Ultrasonographic Measurement of Endometrial Thickness and Histopathological Diagnosis of Endometrial Hyperplasia in Abnormal Uterine Bleeding - A Correlative Study

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Abstract
Context: Women with abnormal uterine bleeding (AUB) had compromised quality life expresses burden socioeconomically, emotionally. Delay in pursuing medical help leads to development of simple hyperplasia to complex carcinoma. Early detection, treatment of hyperplasias prevents progression to malignancy. This study was taken for early detection of hyperplasia with the help of endometrial thickness (ET) through ultrasound (U/S)

Aim: To study clinical presentation, ultrasound ET measurement and correlate histopathological endometrial hyperplasias in AUB.

Materials and methods: Prospective study - 170 patients with AUB in Government maternity hospital, Tirupati

Statistical analysis: M. S. Excel, SPSS

Results: AUB patients 90.2% were reproductive age, 8.8% postmenopausal. Postponement for medical help for 3-6 months, multiparous women observed 60.6%. AUB presentation was significantly observed with advanced age. Ultrasound graphical ET of less than 8 mm displays few hyperplasia, more than 8 mm to 15 mm ET reveals significant increase in hyperplasia, carcinoma without normal endometrium.

Conclusion: Delay in medical help owing to low socioeconomic, illiteracy. Advanced aged women with AUB presentation requires clinical, ultrasonographical ET, histopathological endometrial assessment. Ultrasonographical ET more than 8 mm in reproductive age, more than 4 mm in peri and postmenopausal women necessitates evaluation.

Recommendations: Ultrasonographic ET measurement is valued for guiding histopathological detection of hyperplasias.

Key words: Endometrial thickness, endometrial hyperplasia, histopathology.

I. Introduction

The normal menstrual cycle is an average of 28 days ranging from 21-35 days, with menstrual flow of 3-5 days with an average blood loss of 30 ml.

Alteration in the duration, menstrual frequency and amount of blood loss is defined as Abnormal Uterine bleeding (AUB). Clinically AUB presented as polymenorrhea (frequent menstruation), oligomenorrhea (infrequent menstruation), menorrhagia (increased amount and duration of flow), metorrhagia (inter menstrual bleeding) polyomenorrhagia (both polymenorrhea, menorrhagia) peri and post-menopausal bleeding etc.

The etiology of AUB is classified as organic causes includes fibroids, endometriosis, adenomyosis, polyps, uterine anomalies, systemic causes deep vein thrombosis, coagulatory defects, hypothyroidism, trauma, tumours, and drugs and Dysfunctional uterine bleeding (DUB) is purely hormonal.

PALM-COEIN is a new classification system in which Structural causes - leiomyoma, adenomyosis, polyps, malignancies and hyperplasia sand non-structural causes include ovulatory causes coagulation defects, endometrial, iatrogenic and not yet classified.

Federation of International Gynecologists and Obstetricians (FIGO) introduced new terminologies - Heavy menstrual bleeding (HMB) instead of menorrhagia, Inter menstrual bleeding (IMB) replaces metorrhagia, Heavy and prolonged bleeding (HPB) in place of menometrorrhagia and frequent menstrual bleeding (FMB) substitute ‘polyomenorrhagia’.

AUB is the presenting feature in 20-30% reproductive and 69% in peri or postmenopausal women. Etiology of AUB may single or multiple, the different causes of AUB can be diagnosed by ultrasonography (U/S) like fibroids, endometriosis, polyps etc. and the endometrial thickness measurement.
If endometrial thickness is more than 8mm in reproductive age, more than 4mm in post-menopausal women are abnormal, the abnormal endometrial patterns like endometrial hyperplasias and carcinomas are high. Histopathological examination of endometrium is necessary if ET is more in U/S.

Endometrial changes takes place in AUB are from normal (proliferative, secretory, biphasic, atrophic) to abnormal (endometrial hyperplasia- simple, complex, atypical, cystoglandular hyperplasia, and carcinoma). The endometrial hyperplasias if diagnosed early, the treatment is simple, easy and complications are minimal. Delay in diagnosing and treating the endometrial hyperplasia, may progress to carcinoma which is a dreadful disease to treat and complications are more even after treatment. Most of the women with endometrial carcinoma usually present as either peri menopausal or postmenopausal bleeding.

Blood loss in AUB causes health problems in women like anemia leading to congestive cardiac failure, opportunistic infections and absenteeism from work etc.

The women suffering with AUB were taken in present study to diagnose the endometrial thickness by ultrasonography and correlate with histopathological study of endometrium by endometrial sampling. This study will help in future to early diagnosis of endometrial hyperplasia and treat the women before malignancy develops.

II. Aims And Objectives

1. To study clinical presentation of AUB.
2. To evaluate the endometrial thickness by ultrasound and endometrial hyperplasias by histopathological examination of endometrium in AUB.
3. To correlate ultrasonographical endometrial thickness with histopathological endometrial hyperplasia in AUB.

III. Materials And Methods

3.1. Study Design: A prospective study was conducted in department of Obstetrics and Gynecology, Government maternity hospital, Sri Venkateswara Medical College, Tirupati, from October 2015 to October 2016.

3.2. Study Subjects: In the present study, 170 subjects were patients with AUB came to Gynecological outpatient department and admitted in Government maternity hospital, Tirupati.

3.3. Inclusion Criteria: All patients with abnormal uterine bleeding, age group between 21 to 60 years, women who are willing to participate.

3.4. Exclusion Criteria: Pregnancy and related conditions, females less than 21 and more than 60, infection in genital tract, cases of carcinoma cervix.

3.4. Study Methods: Data was collected on standardized proforma from women with AUB after taking consent. Demographic details collected. Complaints, careful history and detailed menstrual history weretaken. A detailed clinical examination including general, systemic, vital data noted, per abdominal examination, per speculum, per vaginal bimanual examination and per rectal examination conducted. Routine investigations hemoglobin estimation, Bleeding Time, Clotting Time, blood grouping Rh typing, thyroid profile, blood sugar, and urine routine for albumin, sugar, microscopy done. Trans abdominal ultrasound examination was done to all patients the size, position of uterus, endometrial thickness, size of the ovaries, presence of pathology were noted. Endometrial samples were taken by dilatation and curettage sent for histopathological analysis.

3.5. Analysis: Data was analyzed by M.S.Excel and Statistical package for Social Sciences (SPSS) version 17.0 for windows. Decimals were corrected to digit 1.

IV. Results

A prospective study of 170 patients with Abnormal Uterine Bleeding who attended outpatient and inpatient ward in Gynecology department, Government Maternity Hospital, Sri Venkateswara medical college, Tirupati from October 2015 to October 2016 was undertaken.

In the present study, a total of 170 subjects were taken and analyzed. 16 (9.4%) patients were in the age group of 20-29 years, 38 (22.4%) patients in 30-39 years, 101 (59.4%) patients stood in 40-49 years, and 15 (8.8%) patients remained 50-60 years.
Out of total 170 patients, 117 (68.9%) patients belong to rural areas, 53 (31.1%) patients residing in urban sector. Most of the patients i.e., 142 (83.5%) women were illiterates, 28 (16.5%) literates. Patients of 108 (63.5%) belong to low socioeconomic class, 42 (24.7%) patients fit in to middle class, 20 (11.8%) patients go to upper class.

Among 170 patients 11 (6.5%) patients nulliparous, 8 (4.7%) primi para, 48 patients (28.2%) second para and 103 (60.6%) women more than 3 parity.

Women taken medical help with symptoms of AUB were six (3.5%) before one month, 51 (30%) consulted hospital 1-3 months after complaints, 69 (40.6%) with 3-6 months duration and 44 (25.9%) after 6 months.

Table-1: Age wise distribution and pattern of bleeding in AUB patients

<table>
<thead>
<tr>
<th>Presentation</th>
<th>20-29 Years</th>
<th>30-39 Years</th>
<th>40-49 years</th>
<th>50-60 years</th>
<th>Total No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menorrhagia</td>
<td>5</td>
<td>17</td>
<td>53</td>
<td>3</td>
<td>78</td>
<td>45.9%</td>
</tr>
<tr>
<td>Polymenorrhagia</td>
<td>7</td>
<td>13</td>
<td>29</td>
<td>2</td>
<td>51</td>
<td>30%</td>
</tr>
<tr>
<td>Polymenorrhea</td>
<td>3</td>
<td>5</td>
<td>8</td>
<td>0</td>
<td>16</td>
<td>9.4%</td>
</tr>
<tr>
<td>Metrorrhagia</td>
<td>1</td>
<td>3</td>
<td>10</td>
<td>0</td>
<td>14</td>
<td>8.2%</td>
</tr>
<tr>
<td>Postmenopausal bleeding</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>6.5%</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>38</td>
<td>101</td>
<td>15</td>
<td>170</td>
<td>100%</td>
</tr>
</tbody>
</table>

The above “Table-1” shows that among 170 patients, 78 (45.9%) had menorrhagia, polymenorrhagia in 51 (30%), Polymenorrhea was the complaint in 16 (9.4%), Metarrhagia seen in 14 (8.2%), Most of the complaints observed in patients with age group of 40-49 years. Postmenopausal bleeding was seen in 11 (6.5%) observed in 50-60 years.

The above table shows as the age of the patient was increased there remained a rise of complaints due to AUB. P value=0.0001.

Ultrasonographic examination of women with AUB shows 67 were fibroid uterus, 38 patients had no abnormality, adenomyosis in 28 women, ovarian cysts were seen in 24 members, 18 patients had polyp, polycystic ovarian disease was seen in four patients and one patient had endometrial carcinoma.

Table-2: Comparing ET by ultrasonography with endometrial patterns in histopathology.

<table>
<thead>
<tr>
<th>Endometrial thickness (mm)</th>
<th>Proliferative endometrium</th>
<th>Secretory endometrium</th>
<th>Disordered proliferative endometrium</th>
<th>Endometrial hyperplasia</th>
<th>Atrophic endometrium</th>
<th>Biphase endometrium</th>
<th>Endometrial Cancer</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4mm</td>
<td>3</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>4-8 mm</td>
<td>34</td>
<td>39</td>
<td>18</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>94</td>
</tr>
<tr>
<td>8-15 mm</td>
<td>49</td>
<td>1</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>55</td>
</tr>
<tr>
<td>15 mm and above</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>86 (50.6%)</td>
<td>45 (26.5%)</td>
<td>26 (15.3%)</td>
<td>10 (5.8%)</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td>1 (0.6%)</td>
<td>170 (100%)</td>
</tr>
</tbody>
</table>

Simple hyper-8 (80%), complex-2 (20%)
The above “Table-2” shows 77.1% normal proliferative and secretory endometrium, 15.3% disordered proliferative endometrium, 5.8% endometrial hyperplasias, 0.6% atrophic, biphasic each and 0.6% carcinoma were noted.

ET of less than 4 mm shows normal endometrium with few cases of disordered proliferative endometrium. 4-8 mm thick endometrium shows mostly normal, 18 among 94 shows disordered, one each atrophic, biphasic endometrium and one hyperplasia. Women with 8-15 mm ET were 55, among them four had disordered endometrium and one hyperplasia and remain normal. ET of more than 15 mm was seen in 10 patients amongst hyperplasia observed in 8, one disordered proliferative endometrium and one case of carcinoma.

### Table 3: Endometrial thickness by ultrasonography correlated with endometrial hyperplasia on histopathology in reproductive age group.

<table>
<thead>
<tr>
<th>Endometrial thickness</th>
<th>Endometrial hyperplasia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>&lt;8 mm</td>
<td>1</td>
<td>98</td>
</tr>
<tr>
<td>8-15 mm</td>
<td>0</td>
<td>52</td>
</tr>
<tr>
<td>&gt;15 mm</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>6</td>
<td>153</td>
</tr>
</tbody>
</table>

The above “Table-3” show ET of more than 8 mm was seen in 99 patients of whom one patient had endometrial hyperplasia remain doesn’t express. ET between 8-15 mm was seen in 52 patients, none of them had endometrial hyperplasia among them. Eight patients had endometrial thickness more than 15 mm shows hyperplasia in five patients. P value -0.0001 is significant.

### Table-4: Correlation of endometrial thickness and endometrial hyperplasia (cut off 4mm) on histopathology among postmenopausal age group.

<table>
<thead>
<tr>
<th>Endometrial thickness</th>
<th>Endometrial hyperplasia</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>&lt;4 mm</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>&gt;4 mm</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>

The above” Table-4” reveals ET of less than 4 mm was seen in five patients, none of them had hyperplasia. In the present study more than 4 mm seen in six patients among them 4 patients had endometrial hyperplasia. P value - 0.061 is not significant.

### V. Discussion

Present study was carried out at Government Maternity hospital, Tirupati. Total number of 170 cases outpatients and inpatients in Gynecology department were included in the present study.

Maximum numbers of AUB patients 91.2% in reproductive age amongst 59.4% in 40-49 years of age in present study. Nearly similar percentage was 42% reported by Singh et al. Most of the cases of AUB were from rural area, belong to low socioeconomic status and illiterates. Small group of people came from urban, middle, upper socioeconomic and literates.

Most of the cases with AUB were observed in multiparous women, next second para, primi para and nulliparous women in decreasing order, the present study reported that as the parity increases, the incidence of AUB increased was similar to a study by Singh et al, Bhosle et al, the increasing parity will have effect on reproductive tract in developing complications, but it does not show statistical significance as P value is 0.25. According to Muzaffar et al and, Wahda et al low parity had higher incidence of hyperplasia than multiparous women.

Women approached hospital for medical help with duration of presenting complaints ranged one month to 12 months, commonly reported after 3-6 months. Immediate health checkup pursuing was lacking in most of the women even though they were suffering because mainly the women belongs to low socioeconomic status, illiterates and rural areas, loss of daily wages.

Menorrhagia (45.9%) was the chief complaint, next Polymenorrhagia (30%) Poly menorrhagia (9.4%), metarrhagia (8.2%) were the complaints in AUB women decreasing order as represented “Table -1”. This study was associating with other studies Singh et al, Bhosle et al, and Gargi Ray Chaudari et al. Most of the cases in our study were due to uterine causes like fibroids, adenomyosis and polyps.

Postmenopausal bleeding was presenting feature in 6.5% of cases according to present study, is comparable to a study by Singh et al (8.6%). Studies by Gargi et al12 (30.8%) Mahmoud et al13 (16.3%) reported that higher incidence of postmenopausal bleeding was seen in AUB cases. In the present study lower incidence due to reproductive age group were hitherto postmenopausal women.
Age of woman has significant effect over clinical presentation, as the age of the patient increases the problems of AUB also increases. Present study shows statistically significant effect of age to the onset of symptoms in AUB (P value = 0.0001).

Ultrasoundographic measurement of ET less than 4 mm in the present study was 6.47% correlates with (3.6%) shobhitha et al study. The ET with less than 4mm by U/S correlates histopathology major report showed normal endometrium with few disordered proliferative endometrium nearly similarity seen in Shobhitha et al study also had no hyperplasia.

The ET of 4-8 mm was seen in 55.3% of cases, it was high if correlated with a study by Shobhitha et al incidence was 34.5%. ET compared with histopathology shows majority had normal endometrium, few cases of disordered proliferative endometrium and existence of endometrial hyperplasia only one in 94 women. Shobhitha et al study reported 10.5% hyperplasias, it was quiet high percentage because peri menopausal cases were more, whereas in present study reproductive group women and presence of disordered proliferative endometrium.

The ET between 8-15 mm was observed in 32.35% of the cases, it associates a study by shobhitha et al (45.5%). ET compared with histopathology preponderance cases shows normal with few number of disordered proliferative endometrium and presence of hyperplasia. Present study not equated with Shobhitha et al study, high percentage of hyperplasias due to involvement of peri menopausal women.

In present study ET of more than 15 mm in 5.88% of patients and shobhitha et al reported as 16.4%. In present study the incidence was low due to presence more reproductive age and less postmenopausal women. Ultrasoundographic ET versus hyperplasias reveals that more than 15 mm ET illustrates almost hyperplasia including carcinoma without normal endometrium. Present study was allied closely with Shobhitha et al study, all cases ensured hyperplasias.

Disordered proliferative endometrium is significant because at one end of the spectrum proliferative lesions in endometrium that includes carcinoma, at other end intervening stages of hyperplasias. Endometrium is hyperplastic with simple hyperplasia but focal rather than diffuse without increase in endometrial volume. Present study shows 15.3%, comparable 13% with the studies by Vaidya et al, only 7% in Shresta et al study.

Hyperplasias were seen in 5.8% of cases in the present study of which simple hyperplasia in 4.7%, complex hyperplasia 1.1%. Present study shows similar to results as Shresta et al Abid et al. According to Singh et al, Muzaffar et al and Wahda et al reported that higher incidence of hyperplasia observed in low parity than multiparous women. The presence of risk factors like obesity, diabetes, increased intake of animal fat and sedentary life style will have the effect on increased incidence of endometrial hyperplasia. In the present study most patients belong to lower socioeconomic status, daily laborers, early child bearing practices and hard working women, so absence of above risk factors might be the cause for lower incidence of hyperplasia.

Endometrial carcinoma was perceived in one case (0.6%). The incidence of carcinoma in the present study was comparable to previous studies by Singh et al (1%) Abid et al (2%), over all incidence of carcinoma was less than 5%. In the present study carcinoma cases were low oedewery few postmenopausal women.

In reproductive women ET of 8 mm cutoff point is necessary taken, correlated with presence of endometrial hyperplasia in present study and analyzed. It discloses if ET was less than 8 mm the chances of hyperplasia was fewer, whereas the ET was more than 8 mm the chances of hyperplasia development was high. This was evidenced that P value is 0.029 expresses statistical significance; same was quoted by Muhammed Aslam et al.

The ET increasing from 8 mm onwards, the chances of hyperplasia is augmented, if the thickness is 15 mm and above, there is higher occurrence of hyperplasia and even development of carcinoma. It was reported in the present study, illustrated as P-value 0.0001 is statistically significant. Previous studies shobhitha et al and Amna Wajeeh indicate similarly correlation between ET more than 15 mm and endometrial hyperplasia especially in peri and postmenopausal women.

In post-menopausal women the ET of 4 mm or less considered normal, if more than 4 mm the chances of abnormalities like hyperplasia and carcinoma are more. Kaur M et al showed that an ET cut off of 4 mm in postmenopausal women for detecting benign and malignant lesions of endometrium. In the present study among the postmenopausal women, no case of endometrial hyperplasia witnessed with ET less than 4 mm, endometrial hyperplasia was seen in 4 cases with more than 4 mm thickness. Correlation between endometrial thickness and endometrial hyperplasia among postmenopausal age does not show any statistically significant P value = 0.061 the reason for this may perhaps be very few patients are postmenopausal in the present study group.

VI. Conclusion

AUB cases were mostly seen in reproductive age group, half of the women were delay in seeking medical checkup because they belong to rural, low socio economic with illiteracy, loss of wages. AUB occurrence was significantly high as age advances. Early health checkup, meticulous clinical examination by
trained persons, ultrasonography, and endometrial histopathological examination are essential to evaluate the etiology of AUB especially with advanced age.

Ultrasonographic endometrial thickness is more than 8mm in reproductive age and more than 4 mm in peri and post-menopausal women need histopathological examination of endometrium is necessary to know endometrial abnormalities like hyperplasias, and carcinomas. Early detection treatment can avoid most dreadful disease carcinoma.

6.1. Recommendations: Role of ultrasound in diagnosis of endometrial thickness is a ready to lend a hand tool for guidance to histopathological evaluation of endometrial abnormalities. Early health checkup especially advanced aged women with AUB is essential to evaluate the presence of abnormalities.

6.2. Limitations: Small group of study, reproductive age women with less number of peri and post-menopausal women involved in study.

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References
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