Histopathological Study of Endometrium in Abnormal Uterine Bleeding
An Experience in a Tertiary Care Centre of Rural South India

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ABSTRACT

Introduction: Abnormal uterine bleeding continues to be one of the most frequently encountered complaints in Gynecology and one of the most common and perplexing problems both to the patient and the gynecologist. It is defined as a pattern of bleeding that does not correspond with the duration, amount and frequency of the flow of a normal menstrual cycle.

Aim and Objectives: The present study was carried out to document the histomorphological pattern of endometrium in abnormal uterine bleeding, to correlate it with age and symptoms and the incidence of malignancy in this subset of population.

Material and methods: This is a retrospective study done on the patients with chief complaints of AUB and infertility in the Department of pathology, Govt. Dharmapuri Medical College, Dharmapuri, for a period of two years, includes 228 cases, in the age group of 21-65 years, who subjected for endometrial biopsies. The biopsies obtained, were sent in 10% neutral buffered formalin, underwent the routine processing, stained and studied under light microscopy.

Results: Clustering of cases were around 41-50 years representing 48.7%, with metro menorrhagia as chief complaints in 29%. The commonest pathology observed is Disordered Proliferative endometrium in 71 Patients (31.1%) and proliferative endometrium in 25.9%. In perimenopausal age group, Hyperplasia with atypia was frequently noted, with very low incidence of malignancy in this subset of population.

Conclusion: Histopathological examination of endometrial biopsy is an important tool to diagnose, whether benign, pre-malignant and malignant, and help the gynecologist to decide appropriate therapeutic strategy. Hence, the reporting pathologist should be vigilant, as it has an impact on patient's life and treatment.

Key Words: Abnormal uterine bleeding, Endometrium, Infertility, Disordered proliferative endometrium

INTRODUCTION:

Abnormal Uterine Bleeding (AUB) is one of the most common and significant gynaecological complaints in the reproductive age group of women and accounts for about 10-15%. It is defined as a pattern of bleeding that does not correspond with the duration, amount and frequency of the flow of a normal menstrual cycle. The prevalence increases with age, adolescence and perimenopausal women are particularly vulnerable and it is mostly associated with anovulatory menstrual cycles. Histopathological examination of endometrial biopsies and curetting is considered to be the gold

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standard in the diagnosis of its etiology. It is also equally important in evaluating patients for infertility in terms of the dating of the endometrium. Its histological appearance used to document the ovulation and to assess the hormonal status. The endometrial biopsy has been chosen to evaluate DUB as it is safe, relatively easy to perform and can be done as day care procedure. Other investigations like hormonal assays are relatively expensive and laboratories with hormonal assay may not be available in rural areas.

MATRIALS AND METHODS:

This is a retrospective study done on the patients with chief complaints of AUB and infertility in the Department of pathology, Govt. Dharmapuri Medical College, Dharmapuri, for a period of two years from Jan 2015 to Dec 2016. The study material includes a total number of 228 cases, in the age group of 21-65 years, who subjected for endometrial biopsies. The endometrial biopsies obtained, were sent in 10% neutral buffered formalin, and underwent the routine processing; sections were stained by haematoxylin and eosin and studied under light microscopy. Patients were categorised into five groups, Histopathological diagnosis was made and recorded; further categorization was done for all cases. This study was approved by Ethical Committee. The data's were compiled and statically analysed.

A. Criteria for inclusion

1. Patients with complaints of Abnormal Uterine Bleeding.

B. Criteria for exclusion

1. Patients with organic lesions involving the genital tract like leiomyomas, adenomyosis, cervical and vaginal pathology.

2. Patients with systemic disease like haemostatic disorders etc.

3. Patients with pregnancy.

C. Criteria for adequacy of specimen:

Specimens where there is no endometrial tissue or only minimal stromal elements or couldn't be concluded, in spite of the presence of some tissue, a diagnosis of inadequate for evaluation were given.

RESULTS:

The present study included 228 specimens of endometrial biopsies received in the department of pathology, Govt. Dharmapuri Medical College, Dharmapuri, for a period of two years from Jan 2015 to Dec 2016.

The patient age ranges from 21 years to 67 years; they were subdivided into five groups. Maximum numbers of patients were in 41-50 years representing 48.7% which is followed by 31-40 years group 41.2 %. (Table 1)

Table 1. Age wise Distribution

<table>
<thead>
<tr>
<th>AGE</th>
<th>NO OF PATIENTS</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LESS THAN 30</td>
<td>4</td>
<td>1.80%</td>
</tr>
<tr>
<td>31-40</td>
<td>94</td>
<td>41.20%</td>
</tr>
<tr>
<td>41-50</td>
<td>111</td>
<td>48.70%</td>
</tr>
<tr>
<td>51-60</td>
<td>14</td>
<td>6.10%</td>
</tr>
<tr>
<td>MORE THAN 60</td>
<td>5</td>
<td>2.20%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>228</td>
<td>100%</td>
</tr>
</tbody>
</table>

Metromenorrhagia was the common complaints seen in 66 cases out 228 (29%), which is followed by menorrhagia in 44 cases (21.5%). Significant number of patients were with symptoms of menorrhagia (44%), polymenorrhoea (15%), post-menopausal bleeding (8.30%) and infertility (6.1%). (Table 2)
Table 2. Symptom wise distribution

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infertility</td>
<td>14</td>
<td>6.10%</td>
</tr>
<tr>
<td>Post menopausal bleeding</td>
<td>59</td>
<td>26.0%</td>
</tr>
<tr>
<td>Metromenorrhagia</td>
<td>44</td>
<td>19.34%</td>
</tr>
<tr>
<td>Polymenorrhagia</td>
<td>44</td>
<td>19.34%</td>
</tr>
<tr>
<td>Menorrhagia</td>
<td>14</td>
<td>6.09%</td>
</tr>
<tr>
<td>Metrorrhagia</td>
<td>19</td>
<td>31.56%</td>
</tr>
<tr>
<td>Lower abdominal Pain/PM</td>
<td>2</td>
<td>0.90%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>228</strong></td>
<td><strong>100%</strong></td>
</tr>
</tbody>
</table>

The patients were categorized into ten groups depending upon the histomorphological diagnosis. The commonest pathology observed is Disordered Proliferative endometrium in 71 Patients (31.1%), which is followed by Proliferative Endometrium in 59 cases (26%), Secretory endometrium in 47 cases (20.6%) and Atrophic endometrium in five cases (2.2%). Significant number of cases represented with Hyperplasia without atypia 20 cases (8.8%). Cases of Hyperplasia with atypia, chronic endometritis, Squamous cell carcinoma seen in two patients (0.9%). No adeno carcinoma case were found in this study group. Eighteen biopsies were insufficient for evaluation (8%). (Graph 1)

Graph 1. Histomorphological Pattern

While comparing age with symptoms, reproductive age group, 41-50 years, metromenorrhagia seems to be more prevalent, 43 cases (38.7%). Whereas in 31-40 years, commonly presented with metrorrhagia, 33 cases (35.1). In perimenopausal and post-menopausal age group, post-menopausal bleeding seems to be the prominent symptom. (Table 3)

Table 3. Correlation of age with symptoms

<table>
<thead>
<tr>
<th>Age</th>
<th>Infertility</th>
<th>Not menorrhagia bleeding</th>
<th>Metromenorrhagia</th>
<th>Proliferative</th>
<th>Secretory</th>
<th>Atrophic</th>
<th>Pregnancy</th>
<th>Menorrhagia</th>
<th>Metrorrhagia</th>
<th>Lower abdominal Pain/PM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>25.0%</td>
<td>45.0%</td>
<td>10.0%</td>
<td>14.0%</td>
<td>16.0%</td>
<td>12.0%</td>
<td>10.0%</td>
<td>12.0%</td>
<td>13.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>31-40</td>
<td>43.0%</td>
<td>39.0%</td>
<td>11.0%</td>
<td>14.0%</td>
<td>14.0%</td>
<td>12.0%</td>
<td>10.0%</td>
<td>12.0%</td>
<td>13.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>41-50</td>
<td>38.0%</td>
<td>41.0%</td>
<td>11.0%</td>
<td>14.0%</td>
<td>14.0%</td>
<td>12.0%</td>
<td>10.0%</td>
<td>12.0%</td>
<td>13.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>50+</td>
<td>39.0%</td>
<td>41.0%</td>
<td>11.0%</td>
<td>14.0%</td>
<td>14.0%</td>
<td>12.0%</td>
<td>10.0%</td>
<td>12.0%</td>
<td>13.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
</tbody>
</table>

While comparing age with histomorphological findings there were two cases each of proliferative and secretory endometrium in < 30 years of age. In age group of 31-40 years and 41-50 years, disordered proliferative endometrium seems to be the most predominating pattern, that is in 34 cases, which was followed by equal incidence of proliferative 33 cases (Table 4).

Table 4. Correlation of age with histomorphological findings

<table>
<thead>
<tr>
<th>Age</th>
<th>Infertility</th>
<th>Not menorrhagia bleeding</th>
<th>Metromenorrhagia</th>
<th>Proliferative</th>
<th>Secretory</th>
<th>Atrophic</th>
<th>Pregnancy</th>
<th>Menorrhagia</th>
<th>Metrorrhagia</th>
<th>Lower abdominal Pain/PM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>30.0%</td>
<td>40.0%</td>
<td>10.0%</td>
<td>14.0%</td>
<td>14.0%</td>
<td>12.0%</td>
<td>10.0%</td>
<td>12.0%</td>
<td>13.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>6-10</td>
<td>35.0%</td>
<td>35.0%</td>
<td>11.0%</td>
<td>15.0%</td>
<td>15.0%</td>
<td>13.0%</td>
<td>11.0%</td>
<td>13.0%</td>
<td>14.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>11-15</td>
<td>38.0%</td>
<td>38.0%</td>
<td>11.0%</td>
<td>15.0%</td>
<td>15.0%</td>
<td>13.0%</td>
<td>11.0%</td>
<td>13.0%</td>
<td>14.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>16-20</td>
<td>40.0%</td>
<td>40.0%</td>
<td>11.0%</td>
<td>15.0%</td>
<td>15.0%</td>
<td>13.0%</td>
<td>11.0%</td>
<td>13.0%</td>
<td>14.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>&gt;20</td>
<td>35.0%</td>
<td>35.0%</td>
<td>11.0%</td>
<td>15.0%</td>
<td>15.0%</td>
<td>13.0%</td>
<td>11.0%</td>
<td>13.0%</td>
<td>14.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
<tr>
<td>total</td>
<td>30.0%</td>
<td>35.0%</td>
<td>11.0%</td>
<td>15.0%</td>
<td>15.0%</td>
<td>13.0%</td>
<td>11.0%</td>
<td>13.0%</td>
<td>14.0%</td>
<td>0.0%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Of the 228 cases, the most common presenting symptom is metromenorrhagia (62 cases), which is followed by metrorrhagia (45 cases), with these symptoms, Disordered proliferative endometrial pattern (24 cases, 14 cases respectively) is quite common. Among the 40 cases of menorrhagia, proliferative endometrium is the most common histological pattern. In patients with post-menopausal bleeding and polymenorrhagia, disordered proliferative endometrium seems to be the common finding. In infertility cases, the secretory endometrium (7 cases) followed by proliferative endometrium (4 cases) are seen. Inadequate sample is very common with post-menopausal bleeding patients.
DISCUSSION:

Excessive and irregular uterine bleeding (abnormal uterine bleeding) continues to be one of the most frequently encountered complaints in Gynaecology and one of the most common and perplexing problems both to the patient and the gynaecologist. Abnormal uterine bleeding is a diagnosis of exclusion in which no specific organic cause can be attributed to as the reason for the bleeding. The diagnosis is mostly based on patient's symptoms and clinical findings. In most of the cases, a pelvic ultrasonography is done to correlate the clinical findings.

Dilatation and curettage is said to be a diagnostic as well as a therapeutic procedure for these patients. The sensitivity of endometrial biopsy for detection of endometrial abnormalities is very high 96%. Endometrial cancer, the most frequent gynaecologic malignancy in the developing world, which develops through preliminary stages of endometrial hyperplasia, which can be very well picked up even in small endometrial biopsies. Thus, correct diagnosis whether benign, premalignant and malignant, and help the gynaecologist to decide appropriate therapeutic strategy.

Our study significantly reveals that the occurrence of menstrual disorders increases with advancing age. The commonest age group presenting with excessive bleeding was 41–50 years. A similar incidence was reported by Yusuf et al., Muzaffar et al., and Saraswathy et al. The reason for increased incidence of dysfunctional uterine bleeding in this age group (41–50 years) may be due to the fact that these patients are in their climacteric period, as women approach menopause, cycles shorten and often become intermittently anovulatory due to a decline in the number of ovarian follicles and the estradiol level.

AUB can present with many symptoms, varies with the age and causes. Menometrorrhagia is defined as irregular and heavy bleeding, occurs in peri–menopausal women, generally due to anovulatory cycles. Few years following menarche, and certain years before menopause, anovulatory cycles are quite common. Metrorrhagia is defined as excessive flow during regular cycles, might continue for more than a week, seen in ovulatory cycles. The main defect here seems to be a lack of control over the haemostasis mechanism, causes dysregulation of the volume lost. The present study shows, occurrence of metro menorrhagia (29%) commonly compared with menorrhagia (21.5%), as a presenting complaint could be due to the fact that majority of the patients had disordered proliferative endometrium (31.1%), implying anovulatory cycles. This is in concordance with study done by Puneet Kaur et al., and Saraswathy et al.

In this study group, disordered proliferative endometrium seems to be the commonest pattern observed, (31.1%). The term disordered endometrium refers to proliferative phase that does not seem to appropriate for any one time in the menstrual cycle and mimics simple hyperplasia, but the process is focal rather than diffuse. Histologically there show mild disorganization of architecture, with focal dilated glands, with normal gland to stromal ratio.

The higher incidence of disordered proliferative pattern in concordance with the study carried out in Chennai by Saraswathy et al., Revathy et al., Khare et al., and Sarika et al. This could explain the earlier stage of presentation due increasing trend in health awareness.
The study also reveals normal cyclic pattern of proliferative endometrium (25.9) (FIG.2) and secretory endometrium (20.6%) (FIG.3). In anovulatory cycle, bleeding is due to lack of progesterone possibly non-development of corpus luteum, (Fig4) but inovulatory cycle, it includes luteal phase defects and irregular shedding, due to persistence corpus luteum, leading to prolonged progesterone level (Fig.5). This is in agreement with the study conducted by Saraswathy et al., and Amruta Padhye et al., ⁷, ¹³

We labelled our specimens as inadequate, if there were no tissue, or if no diagnosis could be arrived, in spite of the presence of biopsy material, the incidence was the highest, in the post-menopausal age group, due to atrophy of the endometrium. ¹, ⁸, ¹³

In age group less than 30 yrs, commonly presented with infertility with equal incidence of proliferative and secretory pattern possibly due to anovulatory cycle. Endometritis and benign endometrial polyps were common in 41-50 yrs. This in agreement with the many studies that includes, study of Saraswathy et al, Revathy et al and Gredmark et al.⁷, ¹¹, ¹³

Atrophic endometrium was seen predominantly in the 51–60 years age group. The incidence is compared with the study conducted by Batta et al,¹⁴ whereas it's slightly lower when compared with Gredmark et al.¹³ The incidence of endometrial hyperplasia with atypia in this study was comparable with Vani padmaja et al¹⁵ and less as compared to others.¹³, ¹⁶ The possible explanation could be these patients are being identified at a much earlier stage that is in the disordered proliferative phase.

**Figure 1.** H&E Section of Disordered Proliferative Endometrium with mild disorganized glands in loose stroma. (10X)
**Figure 2.** H&E Section of Proliferative Endometrium with tubular glands in compact stroma. (10X).
**Figure 3.** H&E Section of Secretory Endometrium with glands lined by secretory epithelium with basally placed vacuoles. (10X)
While comparing about malignancies the squamous
cell carcinoma was found in less than 1% of cases
with plausible explanation could be from
endocervical origin. No adeno carcinoma was seen
in this group. This in contrast with many studies
which showed incidence less than 1%. Asian women
show lower incidence of endometrial carcinoma
when compared with the west due to early
childbearing, lesser obesity and a more active life
style.

CONCLUSION:

Histopathological examination of endometrial
biopsy is an important tool to diagnose
gynecological conditions, show wide spectrum of
changes ranging from normal endometrium to
malignancy. In the present study, the most frequent
findings seen in patients with DUB in 41-50 years,
with disordered proliferative endometrial pattern.
In perimenopausal age group Hyperplasia with
atypia was frequently noted, with very low
incidence of malignancy in this subset of
population.

REFERENCES

1. Puneet Kaur, Anureet Kaur, Anil Kumar Suri,
Harpreet Sidhu. A two year histopathological
study of endometrial biopsies in a teaching
hospital in Northern India. Indian Journal of
Pathology and Oncology, July-September
2016; 3(3); 508-519.

2. Bhoomika Dadhania, Gauravi Dhruva, Amit
Agravat, Krupal Pujara. Histopathological
study of endometrium in dysfunctional uterine


