ORIGINAL ARTICLE

Diagnostic Accuracy of Doppler Ultrasonography in Diagnosing Endometrial Carcinoma in Post-Menopausal Bleeding Females Taking Histopathology as Gold Standard

UZMA HUSSAIN, SHAZIA BATOOL, ASIA PARVEEN, ALIA NASIR-UD-DIN
Associate Professor FJMC/ SGRH, Lhr, Registrar, Gynae IV/ SGRH, Lhr, Senior Registrar/ Gynae IV/ SGRH, Lhr, Senior Registrar/ Gynae IV/ SGRH, Lhr.

ABSTRACT

Objective: To determine the diagnostic accuracy of Doppler Ultrasonography in diagnosing endometrial carcinoma in females with post-menopausal bleeding taking histopathology as gold standard.

Introduction: Postmenopausal bleeding (PMB) is one of the most common reasons in patients attending gynecological OPD. It is a frequent and alarming sign of endometrial cancer though the commonest cause is an atrophic endometrium. Women with PMB are categorized as those with spontaneous bleeding and those with bleeding whilst on Tamoxifen or HRT. All these patients should be investigated by TVS, hysteroscopy and D&C and accordingly should be managed.

Methods:

Study Design: Cross Sectional Study.

Setting: Unit IV, Department of Obstetrics & Gynecology, Sir Ganga Ram Hospital, Lahore.

Duration: Study was completed (01-07-13 to 30-12-14)

Methodology: Total 250 cases were included in the study of age 50-70 years presented with clinically diagnosed postmenopausal bleeding (as per operational definition) undergoing hysterectomy. After approval from hospital ethical committee, 250 patients who fulfill the inclusion and exclusion criteria was enrolled in the study from OPD of Sir Ganga Ram Hospital, Lahore. Informed consent was obtained. All basic demographic information of each patient was obtained. Females were referred to radiology department for evaluation of endometrial thickness and RI value. If RI was to be <0.70, then patients were labeled as positive. This procedure was done by a single senior radiologist. Then patients were sent for hysterectomy, endometrial sampling was done and sample was sent to the histopathology laboratory of the hospital.

Results: Mean age of all 250 women included in this study was 61.32±7.67 years. Mean endometrial thickness on Doppler ultrasonography was 8.81±4.36 mm. Mean resistive index on Doppler ultrasonography was 0.53±0.17. Sensitivity and specificity of Doppler ultrasound findings was 86.96% and 90.7% respectively. While positive predictive value, negative predictive value and overall diagnostic accuracy of Doppler ultrasound was 97.83%, 59.09% and 87.6% respectively.

Conclusion: Results of this study showed good diagnostic results with the use of Doppler ultrasonography in the diagnosis of endometrial carcinoma in patients presenting with post-menopausal bleeding. Doppler ultrasonography is useful diagnostic tool with good sensitivity (86.97%), specificity (90.7%), PPV(97.83%) and NPV(59.09%). With its use patients can be prevented from unnecessary surgeries.

Key Words: Diagnostic accuracy, Doppler Ultrasonography, Endometrial carcinoma, Post-menopausal bleeding, Histopathology.

INTRODUCTION

Postmenopausal bleeding (PMB) is a common clinical problem that occurs in post menopausal females above 50 years of age. It may occur in 80% of women by age 51 in and 95% of women by age 55, with almost all women facing cessation of menstruation by age 58.[1] Patients with PMB have 10%-15% chance of having endometrial carcinoma.[2]

Common causes for PMB include atrophic endometrium, uterine polyp, leiomyomata, endometrial hyperplasia/cancer, coagulopathy, and lesions of adjacent structures (cervix, vagina, vulva or bladder).[3] PMB is a symptom of possible gynecological malignancy. According to guidelines,

women presenting with this symptom should be referred urgently to a team specializing in the management of gynecological cancer. Examination and investigation of these women should be able to exclude malignancy, while being acceptable to the patient and cost-effective. The gold standard modality of investigation to visualize the uterine cavity is hysteroscopy, but ultrasonographic scanning is recommended as the first-line investigation to select those who need further diagnostic evaluation. Hysteroscopy should be performed in women with a thickened endometrium on scan and women with recurrent episodes of bleeding despite negative scan findings.[4]

Recent studies have reported that endometrial malignancy was diagnosed in 22.7%-24% of the patients with PMB.[5, 6] The value of vascular morphology assessment using color Doppler ultrasonography in the discrimination between benign and malignant endometrium in women with PMB needs to be determined.[7] One study reported that Specificity, sensitivity, positive predictive value and negative predictive value were found to be 97.16%, 76%, 89.56% and 76.92% respectively.[8] Another study reported Sensitivity, 78.8%; specificity, 100%; positive predictive value, 100%; negative predictive value, 89%.

The rationale of this study is to determine the diagnostic accuracy of Doppler ultrasonography (DUS) in diagnosing the endometrial carcinoma in females presenting with postmenopausal bleeding (PMB) taking histopathology as gold standard. International literature has varied the role of DUS but in our setup data is limited about this procedure. Many times cases would found to have benign lesion and would be controlled through proper medication like Hormone Replacement Therapy. Thus, through this study we want evidence that DUS is a reliable tool for diagnosis of endometrial carcinoma as a cause of PMB, so that patients can be prevented from unnecessary surgeries.

MATERIAL AND METHODS
Study Design: Cross Sectional Study.
Setting: Unit IV, Department of Obstetrics & Gynecology, Sir Ganga Ram Hospital, Lahore
Duration of Study: 1st July 2013 to 31st December 2014.
Sample Size: Sample size of 250 cases is calculated with 95% confidence level, 10% margin of error for sensitivity and 2% margin of error for

specificity and taking expected percentage of postmenopausal bleeding i.e. 22.7% and taking specificity and sensitivity of DUS i.e. 97.16% and 76.0% respectively taking histopathology as gold standard.[8]

Sampling Technique: Non-Probability, Purposive sampling.

SAMPLE SELECTION:
INCLUSION CRITERIA:
1. Patients of age 50-70 years presented with clinically diagnosed postmenopausal bleeding undergoing hysterectomy.
2. Females with endometrial thickness>5mm
EXCLUSION CRITERIA:
Females with medical record of taking HRT

DATA COLLECTION PROCEDURE:
After approval from hospital ethical committee, 250 patients who fulfill the inclusion and exclusion criteria was enrolled in the study from OPD of Sir Ganga Ram Hospital, Lahore. Informed consent was obtained. All basic demographic information of each patient (name, age, parity, address and contact) was also obtained. Females were referred to radiology department for evaluation of endometrial thickness and RI value. If RI was be <0.70, then patients were labeled as positive. This procedure was done by a single senior radiologist. Then patients were sent for hysterectomy, endometrial sampling was done and sample was sent to the histopathology laboratory of the hospital. All surgeries were done. Sample was assessed and cases were labeled as positive or negative. This procedure was done by a single senior histopathologist. All this information was recorded through pre-designed proforma.

DATA ANALYSIS PROCEDURE:
The collected data was analysed statistically by using SPSS version 19. Quantitative variables like age was presented in form of mean ± S.D. Qualitative variables like endometrial carcinoma on Doppler USG and histopathology was presented in form of frequency and percentage. 2x2 table was generated to calculate sensitivity, specificity, PPV, NPV and diagnostic accuracy of DUS taking histopathology as gold standard.

RESULTS
- Mean age of all 250 women included in this study was 61.32±7.67 years. Minimum and

maximum age of women was 50 and 70 years respectively. **(Table-1)**

- Mean endometrial thickness on Doppler ultrasonography was 8.81±4.36 mm. Minimum and maximum endometrial thickness was 4.61 and 30.0 mm. **(Table-2)**
- Mean resistive index on Doppler ultrasonography was 0.53±0.17. Minimum and maximum resistive index was 0.23 and 0.86 respectively.**(Table-3)**
- On Doppler ultrasonography there were 184(73.6%) patients who were diagnosed with endometrial carcinoma **(Table-4)**
- Histopathology results showed that there were 207(82.8%) patients who had endometrial carcinoma **(Table-5)**
- Histopathology results showed that 207 patients had endometrial carcinoma while Doppler ultrasound findings showed that 180 patients had endometrial carcinoma and diagnosed 27 patients as negative for endometrial carcinoma. On the other hand histopathology showed that there were 43 patients who were negative for endometrial carcinoma and Doppler ultrasound showed that among 39 patients endometrial carcinoma was negative and it showed 4 patients who were positive on Doppler ultrasound findings. Sensitivity and specificity of Doppler ultrasound findings was 86.96% and 90.7% respectively. While positive predictive value, negative predictive value and overall diagnostic accuracy of Doppler ultrasound was 97.83%, 59.09% and 87.6% respectively. **(Table-6)**

Table-1: Age Distribution of Patients

N	250
Mean	61.32
SD	7.67
Minimum	50
Maximum	70

Table-2: Descriptive Statistics for Endometrial Thickness

N	250
Mean	8.81
SD	4.36
Minimum	4.61
Maximum	30.0

Table-3: Descriptive Statistics For Resistive Index

N	250
Mean	0.53
SD	0.17
Minimum	0.23
Maximum	0.86

Table-4: Diagnosis Of Doppler Ultrasonography

	Frequency	Percentage
Positive	184	73.6%
Negative	66	26.4%
Total	**250**	**100%**

Table-5: Diagnosis Of Histopathology

	Frequency	Percentage
Positive	207	82.8%
Negative	43	17.2%
Total	**250**	**100%**

Table-6: Diagnostic Accuracy of Doppler Ultrasonography Taking Histopathology As Gold Standard

	Histopathology		
	Positive	Negative	Total
Positive	180	4	**184**
Negative	27	39	**66**
Total	**207**	**43**	**250**

Sensitivity = 180/207 = 86. 96%
Specificity = 39/43 = 90.7%
Positive predictive value = 180/184 = 97.83%
Negative predictive value = 39/66 = 59.09%
Diagnostic Accuracy = 87.6%\

DISCUSSION

Endometrial carcinoma is the most common malignancy of the female genital tract. According to the Surveillance Epidemiology and End Results (SEER) database the incidence of endometrial carcinoma in women aged 30 to 34 years is 2.3/100,000; increases to 6.1/100,000 between ages 35 and 40 years; and rises dramatically to 36.2/100,000 in women aged 40 to 49 years. In post-menopausal women not taking HRT, any bleeding is considered "cancer until proven otherwise," although the incidence of malignancy in such patients ranges from 2% to 10% depending on the risk factors. [9, 10]

Endometrial curettage, first described in 1843, is the most common operation performed on women across the world. As early as the 1950s, a review of 6907 curettage procedures found that the

technique missed endometrial lesions in 10% of cases. Of these, 80% were polyps. In the 1970s, vacuum-suction curettage devices allowed sampling without anaesthesia in clinical setting. The most popular was the Vabra aspirator (Berkeley Medevices, Berkeley, California). This device was found to be 86% accurate in diagnosing cancer. [11, 13]

Lately, less expensive, smaller, less painful plastic catheters with their own internal pistons to generate suction have become popular. One of these, the Pipelle device, was found to have similar efficacy but better patient acceptance compared with the Vabra aspirator.[14]

Transvaginal sonography currently is considered to be the first-step technique to be performed in women with postmenopausal bleeding because it may reliably rule out endometrial cancer when endometrial thickness is 5mm and because it is cost-effective. However, a thickened endometrium is a nonspecific finding, and additional tests are warranted. Most current protocols include the use of sonohysterography or endometrial office biopsy.[15]

Power Doppler or color Doppler energy is a new technology that has some advantages over conventional color Doppler. Power Doppler is based on the amplitude of the Doppler signal but not on the Doppler frequency shift. It is insonation angle independent, does not have aliasing and is more sensitive to low-velocity blood flow. All these features make this technique advantageous for blood flow mapping by facilitating the detection of flow where present and depicting more clearly and reliably the vascular architecture. The advantages of the power Doppler technique have been demonstrated in adnexal masses by Guerriero et al. Another study has demonstrated a high correlation between microvessel density and power Doppler findings in breast carcinoma.[16, 17]
Results of this study showed the sensitivity and specificity of Doppler ultrasound for detecting endometrial carcinoma was 86.96% and 90.7%. While positive predictive value, negative predictive value and overall diagnostic accuracy of Doppler ultrasound was 97.83%, 59.09% and 87.6% respectively.

Results of local study from CMH Lahore determined the accuracy of Doppler ultrasound in the diagnosis of endometrial carcinoma in patients presenting with post-menopausal bleeding while taking histopathological findings as the gold standard. Results showed that Specificity, sensitivity, positive predictive value and negative predictive value were found to be 97.16%, 76%, 89. 56% and 76.92% respectively.[18] Results of this study is consistent with the results reported by Shazia Batool from CMH Lahore. However a slight difference can be seen in sensitivity, specificity, PPV and NPV in both studies.

Mahmoud El-Morsi Aboul-Fotouh from Egypt evaluate the role of transvaginal power Doppler sonography in differentiation between benign and malignant endometrial conditions in women with postmenopausal bleeding. Results regarding predictive values for endometrial carcinoma was sensitivity: 85.71%, Specifcity:97.26%, PPV:75% and NPV:98.61% respectively.[19]

Mahmoud El-Morsi Aboul-Fotouh results are consistent with the results of this study however reported sensitivity, specificity, PPV and NPV was a bit lower in this study. But still results demonstrate that Doppler ultrasonography is still effective for the diagnosis of endometrial carcinoma in women with postmenopausal bleeding.

Alcazar et al. who reported a sensitivity, specificity, positive predictive value, and negative predictive values of power Doppler vascular pattern for endometrial carcinoma of 78.8%, 100%, 100%, and 89%, respectively.[16] Alcazar results are also in line with the results of this study.

The differences in results between studies are probably to be explained by differences in ultrasound equipment, machine settings, experience of the examiners, and by lack of standardized criteria for subjective evaluation of endometrial vascularity. Objective quantification of power Doppler signals using computer analysis has been used in the diagnosis of cervical carcinoma. Cheng and coworkers found that in women with cervical carcinoma a power Doppler vascularity index (defined as vascular area divided by tumor area, i.e. an index similar to our vascularity index) showed a linear correlation with microvessel density and was significantly positively correlated to tumor size, depth of stromal invasion and the presence of lymph node metastases. These facts suggest that tumor vascularity as assessed by power Doppler ultrasound may be useful in the diagnosis and characterization of malignancy.[20, 21]

The use of power Doppler blood flow mapping as a secondary test in women presenting with postmenopausal bleeding and a thickened

endometrium at baseline sonography is useful to discriminate carcinoma from other causes of endometrial thickening. Also, it might be a promising screening tool for asymptomatic postmenopausal women with risk factors for endometrial carcinoma.

CONCLUSION

Results of this study showed good diagnostic results with the use of Doppler ultrasonography in the diagnosis of endometrial carcinoma in patients presenting with post-menopausal bleeding. Doppler ultrasonography is useful diagnostic tool with good sensitivity (86.97%), specificity (90.7%), PPV (97.83%) and NPV (59.09%). With its use patients can be prevented from unnecessary surgeries.

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