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Original Research Article

Endometrial thickness cut-off value by transvaginal ultrasonography for screening of endometrial pathology in postmenopausal women with bleeding

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ABSTRACT

Background: Postmenopausal bleeding is defined as blood loss occurring at least 12 months after menopause. Aims and objectives were to assess the clinical usefulness and diagnostic accuracy of ultrasonographic measurement of endometrial thickness (ET) in women with postmenopausal bleeding.
Methods: It was a prospective study that took place at Government Medical College and Rajindra Hospital Patiala. from June 2018 to May 2019. The study was carried out in 60 patients presenting with postmenopausal bleeding to the OPD of department of obstetrics and gynecology, Government Medical College and Rajindra Hospital, Patiala. Patients with post-menopausal bleeding were included in the study. The endometrial thickness (ET) was measured on TVS. Hysteroscopy was done. Findings were recorded as atrophic endometrium, endometrial hyperplasia, endometrial polyp, fibroid, and endometrial carcinoma (obvious intrauterine growth with necrotic tissue). Endometrial biopsies were taken in all patients. Histopathological examination was done and was considered as the final diagnosis. Data collected was analysed using Microsoft Excel Office software 2019 version 19.11 and Epi info (CDC Atlanta) version 7.2.3.1.
Results: The best diagnostic accuracy for TVS was obtained at endometrial thickness of 4 mm.
Conclusions: TVS is useful for detecting endometrial pathology with a cut-off value for ET of 4 mm having a high sensitivity. Role of endometrial thickness cannot be undermined for detecting patients at high risk especially with comorbid conditions.

Keywords: Cut off value, Endometrial thickness, Hysteroscopy, PMB, TVS

INTRODUCTION

The average age of menopause in Asian women is 46 years.[1] Postmenopausal bleeding is defined as blood loss ocurring at least 12 months after menopause.[2] The prevalence of PMB is approximately 10% immediately after menopause.[1] The goal of evaluation of Postmenopausal bleeding is to achieve the diagnosis with greatest accuracy, the least risk and expense for the patient.[3] Potential screening modalities for endometrial cancer include transvaginal sonography (TVS), saline infusion sonohysterography, 3-D color doppler ultrasound, endometrial sampling through endometrial aspiration biopsy, dilatation and curettage, hysteroscopy, and guided biopsy. Pelvic ultrasonographic examination and, in particular, transvaginal Ultrasonography can suggest the cause of bleeding.[4,5] In the present study, non-invasive TVS, the minimally invasive technique endometrial aspiration, and hysteroscopy have been used for the evaluation of endometrial pathology in patients with PMB.

Aims and objectives

The aim of the present study was to assess the clinical usefulness and diagnostic accuracy of ultrasonographic measurement of endometrial thickness (ET) in women with postmenopausal bleeding.

METHODS

The present study was carried out in 60 patients presenting with postmenopausal bleeding to the OPD of department of obstetrics and gynecology, Government Medical College and Rajindra Hospital, Patiala from June 2018 to May 2019. The study was approved by the institutional ethical and research review board. Inclusion criteria included patients with postmenopausal bleeding. Exclusion criteria included patients taking hormonal replacement therapy, with obvious cause of bleeding from cervix and vagina, known blood dyscrasias, on anticoagulant therapy, with surgical menopause. After history, detailed clinical examination, and routine investigations, all patients were subjected to hysteroscopic guided biopsy for histopathological examination. This was preceded by transvaginal sonography. The characters that were studied on TVS included endometrial thickness, echogenicity of endometrium, uterine size, uterine cavity, cervical canal, myometrium, any uterine growth/polyp, any fluid in endometrial cavity and bilateral adnexa. On TVS, atrophic endometrium is thin, homogenous and echogenic. TVS shows nonspecific thickening of the central endometrial complex, with or without cystic changes. Polyp is seen as a distinct hyperechoic line partially or completely surrounds the abnormal endometrial complex. In endometrial hyperplasia, there is a well-defined endometrial thickening with or without cysts. Endometrial cancer is suspected in presence of heterogenous endometrium with irregular interface between endometrium and myometrium with or without fluid collection. The findings were noted, and the patients were scheduled for hysteroscopy and biopsy after pre-anesthetic checkup. Hysteroscopy was performed with Gebrauchsanweisung- Diagnostic 4 mm rigid Karl Storz Aida @ WD200 and WD 250 endoskope with a 30-degree oblique aperture view with a 5 mm sheath. If normal, biopsy was taken from anterior, posterior, two side walls along with fundus in one vial and sent for histopathological examination. If abnormal, biopsy was taken from suspicious area, and polypectomy was done if it was present. The histopathology report was divided into 5 groups that were atrophic endometrium, endometrial polyp, fibroid, endometrial hyperplasia and endometrial carcinoma. The data collected was analysed using Microsoft Excel Office software 2019 version 19.11 and Epi info (CDC Atlanta) version 7.2.3.1.

RESULTS

Sixty patients presenting with postmenopausal bleeding in outpatient department, after applying both inclusion and exclusion criteria, were enrolled in present study.

Table 1: Demographic details.

Characteristics	
Age group majority at presentation	55-64 years
Parity observed mostly	2
Majority had BMI	More than 25 kg/m²
Majority had menopause in age group	45-55 years
No. of diabetic patients	16
No. of hypertensive patients	25

Table 2: Cut off <3 mm.

	ET (<3 mm)		
HPE group1	**Yes**	**No**	**Total**
Normal	6	18	24
Row %	25.00%	75.00%	100.00%
Col %	100.00%	33.33%	40.00%
Pathology	0	36	36
Row %	0.00%	100.00%	100.00%
Col %	0.00%	66.67%	60.00%
Total	6	54	60
Row %	10.00%	90.00%	100.00%
Col %	100.00%	100.00%	100.00%
Sensitivity		1.000	
Specificity		0.667	
Positive predictive value		0.250	
Negative predictive value		1.000	
Accuracy		0.700	
Youden index		0.667	
Kappa		0.286	

Table 3: Cut off ≤3 mm.

	ET (≤3 mm)		
HPE group1	**Yes**	**No**	**Total**
Normal	14	10	24
Row %	58.33%	41.67%	100.00%
Col %	100.00%	21.74%	40.00%
Pathology	0	36	36
Row %	0.00%	100.00%	100.00%
Col %	0.00%	78.26%	60.00%
Total	14	46	60
Row %	23.33%	76.67%	100.00%
Col %	100.00%	100.00%	100.00%
Sensitivity		1.000	
Specificity		1.000	
Positive predictive value		0.783	
Negative predictive value		0.583	
Accuracy		1.000	
Youden index		0.833	
Kappa		0.783	

Table 4: Cutoff <4 mm.

	ET (<4 mm)		
HPE group1	**Yes**	**No**	**Total**
Normal	22	2	24
Row %	91.67%	8.33%	100.00%
Col %	91.67%	5.55%	40.00%
Pathology	3	33	36
Row %	5.55%	94.45%	100.00%
Col %	8.33%	94.45%	60.00%
Total	24	36	60
Row %	40.00%	60.00%	100.00%
Col %	100.00%	100.00%	100.00%
Sensitivity		0.917	
Specificity		0.944	
Positive predictive value		0.917	
Negative predictive value		0.944	
Accuracy		0.933	
Youden index		0.861	
Kappa		0.861	

The mean endometrial thickness on TVS was 8.68±6.45 mm. Majority of patients (58.33%) had ET>4 mm (Table 10). 41.67% patients were found to have atrophic endometrium. On hysteroscopy, endometrium was hyperplastic in 11 (18.33%) patients, polyp in 11 (18.33%) patients, and growth in 7 (11.67%) patients. On histopathology, majority of patients (40 %) had atrophic endometrium. Endometrial hyperplasia was detected in 11 (18.33%). Endometrial cancer was detected in 8 (13.33%) patients. Mean ET in atrophy was 3.27±1.08 mm, hyperplasia 15.23±4.43 mm, carcinoma 17.32±5.85 mm, fibroid 6.20±0.96 mm, and polyp 8.95±4.66 mm. The maximum diagnostic accuracy of endometrial thickness was found at values of ≤4 mm, <5 mm and ≤5 mm, the lowest limit being ≤4 mm (cut off value) (Tables 2 to 9). Out of 36 patients in whom histopathology confirmed any pathology as above said, ultrasound detected some pathology in 34 and missed in two cases. Similarly, out of 24 patients with atrophic endometrium on histopathology ultrasound could detect the same in 23 cases. The sensitivity of hysteroscopy as compared to histopathological examination for postmenopausal women with PMB was 97.2%, and specificity was 100%. The PPV of hysteroscopy as compared to histopathology was 100%, and NPV was 96% with diagnostic accuracy of 98.3%.

Table 5: Cut off ≤4 mm.

	ET (≤4 mm)		
HPE group1	**Yes**	**No**	**Total**
Normal	23	1	24
Row %	95.83%	4.17%	100.00%
Col %	92.00%	2.86%	40.00%
Pathology	2	34	36
Row %	5.55%	94.45%	100.00%
Col %	8.00%	97.14%	60.00%
Total	25	35	60
Row %	41.67%	58.33%	100.00%
Col %	100.00%	100.00%	100.00%
Sensitivity		0.920	
Specificity		0.971	
Positive predictive value		0.958	
Negative predictive value		0.944	
Accuracy		0.950	
Youden index		0.891	
Kappa		0.897	

Table 6: Cut off <5 mm.

	ET (<5 mm)		
HPE group1	**Yes**	**No**	**Total**
Normal	23	1	24
Row %	95.83%	4.17%	100.00%
Col %	92.00%	2.86%	40.00%
Pathology	2	34	36
Row %	5.55%	94.45%	100.00%
Col %	8.00%	97.14%	60.00%
Total	25	35	60
Row %	41.67%	58.33%	100.00%
Col %	100.00%	100.00%	100.00%
Sensitivity		0.920	
Specificity		0.971	
Positive predictive value		0.958	
Negative predictive value		0.944	
Accuracy		0.950	
Youden index		0.891	
Kappa		0.897	

Table 7: Cut off ≤5 mm.

	ET (≤5 mm)		
HPE group1	**Yes**	**No**	**Total**
Normal	23	1	24
Row %	95.83%	4.17%	100.00%
Col %	92.00%	2.86%	40.00%
Pathology	2	34	36
Row %	5.55%	94.45%	100.00%
Col %	8.00%	97.14%	60.00%
Total	25	35	60
Row %	41.67%	58.33%	100.00%
Col %	100.00%	100.00%	100.00%
Sensitivity		0.920	

Continued.

ET (≤5 mm)	
Specificity	0.971
Positive predictive value	0.958
Negative predictive value	0.944
Accuracy	0.950
Youden index	0.891
Kappa	0.897

Table 8: Cut off <6 mm.

ET (<6 mm)			
HPE group1	**Yes**	**No**	**Total**
Normal	23	1	24
Row %	95.83%	4.17%	100.00%
Col %	79.31%	3.23%	40.00%
Pathology	6	30	36
Row %	16.67%	83.33%	100.00%
Col %	20.69%	96.77%	60.00%
Total	29	31	60
Row %	48.33%	51.67%	100.00%
Col %	100.00%	100.00%	100.00%
Sensitivity		0.793	
Specificity		0.968	
Positive predictive value		0.958	
Negative predictive value		0.833	
Accuracy		0.883	
Youden index		0.761	
Kappa		0.765	

Table 9: Combined table for cut off values.

Parameters	<3 mm	≤3 mm	<4 mm	≤4 mm	<5 mm	≤5 mm	<6 mm
Sensitivity	1	1	0.917	0.920	0.920	0.920	0.793
Specificity	0.667	0.783	0.944	0.971	0.971	0.971	0.968
Positive predictive value	0.25	0.583	0.917	0.958	0.958	0.958	0.958
Negative predictive value	1	1	0.944	0.944	0.944	0.944	0.833
Accuracy	0.7	0.833	0.933	0.950	0.950	0.950	0.883
Sensitivity + specificity	1.667	1.783	0.861	1.891	1.891	1.891	1.761
Youden index	0.667	0.783	0.861	0.891	0.891	0.891	0.761
Kappa	0.286	0.627	0.917	0.897	0.897	0.897	0.765

Table 10: ET overview.

ET classification	Frequency	Percent	Cum. percent	Exact 95% LCL	Exact 95% UCL
≤4	25	41.67%	41.67%	30.59%	56.76%
>4	35	58.33%	100.00%	43.24%	69.41%
Total	60	100.00%	100.00%		

The maximum diagnostic accuracy of endometrial thickness was found at values of ≤4 mm, <5 mm and ≤5 mm, the lowest limit being ≤4 mm (cut off value).

DISCUSSION

PMB is more likely caused by pathologic disease as compared to bleeding in younger women, and it must always be investigated.[6] Following are the common causes of postmenopausal bleeding: exogenous estrogens, atrophic endometritis/vaginitis, endometrial cancer, endometrial or cervical polyps, endometrial hyperplasia.

Other causes of genital tract bleeding in a postmenopausal woman are: vulva- trauma, vulvitis, benign and malignant lesions; vagina- foreign body such as ring pessary for

prolapse, vaginal tumor, and postradiation vaginitis; cervix- cervical erosion, cervicitis, decubitus ulcer in prolapse and cervical malignancy; uterus- tubercular endometritis and submucosal fibroids; fallopian tube malignancy; benign and malignant estrogen secreting tumors of ovary; blood dyscrasia; bleeding from urethra and anus may be mistaken for bleeding from vagina; use of tamoxifen leads to endometrial hyperplasia and thus postmenopausal bleeding; and anticoagulant therapy.[7]

Women with PMB have 10-15% chance of having endometrial cancer. Conversely, 90% of the endometrial cancer in the postmenopausal period present with postmenopausal bleeding. Hence, immediate evaluation is required.[1] Present study was undertaken to assess the clinical usefulness and diagnostic accuracy of ultrasonographic measurement of endometrial thickness (ET) in women with postmenopausal bleeding. Considering atrophic endometrium as normal finding in postmenopausal women, all other diagnosis including carcinoma endometrium, submucosal fibroid, endometrial hyperplasia and polyp were grouped as pathologies in the present study. Out of 36 patients in whom histopathology confirmed any pathology as above said, ultrasound detected some pathology in 34 and missed in two cases. Similarly, out of 24 patients with atrophic endometrium on histopathology ultrasound could detect the same in 23 cases. The overall sensitivity of TVS came out to be 94.4%, specificity 95.8%, PPV 97.1%, NPV 92.1% and diagnostic accuracy 95% in the present study. Similar studies conducted by different investigators, Karlsson et al, Gull et al, Garuti et al, Tinelli et al and Kaur et al, had shown the sensitivity ranging from 89 to 100% while specificity from 54.8 to 86 % at ET of 4 mm.[8-11] Sousa et al found that (66.67%) of patients had ET>4 mm while 33.3% had ET≤4 mm.[12] Thus, all patients with PMB need preliminary evaluation by TVS for ET and endometrial sampling to rule out premalignant and malignant pathology as early as possible. Conduction of hysteroscopy to the diagnostic armamentarium of gynecologist has definitely been beneficial in early diagnosis and treatment in women with PMB. Hysteroscopic guided biopsy can help further evaluation and to guide the choice of treatment in women with PMB. Hysteroscopic guided endometrial Biopsy may be done at the same sitting.[13] Hysteroscopic guided endometrial biopsy allows a targeted Biopsy in localized lesions reducing the possibility of false negatives.[14] Hysteroscopic evaluation is the gold standard with TVS as initial investigating tool.[15]

Limitation of this study is small sample size.

CONCLUSION

Evaluation of PMB at the earliest is essential for diagnosing endometrial status for early intervention. Role of endometrial thickness cannot be undermined for detecting patients at high risk especially with comorbid conditions. The diagnostic accuracy of TVS was found best at cut off value of endometrial thickness of ≤4 mm. Histopathological evaluation is mandatory for ruling out malignancy in selected cases of PMB through hysteroscopy.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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