RESEARCH ARTICLE

ACCURACY OF COLOR DOPPLER IN DETECTING ENDOMETRIAL ABNORMALITIES IN WOMEN WITH PERI AND POSTMENOPAUSAL BLEEDING.

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Manuscript Info	Abstract
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Background: In most women with peri and post menopausal bleeding have non malignant endometrial changes. However' uterine currettage is mandatory to exclude malignant changes. Diagnostic curretage has been the method of choice for many years to diagnose cancer of endometrium in patients with post menopaual bleeding. Although it is a simple technique, however it is an invasive and uncomfortable procedure and not without danger. For this reason many different methods have been developed to minimize the need of currettage. Trans-vaginal sonography and color doppler of uterine artery have shown good accuracy in detecting normal endometrium from abnormal.

Objectives: Aim of this work is to evaluate the role of color doppler study of endometrium and Doppler velocimetric measurement of uterine artery as non invasive screening procedures to detect endometrial pathology in peri and post menopausal bleeding and to correlate the sonographic results with hispathological finding in order to discriminate normal from pathological endometrium.

Methodology: This study was carried out in Department of Obstetrics and Gynaecology with collaboration of Department of Pathology and Department of Radiology. 100 patients were selected and they were presented with chief complaints of peri and post menopausal bleeding and subjected to Trans-vaginal sonography, color Doppler n diagnostic curettage. The data obtained from the ultrasound and Doppler examinations is compared to the results of the Histopatholigical Diagnosis After currettage.

Results: This study included 100 patients with abnormal uterine bleeding, 70 perimenopausal and 30 post menopausal. These patients were initially screened with vaginal ultrasound for endometrial thickness and Doppler indices were obtained from the uterine artery (especially the resistance index RI and the pulsatility index). These results were compared to the histopathological findings. As regards the results of Doppler velocimetric study of the uterine artery in the present study: (i) The resistance index (RI) of the uterine artery, was significantly higher in patients with atrophic endometrium and also in patients with benign endometrial lesions (0.85±0.036) compared to those with abnormal pathological endometrium (mean RI 0.73±0.078)

denoting a decrease in the vascular impedance leading to increase blood flow in pathological endometrium conditions especially malignancy. The present study recommend the use of 0.83 as a cut off values for uterine artery RI as maximum sensitivity and specificity was seen at this value in discriminating normal endometrium from abnormal pathological endometrium. (ii) The pulsatality index (PI) of the uterine artery, was significantly higher in patients with atrophic endometrium and also in patients with benign endometrium lesions compared to those with endometrial abnormalities (mean PI 3.88 ± 0.432 and 1.65 ± 1.17 respectively). When choosing the cut off limit for the PI, a value of 3.80 seemed to be the most appropriate as it was associated with a sensitivity of 92.6% and a specificity 73.9%.

Conclusion: Doppler velocimetric study of the uterine artery offers simple non invasive valuable method in screening cases of peri and postmenopausal bleeding and the present study recommend the use of 0.83 and 3.80 as a cut off values for uterine artery RI and PI respectively to discriminating normal endometrium from abnormal pathological endometrium. This value had resulted in a sensitivity of 92.3% and a specificity of 66.67 % for RI, a sensitivity of 92.6% and a specificity of 73.9% for PI, giving this technique a great reliability in differentiating normal from pathological endometrial patterns in cases of peri and postmenopausal bleeding. Doppler velocimetric study of the uterine artery posses high sensitivity and specificity that makes it clinically useful as a single screening tool in discriminating normal from abnormal pathological endometrium in cases with peri and postmenopausal bleeding. But we emphasize the importance of the combined examination of transvaginal ultrasound and color doppler to increase the screening accuracy and to decrease as much as possible the false results that may occur in either of them alone, as the ultrasonography evaluates the endometrial morphology while Doppler study in concerned with hemodynamic changes and thus both techniques are complementary.

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Introduction:-

Postmenopausal bleeding is often the first and principal symptom of endometrial cancer and should be regarded as a symptom of genital tract malignancy until proved otherwise[1]. Most women with perimenopausal and postmenopausal bleeding have non malignant endometrial changes. In most patients, atrophic changes of the endometrium are the only histological findings. However, uterine curettage is mandatory to exclude malignant endometrial changes[2].

Diagnostic curettage has been for many years the method of choice to diagnose cancer of the endometrium. It is a simple technique, however it is an invasive and an uncomfortable procedure and not without danger[3].

For the above reasons many different methods have been developed to minimize the need for curettage[3].
With Doppler transvaginal ultrasound, the uterine artery and its smaller tributaries can be readily visualized and blood flow velocity waveforms can be measured. A good correlation has been found between the uterine artery flow velocity waveforms and the histopathologic diagnosis in women with peri, and postmenopausal bleeding[4,5,6,2].

Doppler velocimetry is a non-invasive technique that uses high frequency ultrasound for investigation of blood flow. When these high frequency sound waves are directed towards a moving object, the change in -frequency of the back scattered waves (frequency shift) is directly proportional to the velocity of the moving object[7].

Most women with perimenopausal or postmenopausal bleeding (80%-90%) have non-malignant endometrial changes. However, uterine curettage is mandatory to exclude malignancy[8]. With the introduction of transvaginal

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color flow imaging, it has become possible to study the pelvic vasculature and the main vessels supplying the uterus[9,10]. Flow velocity profile can be obtained from these vessels[11]. Wave form analysis may be also useful in discriminating benign from malignant masses[12].

The uterine artery and its smaller tributaries can be readily visualized and blood flow velocity waveforms can be measured using Doppler velocimetry. A good correlation has been found between the uterine artery flow velocity waveforms and the histopathologic diagnosis in women with metrorrhagia[4,2]. A number of studies have reported difference in uterine blood flow or uterine artery impedance in physiological and pathological conditions of the uterus[13,2].

Using Doppler ultrasound techniques, many useful information about the blood flow pattern in blood vessels are obtained which are important in reaching the diagnosis and planning the treatment of many obstetric and gynaecological conditions. These measures depend on the maximum frequency shift during the cardiac cycle (Maximum systolic flow, A), minimum frequency shift - during the cardiac cycle (End diastolic flow, B), the mean value of frequency shift throughout the cardiac cycle (Mean), the angle of incidence (0) and then diameter of the blood vessel[14]. The following indices were developed to represent flow:-

1. Resistance index = (A-B)/A. This index indicates the state of peripheral resistance in the vascular bed distal to the point of measurement. The index value as the peripheral resistance decreases and when the end diastolic flow is approaching zero, the index approaches unity[15].
2. Pulsatility index = (A-B)/Mean. The mean is calculated by the Doppler machine and thus, to obtain accurate measures, the frequency shift should be processed in high accuracy[16], so this index may be the most[17].

Aims and objectives:-
The aim of this work is to evaluate the role of Doppler velocimetric measurement of the uterine artery as non-invasive screening procedures to detect endometrial pathology in case of peri and postmenopausal bleeding and to correlate the sonographic results with histopathological finding in order to discriminate normal from pathological endometrium.

Material and Methods:-
This study was carried out in the Postgraduate Department Obstetrics and Gynecology, Department of Radiology and Department of Pathology, Government Medical College Srinagar for a period of two years. One hundred (100) patients were selected from patients presenting of inpatient Department of Lalla Ded Hospital with chief complaints of peri and postmenopausal bleeding and were subjected to TVS, Color Doppler and diagnostic curettage. Patients with (i) age group 40-70 years, (ii) with no medical disorder like ITP, (iii) with no HRT replacement therapy, and (iv) with no bleeding disorders. Patients (i) < 40 or > 70 years of age, (ii) who are seeking HRT therapy and (iii) history of any other drug intake were excluded from the study.

- General Examination
- Proper Abdominal and Pelvic examination
- Laboratory investigations
- Vaginal sonography
- Study of the uterine artery waveform velocity.

Pulsed Doppler scanning of the uterine artery is to be performed. The left ascending branch of the uterine artery is chosen as it is easier to identify, and for the sake of standardization. A Maesterio 7700 machine with a 7.5 MHz vaginal probe is to be used in this study. The women to be scanned was put in lithotomy position, with an empty bladder. The probe is to be introduced in the vagina covered with a condom filled and covered with echo gel.

Examination starts by viewing the uterine fundus, then the probe is angled to view the area of the internal cervical os. The probe is to be shifted laterally to view the paracervical area and the machine is switched to pulsed wave Doppler mode. The sample volume and angle of insonation are adjusted to obtain the best waveforms of the uterine artery.

Three good quality waveforms are obtained on the same screen before taking the measurements. After using the cursor to trace the wave and to identify the peak systolic and end diastolic flow. The following indices were obtained: 1- Resistance index (RI), 2- Pulsatility index (PI).

Endometrial sampling:-
This is to be done by full curettage of the endometrium under general anesthesia, in the operating theatre and specimen in formalin is to be sent to the Department of Pathology.
The data obtained from the ultrasound and Doppler examinations is to be compared to the results of the curettage and the main clinical findings.

Statistical methods:-
SPSS (Version 20.0) and Microsoft Excel were used for statistical analysis of data. Data was analysed with the help of descriptive statistics viz., percentages, means and standard deviations and presented by bar and pie diagrams. Student's independent t-test was employed for comparison of quantitative data. Sensitivity, specificity and predictive values were used in diagnosis of normal endometrial pattern among peri and post menopausal women. P-value less than 0.05 was considered statistically significant.

Results:-
Table 1:- The Clinical Characteristics Of All Atudied Women.

Clinical Variable	Perimenopausal (Group A) [n=70]		Postmenopausal (Group B) [n=30]		P Value
	Mean±SD	Range	Mean±SD	Range	
Age (years)	45.0±1.345	42-48	58.1±3.614	50-68	<0.001 (SSD)
Menarche (years)	12.7±0.925	11-14.8	12.5±0.824	11-14.3	0.363 (SNSD)
Gravidity	3.1±1.291	0-5	3.6±1.429	0-7	0.098 (SNSD)
Parity	2.5±1.032	0-5	2.8±1.184	0-5	0.591 (SNSD)

A total number of patients taken were 100 in numbers in which 70 were in perimenopausal group (Group A) and 30 in postmenopausal group (Group B). Menarche in perimenopausal group (Group A) was 12.70±0.92 years and in postmenopausal group (Group B) it was 12.50±0.08 with a   p value of 0.363 which was statistically insignificant.

Table 2:- Endometrial Histopathology in women with perimenopausal and postmenopausal bleeeding of all studied women.

Histopathological diagnosis		Perimenopausal (Group A)		Postmenopausal (Group B)		Total	
		No.	%age	No.	%age	No.	%age
Normal end	Atrophic	16	22.86	12	40.00	28	28
	Proliferative	13	18.57	9	30.00	22	22
	Secretary	17	24.29	4	13.33	21	21
Abnormal end	hyperplasia	18	25.71	1	3.33	19	19
	Polyp	4	5.71	1	3.33	5	5
	Cancer	2	2.86	3	10.00	5	5
Total		70	100	30	100	100	100

In group A, the number of patients having normal histopathology were 46 and those having disease were 24. In group B, number of patients having normal histopathology were 25 and those having diseases were 5 in number.

Table 3:- Histopathological Diagnosis Correlated With Endometrial Thickness.

Histopathologic diagnosis	No.	Endometrial thickness (mm)		
		Mean	SD	Range
Atrophic	28	5.18	1.142	3.6-8.0
Proliferative	22	5.34	0.960	3.8-7.1
Secretory	21	3.85	1.021	2.5-6.0
Hyperplasia	19	6.62	1.942	4.1-9.7
Polyp	5	6.94	1.568	4.2-8.0
Cancer	5	15.76	2.124	13.1-18.2

The table shows the endometrial thickness measured with TVS in patients having diseases was higher when correlated with histopathological diagnosis after DNC.

Table 4:- Cof Histopathological Diagnosis After Dnc With Resistance Index Measured by color doppler

Histopathologic diagnosis	No.	Resistance Index		
		Mean	SD	Range
Atrophic	28	0.84	0.044	0.75-0.93
Proliferative	22	0.84	0.029	0.8-0.9
Secretory	21	0.87	0.021	0.83-0.91
Hyperplasia	19	0.71	0.060	0.59-0.83
Polyp	5	0.84	0.034	0.79-0.88
Cancer	5	0.68	0.070	0.59-0.74

Table shows resistance index of uterine artery in diseased group was in low range as compared to resistance index of normal group when compared with histopathological diagnosis after DNC.

Table 5:- Comparison of histopathological diagnosis after dnc with pulsatility index measured by color doppler

Histopathologic diagnosis	No.	Pulsatility Index		
		Mean	SD	Range
Atrophic	28	3.91	0.574	2.6-5
Proliferative	22	3.80	0.311	3.1-4.3
Secretory	21	3.92	0.310	3.3-4.4
Hyperplasia	19	1.46	1.018	0.6-3.9
Polyp	5	2.80	1.643	1-4.0
Cancer	5	1.20	0.447	1-2.0

This table shows that pulsatality index of uterine artery in abnormal group was in lower range than pulsatality index of normal group when compared with histopathological diagnosis.

Table 6:- Comparison of uterine artery resistance index between cases with normal and abnormal endometrium.

Endometrium	No.	Resistance Index			P-value
		Mean	SD	Range	
Normal End	71	0.85	0.036	0.75-0.93	<0.001 (SSD)
Abnormal End	29	0.73	0.078	0.59-0.88	

SSD: Statistically significant difference

The mean uterine artery resistance index was found to be significantly higher in case of bleeding with normal endometrial i.e. 0.85±0.036 compared with cases with abnormal endometrial i.e. 0.73 ± 0.078 with a p value of < 0.001 which was statistically significant.

Table 7:- Comparison of uterine artery pulsatility index between cases with normal and abnormal endometrium

Endometrium	No.	Pulsatility Index			P-value
		Mean	SD	Range	
Normal End	71	3.88	0.432	2.6-5.0	<0.001 (SSD)
Abnormal End	29	1.65	1.174	0.6-4.0	

SSD: Statistically significant difference

There was a significant difference in the mean pulsatality index between women with normal endometrial thickness 3.88±0.432 with those with abnormal endometrial pathology i.e. 1.65±1.174 (p value <0.001). The difference was statistically significant.

RI Cut off	Sensitivity (%age)	Specificity (%age)	PPV (%age)	NPV (%age)
0.82	91.2	55.8	73.24	82.76
0.83	92.3	66.67	83.1	82.76
0.84	91.5	47.2	60.6	86.2

When 0.83 was taken as a cut-off point for resistance index, sensitivity was 92% and specificity was 66.67% which was highest as compared to other cut-off values.

Table 9:- Predictive values of various pulsatility index of uterine artery in diagnosis normal endometrial pattern among all studied women.

PI Cut off	Sensitivity (%age)	Specificity (%age)	PPV (%age)	NPV (%age)
3.70	91.23	55.8	73.4	82.8
3.80	92.6	73.9	80.7	89.5
3.90	91.5	47.2	60.6	86.2

When value 3.80 was taken as cut-off point sensitivity and specificity was maximum i.e. 92.6% and 73.9% which was highest at this cut-off point.

Discussion:-

This study included 100 patients with abnormal uterine bleeding, 70 perimenopausal and 30 post menopausal.

These patients were initially screened with vaginal ultrasound for endometrial thickness and Doppler indices were obtained from the uterine artery (especially the resistance index RI and the pulsatility index). These results were compared to the histopathological findings.

As regards the results of Doppler velocimetric study of the uterine artery in the present study:

Resistance index:-
The resistance index (RI) of the uterine artery, was significantly higher in patients with atrophic endometrium and also in patients with benign endometrial lesions (0.85±0.036) compared to those with abnormal pathological endometrium (mean RI 0.73±0.078) denoting a decrease in the vascular impedance leading to increase blood flow in pathological endometrium conditions especially malignancy.

This is in agreement with:-
Weiner et al. (1993)[2], who reported that the lowest values for the RI among the cases of perimenopausal and postmenopausal bleeding in their study were detected uterine fibroid and endometrial carcinoma.

Merce et al (1991)[4], who examined 45 patients with postmenopausal bleeding, he found a significant decrease in the RI in patients with abnormal endometrial Pathology relative to benign cases (0.77 ± 0.04) and (0.85 ± 0.07) respectively.

Greco et al (1997)[18], also studied cases with endometrial cancer and showed that the mean RI increased with the employment of effective chemotherapy.

In this study, the best cut off value for RI was found to be 0.83 as this was associated with a sensitivity of 92.3%, specificity of 66.67%, positive predictivity of 83.1% and negative predictivity of 82.76%, giving this technique a

great reliability in differentiating normal from pathological endometrial patterns in cases of perimenopausal and postmenopausal bleeding.

Also, the results of the present study agree with the results of Hata et al., (1992)[19]; Kurjak et al., (1993)[20]; and Weiner et al, (1993)[2], who concluded that Doppler velocimetric, studies has a good correlation to endometrial histopathological pattern in peri, and postmenopausal cases.

Hata et al. (1992)[19], studied 16 postmenopausal patients with abnormal uterine bleeding using transvaginal color Doppler sonography and reported sensitivity and specificity of 100% in diagnosing endometrial carcinoma. They concluded that this technique can be used to detect endometrial carcinoma in postmenopausal women with abnormal vaginal bleeding and that this method might be applicable in selecting patients who really require diagnostic surgery for endometrial cancer.

In the study performed by Kurjak et al. (1993)[20], on 750 postmenopausal women to evaluate the role of transvaginal color Doppler sonography in detecting endometrial cancer in postmenopausal women, a sensitivity of 91.4% was reported with a conclusion that transvaginal Color Doppler UItrasonography can depict endometrial carcinoma even in early stage.

Weiner et al. (1993)[2], studied the correlation of the uterine artery RI to histopathological picture of the endometrium in 85 women with peri, and postmenopausal bleeding. They found that the mean uterine artery RI in cases with atrophic, proliferative or secretary was significantly higher than that of cases with endometrial hyperplasia or carcinoma and uterine artery RI has 100% sensitivity in detecting endometrial pathology. They concluded that in the presence of high resistance to flow in the uterine artery a more conservative approach can be offered to patients with peri or postmenopausal bleeding without resorting to invasive diagnostic procedures.

Pulsaltility index:-
Also, the pulsatality index (PI) of the uterine artery, was significantly higher in patients with atrophic endometrium and also in patients with benign endometrium lesions compared to those with endometrial abnormalities (mean PI 3.88 ± 0.432 and 1.65 ± 1.17 respectively).

When choosing the cut off limit for the PI, a value of 3.80 seemed to be the most appropriate as it was associated with a sensitivity of 92.6% and a specificity 73.9%.

The results of the present study agreed with the Results:-
Ronnie a1, (1991) and Ilappard et al., (1999). Ronnie et al. (1991)[21], compared Doppler flow in 3 groups of postmenopausal women: those with postmenopausal bleeding who had endometrial cancer, those with postmenopausal bleeding without endometrial pathology and healthy asymptomatic women. They found that the mean arterial PI values were lower in the first two groups in patients when compared with those of the asymptomatic postmenopausal women.

Conclusion:-
Doppler velocimetric study of the uterine artery offers simple non invasive valuable method in screening cases of peri and postmenopausal bleeding and the present study recommend the use of 0.83 and 3.80 as a cut off values for uterine artery RI and PI respectively to discriminating normal endometrium from abnormal pathological endometrium. This values had resulted in a sensitivity of 92.3% and a specificity of 66.67 % for RI, a sensitivity of 92.6% and a specificity of 73.9% for PI, giving this technique a great reliability in differentiating normal from pathological endometrial patterns in cases of peri and postmenopausal bleeding.

Although both transvaginal sonography endometrial thickness and Doppler velocimetric study of the uterine artery posses high sensitivity and specificity that makes each of them clinically useful as a single screening tool in discriminating normal from abnormal pathological endometrium in cases with peri and postmenopausal bleeding, yet the present study emphasizes the importance of the combined examination using both techniques to increase the screening accuracy and to decrease as much as possible the false results that may occur in either of them alone, as the ultrasonography evaluates the endometrial morphology while Doppler study in concerned with hemodynamic changes and thus both techniques are complementary.

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