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Comparison of evaluation of postmenopausal bleeding between transvaginal sonography, hysteroscopy and histopathology

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Abstract
Transvaginal sonography and hysteroscopy were compared with the histopathological results of the biopsies in 100 women with postmenopausal bleeding in Thanjavur medical college. They underwent transvaginal ultrasound and hysteroscopy. Hysteroscopy directed biopsy was taken. TVS and hysteroscopy was compared with histopathology. Women of all parity were included. Most women were 1-5years post-menopausal. 23% women had associated co morbid illness in the form of 10% obesity, 8% hypertension, 5% diabetes mellitus. When endometrial thickness of > 4mm was taken to define endometrial abnormality sensitivity of 86.36%, specificity 42.30%, positive predictive value 29.68 %, negative predictive value 91.66% was obtained. When accuracy of Hysteroscope was compared with HPE sensitivity 90.90%, specificity 91.02%, PPV 74.07%, NPV 97.26%. Both transvaginal ultrasound and hysteroscopy can be used to evaluate post-menopausal bleeding. Hysteroscopy correlates more with histopathology when compared with transvaginal ultrasound. Hysteroscopy is superior and has higher efficacy in diagnosing endometrial abnormality in women with post-menopausal bleeding.

Keywords: Postmenopausal bleeding, TVS, hysteroscopy, histopathology, endometrial biopsy

Introduction
Menopause is that point when permanent cessation of menstruation occurs following loss of ovarian activities [1]. Any bleeding after 1 year of amenorrhea, after the age of 40years is post-menopausal bleeding. Bleeding even after 6 months of cessation of menstruation, or regular menstruation after the age of 52 years needs evaluation [2]. All post-menopausal bleeding should be considered as genital tract malignancy until proven otherwise. Post-menopausal bleeding occurs in approximately 3% of post-menopausal women [3]. On the other hand 10% of women with postmenopausal bleeding will have endometrial cancer [4].
Indian incidence of endometrial carcinoma is 5-7% of all genital cancers [2]. Endometrial carcinoma when detected earlier can be cured completely. Five year survival rate of stage 1 and 2 endometrial carcinoma is 87% and 76% respectively [4]. Transvaginal ultrasound is a non-invasive tool for evaluation of post-menopausal bleeding [5]. Then the less invasive endometrial biopsy with vacuum suction devices such as vabra aspirator (1970), and pipelle aspirator [8] was introduced. The first step in evaluation of postmenopausal bleeding can be either transvaginal ultrasound (TVS) or endometrial biopsy (EMB) [6].
Hysteroscopy allows direct visualization of the endometrial pathology and biopsy of suspected lesions, hence hysteroscopy is gold standard in evaluation of post-menopausal bleeding [2].
This study compares transvaginal ultrasound and hysteroscopy in evaluation of postmenopausal bleeding.

Materials and Methods
100 women who attended outpatient clinic in Rajamirasudhar Hospital, Thanjavur Medical College in Thanjavur between October 2009 - October 2011 were included in the study were selected according to the inclusion and exclusion criteria. They underwent transvaginal ultrasound and hysteroscopy. Hysteroscopy directed biopsy was taken. TVS and hysteroscopy was compared with histopathology.

Inclusion criteria

1. Women experiencing vaginal bleeding after 1 year of amenorrhea (Post-Menopausal Bleeding).

Exclusion criteria

1. Cancer cervix.
2. Women with demonstrable pelvic pathology.
3. Women with blood Dyscrasis.
4. Women on hormone replacement therapy.
5. Premature menopause.

Through history was elicited, clinical examination done. Informed written consent was obtained, transvaginal ultrasound was done. Anesthetic fitness obtained and patients underwent hysteroscopy and directed biopsy. Patients were asked to empty the bladder and lie in supine position. Transvaginal ultrasound with transducer of 6 MHz was used. Both sagittal and coronal view scanned with emphasis on endometrium. Endometrial echotexture, margins and thickness were noted. The thickness of the endometrium was measured in the sagittal plane. Anteroposterior measurement taken at the thickest portion from one to the other myo-endometrial junction. If there is fluid in the endometrial cavity, layers are measured separately and summed. Small amount of fluid is not pathological in post-menopausal women. Other morphological changes were looked for, such as regularity of the margins, focal or diffuse thickening and presence of sub endometrial halo.

Diagnosis was made as follows

Atrophic: When the endometrium is homogenous and thin, endometrial thickness less than or equal to 4mm.

Thickened: When the margins are regular with thickness <10mm and >4 mm. Endometrium was homogenous.

Polyp: Focal endometrial thickening with regular margins.

Hyperplasia: Uniform diffuse thickening with thickness >10mm

Carcinoma: Thick heterogenous endometrium, irregular myo-endometrial junction with absence of sub endometrial halo.

Under short general anesthesia, Hysteroscopy of 2.9 mm was introduced into the cervical canal under vision. Normal saline was the distension medium. Drip set was attached to the normal saline and connected to the flow channel of the hysteroscope. The inflatable cuff surrounding the distension medium was inflated to 100mmHg, and maintained between 80-100mm Hg. Endocervical canal, endometrial cavity and endometrial surface inspected systematically. Endometrial surface, colour, vascularity, glandular pores, and tubal Ostia were noted. Hysteroscopic biopsy was taken in all patients at the end. If there was suspicious areas, biopsy was taken from that area.

Diagnosis by hysteroscopy was made on the following basis

1. **Atrophic:** Endometrium surface is pale, smooth, flat. Glandular opening and superficial vessels absent. Deep stromal vessels can be seen. Tubal Ostia are obliterated.
2. **Proliferative:** Endometrium surface looks smooth, pink relatively thick. Pores of endometrial glands seen with regularity. Superficial vascularisation is relatively poor, tubal Ostia normal.
3. **Secretory:** Smooth surface, velvety and red in appearance. Endometrium appears very thick. Superficial vessels appears in net like geometrical pattern. Gland opening seen, tubal Ostia seen.
4. **Polyp:** Smooth surface, pink or white in colour. Appears as uniform projection from the endometrium. Gland opening is seen. Vascularisation is normal. Tubal Ostia is visible.
5. **Simple hyperplasia:** Rough surface, color is pink, yellow or white. Height of the endometrium is very thick. Gland opening is seen. Rich superficial vascularisation in network like appearance is seen. Glandular orifice is seen. Tubal Ostium is normal.
6. **Complex hyperplasia:** Rough surface, color is pink, yellow or white. Height of the endometrium is uneven and very thick. Rich superficial vascularisation is seen with no specific pattern. Glandular orifice is seen but not well delineated. Tubal Ostium is normal.
7. **Endometrial carcinoma:** Rough surface, papillary appearance with irregular polylobulated excrescence. Partially necrotic and hemorrhagic. Vascularisation is irregular. Often clear demarcation can be seen between normal and cancerous endometrium.

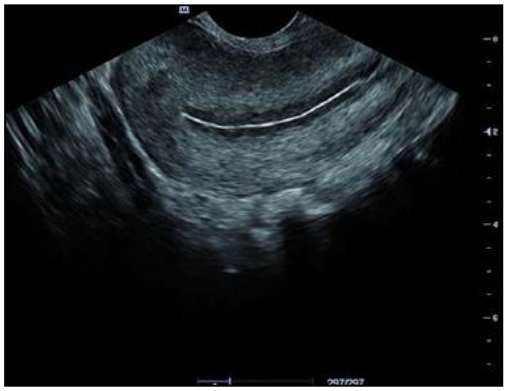

Fig 1: TVS Picture of uterus

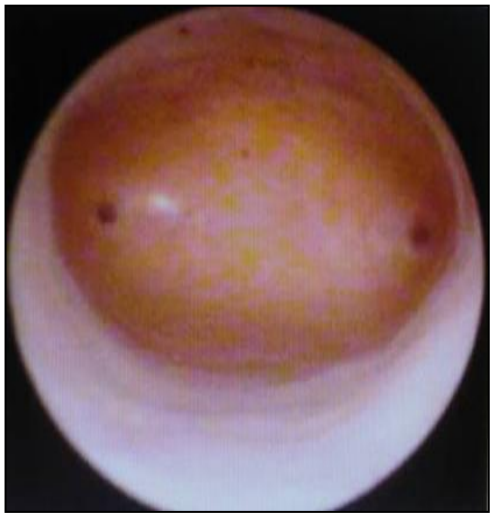

Fig 2: Hysteroscopic view of atrophic endometrium

Results

Table 1: Distribution of findings in TVS

Sl. No	TVS Findings	No of patients	Percentage
1.	Atrophic	36	36
2.	Thickened	40	40
3.	Hyperplasia	15	15
4.	Polyp	03	03
5.	Carcinoma	06	06
Total		100	100

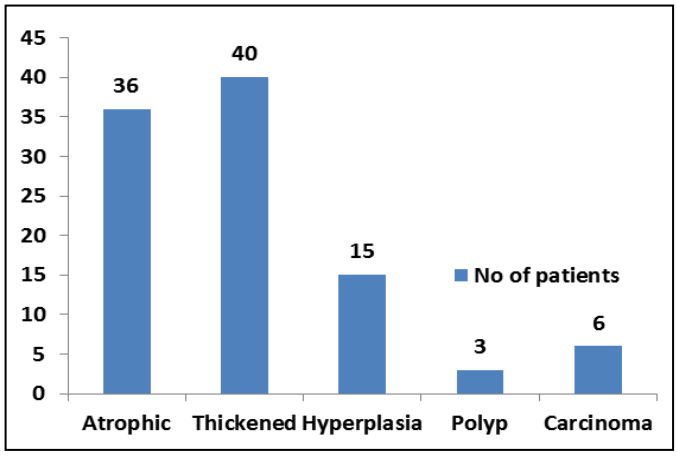

Fig 3: Graphical presentation of TVS findings

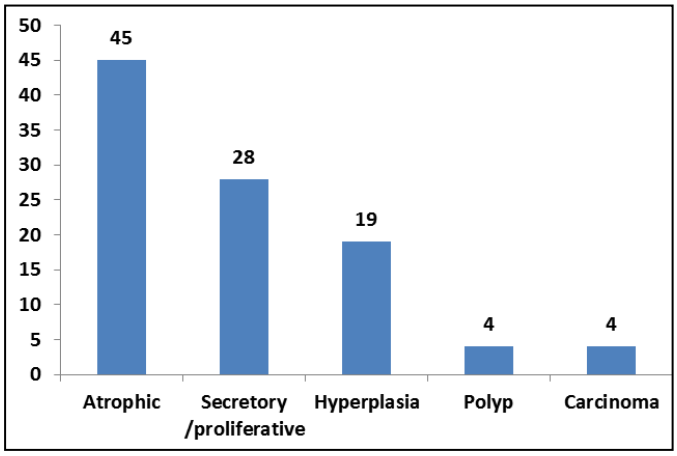

Fig 4: Graphical presentation of hysteroscopic findings

Of the 100 women who underwent TVS 36% were atrophic. 40% thickened, 15% hyperplasia, 3% polyp and 6% carcinoma was diagnosed**.**

Of the 100 women who underwent hysteroscope, 45% atrophic, 28% secretory/proliferative, 19% hyperplasia, 4% polyp and 4% carcinoma was diagnosed.

Table 2: Distribution of findings in hysteroscopy

Sl. No	Hysteroscopy findings	No. of patients	Percentage
1.	Atrophic	45	45
2.	Secretory/proliferative	28	28
3.	Hyperplasia	19	19
4.	Polyp	04	04
5.	Carcinoma	04	04
Total		100	100

Table 3: Comparison of efficacy of TVS and hysteroscopy

	TVS	Hysteroscopy
Sensitivity	86.36 %	90.90 %
Specificity	42.30%	91.02 %
PPV	29.68%	74.07 %
NPV	91.66%	97.26 %
Efficacy	52 %	91 %

Table 4: Comparison of diagnosis by TVS and HPE

TVS	HPE					Total
	Atrophic	Proliferative/ Secretory	Hyperplasia	Polyp	Carcinoma	
Atrophic	29	04	03			36
Thickened	20	17	03			40
Hyperplasia		08	05	02		15
Polyp			01	02		03
Carcinoma			01		05	05
Total	49	29	13	04	05	100

Out of the 36 atrophic endometrium diagnosed by TVS, in HPE 29 was atrophic, 4 came as secretory /proliferative and 3 came as hyperplasia**.** Of the 40 thickened endometrium diagnosed by TVS, in HPE 17 was proliferative /secretory, 20 came as atrophic and 3 turned out to be hyperplasia. 15 Hyperplasia was diagnosed by TVS which on HPE showed 5 hyperplasia, 8 secretory / proliferative changes and 2 polyp. Of the 3 polyp which was diagnosed by TVS, on HPE 2 was polyp and 1 turned out to be hyperplasia. 6 carcinoma was diagnosed by TVS, which on HPE showed 5 carcinoma and 1 came as hyperplasia.

Table 5: Comparison of hysteroscopy with HPE

Hysteroscopy	HPE					Total
	Atrophic	Proliferative/ Secretory	Hyperplasia	Polyp	Carcinoma	
Atrophic	43	02				45
Sec/pro	06	20	02			28
Hyperplasia		07	11		01	19
Polyp				04		04
Carcinoma					04	04
Total	49	29	13	04	05	100

Of the 45 atrophic endometrium diagnosed by hysteroscopy, on HPE 43 were atrophic, while 2 came as proliferative. Of the 28 secretory / proliferative endometrium diagnosed by hysteroscopy, in HPE, 20 was correctly diagnosed as proliferative / secretory, 6 came as atrophic and 2 turned out to be hyperplasia. 19 hyperplasia was diagnosed by hysteroscope, which on HPE showed 11 hyperplasia, 7 came as secretory / proliferative and 1 turned out to be carcinoma. All 4 polyps on HPE were correctly diagnosed by hysteroscopy. Of the 4 carcinoma diagnosed by hysteroscopy, all 4 turned out to be carcinoma by HPE.

Discussion

Post-menopausal bleeding is a common complaint in patient attending the gynecology outpatient department. The main causes of post-menopausal bleeding (excluding carcinoma

cervix) are as follows [4].

- Endometrial atrophy - 60-80%
- Estrogen replacement -15-25%
- Endometrial polyp - 2-12%
- Endometrial hyperplasia -5-10%
- Endometrial carcinoma - 10%

Risk factors for carcinoma endometrium[4] are Nulliparity, Late menopause, Obesity, Diabetes mellitus, Unopposed estrogen action, Tamoxifen, Atypical endometrial hiperplasia, HNPCC syndrome (Heriditary Non Polyposis Colon Cancer).

This prospective comparative study compared between hysteroscopy and transvaginal ultrasound in evaluation of post-menopausal bleeding.In this study most women belonged to the age group 45-50 years. Youngest being 43 years and oldest being 65 years. Mean age was 51.5 years. Kaur *et al*. [7] studied 112 post-menopausal women, mean age was 50 years. Women of all parity were present in his study. In this study majority of the women presented 1-5 years after menopause.

In this study 23% patient had associated comorbid illness, commonest being obesity 10%, 8% were hypertensive and 5% suffered from diabetes mellitus. In study conducted by sunita *et al*. [8] obesity was present in 8%, hypertension in 8% and diabetes mellitus in 2% which was similar to the present study.

In this study diagnosis by TVS, 36% atrophic, 40% thickened 15% hyperplasia, 3% polyp and 6% carcinoma. In the study by Sunita *et al*. [8] atrophic endometrium was found in 58%.Hyperplasia in 5%, carcinoma in 6% and endometrial polyp in 8%, which is comparable with the present study.

In this study histopathological diagnosis of 13% hyperplasia, 4% polyp, 5% carcinoma was reported. While 29% proliferative /secretary and 49% atrophic was reported. Study by Kaur *et al*. [7] showed 52% atrophic, 19% proliferative/secretory 3% hyperplasia, 2% endometrial polyp and 11% endometrial carcinoma, which is comparable with the present study.

In this study when the cut off of >4mm was taken to define endometrial abnormality the TVS sensitivity was 86.36%, specificity was 42.30%, positive predictive value was 29.68% and negative predictive value was 91.66%.Smith beiden *et al*. [9] showed that the meta analysis with 5mm cut off for endometrial disease showed sensitivity-96%, specificity-39%.This study had a better sensitivity than the present study.

Journal of ultrasound 2001. [10] Published a meta-analysis reported of 85 published studies including 5892 women taking endometrial thickness of >5 mm as abnormal the sensitivity was 96%.

In this study the findings by hysteroscopy shows 45% atrophic endometrium, 28% proliferative / secretory, 19% hyperplasia, 4% polyp and 4% carcinoma. Rita *et al*. [11] study in which hysteroscopy was compared with transvaginal ultrasound taking HPE by hysteroscopic biopsy for comparison showed scanty tissue in 17.4%, atrophic 34.8%, cystic atrophy 1.4%, Polyp 7.4%, hyperplasia 5.4% and carcinoma 13%. In this study the accuracy of diagnosis by hysteroscopy when compared with histopathology the sensitivity was 90.90%, specificity 91.02%, positive predicitive value 74.07 %, negative predictive value 97.26 % and efficacy 91%. Stefano bettocchi *et al* [12] analyzing the role hysteroscope alone in 4863 women and showed sensitivity 100%, specificity 99%, positive predictive value 98%, Negative predictive value 100%. Sunita *et al*. [8] studied 60 post-menopausal women and compared TVS with hysteroscope which showed sensitivity-97%, specificity- 98.66 %, comparable with the present study.

Table 6: Comparison of present study with various studies of accuracy for TVS and Hysteroscopy

References	TVS				Hysteroscope			
	Sensi	Speci	Ppv	Npv	Sensi	Speci	Ppv	Npv
Rita [11]	77 %	93.3%	63.%	96.6%	88.9%	98.3%	88.9%	98.3%
Stefano [12]					100%	99%	98%	100%
Sunita [8]	76%				97%	98.66%		
Diaael [13]	73.9%	73.7%	77.3%	70%	78.3%	84.2%	85.7%	76.2%
Present	86.36%	42.30%	29.68%	91.66%	90.90%	91.02%	74.07%	97.26%

When endometrial thickness of > 4mm was taken to define endometrial abnormality sensitivity 86.36%, specificity 42.30%, and positive predictive value 29.68 %, negative predictive value 91.66% was obtained.

When accuracy of hysteroscope was compared with HPE sensitivity 90.90%, specificity 91.02%, PPV 74.07%, NPV 97.26%.

Conclusion

Both transvaginal ultrasound and hysteroscopy are can be used to evaluate post-menopausal bleeding. Hysteroscopy correlates more with histopathology when compared with transvaginal ultrasound. Hysteroscopy is superior and has higher efficacy in diagnosing endometrial abnormality in women with post-menopausal bleeding.

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