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Original Research Article

Correlation of Endometrial Thickness by Transvaginal Sonography with Endometrial Histopathology in Evaluation of Postmenopausal Bleeding: a Prospective Study

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Abstract

Background: Postmenopausal bleeding (PMB) accounts for about 5 percent of patients attending Gynecology Outpatient Department visits. Any postmenopausal bleeding should require prompt and thorough evaluation to exclude endometrial carcinoma particularly in presence of risk factors. The aim of the present study was to evaluate endometrial thickness (ET) by transvaginal sonography in endometrial causes of postmenopausal bleeding (PMB) and its correlation with endometrial tissue histopathology.

Methods: A total 100 patients with PMB fulfilling the inclusion criteria and giving informed consent were selected in this prospective study. Each patient was subjected to transvaginal sonography (TVS) first in which uterus, adnexa and endometrial thickness (ET) were assessed. Dilatation and curettage was then scheduled at subsequent visit as an inpatient procedure. Endometrial tissue was collected and sent for histopathological examination.

Results: Majority (38%) of patients with PMB was in the age group of 46-50 years. Among the risk factors 18% of patients had diabetes mellitus; hypertension was present in 15% of cases and obesity in 14% of cases. Atrophic endometrium (40%) was most common endometrial cause of PMB. Both proliferative endometrium and endometrial hyperplasia without atypia were observed in 18% of cases. Endometrial polyp was found in 5 cases. Endometrial hyperplasia with atypia was observed in 8% of cases. Endometrial carcinoma was seen only in 2 cases.

Conclusions: TVS is an important tool for evaluation of endometrial pathology in all cases of postmenopausal bleeding to exclude endometrial carcinoma. The risk for abnormal endometrial pathology could be ruled outwhen ET<=5 mm. Histopathological diagnosis of endometrium is the gold standard.

Keywords: Postmenopausal bleeding, transvaginal sonography, endometrial thickness, histopathology.

Introduction

Menopause is the permanent stoppage of menstruation resulting from loss of ovarian follicular activity [1]. Bleeding that occurs 12 months or more of amenorrhea is called postmenopausal bleeding (PMB). Postmenopausal bleeding accounts for about 5 percent of patients attending Gynecology Outpatient Department visits [2]. Any postmenopausal bleeding should require prompt and thorough evaluation to exclude endometrial carcinoma and its precursor lesion atypical endometrial hyperplasia. Endometrial carcinoma accounts for approximately 10 percent patients (range 1 to 25 percent, depending upon risk factors) of postmenopausal bleeding [3]. In postmenopausal bleeding, the endometrium is responsible for 50% of the causes. The findings were atrophic endometrium (16.3%), endometrial hyperplasia (13.4%), proliferative endometrium (8.6%), endometrial polyp (2.8%) and endometrial carcinoma (9.6%) [4]. Screening procedures available 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. The aim of the present study was to evaluate the various endometrial causes of postmenopausal bleeding, to correlate endometrial thickness by TVS with histopathology and to determine the diagnostic value of endometrial thickness by TVS in patients with post-menopausal bleeding with histopathological diagnosis taken as gold standard.

Materials and Methods:

The study was conducted in the Department of Obstetrics & Gynecology of Burdwan Medical College & Hospital, Burdwan for a period one year (January 2018 to December 2018). This was a Prospective study. The study was approved by the Institutional Ethical and Research review board. Informed consent was taken from all the participants under study. Total 100 patients presented with postmenopausal bleeding or spotting attending both outpatient and inpatient department who fulfilled inclusion criteria were included in the study considering convenience sampling technique. Postmenopausal women aged 40 years or more with amenorrhea of more than 12 months or more with vaginal bleeding were included in this study. Patients with vaginal infection, underwent hysterectomy, premalignant and malignant lesions of vulva, vagina and cervix, any other cervical and endocervical pathology, any bleeding disorders/ anticoagulant therapy/ medical disorders, adenexal masses, bleeding from urethral and anal orifice, age less than 40 years, patients on tamoxifen and hormonal therapy were excluded from the study. Detailed history was taken regarding age, parity, whether use of exogenous hormones or not and the presence of other gynecological problems if any. History of bleeding disorder, use of anticoagulants, diabetes, thyroid disorders and hypertension were also taken. All patients under study underwent general, systemic, per speculum and per vaginal examinations. Laboratory investigations including CBC, random blood sugar, coagulation profile, liver and kidney function tests were done. Selected patients were subjected to first transvaginal sonography (TVS) prior to the dilatation and curettage. A 7.5 MH transvaginal probe was used in our study. All the patients were asked to evacuate her bladder before examination. TVS examination was done in supine position. The transducer was introduced in the vagina after covering it with a sterile condom containing the acoustic gel. The length, anteroposterior and transverse dimensions of the uterus were measured also to note presence of any pathology like submucous fibroid. The endometrium was examined for thickness, echogenicity and

focal abnormality. Endometrial thickness (ET) was noted by the sum of measurements of both the anterior and posterior layers (double layer thickness) of the endometrium at the thickest segment on a midline longitudinal image. Theendometrium was considered hyperplastic when ET ≥5mm. Endometrium was considered atrophic when ET less than 5mm. The Uterine cavity was examined to note the presence of submucous fibroid, endometrial polyps or any fluid in the endometrial cavity. The endometrial cavity were considered normal if TVS showed a hyperechoic line in middle of the uterus with a homogenous endometrial lining with distinct margins. All other findings such as deformity of endometrial lining, absence or disturbed central hyperechoic line, any solid cystic appearance, any fibroid, growth or polyp with or without well-defined margins were considered abnormal. Endometrial cancer was suspected in presence of heterogenous endometrium with irregular interface between endometrium and myometrium with or without fluid collection. Dilatation and curettage was done in all these patients as an inpatient procedure under anesthesia in OT after TVS examination. Specimens were immediately put in 10% formalin, appropriately labeled and sent for histopathological examination and reporting in Pathology Department. Informed written consent was obtained from each of the patients for the procedure. The findings of TVS were compared with histopathological findings.

Statistical Analysis

Collected data were checked for completeness and consistency. Then the data were entered on Excel data sheets (Microsoft Excel, 2013). Data were analyzed using Statistical Package for Social Sciences (SPSS) [IBM SPSS Statistics for Windows, Version 20.0. (IBM Corp., Armonk, New York, USA)]. Chi-square test was applied as and when applicable basis considering p value <0.05 as statistically significant.

Results:

Total 100 women presented with postmenopausal bleeding fulfilled the inclusion criteria were included in our study. Majority (38%) of patients with PMB was in the age group of 46-50 years, 24% were in the age group of 51-55 years and only 4% were in 40-45 years. In our study most of the women (68%) had parity 1 to 3, 30% had more than 3 children. Nulliparity was observed in 2% of cases. Most of the study participants in our study (60%) presented with postmenopausal bleeding within 5 years of menopause, 25% between 5-9 years of menopause. 15% of patients presented with vaginal bleeding 10 years or more after menopause. Among the risk factors in PMB 18% of patients had diabetes mellitus. Hypertension was present in 15% of cases, obesity in 14% and hypothyroidism was found in 5% of cases. 48% of patients had no significant risk factors. [Table 1]

Table 1: Distribution of Study Participants According To Certain Characteristics (N=100)

Characteristics	Frequency	Percent
Age (Years):		
40-45	4	4.0
46-50	38	38.0
51-55	24	24.0
56-60	20	20.0
>60	14	14.0
Parity:		
Nullipara	2	2.0

1 To 3	68	68.0
>3	30	30.0
Duration Of Menopause (Years):		
< 5	60	60.0
5-9	25	25.0
≥ 10	15	15.0
Comorbid Conditions:		
Diabetes Mellitus(DM)	18	18.0
Hypertension	15	15.0
Obesity	14	14.0
Hypothyroidism	5	5.0
None Of The Above	48	48.0
Total	100	100.0

Majority (52%) of patients had endometrial thickness ≤5 mm. Again, 38 patients had ET between 6-10 mm. Only 10% patients had ET>10 mm. Atrophic endometrium (40%) was most common histopathological finding in our study. Both proliferative endometrium and endometrial hyperplasia without atypia were observed in 18% of cases. Endometrial polyp was found in 5 cases. Endometrial hyperplasia with atypia was observed in 8% of cases. We have reported endometrial carcinoma only in 2 cases in our study [Table 2].

Table 2: Distribution of study participants according to observations on TVS and histopathology (N=100)

Observations	Frequency	Percent
1.TVS Findings [Endometrial Thickness ET (In Mm)]:		
≤5	52	52.0
6-10	38	38.0
>10	10	10.0
2. Histopathology Findings:		
Proliferative Endometrium	18	18.0
Secretory Endometrium	5	5.0
Atrophic Endometrium	40	40.0
Endometritis	2	2.0
Disordered Proliferative Phase	2	2.0
Endometrial Polyp	5	5.0
Endometrial Hyperplasia Without Atypia	18	18.0
Endometrial Hyperplasia With Atypia	8	8.0
Endometrial Carcinoma	2	2.0
Total	100	100.0

In our study all cases of atrophic endometrium were found when endometrial thickness ≤5 mm. Again, 23 had normal endometrium when ET was between 5-10 mm. All cases of endometritis (2) were found when endometrial thickness ≤10 mm. Disordered proliferative phase was found when endometrial thickness was between 6-10 mm. 4 cases of endometrial polyp were noted with the endometrial thickness between 6-10 mm. 6 cases of endometrial hyperplasia without atypia and 5 cases of endometrial hyperplasia with atypia were observed at endometrial thickness >10 mm. All cases of endometrial carcinoma were detected when ET>10 mm. [Table 3]

Table 3: Endometrial thickness on TVS in relation to histopathology findings

Histopathology findings	Endometrial Thickness (Mm)			Total	P-Value*
	≤5	6-10	>10		
	No.	No.	No.		
Proliferative Endometrium	6	12	0	18	<0.001
Secretory Endometrium	2	3	0	5	
Atrophic Endometrium	40	0	0	40	
Endometritis	1	1	0	2	
Disordered Proliferative phase	0	2	0	2	
Endometrial Polyp	1	4	0	5	
Endometrial Hyperplasia Without Atypia	2	10	6	18	
Endometrial Hyperplasia with Atypia	0	3	5	8	
Endometrial Carcinoma	0	0	2	2	

Note: * Fisher's exact test

Table 4 shows transvaginal sonography with the good sensitivity, specificity and diagnostic accuracy of the normal (proliferative and secretory) and abnormal (endometrial polyp and endometrial hyperplasia) endometrium.

Table 4: Sensitivity, Specificity, PPV And NPV Of TVS

TVS	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
Proliferative Endometrium	15	79	3	3	83.3	96.3	83.3	96.3	94.0
Secretory Endometrium	3	92	3	2	60.0	96.8	50.0	97.9	95.0
Endometrial Polyp	4	94	1	1	80.0	98.9	80.0	98.9	98.0
Endometrial Hyperplasia	24	72	1	3	88.9	98.6	96.0	96.0	96.0

Note: TP- True Positive, TN- True Negative, FP- False Positive, FN- False Negative, PPV- Positive Predictive value and NPV- Negative Predictive Value

Discussion:

The present study was conducted with the aim of evaluating various endometrial

causes of postmenopausal bleeding also to correlate various causes of PMB with endometrial thickness. The study also determines the diagnostic value of endometrial thickness by transvaginal ultrasonography with endometrial histopathology which is gold standard. Total 100 women with postmenopausal bleeding who fulfilled the eligibility criteria were taken in our study. We have taken the detailed history of all the cases. Examination and necessary investigations were also performed. TVS was performed and then endometrial biopsy was taken in all the cases.TVS findings of endometrial thickness were correlated with histopathological report. In our study most of the patients (38%) with PMB were in the age group of 46-50 years, 24% were in the age group of 51-55 years and only 4% were in 40-45 years [Table 1]. In their study Verma R et al [5] found that incidence of PMB between the ages of 40-50 years was 45% with mean age as 50.34 years. Naik V et al [6] reported peak incidence for postmenopausal bleeding was 45-50 years and for malignancy 56-65 years. PMB was most commonly found in multiparous women in our study. Kothapally K et al [7] in their study showed 90% were multiparous women also study done by Nirupama V et al [8] where 90% were multiparous women presenting with postmenopausal bleeding. In our study majority (48%) of patients had no risk factors. Most common associated co-morbidities associated with PMB were Diabetes Mellitus (18%), Hypertension (15%), Obesity (14%) and Hypothyroidism (5%) [Table 1]. In their study Sousa R et al [9] reported most common associated risk factors were hypertension (36.2%) and diabetes (11.6%). In other study done by Kaul I et al [10] risk factors were hypertension (20%), Obesity (16%) and diabetes (12%). In this study majority (52%) of patients with PMB had endometrial thickness <5 mm. 38 patients had ET between 6-10 mm and only 10% patients had ET>10 mm [Table 2]. Atrophic endometrium (40%) was most common histopathological finding in our study. Both proliferative endometrium and endometrial hyperplasia without atypia were observed in 18% of cases. Endometrial polyp was found in 5 cases. Endometrial hyperplasia with atypia was observed in 8% of cases. We have reported endometrial carcinoma only in 2 cases [Table 2]. In their study Kaul I et al reported that normal postmenopausal atrophic endometrium was found in 21 (42%) cases. They also observed that hormonal effects were found in 5 cases (10%), endometrial hyperplasia was diagnosed in 9 cases (18%), a polyp was found in 4 cases (8%), endometritis in 2 cases (4%) and endometrial carcinoma was the histopathological report of 5 (10%) cases. Another study done by Sousa R et al [9] observed the following histopathology normal endometrium (7.2%), atrophy (34.8%), cystic atrophy (1.4%), tuberculous endometritis (1.4%), polyps (17.4%), leiomyoma (1.4%), non-atypical hyperplasia (4.3%), atypical hyperplasia (1.4%) and endometrial carcinoma (13.0%) in cases of postmenopausal bleeding. In their study Gao et al [11] also reported that most common cause of postmenopausal bleeding was atrophic endometrium (malignant lesions = 27%; benign lesions = 73%). Naik V et al [6] observed the following histopathological findings in their study: atrophic endometrium with senile cystic atrophy (16.3%), proliferative endometrium (8.6%), endometrial hyperplasia with or without atypia (13.46%), endometrial polyp (2.8 %) and endometrial adenocarcinoma (9.6%). In this study all cases of atrophic endometrium were found when endometrial thickness <= 5 mm. 23 had normal endometrium when ET was between 5-10 mm. All cases of endometritis (2) were found when endometrial thickness <=10 mm. Disordered proliferative phase was found when endometrial thickness was between 6-10 mm. 4 cases of endometrial polyp

were noted with the endometrial thickness between 6-10 mm. 6 cases of endometrial hyperplasia without atypia and 5 cases of endometrial hyperplasia with atypia were observed at endometrial thickness >10 mm. All cases of endometrial carcinoma were detected when ET>10 mm [Table 3]. In their study done by Kothapally K et al it was observed that women with a thick endometrium (endometrial thickness >4 mm) are at risk of developing endometrial carcinoma. Kadakola B et al [12] reported that 34% of the patients with PMB had atrophic endometrium with endometrial thickness <4mm and none had endometrial carcinoma, 14% of the patients with PMB had endometrial carcinoma when ET >4mm. Our study findings were also more or less correlated with study done by Karlsson B et al [13]. Present study showed high sensitivity, specificity, PPV and NPV of TVS [Table 4] which correlates well with the findings of Karlsson B et al[13] and Kaur et al [14] where the sensitivity of TVS was ranging from 89 to 100 % and specificity from 54.8 to 86 %. [15]

Conclusion:

Transvaginal ultrasonography is an important tool and should be used as first line investigation for evaluation of endometrial pathology in cases of postmenopausal bleeding. Transvaginal sonography is relatively cheap, easy, and noninvasive and needs no anesthesia. However, when endometrial thickness measured by TVS was<= 5 mm the risk for abnormal endometrial pathology could be reasonably ruled out. Bulky uterus on P/V examination and endometrial thickness >5mm with or without fluid collection in endometrial cavity on TVS should be further evaluated with endometrial sampling to rule out endometrial carcinoma. Measurement of endometrial thickness by TVS cannot be undermined for detecting patients at high risk especially with comorbid conditions like diabetes, hypertension and obesity. Histopathological diagnosis is gold standard and is mandatory for ruling out malignancy in selected cases of postmenopausal bleeding.

Limitation of the Study

The Present study was done with small sample size and over shorter duration of time in a single centre. TVS findings vary according to the operator's experience, modernization of the instruments and timing. Hysteroscopy is sensitive, more specific, and accurate in evaluation of postmenopausal bleeding particularly with risk factors for endometrial carcinoma and in cases with endometrial thickness greater than 5 mm irrespective of endometrial echotexture. Hysteroscopy along with its guided biopsy for evaluation of AUB was not included in our study due to limitations of resources. However if resources are available, hysteroscopy should be done in all women with postmenopausal bleeding with suspected endometrial pathology. Simultaneously it can also be used for therapeutic interventions if feasible. Follow up was also not included in our study.

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