Histopathological Findings Of Endometrium In Abnormal Uterine Bleeding

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ABSTRACT

Abnormal uterine bleeding (AUB) is defined as any departure from normal menstrual cycle pattern. AUB due to non-obstetric causes has been classified by International Federation of Gynecology and Obstetrics (FIGO) as per PALM-COEIN system which comprises of polyps, adenomyosis, leiomyoma, malignancy, coagulopathy, ovarian dysfunction, endometrial, iatrogenic and not yet classified. The PALM-COEIN classification provides uniform nomenclature which aids clinicians in patient treatment and prognostication.

Aims – To study histopathology of endometrium in cases of abnormal uterine bleeding in non-obstetric causes as per PALM-COEIN classification.

Methods - This study was conducted in department of Pathology, Christian Medical College over a period of two years. A total of 719 endometrial specimens were studied, out of which 295 were endometrial curettings and 424 were hysterectomy specimens.

Results - The most common age group of patients with AUB was 41-50 years. Histopathological examination showed endometrial pathology in 38% cases. Endometrial hyperplasia was seen in 7.7% cases followed by polyps in 6.5%, endometritis in 5.6%, functional endometrium in 5.5%, progesterone effect endometrium in 12% and malignancy was seen in 2.4% of cases. Normal physiological endometrium was seen in majority 62% of the cases.

Conclusion - The PALM–COEIN system gives a structured classification taking into account both the clinical and histopathological features in women with AUB. Persistent unexplained AUB requires definite morphological diagnosis by histopathological examination of endometrium in women especially in age group more than 40 years which should be diligently undertaken.

Keywords: Abnormal uterine bleeding, PALM-COEIN, endometrium.
INTRODUCTION:
Abnormal uterine bleeding (AUB) is defined as changes in frequency of menstruation, duration of flow or amount of blood loss.\(^1\) Abnormal uterine bleeding (AUB) is a commonly encountered gynecological problem.\(^2\) Postmenopausal bleeding is defined as vaginal bleeding occurring after one year of amenorrhea in a woman of the age where the menopause can be expected.\(^3\) It accounts for 5% of cases in gynecological practice.\(^4\) Minimal bleeding at postmenopausal period may be alarming and require in depth evaluation since this may be the only clinical manifestation pointing towards endometrial cancer.\(^5\) AUB has been classified by International Federation of Gynecology and Obstetrics (FIGO) as per PALM-COEIN system which comprises of polyps, adenomyosis, leiomyoma, malignancy, coagulopathy, ovarian dysfunction due to endocrine disorders causing anovulation, endometrial, iatrogenic including drugs and not yet classified.\(^6\) Thus, PALM refers to structural causes whereas COEIN refers to non-structural causes. Endometrial sampling should be performed to evaluate abnormal bleeding in women who are at risk for endometrial polyps, hyperplasia or carcinoma.\(^5\) Histopathological examination of endometrium helps in early diagnosis, management and cannot be overemphasized especially in peri and postmenopausal females who are at a risk of developing malignancy.

MATERIAL & METHODS
This study was conducted in department of Pathology, Christian Medical College over a period of two years. A total of 719 endometrial specimens were studied, out of which 295 were endometrial curettings and 424 were hysterectomy specimens. All the specimens of endometrium sent as curetting, biopsy and hysterectomy with clinical diagnosis of abnormal uterine bleeding were included in the study and those due to obstetrical causes were excluded. All specimens were received in 10% neutral buffered formalin. The gross morphology was recorded with total submission of endometrial samples and representative bits were taken. The tissue bits were processed in Leica automatic tissue processor and paraffin blocks were prepared. Tissue sections of 4–6 microns thickness were cut and stained with Hematoxylin and Eosin stain (H&E). Microscopic examination was done, findings were recorded and descriptive statistics was applied.

RESULTS
The age of the patients ranged from 18 to 85 years with mean age 42.5±8.2. Majority of cases (56%) were in fourth and fifth decades. Menorrhagia was the most common manifestation seen in 33.7% cases followed by polymenorrhagia and metrorrhagia in 27.5% and 14.5% during 41-50 years of age respectively. Out of 719 patients, 343 (47.7%) were perimenopausal in the age group of 41-50 years while 54 (7.5%) were postmenopausal. The prevalence of AUB was highest (90%, 363/403) in perimenopausal age group of 41-60 years followed by (301/719, 41.8%) in women of age group 18-40 years and (12.9%, 54/418) in postmenopausal women in age group 41-85 years of age.

<table>
<thead>
<tr>
<th>Table1-Endometrial findings in patients with AUB</th>
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<tbody>
<tr>
<td>Endometrium</td>
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<td>-------------</td>
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<tr>
<td>Physiological</td>
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<tr>
<td>Functional</td>
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<tr>
<td>Progesterone effect</td>
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<td>Polyp</td>
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<td>Endometritis</td>
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</table>
Histopathological examination showed the physiological endometrium as a predominant finding in 62% patients, out of which secretory phase endometrium was found in 211 (29.3%) followed by proliferative phase endometrium in 190 cases. Organic lesions were found in 21% cases, comprised mainly of endometrial hyperplasia, endometritis, polyps and carcinomas. Endometrial adenomatous polyp was seen in 6.5% cases while endometrial hyperplasia was seen in 7.7% patients with AUB. Of these, 7% cases belonged to simple hyperplasia without atypia and 0.6% cases were of complex atypical hyperplasia. Endometritis was seen in 5.6% cases, out of which granulomatous endometritis was found in 0.3% cases. Malignancies were found in 2.4% cases.

In very young patients of age group 18-20 years, 3 patients showed normal physiological endometrium while endometritis was seen in only one patient. Endometritis and endometrial polyps were more common in women of reproductive age group. Endometrial polyps were found in (37/47, 78%) in the age group 31-50 years. Endometrial hyperplasia was seen more commonly (41/55, 74%) in the age group 41-60 years. Progesterone effect endometrium was common (58%) in the age group 41-60 years where it was possibly due to treatment in view of endometrial hyperplasia.

Malignancies were found more commonly (88%, 15/17) in postmenopausal age group (Table 1) of which all were carcinomas. There were (15/54, 27.7%) cases of carcinomas in postmenopausal age group. Endometrioid carcinoma constituted 15 cases, out of which well differentiated endometrioid adenocarcinoma found in 1, moderately differentiated endometrioid adenocarcinoma in 11 while poorly differentiated in 3 cases. Squamous cell carcinoma of endometrium extending from cervix was seen in 1 patient who was 60 years old while adeno squamous carcinoma was seen in patient aged 78 years. The present study also shows the association of AUB with other lesions comprising of leiomyoma, adenomyosis and endocervical polyp as seen on hysterectomy specimens. (Table 2)
Table 2. Additional findings on hysterectomy specimens:

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. of patients</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Leiomyoma</td>
<td>225</td>
<td>53.1</td>
</tr>
<tr>
<td>Adenomyosis</td>
<td>157</td>
<td>37</td>
</tr>
<tr>
<td>Endocervical polyp</td>
<td>7</td>
<td>1.7</td>
</tr>
</tbody>
</table>

(Figure 1: Endometrial hyperplasia without atypia, Figure 2: complex hyperplasia with atypia)

(Figure 3: Granulomatous Endometritis, Figure 4: Chronic Endometritis)

(Figure 5&6: Endometrioid carcinoma, FIGO grade 1 (architectural grade 1, nuclear grade 1))
DISCUSSION
Endometrium is a dynamic, hormonally sensitive and responsive tissue, which constantly undergoes changes during the active reproductive life. It is a sensitive bioassay for estrogen and progesterone, whose actions are mediated on specific receptors. Histopathological study of endometrium in AUB helps us to determine underlying etiopathogenesis, thus helping in patient management. The youngest patient in our study was of 18 years while the oldest was 85 years, similar to study done by Doraiswami et al. The adolescent age group (less than 20 years) accounted for 1.5% of cases and their endometrium showed normal cyclical pattern similar to the studies done by Doraiswami et al and Bhatta K et al. In the present study, peak incidence of AUB was seen in 4th and 5th decade (47%) which was 8- similar to study conducted by Muzaffar et al, Doraiswami et al, Goel P et al and Betha K et al. Menorrhagia was the most common manifestation similar to the study done by Doraiswami et al while metrorrhagia was seen in 14.5% as compared to 38.5% in study done by Bhatta K et al. Postmenopausal bleeding (PMB) was seen in 12.9% cases during 51-60 years age which was slightly lower than the studies conducted by Tyagi et al (13.5%) and Gredmark T et al (23%). The prevalence of AUB was highest (90%, 363/403) in perimenopausal age group 41-60 years similar to the studies done by Doraiswami et al and Yusuf et al. The important findings in our study group showed the causes of AUB as of normal physiological endometrium in young women, endometritis as common cause in women of reproductive age group, hyperplasia to be more common in women in 41-50 years of age who also received progesterone as therapeutic management while malignancies to be common in postmenopausal women. These findings are similar to other authors. AUB due to organic causes was caused by endometrial hyperplasia, endometritis, endometrial polyp and malignancy. Endometrial hyperplasia seen in 7.6% cases, similar to study by Doraiswami et al, Bhatta K et al and Dangal et al. Identification of endometrial hyperplasia is important because they are thought to be precursors of endometrial carcinoma. Endometrial hyperplasia was seen more commonly (41/55, 74%) in the age group 41-60 years similar to studies done by Doraiswami et al and Bhatta K et al. Endometrial polyp contributed to 6.5% cases, similar to study by Betha K et al. Endometrial polyps were more common (37/47, 78%) in the age group 31-50 years similar to the study done by Bhatta K et al. Carcinoma endometrium was seen in (17/719, 2.4%) of total cases. Moderately differentiated endometrioid adenocarcinoma constituted 1.3% cases. Endometrial carcinoma seen in the age group 41-65 years, most commonly associated with postmenopausal bleeding, similar to the studies done by Doraiswami et al, Bhatta et al and Tyagi et al. Large number of patients showed normal physiological endometrium (62.4%) similar to the studies done by Doraiswami et al. The bleeding in the proliferative phase may be due to anovulatory cycles and bleeding in the secretory phase is due to.
ovulatory dysfunctional uterine bleeding. Endometrial pathology may be isolated or may occur in association with uterine pathologies such as leiomyoma and adenomyosis which also contributes to AUB.

CONCLUSION:
Endometrial cause of non-obstetric AUB is an age related pathology. The endometrial biopsies and curettings on histopathology revealed various patterns ranging from normal endometrium to malignancy. Majority of the patients with AUB presented with normal cyclic endometrium, followed by disordered proliferative endometrium and endometrial hyperplasia. The incidence of endometrial hyperplasia and endometrial carcinoma was more common in postmenopausal women. Hence, histopathological evaluation of the endometrium is specially recommended in women of these age groups presenting with AUB, to rule out possibility of preneoplastic condition or malignancy.

REFERENCES: