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Original article

A study to assess the diagnostic reliability of combined gray scale ultrasound and Doppler flow imaging to differentiate malignant and benign adnexal masses

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Abstract

Aim and Background: *In the present study was investigated that the diagnostic reliability of combined gray scale ultrasound and Doppler flow imaging to differentiate malignant and benign adnexal masses. Ovarian cancer is the most common and highly lethal Gynecological malignancy. Histopathological Examination is considered to be the gold standard for diagnosis. However, Ultrasonography is the primary modality used in the evaluation of the adnexal masses.*

Materials and Methods:*This is a prospective type of study conducted in Meenakshi Medical College Hospital and Research Institute for a period of one and half years. 50 female patients with clinically suspected adnexal masses were evaluated by Transabdominal or transvaginal Ultrasonography with Doppler flow Imaging to detect and categorize adnexal masses. Based on morphological features assessed by the grayscale ultrasound (size, echogenicity, surface contour, papillary projections) and vascularity by Doppler flow imaging (colour Doppler, power Doppler), the lesions were categorized as benign and malignant. Pathological examination of adnexal masses was performed on samples obtained by sonography guided biopsy, ultrasound-guided FNAC, laparoscopic guided aspiration cytology and surgically removed specimens. However, histopathological examination is considered to be the gold standard for the diagnosis of adnexal masses.*

Results:*The present study revealed that the presence of certain morphological features assessed by combined Gray scale ultrasound and colour Doppler comprising of the large size (>10 cms), irregular surface contour, solid & multilocular echogenicity, thick septations, internal papillary projection and low resistance blood flow (PI<1.0, RI<0.4) were statistically significant for malignant tumours.*

Conclusion:*The present study concluded that combined Gray scale ultrasound and Doppler flow imaging had sensitivity of 80 %, specificity of 97 %, the positive predictive value of 80 % and the negative predictive value of 97 % to discriminate between benign and malignant adnexal masses.*

Key words: *Ovarian Cancer, Gray scale ultrasound and Doppler flow imaging*

Introduction

Adnexa (uterine appendages), the most closely related structures adjacent to the uterus includes ovaries, fallopian tubes and ligaments. Adnexal mass represents the broad spectrum of conditions from Gynecologic and Non-Gynecologic sources and is also considered the most common disease in Gynecology. The conditions vary from benign conditions like functional cysts to malignant masses like ovarian cancer. Ovarian pathology alone represents two-thirds of all the cases. Fewer neoplasm's might also occur in the fallopian tube with the inflammatory conditions being more common. In the diagnosis of adnexal masses, the first and foremost clinical parameter to be considered is the age of the patient. Although adnexal cysts are the most common in reproductive-age group, the rate of malignancy is low in this age group. On the contrast, the risk of malignancy is more common among the postmenopausal women. Other factors to be considered while evaluating patients with adnexal masses are symptoms of acute pelvic pain, abdominal distention accompanied by gastrointestinal complaints and weight loss and use of hormonal contraception. The most common causes of pelvic pain are ovarian torsion, endometriosis, pelvic inflammatory disease or an acute hemorrhagic corpus luteal cyst[1]. Weight loss might be attributed to the complications of advanced ovarian cancer while hormonal contraception is implicated with the functional ovarian cysts. Ovarian cancer is the third most common cancer in women and fourth most common cause of cancer-related deaths, worldwide. Approximately 1.6% of women would develop an ovarian malignancy during their lifetime while 10% of women would have a benign tumour of the ovary, requiring surgery [2].

There are no known causative factors in the development of ovarian carcinoma, Factors known to increase the risk of developing ovarian cancer are genetic (BRCA 1, BRCA 2, HNPCC), nulliparity, late childbirth, early menarche, late menopause, family history, obesity, hormone replacement therapy, and high saturated fat diet . The age-specific incidence rate for ovarian cancer increases around 35 years and peaks by 55-64 years . The major drawback is that most of the patients are asymptomatic, presents often at late stages &responds poorly to treatment. Regardless of the numerous advances in treatment, ovarian cancer has consistently had the highest case fatality ratio among all gynecological malignancies, with a 5-year survival rate of 40-50% at all stages of malignancy. The early and accurate diagnosis of ovarian malignancy is of significant clinical importance, because the prognosis entirely depends on early diagnosis. A preoperative diagnosis of malignancy can guide the Gynecologist for appropriate therapy which has been reported to improve the survival period of the patient Further, benign adnexal cysts (such as endometrioma, mature cystic teratoma, and paraovarian cysts) need to be diagnosed correctly. In the event of misdiagnosis it may turn as a risk factor for infertility or ovarian torsion. Therefore, adnexal masses need to be evaluated as benign or malignant, in order to provide better treatment. Ultrasonography is the primary imaging modality used for identification of adnexal mass, Because of its widespread availability, cost-effective, non-invasive technique and higher sensitivity for detection of adnexal masses. USG is considered to be one of the excellent imaging modalities in the determination of the nature of a mass lesion (cystic or solid), origin and its anatomic relation to adjacent structures . Therefore, the correct use of Pelvic Ultrasonography has become an integral part of the Gynecologic evaluation and management. Addition of colour and spectral Doppler imaging that determines the vascular pattern of adnexal disease has been found to be a very useful tool in screening for malignancy. Transvaginal ultrasound is preferred to Trans-abdominal ultrasound; whenever feasible, owing to the higher accuracy with the former[3].

Spectral Doppler analysis with low PI (<1.0) or RI (0.4) indicates malignancy. Transabdominal sonography is helpful for evaluating larger masses or those located superiorly or laterally in the pelvis while Transvaginal USG provides optimal visualization of most adnexal diseases. Doppler sonography is useful in masses with an apparent solid area or septations with vascularity. Other imaging modalities such as computed tomography (CT), Positron emission tomography (PET), or magnetic resonance (MRI) imaging can be helpful in various aspects. Computed tomography helps to assess staging and the extent of disease in patients before and after primary cyto-reductive surgery. Magnetic resonance imaging plays essential role in the characterization of indeterminate adnexal masses. MRI may be used as an adjunct imaging modality when the initial ultrasound characterization of adnexal mass as benign or malignant is inconclusive. In the present study, we characterized the adnexal masses with combined Gray

scale sonography and Doppler flow imaging to identify the malignant potential of the lesion. Further, the sonographic findings were correlated with the final histopathological diagnosis. The sensitivity, specificity, positive and negative predictive values were calculated to assess the accuracy of the involved modalities to differentiate benign from malignant adnexal masses.

Materials and Methods

This is a Prospective study conducted in Meenakshi Medical College Hospital and Research Institute, Kanchipuram. Female patients with complaints of lower abdominal pain, menstrual irregularity referred from the Department of Gynecology, Surgery, General Medicine from MMCH & RI and other hospitals to Department of Radiodiagnosis at Meenakshi Medical College Hospital & Research Institute. After getting informed consent and detailed clinical history from the patients, all the subjects were scanned with Gray-Scale sonography using 3.5-5 MHZ and 8 MHZ probes for Transabdominal and Transvaginal scans respectively and subsequently Color and Spectral Doppler examination was done. Transabdominal USG was done in all cases, followed by transvaginal sonography (TVS) wherever necessary. TVS was not performed in patients who were not willing to undergo TVS and virgin patients with the adnexal mass. The following characteristics of adnexal masses were recorded: Site; laterality (unilateral/bilateral), Size, Surface contour (smooth/irregular), Type of lesion-- [unilocular, unilocular with fibrin strands, unilocular with internal echoes, unilocular solid, solid, multilocular, multilocular with internal echoes, multilocular with solid, solid), Papillary projections, Septations (thin, thick, none), Associated findings (fluid in cul-de-sac and ascites) If possible, a Specific diagnosis was made, e.g Dermoid cyst, Ectopic pregnancy. Following Grey scale examination of mass, Color flow imaging was done to assess the vascularity of the mass. If no blood flow was detected, the tumour was considered avascular tumour. After Color Doppler examination, the masses were evaluated on Spectral Doppler. A range gate was placed across an appropriate vessel and the flow velocity waveform was displayed. In the absence of arterial flow, the mass was considered as benign while in the presence of arterial flow, the mass was considered malignant if RI $\leq$ 0.4 PI $\leq$ 1.0. Pulsatility Index (PI) = Peak systolic flow – end diastolic flow / mean systolic flow. Resistance Index (RI) =Peak systolic flow-end diastolic flow/peak systolic flow. Based on this morphologic characteristic on Grayscale US and Doppler findings, the masses were categorized as benign or malignant. Scanning was performed using Voluson S6 Pro ultrasound machine equipped with a colour and pulsed Doppler and a 3.5 MHZ transabdominal and 8 MHZ transvaginal transducers. Results of the ultrasound studies were correlated with histopathological findings.

Results

Age wise incidence of adnexal masses

The patient‘s age ranged from 16 to 75 years. In the present study, the maximum numbers of cases were in the age group of 36-45 years (34%) and the minimum numbers of cases were in the age group of 66-75 years (6 %). The maximum number of cases were in premenopausal age group <45 years (64%).

Age in years	Frequency	Percentage (%)
16-25	6	12.0
26-35	9	18.0
36-45	17	34.0
46-55	9	18.0
56-65	6	12.0
66-75	3	6.0
Total	**50**	**100.0**

Clinical Diagnosis

In the present study, the most of the patients clinically diagnosed as pelvic masses (38 %). 28 % were diagnosed as dysfunctional uterine bleeding (DUB), 24 % were as pelvic pain, 6 % as dysmenorrhoea and only 2 % diagnosed as polycystic ovaries (PCOD).

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Clinical	**Frequency**	**Percentage (%)**
Pelvic Mass	19	38.0
DUB	14	28.0
PCOD	1	2.0
Dysmenorrhoea	3	6.0
Pelvic Pain	12	24.0
Ectopic Pregnancy	1	2.0
Total	**50**	**100.0**

Distribution of Mass Lesions According to Size

In the present study, 60% of malignant lesions were measured about more than 10 cms in size while only 9 % of benign lesions were in the same size. 49 % of benign masses were measures about 5-10 cms in size, while 40 % of malignant cases were in the same size. 42% of benign lesions were less than 5 cms in size, while no malignant lesions were in that size. P value is 0.005 (significant)

Size in cms	**Histopathological Diagnosis**		**Total**
	Benign	**Malignant**	
<5	19(42.2%)	0(0%)	19(38%)
5-10	22(48.2%)	2(40%)	24(48%)
>10	4(8.9%)	3(60%)	7(14%)
Total	45(100%)	5(100%)	50(100%)
Pearson chi-square	0.005		

Distribution of Mass Lesions Based on Surface Contour

The study shows 91 % of benign lesions have well-defined border and remaining 9 % have an ill-defined border. 60% of malignant lesions have an ill defined border and 40 % have well defined border. P value 0.016 (significant).

USG – Borders/ Surface contour	**Histopathological Diagnosis**		**Total**
	Benign	**Malignant**	
Well defined	41(91.1%)	2(40%)	43(86%)
Illdefined	4(8.9%)	3(60%)	7(14%)

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total	45(100%)	5(100%)	50(100%)
Pearson chi-square	0.016		

Distribution of Mass Lesions Based on Internal Septations

In the present study, 80% of malignant lesions contained thick septations compared to 17.8 % of benign lesions. Also depicts 53.3 % of benign lesions were without septations compared to 20 % of malignant lesions. 28.9 % of benign lesions had thin septations. No malignant lesion contained thin septations. P value 0.008(significant).

USG - Septations	**Histopathological Diagnosis**		**Total**
	Benign	**Malignant**	
Thin	13 (28.9%)	0(0%)	13(26%)
Thick	8(17.8%)	4(80%)	12(24%)
No septations	24(53.3%)	1(20%)	25(50%)
Total	45(100%)	5(100%)	50(100%)
Pearsonchi- square	0.008		

Distribution of Mass Lesions with Ascites

In this study 40 % malignant lesions associated with ascites and 60 % of malignant lesions not associated with ascites. Whereas 97.8 % of benign cases were not associated with ascites, only 2.2 % of the benign lesion was associated with ascites. P value 0.001(significant)

USG – Papillary Projections	**Histopathological Diagnosis**		**Total**
	Benign	**Malignant**	
Present	1(2.2%)	3(60%)	4 (8 %)
Absent	44 (97.8%)	2(40%)	46 (92%)
Total	45(100%)	5(100%)	50(100%)
Pearsonchi- square	0.001		

Distribution of Mass Lesions Based on Colour Uptake
In the present study, all the malignant lesions were vascular (100 %) whereas only 64 % of benign masses were vascular. P value 0.001(significant)

Ascites	Histopathological diagnosis		Total
	Benign	Malignant	
Present	1(2.2%)	2(40%)	3(6%)
Absent	44(97.8%)	3(60%)	47(94%)
Total	45(100%)	5(100%)	50(100%)
Pearsonchi-square	0.001		

Test of Two Proportions
Out of 50 cases, In comparison with histopathology report, combined Gray scale sonography with Doppler imaging found 44 benign cases and 4 malignant cases correctly. One benign and malignant mass was found to be misdiagnosed. In the present study, we found that Gray scale sonography with Doppler imaging had the Sensitivity of 80%, specificity of 97 %, the positive predictive value of 80 % and negative predictive value of 97 % for discriminating between benign and malignant Adnexal masses.

Color uptake	Histopathological diagnosis		Total
	Benign	Malignant	
Present	13(36%)	5(100%)	18(36%)
Absent	32(64 %)	0	32(74%)
Total	45(100%)	5(100%)	50(100%)
Pearsonchi-square	0.001		

Gray scale ultrasound, Doppler flow imaging and Histopathological to differentiate malignant and benign adnexal masses

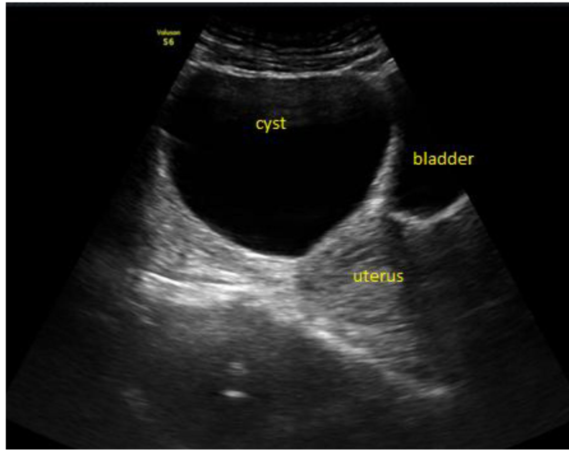

Figure 3a-Transabdominal sonogram showing, a large well defined Unilocular cyst in right adnexa

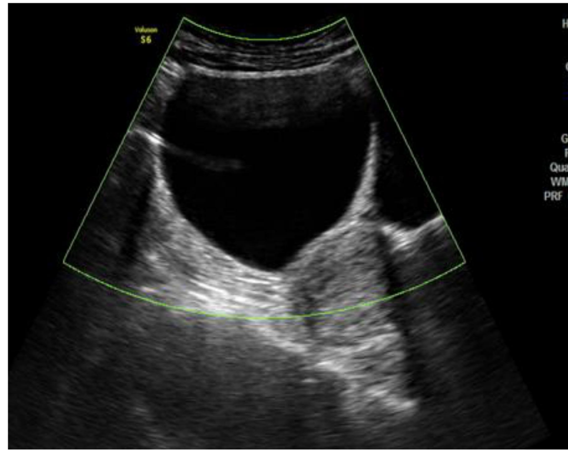

Figure 3b- On color Doppler, no vascularity detected---**Benign Ovarian Cyst**

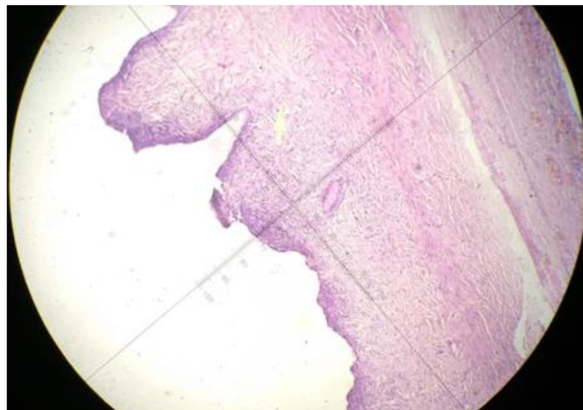

Figure 3b. On Histopathological Examination , diagnosed as **Benign Serous Cystadenoma of Ovary**

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Gray scale ultrasound, Doppler flow imaging and Histopathological to differentiate malignant and benign adnexal masses

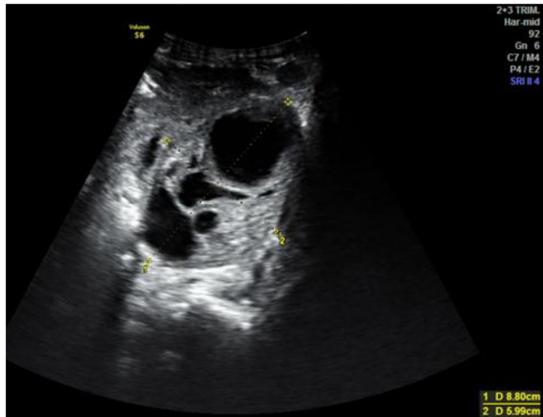

Figure 4a. Transabdominal sonogram showing, a large sized, complex solid and cystic mass lesion in right adnexa

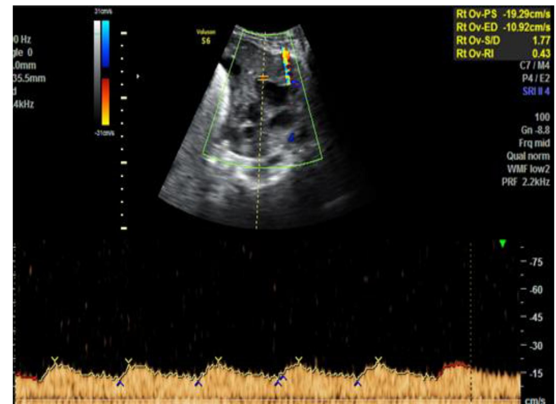

Figure 4b. On Doppler examination, lesion showed internal vascularity, with low resistance blood flow, Resistance Index : 0.43 --**Malignant ovarian mass**

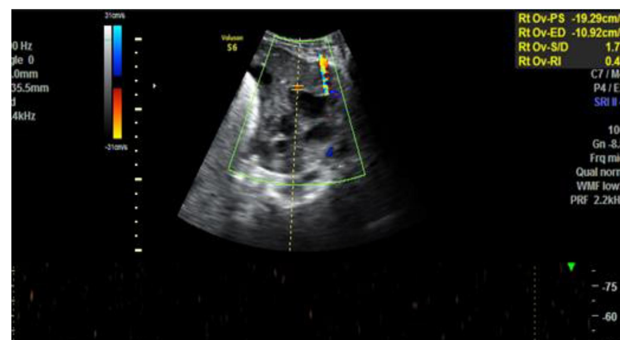

Figure 4c. On histopathology, diagnosed as **Mucinous Cytsadenocarcinoma**

Discussion

Adnexal masses are common among all the age groups but more prevalent among the reproductive age groups. Ovarian cancer is the leading cause of death from Gynecologic malignancies. Most of the patients are asymptomatic, often present at the late stage which in turn leads to poor prognosis. Therefore, pre-operative identification of Adnexal mass as benign or malignant is imperative for appropriate patient triage, referral, and management. In the above mentioned context, the present study was conducted on 50 patients diagnosed with adnexal masses. The study participants were evaluated prospectively on the Gray scale sonography with colour Doppler and spectral Doppler imaging. The common clinical diagnosis observed in the study group were as follows, 38 % patients were as Pelvic masses (19 cases), 28 % were diagnosed of DUB (14 cases), 24 % diagnosed as Pelvic pain, 6% as Dysmenorrhoea, 2% as PCOD and 2% as Ectopic pregnancy This study group comprised of participants ranging in

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age between 16 to 75 years. About 64 % of the participants were individuals less than 45 years of age; The maximum number of benign cases were seen in individuals less than 45 years of age (69%) while the maximum number of malignancies were seen in individuals more than 45 years of age (80 %). This study reveals that relationship between age and status of disease was found to be statistically significant (p=0.01). These findings were also consistent with **Luo H, Yin L et al** (2023)[4].

In the present study, 48 % of masses measured about 5-10 cms in diameter, 38 % of masses measured about less than 5 cms in diameter and remaining 14 % of masses were more than 10 cms in diameter. Most of the benign adnexal masses were found to measure 5-10 cms (49%) in diameter, while maximum numbers of the malignant masses were found to be more than 10 cms in diameter (60 %). The differences in size distribution between the benign and malignant. masses were found to be statistically significant (p=0.005) which was also in concordance with the reports of **Chen L et al** (2019)[5]. In the present study, 86 % of lesions presented with well-defined surface contour, while 14 % of the masses had an irregular surface contour. Most of the benign lesions had well-defined contour (91%), while only 60 % of the malignant masses had an irregular contour. The differences in surface contour abnormality between benign and malignant adnexal masses were also found to be statistically significant (p=0.016). The most common consistency of the lesions were cystic in 70 % (unilocular-54 %, multilocular-16%), while about; 16 % were solid, 8 % had mixed mass with calcifications and 6% had a solid and cystic component. The proportions of benign and malignant lesions that had solid consistency were 13% and 40 % respectively. Also 76% of the benign lesions had cystic consistency whereas only 20 % of the malignant lesions had the same. The differences in echogenicity of the benign and malignant lesion were statistically significant (p=013).

The study findings in this regard were concurrent with the reports of **Chen L et al**., 2019[5]and **Kobal B et al., 1999**[6]

In the present study group, The septa were found in 50 % of cases. About 26 % of the cases had thin septations while 24 % had thick septations. Further thick septations were seen in 80 % and 18 % of the malignant and benign lesions respectively. In addition, 53 % and 20 % of benign and malignant lesions respectively did not contain any septations. Another consistent finding observed in the adnexal masses was the presence of the papillary projection/ solid components. Only 8 % of all the masses had papillary projections (In malignant lesions: 60%; benign lesions : 2.2 %). Thus, it could be inferred that the presence of papillary projections had strong association with malignant disease. Similar pattern was also noted by **L.Valentin**et al**.,2004**[7]and **Kobab et al.,1999**[6]In the present study, only 6 % of the lesions were associated with Ascites. (40 % of malignant cases and 2 % of benign cases).

Further, only 2 % of the lesions were associated with Metastasis. Also, 64 % of lesions were avascular while 36 % of them showed vascularity. It must be noted that all the malignant lesions showed vascularity while only 29 % of the benign masses showed vascularity. The above mentioned findings was concurrent with the study results of **Timor-Tritsch et al.,1993**[8] Among the vascular adnexal masses, 26 % presented with high resistance flow (PI>1.0, RI>0.4) and 10 % of masses had low resistance flow (PI< 1.0, RI<0.4). It was observed that 80 % of malignant lesions had low resistance flow(PI<1.0, RI<0.4). The tumour vessels are morphologically abnormal because of the lack of intimal smooth muscles. The findings was coincided with the study results of **Ha El et al 2021**[9]**.** Of the fifty patients evaluated, ultrasonography guided biopsy and FNAC was perfomed in two patients each, while nine patients underwent laparoscopic guided aspiration cytology and the remaining twenty seven underwent surgical removal. The collected samples/specimens were sent for HPE to the Department of Pathology. Based on the histopathological report, out of 50 cases, 45 adnexal masses were benign, 5 were malignant. In total 45 benign masses, 16 were ovarian cysts. (Of these Serous cysts -4, Mucinous cyst-4, Hemorrhagic cysts-5, Paratubal cyst-1, Endometrioma -2), 5 Mature cystic teratoma, 4 Serous cystadenomas, 4 Mucinous cystadenomas, 2 Ectopic pregnancy, 2 Inclusion cyst, 2 Brenner tumour, 2 Hydrosalpinx and 1 Fibroma, 1 lymphangioma, 1 was Serous papillary adenofibroma, 1 was Broad ligament fibroid, 1 Pyosalpinx, 1 Hematosalpinx, and 1 Ovarian torsion. Out of five malignant cases, one was Serous cystadenocarcinoma, two were Mucinous cystadenocarcinoma, one was Secondary ovarian metastasis and another one was Dysgerminoma. Benign cases far outnumbered the malignant ones. Doppler plays a major role in differentiating benign and malignant lesion. In addition, it is considered important in diagnosing acute pelvic conditions like ectopic pregnancy and ovarian torsion. Ectopic pregnancy

usually exhibits multiple small vessels arranged peripherally (ring of fire) showing high velocity and low impedance flow (RI=0.36-0.45). The sensitivity and specificity of Transvaginal colour Doppler in the diagnosis of ectopic pregnancy analysed in several studies and reported to range between from 73-96% and 87-100% respectively**(Ha EJ et al., 2018)[10].**

The most important sonographic features that indicate ovarian torsion are twisted vascular pedicle and lack of arterial/venous flow in the enlarged ovary. However, partially twisted pedicle with viable ovaries might show central venous blood flow which in turn might lead to an incorrect diagnosis. In such circumstances, local tenderness of affected ovary could be elicited in comparison to the other adjacent structures by Transvaginal ultrasound and this in turn can help in narrowing down to the diagnosis. In the present study, Sonography could not differentiate follicular cysts, serous cysts, and mucinous cysts. However, they were diagnosed as benign ovarian cysts. Sonomorphology has higher sensitivity to identify certain benign ovarian conditions like Dermoids, Inflammatory masses, Endometriomas, and Benign ovarian cysts. Unique diagnostic information was obtained in one 21 year old married woman who had adnexal mass with morphological characteristics of size <5 cms, mixed echogenicity, well-defined border, smooth inner wall without papillary projections had minimal central and peripheral vascularity with PI -0.3, RI -0.8. The above mentioned findings evoked the suspicion of malignancy, which in turn was confirmed by biopsy report as Dysgerminoma. It was highlighted that transvaginal color Doppler was found to be useful in monitoring the progression or early diagnosis of early ovarian cancer in the context of small indeterminate lesions. **Gu Jet al., 2022[11]**reported that that the pulsatility index could be helpful in patient presenting with a very early intraepithelial (or borderline) tumor in a normal size ovary. Transvaginal colour flow imaging could be used to monitor the progression of very small lesions.

In the present study, 44 out of 45 benign cases were diagnosed correctly using Ultrasound with Doppler imaging. Also, out of 5 malignant cases, 4 were diagnosed correctly. The above mentioned Results highlighted that USG with Doppler imaging had sensitivity of 80%, specificity of 97%, the positive predictive value of 80% and negative predictive value of 97% in distinguishing the benign and malignant lesions.

Conclusion

Transvaginal ultrasound depicts sonomorphological characteristics of a mass better than Transabdominal ultrasound. Grayscale ultrasonography combined with Color and Spectral Doppler has been used to achieve better characterization and discrimination between benign and malignant adnexal masses. Transvaginal colour flow imaging can be used to screen for early ovarian cancer or indeterminate small ovarian lesions. The present study highlighted that all the Grayscale ultrasonography and Doppler findings including size, age, consistency, papillary projections, septa and vascularity assessed in the study as showed statistically significant differences between benign and malignant masses.

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