21 to 35) days. Metrorrhagia refers to acyclical and irregular bleeding in between normal cycles. Postmenopausal bleeding refers to bleeding recurring in a menopausal woman atleast one year after cessation of cycles. Dysfunctional uterine bleeding is diagnosed by excluding pregnancy or its related disorders, iatrogenic causes, systemic
conditions, and genital tract pathology [3,4]. The important local pathologies like malignancy, benign tumours and infections were the causes for bleeding in elderly women. The risk of both endometrial carcinoma and hyperplasia increases due to unopposed estrogenic stimulation of the endometrial lining [5]. This study was carried out to evaluate the endometrial causes of abnormal uterine bleeding and to study the frequency of various histopathological patterns of endometrium across different age groups.

Materials and Methods

One-year retrospective study from November 2017 to December 2018 was done in the department of pathology at MMCHR&I, Kanchipuram.150 cases with abnormal uterine bleeding in the 20 to 74 years of age group were included in the study. The Endometrial samplings were obtained either by biopsy or hysterectomy. 100 endometrial biopsies and 50 hysterectomy specimens were taken and fixed in 10% formalin. After gross examination, the specimens were processed in an automated tissue processor and the sections were stained with haematoxylin and eosin stain. The specimens were examined histopathologically.

Inclusion criteria:

The women included in the study were presented with the history of abnormal uterine bleeding (Menorrhagia, metrorrhagia, postmenopausal bleeding).

Exclusion criteria:

The Patients who were excluded from the study were those having pregnancy complications, known case of leiomyoma, and cervical pathology.

Results

A total number of 150 patients with age groups ranged from 20 to 74 years were included in the study and they are categorised in 5 different groups (Table 1). The maximum number of patients with abnormal uterine bleeding presented in the age group of 41 to 50 years was 82(54.67%) and 26 cases (17.33%) were in the age group of 51-60 years. Among 150 patients, 130(86.67%) were premenopausal age group and 20 (13.33%) were postmenopausal age group. Majority (66%) of the patients were multiparous (para 1-2) and 13.3% were nulliparous.

The most common complaint was menorrhagia 75(50%) followed by metrorrhagia 55(36.67%) and postmenopausal bleeding was noted in 20 cases (13.33%). Histopathological examination of the endometrial tissue showed predominantly proliferative endometrium 65(43.33%) followed by disordered proliferative endometrium 26(17.33%) and then hyperplasia with atypia 6(4%). Endometrial carcinoma was found only in 3 (2%) cases. Mixed pattern was seen in 2 (1.3%) cases. 6 cases were inadequate for any diagnostic opinion due to abundant blood clots. Table 2 shows the histopathological diagnosis of endometrial biopsy.

All three cases of endometrial carcinoma were adenocarcinoma, out of which two were in the age group of >60 years and one was in 31-40 years of age. The benign endometrial polyp was more common in 41-50 years of age group than in the other age groups. In elderly patients, atrophic endometrium was commonly seen and the most common pattern in postmenopausal bleeding 9/20 (45%) followed by endometrial hyperplasia and endometrial carcinoma 7/20(35%) and 2/20 (10%) respectively. Table 3 shows the histopathological diagnosis of endometrial sample according to age groups.

In <30 years of age group, the predominant endometrial pattern was proliferative 6/10. Hence no significant pathology was found in this group.

In >60 years of age group 2 cases of malignancy were noted. Hence significances were found.

Depending on the age, severity of the bleeding, histopathological findings and willingness of the patient, all the cases in our study were treated either conservatively or by surgical management. The conservative treatments such as tranexemic acid, oral contraceptive pills, oral progesterone and Levonorgestrel-intrauterine delivery system (LNG-IUD). Surgical treatments such as abdominal hysterectomy, vaginal hysterectomy and total laparoscopic hysterectomy with or without oophorectomy. Table 4 shows management of AUB in different age groups.

Conservative treatments were given to all the patients under group I. In group II, most of the patients were conservatively managed while surgery was
performed in only one patient with endometrial carcinoma. In group III, 23 cases were undergone surgery who were having hyperplasia, disorderly proliferative endometrium and severe degree of bleeding and unwillingness to conservative treatment and follow up. In group IV, most of them were surgically treated. In group V, 3 cases with atrophic endometrium were conservatively managed and 2 cases with endometrial carcinoma were surgically treated.

Discussion:
Abnormal uterine bleeding is a frequently encountered problem affecting the women of reproductive age group that has an economic and social impact significantly by causing anaemia, disturbance of women’s sexual life and daily activities [6]. It is the challenging problem to the gynaecologist regardless of age [7]. The cause of AUB includes a wide spectrum of diseases of the reproductive system as well as non-gynaecological issues. The diagnosis of DUB is made when organic causes of AUB are ruled out. The sensitivity for detection of endometrial pathologies by endometrial biopsy is very high 96% [8].

The significance of this study was that the menstrual disorders increase with increase in age.

In our study, the highest incidence of AUB was noted in the 41-50 years of age group. A similar incidence was reported by Yusuf et al, Muzaffar et al, Saraswathi et al [9,10, and 11].

This may due to the fact that, the ovarian follicles are reduced in number and their resistance to gonadotrophic stimulation have been increased during menopausal period, which results in decreased estrogen level. Hence the normal growth of endometrium is affected.

In patients with age >60years, the incidence of AUB was low (5.3%) probably due to an early diagnosis and treatment.

In the present study, menorrhagia was the most common clinical complaint (50%). Similar results were observed in studies done by Archana et al (43.85%) and Sajitha et al (47%) [12,13].

Most of our patients were in the multiparous category. Other studies also reported a higher incidence of AUB with increase in parity [14,15,16].

The commonest endometrial pattern in this study was proliferative endometrium (Fig 1) in 65 cases (43.33%) followed by disordered proliferative endometrium (Fig 5) in 26 cases (17.33%) which is similar to study of Kumari SR et al [17]. The secretory endometrium (Fig 2) was found in 21 cases (14%). The bleeding in proliferative endometrium may be due to anovulatory cycles and in secretory phase due to ovulatory dysfunctional uterine bleeding.

Atrophic endometrium (Fig 3) was mostly seen in postmenopausal women [18]. Atrophy of endometrium is due to prolonged absence of any endogenous or exogenous estrogenic stimulation. The incidence of atrophic endometrium in our study was (6.6%) and they presented as postmenopausal bleed. A similar incidence was noted in studies of Sajitha et al (5.13%) and Ara S et al (7%) [13,19].

The incidence of benign endometrial polyp (Fig 4) in our study was 2%. Bolde SA et al. found the same (1.79%) [20].

In our study, endometrial hyperplasia (Fig 6,7) (9.3%) was the most common pathological cause for AUB. The incidence was lower than quoted by study of Afgan S et al (20.6%) [21]. The diagnosis of endometrial hyperplasia is very important as it is thought to be the precursors for endometrial carcinoma.

The endometrial carcinoma (Fig 8) was seen in 2% of cases as it is the least common pathology in this study. Studies by Bolde SA et al. [20] and Gerald et al. [22] showed the incidences of 1.49% and 1.7% respectively. The histological type of endometrial carcinoma in this study was endometrioid adenocarcinoma with no lymphovascular invasion noted.

Among three, less than half of the myometrium were involved in 2 cases and more than half of the myometrium was involved in one patient.

Many studies have showed that majority of malignant cases were in the postmenopausal age group [23].

The safest and effective diagnostic method in the evaluation of AUB after medical causes has been ruled out is endometrial biopsy.

The management of AUB is mainly based on histopathological patterns of endometrium. Medical
and hormonal therapy were given to young patients with normal endometrium while surgery was usually required for perimenopausal and postmenopausal females with an abnormal endometrial pathology.

**Conclusion:**

The Endometrial lesions vary according to the patient’s age.

Histopathology showed wide spectrum of endometrial changes ranging from normal endometrium to malignancy. Hence the endometrial sampling by dilatation and curettage is a necessary diagnostic tool to manage AUB. Especially in premenopausal and postmenopausal age groups it is important to rule out pre-neoplastic and neoplastic conditions.

**Acknowledgement:**

I wish like to express my gratitude to Dr. Archana S, Assistant professor of pathology for her guidance and support.

I would also like to thank to my HOD, Dr.V.Eswari for giving me the opportunity to do this study.

**References:**


17. Kumari SR, Anuradha M. Endometrial patterns in abnormal uterine bleeding: a
FIGURE LEGENDS:

1. Figure 1 – Secretory endometrium (H&E10x): The endometrial glands are tortuous and dilated with loose edematous stroma.
2. Figure 2 – Disorderly proliferative endometrium (H&E10x): The endometrial glands are varying in size and shapes with some of the glands are cystically dilated in a compact stroma.
3. Figure 3– Hyperplasia with atypia (H&E 40x): The endometrial glands show stratification, increased gland stroma ratio, abundant back to back arrangement of glands, minimal intervening stroma and cytological atypia - loss of nuclear polarity, pleomorphic vesicular nucleus and clumped chromatin with prominent nucleoli.
4. Figure 4– Endometrial carcinoma (H&E 40x): The malignant epithelial cells are arranged in papillary and glandular pattern. Closely packed endometrial glands show increased gland stroma ratio, stratification, cytological atypia - high nucleocytoplasmic ratio and irregular clumping of nuclear chromatin with sparse to absent intervening stroma. Necrosis seen.

Table 1: Distribution of AUB in different age groups

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>AGE IN YEARS</th>
<th>NO.OF PATIENTS</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≤30</td>
<td>10</td>
<td>6.67%</td>
</tr>
<tr>
<td>2</td>
<td>31-40</td>
<td>24</td>
<td>16%</td>
</tr>
<tr>
<td>3</td>
<td>41-50</td>
<td>82</td>
<td>54.67%</td>
</tr>
<tr>
<td>4</td>
<td>51-60</td>
<td>26</td>
<td>17.33%</td>
</tr>
<tr>
<td>5</td>
<td>&gt;60</td>
<td>8</td>
<td>5.33%</td>
</tr>
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</table>

### Table 2: Histopathological diagnosis of endometrial biopsy

<table>
<thead>
<tr>
<th>Histopathological diagnosis</th>
<th>No of patients</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Proliferative</td>
<td>65</td>
<td>43.33%</td>
</tr>
<tr>
<td>Disordered proliferative</td>
<td>26</td>
<td>17.33%</td>
</tr>
<tr>
<td>Secretory</td>
<td>21</td>
<td>14%</td>
</tr>
<tr>
<td>Atrophic</td>
<td>10</td>
<td>6.67%</td>
</tr>
<tr>
<td>Hyperplasia without atypia</td>
<td>8</td>
<td>5.33%</td>
</tr>
<tr>
<td>Hyperplasia with atypia</td>
<td>6</td>
<td>4%</td>
</tr>
<tr>
<td>Unsatisfactory</td>
<td>6</td>
<td>4%</td>
</tr>
<tr>
<td>Carcinoma</td>
<td>3</td>
<td>2%</td>
</tr>
<tr>
<td>Polyp</td>
<td>3</td>
<td>2%</td>
</tr>
<tr>
<td>Mixed pattern</td>
<td>2</td>
<td>1.33%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>150</strong></td>
<td><strong>100%</strong></td>
</tr>
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### Table 3: Age wise distribution of different endometrial patterns

<table>
<thead>
<tr>
<th>Age group</th>
<th>P</th>
<th>DPE</th>
<th>S</th>
<th>A</th>
<th>H</th>
<th>H</th>
<th>US</th>
<th>CA</th>
<th>EP</th>
<th>MP</th>
<th>TOTAL</th>
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</thead>
<tbody>
<tr>
<td>21-30</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>31-40</td>
<td>12</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>24</td>
</tr>
<tr>
<td>41-50</td>
<td>35</td>
<td>18</td>
<td>15</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>82</td>
</tr>
<tr>
<td>51-60</td>
<td>12</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>26</td>
</tr>
<tr>
<td>&gt;60</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>65</strong></td>
<td><strong>26</strong></td>
<td><strong>21</strong></td>
<td><strong>10</strong></td>
<td><strong>8</strong></td>
<td><strong>6</strong></td>
<td><strong>3</strong></td>
<td><strong>3</strong></td>
<td><strong>2</strong></td>
<td></td>
<td><strong>150</strong></td>
</tr>
</tbody>
</table>

1. Proliferative endometrium
2. Disordered proliferative endometrium
3. Secretory endometrium
4. Atrophic endometrium
5. Hyperplasia without atypia
6. Hyperplasia with atypia
7. Unsatisfactory
8. Carcinoma endometrium
9. Endometrial polyp
10. Mixed pattern
Table 4: Management of AUB in different age groups

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>NO. OF CASES</th>
<th>CONSERVATIVE TREATMENT</th>
<th>SURGERY</th>
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<tbody>
<tr>
<td>1</td>
<td>10</td>
<td>10 (100%)</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>23 (95.8%)</td>
<td>1(4.2%)</td>
</tr>
<tr>
<td>3</td>
<td>82</td>
<td>23(28%)</td>
<td>59(72%)</td>
</tr>
<tr>
<td>4</td>
<td>26</td>
<td>6(23%)</td>
<td>20(77%)</td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>3(37.5%)</td>
<td>5(62.5%)</td>
</tr>
</tbody>
</table>

Figure 1 – Secretory endometrium (H&E10x)

Figure 2 – Disorderly proliferative endometrium (H&E10x)
Figure 3– Hyperplasia with atypia (H&E 40x)

Figure 4– Endometrial carcinoma (H&E 40x)