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ORIGINAL RESEARCH

Colour Doppler Transvaginal Ultrasonography and Histopathological Diagnosis in Abnormal Uterine Bleeding Cases

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Abstract
Objectives- To find out role of colour Doppler transvaginal ultrasonography (CDTU) in diagnosis ofabnormal uterine bleeding (AUB) cases and to confirm etiological diagnosis by histopathological examination.
Methods- In this cross sectional study, 141 patients with AUB arriving in Gynaecology OPD of SantokbaDurlabhji Memorial Hospital underwent CDTU.Then endometrial biopsy was done. Endometrial thickness, pulsatility index (PI) and resistive index (RI) of uterine arteries were measured.
Results-The sensitivity of CDTU in diagnosis of abnormal HPR taking RI and/or PI abnormal- 62.86 %, specificity- 92.45%, positive predictive value- 73.33%, negative predictive value- 88.29% and diagnostic accuracy- 85.11%. Endometrial carcinoma had minimum RI (0.524 ± 0.135) and minimum PI (1.054 ± 0.534).
Conclusions- CDTU can be used to select women with AUB who would further benefit from use of endometrial biopsy to make a definite diagnosis at an earlier stage and to identify those who donot need further invasive procedures
Keyword- Colour Doppler, Transvaginal ultrasonography, Resistive index, Pulsatility index, Endometrial thickness

Introduction

Abnormal uterine bleeding (AUB) is one of the most common problems that challenge the gynaecologists.To diagnose endometrial pathology women are subjected to diagnostic curettage. However, diagnostic curettage is an invasive procedure and not without danger especially in the elderly. The false negative rate for curettage is 2-6% because curettage may not empty the uterine cavity completely. Therefore, non invasive technique like ultrasonography is being utilizednowadays to detect endometrial pathologies. Recently, transvaginalcolour and pulsed doppler ultrasound has increased the reliability of ultrasonographic diagnosis of women with certain endometrial pathologies.[1]

It is able to detect subtle changes in the endometrium and it has been observed that endometrial thickness <4 mm is usually associated with normal morphology.[2]This would help in selecting those patients who require diagnostic curettage, thus preventing an unnecessary operation. It also helps in localizing the tumour prior to diagnostic curettage there by minimizing the chances of missing the lesion.[1]

It also helps in the distinction between benign and malignant conditions based on the detection of low impedance and high diastolic blood flow in tumoral blood vessels in malignant pathologies. Correlation between ultrasound estimated endometrial thickness and pathologically confirmed thickness may be as close as one millimeter.[3]

CDTU is non-invasive, low in cost procedure that does not cause patient discomfort and can be performed without extensive preparation.[4]It is used to obtain a better image of the endometrium, allowing visualization of abnormal thicknesses, polyps, and leiomyomas, which may not be detected by endometrial biopsy[5]. CDTU of

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the genital vessels can improve the sensitivity and specificity of TVS for the prediction of endometrial pathologies[6,7]The presence or absence of flow is considered and the values of resistivity index (RI) and the pulsatility index (PI) are measured.
This study aimed at role of colour dopplertransvaginalsonographic findings in abnormal uterine bleeding cases and to establish etiological diagnosis of abnormal uterine bleeding cases by histopathological examination.

Materials and methods

The present study was conducted indepartment of Obstetrics and Gynaecology, SantokbaDurlabhji Memorial Hospital cum Medical Research Institute, Jaipur, India. It was a descriptive type of observational study. Sample size was calculated at 95% confidence level assuming standard deviation of 0.55 in pulsatility index as observed in the study of Kucuret al.[8]
At precision of 0.1 in pulsatility index minimum 121 abnormal uterine bleeding cases are required as sample size.It was further enhanced and rounded off to 140 cases assuming 15% drop outs/attrition.This study was conducted on patients with abnormal uterine bleeding during the period of 1st June 2014 to 30th April 2015.Women with a known genital tract malignancy, pelvic pathology like endometriosis, fibroid, pelvic inflammatory disease, pregnancy, any bleeding diathesis, drugs intake or history of intra uterine device insertion were excluded.
Patients with abnormal uterine bleeding arriving in Obstetrics and Gynaecology department of our hospital were evaluated initially with complete history regarding bleeding per vaginum,other routine history and examination.Thentheywere referred to radiology department for transvaginalsonography with colour doppler. The patients were examined by standard B mode transvaginalsonography with colour doppler in the mid follicular phase.The primary outcome measures were endometrial thickness, pulsatility index (PI) and resistive index (RI) of uterine arteries.All ultrasound scans were performed by the same examiner to avoid interobservervariability.Radiological findings like endometrial thickness >8 mm[9], RI < 0.715[10] and PI < 1.450[10] were considered as abnormal in this study.
After thatpatients were prepared for endometrial biopsy, specimens were sent to histopathology department of our hospital. Processing, paraffin embedding, section cutting and staining was done by standardized methods in the department. Slides were stained by Hematoxylin (Meyer's) and Eosin.The results of the radiological examinations were compared with the histopathological diagnosis of the endometrial specimen.
Parametric tests like unpaired t test and anova test were used for comparison of continuous variables while chi-square test was used for categorical variables.P value < 0.05 was taken as significant.Medcalc 14.0.0 version software was used for statistical analysis. No additional tests/ procedures were carried out specifically for the requirement of the study. Hence, there was no additional financial inputs required from the part of the patient.

Observations and Results

Table 1-Histopathological (HPR) distribution

HPR	No.	%
Endometrial carcinoma	4	2.84
Sub mucous myoma	9	6.38
Endometrial polyp	9	6.38
Proliferative phase	51	36.17
Secretory phase	55	39.01
Endometrial hyperplasia	13	9.22
Total	141	100.00

Maximum patients had normal endometrium i.e. secretory (39.01%) and proliferative (36.17%) while only 2.84 % patients had endometrial carcinoma (Table-1)

Table 2-Color Doppler distribution

Doppler	No.	%
Abnormal	30	21.28
Normal	111	78.72
Total	141	100.00

Out of 30 abnormal color doppler , 20 patients had both RI and PI abnormal, while 6 had only abnormal RI and 4 had only abnormal PI and 78.72% patients had normal color doppler i.e. both RI and PI normal (Table-2).

Table 3- Comparison of endometrial thickness with histopathology

Endometrial Thickness	HPR	Total

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	Abnormal		Normal			
	No.	%	No.	%	No.	%
<8	11	10.9	90	89.1	101	100
≥8 mm	24	60.0	16	40.0	40	100.00
Total	35	24.8	106	75.2	141	100.00

Chi-square = 37.029 with 1 degree of freedom; P <0.001

60 % patients having ET ≥ 8 mm had abnormal HPR while 89.1 % patients having ET < 8 mm had normal HPR making this correlation significant (Table 3).

Table 4- Comparison of color doppler with histopathology

Doppler	HPR				Total	
	Abnormal		Normal			
	No.	%	No.	%	No.	%
Abnormal	21	70.00	9	30.00	30	100.00
Normal	14	12.60	97	87.40	111	100.00
Total	35	24.82	106	75.18	141	100.00

Chi-square = 41.679 with 1 degree of freedom; P <0.001

70 % patients having abnormal HPR had abnormal color doppler while 87.40 % patients having normal HPR had normal color dopplermaking this correlation significant (Table-4)

Table 5-Efficacy of RI, PI, color doppler and ET in diagnosis of abnormal HPR

	Sensitivity	Specificity	PPV	NPV	Dignostic Accuracy
RI	18/35	98/106	18/26	98/115	116/141
	51.43%	92.45%	69.23%	85.22%	82.27%
PI	16/35	98/106	16/24	98/117	114/141
	45.71%	92.45%	66.67%	83.76%	80.85%
Doppler	22/35	98/106	22/30	98/111	120/141
	62.86%	92.45%	73.33%	88.29%	85.11%

The sensitivity of RI in diagnosis of abnormal HPR taking 0.715 as cut off value was 51.43 %, specificity was 92.45 %, positive predictive value was 69.23%, negative predictive value was 85.22% and diagnostic accuracy was 82.27 % (Table-5).

The sensitivity of PI in diagnosis of abnormal HPR taking 1.450 as cut off value was 45.71 %, specificity was 92.45 %, positive predictive value was 66.67 %, negative predictive value was 83.76% and diagnostic accuracy was 80.85 % (Table-5).

The sensitivity of color doppler in diagnosis of abnormal HPR taking RI and/or PI abnormal was 62.86 %, specificity was 92.45 %, positive predictive value was 73.33 %, negative predictive value was 88.29% and diagnostic accuracy was 85.11 % (Table-5).

Table 6-Comparison of the uterine artery resistive indices (RI) in between various endometrial pathologies

Endometrial histology	Mean	SD	P value*
Endometrial carcinoma	0.524	0.135	<0.001
Sub mucous myoma	0.701	0.169	
Endometrial polyp	0.728	0.158	
Proliferative phase	0.768	0.093	
Secretory phase	0.787	0.101	
Endometrial hyperplasia	0.653	0.166	

Mean RI of various endometrial pathologies, endometrial carcinoma had minimum RI (0.524±0.135) making P value significant (Table-6).

Table 7- Comparison of the uterine artery pulsatility indices (PI) in between various endometrial pathologies

Endometrial histology	Mean	SD	P value*
Endometrial carcinoma	1.054	0.534	<0.001
Sub mucous myoma	1.446	0.650	
Endometrial polyp	1.568	0.489	
Proliferative phase	1.731	0.363	

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Secretory phase	1.802	0.372	
Endometrial hyperplasia	1.327	0.549	

Mean PI of various endometrial pathologies, endometrial carcinoma had minimum PI (1.054 ± 0.534) making P value significant (Table-7).

Discussion

Over recent years colourdopplersonography (CDTU) is being used to predict endometrial pathologies [11,12] In this study we enrolled 141 patients with abnormal uterine bleeding and compared the doppler indices of uterine arteries with the final histopathological diagnoses.

In our study, mean endometrial thickness (ET) was 6.7 mm, with minimum ET 2.0 mm and maximum ET 14.0 mm. Out of 141 patients, 51 (36.17 %) patients had proliferative endometrium, 55 (39.01 %) had secretory endometrium, 13(9.22%) had endometrial hyperplasia, 9 (6.38%) had sub mucous myoma, 9 (6.38%) had endometrial polyp and 4 (2.84%) had endometrial carcinoma . Secretory and proliferative endometrium were considered as normal endometrium including 106 i.e. 75.18% patients and rest all others as abnormal endometrium including 35 i.e. 24.82% patients. Malignant endometrium included 4 i.e. 2.84% patients and rest all were benign endometrium including 137 i.e. 97.16% patients

Among 141 patients, 26 i.e. 18.4 % had abnormal resistive index i.e. RI < 0.715, mean RI was 0.71, minimum RI 0.410, maximum 0.890. 24 patients i.e. 17.02% had abnormal pulsatility index i.e. PI < 1.450, mean PI 1.67, minimum PI 0.700, maximum PI 2.875. 30 patients i.e. 21.28% had abnormal colourdoppler i.e. any patient with RI < 0.715 and/or PI < 1.450. Out of 30 abnormal colourdoppler, 20 patients had both RI and PI abnormal, while 6 had only abnormal RI and 4 had only abnormal PI.

In our study, out of 40 patients with abnormal ET i.e. ≥ 8, 24 (60%) had abnormal HPR and out of 101 patients with normal ET i.e. < 8, 90 (89.1 %) patients had normal HPR. The sensitivity of ET in diagnosis of abnormal HPR taking 8 mm as cut off value was 68.57%, specificity was 84.91%, positive predictive value was 60%, negative predictive value was 89.11% and diagnostic accuracy was 80.85%.

In our study, out of 26 patients with abnormal RI, 18 patients i.e. 69.23% had abnormal HPR, and out of 115 patients with normal RI, 98 patients i.e. 85.22% had normal HPR , out of 24 patients with abnormal PI, 15 patients i.e. 62.5% had abnormal HPR, and out of 117 patients with normal PI, 97 patients i.e. 82.9% had normal HPR , out of 30 patients with abnormal colourdoppler, 21 patients i.e. 70 % had abnormal HPR, and out of 111 patients with normal colourdoppler, 97 patients i.e. 87.40% had normal HPR. This shows that the abnormal RI, PI and doppler are associated with abnormal HPR with significant p value.

So the sensitivity of RI in diagnosis of abnormal HPR taking 0.715 as cut off value was 51.43%, specificity was 92.45%, positive predictive value was 69.23%, negative predictive value was 85.22% and diagnostic accuracy was 82.27%. The sensitivity of PI in diagnosis of abnormal HPR taking 1.450 as cut off value was 45.71%, specificity was 92.45%, positive predictive value was 66.67%, negative predictive value was 83.76% and diagnostic accuracy was 80.85%. The sensitivity of colourdoppler in diagnosis of abnormal HPR taking RI and/or PI abnormal was 62.86%, specificity was 92.45%, positive predictive value was 73.33%, negativepredictive value was 88.29% and diagnostic accuracy was 85.11 % In our study, among mean RI and PI of various endometrial pathologies, endometrial carcinoma had minimum RI (0.524 ± 0.135) and minimum PI (1.054 ± 0.534) making P value significant predictive value was 88.29% and diagnostic accuracy was 85.11 %

Conclusion

Colour dopplertransvaginal ultrasonography of the endometrium has become an important part of the evaluation of women presenting with abnormal uterine bleeding. It is a sensitive, specific, non invasive, low cost procedure that does not cause patient discomfort. In this cross sectional study, colour doppler in evaluation of abnormal uterine bleeding is compared with histopathology after endometrial biopsy. It was concluded thatendometrial pathologies are associated significantly with uterine artery doppler changes.

In conclusion our data shows that colourdopplertransvaginalultrasonography can be used to select women with abnormal uterine bleeding who would further benefit from the use of endometrial biopsy to make a definite diagnosis at an earlier stage and to identify those who donot need further invasive procedures.

The role of colour dopplersonography to discriminate between benign and malignant endometrial condition in women presenting with abnormal bleeding and thickened endometrium is significant in this study but further study in a large population may be conducted to substantiate its significance.

Colourdoppler has a good role in supplementing the diagnosis after transvaginal ultrasonography has been performed for visualizing endometrial thickness and to predict endometrial carcinoma at an earlier stage.

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