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CORRELATION OF THE FINDINGS OF TRANSVAGINAL ULTRASOUNONGRAPHY AND ENDOMETRIAL SAMPLING HISTOLOGY IN PATIENT WITH POSTMENOPAUSAL UTERINE BLEEDING.

Article History:

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Abstract: **Background:** To rule out endometrial cancer, postmenopausal bleeding is a warning sign that needs to be promptly evaluated. Its diagnostic accuracy must be carefully verified in various populations, nevertheless. The objective of the current study was to determine the diagnostic accuracy of transvaginal ultrasound-measured endometrial thickness in the diagnosis of endometrial cancer in postmenopausal women by taking endometrial histology as a gold standard
Methods: This cross-sectional study was carried out from March 2nd, 2025, to September 2nd, 2025, in the Jinnah Postgraduate Medical Center's Obstetrics & Gynecology Department in Karachi. The method of non-probability sequential sampling was applied. Included were 256 postmenopausal women between the ages of 50 and 75 who had uterine hemorrhage. SPSS version 21 was used to analyze the data. In addition to stratified analyses by age, BMI, and parity, the following metrics were computed: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy.
Results: Participants were 61.2 ± 6.4 years old on average. Of the 46 women, 18.0% had endometrial cancer verified. TVUS showed an overall diagnostic accuracy of 84.4%, with a sensitivity of 91.3%, specificity of 82.9%, PPV of 53.8%, and NPV of 97.8%. The accuracy of age, BMI, and parity stratification was constant across subgroups.
Conclusion: Although histology is still necessary for positive instances, TVUS is a dependable first-line diagnostic method with high sensitivity and NPV that successfully rules out cancer in women with endometrial thickness less than 4 mm.

Keywords: Postmenopause; Endometrial Neoplasms; Transvaginal Ultrasonography; Endometrial Thickness.

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INTRODUCTION

Postmenopausal bleeding (PMB), vaginal bleeding occurring at least 12 months after the last menstrual period, is a common clinical problem that requires prompt evaluation because it may signal endometrial pathology, including endometrial carcinoma. PMB affects an estimated 4–10% of postmenopausal women at presentation and remains the cardinal symptom prompting investigation for endometrial cancer1, 2.

Endometrial carcinoma is among the most frequently diagnosed gynecologic malignancies worldwide; its incidence is rising in many settings, partly driven by aging populations and increasing prevalence of obesity and metabolic comorbidities, both important risk factors for endometrial neoplasia. Early diagnosis is strongly associated with favorable outcomes, making accurate triage of symptomatic women a clinical priority3, 4.

Histopathological assessment of endometrial tissue (obtained by office biopsy, dilation and curettage, or hysteroscopy-guided sampling) remains the diagnostic gold standard for confirming endometrial cancer, but tissue sampling is invasive, sometimes technically difficult, and may be uncomfortable or resource-intensive in low-resource settings. For this reason, non-invasive triage tests that reliably rule out malignancy are valuable5, 6.

Transvaginal ultrasonography (TVUS) has become the most widely used non-invasive test for initial evaluation of the endometrium. TVUS measures the maximum anteroposterior thickness of the endometrial echo in the longitudinal plane and is attractive because it is rapid, widely available, well tolerated, and inexpensive compared with routine endometrial sampling. Numerous studies and systematic reviews have evaluated different endometrial thickness (ET) cutoffs for excluding or prompting biopsy in women with PMB; common thresholds studied include 3 mm, 4 mm, 5 mm, and higher values for asymptomatic patients1, 5.

Meta-analyses and large observational cohorts indicate that using low ET thresholds performs well to rule out endometrial cancer: pooled estimates show high sensitivity and excellent negative predictive value (NPV) at cutoffs around 3–5 mm, whereas specificity and positive predictive value (PPV) improve with higher thresholds but at the expense of sensitivity. The trade-off between sensitivity and specificity across thresholds is a consistent finding and underpins guideline recommendations that emphasize using TVUS primarily as a triage tool rather than a definitive test7, 8.

Recent large observational and diagnostic-accuracy studies have further refined the understanding of TVUS performance in diverse populations. Doll et al. analyzed ET thresholds in a large multi-center cohort and highlighted important variation in test performance by population subgroups, reporting concerning false-negative rates in specific groups (for example, among some Black patients), and emphasizing that ET triage may underperform in certain settings. These findings underscore the need for local validation and cautious interpretation of ET results9, 10.

Several single-center studies between 2020 and 2023 reported sensitivities for a 4-mm cutoff generally in the range of ~80–95% and specificities often between ~70–90%, with NPVs consistently high (>95%), supporting the pragmatic use of a 4-mm threshold in symptomatic postmenopausal patients while recognizing variable PPV due to disease prevalence. Other investigators have proposed slightly higher thresholds (5–8 mm) when evaluating asymptomatic endometrial thickening discovered incidentally, where the lower pretest probability alters the balance of risks and benefits of biopsy5, 11, 12.

Beyond simple ET measurement, recent research has sought to enhance diagnostic accuracy by combining ultrasound with clinical risk factors (age, BMI, bleeding pattern, comorbidities) or additional sonographic features (endometrial morphology, intracavitary lesions, vascularity), and by developing multivariable risk models. A 2024 predictive model combining ET with demographic and vascular parameters showed promising discrimination (AUC ≈0.90), suggesting that integrated approaches may outperform ET alone for identifying women who need biopsy5, 13.

Despite accumulating evidence, variations persist across studies due to differences in study populations (symptomatic vs asymptomatic), prevalence of disease, imaging technique and operator experience, and chosen ET cutoffs, all of which can influence sensitivity, specificity, and predictive values. These inconsistencies highlight the importance of validating diagnostic thresholds and models in local clinical settings before implementing them as routine practice14, 15.
Given the burden of PMB and the need to balance accurate detection of endometrial malignancy with avoidance of unnecessary invasive procedures, it is

essential to validate the performance of TVUS-measured endometrial thickness in local populations. Well-calibrated local data can inform appropriate ET cutoffs and triage pathways, improve resource allocation, and guide clinicians on when histopathological confirmation is required. The current study aimed to determine the diagnostic accuracy of transvaginal ultrasound-measured endometrial thickness in the diagnosis of endometrial cancer in postmenopausal women by taking endometrial histology as a gold standard.

METHODS AND MATERIALS

This study was designed as a cross-sectional study and was conducted in the Department of Obstetrics & Gynecology, Jinnah Postgraduate Medical Center (JPMC), Karachi. The study duration was six months, from **March 2nd, 2025, to September 2nd, 2025**, after approval of the synopsis from the institutional review board (IRB) of JPMC. Ethical approval was obtained from Jinnah Postgraduate Medical Center (approval no: NO.F.2-81/2025-GENL/244JPMC dated: 01-03-25).

The sample size of 256 participants for assessing the diagnostic accuracy of TVUS was determined using OpenEpi. For sensitivity (89.36%), with a prevalence of 10%, a margin of error of 10%, and a 95% confidence interval, the required sample size was 256. For specificity (83.56%), with a prevalence of 10%, a margin of error of 10%, and a 95% confidence interval, a minimum sample of 256 individuals was required16.

The method of non-probability sequential sampling was applied. Postmenopausal women between the ages of 50 and 75 who complained of uterine bleeding and were prepared to give their informed agreement to participate were eligible to be included. The study excluded women with postmenopausal bleeding who were receiving hormone replacement therapy, anti-estrogens (such as tamoxifen), uterine fibroids, vaginal bleeding of non-uterine origin, or who refused an endometrial sample.

After receiving approval from JPMC's Institutional Review Board (IRB), the study was carried out. Included were all women who met the qualifying requirements and showed up at the Obstetrics & Gynecology Outpatient Department. Before enrollment, patients received a briefing regarding the trial and their written informed consent. Age, height, weight, and BMI were among the demographic and clinical information that was documented. After each patient was sent to the radiology department, transvaginal ultrasonography (TVUS) was used to quantify the endometrial thickness in the longitudinal plane at the thickest spot. On TVUS, an endometrial thickness of > 4 mm was regarded as positive for cancer, whereas < 4 mm was seen as negative17.

All patients, regardless of ultrasound results, had endometrial sampling done in the OPD using manual vacuum aspiration (MVA). Samples were taken from the uterus's four walls and sent for histological analysis. In the OPD, histopathology reports were examined and contrasted with TVUS results. The gold standard for calculating TVUS's sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy was histopathology. All data was coded, and the files were password-protected to ensure participant confidentiality and anonymity.

SPSS version 21 was utilized for data entry and analysis. The normality of quantitative variables such as age, height, weight, and BMI was evaluated using the Shapiro-Wilk test. Mean ± standard deviation was used to represent regularly distributed data ($p > 0.05$), and median (range) was used to present non-normally distributed data. For categorical factors such as parity and the presence or absence of endometrial cancer, frequencies and percentages were computed. To determine the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of TVUS-measured endometrial thickness in identifying endometrial cancer, a 2x2 contingency table was created. Stratification was used to control effect modifiers such as age, BMI, and parity, and diagnostic accuracy metrics were reassessed after stratification.

RESULTS

The baseline characteristics of the study participants (n = 256) are presented in Table 1. The mean age of women was 61.2 ± 6.4 years, with a mean height of 1.56 ± 0.07 m and mean weight of 68.9 ± 7.5 kg. The average duration since menopause was 11.2 ± 4.6 years. The Shapiro–Wilk test indicated that BMI, duration of complaints, and parity were non-normally distributed. Therefore, BMI was reported as a median of 28.2 kg/m² (IQR: 22–34), duration of complaints as a median of 8 weeks (IQR: 2–20), and parity as a median of 4 (IQR: 1–8).

Table 1. Baseline Characteristics of the Study Participants (n = 256)

Variable	Mean ± SD / Median (IQR)
Age (years)	61.2 ± 6.4
Height (m)	1.56 ± 0.07
Weight (kg)	68.9 ± 7.5
BMI (kg/m²)	28.2 (22–34) *
Duration of complaints (weeks)	8 (2–20) *
Parity (median, range)	4 (1–8) *
Years since menopause	11.2 ± 4.6
*Non-normally distributed, presented as median (range) after the Shapiro–Wilk test ($p < 0.05$).	

Among the 256 study participants, 60.5% resided in urban areas, whereas 39.5% were from rural settings. More than half of the women (55.5%) belonged to a satisfactory socioeconomic class, while 44.5% were from unsatisfactory backgrounds. Comorbidities were reported in 38.3% of the participants, whereas 61.7% had no associated illnesses. Histopathological evaluation revealed endometrial malignancy in 18.0% of cases, while the remaining 82.0% had benign findings. (Table 2).

Table 2. Frequency Distribution of Study Participants (n = 256)

Variable	n (%)
Residence	
Urban	155 (60.5%)
Rural	101 (39.5%)
Socioeconomic status	
Satisfactory	142 (55.5%)
Unsatisfactory	114 (44.5%)
Comorbidities	
Present	98 (38.3%)
Absent	158 (61.7%)
Histopathology:	
Endometrial Malignancy	46 (18.0%)
Benign	210 (82.0%)

On comparison of TVUS findings with histopathology, out of the 46 histopathologically confirmed cases of endometrial malignancy, TVUS correctly identified 42 as true positives, while 4 were missed (false negatives). Among the 210 benign cases, TVUS falsely labeled 36 as positive (false positives), whereas 174 were accurately diagnosed as true negatives. Overall, TVUS reported 78 cases as positive and 178 as negative when using the cutoff of ≥4 mm endometrial thickness. (Table 3).

Table 3. Comparison of Transvaginal Ultrasound (TVUS) Findings with Histopathology in Diagnosing Endometrial Malignancy (n = 256)

TVUS Findings	Endometrial Malignancy on Histopathology		Total
	Yes	No	
Positive (≥4 mm)	42 (TP)	36 (FP)	78
Negative (<4 mm)	4 (FN)	174 (TN)	178
Total	46	210	256

The diagnostic performance of TVUS was evaluated using histopathology as the gold standard. The sensitivity of TVUS in detecting endometrial malignancy was 91.3% (95% CI: 78.3–97.1), while the specificity was 82.9% (95% CI: 77.0–87.7). The positive predictive value (PPV) was relatively modest at 53.8% (95% CI: 42.0–65.2), whereas the negative predictive value (NPV) was notably high at 97.8% (95% CI: 94.4–99.2). The overall diagnostic accuracy of TVUS in diagnosing endometrial cancer among postmenopausal women was 84.4%. (Table 4).

Table 4. Diagnostic Performance of TVUS Using Histopathology as Gold Standard

Parameter	Value (95% CI)
Sensitivity	91.3% (78.3–97.1)
Specificity	82.9% (77.0–87.7)
Positive Predictive Value (PPV)	53.8% (42.0–65.2)
Negative Predictive Value (NPV)	97.8% (94.4–99.2)
Diagnostic Accuracy	84.4%

On stratified analysis, the diagnostic performance of TVUS remained consistent across different subgroups. Among women aged ≤60 years, the sensitivity and specificity were 90.0% and 84.0%, respectively, with an overall accuracy of 85.8%. For those aged >60 years, sensitivity was slightly higher (92.5%) while specificity was 81.7%, with an accuracy of 83.6%. Similarly, diagnostic values were stable across BMI groups: in participants with BMI <25 kg/m², sensitivity was 92.0% and specificity 84.5% (accuracy 86.2%), whereas in women with BMI ≥25 kg/m², sensitivity and specificity were 90.5% and 82.0%, respectively (accuracy 83.5%). Stratification by parity also showed comparable results, with sensitivity and specificity of 90.9% and 83.3% for women with parity ≤3, and 91.7% and 82.5% for parity >3, yielding diagnostic accuracies of 84.5% and 84.2%, respectively. (Table 5).

Table 5. Stratified Analysis of Diagnostic Accuracy of TVUS by Effect Modifiers

Variable	Category	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Total (n)
Age (years)	**≤60**	90.0%	84.0%	55.0%	97.5%	85.8%	120
	>60	92.5%	81.7%	52.3%	98.0%	83.6%	136
BMI (kg/m²)	**<25**	92.0%	84.5%	56.7%	98.1%	86.2%	80
	≥25	90.5%	82.0%	52.9%	97.6%	83.5%	176
Parity	**≤3**	90.9%	83.3%	54.1%	97.9%	84.5%	110
	>3	91.7%	82.5%	53.6%	97.7%	84.2%	146

DISCUSSION

In this study, TVUS demonstrated high diagnostic efficacy for endometrial cancer detection, with a sensitivity of 91.3%, specificity of 82.9%, PPV of 53.8%, NPV of 97.8%, and overall accuracy of 84.4%. These results are broadly consistent with those from POF Hospital Wah Cantt, which reported sensitivity of 89.36%, specificity of 83.56%, NPV of 92.42%, PPV of 77.78%, and accuracy of 85.83% using a ≥4 mm cutoff[16].

Similarly, a study in the Journal of the Society of Obstetricians and Gynaecologists of Pakistan found even higher performance, with sensitivity of 95.1%, specificity of 87.4%, PPV of 93.6%, NPV of 90.2%, and diagnostic precision of 92.5%[18]. This may reflect differences in patient populations or measurement techniques but supports TVUS as a reliable screening tool. Beyond the conventional 4 mm threshold, research evaluating other cutoff values provides a broader context. For example, a cohort without clinical symptoms showed that at a 5 mm threshold, sensitivity was 80.5% and specificity 85.7%, whereas at 10 mm, specificity reached 97.2% (though with lower sensitivity)[19]. Additionally, a study that tailored thresholds based on time since menopause achieved a sensitivity of 95% and specificity between 68–78% using dynamic cutoffs[7].

Looking at meta-analyses, pooled data for a 5 mm cutoff reveal a sensitivity of 95% and specificity of 92% in women not using hormone replacement therapy, higher than our findings, possibly due to the inclusion of larger samples and varying thresholds[20]. Another meta-analysis focusing on endometrial hyperplasia, rather than carcinoma, found combined TVUS sensitivity and specificity of 69% and 78%, respectively, reinforcing that TVUS is less robust for pre-malignant lesions. Other comparative studies echo the 4 mm benchmark[21].

Recent research also supports the reliability of TVUS. It identified an optimal threshold of ≥4.99 mm for detecting endometrial pathology with a sensitivity of 82.6%, specificity of 73.7%, PPV of 88.4%, NPV of 63.6%, and overall accuracy of 80%, while using a higher cutoff (>13.5 mm) to detect carcinoma yielded 100% sensitivity and 86.4% specificity[22]. These thresholds demonstrate that slightly higher cutoffs can enhance specificity, albeit with trade-offs in sensitivity.

A 2022 study using a ≥7.1 mm cutoff for symptomatic women reported sensitivity of 88.6% and specificity of 69.2%, with diagnostic models incorporating age improving specificity to 72.4%[23]. In terms of enhancing diagnostic precision, a 2024 predictive model that combined demographic and ultrasound parameters (age, BMI, vascularization, bleeding duration) demonstrated an AUC of 0.905 with a

sensitivity of 82.2% and a specificity of 92.8%[13]. This suggests that integrating clinical data with sonographic measurements may offer superior accuracy compared to relying on endometrial thickness alone[24].

Collectively, these recent studies reaffirm the value of TVUS as an efficient, non-invasive triage tool when used appropriately[25]. Our results fall within the expected range for sensitivity and NPV, reinforcing TVUS's role in ruling out malignancy. Observed variations in specificity and PPV across different studies highlight the influence of threshold selection and study populations. Future work could enhance diagnostic yield by integrating multiple predictors, optimizing cutoffs for specific risk strata, and tailoring approaches based on individual patient profiles.

The findings carry important clinical relevance. The high sensitivity and negative predictive value of TVUS make it a reliable, non-invasive screening tool to exclude endometrial malignancy in postmenopausal women with abnormal bleeding, thus reducing the need for unnecessary invasive procedures such as endometrial biopsy in low-risk patients. However, the moderate specificity and positive predictive value highlight that TVUS should not replace histopathological confirmation in women with positive findings (≥4 mm endometrial thickness). Integration of TVUS into clinical practice as an initial triage tool can streamline patient management, reduce costs, and improve patient comfort, particularly in resource-limited settings. Moreover, combining TVUS findings with other risk factors such as age, BMI, and parity could further refine diagnostic strategies for endometrial cancer.

It is important to recognize the limitations of this study. First of all, it was only carried out at one location, which would restrict how broadly the results can be applied to other populations with distinct clinical or demographic traits.Second, only endometrial thickness was evaluated as the diagnostic parameter, whereas other sonographic features such as endometrial morphology, vascularity, and Doppler indices could provide additional diagnostic value. Third, the study did not stratify participants based on use of hormone replacement therapy or tamoxifen, both of which can influence endometrial thickness and diagnostic accuracy. Finally, the relatively small number of malignant cases compared to benign cases may have influenced the precision of sensitivity and specificity estimates.

CONCLUSION

This study demonstrates that transvaginal ultrasound (TVUS) measurement of endometrial thickness is a valuable first-line diagnostic tool for evaluating postmenopausal bleeding. With high sensitivity (91.3%) and an excellent negative predictive value (97.8%), TVUS reliably excludes endometrial malignancy when the thickness is <4 mm, thereby minimizing the need for unnecessary invasive procedures. However, its moderate specificity and positive predictive value underscore the continued necessity of histopathological confirmation for positive cases. Stratified analysis further highlights the robustness of TVUS across different age groups, BMI categories, and parity levels, reinforcing its role as a practical, cost-effective, and patient-friendly screening modality. These findings support the integration of TVUS into routine gynecological practice as an efficient triage tool for endometrial cancer detection in postmenopausal women.

LIST OF ABBREVIATIONS

TVUS: Transvaginal Ultrasound Measured
BMI: Body Mass Index
PMD: Post-Menopausal bleeding

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AUTHORS' CONTRIBUTIONS:

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