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ROLE OF TRANSVAGINAL ULTRASONOGRAPHY IN INITIAL EVALUATION OF AUB IN PREMENOPAUSAL WOMEN

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Abstract

Introduction

This study aimed to evaluate the diagnostic accuracy of ultrasound parameters in assessing endometrial pathology and to determine the most sensitive cut-off value of endometrial thickness

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for the exclusion of endometrial lesions in premenopausal women with abnormal uterine bleeding (AUB).

Method

This study was conducted in the Department of Obstetrics and Gynecology, P.B.M. Hospital and S.P. Medical College, Bikaner, from February 2012 to January 2013. During this period, 80 premenopausal women who presented with abnormal uterine bleeding were evaluated with transvaginal sonography (TVS) and followed by endometrial biopsy within 48 hours. We conducted a statistical evaluation using SPSS 17. Receiver operating characteristics (ROC) curves for endometrial thickness and abnormal endometrial histopathology were analyzed.

Result

Abnormal endometrial pathology (hyperplasia and polyp) was confirmed in 10 women (9 with endometrial hyperplasia and no polyp). The area under the Receiver Operating Characteristics (ROC) curve (AUC) was 0.92 (95% CI, 0.85–0.98). The best negative likelihood ratio was obtained at an endometrial thickness of 11.5 mm with a negative predictive value (NPV) of 96.7% and a positive predictive value of 42.1%. The sensitivity and specificity of using an endometrial thickness cut-off value of 11.5 mm were 80% and 84.3% respectively.

Conclusion

In premenopausal women presenting with AUB, TVS measurement of endometrial thickness is efficacious in ruling out endometrial pathology; however, the diagnostic accuracy is not good. Endometrial thickness of 11.5 mm in premenopausal women with AUB may serve as a cutoff point for predicting pathology-negative cases, and diagnostic uterine curettage may be avoided in these patients.

Keywords: Abnormal uterine bleeding(AUB),Premenopausal women, Dilatation and Curettage(D&C),Transvaginal ultrasonography(TVS), Perimenopausal bleeding, Endometrial thickness

Introduction:-

Abnormal uterine bleeding (AUB) is a common problem that prompts more than 20% of all visits to outpatient clinics and may account for more than 25% of all hysterectomies(1,2).· Abnormal uterine bleeding refers to a symptom of excessive, prolonged, unexpected, or acyclic bleeding regardless of cause or diagnosis. It not only affects the quality of life, such as intimate

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relationships, day to day living but can have serious adverse consequences as anemia or malignancy(3,4). Abnormal premenopausal bleeding should always be taken seriously and be properly investigated, no matter how minimal or nonpersistent(5,6)..FIGO (2010) classified AUB into 9 main categories, which are arranged according to the acronym PALM-COEIN (pronounced "palmkoin"): polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified. In general, the components of the PALM group are discrete (structural) entities that can be measured visually with imaging techniques and/or histopathology, whereas the COEIN group is related to entities that are not defined by imaging or histopathology (non-structural)(7). Various methods to evaluate pre and postmenopausal bleeding are Transvaginal sonography (TVS), endometrial biopsy, dilatation and curettage (D&C), and hysteroscopy. Diagnostic procedures obtaining material for histological assessment (e.g., dilatation and curettage, hysteroscopy, and endometrial biopsy) can be more accurate but are also more invasive. TVS can be safely used as an initial investigation in the management of AUB as it is a non-invasive method for the detection of endometrial pathology.

In the past, D & C was the gold standard investigation to exclude endometrial pathology. However, in approximately 60% of the D&C procedures, less than half of the uterine cavity is curetted, hence it may miss focal lesions such as polyps, submucosal fibroids, and endometrial carcinoma. Another drawback is that it has to be done under anesthesia, so it cannot be applied repeatedly in high-risk patients and those with recurrent bleeding. Uterine cancer, the most serious cause of uterine bleeding is diagnosed in fewer than 10% of specimens obtained by endometrial biopsy, in women presenting with AUB. This means that more than 90% of endometrial biopsies reveal benign findings (8,9). Thus, it is highly required to develop a method that is safe, less or noninvasive, and simple with a quick result.

The answer to the above problem could be transvaginal sonography, which is less invasive, painless, has no complications, and will also help gynecologists in diagnosing various

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problems related to the female genital tract. TVS provides valuable information in the evaluation of a wide range of gynecological disorders, including the evaluation of uterine and adnexal masses, inflammatory processes, and neoplasms(10,11). In general, an endometrial thickness of more than 8mm is considered suspicious of endometrial pathology in perimenopausal women with AUB, and further investigation is recommended (12,13). TVS is advantageous in obese patients, in patients with extensive anterior abdominal wall scarring, or when the uterus is retroverted (6).TVS scan on the contrary, in regards to transabdominal sonography should be performed with an empty bladder, thus eliminating patient discomfort. There are a few limitations of USG that it may not be able to distinguish between benign proliferation, hyperplasia, polyp, and malignancy. TVS is a cost-effective and sensitive method to evaluate most women with abnormal bleeding in combination with physical examination and endometrial biopsy.

This study was done to compare transvaginal sonography endometrial assessment with the histopathology report obtained by D&C and to determine the cut-off point for endometrial thickness to reduce the unnecessary diagnostic curettage for premenopausal bleeding.

AIMS & OBJECTIVES

- To compare endometrial assessment by TVS with histology obtained by endometrial curettage in premenopausal women.
- To determine a cutoff point for endometrial thickness to reduce unnecessary diagnostic curettage for premenopausal bleeding.

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Material and methods:- The present study was conducted in the Department of Obstetrics & Gynecology, P.B.M. Hospital attached to S.P. Medical College, Bikaner.

- Study Period: February 2012 to January 2013
- Study design: Prospective study
- Case Collections: OPD and indoor cases.

A total of 80 cases were taken. Informed consent was taken from all the patients in their native language. Details the of study were explained to participants and also provided information on benefits as well as risks during procedures. Participants can withdraw their participation at any point of research but it will not affect their treatment.

- **Inclusion criteria**

  Any patient above the age of 40 years with a history of abnormal uterine bleeding.

Exclusion Criteria

- Women on any hormonal treatment
- Women who have vaginal bleeding
- Women who are known cases of blood dyscrasia.

All patients with the above eligibility criteria were examined by taking a detailed history which includes age, parity, menstrual pattern, (present and past) including duration, severity, cyclic or acyclic, method of contraception used, or any other medical and gynecological complaints.

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All patients were examined for general physical examination, systemic examination, per abdomen, per speculum, and per vaginal examination.

Investigations

All routine investigations like

- HB, BT, CT
- Urine Complete

Then all the patients were subjected to TVS. TVS was performed using a vaginal transducer of 6.5 MHZ frequency. Endometrial thickness was measured in the postmenstrual period (7-10 days) at the thickest part of the endometrium, 1cm from the endometrial-myometrial interface at the fundus in the longitudinal plane as described (14). The thickness measured includes both the endometrial layers. Detection of a hyperechoic area within the endometrial layers is taken as suggestive of endometrial pathology. Endometrial layers represent the inner layer of compact and vascular myometrium. This layer is symmetrical and intact in all normal postmenopausal uteri, and also in all those with endometrial polyps and simple and atypical hyperplasia. It is absent or irregular in uteri with endometrial carcinoma.

All patients were subjected to D&C. D&C was done under sedation. The tissue was put in formalin and sent for histopathological examination.

Primary outcomes were compared for the effectiveness of endometrial assessment by TVS and histopathological specimens obtained by D&C.

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The secondary outcome was to determine a cutoff value of endometrial thickness in premenopausal women to avoid unnecessary curettage in every patient presented with complaints of AUB.

Statistical Analysis: The results were tabulated, and data analyzed as per percentage and included sections on patient demographics, preoperative characteristics, and postoperative outcomes. Statistical evaluation was done using SPSS 17. Receiver operating characteristics (Receiver Operating Characteristics (ROC)) curves for endometrial thickness and abnormal endometrial histopathology were analyzed. Statistical analysis was done by calculating the mean, standard deviation, and p-value.

OBSERVATIONS AND RESULTS

Table 1

Distribution of Cases according to Age group (years)

Age Group	**No.**	**%**
40-44	35	43.75%
45-49	43	53.75%
50-54	2	2.5%

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55-59	0	0
≥60	0	0
Total	80	80

Table 1 shows the distribution of cases according to age group.

The most common age group in our study is 40-49 years of 97.5% of patients. In our study, most of the patients (73%) had their BMI within the normal range while overweight (BMI 25-29.99kg/m2) was found in 20% of cases, and obesity (BMI >30) was found in 7% of cases.

Out of a total of 80 patients, medical/surgical illness was present in 14 patients, and out of them 5 had hypertension, 2 each had diabetes, psychiatric disorder, breast cancer, and cardiac disease while 1 patient had chronic hepatitis B.

Table 2

Distribution of cases according to parity

Parity	**No.**	**%**
Nulli	0	0
1-2	13	16.25%

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3-6	66	82.5%
>6	1	1.25%
Total	80	100

According to Table 2, no case was found in nulliparity, while 13 patients had their parity 1-2, 66 patients had a parity of 3-6, and only 1 patient had a parity >6.

Table 3

Distribution of cases according to Duration of Symptoms (months)

Duration (months)	**No.**	**%**
≤ 3	28	35%
>3	52	65%
Total	80	100

65% of cases had their symptoms since >3 months, while the remaining 35% of patients had symptoms since <3 months.

Table -4 Distribution of cases according to Uterus Size

Uterus Size	**Premenopausal**

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(weeks)	No.	%
Senile	0	-
Normal	37	46.3
6	20	25.0
8	11	13.7
10	7	8.8
12	5	6.2
Total	80	100

According to the table, normal size and up to 6 weeks of uterus were observed in premenopausal women in 71.3%. 28.7%of patients had more than a 6week- size uterus.

Table 5

Distribution of cases according to other USG findings in the premenopausal group

USG Findings	**No.**	**%**
Uterus		
Normal	45	56.25
Normal with Adenaxal Mass	10	12.5
Bulky	13	16.25
Polyp	03	3.75
Myoma	8	10.0
Adenomyosis	1	1.25
Total	80	100

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The Maximum number of patients (n=45) had their USG findings normal, while 10 patients had their uterus normal with adenaxal mass. A bulky uterus was found in 13 patients, polyp in 3 patients, myoma in 8, and adenomyosis in 1 patient.

Table 6:Distribution of cases according to endometrial thickness on TVS

Endometrial Thickness (mm)	**Pre**menopausal	
	No.	%
<5	0	-
5-10	46	57.4
11-15	21	26.3
16-20	10	12.5
>20	3	3.8
Total	80	100

Out of a total of 80 patients, 46 patients had their endometrial thickness between 5and10mm. 11-15mm endometrial thickness was present in 21 patients, and 10 patients came in the16-20mm ET category, while >20mm endometrial thickness was present in 3 patients.

Table 7

Endometrial histopathology women with premenopausal bleeding of all studied women

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Endometrium		Premenopause	
		No.	%
Normal	Atrophic	0	-
	Proliferative	48	60.0
	Secretary	22	27.5
Abnormal	Endometrial hyperplasia	9	11.3
	Polyp	1	1.2
	Cancer	0	-
Total		80	100

According to histopathology of the endometrium, normal histopathology was found to be 70 in the premenopausal group. Only 10 patients had abnormal endometrium. Out of 10 patients which show abnormal endometrium. Simple hyperplasia was found in 5 patients, simple hyperplasia with atypia in 2 patients, complex hyperplasia without atypia in 2 patients, and endometrial polyp was found in 1 patient.

Table 8 Correlation between endometrial thickness and histopathology in premenopausal women

Histopathology	Endometrial Thickness (mm)										Total	
	<5		5-10		11-15		16-20		>20			
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Atrophic	0	-	0	-	0	-	0	-	0	-	0	-
Proliferative	0	-	34	42.5	10	12.5	4	5.0	0	-	48	60.0
Secretary	0	-	12	15.0	8	10.0	2	2.5	0	-	22	27.5

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Endometrium hyperplasia	0	-	0	-	3	3.8	3	3.7	3	3.7	9	11.3
Polyp	0	-	0	-	0	-	1	1.2	0	-	1	1.2
Malignancy	0	-	0	-	0	-	0	-	0	-	0	-

Table 8 shows the correlation between endometrial thickness and histopathology in premenopausal women. In this study, no patients had histopathology of atrophic, while normal histopathology was found in 70 patients out of whom 56 patients had their endometrium thickness between 5and10mm. Endometrium hyperplasia was present in 9 patients and out of them 3 each had endometrial thickness 11-15, 16-20, and >20 respectively, while polyp was present in only 1 patient and he belonged to the 16-20mm endometrium thickness group.

Table 9

Endometrial thickness measured by TVS with regards to histopathological diagnosis of curettage specimen in premenopausal women

Histopathological Findings	**No.**	**Endometrial Thickness**	
		Mean	SD
Atrophic	0	-	-
Proliferative	48	8.56	3.14
Secretary	22	9.82	2.46
Hyperplasia	9	16.33	4.36
Polyp	1	17.00	0.00

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Cancer	0	-	-

Table 9 shows endometrial thickness measured by TVS with regard to histopathological diagnosis of curettage specimens in premenopausal women. In the proliferative group, the Mean endometrial thickness was 8.563.14, the mean ET of secretary was 9.822.46, the mean ET of hyperplasia was 16.334.36, and the mean ET of the polyp was 17.000.00.

Table 10

Mean endometrial thickness of normal and abnormal endometrium in premenopausal women

Endometrium	**No.**	**Range**	**Mean**	**SD**	**P**
Normal	70	6-17	8.96	2.99	<0.001
Abnormal	10	11-22	16.40	4.11	0.836

According to endometrium, the mean of normal endometrium and abnormal endometrium in premenopausal was 8.962.99 and 16.404.11, respectively and the difference was found to be statistically insignificant ($p>0.05$). The area under the Receiver Operating Characteristics (ROC) curve (AUC) was 0.92 (95% confidence interval, 0.85 -0.98). The best negative likelihood ratio was obtained at an endometrial thickness of 11.5 mm with a negative predictive value of 96.7% and a positive predictive value of 42.1%. The sensitivity and specificity of using endometrial thickness cut-off values of 11.5mm were 80% and 84.3% respectively.

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AREA UNDER THE CURVE				
Test result variables(s):endometrial thickness(mm)				
Area	Standard Error	Asymptomatic sig	Asyptomatic 95%Confidence Interval	
.924	0.36	.000	.853	.994

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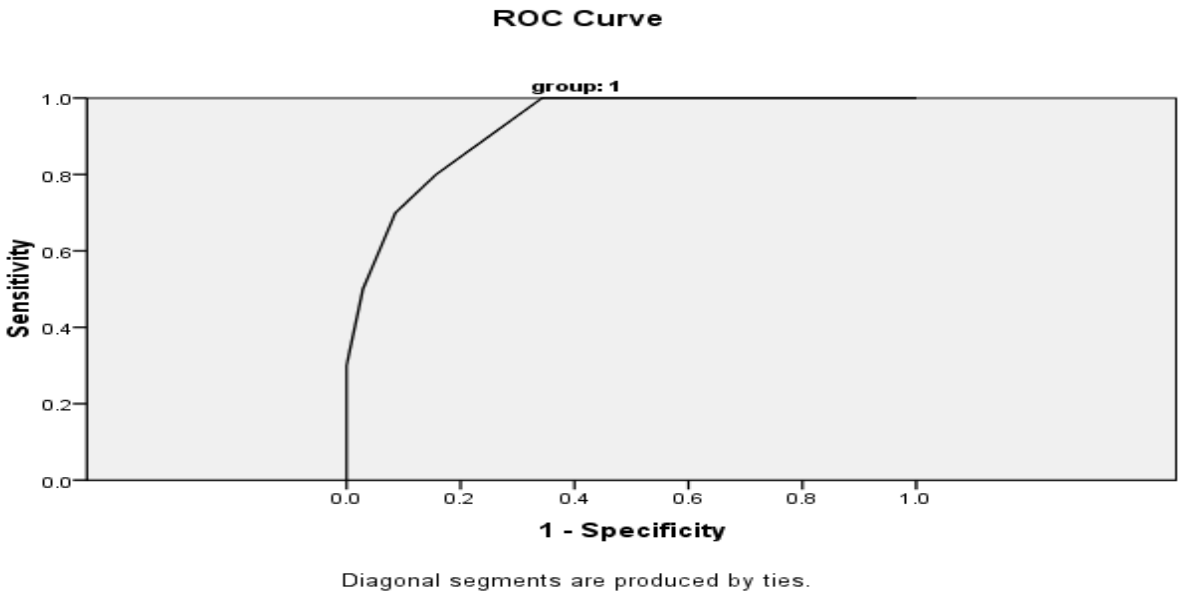

DISCUSSION

Abnormal Uterine bleeding is a common problem, accounting for more than 70% of all gynecological consultations in the peri-and postmenopausal years. The main aim of investigating these women was to rule out endometrial cancer and its precursor lesions and endometrial hyperplasia. The probability of endometrial cancer in women presenting with postmenopausal bleeding is 10% and approximately 15% for endometrial hyperplasia(13). The prevalence of benign intrauterine structural pathology (for example, endometrial polyps and intracavitary fibroids) found in association with bleeding was 25%(13,15)

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However, the majority of women with irregular uterine bleeding have no endometrial pathology and thus undergo the risk of unnecessary surgical procedures.

Transvaginal sonography allows the detection of endometrial pathology in the vast majority of cases and as it is easy, relatively cheap, needs no anesthesia, and is non-invasive, it can be used as a first-line investigation in the evaluation of women with abnormal uterine bleeding. It can be supplemented by procedures like hysteroscopy, allowing visualization of the endometrial cavity. This can minimize the cost, time, and hospital stay when compared to the endometrial sampling technique of dilatation and curettage for evaluating this common complaint in the premenopausal age group.

In our study, the maximum number of cases were seen in the 40-49-year-old age group 97.5%; otherwise, this was the commonest premenopausal AUB age group. (Table 1).

Marcato et al in the year 2005 and Ferrezzi et al in 1996 also concluded that AUB is a more common problem in the premenopausal age group (16,17). So these studies are correlated with our findings.

In our study, the majority of cases were in parity 3-6 (82.%) and 1.25% were in grand multipara and 1-2 para 16.25% (Table 2). Among the 80 cases, none was nullipara. The incidence of AUB increases as the parity increases.

Cornitescu et al and Khan et al studies showed that most of the women were multiparous, and this indicated that the incidence of AUB increases with age and parity (18,19). In our study, symptoms like heavy bleeding, and combinations of different bleeding patterns were present since >3 months in 65% of cases and since <3 months in 35% of cases (Table 3). De Vries et al

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(2011) did a descriptive study that also showed that 2/3rd patients in their study had symptoms lasting more than 3 months 19(20). Thus, our study was comparable with the above study.

In the present study, the uterus was normal in premenopausal women at 46.3%, 6 weeks at 25%, 8 weeks at 13.7%, 10 weeks at 8.8%, and 12 weeks at 6.2% Thus, our study shows that normal and up to 6-week size of uterus was observed in premenopausal women in 71.3% (Table 4).

In the present study, endometrial thickness on TVS was done before D&C in premenopausal patients who presented with abnormal uterine bleeding. The commonest endometrial thickness in the premenopausal group was 5-10mm in 57.4% of cases, between 11-15mm in 26.3% of cases, < in 0% of cases, and between 16-20mm in 12.5% of cases and >20mm in 3.8% of cases (Table 5). In our study, TVS was done along with endometrial thickness, and other findings were also recorded. The uterus was found normal in 49% of cases with adnexal mass in 15% of cases, and bulky in 18%. Polyp was found in 4%, of cases, myoma was found in 11% of cases, and adenomyosis was in 3% of cases (Table 5).

Bakos and Heimen et al studied 196 women with abnormal uterine bleeding as well and Curic et al found that by TVS both normal and pathological endometrial changes could be detected and 82% of patients had an endometrium characterized as normal(21). Endometrial hyperplasia was found in 12% and endometrial polyps in 4% of patients. Curic et al found the same results (22).

Najeeb et al did a study on 141 women in the premenopausal age group. TVS detected polyp in 38 cases, proliferative phase in 46 cases, hyperplasia in 21 cases, suspicious-looking endometrium in 2 cases, atrophy in 10 cases, IUCD in 3 cases, and myoma in 21 cases(23).

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These findings were compared with histopathological findings and concluded that TVS allows the detection of endometrial pathology in the majority of cases.

In our study, the most common endometrial pattern in premenopausal women was normal i.e. proliferative and secretary in histopathological reports.(Table7) Normal endometrium was 87.5%, endometrium hyperplasia was found in 11.3% of cases, and endometrium polyp was found in 1.2% of cases.

In the year 2010, Ozdemir et al did a study and observed that of the 144 women, 113 (78.4%) had normal and 31 (21.6%) had an abnormal endometrium. The abnormal endometrium was composed of 11.8% hyperplasia (simple + atypical complex), 4.2% endometrial polyp, and 5.5% adenocarcinoma. Optimal sensitivity and specificity (83.6 and 56.4%, respectively) and a negative predictive value of 95.6% for detection of abnormal endometrium were obtained with an endometrial thickness of 8 mm(24).

In our study,(table-8) correlation between endometrium thickness by TVS and histopathological reports in premenopausal women showed an HPR proliferative pattern was found in 48 cases out of them:42.5% had their endometrium thickness between 5-10mm and 12.5% had endometrium thickness between 11-15mm and 5% had endometrium thickness between $^{16\text{-}20}$. The secretary pattern was present in 22 patients, and out of them, 15% cases had endometrium thickness between 5-10, 10% cases had endometrium thickness between 11-15, and 2.5% cases had endometrium thickness had 16-20mm. On HPR, hyperplasia was present in 9 patients out of them, 3 each had endometrium thickness 11-15, 16-20, and >20mm. Polyp was

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present in 1 case, and it belonged to the endometrium thickness 16-20mm group, while no case was found in the malignant group.

Paraskevaids and Kalantaridou et al did a study on 80 women, and out of them, 67 had normal histological findings, and 13 patients had abnormal findings. In the 67 women with a histological diagnosis of normal endometrium, the mean thickness was 10.54.0mm, whereas the corresponding value in the 13 women with abnormal findings was 18.70.8mm(25). Machado et al found that endometrial thickness ranged from 2.5-22.5 mm in perimenopausal bleeding women(16). The same results were also found by, Ozdemir et and Stachowicz et al (24,26).

Stachowicz et al in the year 2002, did a study that showed that the mean volume of endometrium in women with endometrial cancer was 19.9+7.5 ml · The mean volumes measured in women with endometrial hyperplasia and normal endometrium were 12.2+7.9 ml and 7.4+4.8 ml, respectively. There was a significant difference in endometrial volume between each pair of study groups ($p< 0.05$). Moreover, significant differences were found in mean endometrial thickness between endometrial cancer and benign but not in hyperplastic endometrium(26).

In our study, we found that mean endometrium thickness in women with normal endometrium and abnormal endometrium was 8.962.99 and16.40±4.11 respectively. (Table 10)

Comparison of endometrium thickness in premenopausal women with various authors

Authors	Year	No. of Patients	Cut Off
Zlatkov et al[61]	2001	45	>8mm
Machado et al[73]	2005	100	>8mm
Ozedemir et al[81]	2010	144	>8mm
Najeeb et al[80]	2010	141	>8mm

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Present Study	2013	80	>8mm

CONCLUSION

Our study showed that TVS could be a good initial screening method for the evaluation of women with AUB in premenopausal patients. We found that TVS is an efficacious, noninvasive screening method for abnormal uterine bleeding and an endometrial thickness of 8.96 +/- 2.99mm in premenopausal patients may serve as a cutoff point for predicting pathology-negative cases and diagnostic uterine curettage may be avoided in these patients. However, since this is a small study, large trials are still recommended.

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