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MORPHOLOGICAL SPECTRUM OF ENDOMETRIAL PATHOLOGIES IN PATIENTS WITH DYSFUNCTIONAL UTERINE BLEEDING AND IT'S CORRELATION WITH ENDOMETRIAL THICKNESS ON ULTRASONOGRAPHY

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Abstract

Background: *Abnormal uterine bleeding (AUB) is a common gynecological presentation with a wide spectrum of underlying etiologies. Transvaginal ultrasound is a non-invasive procedure, while histopathological examination is considered the gold standard for evaluating endometrial pathologies. This study correlated endometrial thickness observed on transvaginal ultrasound with histopathological findings in patients with AUB.*

Methods: *The present study was a hospital-based prospective, cross-sectional study conducted in the Department of Pathology, Lahore General Hospital, Lahore, over 12 months from May 2024 to April 2025. Transvaginal ultrasonography and endometrial biopsy were performed in 70 women presenting with AUB. Endometrial thickness was categorized into five groups (<4 mm, 4-10 mm, 11-15 mm, 16-20 mm, and >20 mm), and histopathological outcomes were classified into eight diagnostic categories. Chi-square tests, ANOVA, and Pearson correlation were used for analysis.*

Results: *The most common diagnoses were endometrial hyperplasia (21.4%), endometrial polyp (20.0%), and secretory endometrium (17.1%), while endometrioid adenocarcinoma was found in 11.4% of patients. A significant association was observed between endometrial thickness category and histopathological diagnosis ($p < 0.001$). All cases with thickness >20 mm were diagnosed with endometrioid adenocarcinoma. Mean thickness values were significantly higher in hyperplastic and malignant cases ($p < 0.001$). Pearson correlation analysis showed a weak but statistically significant positive relationship between endometrial thickness and histopathological severity ($r = 0.275$, $p < 0.05$).*

Conclusion: *Endometrial thickness measured by transvaginal ultrasonography demonstrates a reliable correlation with underlying histopathological patterns in*

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AUB. Thickness >11 mm, and particularly >20 mm, should undergo histological evaluation as they have high suspicion of hyperplasia or malignancy.

INTRODUCTION

Abnormal uterine bleeding (AUB) is a prevalent gynecological presentation and manifests in various forms, such as heavy menstrual bleeding (HMB), frequent or irregular cycles, bleeding after intercourse, or post-menopausal bleeding (PMB). Bleeding is considered abnormal when it is irregular in pattern, lasts for an unusual duration, or involves an excessive amount (>80 ml per menstrual cycle). Internationally, the prevalence of AUB in women of reproductive age ranges from 10% to 30%, with higher rates noted in the perimenopausal age group, reflecting hormonal fluctuations and structural pathologies as contributing factors [1,3]. Locoregional studies in South Asia, including India and Iran, report AUB prevalence rates between 15% and 35% among gynecological outpatient visits, underscoring its significance as a leading cause of hospital admissions and diagnostic interventions [1,3,6].

While transabdominal pelvic ultrasound is commonly used as the first-line imaging modality in the general evaluation of gynecological complaints, its limited resolution for endometrial assessment necessitates further evaluation in cases of AUB [4]. Transvaginal ultrasonography (TVS) offers superior resolution and accuracy in assessing endometrial thickness (ET) and echotexture, making it a valuable tool in the evaluation of AUB. Diagnostic procedures include hematological investigations, ultrasound with endometrial thickness (ET) measurement, and endometrial biopsy, with the latter being regarded as the gold standard [1,2]. TVS serves as a crucial non-invasive and cost-effective screening method to assess structural causes of AUB. Measuring endometrial thickness and identifying different echotextures through TVS is a key initial step in evaluating AUB [3]. Numerous ultrasonography studies on women with AUB have focused on endometrial thickness measurements to rule out endometrial cancer, as a thin endometrium is linked to a lower risk of malignancy, while a thicker endometrium suggests a higher risk [4]. An ET threshold of ≥4 mm in postmenopausal women and ≥14 mm in premenopausal women indicates potential endometrial pathology, necessitating histopathological evaluation [5]. Endometrial sampling is a valuable tool for assessing women with AUB and guiding treatment referrals [6]. Endometrial biopsy, whether through dilation and curettage or office biopsy, is considered the gold standard for AUB [7]. This study aims to correlate endometrial thickness observed via ultrasound with histopathological findings in patients with abnormal uterine bleeding, aiding in the detection of various endometrial pathologies.

Materials & Methods

Study Design and Setting

The present study was hospital-based prospective cross-sectional study, conducted at the Department of Pathology, Lahore General Hospital, Lahore, Pakistan. Study duration was of 12 months (May 2024 to Aril 2025).

Sample Size

Assuming the prevalence of abnormal uterine bleeding of 50% with desired precision of 12.5%, level of significance of 5% and power of 80%, the total sample size taken was calculated to be approximately 70. A non-probability consecutive sampling technique was used, enrolling all eligible patients with AUB meeting the inclusion criteria until the target sample size was achieved.

Inclusion and Exclusion Criteria

Women of reproductive and perimenopausal age presenting with abnormal uterine bleeding (AUB) and undergoing dilatation and curettage for gynecological indications were included in the study. Unmarried women, those with pregnancy and pregnancy-related causes of bleeding, and cases of menorrhagia were excluded.

Ethical Considerations

Approval for the study was obtained from the Ethical Review Committee, Postgraduate Medical Institute/Ameer-ud-Din Medical College/Lahore General Hospital, Lahore, reference number 00-

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143-S-2023, dated 08 May 2023. Informed consent was obtained from each patient after explaining the objectives and procedures of the study.

Data Collection

All reproductive and perimenopausal women presenting with AUB and undergoing dilatation and curettage for gynecological indications were included in the study. Patient name, age, menopausal status, and pelvic ultrasonography reports were recorded. Pelvic ultrasonography was initially performed, followed by transvaginal ultrasonography (TVS) for detailed assessment of endometrial thickness. TVS was performed using a GE Voluson P8 ultrasound machine with a 5–9 MHz transvaginal probe. Endometrial thickness was categorized into five groups: <4 mm, 4–10 mm, 11–15 mm, 16–20 mm, and >20 mm. Following imaging, endometrial sampling was performed using dilatation and curettage under aseptic precautions in the operating theatre. The endometrial tissue obtained was fixed in 10% formalin, processed using standard histopathological protocols, and stained with Hematoxylin and Eosin (H&E) for microscopic examination by an experienced pathologist.

Data Analysis

Data were compiled in Microsoft Excel and analyzed using SPSS version 27.0. Quantitative variables (age, endometrial thickness) were summarized using mean ± standard deviation (SD), while qualitative variables (menopausal status, histopathological patterns, endometrial thickness categories) were presented as frequencies and percentages. The Chi-square test (χ^2) was applied to analyze associations between endometrial thickness categories and histopathological findings, while one-way Analysis of Variance (ANOVA) was used to compare mean endometrial thickness across different histopathological patterns. A p-value of ≤ 0.05 was considered statistically significant.

The study included 70 women with a mean age of 47.5 ± 11.3 years. Most patients were 40–49 years old (55.7%), followed by ≥50 years (30.0%); 68.6% were pre-menopausal and 31.4% were post-menopausal.

Table 1: Frequency of Endometrial Thickness Categories

Endometrial Thickness Category	Frequency	Percentage
<4mm	3	4.3%
4-10mm	43	61.4%
11-15mm	12	17.1%
16-20mm	7	10.0%
>20mm	5	7.1%

The majority of patients (61.4%) exhibited endometrial thickness in the range of 4-10mm. A smaller subset showed significantly increased measurements: 11-15mm (17.1%), 16-20mm (10%), and >20mm (7.1%). Conversely, only 4.3% patients had <4mm thickness as shown in Table 1.

Table 2: Frequency of Histopathological Patterns

Histopathological Pattern	Frequency	Percentage
Atrophic Endometrium	3	4.3%
Secretory Phase	12	17.1%
Disordered Proliferative Phase	6	8.6%
Endometrial Polyp	14	20%
Chronic Endometritis	7	10.0%
Hormonal Imbalance	5	7.1%

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Endometrial hyperplasia	15	21.4%
Endometrioid adenocarcinoma	8	11.4%

Histopathological findings of endometrium showed 21.4% had endometrial hyperplasia, 20% had endometrial polyp, 17.1% had secretory endometrium and 10% had chronic endometritis. Endometrioid adenocarcinoma was detected in 11.4% of patients. Other findings included disordered proliferative endometrium (8.6%), hormonal imbalance (7.1%) and atrophic endometrium (4.3%) as shown in Table 2.

Endometrial thickness	**A.E**	**S.P**	**D.P**	**E.P**	**C.E**	**H.I**	**E.H**	**E.C**	**Total**	**(χ^2)**	**p-value**
<4mm	3(100%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	3(100%)	70.00	<0.001
4-10mm	0(0%)	12(27.9%)	6(14.0%)	14(32.6%)	6(14.0%)	5(11.6%)	0(0%)	0(0%)	43(100%)	66.382	<0.001
11-15mm	0(0%)	0(0%)	0(0%)	0(0%)	1(8.3%)	0(0%)	11(91.7%)	0(0%)	12(100%)	43.31	<0.001
16-20mm	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	4(57.1%)	3(42.9%)	7(100%)	16.57	0.020
>20mm	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	5(100%)	5(100%)	41.731	<0.001
Total	3(4.3%)	12(17.1%)	6(8.6%)	14(20%)	7(10%)	5(7.1%)	15(21.4%)	8(11.4%)	70(100%)		

Table 3: Correlation of Histopathological Pattern with Endometrial Thickness

Abbreviations: A.E., atrophic endometrium; S.P., secretory phase; D.P., disordered proliferative phase; E.P., endometrial polyp; C.E., chronic endometritis; H.I., hormonal imbalance; E.H., endometrial hyperplasia; E.C., endometrioid adenocarcinoma.

E.H: Endometrioid hyperplasia E.C: Endometrioid adenocarcinoma

Statistically significant association was observed between endometrial thickness category and histopathological diagnosis. In ET<4mm there were 3 patients in atrophic endometrium while there were no cases in the rest. Histopathological, there was statistically significant relation between histopathology and endometrial thickness<4mm with p-value <0.001 as shown in Table 3.

In ET 4-10mm there were 27.9% patients in secretory endometrium, 32.6% patients in endometrial polyp,14.6% patients in disordered proliferative endometrium,11.6% patients in hormonal imbalance, as for endometrioid adenocarcinoma there were no cases at

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endometrial thickness 4-10mm. There was statistically significant relation between histopathology and endometrial thickness 4-10mm with p-value <0.001.

The endometrial thickness 11-15mm was highly indicative of hyperplasia(91.7%). The endometrial thickness 16-20mm, showed 57.1% patients in hyperplasia and 42.9% endometrioid adenocarcinoma. There were no benign pathology at endometrial thickness 16-20mm. There was statistically significant relation between histopathology and endometrial thickness with p-value <0.001, which was highly significant. This indicates that hyperplasia and adenocarcinoma related endometrial thickness 16-20mm as shown in Table 3.

Endometrial thickness > 20mm was exclusively associated with malignancy (100%); there was statistically significant relation between histopathology and endometrial thickness >20mm with p-value<0.001.

Additional statistical summary: Mean endometrial-thickness category differed significantly across histopathological patterns (ANOVA=96.468, p<0.001). The highest mean category was seen in endometrioid adenocarcinoma (4.62 ± 0.52), followed by endometrial hyperplasia (3.27 ± 0.46), while atrophic endometrium showed the lowest value (1.0 ± 0.0).

Correlation summary: Endometrial thickness showed a statistically significant positive relationship with histopathological severity (r=0.275, p<0.05), indicating that more severe endometrial pathology was associated with greater thickness.

Microscopic examination of endometrial polyp (Figure 1), endometrioid carcinoma (Figure 2), endometrial hyperplasia (Figure 3), showed various histological findings.

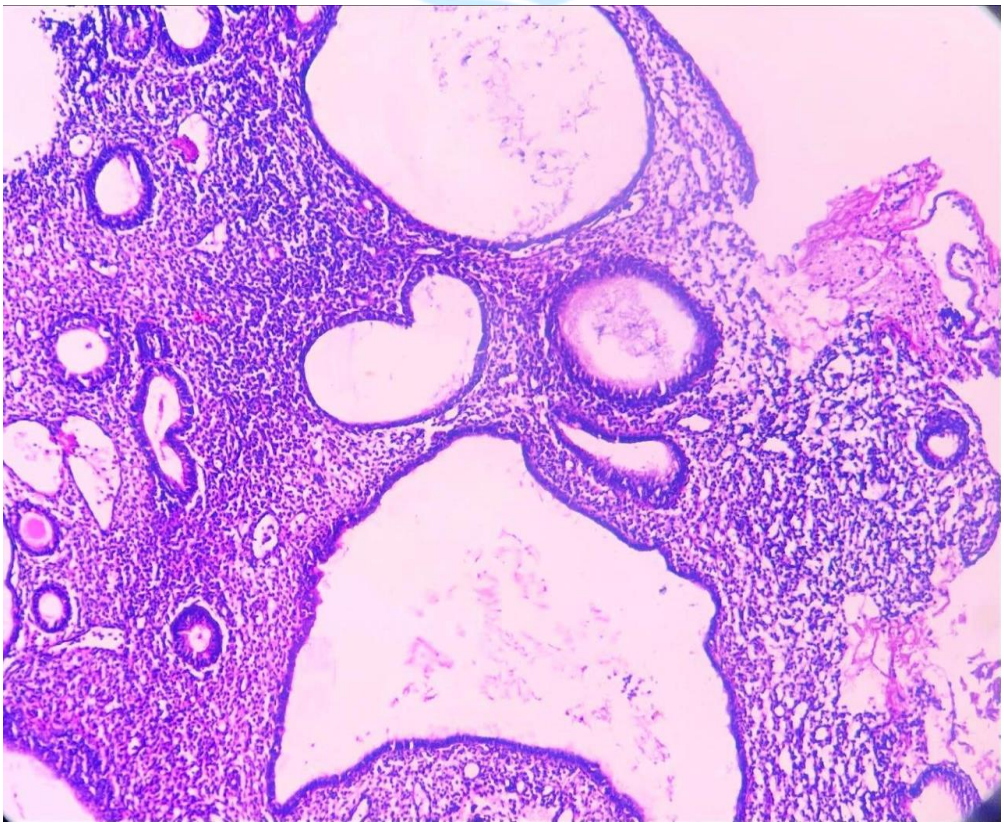

Figure 1: Endometrial polyp, hematoxylin and eosin stain.

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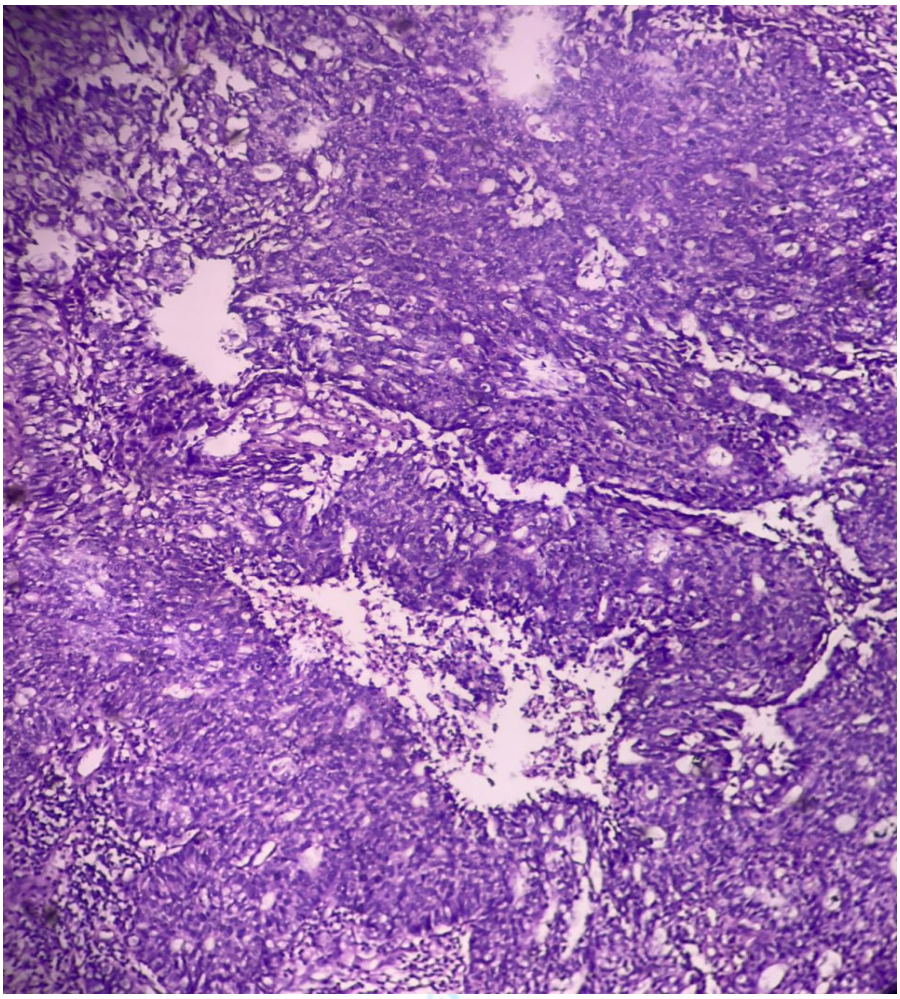

Figure 2: Endometrioid adenocarcinoma, hematoxylin and eosin stain.

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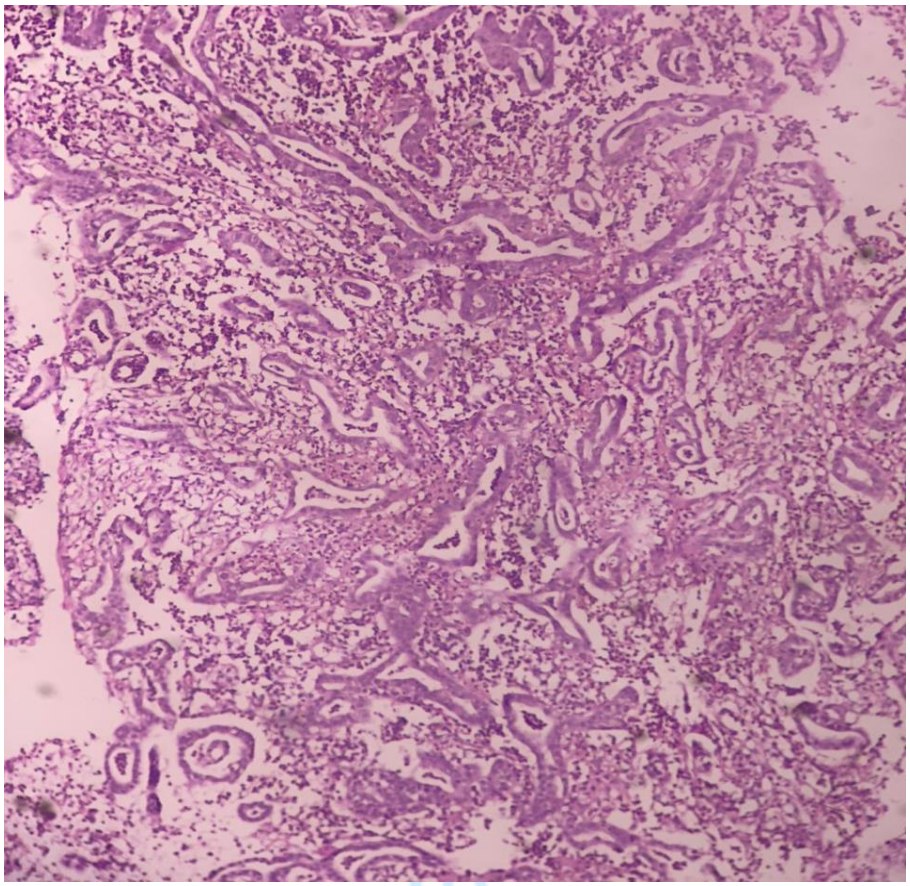

Figure 3: Endometrial hyperplasia, hematoxylin and eosin stain.

Discussion:

Abnormal uterine bleeding is a broad term that describes irregularities in the menstrual cycle involving frequency, regularity, duration and volume of flow outside of pregnancy [7]. Endometrial sampling is a safe procedure that helps to evaluate endometrium and brings out diagnosis though it has limitations of being a blind procedure [1]. Sonography in combination with histological assessment of endometrial cavity remains diagnostic modality in current practice [3].

This study aimed to correlate endometrial thickness (ET) as measured by transvaginal sonography (TVS) with histopathological findings in 70 women presenting with abnormal uterine bleeding (AUB). The results demonstrate a strong and statistically significant association between increasing ET and the severity of endometrial pathology ($p<0.001$). Our primary findings indicate a high prevalence of significant pathologies within the study cohort, with endometrial hyperplasia (21.4%) and endometrial polyps (20.0%) being the most common diagnoses. Most notably, the incidence of endometrioid adenocarcinoma was found to be 11.4%, a figure that underscores the critical importance of diligent investigation in this patient population.

A key finding of this study is the clear risk stratification provided by ET measurements. An endometrial thickness of less than 4 mm was exclusively associated with benign atrophic endometrium, suggesting a high negative predictive value for malignancy in this range. Conversely, a thickness greater than 11 mm was strongly indicative of pathology, with 91.7% of cases in the 11-15 mm range showing endometrial hyperplasia. The risk of malignancy increased sharply with greater thickness; the 16-20 mm range contained both hyperplasia (57.1%) and

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adenocarcinoma (42.9%), while an ET greater than 20 mm was found to be 100% predictive of endometrioid adenocarcinoma in our cohort. While the Pearson correlation coefficient indicated a weak positive relationship ($r=0.275$), its statistical significance ($p<0.05$) confirms that as endometrial thickness increases, so does the likelihood of encountering more severe pathology. This weak 'r' value is expected, as the relationship is not perfectly linear due to the varied nature of pathologies like polyps and hyperplasia, which can present with overlapping ET measurements.

This research was designed as a hospital-based, prospective, cross-sectional study conducted at Lahore General Hospital, Lahore. The prospective nature of the study is a methodological strength, as it minimizes recall bias and allows for standardized data collection. The sample consisted of 70 reproductive and perimenopausal women presenting with AUB. A notable aspect of our patient selection was the exclusion of cases with pregnancy-related bleeding and menorrhagia. While this focused the study on other patterns of AUB, it is an important consideration when interpreting the results. For endometrial sampling, dilatation and curettage (D&C) was employed, which, while invasive, is a standard and robust method for obtaining adequate tissue for histopathological examination, considered the gold standard for diagnosis.

The statistical analysis was designed to rigorously evaluate the relationship between the study variables. The Chi-square ($\chi 2$) test was appropriately used to determine the association between categorical variables, namely the pre-defined endometrial thickness categories and the various histopathological diagnoses. To compare the mean endometrial thickness across the different pathology groups, a one-way Analysis of Variance (ANOVA) was employed, which effectively demonstrated that the mean ET was significantly higher in hyperplastic and malignant conditions. Finally, the Pearson correlation test was used to quantify the linear relationship between ET as a continuous variable and the ordered severity of the pathology, confirming a positive, albeit weak, trend. The use of these statistical tools is standard for this type of study design and provides confidence in the reported associations.

The primary strengths of this study lie in its prospective design and its use of D&C for obtaining high-quality tissue for histopathological correlation. This provides robust, real-time data and minimizes diagnostic ambiguity. Furthermore, the study offers clear, clinically actionable ET thresholds (e.g., >11 mm, >16 mm, and >20 mm) that can guide decision-making for clinicians in our local setting.

To build upon the important findings of this research, future studies should aim to address its limitations. A large-scale, multi-center prospective study conducted across various hospitals in Pakistan is recommended to validate our proposed ET cut-off values and to establish their generalizability. Future research should also employ broader inclusion criteria that encompass all patterns of AUB, including menorrhagia, to provide a more complete epidemiological picture. To move beyond the weak correlation coefficient and improve predictive power, a multivariable regression model could be developed, incorporating not only ET but also other sonographic features (e.g., IETA terminology), patient age, BMI, and clinical risk factors.

Our findings, when placed in the context of existing literature, are both corroborative and unique. The demographic finding that the perimenopausal age group (40–49 years) is most affected (55.7%) is highly consistent with multiple studies that report a similar peak incidence [1,2,3], confirming this as a high-risk period for AUB presentations requiring investigation.

The prevalence of endometrial hyperplasia in our study (21.4%) is considerably higher than rates reported in several studies, which range from 7% to 17.5% [2,3,6,8], though lower than an outlier finding of 56% in a small cohort [7]. This suggests a potentially higher burden of this pre-malignant condition in our local population. Most notably, our malignancy rate of 11.4% is exceptionally high. It surpasses the 9% rate in a post-menopausal cohort [10] and the 6.2% in a large international study [4], and is significantly higher than the 0.7-4% range reported across numerous other studies [1,2,3,6,7,8,9]. This striking finding strongly advocates

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for an aggressive diagnostic approach in our patient cohort.

Regarding endometrial thickness, our observation that an ET < 4 mm is associated with benign atrophy aligns perfectly with findings from other studies, which report a very high negative predictive value for malignancy below this threshold [4,10]. Our recommendation to investigate ET > 11 mm is consistent with other research focused on perimenopausal women, where cut-offs of ≥8 mm [8] and ≥10.5 mm [9] were proposed to detect pathology. The most critical correlation in our study—that 100% of cases with ET > 20 mm were malignant—is a powerful clinical indicator. While no other single study reported an identical 100% figure, this trend is strongly supported by findings that associate extreme endometrial thickening with malignancy; one study found 3 of its 4 cancer cases had an ET > 20 mm [3], and another reported a mean ET of 15.67 mm for adenocarcinoma [10], firmly establishing that significant endometrial thickening is a major red flag as summarized in the literature comparison.

Literature comparison summary: Previous studies generally report peak AUB presentation in the perimenopausal age group, with hyperplasia rates ranging from 7% to 30% in most cohorts and carcinoma rates commonly below the present study. Reported ET thresholds such as ≥8 mm, ≥10.5 mm, and >12 mm support histopathological evaluation when endometrial thickness is increased, while <4 mm is repeatedly associated with low malignant risk. Recent studies and reviews further support the use of endometrial thickness together with histopathological assessment for risk stratification in AUB and peri-/postmenopausal bleeding[11-15].

Limitations

However, several limitations must be acknowledged. The most significant is the small sample size (N=70). This limits the generalizability of our findings; for instance, the 100% rate of malignancy in the >20 mm ET group is a striking result but is based on only five patients and may be subject to the effects of random chance. Second, as a single-center study, the results may reflect local population demographics and referral patterns at Lahore General Hospital, and may not be representative of other regions. Third, the exclusion of patients with menorrhagia is a notable limitation. As menorrhagia is a very common presentation of AUB and is often linked to pathologies like leiomyomas and adenomyosis, its exclusion may have influenced the prevalence rates of the diagnosed conditions. Lastly, the use of non-probability consecutive sampling, while practical, may also limit the external validity of the results compared to random sampling.

Conclusion:

Transvaginal ultrasonography is a reliable, non-invasive, and effective screening tool for evaluating women with abnormal uterine bleeding. This study confirms a significant correlation between increasing endometrial thickness and the risk of underlying pathology, particularly endometrial hyperplasia and malignancy. An endometrial thickness >11 mm warrants histopathological evaluation, with thicknesses >16 mm being highly suspicious for malignancy. Conversely, an ET <4 mm is strongly associated with benign or atrophic changes, suggesting that invasive sampling may be safely deferred in these low-risk patients. These findings support the use of TVS to stratify patient risk, thereby optimizing diagnostic pathways, reducing unnecessary invasive procedures, and improving the standard of care, especially in resource-limited clinical settings.

Conflict-of-interest statement:

All authors declared no conflict of interest exists.

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Author Contribution Statement:

DA: Conceptualization, investigation, data curation, writing-original draft, discussion, and references.

RA: Investigation, data curation, writing-original draft, introduction, and references.

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AA: Formal analysis, abstract preparation, critical review, and data analysis.
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All authors reviewed and approved the final manuscript and agreed to be accountable for the integrity and accuracy of the work.

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The authors verified all scientific content, data, analysis, references, and conclusions and remain fully accountable for the integrity and accuracy of the work.

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