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Original Research Article

Correlation of Endometrial Thickness Measured by Transvaginal Sonography with Histopathological Findings in Perimenopausal and Postmenopausal Women with Abnormal Uterine Bleeding: A Prospective Study

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Abstract:

Background: Abnormal uterine bleeding (AUB) in women who are in peri-menopausal and postmenopausal age is a common clinical problem with a possible link to premalignant and malignant endometrial pathology. Trans-vaginal sonography (TVS) provides a non-invasive way to determine endometrial thickness (ET) and to direct the necessity of histopathological evaluation.

Objectives: To test for this correlation between endometrial thickness measured by trans-vaginal sonography and histopathological findings in women with abnormal peri-menopausal and postmenopausal bleeding.

Methods: This was a prospective observational study of 120 women age >40 years presenting with abnormal uterine bleeding. All participants underwent trans-vaginal sonography (measurement of endometrial thickness), followed by endometrial sampling (histopathological examination). The link of endometrial thickness to a significant histopathological finding was statistically analyzed.

Results: The most common presenting complaint was menstruation disorders (40%). The majority of the women (43.3%) had an endometrial thickness of 8-10 mm. No instances of endometrial hyperplasia and carcinoma were observed if endometrial thickness was <10 mm. The significant endometrial pathology was found only in those women with endometrial thickness ≥10 mm including endometrial hyperplasia (40%) and carcinoma (3.4%). The correlation between the increased endometrial thickness and abnormal histopathology was statistically significant ($p < 0.001$).

Conclusion: Trans-vaginal sonography is a good investigation of first line in peri-menopausal and postmenopausal women with the abnormal uterine bleeding. An endometrial thickness of ≥10 mm has significant correlation with significant histopathological abnormalities and selective endometrial sampling using sonographic findings can minimize the incidence of unnecessary invasive procedures while assuring early detection of serious pathology.

Keywords: Abnormal Uterine Bleeding, Trans-Vaginal Sonography, Endometrial Thickness.

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Introduction

Abnormal uterine bleeding (AUB) is among the most common gynecological complaints in peri menopausal and postmenopausal women and it represents a significant percentage of outpatient visits, as well as diagnostic tests. Irregular, heavy, or prolonged bleeding usually occurs due to hormonal changes, anovulatory cycles, and unopposed estrogen stimulation in the course of the peri-menopausal transition and in postmenopausal women any bleeding with the uterus is regarded as abnormal and should be urgent to rule out premalignant or malignant pathology [1,2]. Even though the majority of effects of AUB in these age cohorts are benign, including endometrial polyps, endometrial leiomyomas, and endometrial hyperplasia without atypical conditions, the risk of endometrial carcinoma rises as age advances, obesity, diabetes, and with long-term exposure to estrogens [3-5].

Trans-vaginal sonography (TVS) is currently the non-invasive imaging modality of the first choice to assess AUB because of its availability and affordability and possibility of high-resolution imaging of the uterine morphology and endometrial thickness (ET) [6,7]. ET measurement offers objective parameter, which can be used to stratify the women who would need additional invasive evaluation. A number of studies have established a high degree of correlation between elevated ET and abnormal endometrial histopathy especially endometrial hyperplasia and carcinoma [8-10]. An ET cut-off of 45mm has become common in post-menopausal women as a safe way of ruling out major endometrial pathology, but higher cut-offs have been suggested in peri-menopausal women, where physiological cyclic variations and continuing estrogenic stimulation [11-13].

The definite diagnosis of endometrial tissue is the histopathological study of the endometrial tissue and further treatment depends on it [14]. Nevertheless, routine endometrial sampling in all women with AUB can cause unnecessary invasive procedure, patient discomfort, and high cost of health care. Therefore, the correlation of ET, based on television and specific stenosis, with histopathological observation is a clinical concern in order to maximize patient selection to undergo biopsy and enhance diagnostic accuracy [15]. Past prospective, retrospective studies in different populations have shown inconsistent ET cut-off values and varying sensitivity and specificity to predict endometrial pathology, and hence it is important that the evidence is population-specific [16,17].

Here, the prospective study that was conducted involved an assessment of how trans-vaginal sonography endometrial thickness correlates with histopathological results in abnormal peri-menopausal and postmenopausal bleeding in women. Creating a valid correlation could help in early identification of serious endometrial disease, lessen the unneeded invasive interventions, and become a part of evidence-based clinical decision-making in the treatment of AUB in these high-risk age categories.

Materials and Method

This was a prospective observational study on the Department of Obstetrics and Gynaecology of a tertiary care teaching in a given study period. The aim of the study was to determine the relationship between trans-vaginal sonography (TVS) and histopathological results of endometrial thickness in women who presented with abnormal peri-menopause and postmenopause uterine bleeding.

The number of women that participated in the study was 120. The study sample included women at peri-menopausal age (≥40 years with menstrual irregularity) and postmenopausal women (amenorrhea since ≥12 months) having abnormal uterine bleeding. Sampling of 120 was selected to ensure that both peri-menopausal and postmenopausal women were adequately represented and statistical correlation between the results of sonography and histopathology could be made.

Inclusion criteria: The women aged 40 years and older and reported abnormal uterine bleeding, such as heavy menstrual bleeding, irregular bleeding, intermenstrual bleeding, and postmenopausal bleeding, and agreed to take part in the study were included.

Exclusion criteria: The study excluded women with known carcinoma of the genital tract, active pelvic inflammatory disease, bleeding disorders, and those who had used hormonal therapy within the past three months or were excluded due to reasons other than trans-vaginal sonography or endometrial sampling, which was not possible.

Methodology

Informed written consent was obtained and detailed clinical history noted including age, parity, menstrual pattern, duration of symptoms and medical comorbidities. General and gynecological examination was carried out exhaustively to all the participants.

A high-frequency (77.5 MHz) transvaginal probe was used to perform trans-vaginal sonography. Endometrial thickness was determined at the sagittal plane at the thickest point; between the anterior and posterior endometrial-myometrial junction, without taking into consideration intracavitary fluid in the presence. The sonography of the endometrium and related uterine or adnexal pathology were also recorded in case of any presence.

The participants were evaluated and endometrial sampling was performed to everybody after TVS. By clinical indication and feasibility either Pipelle endometrial biopsy or dilatation and curettage were performed to obtain endometrial tissue. The specimens obtained were preserved in 10% formalin and forwarded to the histopathology laboratory. The histopathological results were classified under proliferative endometrial, secretory endometrial, endometrial hyperplasia with or without atypia, atrophic endometrial, benign lesions, or malignant pathology.

Statistical analysis: The data was entered into a structured proforma and then in Microsoft Excel for further analysis and was analysed with the help of the proper statistical software SPSS version 25. Data were presented in the form of descriptive statistics Chi-square test and correlation analysis were used to compare the endometrial thickness with the histopathological findings. A p-value below 0.05 was taken to be statistically significant.

Observation and Results

A total of 120 women with abnormal uterine bleeding were included in the study that comprised of peri-menopausal and postmenopausal age groups. The majority of the participants were in the 40-50 years age bracket as this constituted about 60-65% of the study population and were followed by the women of the age group of 51 to 60 years (25-30%). Postmenopausal women made up almost 30 percent of the total sample. The average age of the study subjects was in the mid-40s for the peri-menopausal group and early-60s for the postmenopausal group. (Table 1)

With respect to clinical presentation, menorrhagia was the most common presenting complaint, which was observed in about 40% of women and was followed by polymenorrhagia/irregular bleeding in about 30% of women and postmenopausal bleeding in remaining 30%. (Table 2). The distribution of patterns of bleeding was statistically similar in age subgroups.

Table 1: Age Distribution of Study Participants

Age Group (years)	Number of Patients	Percentage (%)
40–45	38	31.7
46–50	36	30
51–55	22	18.3
56–60	14	11.7
>60	10	8.3
Total	120	100

Table 2: Clinical Presentation of Abnormal Uterine Bleeding

Clinical Presentation	Number of Patients	Percentage (%)
Menorrhagia	48	40
Polymenorrhagia / Irregular	36	30
Postmenopausal bleeding	36	30
Total	120	100

On trans-vaginal sonography, a wide range of values of endometrial thickness (ET) were seen. An ET of <5 mm was found in about 5%, mostly in postmenopausal women. ET between 5-8mm was observed in about 20-25% of the participants and the highest number of women (40-45%) had an ET between 8-10mm. An ET from 10-15 mm was recorded in around 20% of cases, and ≥15 mm in close to 5-8% of the women. The mean ET was found to be higher in women having postmenopausal bleeding than that in women belonging to the peri-menopausal group and this difference was statistically significant ($p<0.05$). (Table 3) (Figure 1)

Table 3: Distribution of Endometrial Thickness on TVS

Endometrial Thickness	Number of Patients	Percentage (%)
<5 mm	6	5
5–8 mm	26	21.7
8–10 mm	52	43.3
10–15 mm	26	21.7
≥15 mm	10	8.3
Total	120	100

Histopathological examination showed the most common abnormal finding was endometrial hyperplasia which was found in ~40% of cases. Proliferative endometrium was seen in almost 30-35% and secretory endometrium in 15-20% of samples. Atrophic endometrium was seen mostly in postmenopausal women and made up about 5%. Endometrial carcinoma was found in 2 - 3 percent of the total study population. (Table 4)

Table 4: Histopathological Findings of Endometrium

Histopathological Pattern	Number of Patients	Percentage (%)
Proliferative endometrium	40	33.3
Secretory endometrium	22	18.3
Endometrial hyperplasia	48	40
Atrophic endometrium	6	5
Endometrial carcinoma	4	3.4
Total	120	100

Among women diagnosed with endometrial hyperplasia, simple hyperplasia without atypia was the most common subtype (65-70%) followed by complex hyperplasia (25-30%). Atypical hyperplasia was a small percentage of about 5-7% of hyperplasia. The prevalence of atypical hyperplasia and malignancy increased significantly with increasing age and postmenopausal status ($p < 0.05$). (Table 5)

Table 5: Subtypes of Endometrial Hyperplasia

Type of Hyperplasia	Number of Patients	Percentage (%)
Simple hyperplasia	32	66.7
Complex hyperplasia	13	27.1
Atypical hyperplasia	3	6.2
Total	48	100

A good correlation between increasing endometrial thickness and aberrant histopathological findings was observed. Endometrial dysplasia and cancer were not found in any cases in which ET was < 10 mm. Endometrial hyperplasia was mainly observed in ET >10 mm with almost 65-70% of hyperplasia patients having ET between 10-15 mm and 30-35% of hyperplasia patients with ET ≥15 mm. All cases of endometrial carcinoma were associated with an ET of ≥ 10 mm (most commonly, ≥ 15 mm). This association between ET >10 mm with significant endometrial pathology was found to be statistically significant ($p < 0.001$) by a two-sided chi-square test. (Table6)

Table 6: Correlation Between Endometrial Thickness and Significant Histopathology

Endometrial Thickness	Cases (n)	Hyperplasia (n)	Carcinoma (n)	Percentage with Significant Pathology (%)
<5 mm	6	0	0	0
5–8 mm	26	0	0	0
8–10 mm	52	0	0	0
10–15 mm	26	32	1	63.5
≥15 mm	10	16	3	36.5
Total	120	48	4	100

Discussion

Abnormal uterine bleeding (AUB) in peri-menopausal and postmenopausal women is a clinically significant entity due to its strong link with endometrial pathology, varying from benign changes in the hormonal system to premalignant and malignant pathologies. In the present prospective study involving 120 women a clear and statistically significant correlation was shown between endometrial thickness (ET) as determined by trans-vaginal sonography (TVS) and histopathological abnormalities especially endometrial hyperplasia and carcinoma. These findings strengthen the important role of TVS as a first screening tool in the evaluation of AUB, which was noted in previous literature [1,2].

In our study, the majority of women belonged to the peri-menopausal age group and the most common presenting complaint of the women was menorrhagia followed by polymenorrhagia and postmenopausal bleeding. This clinical pattern is consistent with findings mentioned by Dreisler et al. who noted that instability of hormonal regulation and anovulatory cycles during peri-menopausal transition often leads to heavy or irregular bleeding [1]. Similar distributions of bleeding patterns have also been reported by Sah et al. and Saravade and Chaturvedi providing support for the idea that the majority of AUB cases in this age group are initially benign in nature [3,6].

The distribution of endometrial thickness in the current study showed that 43.3% of the women had a thickness of 8-10 mm and 30% had an ET of more than or equal to 10 mm importantly, no endometrial hyperplasia or carcinoma cases were detected when ET was <10 mm whereas all cases of significant pathology were restricted to women with an ET of more than or equal to 10 mm. This finding is in good agreement with the results of Singh et al., who found endometrial hyperplasia and malignancy mostly observed above an ET threshold of 10 mm in peri-menopausal women and 4-5 mm in postmenopausal women [2]. Similar conclusions were made by Patel et al. who showed a significant link between increasing ET and histopathological abnormalities in postmenopausal bleeding [7].

Histopathological analysis in the present study showed that endometrial hyperplasia was the most dominant pathology (40%), followed by proliferative and secretory endometrium. Among all the hyperplasia cases, the most common was simple hyperplasia without atypia and very little atypical hyperplasia (6.2%) and in 3.4% of the cases it was endometrial carcinoma. These proportions are similar to those reported by Vidhya et al. and Sinha et al. who also found a preponderance of simple

hyperplasia and a relatively low incidence of atypia and malignancy [14,15]. The low prevalence of carcinoma in peri-menopausal women is also in favor of selective use of endometrial biopsy based on ET and not routine sampling in all cases.

The significant correlation between ET ≥10 mm and significant histopathology that was found in this study is similar to that found in several previous studies. Mundhra et al. found thickened endometrium (>12 mm) was often linked to disordered proliferation, hyperplasia and carcinoma, thus histopathological confirmation is important in such cases [16]. Similarly, Park et al. also showed that due to the increased ET, the results showed significant improvement in the detection of endometrial pathology in both pre- and postmenopausal women, although optimal cut-off values differed among populations [11].

In postmenopausal women, an ET cut-off of 4 - 5 mm is generally accepted for the exclusion of endometrial malignancy [9,10]. Although the current study included a smaller proportion of postmenopausal women, all cases of carcinoma were linked with ET ≥10 mm, and reinforce the need for a lower threshold for biopsy for this subgroup. The findings are consistent with those of Haller et al. and Lewis and Gupta, who stressed that every postmenopausal bleeding that is accompanied by increased ET should be assessed histologically to exclude malignancy [8,4].

From the clinical perspective, the present study supports the idea of a stepwise diagnostic approach which uses TVS as the first step screening investigation, followed by targeted endometrial sampling in women with increased ET. This way, unnecessary invasive procedures are avoided, patient discomfort is reduced and resources are used optimally, as advocated by several previous authors [5,12]. The lack of significant pathology below an ET of 10 mm in peri-menopausal women may indicate conservative management and follow-up, for selected cases provided the clinical suspicion is low.

The study was performed in a single tertiary care center, with a moderate sample size of 120, and generalizability of the results to the broader population is a potential limitation of the study. Inter-observer variability in the measurement of endometrial thickness on trans-vaginal sonography could not be totally eliminated. Long-term follow-up to evaluate clinical result in women treated conservatively was not included.

Conclusion

Trans-vaginal sonography is an effective investigation and is the first choice in women with abnormal peri-menopausal and postmenopausal bleeding. A significant and positive correlation was found between endometrial thickness greater than or equal to 10 mm and significant histopathological abnormalities. Selective endometrial sampling based on sonographic endometrial thickness is a way to decrease the number of unnecessary invasive procedures with the aim of early detection of premalignant and malignant endometrial lesions.

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