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Original Research Article

Endometrial thickness by ultrasonography and its correlation with histopathology in abnormal uterine bleeding among peri and post menopausal women

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ABSTRACT

Background: The endometrium constitutes a dynamic organ in female reproductive years, as it is subjected to hormonal variations in every cycle. Present study was conducted with the aim to correlate the endometrial thickness with the histopathology in the peri-menopausal females presenting with abnormal uterine bleeding (AUB) and to identify cut off value of endometrial thickness in order to reach at some consensus regarding when to intervene so that not a single endometrial pathology will be missed.**Materials and Methods:** This was an observational study conducted on 242 peri-menopausal and post-menopausal women ≥ 40 years of age presenting with abnormal uterine bleeding (AUB).**Results:** Based on the ROC curve, the cutoff point that delineates the abnormal histology and normal histology for endometrial thickness was 14.20 mm. Area under the curve (AUC) was 0.783 with 95% CI as 0.686 - 0.880 having sensitivity 71% and specificity 90% ($p < 0.001$).**Conclusion:** Heavy menstrual bleeding and frequent cycle were found to be commonly associated with gynecological pathology in these age groups. In all post and peri-menopausal AUB trans vaginal sonography for endometrial thickness is the initial best modality of investigation. Endometrial thickness cutoff in the range of ≥ 14 mm is of prime importance.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

The endometrium constitutes a dynamic organ in female reproductive years subjected to cyclical hormonal variations. Perimenopause is a transition phase of women's life marked by erratic cycle and fluctuating hormonal milieu. Abnormal uterine bleeding constitutes majority of gynecological consultations and responsible for all two - third hysterectomies.¹⁻⁷ The investigations in them should be targeted to exclude serious pathology such as endometrial cancer and its precursor lesion endometrial

hyperplasia. Trans vaginal sonography (TVS), which is a simple, non-invasive technique for endometrial evaluation plays a major role in this regard. Use of high resolution transvaginal probes and colour Doppler further enhanced the ability to study the endometrium beyond its thickness. Findings such as focal thickening, heterogeneity in the endometrium, irregular endometrial thickening, polypoidal mass lesion, intrauterine fluid collection and disruption of sub endometrial halo prompt further evaluation to rule out serious pathology even if the endometrial thickness is normal.^{1,8,9} In postmenopausal lady the cut-off for endometrial thickness for further evaluation is almost defined. However, there is a lack of clear cut-off criteria

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for abnormal endometrial thickness for peri-menopausal women. The present study tries to correlate the endometrial thickness in TVS evaluation with the histopathological abnormality in the peri menopausal and post-menopausal women. Present study was conducted with the following objectives:

1. To assess the endometrial thickness by trans vaginal ultrasonography.
2. To see correlation of histopathology with endometrial thickness in abnormal uterine bleeding (AUB) in peri-menopausal and post-menopausal women.
3. The current study also throws some light about various causes of AUB as per PALM-COIEN prevalent in our locality.
4. To find the cutoff for endometrial thickness that delineates the abnormal from normal histology.

2. Materials and Methods

This was a prospective observational study conducted in the Department of O&G, Pradyumna Bal Memorial hospital, KIMS, BBSR, Bhubaneswar, Odisha for the period of two year October 2020 to October 2022 after taking clearance from the Institutional ethics committee. In the present study 250 consecutive peri-menopausal and post-menopausal women ≥ 40 years of age presenting with abnormal uterine bleeding (AUB) with informed consent and willing to undergo hysteroscopy and endometrial biopsy were included in the present study. Patients < 40 years age; and ≥ 1 year of final menstification (post menopausal) having Acute pelvic infections or pregnant females or women on drugs/hormones and with (endometrial carcinoma, vulvar, vaginal or cervical cancer, cervical polyp, myomatous polyp) or females having vaginal or cervical causes of bleeding were excluded from the present study. A pre-designed structured data collection tool was used for the collection of the information. Variables such as age, BMI, socioeconomic status, parity, menstrual pattern, pelvic examination findings, endometrial thickness by TVS etc. were noted. A midline sagittal image of the uterus was used to obtain the endometrialecho complex (EEC). It was noted if the complex is indistinct, heterogeneous or focally thickened. Those with thickened endometrium were subjected to hysteroscopy and endometrial biopsy.

Peri-menopausal-It is the transition period starting immediately before and up to 1 year after the final menstrual period. It may last for 3-4year.^{10,11}

Postmenopausal bleeding (PMB): "It is bleeding that occurs 12 months after the last normal period. However, it is recommended that any vaginal bleeding that occurs 6 months after the last period (presumed menopause) should be investigated".¹²

Data obtained were entered in the excel sheet and analyzed using standard descriptive methods such as

frequency and percentages for categorical variables, and mean and SD or median and range for continuous variables. Comparisons between categorical variables were calculated by chi-square test. Receiver operating characteristic (ROC) curve was used to determine the best cut-off point of endometrial thickness for detection of endometrial pathology with highest possible sensitivity and specificity along with the cut off value of endometrial thickness to classify the abnormality. In this study, sensitivity, specificity of endometrial thickness by TVS were evaluated in detecting endometrial pathology. All calculated P values were 2 sided and $P < 0.05$ was considered as statistically significant. Data entry was performed on Microsoft Excel Software (Window-10). Statistical analysis was done using Statistical Package for Social Science for Windows (SPSS-20).

3. Results

In the present study 242 participants were included with mean age as 44.73 ± 3.67 years. Most of the females were in the age group 40-45 years (61.15%) (Table 1). Majority of the patients belonged to normal BMI category (78.8%). Distribution of study participants according to their socio-demographic profile showing most of the females belonged to lower socio-economic class (48.34%) and were multiparous (82.63%).

Heavy menstrual bleeding was the commonest pattern amongst half (51.2%) of the females. In present study the most common comorbid condition associated was hypertension ($n=32$, 13.2%) followed by diabetes mellitus ($n=18$, 7.2%) and Hypothyroidism ($n = 21$, 8.4%).

79 patients (32.64%) were without any significant ultrasonography abnormality. The most common pathology associated was fibroid (21.9%) followed by adenomyosis (13.64%) and Thickened Endometrium (11.57%). Few patients also had more than one pathology, fibroid with adenomyosis being the most common association (3.72%) (Table 2).

In present study, mean endometrial thickness (mm) was 44.78 ± 3.68 mm. Most frequently observed endometrial thickness (mm) was 10-14.9mm (118, 47.2%). Endometrial thickness ≥ 20 mm were observed in 7.6% ($n=19$). A wide spectrum of endometrial pattern was noted on histopathology, Secretory pattern being the commonest (35.12%) observation followed by Proliferative pattern (30.99%). Endometrial hyperplasia was observed in 11.16% ($n=27$). 12 (4.95%) showing atypical change. Benign endometrial polyp was observed in 5.37% cases where as Adenocarcinoma was found in 2.89%.

Comparison of endometrial thickness with histopathology revealed that for the endometrial thickness 10 mm-14.9 mm, secretory endometrium (50%) was the most common finding followed by proliferative endometrium (29.46%). For the endometrial thickness

Table 1: Distribution of the patients for their socio-demographic and clinical profile

		N (%)
Age	40-45 Years	142 (61.15)
	46-50 Years	82 (33.88)
	> 50 Years	12 (4.95)
Socio Economic Status	Lower	117 (48.34)
	Lower middle	50 (20.66)
	Middle	45 (18.59)
	Upper middle	25 (10.33)
Parity	Uper	5 (2.06)
	Nulli para	2 (0.82)
	Para 1	40 (16.52)
	Para 2	128 (52.89)
	Para 3	48 (19.83)
	Para ≥ 4	24 (9.91)

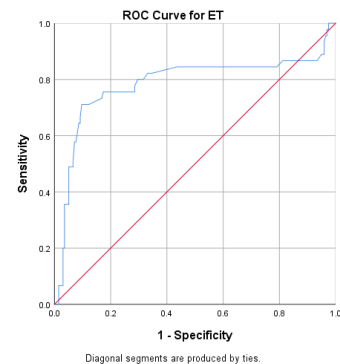
Table 2: Distribution of the patients according to the USG findings (PALM-COEIN)

		N(%)
USG Findings showing the single pathology:	Normal	79 (32.64)
	Fibroid	53 (21.9)
	Adenomyosis	33 (13.64)
	Endometrial Hyperplasia	28 (11.57)
	Ovarian Simple Cyst	10 (4.13)
	Endometrial Polyp	9 (3.72)
	PCOD	4 (1.65)
	Hydrosalpinx	2 (0.83)
	Dermoid Ovarian Cyst	1 (0.41)
	Collection In Endometrial Cavity	1 (0.41)
	Fibroid, Adenomyosis	9 (3.72)
USG Findings showing the more than one pathology:	Fibroid, Ovarian Simple Cyst	3 (1.24)
	Adenomyosis, Ovarian Simple Cyst	3 (1.24)
	Fibroid and Polyp	2 (0.83)
	Fibroid and Endometrial Polyp	2 (0.83)
	Adenomyosis, Endometrial Polyp	1 (0.41)
	Thickened endometrium, Polyp	1 (0.41)
	Fibroid, Thickened Endometrium	1 (0.41)

15 mm-19.9 mm, endometrial hyperplasia (40%) was the most common finding having equal proportion of non atypical (20%) and typical endometrial hyperplasia (20%) of followed by secretory endometrium (16.67%) and benign endometrial Polyp (16.67%). For the endometrial thickness ≥ 20 mm, endometrium with progestational effect (22.22%). Atypical Endometrial Hyperplasia (33.33%), Adenocarcinoma (22.22%), was the commonly noted observation (Table 3).

Based on the ROC curve, the cutoff point that delineates the abnormal histology and normal histology for endometrial thickness was 14.20 mm. Area under the curve (AUC) was 0.783 with 95% CI as 0.686 -0.880 and p value < 0.001 having 71% sensitivity and 90% specificity. (Figure 1)

The cutoff point of Endometrial Thickness to predict the malignancy was 18.65mm. AUC was 0.907 with 95% CI was 0.822 – 0.922 having sensitivity of 85% and specificity

**Figure 1:** ROC curve for abnormal histology

of 92% ($p < 0.001$) (Figure 2).

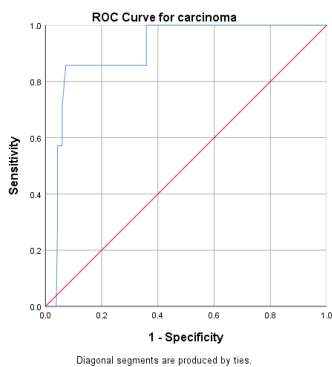
Table 4 showing that more than half of the patients (62.70%) with endometrial thickness ≥ 14.20 were having

Table 3: Association of endometrial thickness with histopathological findings

Histopathological Findings	Endometrial Thickness					Total
	<5	5 - 9.9	10 - 14.9	15 - 19.9	≥ 20	
Adenocarcinoma	0	0	1	2	4	7
Benign Endometrial Polyp	0	5	3	5	0	13
Atypical endometrial hyperplasia	0	0	0	6	6	12
Disordered Proliferative Endometrium	1	3	6	0	0	10
Endometritis	1	1	2	0	0	4
Endometrium with Progestational Effect	3	7	9	4	4	27
Proliferative	1	39	33	2	0	75
Secretory	0	21	56	5	3	85
Non-atypical endometrial hyperplasia	0	0	2	6	1	9

Table 4: Association of endometrium pathology and endometrial thickness cutoff value

Histo Findings	Endometrial Thickness		P Value
	< 14.20 mm	≥ 14.20 mm	
Normal Histo	178 (93.2%)	19 (37.3%)	<0.001
Abnormal Histo	13 (6.8%)	32 (62.7%)	

**Figure 2:** ROC curve for malignancy

abnormal histology while only 6.80% of patients with the endometrial thickness <14.20 were reported to have abnormal histology which was statistically significant ($p < 0.001$).

4. Discussion

Present study was conducted on 242 participants with average age of the patients recorded as 45.28 ± 4.76 years and majority of them belong to lower socioeconomic status. Our age distribution profile is similar to several studies.^{13–15}

In our study most of the women are multiparous and have normal BMI similar to study of Pillai and Shrestha et al.^{2,16} Present study recorded mean hemoglobin level as 10.55 ± 1.50 gm/dl. Half of the patients had mild anaemia and 4.4% with severe anaemia which correlates with the study of many others.^{6,7}

HMB was the most common menstrual disturbance ($n=128, 51.2\%$) observed in our study followed by Frequent menstrual bleeding ($n=39, 15.6\%$). Our finding is in resonance with the study conducted by Jaiswal et al. and Shobhita et al, where a higher percentage of HMB was reported by Katke et al (74.24%).^{17–19}

Distribution of USG findings in perimenopausal age group reflects various pathology in different studies. Fibroid uterus is the most common observation in majority of studies.^{2,3,20–22} Our study also recorded fibroid uterus as common association (21.6%) followed by Adenomyosis (13.2%).

Regarding the endometrial thickness observed in our study majority fall in the category of 11–15mm which is similar to several studies.^{2,5,7,16,23}

In the present study, secretory and proliferative pattern was noted in similar frequency in the current study (34% v/s 30%) which was in contrast to other study made by Pillai et al., Shrestha et al. and Acharya et al.^{2,16,24} who observed proliferative pattern to be the commonest. It could be due to equal distribution of ovulatory and anovulatory AUB in premenopausal group in our studies. Around 0.4% of our cases revealed atrophic endometrium which is in contrast to Pillai's study who obtained a higher percentage (4.6%) of the same. Benign Endometrial Polyp was observed in 6.4% cases where as some other study of Lohit et al. found the same in 3.8%.^{2,3,16,24} In our study disordered proliferative endometrium was in 4.4% whereas some other study by Pillai et al. found higher percentage (22.7%) of it.² Around 8.7% of cases had endometrial hyperplasia out of them the complex hyperplasia was obtained in 4.9% and adenocarcinoma was found in 2.9% of cases where as

Table 5: Comparison of endometrial thickness

Endometrial Thickness	Pillai SS - 2014	Sur D & Chakravorty R(2016)	Bishnu Prasad Das(2017)	Shrestha et al - 2018	Sujana G (2020)	Present Study
<5mm	3.41%	17.07%	3%	1.90%	3.66%	2.80%
5-10mm	46.59%	32.32%	34%	35.24%	46.86%	30.00%
11-15mm	22.73%	42.07%	42%	48.57%	39.01%	47.20%
16-20mm	17.04%	6.71%	15%	11.43%	8.38%	12.40%
>20mm	10.23%	1.83%	6%	2.86%	2.09%	7.60%

in study done by Pillai et al. and Shrestha et al. atypical hyperplasia (5.7% and 8.5%) and adenocarcinoma (4.6%) was found in higher percentage.²⁻¹⁶

In the present study based on the ROC curve and Youden's Index, the cutoff point for the endometrial thickness with the highest sensitivity and specificity for Abnormal Histology is 13.75 mm. Several other studies reported variable endometrial thickness with cut-off value of 13.0 mm, >11 mm, ≥ 10 mm and 10.5 mm respectively for Abnormal Histology.^{6,25-27} Hence it is not easy to pinpoint the critical cut-off range for abnormal histology. However, the cut-off can be put in between range of 10-14 mm. None of the critical values decided in the cited studies above had been performed with optimal standardization of ultrasound schedule in regard to the menstrual cycle.

5. Limitation of Study

1. The study has combined both peri-menopausal and postmenopausal women where the cut-off value for finding significant endometrial pathology is different.
2. USG was performed independent of phase of menstrual cycle.

5.1. Strength of Study

Our study adds to the small sphere knowledge that has targeted endometrial thickness in peri-menopausal and post-menopausal females with AUB. The current study also had the advantage of the direct visualization of endometrial pathology as majority of the cases underwent hysteroscopic evaluation and hysterectomy.

6. Conclusion

In the present study peri menopausal AUB may present to gynecological outpatient department with varied complaints. Out of them heavy menstrual bleed and frequent cycle were found to be commonly associated with gynaecological pathology in these age groups. In all peri menopausal AUB Trans vaginal sonography for endometrial thickness is the initial best modality of investigation. Combining colour Doppler is complementary and it enhances further diagnostic accuracy of endometrial evaluation. Endometrial biopsy for histopathological

examination should be offered to all perimenopausal AUB with cut off value equal to or more than 13mm. However, with positive doppler findings, focal abnormality, coexisting risk factors such as obesity, diabetes, age greater than or equal to 45 years or presence of post-menopausal bleeding, endometrial biopsy should be considered irrespective of the thickness as there is increased chance of having significant endometrial pathology.

7. Source of Funding

Nil.

8. Conflict of Interest

Nil.

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