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Correlation of the role of Transvaginal Sonography and Doppler with endometrial biopsy in detection of carcinoma endometrium in postmenopausal bleeding

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ABSTRACT

To evaluate the diagnostic accuracy of transvaginal sonography (TVS) with Doppler compared to histopathological examination in diagnosing endometrial pathology in patients with postmenopausal bleeding; to determine whether the number of diagnostic dilatation and curettage (invasive) can be reduced by TVS (non-invasive) examination. 100 women were selected by Simple Random Sampling method, satisfying the inclusion criteria from January 2015 to June 2016. After obtaining written informed consent and detailed clinical examination TVS with doppler followed by dilatation and curettage were done and specimen were sent for histopathological examination. Patients with postmenopausal bleeding were included and those on Hormone Replacement Therapy**,** with bleeding disorders**,** known cases of malignancies**,** cervical polyp were excluded from the study. Statistical analysis was done for these parameters. TVS with Doppler parameters had sensitivity of 72.92% and specificity of 57.69% as a diagnostic tool in order to detect endometrial hyperplasia and endometrial carcinoma in such patients. It had a positive predictive value of 61.40% and negative predictive value of 69.77% with capability of diagnosing endometrial pathology with an accuracy of 65%. 48 patients had endometrial atrophy. There is a high incidence of endometrial atrophy in patients presenting with postmenopausal bleeding. The relatively good sensitivity and accuracy of TVS with doppler in detection of endometrial pathology encourage us to suggest that it can be utilized as a first line investigation in these patients to rule out endometrial hyperplasia or endometrial cancer.

Keywords: Transvaginal Sonography, doppler, postmenopausal bleeding, endometrial pathology or cancer

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INTRODUCTION

Postmenopausal uterine bleeding is defined as uterine bleeding 12 months or more after permanent cessation of menstruation. Bleeding can be spontaneous or related to hormone replacement therapy or due to use of selective estrogen receptor modulators.[1] Its prevalence is approximately 10% immediately or 1-2years of menopause; signifies endometrial carcinoma in about 10% cases and further benign causes like endometrial atrophy or polyp.[2]Most common finding on histopathology being endometrial atrophy, being 60%-80% followed by endometrial polyp; endometrial carcinoma.[3] Carcinoma endometrium is the fourth common carcinoma ranking after breast, lung, colorectal carcinomas; eighth leading cause of death of malignancy in women.[3] The probability of endometrial carcinoma is 5-10% and hence further evaluation is mandatory within 2-6weeks.[4,5]Depending on patient's characteristics the incidence has been reported to be as high as 29%.[6]

TVS has a moderate diagnostic accuracy in detecting endometrial hyperplasia as it is safe, acceptable and easily available in most secondary and tertiary care settings and is non-invasive in nature and hence to be used as a first line diagnostic tool in patients who present with abnormal uterine bleeding.[5]Diagnostic procedures obtaining material for histopathological examination (e.g., dilatation and curettage, hysteroscopy, and endometrial pipelling) can be more accurate but are also more invasive.[6]

This study has been conducted to compare the diagnostic accuracy of TVS with Doppler parameters and correlate with findings of endometrial biopsy; assess role of TVS in reducing invasive procedures in detection of endometrial carcinoma in patients with PMB.

MATERIALS AND METHOD

Inclusion criteria:

The study has been conducted on 100 women with one or more episodes of postmenopausal bleeding in the Department of Obstetrics and Gynecology at Vydehi Institute of Medical Sciences and Research Centre, Bangalore, over 2 years (2014-2016).

Exclusion criteria:

Women on hormone replacement therapy, with bleeding disorders, known cases of malignancy, with local cervical pathology (polyp, growth) were excluded.

Consent:

Permission was taken from institutional ethical committee. After obtaining written informed consent detailed history was taken and thorough physical examination was done.

TVS with Doppler parameters (irregular branching of vessels, areas of densely packed vessels, number of vessels, large vessels and Colour 'splashes') was done in all the patients followed

by endometrial biopsy obtained by dilatation and curettage under intravenous sedation (pentazocin , promethazine).

Statistical analysis was done with SPSS software. Sensitivity, specificity, and positive and negative predictive values of TVS and dilatation and curettage for endometrial biopsy in diagnosing the cause of PMB were assessed.

RESULTS AND DISCUSSION

The age of my patients ranged from 45 to 77yrs. Maximum number of patients with PMB belonged to age group 55-64yrs (n=38) ; 2 patients were above 74years as shown in **Table I**. All the patients had complaints of postmenopausal bleeding. In addition to that 60% of them had complaints of hot flushes and 40% had dyspareunia. 18 of them were nulliparous, 24 were primipara and 58 were multiparous women. 45% patients had BMI varying from 25-30Kg/m^2. 28% patients were obese. 35% patients had Diabetes Mellitus; 30% had hypertension; 15% patients had both.

Table I: Incidence of PMB in different age groups

Age in years	PMB cases	Total OPD patients	Incidence(per 1000)
45– 54	36	2184	16.4
55-64	38	2728	13.9
65-74	26	1996	13
>74	2	289	6.9
Total	100	7197	13.8

On per speculum examination, 54% of patients had normal cervix and vagina. 38% had dry vagina, 4% had bleeding through external os at the time of examination. 3% patients had cervical erosion over anterior and posterior lip. 1patient had cervix flushed with vagina. On per vaginal examination 48% patients had normal size uterus; 36% patients had atrophied uterus.

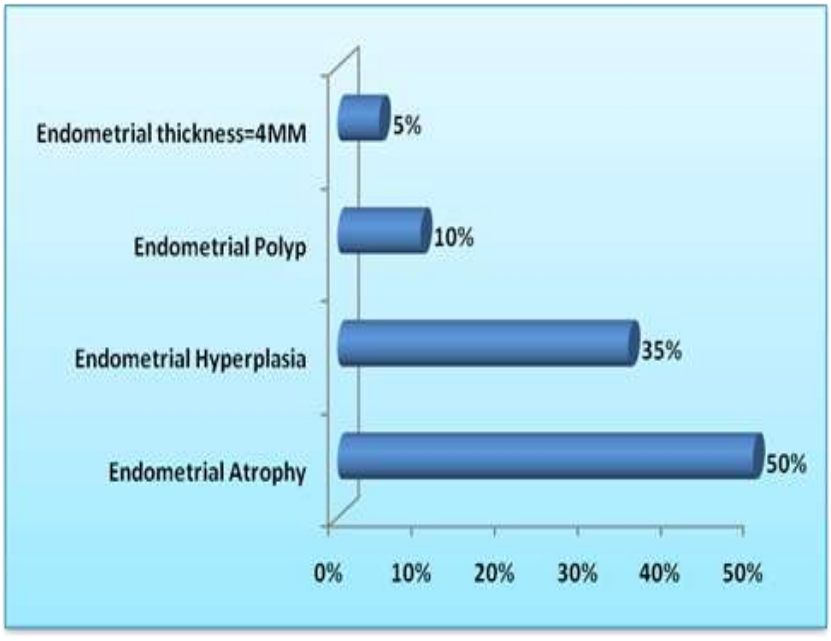

Figure 1: TVS findings of the patients

TVS showed 50% patients had atrophic endometrium, 35% had hyperplasia,10% had polyp; 5% had endometrial thickness of 4mm.

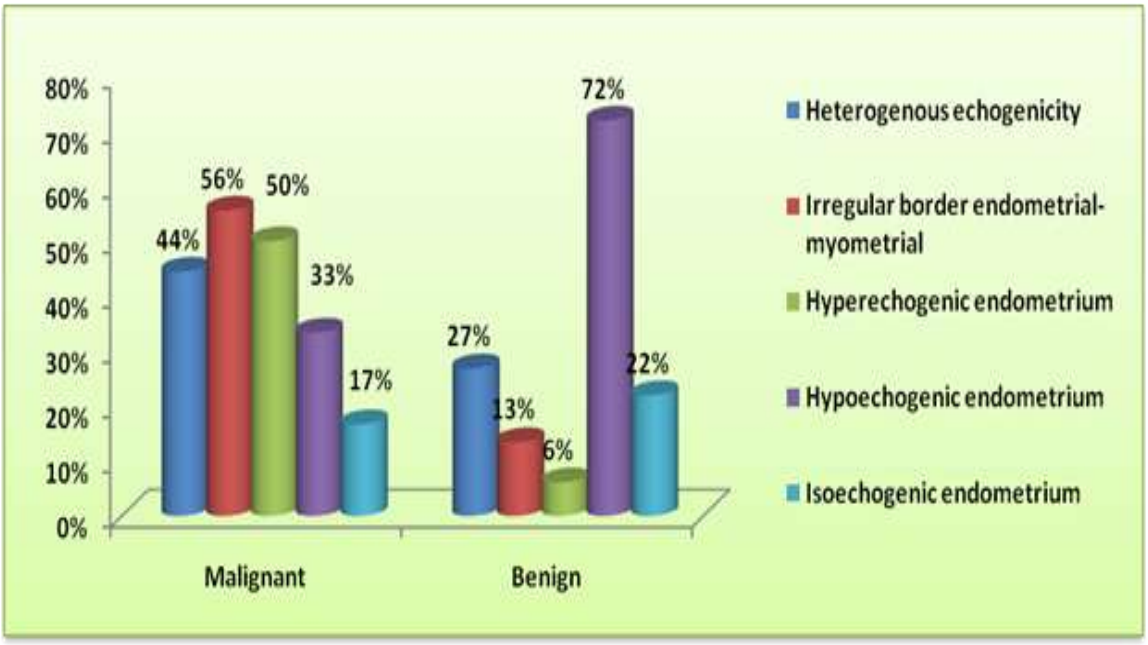

Figure 2: Gray-scale ultrasound analysis of endometrium

On gray-scale ultrasound 82 patients were diagnosed to have benign pathology and 18 patients were diagnosed to have endometrial carcinoma. In patients with carcinoma endometrium, 44% had heterogenous echogenicity of the endometrium; 56% had irregular endometrial-myometrial borders; 50% had hyperechogenic endometrium.72% patients with benign endometrial pathology had hypoechogenic endometrium.

Out of 18 patients diagnosed with endometrial carcinoma 61% had irregular branching of vessels; 78% patients had many vessels and large vessels in the endometrium. There were areas of densely packed vessels in 79% of benign patients and colour 'splashes' in 63% of benign patients according to Doppler as shown in **Table II.**

Table II-Doppler analysis

	Malignant cases	**Benign cases**
Irregular branching of vessels	11/18	38/82
Areas of densely packed vessels	12/18	65/82
Many vessels(one, two, many)	14/18	38/82
Large vessels	14/18	22/82
Colour 'splashes'	9/18	56/82

According to histopathology reports (gold standard), as depicted in **Table III**, out of 100 women with PMB 48% patients had endometrial atrophy; 18% patients were diagnosed to have endometrial carcinoma; 17% of patients had endometrial polyp; 17% of the patients had endometrial hyperplasia.

Table III-Diagnosis (mainly based on histopathology)

Diagnosis	Number of patients	Percentage
Atrophic endometrium	48	48
Endometrial polyp	17	17
Hyperplastic endometrium	17	17
Carcinoma endometrium	18	18
Total	100	100

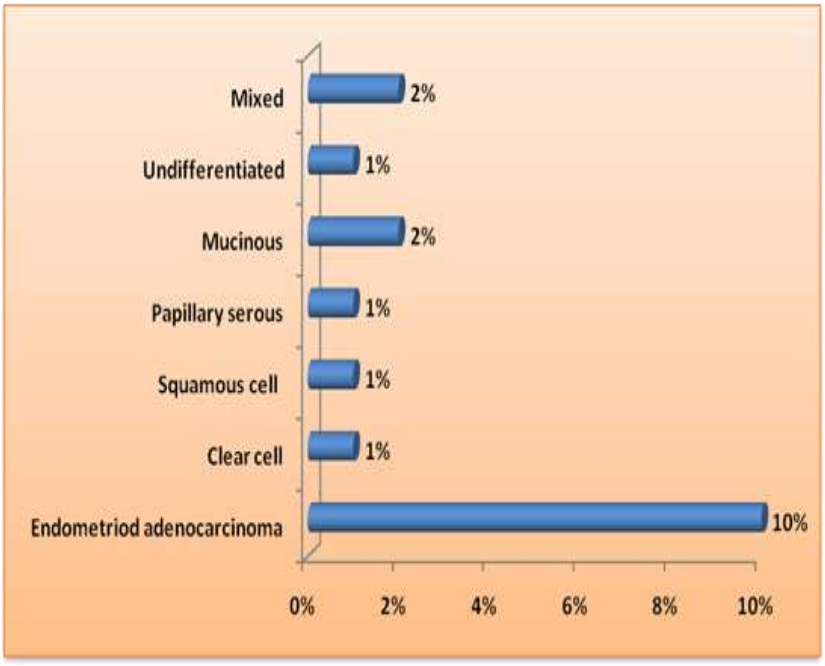

Figure 3: Classification of carcinoma

10% of the patients had endometriod carcinoma; 2% had mucinous and mixed carcinoma; 1% patient had papillary serous carcinoma, squamous cell carcinoma, clear cell carcinoma and undifferentiated carcinoma**.**

Table IV-TVS with Doppler vs histopathology

TVS with Doppler versus histopathology	TP	TN	FP	FN	Sensitivity(%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy	P value
Endometrial atrophy	5	3	43	49	10.42	94.23	62.5	53.26	54	0.001
Endometrial hyperplasia	16	9	32	43	33.3	84.89	64	57.3	59	<0.001
Endometrial polyp	2	46	1	51	4.17	98.08	66.6	52.58	53	0.001
Carcinoma	27	21	31	21	56.25	40.38	46.5	50	48	<0.001

As shown in **Table IV** TVS with the Doppler parameters has sensitivity of 72.92% and specificity of 57.69% as a diagnostic tool in order to detect endometrial hyperplasia and endometrial carcinoma in patients with postmenopausal bleeding. It has a positive predictive value of 61.40% and negative predictive value of 69.77%. It is capable of diagnosing endometrial pathology with an accuracy of 65%.

DISCUSSION

Postmenopausal bleeding is often caused by abnormalities of the endometrium, whether they are benign or malignant. Amongst postmenopausal women with vaginal bleeding, 10%–15% have endometrial carcinoma.[7]Endometrial cancer is the most common malignancy of the female genital tract in developed countries. Relevant investigations leading to diagnosis in such patients help in determining adequate management and avoid unnecessary interventions and major surgeries. [8]

Commonly used diagnostic procedures in patients with postmenopausal bleeding can be classified as non-invasive and invasive tools. Non-invasive methods include – transvaginal ultrasound, saline infusion sonohysterography. Invasive procedures are endometrial pipelling, dilatation and curettage for endometrial sampling and hysteroscopy. [9] These methods are used alone or in combination to get a correct diagnosis.

TVS has been proposed as an alternative or a compliment to hysteroscopy in the workup of patients with Postmenopausal bleeding**.**[10,11,12] Reliability of TVS in excluding the presence of intra cavitary disorders in pre and postmenopausal females has been demonstrated repeatedly and the necessity of hysteroscopy after a negative TVS has been questioned.[13.14]

In the study done by Indu Kaul et al [9] transvaginal ultrasound had detected 24(48%) out of 50 women with postmenopausal bleeding, had endometrial atrophy which correlates with this study in which TVS detected 50 patients to have atrophic endometrium.

Ali Babacan et al [15]showed that transvaginal ultrasound could detect endometrial polyp in 129 out of 285 patients with 12% & 8.3% sensitivity in detecting polyp when compared to hysteroscopy. N. van Hanegem et al[2] showed the sensitivity and specificity of transvaginal ultrasound was 96% and 50% respectively in detecting endometrial carcinoma which correlates with the higher sensitivity of ultrasound in the present study. Showkat MS et al [16]performed a study in which transvaginal ultrasound could be used to rule out endometrial hyperplasia or carcinoma like in the present study in which accuracy of ultrasound with Doppler is 65%.As stated by Mortakis et al [17], Dijkhuizen et al [18] transvaginal ultrasound seems to be an excellent initial diagnostic method with high sensitivity in diagnosing endometrial abnormalities as a first step as described in the present study.

According to E.Epstein et al [19], Guida et al [20],Garuti et al [21] hysteroscopy was superior to both saline contrast sonography and conventional ultrasound with regard to discriminating between benign and malignant lesions with sensitivity of 84% , 44% ,60% respectively and false-positive rate as 15%, 6% , 10% respectively which does not correlate with this study in which TVS has been seen to have good sensitivity and accuracy of 65%.

Power Doppler ultrasound can contribute to a correct diagnosis of endometrial malignancy, especially if the endometrium measures 5–15 mm. as stated by E.Epstein et al [22].83 women

with postmenopausal bleeding and endometrial thickness ≥ 5 mm underwent gray-scale and power Doppler ultrasound examination and it was concluded that ultrasound findings may guide to decide the optimal timing for biopsy and may refrain us from invasive diagnostic procedures in low risk women which supports the present study. G.Opolskiene et al[6],assessed different parameters like vascularization index, flow index , vascularization flow index, irregular branching of endometrial blood vessels along with endometrial thickness >4.5mm ;and concluded that diagnostic performance was not superior to two-dimensional ultrasound in detection of benign or malignant endometrial pathology unlike the present study.

In postmenopausal women endometrial sampling with both the Pipelle and the Vabra device (USA) were found to be very sensitive techniques for the detection of endometrial carcinoma, with detection rates of 99.6% and 97.1%, respectively. It has been concluded that the sensitivity of TVS alone to rule out endometrial malignancy to be controversial.[8] Hence TVS can be used as a complementary tool along with endometrial biopsy in order to rule out carcinoma endometrium which has similar opinion as the present study. Clark et al[23]suggested that ultrasonographic measurement of endometrial thickness has limited diagnostic prediction for endometrial cancer but is a good test for exclusion of malignancy. In similarity with this study although ultrasound has significant role to rule out endometrial malignancy and can help in reducing unwanted invasive procedures endometrial sampling is the gold standard in order to diagnose endometrial carcinoma.

CONCLUSION

Transvaginal ultrasound with Doppler parameters can have an important role in patients , with postmenopausal bleeding, as it can discriminate between benign and malignant pathologies of the endometrium. Ultrasound with Doppler has a good sensitivity and accuracy in detecting endometrial malignancy. Moreover patient compliance is seen to be good with this tool as it is done on outpatient basis it is non-invasive , and there is no unnecessary exposure to anesthetic drugs. TVS with Doppler can be suggested as an excellent tool in stratifying patients in high and low risk groups. It has been seen to play an integral role in detection of patients with endometrial hyperplasia or malignancy. Hence it is suggested that transvaginal ultrasound with Doppler parameters to be used as the first or initial tool to detect endometrial pathology. In order to avoid unwanted invasive procedures in patients in whom endometrial thickness <4.5mm and there are negative Doppler findings, TVS can be used to rule out endometrial malignancy considering endometrial biopsy as the gold standard.

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