Histopathological Spectrum of Endometrial Changes in Women Presenting with Abnormal Uterine Bleeding with Special Reference to Endometrial Malignancies: A Two Years Hospital Based Study.

Riju Rani Deka*, Tanma Saikia, Amitabh Handique, Basanta Sonowal

1Dept. of Pathology, Tezpur Medical College, Assam, India
2Department of O&G, Tezpur Medical College, Assam, India

Keywords: Abnormal Uterine Bleeding, Clear Cell Carcinoma, Endometrial Hyperplasia, Endometrial Malignancy, Proliferative Endometrium.

ABSTRACT

Background: Abnormal uterine bleeding (AUB) is a common symptom of the patients in all age groups attending the patient department of O&G. AUB is caused by a wide variety of causes in different age. Histopathological examination of endometrial biopsy is a major diagnostic tool in evaluation of AUB. Aim: To study the spectrum of endometrial changes in all age groups presenting with AUB and to find the incidence of endometrial malignancies in this area of upper Assam.

Methods: The study was a retrospective cross sectional study of cases presenting with AUB. D&C material and endometrial biopsy specimens were collected in Pathology Department of Tezpur Medical College from 2013 July to 2015 June. Specimens were routinely processed and stained with H&E stain and morphological evaluation was done. Patients were categorized into reproductive age group (18-40 yrs), perimenopausal (41yrs-50 yrs) and postmenopausal (>50 years).

Result: A total of 150 specimens of D&C materials and endometrial biopsies were collected of which 18 cases were excluded due to inadequate sampling and finding of 132 cases were analysed. Maximum number of cases were received from reproductive age group (51.6%). Functional causes (64.4%) were the predominating irrespective of age, proliferative phase endometrium (37.2%) was the overall predominant histopathological finding. Most common cause of organic lesion was pregnancy related complications (PRC) (63%). In reproductive age PRC (35.3%) and perimenopausal age groups proliferative endometrium (35.6%) was commonest. In post menopausal age atrophic endometrium (57.8%) was the commonest finding. One case of endometrial carcinoma (0.75%) which was clear cell carcinoma, was recorded in 31-40 years group.

Conclusion: Histopathological evaluation of endometrial samples can be used as first step for diagnosis of abnormal uterine bleeding specially in post menopausal women who are at increased risk of malignancy. However histopathological evaluation is a challenge for the pathologist due to the frequent receipt of inadequate endometrial samples.

*Corresponding author:
Dr. Riju Rani Deka, C/O P. C. Deka, Bishnu Nagar, Bishnu Rabha Path, P.O- Tezpur, Dist-Sonitpur, State-Assam, Pin-784001,
Phone: +91-09435180795
E-mail: dr.rijurdeka82@gmail.com

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Introduction:
Abnormal uterine bleeding (AUB) is defined as any departure from normal menstruation or from a normal menstrual cycle pattern.\(^1\) bleeding is considered abnormal when the pattern is irregular, abnormal duration (>7 days), or menorrhagia or abnormal amount (>80ml/menses).\(^2\) Causes include functional causes like normal cyclical endometrium, abnormal physiological changes of endometrium (atrophic endometrium, weakly proliferative endometrium, disordered proliferative) and organic lesions like chronic endometritis, hyperplasia, polyp, carcinomas and pregnancy related complications. Dysfunctional uterine bleeding is defined as a type of AUB where no underlying cause can be defined. But with passing time more and more causes are being defined.\(^3\) therefore diagnosis earlier included in DUB category are now classified\(^4\) under 3 headings.

Disorders of endometrial origin (disturbances of molecular mechanisms responsible for regulation of the volume of menstrual bleeding )

Disorders of hypothalamic-pituitary-ovarian axis.

Disorders of haemostasis (coagulopathy)

These three together are called non-structural causes of abnormal uterine bleeding.\(^5\)

In reproductive age group heavy menstrual bleeding accounts for about 30% of cases,\(^6\) while postmenopausal bleeding accounts for 5% of all gynaecological visits.\(^7\) Histopathological examination of endometrial biopsy is a major diagnostic tool in evaluation of abnormal uterine bleeding.\(^8\)

AIM: Varied causes of AUB and availability of endometrial samples led us to find out the endometrial causes of abnormal uterine bleeding in women of all age groups.

Materials and Methods
This study was a retrospective cross sectional study carried out in the Department of Pathology, Tezpur Medical College, Assam for a period of two years from July 2013 to June 2015. 150 samples collected mainly were D& C material and endometrial biopsy from specimens from women presenting with AUB, sent to the histopathology section of the Department of Pathology. Samples were fixed in 10% formalin and routinely processed, stained with H&E stain. Histopathological evaluation was done under light microscope.

A recent study showed that there is a considerable controversy among gynaecological pathologists about the definition of an adequate endometrial biopsy specimen.\(^9,10,11,12,13,14\) Here material was termed inadequate when only a strip of cervical tissue and a very small amount of endometrial tissue composed of endometrial surface lining epithelium only was seen in the sample. A total of 18 cases were excluded from the study considering them as inadequate samples.

The age of the patients were categorized as reproductive (18-40 years), peri-menopausal (41-50 years) and postmenopausal (>50 years) age groups.

The histopathological findings were classified as functional and organic causes. Functional causes included physiological cyclical changes i.e proliferative and secretory phases, atrophic and weakly proliferative endometrium, disordered proliferative endometrium, nonspecific degenerative changes. Organic causes included endometrial polyp, chronic endometritis, hyperplasia, carcinomas and pregnancy related complications which again comprises of retained product of conceptus (RPOC) and gestational trophoblastic diseases (GTD).

Result
In our study, functional cause (64.4%) was the predominant finding for AUB [figure:1]. Majority of cases were observed in reproductive age group (51.6%) [table:1]. Organic lesions (27.3%) were the major cause of AUB in reproductive age group while functional issues were predominating in perimenopausal and post menopausal age groups. [figure:2]

<table>
<thead>
<tr>
<th>Age group</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive</td>
<td>68 (51.6%)</td>
</tr>
<tr>
<td>Perimenopausal</td>
<td>45 (34%)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>19 (14.4%)</td>
</tr>
</tbody>
</table>

Fig. 1: Diagram showing the distribution of causes:
In our study it was observed that in early period of life, organic lesions were the main cause of AUB while with increasing age incidence of functional cause predominated. (fig:3)

The common findings recorded in functional issues were normal cyclical endometrium i.e proliferative phase (37.2%), secretory phase (18.6%) and atrophic endometrium (26.7%) [table.2]. Most commonly seen lesions in the list of organic lesions were pregnancy related complications (63%) and endometrial hyperplasia (32.6%). [table.3]. pregnancy related complications in histopathological sections showed retained product of conceptus (54.3%) and hydatidiform mole (8.7%).

18-20 years of age group had minimum number of cases which were mainly pregnancy related endometrial finding with equal frequency i.e retained product of conceptus(50%) and hydatidiform mole(50%).[table.4]

In 21-30 years of age RPOC was the predominant change (13, 46.4%) while in 31-50 years of age proliferative endometrium (30.5%, 35.6%) predominated. In 51-60 years atrophic endometrium(58.3%) was mainly seen. Atrophic changes were the common finding seen at old age.[table4.]

One case of clear cell carcinoma of endometrium was recorded at 33years of age. Other histopathological finding of endometrium noted in our study were non specific degenerative changes, chronic endometritis. Endometrial hyperplasia which was mainly simple hyperplasia without atypia, seen mainly in perimenopausal age.

**Discussion**

Our study received maximum number of cases from reproductive age group which is comparable to the study carried out in Meerut by Khare et al who reported 62% and by Saera et al in Pakistan who reported 64.8% cases from reproductive age group.15,16 But literature have mentioned studies where majority of cases were from perimenopausal age group .17,18,19

Functional cause was the main reason of AUB in our study of which proliferative phase endometrial change(32 cases) followed by pregnancy related complications (29cases) which come under the category of organic lesions, were the predominating histopathological finding. This finding of proliferative endometrial change as a leading cause of AUB is comparable to studies by Anuradha Salvi et al (37.2%) and Agrawal et al. Proliferative endometrium was the commonest finding in Khare et al(26.8%) and Saera et al(34.6%) too though cases with pregnancy related complications were not taken into account in their studies.15,16 Again Vaidya et al found secretory phase endometrial change(22.58%) as major cause of AUB in their study but pregnancy related complications were their exclusion criteria.17

In reproductive age group, pregnancy related complications were the commonest finding bellow 30 years of age and in 31-40 years of age cyclical endometrial change was predominant finding which is comparable to the study by Doraiswami et al in 2011.7

In perimenopausal age, cyclical endometrial change, mainly proliferative endometrium (35.6%) was the major cause which is comparable to the findings in Doraiswami et al(41%), Salvi et al(53%), Bhatta et al(29.8%) and also in Damle et al(34%) although the later considered only women above 40 years in their study.7,19,20,31 On the contrary, Vaidya et al found secretory phase as the predominating change in endometrial biopsy in perimenopausal age.17 Again distribution of cases of simple endometrial hyperplasia was highest in this age group. Literature mentioned studies where simple endometrial hyperplasia was one of the leading cause of AUB in perimenopausal age.15,21,22 This supports the anovulatory cycles in this age due to which excessive and prolonged estrogenic stimulus leads to these spectrum of changes in endometrium and hence bleeding.

In this study, atrophic endometrium was the major finding in postmenopausal group. This finding is comparable to the
Table 2: functional causes of abnormal uterine bleeding:

<table>
<thead>
<tr>
<th>Functional causes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Proliferative phase</td>
<td>32 (37.2%)</td>
</tr>
<tr>
<td>Secretory phase</td>
<td>16 (18.6%)</td>
</tr>
<tr>
<td>Atrophic endometrium</td>
<td>23 (26.7%)</td>
</tr>
<tr>
<td>Weakly proliferative</td>
<td>04 (4.7%)</td>
</tr>
<tr>
<td>Disordered proliferative</td>
<td>10 (11.6%)</td>
</tr>
<tr>
<td>Non specific degenerative change</td>
<td>01 (1.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>86(100%)</td>
</tr>
</tbody>
</table>

Table 3: organic lesions of abnormal uterine bleeding:

<table>
<thead>
<tr>
<th>Organic lesions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Retained product of conceptus</td>
<td>25(54.3%)</td>
</tr>
<tr>
<td>Chronic endometritis</td>
<td>01(2.2%)</td>
</tr>
<tr>
<td>Endometrial hyperplasia</td>
<td>15(32.6%)</td>
</tr>
<tr>
<td>Endometrial carcinoma</td>
<td>01(2.2%)</td>
</tr>
<tr>
<td>H. mole</td>
<td>04(8.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>46(100%)</td>
</tr>
</tbody>
</table>

Table 4: distribution of study subjects (n=132) according to histological diagnosis in different age groups.

<table>
<thead>
<tr>
<th>Histopathological diagnosis</th>
<th>18-20 yrs (%)</th>
<th>21-30 yrs (%)</th>
<th>31-40 yrs (%)</th>
<th>41-50 yrs (%)</th>
<th>51-60 yrs (%)</th>
<th>61-70 yrs (%)</th>
<th>&gt;70yrs (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proliferative endometrium</td>
<td>0</td>
<td>4 (14.3%)</td>
<td>11 (30.5%)</td>
<td>16 (35.6%)</td>
<td>0</td>
<td>1 (33.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Secretary endometrium</td>
<td>0</td>
<td>3 (10.8%)</td>
<td>1 (2.8%)</td>
<td>0</td>
<td>1 (2.8%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Atrophic</td>
<td>0</td>
<td>1 (3.6%)</td>
<td>1 (2.8%)</td>
<td>10 (22.2%)</td>
<td>7 (58.3%)</td>
<td>1 (33.3%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>Weakly proliferative</td>
<td>0</td>
<td>0</td>
<td>1 (2.8%)</td>
<td>1 (2.2%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Disordered proliferative</td>
<td>0</td>
<td>01 (3.6%)</td>
<td>4 (11.1%)</td>
<td>5 (11.1%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Non-specific degenerative change</td>
<td>0</td>
<td>1 (3.6%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RPOC</td>
<td>2 (50%)</td>
<td>13 (46.4%)</td>
<td>9 (25%)</td>
<td>1 (2.2%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Chronic endometritis</td>
<td>0</td>
<td>0</td>
<td>1 (2.8%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Simple endometrial hyperplasia</td>
<td>0</td>
<td>3 (10.7%)</td>
<td>3 (8.3%)</td>
<td>7 (15.6%)</td>
<td>1 (8.3%)</td>
<td>0</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Endometrial carcinoma</td>
<td>0</td>
<td>0</td>
<td>1 (2.8%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>H.mole</td>
<td>2 (50%)</td>
<td>2 (7.2%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>04</td>
<td>28</td>
<td>36</td>
<td>45</td>
<td>12</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
findings in most of the studies in literature.\textsuperscript{19,20,21,22} Khare et al found equal number of cases of atrophic endometrium and complex hyperplasia of endometrium without atypia.\textsuperscript{15} Again Vaidya et al found secretory endometrium and Sweta et al found histopathological finding of proliferative endometrium(45\%) to be the major cause of AUB in postmenopausal age.\textsuperscript{17,18} Mechanism of bleeding due to atrophic endometrium in old age is stated in different studies as sclerotic degeneration of vessel wall or local abnormal haemostatic mechanism.

Incidence of endometrial carcinoma in our study was 0.75\% (1) which was seen at 31-40 years of age group. This finding is comparable to the finding in Mahapatro et al (0.7\%), Prajapati et al (0.99\%), closely to Sandeepa et al(1.1\%). On the contrary, this finding is lower than the incidence recorded by Doraiswami et al(4.4\%), Khare et al(3.7\%), Agrawal et al(3.5\%) and Bhatta et al(5.7\%).\textsuperscript{7,15,18,20} This dissimilarity may be explained by the majority of the population in our study which was mainly from reproductive age group and only endometrial cause of AUB was considered in our study. The only case of carcinoma was Clear cell carcinoma of endometrium confined to endometrial layer at the time of presentation. Most of the studies found majority of cases of carcinoma in postmenopausal age.\textsuperscript{23,25} Karmakar et al found endometrioid carcinoma to be the main histopathological variant.\textsuperscript{25} Incidence of clear cell carcinoma in literature were 20\% and 5.5\% (26,27) This difference in finding is due to the study
population in their studies which were mainly the women with endometrial carcinomas and proportion of different histopathological types were mainly evaluated.

**Conclusion**

Histopathological evaluation of endometrial samples can be used as first step for diagnosis of abnormal uterine bleeding specially in post menopausal women who are at increased risk of malignancy. However histopathological evaluation is a challenge for the pathologist due to the frequent receipt of inadequate endometrial samples.

**Acknowledgements**

NONE

**Funding**

None

**Competing Interests**

None Declared

**Abbreviation**

AUB: Abnormal uterine bleeding

RPOC: Retained product of conceptus

GTD: Gestational trophoblastic disease

PRC: Pregnancy related complication

**Reference**

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