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Uterine blood flow assessment by colour Doppler for prediction of malignant endometrial pathologies in women with abnormal uterine bleeding

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Abstract

Introduction: Colour Doppler has emerged as useful adjunct to transvaginal sonography in evaluation of women with AUB. This study was carried out to evaluate the role of measurement of the Resistance index (RI) and Pulsatility index (PI) of the uterine arteries by Colour Doppler sonography to discriminate between benign and malignant endometrial condition in women with abnormal bleeding.

Material and Methods: This prospective analytical study was performed to evaluate 70 women (30-60 years) with AUB. Spiral arterioles flow patterns, Resistance index (with 0.81 as cut off) and Pulsatility index (with 1.83 as cut off) of uterine arteries were analysed by colour Doppler after detailed TVS. They were compared with Histopathological report of Endometrial Aspiration biopsy.

Results: 10 patients (14.3%) had RI in malignancy range (> 0.81) and 9 patients (12.9%) had PI in malignancy range (< 1.83). Out of these 8 had both RI and PI in malignancy range. Thus 11 cases (15.7%) having either RI/PI or RI and PI both, in malignancy range were considered to be suspected of malignancy. Out of these 11 cases, 5 patients were diagnosed to have Hyperplasia/Malignancy on histopathology. There were no False Negative cases, making the sensitivity 100% and specificity 90.7% of TVS with colour Doppler. For the vascular patterns, both cases of hyperplasia had scattered vessel pattern and all 3 cases of carcinoma had multiple vessel pattern, making the association of vascular pattern with AUB diagnosis significant ($p < 0.001$).

Conclusion: Colour Doppler of the uterine artery and endometrial spiral arteries, improves the diagnostic accuracy of TVS for the prediction of endometrial pathologies and facilitates in screening for malignant and premalignant lesions. Therefore, it is recommended that CDTU with TVS should be used as screening modality in all AUB patient.

Keywords: Colour Doppler (CDTU), transvaginal sonography (TVS), Abnormal Uterine bleeding (AUB), Endometrial Carcinoma

Introduction

Abnormal Uterine Bleeding (AUB) is a frequently encountered problem among women in the perimenopausal age group. It can have significant medical implications and greatly impact the overall quality of life. Given the heightened risk of endometrial carcinoma in perimenopausal and post-menopausal women, it is crucial to confirm the diagnosis in order to provide appropriate management. Unfortunately, many women tend to perceive menstrual irregularities as normal during the perimenopausal phase and thus avoid seeking treatment. This delay in diagnosis and treatment often leads to unfavourable outcomes, including poor prognosis, increased morbidity, and mortality among patients

Transvaginal sonography (TVS) has emerged as a crucial diagnostic tool for investigating Abnormal Uterine Bleeding (AUB). The measurement of endometrial thickness using TVS has shown a strong correlation with histopathology results^[1]. Furthermore, the integration of Colour Doppler to TVS (CDTU) can aid in the diagnosis of intrauterine pathologies by assessing differences in blood flow between benign and malignant lesions. Evaluating vascular flow patterns can help distinguish between benign and malignant uterine pathologies. Malignant conditions typically exhibit increased vascularity due to neo-angiogenesis, resulting in decreased pulsatility index and resistive index^[2]. TVS offers numerous advantages, including non-invasiveness, wide availability, affordability, and patient comfort, making it a widely accepted method for ultrasound-based triage. The addition of CDTU to TVS may enhance the accuracy of predicting malignancy in women with AUB.

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Endometrial histopathology is widely regarded as the definitive method for evaluating Abnormal Uterine Bleeding (AUB) and confirming or excluding the presence of endometrial carcinoma [3]. Therefore, the purpose of this study was to assess the effectiveness of Colour Doppler sonography in distinguishing between benign and malignant endometrial conditions by comparing it to the results of endometrial biopsy.

Methodology

A tertiary care hospital based prospective observational study was carried out after clearance from the institutional ethics committee on 70 women with abnormal uterine bleeding of age between 30-70 year of age group. Detailed history, examination and investigations were done after informed consent.

TVS was performed with an endo-vaginal probe and equipped with color and power Doppler capabilities. First, conventional gray scale sonography was done where the uterus and adnexa were scanned in longitudinal and transverse planes making note of any abnormality. Double layer endometrial thickness was measured on the midline sagittal scan. The power Doppler gate was then activated for blood flow mapping of the endometrium. The power Doppler settings to be set to achieve maximum sensitivity for detecting low velocity flow.

The flow velocities were obtained from both main uterine arteries at the level of internal Os. The image then was frozen including at least three waveform signals. Areas of maximum colour intensity, representing the greatest Doppler frequency shifts, were selected for pulsed Doppler examinations. Blood flow velocity waveforms were detected and recorded.

Uterine vessels (flow) were observed, RI and PI (Resistance index and Pulsatility index) were calculated using the formula. The operator typically recognizes and demarcates peak systolic and end diastolic velocity, while time average velocity was calculated by ultrasound machine.

$PI = (\text{Peak Systolic velocity} - \text{End Diastolic Velocity}) / \text{Time average Velocity}$

$RI = (\text{Peak Systolic velocity} - \text{End Diastolic Velocity}) / \text{End Diastolic Velocity}$

By CDTU, by measuring PI, taking 1.83 as cut off (< 1.83 was considered as malignant, and > 1.83 was considered benign), and by measuring RI, taking 0.81 as cut off (< 0.81 was considered as malignant, and > 0.81 will be considered benign) [4].

The endometrium and sub-endometrial area were magnified to look for blood vessel pattern within 5 mm of endometrium indicating the changes in blood supply from spiral arterioles. This spiral artery flow pattern (flow) vessel patterns were also used to help in prediction of pathology. They were described as following

- No flow pattern:** When no blood flow is seen in the endometrium and this is regarded as normal.
- Single vessel pattern:** When one echogenic focus is seen supplied by a single blood vessel which enters the endometrium from myometrium, it is usually seen in endometrial polyps.
- Rim vessel pattern:** In this pattern a circular or

semicircular vessel surrounding the focal endometrial lesion is seen. The leiomyoma is usually associated with blood vessel pattern like this as blood vessel surrounds the fibroid all around it.

- The scattered vessel pattern:** When scanty blood vessels are seen scattered in endometrium, and this is generally associated with endometrial hyperplasia.
- Multiple vessel pattern:** In this pattern, multiple vessels of variable caliber indicating the neo angiogenesis, were found within the endometrium and in the myometrial endometrial interface seen in Endometrial carcinomas

Finally, the endometrial biopsy was taken for histopathology in premenstrual phase. The report was compared with the observations of Color Doppler sonography.

Results

The mean age of 70 women who came with AUB was 39.2 ± 6.6 . Most common presenting symptom was menorrhagia, seen in 55 (88.6%), irregular bleeding was seen in 14 (20%) and one patient (1.4%) presented with post-menopausal bleeding. On TVS, abnormal findings were detected in 31 cases (44.2%).

Leiomyoma was the most common finding on TVS seen in 12 patients (17.1%). Endometrial Polyp was seen in 5 (7.1%) cases, Adenomyosis was seen in 5.7% cases. Endometrial growth was seen in 2.8% cases.

On endometrial biopsy, Histopathology was found to be normal (endometrium in either Secretary (26.5%), Proliferative phase (63.2%) or Atrophic) in 65 (91.1%) of cases.

Hyperplasia with Atypia and Hyperplasia without Atypia, were both seen in 1 case (1.4%). Endometrial Carcinoma was detected in 3 cases (4.7%).

Qualitatively, color and Power Doppler flow pattern was evaluated in the endometrium. No flow pattern seen in 57 (81.4%) cases. 5 (7.1%) cases showed single vessel pattern (Fig. No. 1). 1 (1.4%) case showed rim vessel. There were 4 (5.7%) cases in whom scattered vessel pattern was observed and 3 (4.3%) cases showed multiple vessel pattern (Fig. No. 2).

Out of 57 cases with no flow vascular pattern on CDTU none of them had malignant lesion on histopathology (p value < 0.001). All the 5 endometrial polyps diagnosed by TVS, had single pedicle feeding vessel pattern on CDTU (p value < 0.001). All the three cases of endometrial carcinoma were associated with multiple vessel pattern and both cases of hyperplasia had scattered vessel pattern. However, leiomyoma was associated with rim vessel pattern in 1 out of 12 cases of fibroid.

Table 1: Vascular Pattern of spiral Arterioles of endometrium

Vascular Pattern	Malignancy histopathology			
	Yes		No	
	Count	Row N %	Count	Row N %
No Flow	0	0.0%	57	100.0%
Single feeding vessel pattern	0	0.0%	5	100.0%
Scattered Vessel Pattern	2	50.0%	2	50.0%
Multiple vessel Pattern	3	100.0%	0	0.0%
Rim vessel Pattern	0	0.0%	1	100.0%
Total	5	7.1%	65	92.9%

Chi-square = 54.92, DF=4, $p < 0.001$

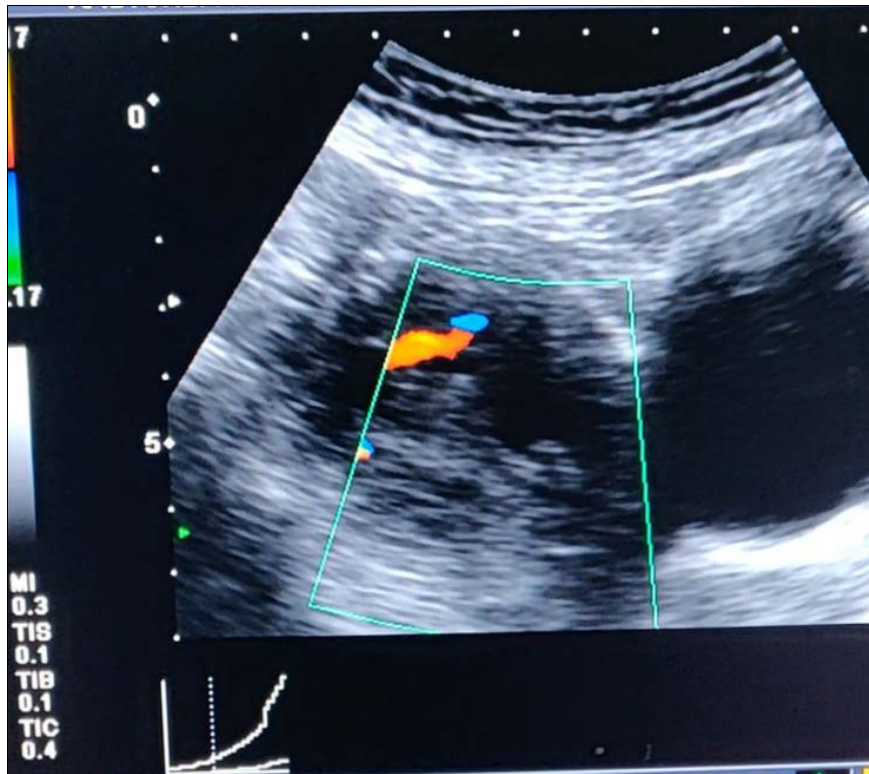


Fig 1: Single Vessel pattern in endometrial Polyp

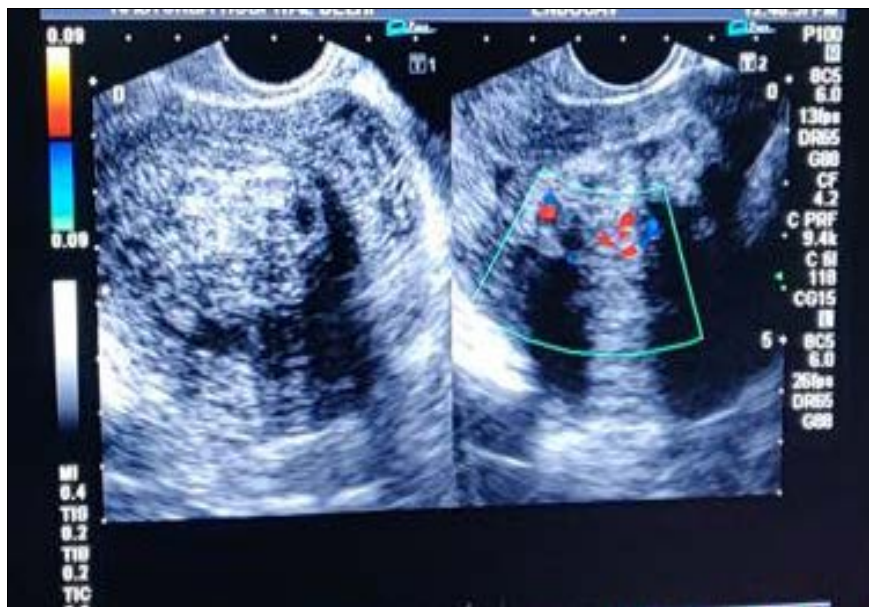


Fig 2: Multiple Vessel pattern in endometrial growth

On CDTU, RI and PI (Resistance index and Pulsatility index) of uterine artery were calculated and it was found that 10 patients (14.3%) had RI in malignancy range (< 0.81) and 9 patients (12.9%) had PI in malignancy range (< 1.83) (Fig. No. 3). The Mean PI for suspected malignant case was 1.55 ± 0.37 and Mean PI for Suspected Benign case was 2.84 ± 0.77 . 11 cases (15.7%) having either RI/PI or RI and PI both, in malignancy range were considered to be suspected of malignancy.

On comparing the histopathology with RI/PI, all 5 cases with malignancy or premalignant hyperplasia (AUB-M) (as confirmed by histopathology) had RI in malignant range and 4 had PI in malignant range. Mean RI for Malignant Change by histopathology, was 0.71 ± 0.08 . Mean RI for Benign Change was 1.48 ± 0.46 . Mean PI for Malignant Change was 1.55 ± 0.37

and Mean PI for Benign Change was 2.84 ± 0.77 . With respect to flowmetric parameters, we found mean pulsatility and resistive indices of patients with malignancy and hyperplasia to be significantly lower as compared to those with normal endometrium and polyp/fibroid pathology (p -value < 0.001).

Specificity and Sensitivity of RI for malignant change was 80% and 92.31%. PPV and NPV for RI are 44.4 and 98.3% respectively. Specificity and Sensitivity of PI for malignant change was 100% and 92.31%. PPV and NPV for PI are 50 and 100% respectively.

Specificity and Sensitivity of RI/PI or RI and PI for malignant change was 100 and 90.77%. PPV and NPV are 45.45 and 100% respectively.

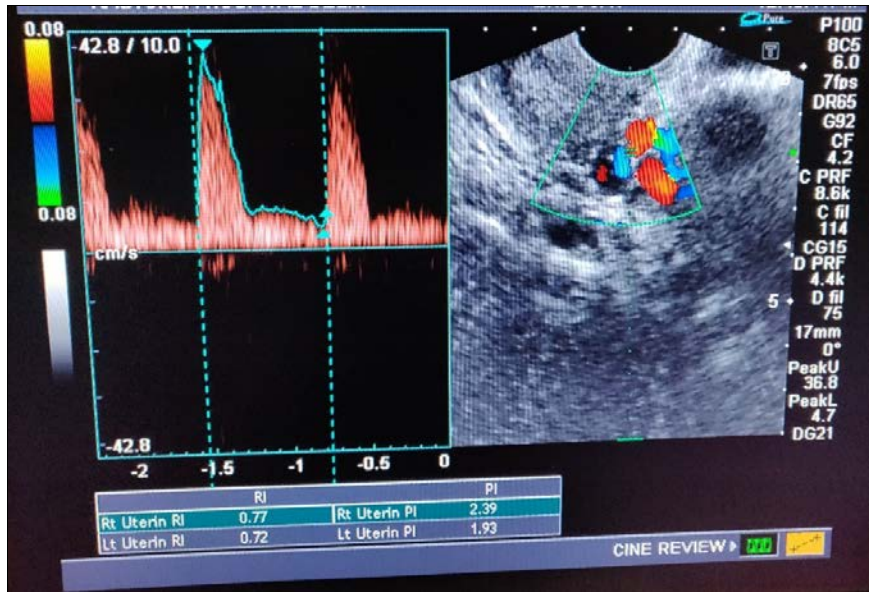


Fig 3: Calculation of RI and PI in Uterine artery

Table 2: comparative evaluation of RI and pi by CDTU against HPE

Variables	Cut off	HPE of Endometrium			
		Malignant		Benign	
		Count	Row N %	Count	Row N %
RI of Uterine Artery	Malignant (≤ 0.81)	5	50.0%	5	50.0%
	Benign (> 0.81)	0	0.0%	60	100.0%
PI of Uterine Artery	Malignant (≤ 1.83)	4	44.4%	5	55.6%
	Benign (> 1.83)	1	1.6%	60	98.4%
RI/PI of Uterine Artery	Malignant	5	45.5%	6	54.5%
	Benign	0	0.0%	59	100.0%

Discussion

- Endometrial carcinoma is the most prevalent gynaecological malignancy, often presenting as abnormal uterine bleeding in perimenopausal or post-menopausal women. Transvaginal sonography (TVS) has demonstrated its effectiveness in triaging abnormal uterine bleeding in postmenopausal women by measuring endometrial thickness. It is widely acknowledged that the risk of endometrial cancer in women with postmenopausal bleeding and an endometrial thickness (E.T.) of less than 4 mm is less than 1% [5]. However, the diagnostic role of endometrial thickness in abnormal uterine bleeding among premenopausal women is still under investigation. This is due to the existence of an overlap between normal endometrial thickness and thickness caused by endometrial disease. Nonetheless, an endometrial thickness of less than 8mm is less likely to be associated with a pathological endometrium in low-risk premenopausal women experiencing abnormal uterine bleeding
- Dilation and Curettage (D & C) and Endometrial aspiration are procedures commonly used to obtain tissue samples for histopathology, but they are considered blind procedures. In contrast, hysteroscopic biopsy is considered the most reliable method for confirming the diagnosis of uterine malignancy or preinvasive lesions. However, despite its effectiveness, hysteroscopic biopsy cannot be used as a screening modality due to several limitations. These include its invasive nature, high cost, limited availability, the requirement for skilled operators, and its nonavailability in all healthcare settings.
- The addition of Colour Doppler to Transvaginal

Sonography (CDTU) can provide valuable assistance in diagnosing intrauterine pathologies, as there are distinct differences in the blood flow patterns between benign and malignant lesions. Evaluating vascular flow through Colour Doppler can aid in differentiating between benign and malignant uterine pathologies. Malignant conditions typically exhibit decreased pulsatility index and resistive index of uterine artery due to increased vascularity². Additionally, Colour Doppler has several advantages, including its non-invasive nature, widespread availability, affordability, and minimal patient discomfort. As a result, ultrasound-based triage has gained significant acceptance in clinical practice. Therefore, the objective of this study was to utilize uterine artery flowmetry via Colour Doppler to predict premalignant or malignant lesions of the endometrium

- In our study, no flow pattern was observed in 57 cases, accounting for 81.4% of the total sample. It is noteworthy that all of these cases exhibited benign histopathology in the endometrium. This finding suggests a strong association between the absence of flow in the endometrium and the absence of malignancy, with a statistically significant P-value of less than 0.001.

In our study, we observed that all five cases of endometrial polyps had a single feeding vessel to the polyp. Based on this finding, it can be concluded that a single vessel pattern is both characteristic and confirmatory of endometrial polyps. Aboul-Fotouh ME, in their study, reported a frequency of 23.75% for the single vessel pattern [6]. Among the 19 cases displaying a single vessel pattern on Colour Doppler Transvaginal

Ultrasound (CDTU), 13 patients were confirmed to have polyps upon histological examination. Therefore, the sensitivity and specificity for detecting endometrial polyps were found to be 81.25% and 93.54%, respectively

- Among the cases included in our study, we observed a scattered vessel pattern in 4 individuals, accounting for 5.7% of the sample. Out of these cases, 2 had normal histology, while both cases of hyperplasia exhibited a scattered vessel pattern on Colour Doppler Transvaginal Ultrasound (CDTU). In all three cases of endometrial carcinoma, a multiple vessel pattern was observed. These findings indicate that none of the subjects with premalignant hyperplasia or malignancy (AUB-M) were missed when evaluating the vascular pattern of the endometrium, with a statistically significant p-value of less than 0.001. Our study demonstrates that Colour Doppler, when used to assess vascular patterns, plays a crucial role in aiding the diagnosis of structural abnormalities visualized on Transvaginal Sonography (TVS) and differentiating early-stage malignancy from benign causes.
- In our study, which included a total of 70 cases, including 5 cases of Abnormal Uterine Bleeding with Malignant changes or premalignant hyperplasia (AUB-M), we calculated the specificity and sensitivity of the uterine artery Resistive Index (RI) for detecting malignant changes as 80% and 92.31% respectively. The Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for RI were found to be 44.4% and 98.3% respectively. Additionally, the specificity and sensitivity of the uterine artery Pulsatility Index (PI) for detecting malignant changes were calculated as 100% and 92.31% respectively. The PPV and NPV for PI were determined to be 50% and 100% respectively.
- In a study conducted by Alcazar *et al.* [7], a total of 91 women with abnormal uterine bleeding and an endometrial thickness greater than 5mm were enrolled. Transvaginal sonography and Power Doppler were used for evaluation. The diagnostic performance of Power Doppler pattern for detecting carcinomas with a Multiple-vessel pattern was found to have a sensitivity of 78.8%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 89%. On the other hand, the diagnostic performance of Power Doppler pattern for detecting polyps with a Single-vessel pattern showed a sensitivity of 89.2%, specificity of 87%, positive predictive value of 82.5%, and negative predictive value of 92.2%. Based on these findings, the study concluded that the use of Power Doppler blood flow mapping as a secondary test in women experiencing postmenopausal bleeding, not on hormone replacement therapy or tamoxifen, and with a thickened endometrium on baseline sonography, can be beneficial in distinguishing between carcinoma, polyps, and other causes of endometrial thickening.
- In the study conducted by Chaudhary *et al.* [8], the sensitivity of uterine artery indices for detecting Endometrial carcinoma was determined to be 71.43%. The specificity of the uterine artery indices in the same context was found to be 100%. The Positive Predictive Value (PPV) was calculated as 100%, indicating a high probability of true positive results. The Negative Predictive Value (NPV) was determined to be 95.5%, indicating a high probability of true negative results. These findings suggest that the uterine artery indices show good specificity and high PPV for detecting endometrial carcinoma in the studied

population.

- Based on the values obtained from the present study, it can be inferred that Transvaginal Sonography (TVS) with Colour Doppler for Uterine artery indices can serve as a reliable screening test for patients with Abnormal Uterine Bleeding (AUB). An ideal screening test should meet certain criteria, such as being inexpensive, easy to perform, causing minimal discomfort, and demonstrating high reliability and validity in accurately identifying both diseased and non-diseased individuals. Ideally, a screening test should be highly sensitive and highly specific. Based on the sensitivity and specificity values being very close to 100 in the present study, TVS with Colour Doppler appears to fulfil these requirements and can therefore be considered an effective screening modality for patients with AUB.

Conclusion

Based on the observations of the present study, it can be inferred that Colour Doppler Transvaginal Ultrasound (CDTU) can be considered a reliable screening modality for patients with Abnormal Uterine Bleeding (AUB) due to its high accuracy and validity. Additionally, the study concluded that when Transvaginal Sonography (TVS) is combined with Colour Doppler for visualizing the vascular pattern and assessing uterine artery indices, the diagnostic accuracy is further improved. This suggests that the combination of TVS and Colour Doppler provides enhanced information for accurate diagnosis for malignant or premalignant changes in endometrium.

In cases where the TVS with Colour Doppler is inconclusive or shows abnormal thickness, invasive methods such as endometrial aspiration biopsy should be considered. This is particularly important to obtain endometrial tissue and exclude pre-cancerous lesions or endometrial cancer in patients with a high suspicion. By incorporating these approaches, clinicians can effectively utilize non-invasive techniques like CDTU as a screening tool and reserve invasive methods for cases requiring further evaluation or confirmation.

Conflict of Interest

Not available

Financial Support

Not available

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