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Research Article

Comparison of Transvaginal Ultrasonography and Hysteroscopy for Evaluation of Postmenopausal Bleeding: A Cross Sectional Study

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ABSTRACT

Aim: To compare the sensitivity and specificity of transvaginal ultrasonography (TVS) and hysteroscopy with endometrial biopsy in patients of postmenopausal bleeding.

Methods: A hospital-based cross-sectional study was performed among 40 postmenopausal women with a history of amenorrhea for more than one year. The enrolled patients underwent TVS and hysteroscopy along with hysteroscopy-guided endometrial biopsy. Histopathological findings were considered as definitive diagnosis; which was compared with presumptive diagnosis of TVS and hysteroscopic findings. Data entry and statistical analysis were performed using SPSS v21.

Results: The mean age of the patients was 55.1 ± 6.5 years. Among the 40 patients, 22 (55%) had normal endometrial thickness (< 4 mm). The two most common causes of postmenopausal bleeding were found to be atrophic endometrium (37.5%) and endometrial hyperplasia (37.5%). The sensitivity and specificity of TVS in diagnosis of atrophic endometrium were found to be 66.7% and 64% respectively. Additionally, the sensitivity and specificity in endometrial hyperplasia were 60% and 76% respectively, and the sensitivity in sub-mucosal fibroid was 100%. Similarly, the sensitivity of hysteroscopy in diagnosis of atrophic endometrium, endometrial polyp, endometrial hyperplasia, sub-mucosal fibroid and endometrial carcinoma was 66.7%, 100%, 66.7%, 50% and 33.3% respectively. No any cases of endometrial carcinoma were detected in TVS, though three patients (7.5%) were biopsy proven cases of endometrial carcinoma.

Conclusion: Atrophic endometrium and endometrial hyperplasia are the two most common causes of postmenopausal bleeding. TVS and hysteroscopy may be used as effective tools for evaluation of postmenopausal bleeding, however; further larger scale study is required to confirm this finding.

Keywords

postmenopausal bleeding; transvaginal ultrasonography; TVS; hysteroscopy

Introduction

The incidence of post-menopausal bleeding (PMB) is 10% and accounts for 5 % of referral [1]. PMB can either be due to genital (benign/malignant) or extra-genital causes (urethral caruncle, bladder and rectal cancer). The common benign genital causes of PMB include atrophic vaginitis, endometrial and cervical polyps, endometrial hyperplasia, pyometra and submucous fibroids and overal the most common cause is atrophic vaginitis [2]. Endometrial, cervical, ovarian, vaginal and vulval cancers are the common malignant genital causes of PMB [2]. Overall, the most common cause of PMB is atrophic vaginitis [3]. However, all the patients with PMB should be evaluated for endometrial carcinoma, as it accounts for 10% of the cases (range 1 to 25%, depending upon risk factors) and is potentially lethal [4].

Uterine curettage is investigation of choice for PMB [5]. However, it is a blind procedure and often results in unrepresentative biopsies (false negative rates 2-10%) as in approximately 60% of the curettage procedures, less than half of the uterine cavity is curetted [6]. Transvaginal ultrasonography (TVS) is a non-invasive method that could predict endometrial lesions accurately. Diagnostic hysteroscopy allows direct visualization and biopsy of diffuse or focal abnormalities of the endometrium and is well-tolerated, accurate, and sensitive outpatient procedure [7]. In this study, we aimed to determine the diagnostic accuracy of TVS and hysteroscopy for the diagnosis of endometrial pathology in patients with PM.

Materials and methods

This was a single center, descriptive, cross-sectional study conducted at B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan, Nepal over a period of 12 months from 27th November 2018 to 26th October 2019. BPKIHS is a tertiary care hospital located in the Eastern part of Nepal.

Patients attending outpatient and emergency department of Obstetrics and Gynecology were recruited for the study by a method of non-probability. All the patients with PMB at least one year of amenorrhea were included. They were excluded if were under hormonal replacement therapy (HRT) or anticoagulation therapy, had prior history of bleeding dyscrasias. Patients with obvious cause of bleeding from cervix/vagina, bleeding secondary to adnexal pathology and surgical menopause were also excluded. Ethical clearance was obtained from Institutional Review Committee (IRC) of BPKIHS. A prior written informed consent was gained from the patients after explaining the nature and purpose of study.

Sample size:

Sample size was calculated based on sensitivity (97.5%) of hysteroscopy to diagnose atrophic endometrium. [8]

$n=z^2pq/L^2$

where,

n= sample size

z= variate= 1.96

p= sensitivity of hysteroscopy=97.5% [9]

q= 100 – p= 100- 97.5 = 2.5%

L= allowable error = 5% of p = 5% of 97.5% = 4.87%

By applying above formula, the sample size was estimated to be 40.

Transvaginal Sonography:

For all the enrolled patients, TVS [machine name] was performed by an expert radiologist or ultrasonologist with a transvaginal transducer of frequency C8-V4 either on the same day or prior to hysteroscopy.

Endometrial thickness (ET) was calculated as the maximal distance between the two myometrial interfaces in a longitudinal scan. A cut off value of <4 mm was taken to classify as normal or abnormal ET [10].

Other significant findings in TVS was noted like echogenicity of endometrium, uterine size, uterine cavity, cervical canal, myometrium, any uterine growth/polyp, any fluid in endometrial cavity and bilateral adnexa. The endometrium and uterine cavity were considered normal if transvaginal sonography 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 ..Endometrial cancer was suspected in presence of heterogenous endometrium with irregular interface between endometrium and myometrium with or without fluid collection. In invasive uterine cancer, sub endometrial halo is lost[11]. The intrauterine cavity was seen for any intracavitary collection.

Hysteroscopy was performed for all enrolled patient irrespective of TVS finding by vaginoscopy method using a 5-mm sheath rigid hysteroscope with a 0-degree optic lens and with normal saline solution 0.9% as distention media at 100 mm Hg pressure bag and viewed on high resolution color monitor.

At the end of hysteroscopy, endometrial eye-directed biopsy of focal areas of pathologic endometrium was performed with a 5-Fr punch biopsy forceps and sent for histological assessment. Four biopsy specimens of an appropriate amount of tissue for the histologic examination was obtained from the uterine walls, if no visible areas of pathologic endometrium were seen. Therapeutic intervention was done in same setting for benign pathology like polyp.

Histopathological examinations:

Endometrial samples were analyzed at the Department of Pathology of our hospital. The specimen for histopathological examination preserved in 10% formalin was processed with hematoxylin and eosin staining and visualized under microscope.

Five histologic categories were defined: atrophic endometrium, endometrial polyp, submucous myoma, endometrial hyperplasia, and endometrial carcinoma.

After completing the protocol examinations, women underwent medical or surgical therapy if necessary.

DATA MANAGEMENT AND STATISTICAL ANALYSIS

Statistical methods proposed:

The excel data was converted it into Statistical package for Social Science (SPSS, version 11.5) for statistical analysis. Percentage distribution of subjects with post-menopausal bleeding with different endometrial abnormalities in TVS, hysteroscopy and histopathological examinations was tabulated. Descriptive statistics was calculated (mean, standard deviation, % and proportion) and different graphs for exploring characteristics of variables was constructed. Histologic diagnoses were considered definitive and compared with the ultrasonographic and hysteroscopic findings. Sensitivity (TP [true positive]/TP+FN [false negative]), specificity (TN [true negative]/TN+FP [false positive]), positive predictive value (TP/TP+FP) and negative predictive value (TN/TN+FN) were calculated.

Result

Demography

The mean ±SD age of enrolled participants was 55.1±6.5 years. Among them most of the participants developed postmenopausal bleeding in 51-55 years of age. The mean ±SD duration of postmenopausal bleeding of the participants was 5.82±7.18 weeks and 35% of participants had postmenopausal bleeding for less than two weeks and 65% of participants had postmenopausal bleeding for more than two weeks.

Transvaginal sonography

Out of 40 participants, 22 (55%) had normal endometrial thickness (< 4mm), 14 had endometrial thickness between 4 to 12 mm, and 4 had endometrial thickness >12 mm. The mean endometrial thickness was 6.17±3.92 mm. On TVS, the most common cause of PMB was found to be atrophic endometrium (n= 18; 45%). [Figure…1]. No cases of suspicious malignant growth detected on TVS.

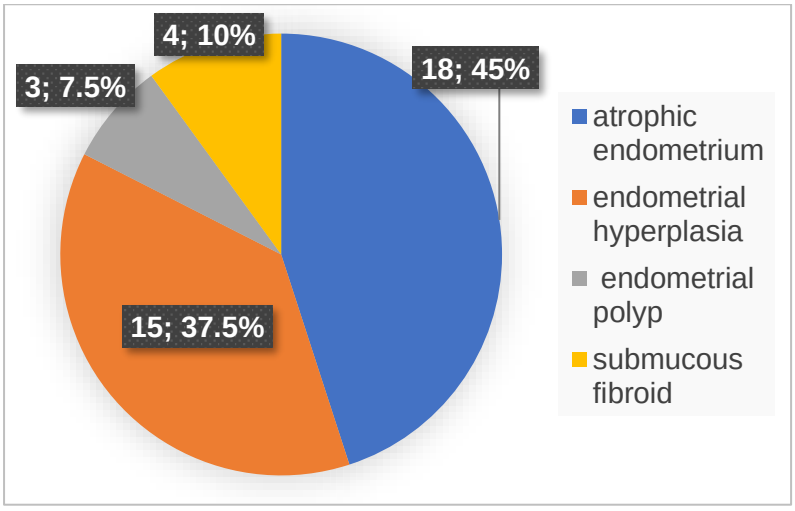

Figure 1: TVS finding in postmenopausal bleeding

Out of 17 patients of endometrial hyperplasia, 11 (64.7%) had abnormal ET (i.e., > 4 mm) [Figure…1.].

Table 1: Correlation between hysteroscopic finding and endometrial thickness

		TVS finding		Total
		Abnormal ET>4mm	**Normal ET<4mm**	
Hysteroscopic finding	Atrophic endometrium	3 (23.1%)	10(76.9%)	13(100%)
	Endometrial hyperplasia	11(64.7%)	6(35.3%)	17(100%)
	Endometrial polyp	3(37.5%)	5(62.5%)	8(100%)
	Submucous fibroid	0 (0%)	1(100%)	1(100%)
	Suspicious malignant growth	1(100%)	0(0%)	1(100%)

Hysteroscopy

In the hysteroscopic finding of participants, majority (n=17; 42.5%) of had endometrial hyperplasia [Figure…2.].

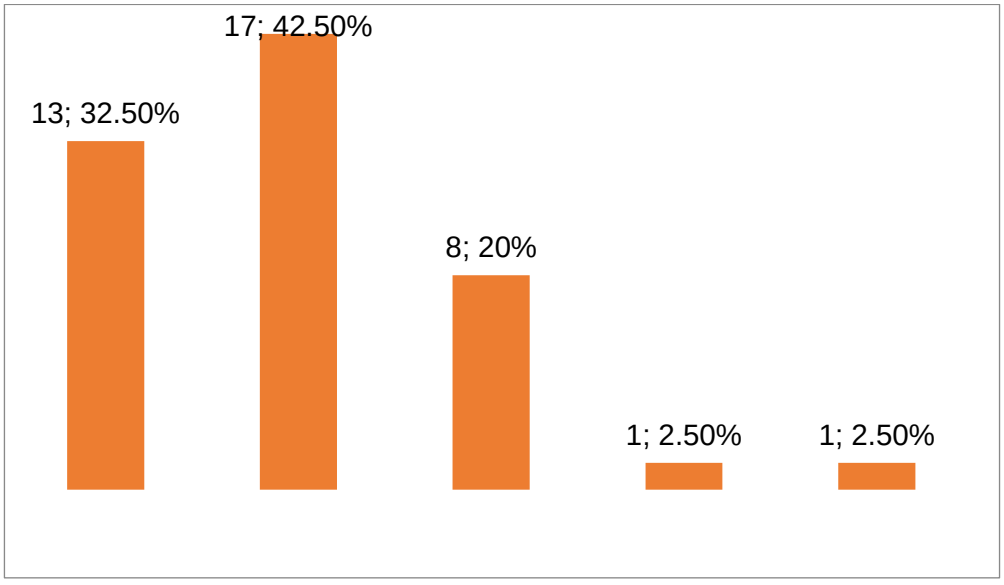

Figure2: Hysteroscopic finding among participants (n=40)

Histopathology evaluation

Equal proportion (37.5%) of atrophic endometrium and endometrial hyperplasia was confirmed histologically among postmenopausal women.

Table 2: Histopathology finding of participants

Characteristics	Categories	Frequency	Percentage
Histopathology evaluation	Atrophic endometrial	15	37.5%
	Endometrial hyperplasia	15	37.5%
	Endometrial polyp	5	12.5%
	Carcinoma endomerium	3	7.5%
	Submucous fibroid	2	5.0%
Total		40	100%

Correlation between histopathology and endometrial thickness

Most of the cases with atrophic endometrium (73.3 %) was found normal (endometrial thickness) by transvaginal sonography.

Table 3: Correlation between histop athological finding and endometrial thickness

		TVS finding		Total
		Abnormal ET>4mm	Normal ET<4mm	
Histopathological finding	Atrophic endometrium	4(26.7%)	11 73.3%	15(100%)
	Endometrial hyperplasia	10(66.7%)	5(33.3%)	15(100%)
	Endometrial polyp	1(20%)	4(80%)	5(100%)
	Submucous fibroid	0(0%)	2(100%)	2(100%)
	Carcinoma of endometrium	3(100%)	0(0%)	3(100%)

Sensitivity and specificity of TVS and hysteroscopy

In our study, the sensitivity and specificity of TVS in diagnosing atrophic endometrium was 66.7% and 64% respectively whereas sensitivity and specificity of TVS in diagnosing in endometrial hyperplasia was 60% and 76% respectively. The sensitivity of TVS in diagnosing of submucous fibroid was 100%. Similarly, the

sensitivity of hysteroscopy in diagnosing of atrophic endometrium and endometrial hyperplasia was 66.7% and sensitivity of hysteroscopy for diagnosing of endometrial polyp, sub mucous fibroid and carcinoma of endometrium was 100%, 50% and 33.3% respectively (Table 7).

Table 4: Sensitivity and specificity of TVS and hysteroscopy for diagnosing endometrial pathologies casing PMB

Diagnosis	TVS		Hysteroscopy	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Atrophic endometrium	66.7	64.0	66.7	88.0
Endometrial hyperplasia	60.0	76.0	66.7	72.0
Endometrial polyp	20	94.3	100.0	91.4
Submucous fibroid	100	94.7	50.0	100.0
Suspicious malignant growth	-	100	33.3	100.0

TVS has maximum positive predictive value (PPV) of 60% for endometrial hyperplasia and maximum negative predictive value (NPV) of 89.2% for endometrial polyp whereas PPV and NPV was least for carcinoma endometrium. Hysteroscopy has maximum PPV of100% submucous fibroid and carcinoma endometrium whereas it was least for endometrial hyperplasia (58.82%). Similarly, NPV was maximum (100%) for endometrial polyp and least for atrophic endometrium (81.48%).

Table 5:PPV and NPV of hysteroscopy and transvaginal sonography for diagnosing endometrial pathoogies

Diagnosis	TVS		Hysteroscopy	
	PPV (%)	NPV (%)	PPV (%)	NPV (%)
Atrophic endometrium	52.63	31.25	76.92	81.48
Endometrial hyperplasia	60.0	76.0	58.82	78.26
Endometrial polyp	33.3	89.2	62.5	100
Submucous fibroid	50	100	100	97.43

Suspicious malignant growth	8.1	-	100	94.87

Correlation between age of attaining menopause and carcinoma of endometrium

Two out of 11 (i.e., 18.2%) women of more than 55 years of age were subsequently found to have been suffering from endometrial carcinoma and one out of 15 (i.e., 6.7%) woman of 50-55 years of age found to have endometrial carcinoma. (Table 6)

Table 6: Correlation between age of attaining menopause and carcinoma of endometrium

Age of attaining menopause(years)	No. of women with PMB	No. of cases detected with carcinoma of endometrium on histopathology report (HPR)
<45years	2	0
45-50years	12	0
50-55years	15	1(6.7%)
>55years	11	2(18.2%)

Discussion

This comparative cross-sectional study was designed for evaluation of postmenopausal bleeding by two different methods: TVS and hysteroscopy with reference to histopathological examinations.

The mean±SD age of enrolled participants was 55.1± 6.5 years. In our study sensitivity of TVS for atrophic endometrium, endometrial hyperplasia, endometrial polyp, submucous fibroid and suspicious malignant lesion were 66.7%,60%,20%,100% and 0% respectively. In a similar study conducted by Sunita tandulwadkar, et al. [8], sensitivity of TVS for detecting atrophic endometrium, endometrial hyperplasia, endometrial polyp,submucous fibroid and carcinoma endometrium were 87.5%,75%,71%,100%,and 100% respectively [Table…4.]. Similarly, sensitivity of hysteroscopy for atrophic endometrium,endometrial hyperplasia,endometrial polyp,submucous fibroid and endometrial carcinoma were 66.7%,66.7%,100%,50%,33% respectively in our study whereas in the study done by Sunita tandulwadkar,it was found to be 97%,100%,100%,100%and 87% [Table 7]. Most common cause of PMB in the study done by Sunita tandulwadkar et al was atrophic endometrium (40%), this is in contrast to our study; where we found that atrophic endometrium and endometrial hyperplasia was equally account for postmenopausal bleeding (37.5%) [12].

Table: 7

Variables	Sunita et al	Present study
Commonest cause	Atrophic endometrium	Atrophic endometrium and endometrial hyperplasia
TVS		
Atrophic endometrium	87.5%	66.7%
Endometrial hyperplasia	75%	60%
Endometrial polyp	71%	20%
Submucous fibroid	100%	100 %
Endometrial carcinoma	100%	0%
Hysteroscopy		
Atrophic endometrium	97%	66.7%
Endometrial hyperplasia	100%	66.7%
Endometrial polyp	100%	100%
Submucous fibroid	100%	50%
Endometrial carcinoma	87%	33%

In our study, the detection of endometrial polyp by transvaginal sonography was 20% and by hysteroscopy was 100%; which is in contrast to study of Cepni et al. (24% by TVS and 70% by hysteroscopy) [13]

In our study, hysteroscopy had sensitivity of 66.7% and specificity of 72% for endometrial hyperplasia; whereas it was 56% and 89% respectively in study done by Lasmar et al [14]. Similarly, in our study we discovered that sensitivity and specificity of hysteroscopy in diagnosing endometrial carcinoma were 100 % and 33% respectively, in contrast to study of Lamsar et al., who found that the sensitivity and specificity were 80 % and 99 % respectively [14].

According to our study, the most common cause of PMB were endometrial hyperplasia and atrophic endometrium (table 2) whereas; in the study done by sheeba Rani ,it was found to be oestrogen administration as most common cause(12.5)% followed by atrophic endometrium (11.9)%[15]. The prevalence of endometrial carcinoma was 7.5% in our study contrast to 0.6 % the study by Litta et al [16]. Finding of abnormally high prevalence of endometrial carcinoma could have occurred by a chance due to smaller sample size. A further large-scale study is required for the interpretation.

Variables	Puspa et al	Present study
Mean age	45-50 years	51-55years

ET<4mm	40%of cases	55%of cases
HPE-		
Atrophic endometrium	38.3%	37.5%
Endometrial hyperplasia	23.3%	37.5%
Hysteroscopy		
Endometrial hyperplasia	30%	42%
Endometrial polyp	10%	20%
Malignant growth	11.6%	2.5%

Conclusion

Atrophic endometrium and endometrial hyperplasia are two main causes of PMB with equal prevalence. TVS and hysteroscopy are equally sensitive for diagnosing atrophic endometrium however, specificity was more for hysteroscopy. Hysteroscopy was found to be highly sensitive for diagnosing endometrial polyp. TVS had highest sensitivity for submucous fibroid. This is to conclude both hysteroscopy and TVS are helpful tool in evaluation of PMB. We recommend a further large-scale multicenter study to be done for diagnosing PMB before taking our finding for interpretation.

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