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Original Research Article

A prospective study on postmenopausal bleeding-causes and its diagnosis using transvaginal ultrasound and hysteroscopy

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ABSTRACT

Background: Postmenopausal bleeding (PMB) is considered a red flag symptom and warrants further examination and evaluation. Trans-vaginalsonography (TVS) can be used reliably to diagnose fibroids, polyps and thickened endometrium. Hysteroscopy is considered "gold standard" for evaluating endometrial cavity. It provides direct visualization of endometrial cavity. It can have both diagnostic as well as operative purpose however, it is not cost effective, an invasive procedure and requires anesthesia and expertise. Present study was designed and carried out to study aetiology and prevalence of PMB in Central India as well as to evaluate the efficacy of TVS and hysteroscopy in diagnosis of different endometrial pathologies in patients with PMB.
Methods: This prospective study included 82 post-menopausal women with PMB who attended the gynaecological clinic from December, 2019 to December, 2020 at Motherhood hospital, Indore, India after ethical clearance. A detailed history, examination followed by transvaginal sonography was made. Hysteroscopy was then performed, and biopsy was obtained in all patients. Hysteroscopic and sonographic images were then analyzed and conformed with the histopathologic diagnosis.
Results: Most common endometrial pathology was atrophic endometrium followed by endometrial polyp and hyperplasia. Endometrial carcinoma was observed in (3.66%) females. Other findings in cases of secretory, proliferative endometrium and endometritis accounted for 6.09%. The diagnostic accuracy of ET by TVS at a cut-off point of 5 mm was 94% with sensitivity 89.3%, specificity 100%, PPV 100% and NPV 88%. The diagnostic accuracy of hysteroscopy was 98% with sensitivity 96.4%, specificity 100%, PPV 100% and NPV 95.7%.
Conclusions: TVS with ET measurement should first line investigation in the evaluation of women with PMB with suspected endometrial pathology because of cost effectiveness, easy accessibility and non-invasive method of diagnosis. Although hysteroscopy is more specific and sensitive, in poor resource settings it should be limited to cases with illdefined endometrial lining, recurrent/ persistent bleeding and cases with endometrial thickness greater than 5 mm irrespective of endometrial echotexture.

Keywords: PMB, Endometrial thickness, Transvaginal sonography, Hysteroscopy

INTRODUCTION

Menopause is the permanent cessation of menstruation that results from loss of ovarian follicular activity. Natural menopause is recognized after 12 consecutive months of amenorrhea. For which no other pathological or physiological cause is present.[1]

Bleeding which occurs from genital tract after 12 months of menopause is considered as PMB.[2] PMB is considered a red flag symptom and warrants further examination and evaluation.[1]

PMB is primarily caused by endometrial and vaginal atrophy. However, as approximately 15% of these women

will have some form of hyperplasia and 7-10% will have endometrial cancer. PMB suggests malignancy until proven otherwise.[3]

TVS can be used reliably to diagnose fibroids, polyps and thickened endometrium. Hysteroscopy is considered "gold standard" for evaluating endometrial cavity. It provides direct visualization of endometrial cavity. It can have both diagnostic as well as operative purpose however, it is not cost effective, an invasive procedure and requires anesthesia and expertise.[2,3] Hysteroscopic evaluation can be diagnostic for direct visualization of the uterine cavity as well as therapeutic like targeted endometrial biopsy, polypectomy etc.[4]

Present study was designed and carried out to aetiology and prevalence of PMB in central India as well as to evaluate efficacy of TVS and hysteroscopy in diagnosis of different endometrial pathologies in patients with PMB.

METHODS

This prospective study included 82 postmenopausal women with PMB who attended the gynaecological clinic from December, 2019 to December, 2020 at Motherhood hospital, Indore, India after ethical clearance. The exclusion criteria for women included in the study were women on hormonal replacement therapy and anticoagulant therapy. Patients with bleeding from sites other than the uterus such as the cervix and vagina and medical disorders such as blood dyscrasias, history of trauma, radiotherapy or surgical menopause were excluded from the study. Patients participating in the study were subjected to a thorough clinical examination and a detailed anamnesis. History included comorbidities, past illness, drug intake and surgeries, and obstetric and gynaecological abnormalities.These patients were subjected to TVS. A thorough pelvic examination was performed and endometrial thickness was measured in the longitudinal plane. Hysteroscopy was performed for both diagnoses and therapeutic procedure as well as for collection of guided biopsy. Hysteroscopic and sonographic images were then analyzed and compared with the histopathologic diagnosis.

Transvaginal sonography

TVS was done using ssonoscape-4000 ultrasound machine using TVS probe with frequency of 5-7.5MHz Endometrial thickness measured and abnormalities noted like, hyperplasia if thickness was >5mm, endometrial polyp, urine myoma, atrophy of endometrium and adnexal pathology. Endometrial malignancy was suspected when endometrium seen irregular with loss of sub endometrial halo and fluid collection in the endometrial cavity.

Hysteroscopy

Hysteroscopy was done using 5 mm hysteroscope with 30-degree telescope (KARL STORZ). Normal saline was used as distending medium. Uterine cavity was observed for features of polyps, atrophy, hyperplasia, myoma and malignancy. Directed biopsies were taken from the suspected areas, curettage done and whenever warranted resection of lesions done.

SPSS version 21 was used for statistical analysis.[5] Sensitivity, specificity and diagnostic accuracy were calculated for TVS and hysteroscopy individually, combined and in comparison, to histopathology.

RESULTS

Among 82 patients studied, mean age of the subjects was 54.85±5.25 years with max patients belonging between 56-65-year age group accounting for 63% (Table 1).

Table 1: Age-wise distribution of the study population, (n=82).

Age group (Years)	No. of patients, n (%)
50-55	13 (15.85)
56-60	42 (51.22)
61-65	21 (25.61)
>65	6 (7.32)

Mean age: 54.85±5.25 years

Among study group, 73 patients (89.02%) were multipara (Table 2).

Table 2: Distribution of the study population on basis of parity, (n=82).

Parity of the patient	No. of patients, n (%)
Nullipara	2 (2.44)
Para 1	7 (8.54)
Multipara	73 (89.02)

The study population comprised of 62 (75.61%) women with menopause of less than 8 years duration, 20 (24.39%) had menopause of more than 9 years of duration and only 2 (2.44%) women had menopause of more than 15 years of duration (Table 3).

Table 3: Distribution of study subjects according to duration of menopause, (n=82).

Years	N	Percentage (%)
1-4	37	45.12
5-8	25	30.49
9-12	18	21.95
>13	2	2.44

Based on HPE findings, atrophic endometrium was the most common pathology in 45 (54.87%) patients with PMB, followed by endometrial polyp in 18 (21.95%) and endometrial hyperplasia in 11 (31.41%). Endometrial cancer accounted for 3 (3.66%) cases and 5 (6.09%) had other findings like secretory/ proliferative endometrium or endometritis (Table 4).

Table 4: Distribution of study population on the basis of histo-pathological findings, (n=82).

HPE findings	N	Percentage (%)
Atrophic endometrium	45	54.87
Endometrial polyp	18	21.95
Endometrial Carcinoma	3	3.66
Endometrial hyperplasia	11	13.41
Others (secretory, proliferative, endometritis)	5	6.09

When the HPE results were compared with TVS and hysteroscopy, TVS had 100% sensitivity in diagnosing the atrophic endometrium, but the specificity was 67.5%. Sensitivity with hysteroscopy was also 100% for atrophic endometrium, however specificity was increased with hysteroscopy to 86.49%. For diagnosis of fibroid and polyp, TVS had sensitivity of 77.78% and specificity of 100% and with hysteroscopy both sensitivity and specificity were 100%. For endometrial malignancy, sensitivity and specificity were 66.67% and 100% by TVS, but with hysteroscopy sensitivity and specificity was 100%. For diagnosis of endometrial hyperplasia, TVS showed sensitivity of 81.82% and specificity 100% and hysteroscopy revealed 100%sensitivity and specificity (Table 5 and 6).

Based on endometrial thickness, TVS can detect polyps more accurately when the endometrial thickness (ET) is more than 8 mm. Hysteroscopy could visualize all the polyps directly, but maximum polyps were diagnosed at ET of more than 10 mm, 14 (77.77%) out of 18 cases of endometrial polyp/ fibroid.

Maximum cases of endometrial hyperplasia were observed in younger age group. All the 11(13.41%) patients were less than 60 years of age group. Atrophic endometrium was seen more commonly in 56 and above age group accounting for 33 (73.33%). Polyps were also common in younger age group, especially in less than 58 years of age.

Endometrial malignancy was observed in older age group, 1 patient was 63 years old and 2 were more than 70 years old among the 3 diagnosed cases (Table 7).

Table 5: Distribution of endometrial pathologies based on TVS and hysteroscopy findings in patients of PMB.

Visual findings	TVS	Hysteroscopy	HPE
Atrophic endometrium	57	50	45
Endometrial polyp/ fibroid	14	18	18
Endometrial malignancy	2	3	3
Endometrial hyperplasia	9	11	11
Others (secretory, proliferative, endometritis)	0	0	5

Table 6: Comparison of TVS and hysteroscopy with histopathological finding.

Visual findings	TVS	Hysteroscopy	HPE	TVS Vs HPE		HYS vs HPE	
				Sensitivity	Specificity	Sensitivity	Specificity
Atrophic endometrium	57	50	45	95	67.57	100	86.49
Endometrial polyp/ fibroid	14	18	18	77.78	100	100	100
Endometrial malignancy	2	3	3	66.67	100	100	100
Endometrial hyperplasia	9	11	11	81.82	100	100	100
Others (secretory, proliferative, endometritis)	0	0	5	0	100	0	100

Table 7: Relation of age with endometrial lesions, (n=82).

Endometrial histopathology	Age (45-55 years)	Age (56-65 years)	Age (65-75 years)	Total
Hyperplasia (Simple and complex)	8	3	0	11
Atrophic endometrium	12	23	10	45
Polyp	10	8	0	18
Proliferative endometrium	1	0	0	1
Secretory endometrium	1	0	0	1
Endometritis	0	3	0	3
Endometrial adenocarcinoma		1	2	3
Total	32	38	12	82

DISCUSSION

Present study was conducted in 82 patients who presented with post-menopausal bleeding, to evaluate the various endometrial causes for post-menopausal bleeding and to assess the diagnostic accuracy with the use of TVS and hysteroscopy to assess different pathologies which were confirmed by histopathological examination as gold standard.

Among 82 patients studied, mean age of the subjects was 54.85±5.25 years with maximum patients belonging between 56-65-year age group accounting for 63%. The mean age in the study by Sousa et al 62.1 years, whereas Yela et al, Kaul et al and Bhangale et al reported the mean age as 61.9, 54.4 and 52.32 years, respectively.[6-9]

Study conducted by Verma et al reported the incidence of PMB between the ages of 40-50 years (45%) with mean age as 50.34 years.[10] Highest incidence found by Naik et al was between age group 45-50 years for PMB and 56-65 years for malignancy.[11] Sengupta et al found maximum number of PMB cases in the age group of 50-59 years accounting for 80% of the cases.[12]

Most of the cases in the present study were multiparous accounting for 73% followed by nullipara and primipara. Bhangale et al also reported most (90%) cases between para 1 to para 4 and only one female (2%) as nulliparous.[9] In a study by Yela et al only (5%) females were nullipara.[7] In a study by Kaul et al (4%) females were nulliparous while (6%) were para >6.13.[8] Sengupta and Verma et al also showed similar distribution.[10,12]

Most common endometrial pathology observed in the present study was atrophic endometrium followed by endometrial polyp and hyperplasia. Endometrial carcinoma was observed in (3.66%) females. Other findings in cases of secretory, proliferative endometrium and endometritis accounted for 6.09%. Study by Kaul et al revealed normal postmenopausal atrophic endometrium in 21 (42%), hormonal effects in 5 (10%), endometrial hyperplasia in 9 (18%), polyp in 4 (8%), endometritis in 2 (4%) and endometrial carcinoma in 5 (10%) cases.[8] Sousa et al in their study observed following pathologies in cases of PMB: 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%).[6] Gao et al also observed that most common cause of PMB was atrophic endometrium (malignant lesions=27%; benign lesions=73%).[13] Naik et al observed atrophic endometrium with senile cystic atrophy (16.3%), proliferative endometrium (8.6%), endometrial hyperplasia with or without atypia (13.46%), endometrial polyp (2.8 %), endometrial adenocarcinoma (9.6%).[11] In present study, higher number of patients (17 cases) showed endometrial thickness between 5-6 mm followed by >7 mm and up to 4 mm in 9 and 6 cases, respectively. The diagnostic accuracy of endometrial thickness was relatively higher by TVS in comparison to hysteroscopy. Kaul et al observed that at a cut-off limit of >5 mm for endometrial thickness indicating pathologic endometrium, the sensitivity and specificity of TVS was 100% and 80% respectively and a predictive value as a positive test, as a negative test and accuracy was 76.9%, 100% and 89% respectively.[8] Ahmed et al observed that by using 5 mm endometrial thickness as cut off value for atrophic endometrium, TVS had 85% sensitivity, 96.7% specificity and accuracy of 92% in cases of PMB.[14] Karlson et al in a similar study observed that at endometrial thickness of 4 mm or more the sensitivity and specificity of TVS to diagnose endometrial abnormality were 100% and 75% respectively.[15] On hysteroscopy, atrophic endometrium was seen in (46%) cases while abnormal thickened endometrium was seen in (36%) cases. Other specific lesions like endometrial polyps and leiomyomas were seen in (18%) cases. The diagnostic accuracy of hysteroscopy for cases of PMB was 98% with sensitivity and specificity of 96.4% and 100% and positive predictive value and negative predictive value of 100% and 95.7% respectively. In the study by Sousa et al for the assessment of endometrial pathology as a whole, transvaginal sonography revealed sensitivity 79.5%, specificity 88%, positive predictive value 92.1%, negative predictive value 71%; and hysteroscopy revealed sensitivity 97.7%, specificity 92%, positive predictive value 95.5%, negative predictive value 95.8%.[6,11] In a study, Yela et al observed that, ultrasound showed high sensitivity and low specificity, with diagnostic accuracy of 53.7%, whereas hysteroscopy showed high sensitivity and specificity, with accuracy of 88.7%.[7] In a study by Mathlouthi et al the sensitivity, the specificity, the positive and negative predictive values of the transvaginal ultrasonography was respectively 93.75%, 87.5%, 83.3% and 95.45%.[16] Further, hysteroscopy seems to be more effective in the diagnosis of intrauterine abnormalities with the respective values of 100%, 95.83%, 94.11% and 100%.

Study conducted by Bhangale et al revealed that most common endometrial cause of PMB was atrophic endometrium (44%).[9] The other causes were endometrial carcinoma (18%), endometrial hyperplasia (18%), endometrial polyp (12%), endometritis (4%), and leiomyoma (4%). The diagnostic accuracy of ET by TVS at a cut-off point of 5 mm was 94% with sensitivity 89.3%, specificity 100%, PPV 100% and NPV 88%. The diagnostic accuracy of hysteroscopy was 98% with sensitivity 96.4%, specificity 100%, PPV 100% and NPV 95.7%.

The findings of the present study concluded that both TVS and hysteroscopy could be considered as useful investigations for evaluation of endometrial pathology in cases of PMB. However, hysteroscopy showed higher sensitivity, specificity and accuracy in comparison to TVS. TVS is relatively cost effective, easy, non-invasive and needs no anesthesia, hence should be considered as first line investigation in the evaluation of patients with PMB

with suspected endometrial pathology. Though hysteroscopy is more specific and sensitive, but in poor resource settings this method should be limited to cases with ill-defined endometrial lining, recurrent/ persistent bleeding, risk factors for endometrial carcinoma and cases with endometrial thickness greater than 5 mm irrespective of endometrial echo texture. This study was conducted in hospital-based setup with relatively small sample size, hence extrapolation of the results of this study cannot be considered for larger population. Inter observer variation are possible during transvaginal ultrasonography and hysteroscopic evaluation. Considering the above facts, further study is proposed encompassing larger population size and involving multiple parameters for precision of various techniques at tertiary healthcare centre to overcome the limitations.

CONCLUSION

This study highlighted the importance of transvaginal ultrasonography for evaluation of endometrial pathology in cases of PMB. Transvaginal ultrasonography is relatively effective, easy, non-invasive and needs no anesthesia and hence should be considered as first line investigation in the evaluation of women with PMB with suspected endometrial pathology. Although hysteroscopy is more specific, sensitive and accurate, in poor resource settings it should be limited to cases with ill-defined endometrial lining, recurrent/ persistent bleeding, risk factors for endometrial carcinoma and cases with endometrial thickness greater than 5 mm irrespective of endometrial echotexture. Hysteroscopy should be employed in patients with PMB with suspected endometrial pathology.

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