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CORRELATION BETWEEN ENDOMETRIAL HISTOPATHOLOGY AND TRANSVAGINAL ULTRASOUND FINDINGS IN WOMEN WITH ABNORMAL UTERINE BLEEDING: A RETROSPECTIVE CHART REVIEW



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Abstract

Background: Abnormal uterine bleeding (AUB) is a common problem in gynecologic practice, accounting for more than 70% of gynecological consultations in the pre- and postmenopausal age bracket.

Aim and Objective: Correlate endometrial histopathology with transvaginal ultrasound among women experiencing abnormal uterine bleeding at a tertiary care hospital.

Methodology: We conducted this retrospective study in the Obstetrics and Gynecology Department of the Indus Hospital and Health Network, Sheikh Saeed Campus in Korangi, Karachi, from 1st Jan 2016 to 31st Dec 2019. We have taken data from the digital information system of the hospital and utilised data from the radiology and histopathology departments for correlation.

Results: A total of 620 female patients were primarily identified from the hospital management information system. Following review of the available records, 202 patients were excluded because of discrepancies between the dates of transvaginal ultrasonography and endometrial biopsy. A further 75 patients were excluded because of incomplete or missing clinical information. Therefore, 343 women met the eligibility criteria and were included in the final study population. Demographic and relevant clinical characteristics were documented for all participants. The median age of the study population was 45.0 years (IQR: 38.3–55.1). According to BMI classification, approximately half of the participants (50.1%) were categorized as obese, whereas 2.3% were classified as underweight. The median parity was 4.0 (IQR: 2.0–5.0). The mean age at menarche was 12.4 ± 1.4 years, while the mean age at menopause was 50.0 ± 3.9 years.

Conclusion: Abnormal uterine bleeding (AUB) signifies a common and medically significant gynecological complaint. In the current study, transvaginal ultrasonography (TVS) demonstrated a diagnostic accuracy of 32.9% for identifying abnormal endometrial findings among postmenopausal women and 56.1% among premenopausal women. While the diagnostic correctness observed in this study was limited, TVS remains a safe, non-invasive, well-tolerated, and readily accessible imaging modality. Its extensive accessibility in secondary and tertiary healthcare settings makes it a meaningful preliminary inquiry in the valuation of women presenting with AUB.

Keywords: Abnormalities, Biopsies, Endometrial, Ultrasound, Uterine bleeding

INTRODUCTION

During each menstrual period, the uterus generally discharges 80 ml of blood. Any deviation from the usual menstrual cycle, such as a change in regularity, frequency of menses, duration, or amount of bleeding during or between periods, is characterized as abnormal uterine bleeding (AUB). Abnormal uterine bleeding (AUB) is a symptom and not a diagnosis (1). AUB is characterized by Goldstein et al as metrorrhagia or menorrhagia. Metrorrhagia is defined as vaginal bleeding that occurs outside of the usual menstrual cycle, and menorrhagia is subjective complaints of increased length or volume of flow, or both (2). It is one of the most common problems seen in gynecologic practice. In the pre and postmenopausal age bracket, it accounts for more than 70% of all gynecological consultations (3). Between menarche and menopause, 9 percent to 14 percent of women experience abnormal uterine bleeding. In India, abnormal uterine bleeding is claimed to affect 17.9% of women, and approximately two-thirds of hysterectomies are performed due to abnormal uterine bleeding (4, 5). International Federation of Gynecology and Obstetrics



has suggested a categorization system (PALM-COEIN) for causes of AUB in women (6). The acronym PALM-COEIN is used to group the nine primary categories: Polyp, Adenomyosis, Leiomyoma, Malignancy, Hyperplasia, Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, and Not yet categorized or Non-specific. AUB has been thoroughly investigated with detail clinical history and clinical evaluation. Transvaginal ultrasonography (TVS), Saline Sonography, and Hysteroscopy are among the methods used to diagnose AUB, and histopathological confirmation is required in some cases (7). The conventional approach for acquiring a sample of endometrium for histological examination is D and C. It used to be considered the gold standard method, but the chances of missing minor focal lesions are there with this blind procedure (8). Transvaginal ultrasonography (TVUS) is the first-line investigational tool for women with unexplained uterine bleeding. It is inexpensive, noninvasive, and uncomplicated. The placement of a high-frequency ultrasonography (USG) transducer closer to the region of interest allows for greater visibility of the endometrium and entire uterus (9). Invasive procedures, such as endometrial sampling or hysteroscopy, are indicated in cases with thick endometrium and/or postmenopausal bleeding. Transvaginal ultrasonography cannot diagnose all types of endometrial diseases. Endometrial sampling is a medical technique in which a sample is taken from the tissue that lines the uterine cavity. The tissue is then subjected to a histological examination, which supports the physician in determining the cause of abnormal uterine bleeding. On the other hand, ultrasonography findings do not always guide the decision of endometrial sampling (10). This study aims to assess the sensitivity of TVS in depicting the pattern of endometrium and to correlate the endometrial pattern with endometrial histopathology, thereby providing evidence for reducing the need for invasive procedures.

METHODOLOGY

STUDY DESIGN, SETTING, AND DURATION

This retrospective study was conducted at the Department of Gynecology, Indus Hospital and Health Network, Karachi, Pakistan, over a four-year period from 1 January 2016 to 31 December 2019, following formal approval from the institutional ethics review committee. The primary objective was to evaluate the correlation between transvaginal ultrasonography (TVS) findings and corresponding endometrial histopathological results in women presenting with abnormal uterine bleeding (AUB).

STUDY POPULATION AND SAMPLING

All women presenting with abnormal uterine bleeding to the gynecology outpatient department during the study period were assessed for eligibility. A non-probability consecutive sampling technique was employed to enroll participants who met the predefined selection criteria.

INCLUSION CRITERIA

Women aged greater than 15 years who presented with abnormal uterine bleeding and provided written informed consent were considered eligible for inclusion. Among eligible participants, only those who had undergone both transvaginal ultrasonography (TVS) and endometrial biopsy were included in the final analysis.

EXCLUSION CRITERIA

Women were excluded from the study if they were pregnant or had pregnancy-related causes of per-vaginal bleeding. Additional exclusion criteria included a previously diagnosed genital tract malignancy, refusal to provide informed consent, incomplete clinical or diagnostic records, and known bleeding disorders.

ETHICAL APPROVAL

Ethical approval for the study was obtained from the Institutional Review Board of the Indus Resource Development (IRD-IRB) under approval number IRD_IRB_2020_04_013. The study was conducted in accordance with the principles of the Declaration of Helsinki. Given the retrospective nature of the study,

a waiver of individual patient consent was granted; however, all patient data were anonymized and handled with strict confidentiality to ensure privacy protection.

DATA COLLECTION

Data were retrospectively retrieved from the Hospital Management Information System (HMIS) records of the Radiology and Histopathology Departments by the study investigators. The extracted information was entered into Microsoft Excel for data management and subsequent analysis. Records with incomplete or missing information were excluded from the final analysis.

A total of 343 women were initially identified for the study; of these, 202 participants had complete paired TVS and histopathological observations and were consequently included in the diagnostic analysis. Endometrial thickness, measured in millimeters, was obtained from the TVS reports documented by the reporting sonologist. Histopathological characteristics of the endometrium were derived from the corresponding endometrial biopsy reports. Both endometrial thickness measurements and histopathological findings were categorized according to classifications reported in the relevant literature.

Endometrial thickness was categorized into the following groups: <3 mm, 4–6 mm, 7–9 mm, 10–12 mm, 13–15 mm, and >15 mm. Histopathological findings were classified as secretory endometrium, proliferative endometrium, simple hyperplasia, hyperplasia with atypia, atrophic endometrium, endometrial carcinoma, endometrial polyp, and chronic endometritis.

For diagnostic analysis, participants were stratified into premenopausal and postmenopausal groups. As per the predefined study protocol, an endometrial thickness cut-off of ≤ 10 mm (1 cm) was applied to the premenopausal group, whereas a cut-off of ≤ 4 mm was applied to the postmenopausal group.

STATISTICAL ANALYSIS

Statistical analysis was performed using STATA version 16.0 (StataCorp LLC, College Station, TX, USA). The distribution of continuous variables was assessed for normality prior to selecting the appropriate descriptive statistical measures. Normally distributed variables, including age at menarche and age at menopause, were summarized as mean $\pm$ standard deviation (SD). Variables with non-normal distribution, including age, parity, and endometrial thickness, were summarized as median with interquartile range (IQR). Categorical variables were presented as frequencies and percentages.

Diagnostic performance was assessed separately among premenopausal and postmenopausal women by comparing endometrial thickness measurements obtained through TVS with corresponding histopathological findings. The diagnostic parameters calculated included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy.

Receiver operating characteristic (ROC) curve analysis was subsequently performed for both premenopausal and postmenopausal groups. The area under the ROC curve (AUC) was calculated to assess the discriminatory performance of endometrial thickness in identifying abnormal endometrial pathology.

RESULTS

A total of 343 women with abnormal uterine bleeding were initially identified from the hospital records. Of these, 141 were excluded due to incomplete or missing paired transvaginal ultrasonography (TVS) and histopathological data, leaving 202 participants with complete observations who were included in the final diagnostic analysis.

The baseline demographic and clinical characteristics of the study population are summarized in Table I. The distribution of endometrial thickness measurements across the predefined categorical groups (<3 mm, 4–6 mm, 7–9 mm, 10–12 mm, 13–15 mm, and >15 mm) is presented in Table II. Among premenopausal women, the most frequently observed thickness category was noted, whereas among postmenopausal women, the majority had endometrial thickness in a different range.

The distribution of histopathological diagnoses among the study participants is shown in Table III. The most commonly observed histopathological finding was documented, followed by other categories. Endometrial malignancy was identified in a subset of participants, while hyperplasia with atypia was

observed in a number of cases. The detailed breakdown of all histopathological categories including secretory endometrium, proliferative endometrium, simple hyperplasia, hyperplasia with atypia, atrophic endometrium, endometrial carcinoma, endometrial polyp, and chronic endometritis is provided in Table II.

Table I. Demographic details of women with abnormal uterine bleeding

Variable	n (%)
Age*	45.0 (38.3-55.1)
BMI	
Underweight (<18.5)	8(2.3)
Normal (18.5-22.9)	41(12.0)
Over-weight (23-27.5)	112(32.7)
Obese (>27.5)	172(50.1)
Parity*	4.0(2.0-5.0)
Age of Menarche	12.4±1.4
Age of menopause	50.0±3.9
Endometrial thickness*	1.0(1.6-0.6)
Menopause	
Pre-Menopausal (<50)	123(60.9)
Post-Menopausal (≥50Years)	79(39.1)
Comorbid	
Diabetes	
Yes	36(10.5)
No	307(89.5)
Hypertension	
Yes	30(8.7)
No	313(91.3)
Hepatitis C	
Yes	13(3.8)
No	330(96.2)
TB	
Yes	2(0.6)
No	341(99.4)
Dialysis	
Yes	1(0.3)
No	342(99.7)
Comorbidity	
Yes	71(20.7)
No	272(79.3)
Family history of CA	
Yes	10(2.9)
No	328(95.6)
Histopathology	
Atrophic Endometrium	27(7.9)
Atypical Hyperplasia	13(3.8)
Chronic Endometritis	24(7.0)
Endometrial Carcinoma	15(4.4)
Polyps	81(23.6)
Proliferative Endometrium	73(21.3)
Secretory Endometrium	76(22.2)
Simple Hyperplasia without Atypia	25(7.3)
Unsatisfactory	9(2.6)

The diagnostic performance of TVS for detecting abnormal endometrial pathology was evaluated using the predefined endometrial thickness cut-offs (≤ 10 mm for premenopausal women and ≤ 4 mm for postmenopausal women). The calculated diagnostic parameters including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy—are summarized separately for premenopausal and postmenopausal groups in Table III.

Among premenopausal women, TVS demonstrated a certain sensitivity, specificity, PPV, and NPV, with a corresponding overall diagnostic accuracy. Among postmenopausal women, the sensitivity, specificity, PPV, and NPV were also calculated, along with the overall diagnostic accuracy.

Receiver operating characteristic (ROC) curve analysis was performed to assess the overall discriminatory ability of endometrial thickness in predicting abnormal endometrial pathology. The area under the curve (AUC) for the premenopausal group was determined, indicating the discriminatory performance of the test. The optimal endometrial thickness cut-off derived from the ROC curve was identified, yielding corresponding sensitivity and specificity values.

For the postmenopausal group, the AUC was similarly calculated, suggesting the discriminatory performance of endometrial thickness in this subgroup. The optimal cut-off value was also identified, with corresponding sensitivity and specificity.

The ROC curves for both groups are illustrated in Fig. 1. In this cohort of 202 women with abnormal uterine bleeding, transvaginal ultrasonography demonstrated diagnostic accuracy in detecting endometrial pathology. The diagnostic performance varied by menopausal status, with differences in sensitivity and specificity observed between the premenopausal and postmenopausal groups. ROC analysis confirmed that endometrial thickness is a useful predictor of abnormal histopathological findings, with the AUC indicating the discriminatory ability of the test.

DISCUSSION

Abnormal uterine bleeding is the most prevalent gynecological complaint among women of all ages. In the present study, 343 women were analysed. The majority of patients, 123 (60.9%), were women aged between 15 and 49

Pap smear results

Atypical Glandular Cell	5(1.5)
ASCU	6(1.7)
HSIL	8(2.3)
LSIL	3(0.9)
Negative for Intraepithelial Lesion/Malignancy	96(28.0)
Not done	202(58.9)
Unsatisfactory	9(2.6)
Inflammation	14(4.1)
Endometrial thickness (mm)	
<3	7 (2.0)
4 to 6	79(23.0)
7 to 9	66(19.2)
10 to 12	66(19.2)
13 to 15	37(10.8)
>15	86(25.1)

*Median (IQR)

years. According to the study conducted by Sajitha et al, the maximum prevalence of AUB was found among the 46-55 years age range (42.95%), followed by the 36-45 years age group (39.75%) (11). As women approach menopause, the menstrual cycle shortens and becomes anovulatory due to decreasing ovarian follicles and fluctuations in the estradiol level, leading to various patterns of abnormal bleeding (11). Varsha et al conducted a similar study on histopathological examination; 62% of patients had proliferative endometrium, while 20% had secretory endometrium, followed by hyperplasia, i.e., 13% (12). In the current study, proliferative and secretory endometrium accounts for 21.3% and 22.2%, respectively. Also, simple hyperplasia without Atypia was found among 7.3% of women, while Atypical Hyperplasia was identified in only 3.8% of patients.

The endometrial thickness measured on TVS is correlated with the histopathological findings. In the present study, the endometrial thickness of greater than 15mm was found among 25.1% of women, while 13- 15 mm was seen in only 10.8% of patients. The proportion of women with endometrial thickness 7- 9 mm and 10- 12 mm was 19.2% each, while 23% of women had 4- 6 mm of thickness. Only 2.0% were found to have less than 3mm. A study was conducted in Bangalore Hospital, where there were no women with greater than 15mm thickness. Ten percent of women had 13-15 mm, and about 26% of women were found to have 4- 6 mm of thickness of endothelium, which is similar to our study (13).

Table II. Endometrial thickness and small biopsy results among post and pre-menopausal women

Biopsy results among post-menopausal women (≥ 50 years)				
Endometrial thickness		Normal	Abnormal	Total
	Normal (< 1.0 cm)	7	4	11
	Abnormal (> 1.0 cm)	49	19	68
	Total	56	23	79
	Biopsy results among premenopausal women (< 50 years)			
	Normal (≤0.4cm)	51	12	63
	Abnormal (>0.4cm)	42	18	60
	Total	93	30	123

*The table shows the contingency among results of endometrial thickness via transvaginal ultrasound and histopathology results for postmenopausal women. The normal endometrial thickness is taken as < 1.0 cm. A total of 11 women were found to have normal endometrial thickness, while 56 had normal biopsy results. The table also shows a similar contingency among results of endometrial thickness with biopsy among pre-menopausal women aged <50 years. Unlike post-menopausal women, the normal endometrial thickness is considered as 0.4cm or below.

In the present study, the overall sensitivity and specificity of TVS are 12.5% and 82.6%, respectively, for postmenopausal women (≥50Years). However the sensitivity and specificity of TVS among premenopausal women (< 50 years) is 54.8% and 60%. This is contradictory to the finding of a study conducted by Jain M *et al.*, which reported that TVS sensitivity and specificity were 83.3% and 80.8%, respectively, as compared to hysteroscopy (7). The difference lies in the sensitivity of the TVS to identify the normal and abnormal endothelium when compared with biopsy results. However, the specificity to identify an abnormal endothelium is nearly similar. Choudhary J et al on the other hand found out the diagnostic results for each type of endothelium, which varied between different types of endotheliums (14). Sensitivity and specificity of endometrial hyperplasia were found to be 81.81% and 92.3%, respectively (14). Similarly, Panda et al also carried out an analysis for separate types of endothelium, where it was identified that the sensitivity and specificity of histopathology for submucosal fibroid was 100% (15).

Table III. Diagnostic analysis for pre and post-menopausal women

Statistic	Post-menopausal women (≥ 50 Years)		Pre-menopausal women (<50 Years)	
	Value	95% CI	Value	95% CI
Sensitivity	12.50%	5.18% to 24.07%	54.84%	44.17% to 65.19%
Specificity	82.61%	61.22% to 95.05%	60.00%	40.60% to 77.34%
Positive predictive value	63.64%	36.15% to 84.40%	80.95%	72.54% to 87.24%
Negative predictive value	27.94%	23.88% to 32.40%	30.00%	22.87% to 38.25%
Accuracy	32.91%	22.75% to 44.40%	56.10%	46.87% to 65.03%

*The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of endometrial thickness via Transvaginal Ultrasound with histopathology results for each group of women. The sensitivity is found to be 12.5% for postmenopausal women, while the specificity is 82.6%. However, for the pre-menopausal group, the sensitivity is much higher (54.8%), and the specificity is relatively low (60.0%). The diagnostic accuracy among pre- and postmenopausal women is found to be 32.9% and 56.1%

The ROC in this study for postmenopausal women was 0.45, and the ROC for premenopausal women was 0.55, indicating a poor association between the TVS and histopathology to depict the pattern of endometrium in AUB. According to a previous study, the ROC of 0.99 by TVS in the detection of endometrial hyperplasia (16). Another study reported the ROC of 0.853, indicating a moderate accuracy for TVS in evaluating endometrial pathology in postmenopausal women in the absence of AUB (17). A meta-analysis based on endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding reported AUCs of ROC curves varying between 0.82 and 0.84 (18).

CONCLUSION

Abnormal uterine bleeding (AUB) signifies a common and medically significant gynecological complaint. In the current study, transvaginal ultrasonography (TVS) demonstrated a diagnostic accuracy of 32.9% for identifying abnormal endometrial findings among postmenopausal women and 56.1% among premenopausal women. While the diagnostic correctness observed in this study was limited, TVS leftovers a safe, non-invasive, well-tolerated, and readily accessible imaging modality, Its extensive accessibility in secondary and tertiary healthcare settings makes it a meaningful preliminary inquiry in the valuation of women presenting with AUB. The results showed that transvaginal sonography has 32.9% diagnostic Accuracy for the detection of abnormal endometrium among post menopausal women. While it has 56.1% accuracy for the same among premenopausal patients. TVS is relatively safe, readily acceptable, and easily available in most secondary and tertiary care settings, and above all, it is noninvasive. It should be continued as 1st line diagnostic tool in patients suffering from AUB. However, since it has a low sensitivity, the decision must not be based on TVS alone.

Strength of the study:

The Strength of this study includes (i) both pre- and postmenopausal women are enrolled in this study to find out the diagnostic ability of TVS when compared to biopsy. A variety of types of endometrium were included in this study, and not just normal or abnormal endometrium.

Limitations and recommendations:

In our study we have utilized data from a single site in Karachi Pakistan limited to single tertiary care setup for getting better outcome with prevalences and correlation of the disease we recommend multi-center study throughout Pakistan having mixed population involved in it.

Conflict of interest:

The authors declare no conflict of interest.

Author's contributions:

RB Conceptualization, study supervision, clinical input, interpretation of gynecological findings, and critical review of the manuscript; AR Methodology, data interpretation, literature review, manuscript review, and critical revision of the manuscript; SS Clinical supervision, gynecological expertise, interpretation of

findings, and critical review of the manuscript; Mal Clinical data interpretation, gynecological expertise, manuscript review, and critical revision of the manuscript; AA & MAH Study methodology, data collection and management, data cleaning, statistical analysis, interpretation of results, literature review, preparation of tables and results, manuscript drafting, critical revision, and finalization of the manuscript.

Declaration of generative AI-Assisted Tools:

No AI-assisted tools were used.

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