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DIAGNOSTIC ACCURACY OF ENDOMETRIAL THICKNESS ON ULTRASOUND AND ITS CORRELATION WITH HISTOPATHOLOGY IN FEMALES WITH POSTMENOPAUSAL BLEEDING

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ABSTRACT

Background: The ultrasonic diagnostic represents an accurate and noninvasive approach to examine endometrial thickness in the early diagnosis of endometrial cancer as well as during postmenopausal bleeding. However, there is a paucity of studies in the Pakistani population assessing risk in PMB patients through demographic and clinical factors to inform low-risk early detection strategies.

Objective: To compare the diagnostic accuracy of endometrial thickness on ultrasound with histopathological results and investigate associations of endometrial thickness with demographic and clinical risk factors.

Methods: This prospective cross-sectional study was carried out in Department of Obstetrics and Gynecology, Hameed Latif Hospital, Lahore, Pakistan. Demographic and clinical information such age, BMI, smoking, and other risk factors were documented which were independent variables, and ultrasound (US) was conducted to assess ET, which was dependent variable and abnormal if >4 mm. Endometrial biopsy for histopathological diagnosis was done in all the participants. Data was analyzed using SPSS V. 27.

Results: Participants' mean age was 59.9 ± 6.3 years, mean BMI was 29.1 ± 4.5 kg/m², and mean endometrial thickening was 5.1 ± 3.6 mm. Upon ultrasound, 30.5% had elevated ET, whereas histopathology established abnormalities in 20.5%. Ultrasound showed 90.2% sensitivity, 84.9% specificity, 60.7% positive predictive value PV, 97.1% negative predictive value (NPV), and overall diagnostic accuracy of 86.0%.

Conclusion: Endometrial thickening measured by US has been found to be highly sensitive and specific diagnostic test for assessment of PMB with an excellent NPV, and thus an ideal non-invasive screening test.

KEYWORDS: Body Mass Index; Endometrial Neoplasms; Post menopause; Smoking; Ultrasonography, Transvaginal

INTRODUCTION

Postmenopausal bleeding [PMB] represents a significant clinical concern, serving as the presenting symptom in over 90% of women diagnosed with endometrial carcinoma and warranting immediate evaluation to exclude malignancy [1]. Globally, endometrial cancer ranks as the most common gynecologic malignancy in developed countries, with over 66,000 new cases reported in the United States in 2023 alone [2]. Research illustrates that although about 90% of women with endometrial cancer develop postmenopausal bleeding, barely 9% of women who present with PMB eventually develop endometrial cancer [3-4]. The histopathological spectrum illustrates that 60-80% of cases of atrophic endometrium are followed by endometrial hyperplasia and malignancy; around 11% of postmenopausal bleeding episodes are due to endometrium atrophy [5]. Recent Pakistani studies have reported high rates of malignancy (16%–30%) in PMB patients, which is higher than typical global trends [6].

Asymptomatic endometrial thickening is an ordinary occurrence in postmenopausal women and is usually incidentally revealed during routine ultrasound normal examinations of PMB [7]. Most of these cases have a benign course, but a potential risk of underlining malignancy, including endometrial carcinoma and precursor lesions, necessitates careful consideration. Smith-Bindman et al presented early hints into this issue as early as 2004 [8]. Their theoretical-cohort based decision-analysis showed that in the case of asymptomatic postmenopausal women, with an endometrial biopsy being conducted when the transvaginal ultrasonographic endometrial thickening is at least 11.0 mm, it will be necessary to appropriately assess risks to avoid the delay of malignancy diagnosis [9]. The existing evidence indicates

that endometrial thickness of 5mm or above in a sonogram is highly correlated with a high probability of endometrial malignancy and is thus required to further undergo histopathological testing [10]. The difficulty is to decide which patients require additional tests because unnecessary tests can cause physical, psychological and financial burden to patients and health systems. The risks of malignancy against the cost-effectiveness and the impact of diagnostic procedures is a significant issue in the management of this condition [11].

The PMB has become the most relevant sign of endometrial disease, including cancer and hyperplasia. In the Pakistani context, regional data indicates that benign endometrial pathology accounts for 98% of abnormal uterine bleeding cases, with endometrial cancer representing the third most common female malignancy at 2.49% [12]. Although useful when screening rapidly for potential disease, the accuracy of endometrial thickening as a diagnostic tool varies. Correlating endometrial thickening to the histology of the specimen is the gold standard, and thus is helpful when determining how endometrial thickening can provide reliable means of detecting significant endometrial lesions [13]. Additionally, there is a lack of studies among Pakistani population regarding measuring risk by evaluating PMB patients' associations with demographic and clinical risk factors, which could provide direction for developing low-risk early detection strategies. Thus, this study is aimed to compare the diagnostic accuracy of endometrial thickness on ultrasound with histopathological results and investigate associations of endometrial thickness with demographic and clinical risk factors among Pakistani patients with PMB.

METHODOLOGY

This prospective cross-sectional study was undertaken at the Department of Obstetrics and Gynecology, Hameed Latif Hospital, Lahore, during six months from 10th September 2025 to 10th March 2026 with approval of Institutional Ethics Committee (HLH/ADM/IRB/2025-026) on 03 September 2025.

To calculate the sample size, we used a confidence level of 95% with a sensitivity of 90.2% for detecting endometrial pathology by transvaginal ultrasound and a prevalence of 20.5% of endometrial pathology based on prior research. Using the standard formula for diagnostic accuracy studies, we arrived at an estimated sample size of 200 patients [14].

Women aged 45–75 years with postmenopausal bleeding (vaginal bleeding >12 months after the last menstrual period) were included. Patients with vaginal infection, premalignant or malignant vulval, vaginal, or cervical lesions, cervical/endocervical disease, adnexal masses, bleeding disorders, or previous tamoxifen or hormone therapy were excluded.

All the enrolled women were subjected to standardized transvaginal ultrasonography by experienced sonographers of at least 5-year experience. The thickness of endometrium was taken at the thickest point in the sagittal plane. Endometrial thickness >4 mm was regarded as positive endometrial disorder. All patients were then subjected to hysteroscopy, and biopsy samples were taken for histopathological examination, which was considered the reference standard. Endometrial pathology was any histologically proven abnormality such as hyperplasia, polyp, fibroid, or malignancy. Baseline demographic and clinical information such as age, BMI, parity, marital status, number of vaginal deliveries, symptom duration, smoking status (>5 pack-years), family history of endometrial pathology, and intrauterine contraceptive use were documented on a pre-designed proforma.

Data were statistically analyzed with SPSS version 27.0. Descriptive statistics were performed to compute continuous variables in mean ± SD and categorical variables using frequencies and percentages. The diagnostic accuracy metrics (sensitivity, specificity, positive predictive value, negative predictive value, false positive/negative rates, and overall accuracy) were calculated using histopathology as the gold standard by comparing to the ultrasound findings. After performing normality test with the Shapiro-Wilk test, Chi-square test and Spearman correlation were performed to determine the relationships between ultrasound and histopathological results and a p-value of less than 0.05 as significant.

RESULTS

The study population was 59.9 years with a standard deviation of 6.3 years, thus having a late postmenopausal population. The average body mass index of was 29.1 4.5kg/m 2 indicating an overweight population, a known risk factor in endometrial pathology. The mean endometrial thickness was 5.1 ± 3.6 mm which is above the generally validated threshold of 4mm of abnormality indicating a relatively higher abnormality burden in this group. Participant population consisted of mainly multiparous (89.0%), who had a history of vaginal delivery (76.5%) and were mainly married (94.0%). The prevalence of smoking was significant (22.5%), and it could lead to pathological alterations according to the following analyses. The family history of postmenopausal bleeding and endometrial cancer were comparatively low, 9.0% and 4.5% of the participants, respectively.

Table 1: Demographic and clinical profile of participants(n=200)

Variable	Mean ± SD / n (%)
Age (years)	59.9 ± 6.3
BMI (kg/m²)	29.1 ± 4.5

Endometrial Thickness (mm)	5.1 ± 3.6
Duration of Symptoms (months)	5.06 ± 3.38
Parity	
Nulliparous	22 (11.0%)
Multiparous (≥1)	178 (89.0%)
Vaginal Deliveries	
None	47 (23.5%)
≥1	153 (76.5%)
Marital Status	
Married	188 (94.0%)
Unmarried	12 (6.0%)
Smoking Status	
Non-smokers	155 (77.5%)
Smokers	45 (22.5%)
Family History of PMB	
Yes	18 (9.0%)
No	182 (91.0%)
Family History of Endometrial Cancer	
Yes	9 (4.5%)
No	191 (95.5%)
IUCD Use	
Yes	12 (6.0%)
No	188 (94.0%)

The normality test showed that age and BMI were normally distributed ($p > 0.05$), indicating that parametric tests (independent t-test or Pearson correlation) could be used to test these variables. Conversely, endometrial thickness and duration of symptoms did not follow a normal distribution ($p < 0.05$), suggesting that both had skewed distribution. This difference guarantees the statistical validity and enhances the methodological rigor of the study.

Table 2: Tests of Normality for Continuous Variables

Variable	Kolmogorov-Smirnov (p-value)	Shapiro-Wilk (p-value)
Age	0.072	0.089
BMI	0.065	0.078
Endometrial Thickness	0.001	0.001*
Duration of Symptoms	0.003	0.001*

** denotes significant correlation due to ≤ 0.05*

Statistically significant results were found for the association of smoking with both ultrasound and histopathological findings ($p < 0.001$). Of the non-smokers, 80.6% of patients had negative ultrasound findings and 88.4% had negative histopathological findings, while 68.9% of smokers had positive ultrasound findings and 51.1% had positive histopathological findings, indicating that smoking can significantly increase the likelihood of having abnormal endometrial findings.

Table 3 Association Between Smoking and Ultrasound and Histopathological Finding of Endometrial Disorder(n=200)

Category	Smoking No (n=155) n (%)	Smoking Yes (n=45) n (%)	p-value
Ultrasound Findings			<0.001*
Negative	125 (80.6%)	14 (31.1%)	
Positive	30 (19.4%)	31 (68.9%)	
Histopathology Findings			<0.001*
Negative	137 (88.4%)	22 (48.9%)	
Positive	18 (11.6%)	23 (51.1%)	

** denotes significant correlation due to ≤ 0.05*

Ultrasound showed an excellent negative predictive value of 97.1%, a positive predictive value of 60.7%, and a sensitivity of 90.2% and specificity of 84.9%. With a false positive rate of 15.1% and a false negative rate of 9.8%, the overall diagnostic accuracy was 86.0%.

Table 4. Diagnostic accuracy of transvaginal ultrasound compared with histopathology (gold standard) for detection of endometrial pathology (n=200).

	Histopathology Positive (n=41)	Histopathology Negative (n=159)	Total
Ultrasound Positive	37 (90.2%) (TP)	24 (15.1%) (FP)	61
Ultrasound Negative	4 (9.8%) (FN)	135 (84.9%) (TN)	139
Total	41 (100%)	159 (100%)	200

Values are presented as frequency (percentage). Percentages are calculated column-wise using histopathology as the gold standard. TP: True Positive; FP: False Positive; FN: False Negative; TN: True Negative.

Spearman's correlation analysis revealed a statistically significant positive relationship between endometrial thickness and age ($r_s = 0.21$, $p = 0.003$), suggesting that increasing age is modestly associated with greater endometrial thickness. A stronger correlation was observed with BMI ($r_s = 0.34$, $p < 0.001$), indicating that higher body mass index may contribute to increased endometrial proliferation, possibly due to estrogenic effects of adipose tissue. Likewise, there was a strong positive correlation between duration of symptoms ($p<0.001$) suggesting that the longer the bleeding, the greater the endometrial thickness. Smoking status was the most correlated ($p < 0.001$) and supports its importance as an important risk factor of endometrial pathology.

Table 5. Correlation of Endometrial Thickness with Clinical Variables

Variable	Correlation Coefficient (r_s)	p-value
Age	0.21	0.003*
BMI	0.34	<0.001*
Duration of Symptoms	0.29	<0.001*
Parity	-0.12	0.089
Smoking Status	0.41	<0.001

** denotes significant correlation due to ≤ 0.05*

DISCUSSION

This research was aimed to compare the diagnostic accuracy of endometrial thickness on ultrasound with histopathological results and investigate associations of endometrial thickness with demographic and clinical risk factors. Significant associations between increased endometrial thickness and histopathological abnormalities in women who present with postmenopausal bleeding are highlighted by this cross-sectional study. In this study, the average endometrial thickness was 5.1 ± 3.6 mm, with 20.5% of cases confirmed endometrial disorders on biopsy and 30.5% exhibiting increased thickness on ultrasound. These results are consistent with recent qualitative research that found comparable mean thickness of the endometrium thresholds linked to pathology. The diagnostic significance of thickened endometrium in this population was highlighted by Ai et al. (2023), who determined a cut-off of ≥14 mm to define abnormal histology, with a sensitivity of 71% and specificity of 90% in cases of perimenopausal and postmenopausal bleeding [15]. A statistically significant association between thickness and pathology was confirmed by another study from by Wang et al., (2025), which found that 70.8% of PMB women had abnormal histopathology, mainly endometrial hyperplasia, and 58.5% of them had thickness >5 mm (mean 9.1 ± 6.1 mm) (p=0.001) [16]. These support the current study's conclusion that ultrasound has a high diagnostic accuracy of 86%, with sensitivity and specificity of 90.2% and 84.9%, respectively.

Additionally, our findings showed that women who had positive histopathological or ultrasound results were much older as well as had higher BMIs ($p<0.001$). This is in line with a number of recent analytical studies that found that increased BMI and advanced age are associated risk factors for endometrial pathology in women who are bleeding after menopause. A Chinese observational study, for instance, found a strong correlation between age and BMI and histopathological endometrial disorders [17]. This finding reflects the effects of hormones and metabolism on endometrial proliferation. Clinical risk classification models should take these demographic factors into account in order to customize PMB diagnosis and treatment pathways. The statistically significant correlation between smoking and increased thickness of endometrium on ultrasound as well as histopathology ($p<0.001$) is a novel finding of our study. Although smoking is traditionally thought to protect against endometrial cancer because it has anti-estrogenic properties, new research indicates that it may have complex modulating effects on endometrial tissue structure and vascularity, which may affect ultrasound parameters. This finding calls for additional research using analytical cohorts to define the contribution of smoking to endometrial disorders and imaging features in postmenopausal women.

The ultrasound performance metrics from our study show good agreement with those found in recent research. In this study, 97.1% negative predictive value (NPV) is comparable to a study from Pakistan that found that endometrial thickness of less than 4 mm had a low likelihood of malignancy and that transvaginal ultrasound had a high NPV in ruling out pathology. With a moderate positive predictive value (PPV) of 60.7%, ultrasound is known to have limitations in distinguishing benign thickening from precancerous or cancerous lesions. It was consistent with a recent

study by Thoprasert et al., (2023) which showed that 28.4% of endometrial cancers arise in postmenopausal women between 51-60years of age and 80% of them endometrioid. The endometrial thickness and histopathological results have a correlation of mean endometrial thickness of 5.97mm in atrophic and 11.95mm in carcinomatous lesions [18]. The sensitivity and specificity rates of ultrasound were 71-90%, as reported in other recent studies, indicating that it is a reliable first-line examination in PMB studies [19].

In our study, we suggest a threshold of 5 mm, which aligns with international standards and several recently-published reviews that recommend 5 mm or less endometrial thickness as a reliable PMB predictor, and which differ with other reports that recommend higher cut-offs (10 mm or more) [20]. This or reduced cut-off reduces unnecessary invasive interventions in low-risk women such as biopsy and weighs the possibility of false-negative pathology. Although other analytical researches focus on the importance of metabolic and endocrine risk factors over the past reproductive history in PMB pathogenesis, the frequency of observed parity with various birth studies and a higher proportion of married women are in line with the local demographic profile [21]. These variables however, had less direct relationships with endometrial pathology as compared to age and BMI. The new evidence this paper presents in a tertiary care environment on the high correlation between smoking and endometrial thickness and histopathology can be used in future risk assessment frameworks. Moreover, the NPV and the good correspondence between ultrasound and histopathological results justify the role of ultrasound as a necessary first modality in the work at the PMB in the centers having limited resources [22].

The research study has many limitations. The results obtained in one center only, tertiary health care facility, restricts the generalizability of these findings to the wider population. The technique of a successive non-probability sampling could contribute to the selection bias. Since the sample size of 200 is not large, this restricts the power of any subgroup analysis. Additionally, there is possible operator dependency associated with the accuracy of ultrasound measurements. It was not possible to exclude possible confounding factors in the study, such as hormonal status, specific metabolic problems or the use of medications. The research was cross-sectional meaning that no conclusions on any causal associations could be drawn. Lastly, there is no long-term follow-up at the time of writing to determine the development and progression of any endometrial abnormalities detected.

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CONCLUSION

The findings revealed that in postmenopausal bleeding patients, especially in older and women with high BMI, higher endometrial thickness on transvaginal ultrasonography is strongly correlated with histopathological abnormalities. The diagnostic accuracy and predictive variables are reinforcing the application of ultrasound as a non-invasive screening method with histopathology preserved in cases that are thicker than 5 mm or other risk factors.

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