ABSTRACT

BACKGROUND
The climacteric marks the phase in ageing process that signals transition from reproductive to nonreproductive. One of the common complaints in this period is vaginal bleeding, which in 10% of people can be due to underlying endometrial malignancy. Invasive office biopsy of the endometrium is the first choice for the diagnosis of these endometrial pathologies. Since, only 10% of women with postmenopausal bleeding have endometrial carcinoma, a simpler less expensive safe and noninvasive diagnostic method was searched for. Hence, transvaginal sonography with Doppler study of the endometrium was looked into as a replacement for the invasive office biopsy.

The aim of the study is to study the efficacy of transvaginal sonography with Doppler for predicting endometrial carcinoma in women with postmenopausal bleeding.

MATERIALS AND METHODS
It was a study carried out in 30 women who presented with postmenopausal bleeding after one year of amenorrhea. Endometrial biopsy was taken in all patients. Transvaginal sonography with colour Doppler was performed just prior to the endometrial biopsy in these patients.

RESULTS
Total number of patients evaluated with transvaginal sonography and Doppler were 30. Histologically proven malignant cases were 18 and benign were 12. Majority of the women were parous and had achieved menopause after age of 50. Endometrial thickness measured by transvaginal sonography was significantly higher in malignancy as compared to benign. Resistance index measured by Doppler in the uterine arteries and endometrial vessels were studied and though resistance index was lower in patients with neoplastic pathology, it was not of statistical significance.

CONCLUSION
Endometrial thickness and colour Doppler measurements in the detection of endometrial pathologies are a useful adjuvant to endometrial biopsy in the detection of malignancy, but not a substitute for biopsy.

KEYWORDS
Endometrial Malignancy, Transvaginal Sonography with Doppler Study, Uterine Artery Resistance Index, Statistical Significance.

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BACKGROUND
When uterine bleeding occurs more than 12 months after the last regular menstrual period, it is defined as postmenopausal bleeding. It should always be taken seriously and investigated no matter how minimal or nonpersistent. Causes maybe nongenital, genital extrauterine or uterine.1

According to Hacker NF and Moore JG, the genital causes for postmenopausal bleeding are exogenous oestrogen, atrophic endometritis, endometrial cancer, endometrial/cervical polyp, endometrial hyperplasia and miscellaneous causes like cervical cancer, trauma, etc.

Endometrial carcinoma is the fourth most common cancer ranking behind breast, lung and bowel cancers and the seventh leading cause of death from malignancy in women. Overall, about 2% to 3% of women develop endometrial cancer during their lifetime.2

There appear to be two different pathogenetic types of endometrial cancer.3 The more common and better differentiated “oestrogen-dependent” and the less common, less differentiated “oestrogen-independent” varieties.

Endometrial cancer occurs most commonly in women in the sixth and seventh decade of life at an average of 60 years- 75% occur in women older than 50 years of age. 90% of women with endometrial carcinoma have vaginal bleeding or discharge as their only presenting complaint.4

Screening for endometrial cancer is currently not undertaken because of lack of an appropriate, cost effective...
and acceptable test that reduces mortality.\textsuperscript{5,6,7} Transvaginal ultrasound examination of the uterus and endometrial biopsy are too expensive to be employed as screening tests.\textsuperscript{4} Screening maybe justified for certain high-risk women like those receiving postmenopausal oestrogen therapy without progestins and members of families with hereditary nonpolyposis colorectal cancer.

Office endometrial aspiration biopsy is the accepted first step in evaluating a patient with abnormal uterine bleeding or suspected endometrial pathology.\textsuperscript{8} The diagnostic accuracy of office-based endometrial biopsy is 90% to 98% when compared with subsequent findings at dilatation and curettage or hysterectomy.\textsuperscript{9,10,11} Hysteroscopy is more accurate in identifying polyps and myomas than endometrial biopsy or D and C alone.\textsuperscript{12,13} Transvaginal sonography may be a useful adjunct to endometrial biopsy for evaluating abnormal uterine bleeding and selecting patients for additional testing.\textsuperscript{14,15,16}

Ultrasound is the modality of choice for initial evaluation of female pelvic organs. Typical examinations include transabdominal sonography and transvaginal sonography, which are supplemented by colour Doppler imaging as needed. Transvaginal sonography has the advantage of using high frequency transducers placed close to the pelvic organ and high-resolution images of better quality than transabdominal sonography. Transvaginal sonography is clinically established as the preferred technique for the evaluation of endometrial disorders especially useful in the workup of abnormal uterine bleeding.

In endometrial carcinoma, transvaginal sonography findings are as follows;

The earliest depicted finding is thickened endometrium that usually is heterogenous and poorly defined or has irregular contours. In most patients, endometrium is more echogenic than the myometrium. These findings are nonspecific as there is overlap of the findings of the endometrium in patients with carcinoma, hyperplasia or polyp.

The endometrium is measured at its maximal thickness on a sagittal image of the uterus obtained by transvaginal sonography. Endometrial thickness is a bilayer measurement combining the anteroposterior width of both the anterior and posterior layers of the endometrium exclusive of possible intracavitary content. The normal range of endometrial thickness is up to 5 mm in postmenopausal women not receiving hormones and up to 8 mm in asymptomatic postmenopausal women on hormone replacement therapy. The Doppler ultrasound is based on the Doppler effect, a physical phenomenon, which is valid for various types of wave energies. When applied, the ultrasonic waves are transmitted by a piezoelectric crystal (the transducer) into the tissue at a given frequency when it is reflected by the moving blood cells within a vessel; the returning ultrasound is received with different frequency. This change in the ultrasound frequency is called the Doppler shift. The blood velocity can be calculated from the Doppler shift if the angle between the ultrasound beam and the blood flow within the vessels is known. The pulsed wave Doppler velocimetry provides information about 3 aspects of blood flow. 1 - velocity, 2 - resistance to blood flow through a particular vessel and 3 - volume of blood flow. Analysis of waveform can be accomplished using standard indices such as resistance index and pulsatility index. These indices depend on systolic and diastolic velocity. If diastolic flow is absent or reversed, resistance index cannot be used and pulsatility index is needed.

**Aims**

To study the endometrial pathology in patients with postmenopausal bleeding by using transvaginal sonography, colour Doppler and histopathology.

1. To compare the sonographically measured endometrial thickness and colour Doppler parameters with histopathological diagnosis in women with postmenopausal bleeding.
2. To determine whether measurements of blood flow in endometrial vessels by transvaginal colour Doppler and endometrial thickness was valuable in the diagnosis of endometrial neoplasia in women with postmenopausal bleeding.

**MATERIALS AND METHODS**

30 women with postmenopausal bleeding were evaluated. Postmenopausal bleeding was defined as women who presented with bleeding after 1 year of amenorrhea. Transvaginal sonography of the uterus and Doppler analysis of the blood flow were performed using vaginal probe at 5-7.5 megahertz. On transvaginal sonography, endometrial thickness as well as other pathologies in the cavity were noted. Transverse and longitudinal sections of the endometrial echoes were obtained and maximal double-layer endometrial thickness in the sagittal plane was measured. Vascularity of the uterus was assessed systematically. Both uterine arteries could be detected in the transverse and longitudinal plane above the supravaginal portion of the cervix. Colour flow images of the uterine arteries were obtained and Doppler signals in the form of flow velocity waveforms displayed. In the velocimetric analysis of flow velocity, waveform determined the resistance index (RI). RI = ($S-D)/S$.

$S$ = Maximum systolic velocity.

$D$ = Diastolic velocity.

**RESULTS**

30 cases of postmenopausal bleeding were evaluated. Histologically proven malignant cases were 18 and 12 were benign.

<table>
<thead>
<tr>
<th>Histologically Proven</th>
<th>Total Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>12</td>
<td>40%</td>
</tr>
<tr>
<td>Malignant</td>
<td>18</td>
<td>60%</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table 1**
Age Group

Parity status of the women evaluated.

Age of menopause of the women with malignancy (n=18).

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>8</td>
<td>44.44</td>
</tr>
<tr>
<td>&gt;50</td>
<td>10</td>
<td>55.55</td>
</tr>
</tbody>
</table>

Table 2. Age of Menopause

Body Mass Index (BMI) in women with malignancy (n=18).

<table>
<thead>
<tr>
<th>BMI</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-25</td>
<td>12</td>
<td>66.66</td>
</tr>
<tr>
<td>25-30</td>
<td>5</td>
<td>27.77</td>
</tr>
<tr>
<td>&gt;30</td>
<td>1</td>
<td>5.55</td>
</tr>
</tbody>
</table>

Table 3. Body Mass Index (BMI)

Endometrial Thickness.

<table>
<thead>
<tr>
<th></th>
<th>Endometrial Thickness (Mean)</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>8.4 mm</td>
<td>2.35</td>
</tr>
<tr>
<td>Malignant</td>
<td>14.49 mm</td>
<td>7.387</td>
</tr>
</tbody>
</table>

Table 4. Endometrial Thickness

The endometrial thickness (Mean±SD) in patients with malignancy was 14.49±7.9 and that of benign was 8.4±2.35. The endometrial thickness in patients with neoplastic endometrial pathology was significantly higher than that in patients with nonneoplastic endometrial pathology. The P value was <0.05 and hence significant.

Resistance Index

<table>
<thead>
<tr>
<th></th>
<th>Malignant</th>
<th></th>
<th>Benign</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Number</td>
<td>Percentage</td>
<td>Number</td>
<td>Percentage</td>
</tr>
<tr>
<td>ERI</td>
<td>0.497</td>
<td>0.105</td>
<td>0.63</td>
<td>0.075</td>
</tr>
<tr>
<td>LURI</td>
<td>0.69</td>
<td>0.063</td>
<td>0.82</td>
<td>0.056</td>
</tr>
<tr>
<td>RURI</td>
<td>0.674</td>
<td>0.086</td>
<td>0.79</td>
<td>0.066</td>
</tr>
</tbody>
</table>

Table 5. Resistance Index

ERI - Endometrial Resistance Index.
LURI - Left Uterine Artery Resistance Index.
RURI - Right Uterine Artery Resistance Index.
The Resistance Index (RI) of endometrial and both right and left uterine arteries were determined in all benign and malignant patients. The resistance index (Mean±SD) of the endometrial arteries of benign and malignant were 0.063±0.075 and 0.497±0.105. The P value was >0.05, not statistically significant. Resistance index of left uterine artery in benign and malignant lesions were 0.82±0.05 and 0.69±0.063 with P>0.05. Resistance index of right uterine artery in benign and malignant tumours were 0.79±0.0663 and 0.674±0.086 with P>0.05. Resistance index was lower in patients with neoplastic endometrial pathology than in patients with nonneoplastic endometrial pathology. But, the differences did not reach a statistical significance.

DISCUSSION

30 patients with postmenopausal bleeding were evaluated. 18 had underlying malignant lesion whereas 12 had benign lesions. Probably the 60% incidence of malignancy was due to the fact that the study institute is a referral hospital.

Majority of the benign as well as malignant lesions belonged to 50-60 years age group.

27.7% of malignant tumours were seen in the nulliparous age group. Of the total number of malignant lesions, 94.45% of cases belonged to nulliparous and low parity groups. Only 5.55% belonged to parity 4 and above.

Among the 18 patients with malignant disease, 10 attained menopause at or above the age of 50 years and 8 below the age of 50. This indicates that patients with late menopause are at higher risk of endometrial carcinoma. This is due to longer stimulation of endometrium by oestrogen.

In this present study, 66.66% of patients with endometrial malignancy had body mass index 25-30. The risk of endometrial cancer has increased with increase in obesity due to peripheral conversion of adrenally derived androstenedione by aromatisation in fat. A significant association between obesity and malignancy was not seen in present study. This is possibly due to dietary factors in the population studied.

Now coming to the predictive value of transvaginal sonography in the diagnosis of benign and malignant tumours, histological examination of the endometrium is the method of choice in the diagnosis of endometrial pathologies. Noninvasive method may contribute to the diagnostic accuracy of invasive methods in some patients suspected of having an endometrial pathology. The most acceptable noninvasive method is the measurement of endometrial thickness by transvaginal sonography. This method is used primarily for distinguishing patients with minimal endometrial tissue from those with significant amount of tissue in the former group of patients bleeding caused by atrophy. In menopause, the normal endometrium becomes thin and atrophic due to lack of epithelial stimulation by oestrogen. Those with significant amount of tissue need further evaluation. Although, the endometrium was reported to be thicker on transvaginal sonography in the presence of endometrial pathology, the accepted cut-off value (>5 mm) to distinguish benign from malignant lesion did not have a high sensitivity and specificity sufficient to replace invasive method. A few women with endometrial cancer have been reported to have an endometrial thickness of even <3 mm.

Sensitivity of endometrial thickness in the diagnosis of malignancy was 88.89% whereas specificity of endometrial thickness in the diagnosis of malignancy was 8.33%. The positive predictive value was 59.26% and negative predictive value was 33.33%.

CONCLUSION

Thirty patients with postmenopausal bleeding were studied. Endometrial thickness and Doppler flow parameters (endometrial resistance index, left uterine resistance index and right uterine resistance index) were studied in these patients. Histopathology reported 18 as malignancy and 12 as benign. The above-mentioned ultrasonological parameters were compared in these groups.

Significance of these parameters as predictors of malignancy were studied.

Sensitivity, specificity, positive predictive value and negative predictive value of endometrial thickness by transvaginal sonography in malignancy were studied and it was seen that endometrial thickness measurements using transvaginal sonography is a useful noninvasive procedure in patients with postmenopausal bleeding in predicting malignant pathology, but it did not replace the need for invasive diagnostic testing for confirmation.

Even though, endometrial, left uterine and right uterine resistance index values were lower in patients with malignancy than in patients with benign lesions, the difference was not statistically significant (p value >0.05).

In conclusion, endometrial thickness and colour Doppler measurements (resistance index) in the detection of endometrial pathologies are not valuable enough to increase the diagnostic accuracy of transvaginal sonography, because endometrial thickness and Doppler parameters of benign and malignant lesions significantly overlap. Noninvasive methods cannot replace invasive procedures in the evaluation of patients at high risk of endometrial pathology. These measurements can be used as an adjunct along with invasive procedures for diagnosis of malignant lesions.

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REFERENCES


