

# Evaluation of Ovarian Masses by Color Doppler Imaging and Histopathological Correlation

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## A B S T R A C T

**Introduction:** Adnexal masses pose a special diagnostic challenge and suspicion for malignancy is based largely on imaging appearance. As a primary imaging modality, ultrasonography (US) can provide diagnostic information for evaluating ovarian masses. This study had revealed the change of spectral Doppler wave form characteristics (resistive index, pulsatility index) of ovarian masses and differentiates them into benign and malignant lesions and correlate with histopathological findings.

**Material and Methods:** Thirty nine women who were referred to the radiology department for abdomen or pelvis USG from Gynaecology OPD at a tertiary care hospital, Kishanganj, Bihar with a clinical diagnosis of adnexal mass by per abdomen or per vaginal examination or history of irregular lower abdominal pain or bleeding disorder were included in the study. Transabdominal USG with Doppler study was performed in all cases. On spectral Doppler, the lowest resistance index (RI), and maximum peak systolic velocity (PSV) detected at any point in the mass was used for analysis. After USG patients were planned for surgery. Accordingly then post operated excised tumor were send for histopathology. Thus this study was a correlation of USG finding (including grey scale and Doppler) in cases of ovarian/adnexal masses considering with histopathology as a gold standard.

**Results:** Different variables on USG and CDUS were used in diagnosis of benign and malignant ovarian tumors in 39 patients. A total of 56 masses detected in right and left adnexa. Excellent agreement between histopathology and USG (grey scale and CDUS) was found for the diagnosis of benign and malignant tumor of ovary. CDUS shows RI value ranges from 0.4 to 0.9 are malignant and PI value ranges from 0.48 to 1.33 which is comparable with literature. Grey scale USG shows necrosis and calcification present in all malignant cases proved histopathologically. Among 39 patients 13 shows flow within the tumor, but only 4 of them which were proved by histopathology as malignant ranges from 0.4-0.9. however 6 of them shows value ranges from 0.8-0.9 (borderline) but they were proved as benign by histopathology and USG sensitivity found to be 100%, specificity 80%, PPV 36% and NPV 100%.

**Conclusion:** Multiparameter analysis utilizing B-mode USG along with Color Doppler and Spectral Doppler is the mainstay in diagnosis of patients with ovarian tumors.

**Keywords:** Ovarian Mass, Ultrasonography, Color Doppler, Malignancy

## INTRODUCTION

Ovarian mass represents a common problem in clinical practice. Of all gynecologic carcinoma, ovarian carcinoma represents the greatest clinical challenge. The majority of ovarian mass are benign (80%) with cystic, solid, and mixed characteristics and a favorable diagnosis. The other 20% masses are malignant, so we need diagnostic means which permit accurate classification of ovarian masses before surgery.<sup>1</sup> Ultrasonography is considered the primary imaging

modality for confirmation of the ovarian origin of mass and characterization of nature of mass as benign or malignant.<sup>2</sup> It correlates morphologic images with gross macroscopic pathologic features of ovarian masses. However, when morphologic features alone are applied to the prediction of ovarian malignancy, there is tendency to over diagnose malignant tumors because of a substantial overlap between malignant and benign masses. Therefore, addition of color Doppler imaging with pulsed Doppler spectral analysis improves the characterization of ovarian masses by means

of quantitative blood flow measurements obtained from tumor vessels and so increases sensitivity and specificity of characterization of ovarian masses.<sup>3</sup> High operator dependence and extreme variability of characteristics of ovarian tumor make a precise diagnosis still difficult.<sup>4,5</sup>

Determination of a degree of suspicion for malignancy in an adnexal mass is the most critical step after identification of the mass. Many different scoring systems exist for discriminating benign from malignant adnexal masses. These scoring systems evaluate masses for solid elements, cyst wall thickness, number, thickness, and irregularity of septations, and the presence of ascitic fluid. Numerical scores are applied and masses that score higher than a certain cutoff are considered potentially malignant.<sup>6</sup>

In order to ensure the availability of explicit criteria for predicting the nature of ovarian tumors, of late, a number of scoring systems have been proposed by using variables such as the presence of nodularity, solid areas, internal echoes, septae, necrosis, calcification and irregularity of borders.<sup>7</sup> Ovaries are sonographically hypoechoic compared with surrounding structures. Many morphological scoring systems on USG have been proposed, based on the wall thickness inner wall structure, septal characteristic, and echogenicity of the lesion. CDUS of ovarian masses helps in differentiating benign and malignant tumor.<sup>8</sup> It is also used in conjunction with pulsed CDUS to identify vessels for waveform analysis. Two indices have been used in analyzing Doppler waveforms: the PI and the RI. RI less than 0.4-0.8 and PI less than 1.0 are generally considered to be suspicious for malignancy.<sup>9</sup> Benign lesions tend to initiate new tumor blood vessel formation peripherally from pre-existing host vessels; whereas malignant tumors tend to initiate new tumor blood vessel formation centrally. The newly formed tumor vessels have a deficiency of smooth muscle in their walls as opposed to their calibre. Due to muscular paucity, these vessels present a low resistance to the blood flow and thereby receive a large volume flow than normal vessels, which have high impedance. Some differentiation between benign and malignant masses is achieved by quantifying this differences.<sup>10</sup>

This study had revealed the change of spectral Doppler wave form characteristics (resistive index, pulsatility index) of ovarian masses and differentiates them into benign and malignant lesions and correlate with histopathological findings.

## MATERIAL AND METHODS

The study sample comprised of 39 patients having clinically suspected ovarian masses on the basis of a positive history and clinical examination. USG was performed on sonoline G 50 and versa pro machine with 3.5-5.5 MHz trans-abdominal probe. TVS was performed whenever required to obtain additional findings. For transabdominal USG patient was advised to hold urine and examination was performed in supine position. Scanning of lower abdomen and pelvic region was done in different planes using 3.5-5.5 MHz curvilinear transducer.

The presence of a mass was first confirmed on gray scale all masses were awarded morphologic scores as per the Sassone's

scoring system. The scores could range from a minimum of 4 to maximum 15 points. Following gray scale scanning, color flow signals were superimposed in real time and the regions of intratumoral neovascularisation were identified as the areas of color. A cursor was placed at the region of interest and the spectral wave forms were obtained from which the pulsatility and resistive indices were noted (PI and RI). A mass was declared as not to be having a detectable blood flow, in case we failed to obtain color flow signals after 25 minutes of continuous scanning. In such cases, using maximum magnification, the sampling box was moved all over the tumor area, so as to identify any possible areas of color. All the patients underwent surgical exploration and the post surgical histopathology findings were correlated with the morphologic scorings and Doppler indices RI/PI value that had been obtained preoperatively.

Menstrual status	Benign	Malignant
Premeanrche	-	-
Premenopausal	24	2
Postmenopausal	11	2
Total	35 (89.7%)	4 (10.3%)

**Table-1:** Comparison of menstrual status with histopathological findings

Type of tumor	No.	Percentage
Mature cystic teratoma	12	30.8%
Mucinous cystadenoma	6	15.5%
Simple cyst	5	13%
Cystic teratoma	9	23.4%
Serous cystadenoma	2	5.2%
Corpus luteal cyst	1	2.6%
Choriocarcinoma	4	10.4%

**Table-2:** Type of tumor detected in 39 women by histopathological finding

Name of the Tumor	Score
Choriocarcinoma	13-14
Mucinous cystadenoma	10-12
Mature cystic teratoma	12
Cystic teratoma	7
Serous cystadenoma	8
Corpus luteal cyst	8
Simple cyst	7
Thecaluteal cyst	7-8
Mature teratoma (dermoid)	8
Fluid filled cystic lesion	6
Unilocated epithelial lining cyst	6
Physiological/infective cyst	5 (normal)

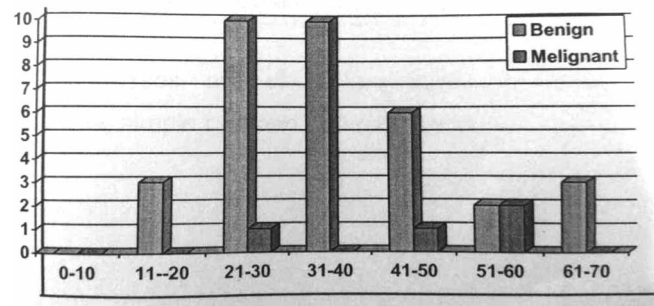
**Table-3:** USG evaluation by grey scale score

Flow [Positive]		Flow [Negative]
Benign	Malignant	
9	4	26
13 (33.33%)		26(66.6%)

**Table-4:** Doppler study for color flow within the tumor

Serial No.	Right	Left
1	-	1.74
2	-	2.55
3	-	3.08
4	-	1.3
5	0.48	-
6	0.61	-
7	1.33	-
8	0.99	-
9	4.1	-
10	3.35	-
11	3.0	-
12	7.4	-
13	1.83	-

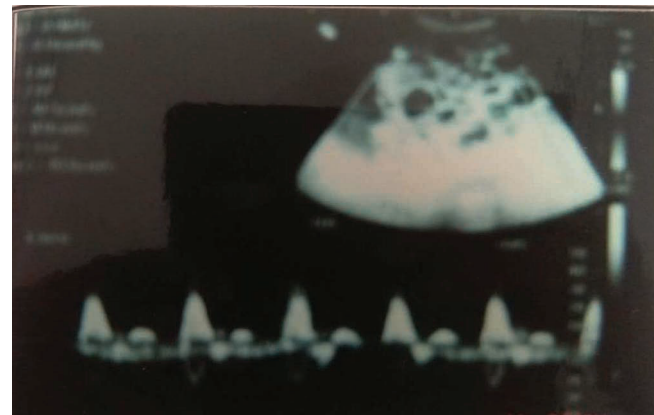
**Table-5:** Range of pulsatility index



**Figure-1:** Distribution of cases in different age groups

Serial No.	Right	Left
1	0.4	-
2	0.45	-
3	0.39	-
4	0.98	-
5	0.81	-
6	0.93	-
7	0.98	-
8	1	-
9	1	-
10	1	-
11	2	0.9
12	-	0.9
13	-	0.9

**Table-6:** Range of resistivity index



**Figure-1:** USG showing Doppler spectral tracing from intratumoral vessel

Calcification- Rt	Calcification- Lt
4 (Positive)	3 (Positive)
35 (Negative)	14 (Negative)
39 (Total)	17 (Total)
Necrosis- Rt	Necrosis-Lt
11(Positive)	4 (Positive)
28 (Negative)	13 (Negative)
39 (Total)	17 (Total)

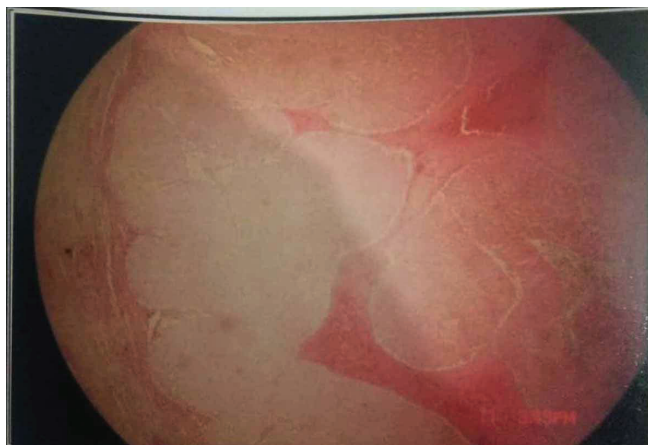
**Table-7:** Calcification and necrosis (by USG) within the tumor



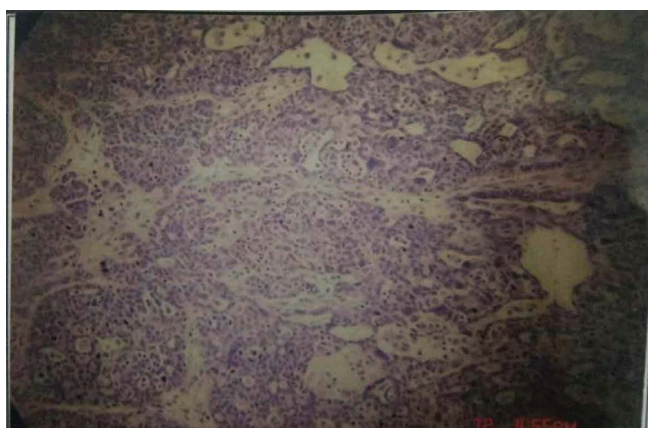
**Figure-2:** Postoperative specimen of solid mature cystic teratoma

	Histopathological findings		Total
	Yes	No	
USG (Benign)	0	35	35
USG (Malignant)	4	0	4
Total	4	35	39
Summetric Measures			
	Value	Asmp. Std. Error	Approx. T
Measure of agreement Kappa	1.000	0.000	6.245
N of valid cases	39		
a. Not assuming the null hypothesis; b. Using the asymptotic standard error assuming the null hypothesis			
According to Cohen's Kappa when both variables have the same number of categories of a value of 1 indicates perfect agreement between two departments			

**Table-8:** USG CA histopathological findings



**Figure-3:** Histopathological slide of haemorrhagic corpus luteal cyst



**Figure-4:** Histopathological slide of sertoli leydig cell tumor (showing tubular)

## RESULTS

Thirty nine women suspected of having ovarian mass referred from Department of Gynaecology over the period of 16<sup>th</sup> month [Feb 2015 to June 2016], were included in the study subjected for pelvis USG after obtaining detail clinical history as per proforma post operative histopathological reports were obtained. A total of 56 masses were detected in 39 patients. On histopathological examination, 4 masses proved to be malignant and 24 masses were benign and rest were physiological cyst/ infective process, which showed only cyst increase in size on follow up USG and these masses were not operated and managed conservatively. Hence they were not included in our analysis. Morphological scores were assigned to all masses. Doppler blood flow could not be identified in 26 patients. In the remaining 13 patients in whom blood flow was obtained, pulsatility and resistance indices were calculated and correlated with their histopathologic results. Among them 9 in which intra tumoral flow noted the Doppler RI and PI values showed nature of masses condition. Among the study participants 89.7% were having benign lesions and rest 10.3% were having malignant lesions [Table 1]. Majority of cases are of mature cystic teratoma, mucinous cystadenoma, simple cyst and cystic teratoma [Table 2, Fig. 2,3]. Grey scale/morphological score show maximum value of 14 for malignant lesion for benign one value ranges from

6-12 [Table 3]. About 13 masses in which intratumoral flow [Fig.1] was present and among them 9 were benign and 4 were malignant [Table 4].

Among 39 patients 13 shows flow within the tumor, but only 5 of them shows PI value ranging from 0.48-1.33 and by histopathological correlation they were found as malignant with sensitivity 100%, specificity 97%, PPV 80% and NPV 100% [Table 5].

Among 39 patients 13 shows flow within the tumor, but only 4 of them which were proved by histopathology as malignant ranges from 0.4-0.9. however 6 of them shows value ranges from 0.8-0.9 (borderline) but they were proved as benign by histopathology and USG sensitivity found to be 100%, specificity 80%, PPV 36% and NPV 100% [Table 6].

All the cases which were proven as malignant by histopathology contain necrosis and calcification in USG (grey scale) [Table 7, Fig.4].

## DISCUSSION

USG finding of different tumors on gray scale CDUS

Choriocarcinoma of ovary showed heterogenous echotexture with irregular or lobulated margin. Areas of necrosis and calcification noted within the lesion.<sup>12</sup> Doppler study showed intratumoral blood flow with low RI/PI values. Serous cystadenoma showed heterogenous echotexture with septation and calcification noted within the lesion. Some of them showed necrotic areas, with intratumoral blood flow but high RI/PI values. Mucinous cystadenoma showed thick walled heterogenous echotexture with multiple varying sizes cystic areas and septation having solid component with blood flow showed high RI/PI values. Mature teratoma showed heterogenous echotexture with solid and cystic areas. Some solid component noted within the tumor. Cystic teratoma showed low level echogenic fluid filled cystic tumor with no internal Doppler flow noted.<sup>13,14</sup>

On color flow imaging we failed to obtain color signals in 26 patients. However, no malignancy was encountered in this group. Blood flow was obtained in all the 4 malignant masses and 9 benign masses. Analysis of color flow data as a predictor of malignancy, we obtained a sensitivity of 100% and NPV of 100% while specificity and PPV were 80% and 36% respectively.

The range of values of PI for malignant masses was 0.48 to 1.33 with a mean of 0.85. PI of benign masses ranged from 1.3 to 7.4 with mean standing at 3.15, by using a PI value of 1.1 as the cut-off point, for differentiating benign and malignant lesions. Decreasing the cut off value to 1 or 0.9 would make the test less sensitive but more specific. The range of values of RI for malignant masses was 0.4 to 0.98 with a mean of 0.5. RI of benign masses ranged from 0.4 to 0.9 with mean standing at 1.05, using an RI value of 0.6 as the cut-off point. Decreasing the cut-off value to 0.5 or 0.4 would make the test less sensitive but more specific. There is a wide variation of results in the works of below mentioned authors with the proposed cut-off values of RI ranging from 0.41 to 0.8. Our results fall within the spectrum of above mentioned studies. Various authors have documented spectrum of USG (grey scale/Doppler study) for evaluation of ovarian masses. Karimi-Zarchi M et al (2016)<sup>15</sup> proved

that four criteria could be combined in malignancy score which was calculated as product of serum CA 125 presence of serum, RI ( $RI < 0.5$ ), PSV ( $PSV \geq 40$  cm). They conducted the sensitivity was 98% and specificity was 85%, PPV was 87.5% and NPV 97.6%. In the present study mean value of RI in malignant lesion is approx 0.5, with sensitivity 100%, specificity 80%, PPV 36% and NPV 100%. Our result fall within the spectrum of above mentioned studies. Valentin L et al proved small proportion of solid issue with papillary projection and intratumoral flow suggest malignant tumor.<sup>5</sup> Brown et al in their study concluded that grey scale and CDUS finding and solid component within the most statistically significant predictor of ovarian malignancy.<sup>16</sup>

Taylor A et al took age, tumor diameter, volume, papillary projection, PSV, time as variables and averaged maximum velocity RI and PI.<sup>17</sup> They included the variables for each patient: (1) age, (2) maximum tumor diameter, (3) tumor volume, (4) unilocularity (presence (0) or absence(1)), (5) papillary projections (presence (1) or absence (0)), (6) random echogenicity (presence (1) or absence (0)), (7) highest peak systolic velocity (PSV), (8) time-averaged maximum velocity (TAMXV), (9) pulsatility index (PI) and (10) resistance index (RI) for predicting the presence or absence of malignancy. The accuracy of this prediction appears to be better than that of morphological or Doppler criteria when the later is used independently. Taylor A et al in their study found complex structures and echogenic lesions were found in ovarian tumor of low malignant potential and malignant tumor than in the cystadenomas and the difference was statistically significant. RI value in this study had showed ( $0.48 \pm 0.07$ ).<sup>17</sup>

Alcazar JC et al studied in ovarian cancer by TVS and CDUS. They concluded that purely solid tumor indicates probability of metastatic carcinoma.<sup>18</sup> However variables such as bilaterality, volume, ecogenecity, speta, papillary projection, soild areas, Doppler indices RI/PI do not show statistical difference. Varras M et al in their study showed the limitations of USG in early detection of ovarian cancer and Doppler USG is not an independent indicator for malignancy. Consistent with the findings of other studies.<sup>19</sup> Consistent with the findings of other studies our result also showed necrosis, solid component and calcification on USG to be features suggesting malignant lesion. However Doppler evaluation helps to confirm the diagnosis.

Szpurek D et al (2006)<sup>20</sup> studied ovarian fibrosarcoma by CDUS (variables were RI/PI and PSV). They concluded low vascular resistance can be encountered in ovarian fibrosarcoma and intratumoral Doppler wave form might help in prediction of rare malignant tumors. Gramellini et al showed central Doppler flow was the only significant parameter among those analyzed using Color Doppler which was useful for the diagnosis of a malignant neoplasm with a diagnostic accuracy of 82.95% sensitivity 55.55% but low false positive 7.95%.<sup>21</sup> Alcazar JL et al studied on adenexal malignancy by USG and color Doppler and histopathological correlation. They concluded sensitivity, specificity, PPV, NPV were 85.7%, 100%, 1005 and 95.4% respectively. Overall accuracy of USG with CDUS was 96.4%.<sup>22</sup> Marret H et al analyzed and established that USG is the gold standard for ovarian cyst

diagnosis. They found papillary formations and masses with a nonhyperechoic solid component are the most statistically significant predictors of malignant ovarian mass.<sup>23</sup> They concluded that DUS and morphologic parameters have a sensitivity of 80% and specificity of 93% that make test as the gold standard for ovarian masses diagnosis. Guerriero S et al studied comparison of conventional color DUS and power Doppler imaging for the diagnosis of ovarian cancer. Using both modalities of color Doppler or was at least one of the two Doppler techniques should be used in conjunction with B-mode imaging in order to diagnose malignant lesion.<sup>24</sup> Sawicki W et al<sup>11</sup> proved their study that Doppler flow within the tumor was 74.5% in benign and 98.6% in malignant masses ( $P < 0.0001$ ). Average value in an echogenic portion defined as malignant by B-mode. They found peripheral vasculature in benign on the other hand, central and peripheral and mixed in malignant and location and intensification of vascularisation in examined masses which permit the differentiation of malignant and benign lesions. Consistence with the finding of others; this study also proved that low vascular resistance and intratumoral flow signify malignant tumor with a diagnostic accuracy of 80% and sensitivity of 100%.

Pascual MA et al analysed grayscale and color Doppler USG feature with histopathological correlation.<sup>25</sup> They concluded when a ovarian cystic mass with papillae, necrosis with Doppler values of low RI value within the mass suggests malignancy. Smolen et al included six variables age, bilaterality, septae, necrosis, volume and color score (RI/PI) in their study. Results were sensitivity 74.6% and specificity 94.7%. For ovarian mass our study showed sensitivity 100% and specificity 80%. That falls within the spectrum of aforementioned study. Varras M et al proved CDUS imaging is very useful in detecting of uterine adnexal malignancy because of revascularization in malignant tumors. Presence of septum, pappillary projections, or solid components present within the lesion supports in favour of malignancy.<sup>19</sup>

Cohen L et al studied in ovarian cancer by using USG and proved that TVS in expert hand is sensitive but not specific for discriminating benign from malignant but judicious use of color Doppler evaluation may help to discriminate benign and malignant lesion.<sup>26</sup> Czekierdowski A et al studied color Doppler blood flow measurements and microvessel density assessment in ovarian tumors. Finally they came to a conclusion that low resistance to blood flow as measured by the RI or PI on CDUS may by positively correlate with the micro vessel density in the malignant ovarian tumors.<sup>27</sup> Valentin L et al came in a conclusion that CDUS examination is helpful only in differentiating multilocular cysts with solid parts. Thus greater the solid parts in multilocular cyst, greater the potential of the Doppler examination to improve diagnostic accuracy.<sup>28</sup> Caruso A et al proved usefulness of color Doppler in the differential diagnosis of adenexal masses.<sup>29</sup> Doppler analysis (vascular score) was compared to that of some morphological scores. The sensitivity was 100% for all the technique used. But Doppler analysis had a higher specificity. Finally they came in a conclusion that color CDUS of ovarian tumors seem to be a reliable method in the differential diagnosis of adnexal masses. Our

study also proved that Doppler evaluation (RI/PI) indices has important role to discriminate benign from malignant ovarian tumor.

Shah D et al (2012)<sup>30</sup> concluded that PI was lesser in malignant lesion than in benign lesions ( $< \text{or} = 1.0$ ). However the PI value sometimes showed considerable overlap between benign and malignant lesions indicating that CDUS has limitations in the differentiation of benign from malignant ovarian masses. Salem S et al came in a conclusion that their results showed a high positive predictive value of high impedance flow in benign adnexal disease and a predominance of low impedance flow in malignant adnexal disease. However, the PI showed considerable overlap between benign and malignant lesions, indicating that DUS has severe limitations in the differentiation of benign from malignant adnexal disease on the basis of low impedance flow ( $\text{PI} < 1.0$ ). But in our study only cases showed overlap in PI value for malignant lesion. However our result fall within the spectrum of proved PI value by different authors; such as value of PI ( $< \text{OR} = 1$ ) for malignant lesion.

The comparison of USG findings with that of histopathology shows good correlation in diagnosing benign and malignant ovarian mass. In overall transabdominal USG with Doppler study is fairly accurate in diagnosing benign and malignant ovarian tumor.

Madan R, et al 2004<sup>31</sup> showed that the sonomorphologic evaluation following Sassone scoring system had a sensitivity of 92.3%, specificity 55.3%, PPV 54.3%, NPV 92.8% and a diagnostic accuracy of 68.9%. Forty six out of 74 masses were considered suspicious of malignancy (Sassone score = 9) of which 25 were malignant and 21 were benign. High scoring (= 9) benign lesions were inflammatory adnexal masses, endometriomas, cystic teratomas, mucinous cystadenomas, and thecoma. Non-suspicious sonomorphology (score < 9) was noted in 28 mass lesions- 26 were benign and 2 were malignant (1 immature teratoma and 1 serous cystadenocarcinoma).<sup>31</sup> Color flow was detected in 77.02% masses- - 92.5% (25/27 masses) malignant masses were vascularised as compared to 68.08% (32/47 masses) benign adnexal masses; increased flow was noted in 92% malignant lesions and only 21.87% benign masses (5 inflammatory masses, one broad ligament fibroid and one thecoma). On pulsed Doppler, the average value of RI in malignant ovarian neoplasms amounted to  $0.40 \pm 0.15$  and was higher in benign masses [ $0.51 \pm 0.11$ ]. The mean PI of  $0.61 \pm 0.19$  in malignant adnexal masses was lower than  $0.89 \pm 0.32$  in benign lesions. The mean PSV in benign masses ( $12.74 \pm 8.4 \text{ cm/sec}$ ) was lower than that in malignant adnexal masses ( $23.92 \pm 13.6 \text{ cm/sec}$ ). The mean vascular score (Caruso et al) was higher in malignant ovarian neoplasms ( $7.64 \pm 2.64$ ) as compared to benign lesions ( $2.34 \pm 2.23$ ).<sup>31</sup>

There is considerable overlap in the morphologic patterns of various ovarian masses. Gray scale ultrasonography in combination with color Doppler, spectral Doppler, and their combination in the form of scoring systems like ALCAZAR is proposed as the foremost diagnostic modality in patients with ovarian tumor, so as to establish the definite diagnosis of malignancy early in the course of the disease.<sup>32</sup>

## CONCLUSION

The present study evaluates ovarian mass by USG and CDUS considering histopathological examination of post operative specimen as gold standard. The purpose of this work was to study the morphological characteristic of ovarian masses by USG and change of spectral Doppler wave form characteristic (RI/PI) of ovarian masses and differentiate them in to benign and malignant lesions with a correlation of histopathological finding. The morphologic scores of benign masses are comparatively lower than that of malignant masses. A mass showing absence of color flow signals on color Doppler is more likely to be benign, though reverse is not true. Low resistance to blood flow with low pulsatility and resistive indices is a feature of malignant masses. High resistance blood flow with high PI and RI values is suggestive of benign masses. An area of overlap exists between the range of values of benign and malignant masses with both on morphologic as well as haemodynamic assessment. In the overall scenario, pulsatility index is more accurate followed by resistive index and then by morphologic scores in predicting the nature of a mass. The limitations of our study were the small sample size and the inability to compare our values in the large scale. Determination of a degree of suspicion for malignancy in an adnexal mass is the most critical step after identification of the mass and has a profound effect on patient survival. Color flow imaging and spectral Doppler have a promising role in the evaluation of adnexal masses. Morphologic analysis of adnexal masses is done to classify them as either low risk or high risk. The most ominous features are non-fatty solid vascularised tissue identified by Color Doppler US. Spectral Doppler waveform characteristics- RI, PI and PSV correlate well with malignancy and are based on the fact that tumor vessels are morphologically abnormal.

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