

## ORIGINAL ARTICLE

# Correlation between Ultrasound-Measured Endometrial Thickness and Histopathological Findings in Postmenopausal Women with Abnormal Uterine Bleeding

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## ABSTRACT

**Background:** Abnormal uterine bleeding (AUB) in postmenopausal women is a clinically recognised symptom commonly associated with endometrial pathology (including malignancy). TVUS is a commonly used, noninvasive way of measuring endometrial thickness (ET), which may assist in directing further management. Nevertheless, additional evaluation is needed in local populations for the correlation between ET and histopathological findings.

**Objective:** The aim is to investigate the correlation between ultrasound-measured endometrial thickness and the histopathological findings in postmenopausal women with AUB.

**Methods:** A cross-sectional study was conducted in Shaikh Hospital and Bolan Medical College Hospital, Quetta, from February 2022 to June 2023. Transvaginal ultrasound and endometrial sampling were performed on seventy postmenopausal women with AUB. Correlation of biopsy-confirmed histopathology with et was recorded. It was also analyzed with demographic data and clinical biomarkers such as BMI, hemoglobin, fasting glucose, and serum estradiol. SPSS v26 was used to calculate Pearson correlation, sensitivity, specificity, and predictive values of ET thresholds.

**Results:** The mean endometrial thickness was  $8.7 \pm 3.5$  mm. The histopathology was 20 cases of hyperplasia without atypia, 10 with atypia, 10 carcinomas, and 30 benign diagnoses. For the detection of premalignant or malignant pathology, the sensitivity and NPV of ET  $\geq 5$  mm were 100%. There was a strong positive correlation between ET and histopathological severity ( $r = 0.76$ ,  $p < 0.001$ ). Patients with pathological findings had metabolic risk factors such as elevated BMI and glucose.

**Conclusion:** TVUS-measured endometrial thickness is strongly correlated with histopathological abnormalities of postmenopausal AUB. Thus, a cutoff of  $\geq 5$  mm is highly sensitive and may be used as an effective triaging tool for endometrial sampling. Clinical and metabolic risk profiling may provide additional diagnostic accuracy when integrated as part of the assessment.

**Keywords:** Postmenopausal bleeding, Endometrial thickness, Transvaginal ultrasound, Endometrial hyperplasia, Endometrial carcinoma, Histopathology, Obesity, Pakistan

## INTRODUCTION

Postmenopausal women with abnormal uterine bleeding (AUB) are one of the more alarming clinical presentations in gynecology, for which the serious underlying pathology of endometrial cancer is associated. The cessation of menstruation for at least 12 consecutive months caused by ovarian senescence is called menopause<sup>1</sup>. Therefore, any bleeding occurring after this period is considered pathological and is thoroughly evaluated. The etiology of postmenopausal bleeding (PMB) may be benign (atrophic endometrium, polyps, hormone therapy), but the main risk is the presence of endometrial cancer, which occurs in about 10-15% of women with PMB worldwide<sup>2</sup>.

While the global incidence of endometrial carcinoma has been increasing, particularly in developing countries, where diagnostic resources are limited and patients are often presented with advanced disease. Endometrial cancer is one of the top five malignancies in women in Pakistan, and the burden of gynecological malignancies is also increasing in the country. This context makes the early and accurate identification of high-risk individuals a clinical imperative to prevent morbidity and mortality by early intervention<sup>3,4</sup>.

TVUS has become the preferred noninvasive, accessible, and highly sensitive first-line imaging modality for investigation of postmenopausal AUB. Endometrial thickness (ET) is one of the key parameters used to assess by TVUS, and ET is a surrogate marker for endometrial pathology. Because ET measurement is so simple and reproducible, it has become widely used in outpatient and inpatient settings<sup>5</sup>. Several international guidelines, such as the American College of Obstetricians and Gynecologists (ACOG) and the Royal College of Obstetricians

and Gynaecologists (RCOG), recommend the use of ET cut-offs to decide whether endometrial sampling is required<sup>6</sup>. However, there is no universal consensus regarding the best threshold (4–5 mm) in symptomatic women. Additionally, there is a well-established association of a thicker endometrium with a higher risk of malignancy, but there are also overlapping values in benign conditions such as polyps or hormone-induced changes, which questions specificity<sup>7</sup>.

The diagnosis of endometrial pathology is still the gold standard of histopathological examination. Sonographic findings, especially endometrial thickness, need to be correlated with histopathological outcome for the validation of the diagnostic utility of TVUS. The correlation between TMD and DM has been studied numerous times across countries in the world; however, regional differences in patient demographics, comorbidities, and healthcare access require local data to accurately guide clinical practice in settings like Pakistan<sup>8,9</sup>.

The aim of this study was to bridge the gap between ultrasound-measured endometrial thickness and histopathological findings in postmenopausal women with AUB. This has been done to determine the diagnostic performance of TVUS in predicting underlying pathology, as well as whether ET measurement alone can reliably guide the need for endometrial biopsy in resource resource-limited clinical environment. In the end, this study aimed to improve the diagnostic algorithm for postmenopausal bleeding in South Asian populations based on noninvasive imaging coupled with confirmatory histological evidence<sup>10</sup>.

## MATERIALS AND METHODS

**Study Design and Setting:** The study was carried out in a hospital-based cross-sectional clinical study conducted at the Department of Obstetrics and Gynecology, Shaikh Hospital and Bolan Medical College Hospital, Quetta, Pakistan. Over a duration of seventeen months, from February 2022 to June 2023, the study

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was carried out. The first aim was to assess the correlation between ultrasound-measured endometrial thickness with histopathological findings in postmenopausal women who reported AUB.

**Study Population and Sample Size:** Seventy postmenopausal women between the ages of 50 to 75 years were enrolled in the study. Participants were purposively sampled from nonprobability purposive sampling in which all participants presented with postmenopausal AUB. It was defined as postmenopausal status, absence of menstruation for at least twelve consecutive months without hormonal or surgical causes. Previously, literature suggested a moderate to strong correlation between endometrial thickness and histopathology, and a sample size of 80% at a confidence level of 95% study power was used to calculate.

**Inclusion and Exclusion Criteria:** Women who had reached natural menopause, had abnormal uterine bleeding of unexplained origin, and were willing to undergo both transvaginal ultrasound and endometrial biopsy were eligible. Subjects excluded from the study were women with a known history of gynecological malignancy, those who were receiving or had recently used hormone replacement therapy, those with bleeding disorders, those with anatomical uterine distortions that interfered with ultrasound accuracy, or who refused biopsy. They were set up to eliminate confounding factors and to be able to count on accurate sonographic and histological assessments.

**Ethical Considerations:** The study was approved by the Institutional Review Board. All participants provided informed consent before enrolment. Patients were informed of study objectives, procedures, possible risks, and benefits. Throughout the course of the study, confidentiality of patient data was strictly maintained.

**Ultrasound Evaluation:** Detailed transvaginal ultrasound (TVUS) was performed by experienced gynecologists using a high-resolution transducer 7.5 MHz in each participant. The patient was placed in lithotomy position with an empty bladder for optimal visualization. One endometrial-myometrial interface was located in the sagittal plane, and the thickest point of the endometrial thickness was measured from one endometrial-myometrial interface to the opposite side. Measurements were recorded in millimeters. The participants were divided based on the ultrasound findings, i.e., endometrial thickness, into three categories: Group A women with endometrial thickness less than 5 mm, Group B women with endometrial thickness between 5 to 10 mm, and Group C women with endometrial thickness more than 10 mm.

**Endometrial Sampling and Histopathological Examination:** All patients then had endometrial sampling one week after their imaging; then the patients were followed for six months. The sampling technique utilized was pipelle suction biopsy in the outpatient department or dilation and curettage (D&C) under anesthesia in some cases where operative evaluation was deemed necessary. Specimens were fixed in 10% buffered formalin, and gross and histopathological analysis was performed at the Department of Pathology. The standard hematoxylin and eosin staining techniques were used for histological processing. The slides were scored independently by senior pathologists blinded to the ultrasound measurements. The histopathology revealed atrophic endometrium, physiological (proliferative or secretory) endometrium, endometrial hyperplasia without atypia, endometrial hyperplasia with atypia, endometrial carcinoma, and other benign conditions, including polyps.

**Data Collection and Statistical Analysis:** We collected all relevant clinical data, ultrasound findings, and histopathology reports in a structured data collection proforma. IBM SPSS version 26.0 was used for statistical analysis. Age and endometrial thickness were expressed as mean  $\pm$  standard deviation or frequencies and percentages for continuous and categorical variables, respectively. Pearson's correlation coefficient was used to determine the correlation between endometrial thickness and the type of histopathological finding. Diagnostic performance indicators of sensitivity, specificity, positive predictive value (PPV),

and negative predictive value (NPV) for an endometrial thickness cut-off of  $\geq 5$  mm were also calculated. The p-value less than 0.05 was taken as statistically significant.

## RESULTS

The study was carried out with 70 postmenopausal women with abnormal uterine bleeding. The age of participants ranged from 50 to 74 years, mean of 61.3, s.d. = 5.8. The mean body mass index (BMI) of 27.4 kg/m<sup>2</sup> ( $\pm 4.2$ ), and the majority of patients were overweight or obese. The median parity was 3, with parity from 1 to 5. Hemoglobin levels were 10.8 g/dL ( $\pm 1.5$ ), and 41 (58.6%) women had mild or moderate anemia. Mean fasting blood glucose was 108.4 mg/dL ( $\pm 12.7$ ), and 27.1% of patients had prediabetic levels. None of the patients were on hormone replacement therapy and averaged 24.2 pg/mL ( $\pm 5.3$ ) for estradiol levels. Transvaginal ultrasound measured ET to be 8.7 mm ( $\pm 3.5$ ), with values from 2.0 to 20.0 mm. The following summarizes the demographic and clinical biomarker findings.

Table 1: Demographic and Clinical Characteristics of Study Population (n = 70)

Variable	Mean $\pm$ SD	Range
Age (years)	61.3 $\pm$ 5.8	50.0 – 74.0
Body Mass Index (kg/m <sup>2</sup> )	27.4 $\pm$ 4.2	18.9 – 35.9
Parity	3.0 $\pm$ 1.2	1 – 5
Hemoglobin (g/dL)	10.8 $\pm$ 1.5	8.1 – 13.5
Fasting Blood Glucose (mg/dL)	108.4 $\pm$ 12.7	85 – 139
Estradiol (pg/mL)	24.2 $\pm$ 5.3	14 – 37
Endometrial Thickness (mm)	8.7 $\pm$ 3.5	2.0 – 20.0

Five categories of primary diagnostic histopathology of endometrial biopsy specimens were identified. The most common diagnosis was hyperplasia without atypia in 20 cases (28.6%) and physiological endometrium (proliferative or secretory phase) in 17 cases (24.3%). Nineteen cases (26.8%) were diagnosed as atrophic endometrium, 10 cases (14.3%) each of hyperplasia with atypia and endometrial carcinoma. In the following table, the details of these distributions are given.

Table 2: Frequency of Histopathological Diagnoses (n = 70)

Histopathological Diagnosis	Frequency	Percentage (%)
Hyperplasia without Atypia	20	28.6
Physiological Endometrium	17	24.3
Atrophic Endometrium	13	18.6
Hyperplasia with Atypia	10	14.3
Endometrial Carcinoma	10	14.3

Three groups of patients were made, based on endometrial thickness: Group A ( $< 5$  mm), Group B (5–10 mm), and Group C ( $> 10$  mm). Group A comprised 13 patients (18.6%) with all of them having atrophic endometria, and no cases of hyperplasia or malignancy. Group B (37 patients, 52.9%) included 20 patients with hyperplasia without atypia and 17 patients with physiological endometrium, and no patients had carcinoma or atypia of hyperplasia. Group C consisted of 20 patients (28.6%) with high-risk pathology, all of whom were 10 cases of hyperplasia with atypia and 10 of endometrial carcinoma. Below is a summary of the relationship between endometrial thickness category and histopathological findings.

A Pearson correlation coefficient was calculated to evaluate the relationship between endometrial thickness (continuous variable) and the histopathological severity (scored 1 (atrophy) to 5 (carcinoma)). The correlation value was  $r = 0.76$ ,  $p < 0.001$ ; a strong, but statistically significant positive relationship. The cut-off value of endometrial thickness of  $\geq 5$  mm was used to assess the diagnostic utility of endometrial thickness. The results showed that the NPV was 100% (no high-risk pathology occurred if ET  $< 5$  mm); the sensitivity was 100%. The specificity was 26%, and the positive predictive value (PPV) was 35.1%, which means that even though many of the benign cases lie above the 5 mm threshold, an

ET is effective at ruling out malignancy. In the following table, these diagnostic performance indices are outlined.

Table 3: Distribution of Histopathological Diagnoses by Endometrial Thickness Group

Endometrial Thickness Group	Atrophic Endometrium	Hyperplasia w/o Atypia	Physiological	Hyperplasia with/ Atypia	Carcinoma
Group A (<5 mm)	13	0	0	0	0
Group B (5–10 mm)	0	20	17	0	0
Group C (>10 mm)	0	0	0	10	10

Table 4: Diagnostic Accuracy of Endometrial Thickness Cut-Off  $\geq 5$  mm

Diagnostic Metric	Value (%)
Sensitivity	100.0
Specificity	26.0
Positive Predictive Value	35.1
Negative Predictive Value	100.0

These findings demonstrate that clinical triage is provided by endometrial thickness alone, but diagnostic accuracy is not, and that endometrial thickness is a useful triaging tool. A strong correlation exists between an endometrial thickness  $\geq 10$  mm and serious pathology, and immediate biopsy; ET <5 mm can defer invasive procedures in low-risk patients. However, endometrial thickness interpreted in a clinical context is further enhanced in its predictive utility by the combination of increased BMI, anemia, and metabolic derangements.

## DISCUSSION

The objective of this study was to correlate transvaginal ultrasound-measured endometrial thickness to histopathological findings in postmenopausal women with abnormal uterine bleeding (AUB). The results suggest that there is a statistically significant and clinically important association between increased ET and pathological changes in the endometrium, in particular, lesions of premalignant and malignant nature<sup>11</sup>.

It was found that all cases of endometrial carcinoma and hyperplasia with atypia had ET values more than 10 mm. On the other hand, women with ET less than 5 mm had all benign histology, except a few with atrophic endometrium<sup>12</sup>. These findings are consistent with existing international guidelines, such as the American College of Obstetricians and Gynecologists (ACOG) recommendations for AUB in postmenopausal women to be investigated further if the thickness is 4–5 mm. Ruling out serious pathology, our data support that an ET <5 mm can be considered a reassuring finding with an excellent negative predictive value (100%)<sup>13</sup>.

A further strong positive correlation between the increasing ET and histopathological severity ( $r = 0.76$ ;  $p < 0.001$ ) was found, validating the use of ET as a stratification tool. Although the sensitivity and NPV of the  $\geq 5$  mm cut-off were 100%, the specificity and PPV were both low (26% and 35.1%, respectively). This implies that the majority of patients who exceed the cut-off of 5 mm also have benign conditions, and very few have serious disease. ET is therefore a sensitive but nonspecific marker<sup>14</sup>.

This study also pointed out the participation of clinical and metabolic biomarkers such as BMI, anemia, and high fasting glucose levels as the contributory risk factors for the endometrial pathology<sup>15</sup>. About 88% of patients were overweight or obese, and 27% were prediabetic. Likely, these risk factors work synergistically to promote endometrial hyperplasia in response to chronic unopposed estrogen stimulation and insulin resistance, both of which have been shown to influence endometrial proliferation<sup>16</sup>.

This is one of the major strengths of the present study, which has performed a comprehensive analysis of ultrasound findings, histopathological confirmation, and biomarker profiling in a regional Pakistani population. Patients from Bolan Medical College Hospital, Quetta, and Shaikh Hospital were included as these results further increase the regional validity and clinical generalizability of the results in a similar resource-limited setting<sup>17</sup>.

Although the study is not without limitations. The data are cross-sectional, so it does not have longitudinal follow-up data to further explain progression from hyperplasia to carcinoma<sup>18</sup>.

Moreover, histopathological diagnoses were restricted to single-time sampling, and hormonal profiles were not always measured extensively. However, the study reveals valuable evidence for the use of ultrasound for the diagnosis of AUB in postmenopausal women and proposes a stratified, biomarker-informed approach for clinical decision making<sup>19</sup>.

## CONCLUSION

Transvaginal ultrasound of endometrial thickness is a noninvasive screening tool of value in the evaluation of postmenopausal abnormal uterine bleeding. Cut off value of  $\geq 5$  mm has excellent sensitivity and negative predictive value to detect premalignant and malignant lesions. Conversely, ET <5 mm is reliably negative for significant pathology. The strong correlation between increased ET and serious endometrial disease when combined with metabolic risk factors such as obesity and prediabetes emphasizes the importance of integrated diagnostic strategies. Transvaginal sonography routine use combined with selective histopathological confirmation based on risk stratification might reduce unnecessary biopsies without compromising early detection of endometrial pathology.

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**Conflict of Interest:** The authors declare that they have no conflicts of interest.

**Data Availability Statement:** The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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**Authors contribution:**

**RRB:** Conceptualization, Study Design, Supervision

**FU:** Data Collection, Patient Recruitment

**SS:** Literature Review, Draft Writing

**NK:** Statistical Analysis, Interpretation of Results

**SG:** Draft Editing, Technical Review

**PA:** Data Curation, Formatting, and References

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