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Diagnostic Accuracy of Endometrial Thickness in Diagnosing Endometrial Hyperplasia by Taking Endometrial Sampling as the Gold Standard in Patients with Post-Menopausal Bleeding

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ABSTRACT

Background: Endometrial hyperplasia is most common with post-menopausal bleeding (PMB). The clinical tests to evaluate the endometrium include transvaginal ultrasound scanning (TVS) to measure endometrial thickness (ET) and endometrial sampling (ES) with hysteroscopy as gold standard. **Objective:** To determine diagnostic accuracy of endometrial thickness in diagnosing endometrial hyperplasia by taking endometrial sampling as the gold standard in patients with post-menopausal bleeding. **Study Design:** Cross-sectional study. **Settings:** Department of Obstetrics & Gynecology, Allied & DHQ Hospitals affiliated with Faisalabad Medical University, Faisalabad Pakistan. **Duration:** January 01, 2022 till March 31, 2022. **Methods:** A total of 150 patients fulfilling the inclusion criteria were recruited. Endometrial sampling was obtained by using a pipelle sampler. Patient's characteristics taken into account were age, parity, body mass index, hypertension and diabetes. Histological findings were compared to measure the diagnostic accuracy of endometrial hyperplasia. **Results:** The mean age of patients was 55.29 ± 2.91 years with minimum and maximum age as 50 and 60 years. Endometrial hyperplasia was diagnosed in 67(44.7%) females on sampling and in 71(47.3%) females on endometrial thickness by USG. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of endometrial thickness was 82.09%, 80.72%, 77.46%, 84.81% and 81.33%. **Conclusion:** It is concluded that endometrial thickness is useful for diagnosis of endometrial hyperplasia in females with post-menopausal bleeding and used even in low source settings as ultrasonography requires basic ultrasound knowledge.

Keywords: *Endometrial thickness (ET), Endometrial sampling (ES), Endometrial hyperplasia, Post-menopausal bleeding(PMB).*

INTRODUCTION

Endometrial hyperplasia is currently the most common disease of the female genital tract in Europe and South Asia. Around 65% of women eventually diagnosed with endometrial hyperplasia initially presented with post-menopausal bleeding (PMB).[1] The aim in the evaluation of PMB is to exclude underlying malignancy. Clinical tests to evaluate the endometrium are transvaginal ultrasound scanning (TVS), endometrial sampling (ES) and hysteroscopy.[1,2]

Transvaginal ultrasound has been recommended as a first-line investigation, because it is less invasive compared to the other tests that require uterine instrumentation. There are however, different endometrial thickness (ET) cut-off values recommended by various professional groups. The Society of Gynecological Oncology and Society of Obstetricians and Gynecologists of Canada recommend <5 mm,[4] the American College of Obstetricians and Gynecologists (ACOG) committee recommends ≤4 mm, and the National Clinical Guideline of the Scottish Intercollegiate Guidelines Network recommends ≥3 or

≥5 mm to be used, depending on whether the patient is using hormone replacement therapy (HRT) or not.[3,4]

Rationale of this study is to determine diagnostic accuracy of endometrial thickness on TVS in diagnosing endometrial hyperplasia by taking endometrial sampling as the gold standard in our population. As Pakistan is resource limited country and transvaginal ultrasound is easy to carry out, requires basic ultrasound knowledge and is cost effective this study was useful addition to diagnostic modalities available here for endometrial hyperplasia. No local study is available.

The clinical importance of diagnosis of EH relates to the long-term risk of progression to endometrial carcinoma and it is generally accepted that cytological atypia is the principal histological characteristic when assessing EHs for malignant potential. However, not all EHs will progress to malignancy; some EHs occur secondary to estrogenic proliferation without an underlying malignant mechanism. These patients may be asymptomatic and, in some cases, the EH may regress without ever being detected. Ultrasonography to measure endometrial echo should be offered as an initial evaluation only to women with postmenopausal bleeding for whom no further evaluation would be needed if a thin echo is found. Persistent or recurrent bleeding should trigger additional evaluation.

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.[5] The best diagnostic strategy for diagnosing endometrial carcinoma in patients with PMB still remains controversial. We took 4mm cut of value for endometrial thickness.

METHODS

The study was conducted at Department of Obstetrics & Gynecology Allied & DHQ Hospitals affiliated with Faisalabad Medical University, Faisalabad Pakistan from January 01, 2022 till March 31, 2022.

By non-probability consecutive sampling, sample size of 150 cases was calculated with 95% confidence level with 12% margin of error and expected percentage of endometrial hyperplasia as 65%, with sensitivity and specificity as 50.0% and 74%. It was Cross-Sectional Study.

All postmenopausal female patients with symptom of postmenopausal bleeding (PMB) were included. All other postmenopausal patients without bleeding and on hormonal therapy (HRT) were excluded. Patients were selected and written informed consent was obtained.

A total of 150 patients fulfilling the inclusion criteria were included. Transvaginal ultrasound of pelvis was done. ES was obtained by using a pipelle sampler. Patient's characteristics taken into account were age, parity, body mass index, hypertension and diabetes. Histological findings were compared to measure the diagnostic accuracy of Endometrial Hyperplasia. Likewise, endometrial thickness cut-off value was tested to measure their diagnostic accuracy for intra-uterine lesions.

Data was analyzed by SPSS v23.0. Quantitative variables like age and BMI were presented as Mean ± S.D. Qualitative variables like parity, hypertension and diabetes and endometrial hyperplasia on ET and ES were presented as frequency and percentages. A 2x2 contingency was generated to calculate sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy. Data was stratified for age, parity, hypertension, BMI and diabetes to address the modifier effect. Post stratification, diagnostic accuracy was calculated.

RESULTS

The mean age of patients was 60.29 ± 2.91 years with minimum and maximum age as 55 and 65 years. There were 61(40.7%) cases who were 55-59 years old and 89(59.3%) cases were 56-65 years old. The mean BMI was 28.99 ± 3.91 with minimum and maximum BMI as 22.20 and 36.90. There were 49(32.7%) obese and 101(67.3%) non-obese cases. A total of 84(56%) female had parity < 3 and 66(44%) females had parity ≥ 3. There were 25(16.7%) females who had hypertension and 41(27.3%) females were diabetic. Endometrial hyperplasia was diagnosed in 67(44.7%) females on ES and was seen in 71(47.3%) females on ET. There were 16 FP and 12 FN. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ET was 82.09%, 80.72%, 77.46%, 84.81% and 81.33%. (Table 1)

Table 1: Comparison of endometrial hyperplasia on ET in endometrial hyperplasia on ES

Endometrial Hyperplasia		on ES		Total
		Yes	No	
on ET	Yes	55	16	71
	No	12	67	79
Total		67	83	150

Sensitivity	82.09%
Specificity	80.72%
Positive predictive value	77.46%
Negative predictive value	84.81%
Accuracy	81.33%

Among 55-59 years old females, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ET was 81.48%, 76.47%, 73.33%, 83.87% and 78.69%. Among 60-65 years old female the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ET was 82.50%, 83.67%, 80.49%, 85.42% and 83.15% respectively. (Table 2)

Table 2: Comparison of endometrial hyperplasia on ET in endometrial hyperplasia on ES with respect to age groups (years)

Age groups (years)	Endometrial Hyperplasia on ET	Endometrial Hyperplasia on ES		Total
		Yes	No	
55-59	Yes	22	8	30
	No	5	26	31
60-65	Yes	33	8	41
	No	7	41	48

Age groups (years)	55-59	60-65
Sensitivity	81.48%	82.50%
Specificity	76.47%	83.67%
Positive predictive value	73.33%	80.49%
Negative predictive value	83.87%	85.42%
Accuracy	78.69%	83.15%

Among obese cases, the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ET was 76.19%, 85.71%, 80.00%, 82.76% and 81.63%. Among non-obese females the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ET was 84.78%, 78.18%, 76.47%, 86.00% and 81.19% respectively. (Table 3)

Table 3: Comparison of endometrial hyperplasia on ET in endometrial hyperplasia on ES with respect to BMI

BMI	Endometrial Hyperplasia on ET	Endometrial Hyperplasia on ES		Total
		Yes	No	
Obese	Yes	16	4	20
	No	5	24	29
Non-obese	Yes	39	12	51
	No	7	43	50

BMI	Obese	Non-obese
Sensitivity	76.19%	84.78%
Specificity	85.71%	78.18%
Positive predictive value	80.00%	76.47%
Negative predictive value	82.76%	86.00%
Accuracy	81.63%	81.19%

The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ET was 79.07%, 78.05%, 79.07%, 78.05% and 78.57% among females who had parity < 3. (Table 4)

Table 4: Comparison of endometrial hyperplasia on ET in endometrial hyperplasia on ES with respect to diabetes mellitus

Diabetes mellitus	Endometrial Hyperplasia on ET	Endometrial Hyperplasia on ES		Total
		Yes	No	
Yes	Yes	8	10	18
	No	7	16	23
No	Yes	47	6	53
	No	5	51	56

Diabetes mellitus	Yes	No
Sensitivity	53.33%	90.38%
Specificity	61.54%	89.47%
Positive predictive value	44.44%	88.68%
Negative predictive value	69.57%	91.07%
Accuracy	58.54%	89.91%

DISCUSSION

Postmenopausal bleeding (PMB) is defined as bleeding that occurs after 1 year of amenorrhea in a woman who is not receiving hormone therapy (HT).[5] Women on continuous progesterone and estrogen hormone therapy can expect to have irregular vaginal bleeding, especially for the first 6 months. This bleeding should cease after 1 year. Women on estrogen and cyclical progesterone should have a regular withdrawal bleeding after stopping the progesterone. Around 90% of women eventually diagnosed with endometrial cancer initially presented with postmenopausal bleeding (PMB). The aim in the evaluation of PMB is to exclude underlying malignancy.[6]

A study reported mean age of the patients was 65.56 ± 6.11 years.[7,8] In current study the mean age of patients was 60.29 ± 2.91 years with minimum and maximum age as 55 and 65 years. In current study the mean age was less, in current study the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ET was 82.09%, 80.72%, 77.46%, 84.81% and 81.33%.

In this study, it was found that the overall sensitivity and specificity of endometrial thickness in diagnosing endometrial hyperplasia were 50.0% and 96.9%. In comparison to another studies, it was found that, the overall sensitivity and specificity of endometrial thickness in diagnosing endometrial hyperplasia were 93.5% and 74.0%.[9, 10] These findings are inconsistent with our findings. Another study was done to determine the diagnostic accuracy of transvaginal ultrasound for detection of endometrial malignancy in females presenting with PMB taking histopathology as gold standard.[11] The sensitivity of TVS was 86.3% with specificity of 93.0%, PPV was 91.3%, NPV was 88.9% and diagnostic accuracy was 89.9% taking histopathology as gold standard. Thus, it can be concluded that the TVS is

safe, acceptable and easily available procedure for detection of endometrial malignancy in females presenting with PMB.

The sensitivity and specificity of TVS endometrial thickness measurement in the prediction of endometrial carcinoma were 0.83 (95% CI, 0.19–1.00) and 0.72 (95% CI, 0.23–0.95) for a 5mm cutoff and 0.33 (95% CI, 0.04–0.85) and 0.94 (95% CI, 0.92–0.96) for a 6mm cut off.[11] So, the study concluded that the results from this systematic review do not justify the use of endometrial thickness as a screening test for endometrial carcinoma and atypical endometrial hyperplasia in asymptomatic postmenopausal women not using HRT. Likewise, in another study the optimum endometrial thickness cutoff for endometrial cancer or atypical EH was 5.15 mm, with sensitivity of 80.5% (95% CI 72.7–86.8) and specificity of 86.2% (85.8–86.6). Sensitivity and specificity at a 5 mm or greater cutoff were 80.5% (72.7–86.8) and 85.7% (85.4–86.2); for women with a 5 mm or greater cutoff plus endometrial abnormalities, the sensitivity and specificity were 85.3% (78.2–90.8) and 80.4% (80–80.8), respectively. For a cutoff of 10 mm or greater, sensitivity and specificity were 54.1% (45.3–62.8) and 97.2% (97.0–97.4).[10,11] Thus, the findings showed that TVS screening for endometrial cancer has good sensitivity in postmenopausal women. The burden of diagnostic procedures and false-positive results can be reduced by limiting screening to a higher-risk group. The role of population screening for endometrial cancer remains uncertain, but the findings are of immediate value in the management of increased endometrial thickness in postmenopausal women undergoing pelvic scans for reasons other than vaginal bleeding.

CONCLUSION

It is concluded that endometrial thickness is useful for diagnosis of endometrial hyperplasia in females with post-menopausal bleeding. Hence endometrial thickness can be used even in low source settings as ultrasonography requires basic ultrasound knowledge. Moreover, this is cost effective method and can be useful for early detection and management.

LIMITATIONS

The limitations of study were due to study design, limited sample size, short duration period, and restricted study setting. Lack of availability of new research studies on this topic for comparison. The diagnostic tools were limited.

SUGGESTIONS / RECOMMENDATIONS

Study method should be prospective and for longer time period with larger sample size.

CONFLICT OF INTEREST / DISCLOSURE

There was no larger conflict of interest in study for financial and other personal considerations.

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REFERENCES

1. The American College of Obstetricians and Gynaecologists The role of transvaginal ultrasonography in the evaluation of postmenopausal bleeding ACOG Obstet Gynecol. 2013;114:409–11.
2. Piróg M, Kacalska-Janssen O, Bereza T, Jach R. The thin red line - postmenopausal abnormal uterine bleeding with endometrial thickness less than 4 mm. Contemp Oncol (Pozn). 2019;23(1):43-46.
3. Aggarwal A, Hatti A, Tirumuru SS, Nair SS. Management of Asymptomatic Postmenopausal Women Referred to Outpatient Hysteroscopy Service with Incidental Finding of Thickened Endometrium - A UK District General Hospital Experience. J Minim Invasive Gynecol. 2021 Oct;28(10):1725-1729.
4. Ozer A, Ozer S, Kanat-Pektas M. Correlation between transvaginal ultrasound measured endometrial thickness and histopathological findings in Turkish women with abnormal uterine bleeding. J Obstet Gynaecol Res. 2016 May;42(5):573-8.
5. Sanderson PA, Critchley HO, Williams AR, Arends MJ, Saunders PT. New concepts for an old problem: the diagnosis of endometrial hyperplasia. Hum Reprod Update. 2017 Mar 1;23(2):232-254.
6. Wong AS, Lao TT, Cheung CW, Yeung SW, Fan HL, Ng PS, et al. Reappraisal of endometrial thickness for the detection of endometrial cancer in postmenopausal bleeding: a retrospective cohort study. BJOG. 2016 Feb;123(3):439-46.
7. Iqbal R, Khan F, Khurshid S. Diagnostic Accuracy of Transvaginal Ultrasound with Histopathological findings in Postmenopausal Bleeding. Age (years). 2018 Jul 1;65:6-11.
8. Breijer M, Peeters JA, Opmeer BC, Clark TJ, Verheijen RH, Mol BW, Timmermans A. Capacity of endometrial thickness measurement to diagnose endometrial carcinoma in asymptomatic postmenopausal women: a systematic review and meta-analysis. Ultrasound in obstetrics & gynecology. 2012 Dec;40(6):621-9.
9. Elsandabesee D, Greenwood P. The performance of Pipelle endometrial sampling in a dedicated postmenopausal bleeding clinic. Journal of obstetrics and gynaecology. 2005 Jan 1;25(1):32-4.
10. Abid M, Hashmi AA, Malik B, et al. Clinical pattern and spectrum of endometrial pathologies in patients with abnormal uterine bleeding in Pakistan: need to adopt a more conservative approach to treatment. BMC Womens Health. 2014;14:132.
11. Reijnen C, Visser NCM, Bulten J, Massuger LFAG, van der Putten LJM, Pijnenborg JMA. Diagnostic accuracy of endometrial biopsy in relation to the amount of tissue. J Clin Pathol. 2017 Nov;70(11):941-946.