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Original Research Article

Correlation of combined B-mode and uterine artery Doppler with the endometrial pathology in perimenopausal women with abnormal uterine bleeding

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ABSTRACT

Introduction: Heavy menstrual bleeding in perimenopausal women is defined as excessive blood loss that interferes with the woman's physical, emotional, social, and material quality of life. In India, the reported prevalence of abnormal uterine bleeding is around 17.9%.

Background: This study was conducted at AIIMS, Nagpur, where 80 perimenopausal women were recruited with complaints of HMB in our cross-sectional study. We obtained samples of uterine artery PI and RI, endometrial thickness, and performed an endometrial biopsy on the same day. The mean and standard deviation for PBAC, haemoglobin, endometrial thickness, PI, and RI are calculated.

Result: The cohort comprised women with a mean age of 46.06 years (±5.8 years). The mean PBAC score was 342 (±117.2), ranging from 145 to 590. Haemoglobin levels were at a mean of 8.8 g/dl (±1.14), with a range from 6.2 gm/dl to 10.3 gm/dl. A mean endometrial thickness of 11.65 mm (±4.05) with mean values for pulsatility index (PI) and resistance index (RI) were 1.72 (±0.065) and 0.75 (±0.035), respectively. Endometrial pathology distribution in biopsy samples included disordered proliferation endometrium in 29 out of 80 cases (36.25%), proliferative endometrium in 21 out of 80 cases (26.3%), secretory endometrium in 14 out of 80 cases (17.5%), and endometrial hyperplasia without atypia in 9 out of 80 cases (11.2%). Additionally, three cases of endometrial malignancy were identified within the cohort.

Conclusion: The combination of uterine artery doppler to B-mode ultrasound doesn't add much information in detecting endometrial pathologies like malignancy and atypia.

Keywords: Endometrial biopsy, Endometrial thickness, AUB, Uterine artery color Doppler

INTRODUCTION

Abnormal uterine bleeding (AUB) is defined as bleeding from the uterine corpus that is abnormal in regularity, volume, frequency, or duration in the absence of pregnancy.[1] It is the most commonly encountered problem in gynaecological OPD and can affect 10-30% of women in the reproductive age group, and may affect 50% of peri-menopausal women.[2-4] Heavy menstrual bleeding (HMB) is widely accepted as the loss of menstrual blood of ≥60-80 ml per cycle, compared with 30-40 ml for the average woman with 'normal' periods.[6]

The National institute for health and care excellence (NICE) defines HMB more holistically as "excessive blood loss that interferes with the woman's physical,

emotional, social, and material quality of life".[6] In India, the reported prevalence of abnormal uterine bleeding is around 17.9%.[1]

There are many methods for endometrial assessment, including ultrasound measurement of endometrial thickness, endometrial dilation and curettage, and office-based methods such as endometrial samples using a pipelle. An endometrial biopsy with dilation and curettage is the gold standard method, but it needs hospitalization and necessary anaesthesia. However, being an invasive procedure, it has a risk of complications, infection, and uterine perforation. Diagnosis of malignant and non-malignant lesions of the endometrium in heavy menstrual bleeding patients requires an endometrial biopsy, but there is the risk of false-negative results. Despite that, excluding malignant endometrial changes is still mandatory.[2]

Another non-invasive and painless modality is transvaginal sonography, which is routinely done in HMB patients, but it's not specific and can't distinguish between benign proliferation, hyperplasia, polyps, and malignant lesions. Utero-ovarian blood flow is a potentially valuable method to evaluate increased blood flow due to neo-angiogenesis, especially in premalignant and malignant conditions. These parameters effectively assess the impedance to flow in the uterine artery, endometrial vasculature, and subsequent effect on the endometrial receptivity. Hence, this test can be applied to differentiate between malignant and benign cases at least, which is the aim of doing an invasive test, i.e., endometrial biopsy.

Recently, a few studies on uterine artery doppler sonography in heavy menstrual bleeding show sensitivity and specificity as high as 90 to 100% for detecting endometrial pathology, and can be a promising tool in the future to detect endometrial abnormalities.[7,8] The present study will be done to measure uterine artery doppler indices in perimenopausal women with AUB. The addition of uterine artery doppler studies in these women may provide additional information at the time of transvaginal ultrasound evaluation about the uterine blood flow, which may be altered in patients with endometrial pathology.

METHODS

Study design

This was a cross-sectional study

Study duration

The study duration was from October 2023 to December 2023.

Study setting

Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences (AIIMS), Nagpur.

Study population

Patients presenting to the Gynaecology department with complaints of heavy menstrual bleeding above 40 years of age. The National Institute for Health and Care Excellence (NICE) defines HMB more holistically as "excessive blood loss that interferes with the woman's physical, emotional, social, and material quality of life" 7

Inclusion criteria

All patients above 40 years of age presenting with heavy menstrual bleeding.

Exclusion criteria

Fibroids with the size of uterus >4 cm, Adenomyosis, Postmenopausal bleeding (PMB is defined as bleeding after one year of amenorrhoea), patients already on hormonal therapy for AUB, women with coagulation disorders or on anticoagulants, endometrial polyp, the intrauterine device in situ, or any adnexal mass.

All the patients attending the Gynaecology department with abnormal menstrual bleeding were screened for heavy menstrual bleeding. A detailed history was obtained, including age, age of menarche, marital status, parity, pattern of menstrual bleeding (duration and frequency), duration of complaints, and history of medication received, if any. A detailed general examination, including height, weight, Body Mass Index, and signs of pallor, per abdomen examination and speculum, and vaginal examination, was done to exclude local causes of vaginal bleeding. Investigations like blood group, complete blood count, thyroid function test, and Pap smear were done as a part of the routine workup of AUB.

A transvaginal pelvic ultrasound was carried out to rule out structural causes and to measure endometrial thickness. All these women were examined using transvaginal sonography and bilateral uterine artery doppler after taking written, valid informed consent, by using Mindray DC-30,9P-01006663 ultrasonography machine (Mindray Medical System, USA Inc), using an 8 MHz endo-vaginal probe. The transvaginal sonography was performed after the woman emptied her bladder and in the lithotomy position. The thickness of the endometrium was measured at the maximum distance between each myometrium/endometrial interface in a longitudinal plane.

Then, the colour Doppler mode was activated to obtain the flow images. The uterine arteries were traced laterally to the cervix near the internal os bilaterally. Using the colour doppler in the 2D mode, flow velocity waveforms were obtained from the ascending branch of the uterine artery on the right and left sides of the cervix in a longitudinal plane before they entered the uterus. A 2-mm range gate is then placed across the vessel. The angle of the probe was moved to obtain the maximum waveform amplitude and

clarity. After confirming that waveforms are continuous, an average of 3-5 cardiac cycles was selected for the calculation of the Resistive index (RI) and Pulsatility index (PI). Both RI and PI were calculated automatically by the ultrasound machine. RI (Resistance index) = PSV-EDV /PSV, PI (Pulsatility index) =PSV–EDV/MAV, PSV-Peak systolic velocity, EDV-End-diastolic velocity. Endometrial biopsy is the gold standard test to detect endometrial pathology. For any patient with AUB who is above 40 years of age, an endometrial biopsy is recommended by NICE guidelines.[7] All patients underwent endometrial sampling by Pipelle's device on the same day following ultrasound examination. The biopsy specimen was reported by the pathologist who was blinded to the results of the doppler studies.

The endometrial pathology report was considered abnormal if it showed endometrial hyperplasia with or without atypia or endometrial carcinoma. All other reports, including hormonal imbalance, were categorized as normal.

Sample size

Based on a previous study, with an expected sensitivity of 96% and specificity of 100% of uterine artery resistive index to detect endometrial pathology with 95% confidence, the sample size calculated is 68. Considering the 10% dropout rate, the final sample size calculated was 76.

Data analysis

Findings were entered in an Excel sheet, and age matching of the values was done. Continuous variables were calculated as mean, standard deviation if normally distributed, and median with IQR if not normally distributed (PBAC score, haemoglobin, endometrial thickness, uterine artery PI, and RI) and were compared with the student's t-test. Categorical/Discrete variables were expressed as frequency and proportion and were compared.

A one-way ANOVA test was used to correlate RI and PI values with endometrial pathology.

RESULTS

80 women participated and completed the study between October 2023 to December 2023. The demographic distribution is shown in Table 1. The mean age of these women was 46.06±5.8 years. The mean PBAC score for these women was 342±117.2, with a minimum of 145 and a maximum of 590, as shown in Figure 1. The mean haemoglobin of these 80 women was 8.8±1.14 gm/dl with a minimum of 6.2 gm/dl and a maximum of 10.3 gm/dl, suggesting that most of the women had anaemia subsequent to HMB (Figure 2). The mean endometrial thickness as measured on transvaginal ultrasound was 11.65 ± 4.05, as shown in Figure 3.

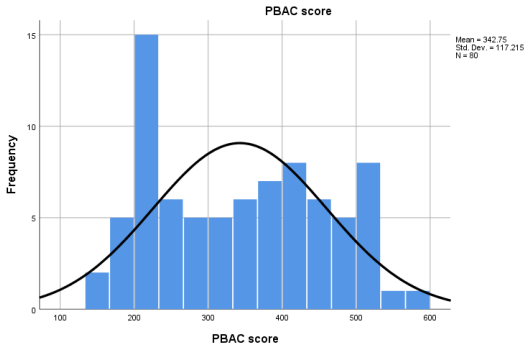

Figure 1: PBAC score mean and standard deviation.

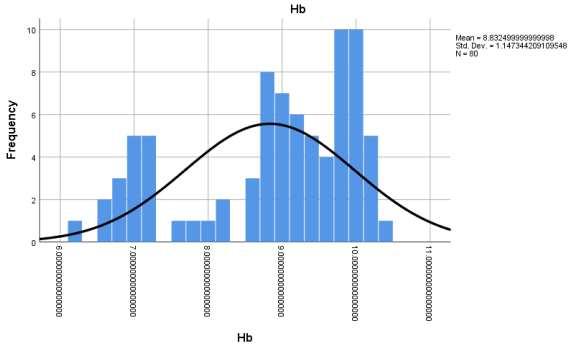

Figure 2: The mean Hb and its standard deviation.

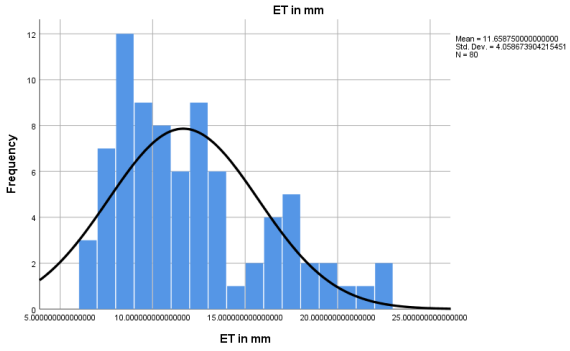

Figure 3: Mean and standard deviation of the endometrial thickness (ET).

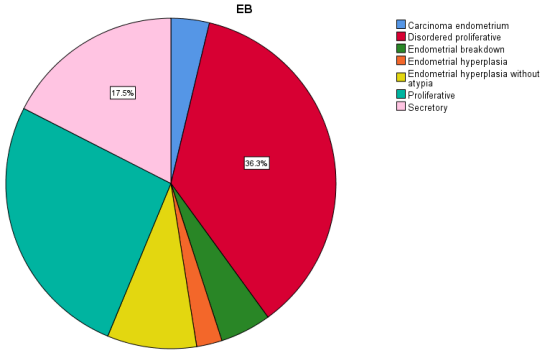

Figure 4: Distribution of histopathological examination of endometrial biopsy (EB).

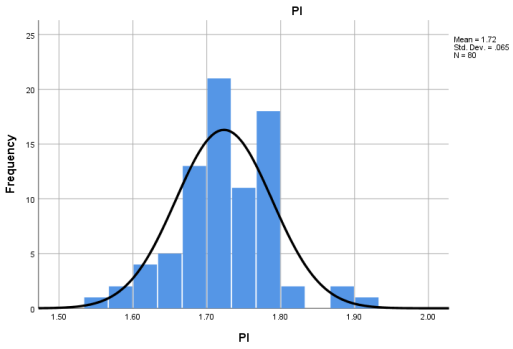

Figure 5- The mean and standard deviation of PI of uterine artery.

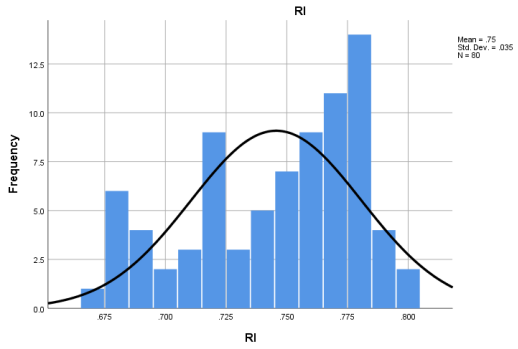

Figure 6: The mean and standard deviation of RI of the uterine artery.

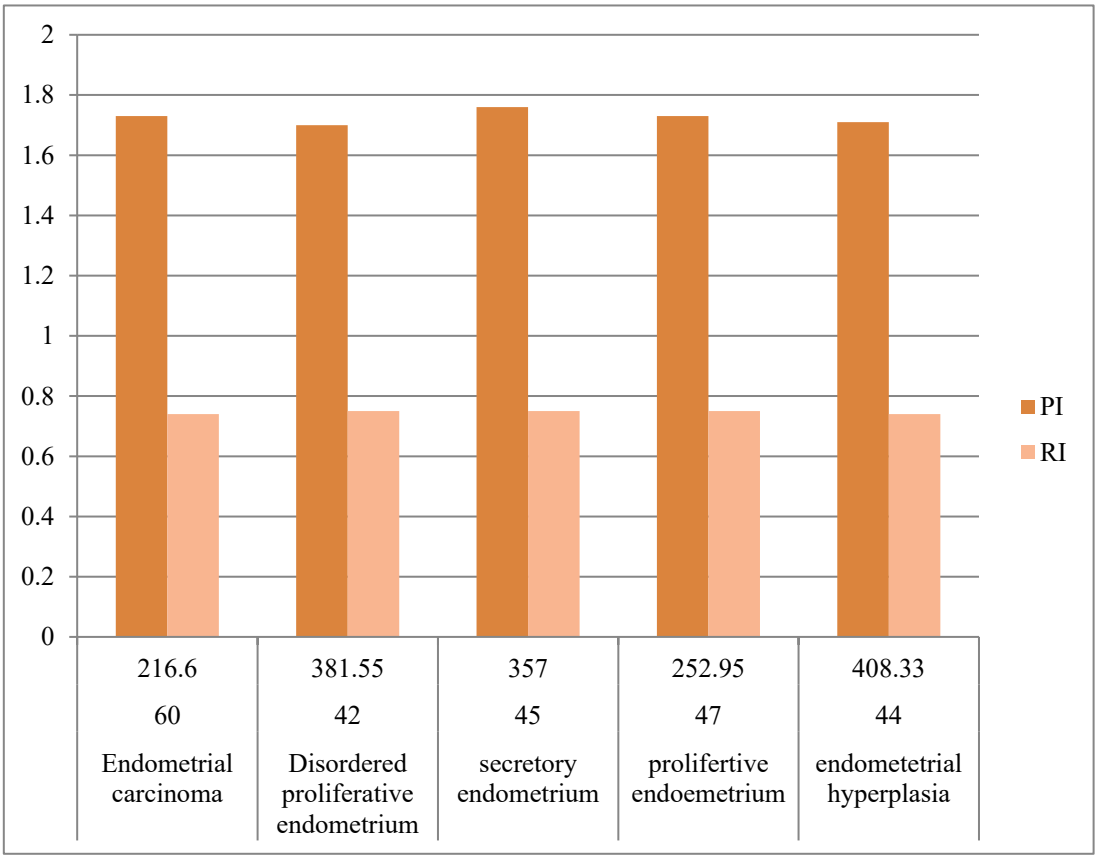

Figure 7: Histopathological examination of endometrium and its mean PI and mean RI distribution.

The distribution of endometrial pathology in the biopsy sample was disordered proliferative endometrium 29/80 (36.25%), proliferative endometrium 21/80 (26.3%), secretory endometrium 14/80 (17.5%), followed by endometrial hyperplasia without atypia 9/80 (11.2%). There were three cases of endometrial malignancy also (Figure 4). The mean ET of disordered proliferative endometrium was 15.23 mm, endometrial carcinoma was 20 mm, endometrial hyperplasia was 18.14 mm, proliferative endometrium was 11.13 mm, and secretory endometrium was 11.05 mm. The mean PI & RI of the uterine artery for 80 women was 1.72 with SD 0.065 (Figure 5) and 0.75 with SD 0.035 (Figure 6), respectively.

Evaluation of mean PI and RI according to different endometrial pathologies is shown in Figure 7. Further analysis upon applying the ANOVA test (Table 1) revealed that in perimenopausal women with abnormal uterine bleeding, there was no significant correlation between the combined B-mode and uterine artery doppler findings and endometrial pathology, as there was no statistically significant difference in mean PI and RI of different endometrial pathologies. This suggests that while these imaging techniques may show promise in some cases, they may not be reliable indicators of endometrial pathology in all perimenopausal women with abnormal uterine bleeding.

Table 1: Demographic distribution.

Demographic details	Values
Mean age (in year)	46.06%
Multipara	93.75%
Nullipara	6.25%
Urban	58.75%
Rural	41.25%
Educated	67.5%
Uneducated	32.5%

Table 2: ANOVA test for PI and RI of the uterine artery with f value 1.08.

Source	SS	Df	MS	F	Prob>F
Between groups	100.816667	21	4.80079365	1.08	0.3951
Within groups	258.183333	58	4.45143678		
Total	359	79	4.5443038		

Barlett's equal-variances test: chi 2 (12)=0.8372 Prob>chi=1.000

DISCUSSION

The study highlights the complexity of diagnosing endometrial pathology in perimenopausal women and emphasizes the need for a comprehensive approach that takes into account a range of clinical and imaging factors. The mean age of the perimenopausal age group is 40-45 years, presenting with AUB. The most common cause of hysterectomy is AUB in this age group, and the main cause is endometrial hyperplasia (56.31%). Similar results can be seen in our study with a mean age of 46.3 years and an endometrial hyperplasia composed cumulative percentage of 56%.[9] In the study, the rate of carcinoma endometrium was 3.7% which is much lower than the study of Jha et al where they found it as 4.7%.[10] It is low as carcinoma endometrium is a disease of postmenopausal women, and the mean age group of carcinoma endometrium is 62 years.[11] Our study analysis revealed that in perimenopausal women with abnormal uterine bleeding, there was no significant correlation between the combined B-mode and uterine artery doppler findings and endometrial pathology. Irrespective of endometrial pathologies, the mean PI and RI of the uterine artery were almost similar.

A study by Noha et al in 50 postmenopausal women concluded that the mean uterine artery RI and PI were lower in cases with Postmenopausal bleeding and cases with malignant causes than benign causes. The mean spiral artery RI & PI were also lower in cases with benign than in cases with malignant causes of postmenopausal bleeding.[12] In a similar study by Nguyen et al, the uterine artery doppler indices, including resistance index (RI), pulsatility index (PI), and peak systolic velocity (PSV), were significantly lower in the malignant group than in the benign group. The threshold values of the Uterine Artery RI were ≤0.73, and PI was ≤1.42, with the sensitivity and specificity being 91.3% and 83.3%, respectively.[13] However, the study by Ahmadzade et al contradicts these findings and suggests that the RI, PI, and PSV indices in endometrial carcinoma were significantly higher than in endometrial hyperplasia ($p<0.0001$). They studied two groups, 10 patients with endometrial hyperplasia and 38 patients with endometrial cancer, and concluded that the Intramural blood flow index was higher in high-grade tumours than in low-grade tumours ($p<0.05$).[14] Our study couldn't find any significant difference, as we didn't consider the spiral arteries' colour doppler.

In a study, they stated that in cases of proliferative or secretory endometrium, the interquartile range for endometrial thickness was 6–13 mm and the colour score was often 1, and in endometrial hyperplasia without atypia, the interquartile range for endometrial thickness was 9–17 mm with the colour score was usually 1 or 2 and, when colour doppler signals were present, the most common vessel morphology was multiple vessels with multifocal origin or a scattered pattern. Whereas in endometrial cancer, the endometrium was thickened, the interquartile range of endometrial thickness being 11–26 mm, and a high colour score of 3 or 4 was common, and if colour-doppler signals were detectable, the most common vessel pattern was multiple vessels of focal or multifocal origin.[15] Similar vascular grading was done by Heremans et al in the study where patients with heavy menstrual bleeding and those without heavy menstrual bleeding were compared and found that moderate to abundant vascularization (colour score 3-4) was seen in cases with endometrial carcinoma compared with those with a benign outcome. Multiple multifocal vessels were recorded in women with Endometrial carcinoma versus those with a benign outcome. In women with endometrial carcinoma, both in those with and those without heavy menstrual bleeding, the endometrium usually manifested heterogeneous echogenicity, but the endometrium was on average 8.6 mm thinner and less intensely vascularized (colour score 3-4) in women compared to those with heavy menstrual bleeding.[16]

The limitation of the study is that we could not sample the small arteries, like the radial and arcuate arteries, to estimate the subendometrially blood flow.

CONCLUSION

Combining uterine Doppler with B-mode ultrasound doesn't significantly improve the detection of malignant or atypical endometrial pathologies. Doppler ultrasound, although capable of assessing blood flow patterns, faces challenges in reliably differentiating between benign and malignant endometrial lesions. Consequently, its utility in this context is limited, offering little additional value in enhancing diagnostic accuracy. Histopathological biopsy remains the gold standard for accurate diagnosis.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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