ABSTRACT: Of all the gynecological cancers, ovarian malignancies represent the greatest clinical challenge. The value of tumor marker and ultrasonography to screen for epithelial ovarian cancers has not been clearly established by prospective studies. In present study the relative value, predictive value and differentiate between benign and malignant ovarian tumors of B mode ultrasonography alone and in combination with colour differentiating benign from malignant ovarian neoplasms and to correlate the imaging findings with histopathological findings. The present study established a multi – fold increase in the specificity and positive predictive value in establishing the pre-operative diagnosis of ovarian masses, especially in terms of benignity and malignancy, when using B-mode ultrasonography in combination with colour and spectral Doppler as compared to B-mode ultrasound alone.

KEYWORDS: Ultrasonography, Benign and malignant cancer, Velocimetric indices.

INTRODUCTION: Of all the gynecological cancers, ovarian malignancies represent the greatest clinical challenge. Epithelial cancers are the most common ovarian malignancies and because they are usually asymptomatic until they have metastasized, patients have advanced disease at the time of diagnosis in more than two thirds of the cases. Ovarian cancer represents a major surgical challenge, requires intensive and complex therapies, and is extremely demanding of the patient’s psychological and physical energy.

The value of tumor marker and ultrasonography to screen for epithelial ovarian cancers has not been clearly established by prospective studies. Rising trend in serum CA 125 levels over time is more predictive of ovarian cancer, than a single elevated marker determination.\(^{(1,2)}\) A number of grey scale and Doppler Sonographic features have been studied for their ability to allow distinction between benign and malignant ovarian masses. Initial reports suggested a high degree of accuracy for some of these features such as Pulsatility index (PI) and Resistance index (RI)\(^{(3)}\). Further experience revealed that no single parameter has sufficiently high sensitivity, specificity or predictive values to allow confident diagnosis or exclusion of malignancy. Subsequently most investigators have found grey scale sonography to be as good as or better than Doppler.\(^{(4)}\) To improve diagnostic sensitivity various scoring systems have been proposed but have important shortcomings.\(^{(5)}\) With this background in mind with conflicting reports available regarding the accuracy of ultrasound in the diagnosis of ovarian malignancy, this study was carried out to make assessment regarding the utility and efficacy of B-mode ultrasonography in combination with Doppler for characterization of ovarian masses.
AIM OF STUDY: To assess the relative value, predictive value and differentiate between benign and malignant ovarian tumors of B mode ultrasonography alone and in combination with colour and spectral Doppler in differentiating benign from malignant ovarian neoplasms and to correlate the imaging findings with histopathological findings.

MATERIALS AND METHODS: This study was carried out in the Department of Obstetrics and Gynecology Konaseema Institute of Medical Sciences, Amalapuram. The study included patients of all age groups presenting with adenexal masses. It was conducted from October 2013 to May 2015.

The patients were included into the study based on the following criteria.

SELECTION CRITERIA:
1. Patients with complaints of mass per abdomen.
2. Patients with complaints of pain abdomen, menstrual symptoms having adenexal mass on bimanual examination.
3. Patients with infertility having adenexal mass on clinical examination or ultrasound examination.
4. Cases of ovarian or adenaxal masses referred from other hospitals.

EXCLUSION CRITERIA (AFTER SCAN):
1. Unilocular cystic masses <5cms.
2. Masses which on HPE turned out to be extra ovarian in origin like uterine or broad ligament cyst etc.
3. Masses which turned out to be inflammatory in pathology (Tubo ovarian masses, abscess etc.).

ULTRASOUND EXAMINATION: Esaote Biomedica Au5ef5 Colour Doppler Ultrasound with 2.5 to 5 MHZ. convex probe and multifrequency transvaginal probe was used.

1. Both transabdominal and transvaginal ultrasound was done.

Initially the lesions were evaluated in terms of morphology in B-mode and then color-Doppler study was done at high sensitivity settings and lowest pulse-repetition frequency possible without aliasing. The spectral Doppler was done and PI and RI values were calculated. 3 readings were obtained and the lowest of PI and RI are recorded. Independent T-test was used to assess the statistical significance of PI and RI.

Several grey scale and Doppler features were analysed and result were recorded which included.

RESULTS: Total number of 57 cases was included in age ranging from 11 to 80 years (Median 45.5 years). TVUS was found to be advantageous over TAUS in analysing masses confined to pelvis, small masses (<12cm), bilateral masses, patients with gross ascites and obese patients. TAUS aided and allowed better morphological characterization of masses (Presence of internal echoes, septations thick and thin, areas of necrosis with solid masses etc) and the detection and delineation of site of neovascularity within the masses.
Of the total masses studied, 3 were bilateral (5.26%) while the rest 54 (94.73%) were unilateral. Amongst the unilateral tumours 35 (64.81%) were right sided, while 19 (35.18%) were left sided. Size of the tumours ranged from 4.2x4 cm to 30x18 cm. Tumors less than 5 cm which were cystic were excluded. The internal consistency of tumours included predominantly cystic in 43 (75.43%), mixed or complex in 10 (17.54%) and predominantly solid in 4 (7.01%).

Among the tumors that were not solid:
- Internal echoes were present in 16 (29.62%).
- Papillary projections were present in 2 (3.70%).
- Septations were present in 19 (35.18%) of which:
  - 5 (26.31%) had thick septations.
  - 14 (73.68%) had thin septations.
- Solid components were present in 8 (14.81%).
  - Septal nodules in 2 (25%).
  - Mural nodules in 6 (75%).

Among the solid tumours, necrosis was not noted in any, tumor echo genecity was low in 2 and mixed in 2. There was ascites in 2. There was no liver metastasis, lymphadenopathy and pleural disease.

When the Doppler was analysed:
1. Presence of tumour neovascularity was found in 27 (47.36%) of 57 cases, in which the site of vascularity was as follows;
   a. Cystic.
      i. Purely cystic;
         - Septal 2.
         - Peripheral 16.
      ii. Mixed.
         - Septal 1.
         - Mural 1.
         - Central and Mural 1.
   b. Solid Lesions.
      - Central 2.
      - Central and peripheral 1.
      - Peripheral.

Both venous and arterial flow was detected in 1 (16.66%) of six proven malignant cases that showed neovasularity. This is explained by the formation of arterio-venous shunts and microaneurysms in malignant tumours.

CORRELATION OF B-MODE ULTRASONOGRAPHIC FEATURES WITH HPE:
- Of the total cases, 50 (87.71%) were benign and 7 (12.28%) were malignant on HPE.
- Of the three bilateral cases, 2 were benign (66.66%) and 1 was malignant (33.33%).
- Among 54 unilateral cases, 48 were benign (88.88%) and 6 (11.11%) were malignant.
CORRELATION OF MORPHOLOGICAL APPEARANCE WITH HPE:

1. Predominantly cystic were 43(75.43%) of which,
   a. Benign were 43(100%).
   b. Malignant were 0.
2. Complex or mixed were 10(17.54%) of which,
   a. Benign were 7(70%).
   b. Malignant were 3(30%).
3. Predominantly solid were 4(7.01%) of which all were malignant (100%).

| Morphology | Number | Percentage |
|------------|--------|------------|
| Cystic     | Benign | 43         | 100%       |
|            | Malignant | 0         | 0%          |
| Solid      | Benign | 0         | 0%          |
|            | Malignant | 4         | 100%        |
| Complex    | Benign | 4         | 70%         |
|            | Malignant | 3         | 30%         |

Table 1

CORRELATION OF HPE WITH COLOUR (AND POWER) DOPPLER: The number of benign neoplasms that showed neovascularity was 21, out of 50 benign tumours (42%).

The number of benign neoplasms that showed neovascularisation amongst tumours 27 showing neovascularisation was 21 (77.77%)

The vascularity pattern among the benign ovarian neoplasms was:

1. In purely cystic lesions.
   a. Septal in 2(9.52%).
   b. Peripheral in 16(76.19%).

2. In mixed lesions.
   a. Mural 1(4.76%).
   b. Septal 1(4.76%).
   c. Mural & Central 1(4.76%)

   • The number of malignant neoplasms among tumours that showed neovascularisation was 6, amongst of a total of 27(22.22%).
   • The number of malignant neoplasms that showed neovascularisation amongst a total number of malignant tumours was 6 out 7(83.33%).
   • The vascularity pattern among the malignant ovarian neoplasms was
     a. In solid tumours.
        1. Central in 2(33.33%).
        2. Peripheral and central in 1(16.66%).
     b. In mixed tumours.
        1. Mural and central vascularity in 3(50%).
The vascularity pattern among the malignant neoplasms was central in 5(83.33%) and central and peripheral in 1(16.66%).

The above findings indicate that mere presence of vascularity doesn’t help in differentiating malignant from benign ovarian tumours. However, malignant tumours have central vascularity and benign tumours haves superficial (Peripheral and septal vascularity).

| Tumor type | Morphology     | Vascularity         | No. | Percentage |
|------------|----------------|---------------------|-----|------------|
| Benign     | Cystic         | Peripheral          | 16  | 76.19%     |
|            |                | Septal              | 2   | 9.52%      |
|            | Mixed          | Mural               | 1   | 4.76%      |
|            |                | Septal              | 1   | 4.76%      |
|            |                | Mural & central     | 1   | 4.76%      |
| Malignant  | Mixed          | Mural & central     | 3   | 50%        |
|            | Solid          | Central             | 2   | 33.33%     |
|            |                | Central & Peripheral| 1   | 16.6%      |

Table 2

CORRELATION OF HPE WITH SPECTRAL DOPPLER: Following is the table of RI and PI in malignant and benign tumours.

| Tumour Type | PI < 0.8 | PI < 1 | PI < 0.8 | PI < 1 |
|-------------|----------|--------|----------|--------|
|             | No. | Sens  | Spec   | PPV   | NPV  | No. | Sens  | Spec   | PPV   | NPV  |
| Malignant   | 5   | 83.33%| 90.47% | 71.42%| 95%  | 6   | 100%  | 71.42% | 50%   | 50%  |
| Benign      | 2   |       |        |       |      | 6   | 100%  |        |      |      |

Table 3

- Out of the 6 malignant tumours, 5 have PI <0.8 and out of 21 benign tumours, 2 have PI <0.8.
- Percentage of malignant tumours with PI <0.8(83.33%).
- Percentage of benign tumours with PI <0.8(9.52%).
- Out of 6 malignant tumours all had PI <1 and out of 21 benign tumours 6 have PI <1.
- Percentage of malignant tumours with PI <1(100%).
- Percentage of benign tumours with PI <1(28.57%).

| Tumour Type | RI < 0.4 | RI < 0.6 |
|-------------|----------|---------|
|             | No. | Sens  | Spec   | PPV   | NPV  | No. | Sens  | Spec   | PPV   | NPV  |
| Malignant   | 2   | 33.33%| 90.47% | 50%   | 33.33%| 5   | 83.33%| 80.95% | 55.55%| 94.44%|
| Benign      | 2   |       |        |       |      | 4   |       |        |      |      |

Table 4
Out of 6 malignant tumours, 5 had RI <0.6 (83.33%).
Out of 21 benign tumours, 4 had RI <0.6 (19.04%).
Out of 6 malignant tumours, 2 had RI <0.4 (33.33%).
Out of 21 benign tumours, 2 had RI < 0.4 (9.52%).

Thus, the present study yielded fairly good specificity and sensitivity with PI and RI <0.8 and <0.6 respectively, despite some overlap in the values between benign and malignant ovarian tumours. When the data of present study was extrapolated using the criterion PI <1 and RI <0.4, 100% of malignant tumours and 28.57% of benign tumours showed PI <1, while only 33.33% of malignant tumours, 9.52% of benign tumours showed RI <0.4. Thus present data was rendered slightly more specific and less sensitive with RI <0.4 and slightly more sensitive and less specific with PI <1. Thus it is established that PI <0.8 and RI <0.6 as the better choice for the threshold values, in terms of optimizing the sensitivity and specificity.

VALUE OF B-MODE ULTRASOUND ALONE AND IN COMBINATION WITH DUPLEX DOPPLER IN DIFFERENTIATING BENIGN AND MALIGNANT NEOPLASMS:

| Method                                | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value |
|---------------------------------------|-------------|-------------|---------------------------|---------------------------|
| B-Mode Ultrasound                     | 85.7%       | 86%         | 46.15%                    | 97.72%                    |
| B-Mode with colour and spectral Doppler | 85.7%       | 96%         | 75%                       | 97.95%                    |

CA125 was estimated in 47 cases.
When a cut-off value for malignancy was taken above 30 U/ml, 13 cases had values above 30 U/ml, in which malignant tumours were 4.
Out of the 33 cases, 2 were malignant, with values less than 30 U/ml. one of them was Sertoli Leydig cell tumour and other was Mucinous cystadenocarcinoma, Sensitivity is 66.66%, Specificity is 78.04%, PPV is 38.46% and NPV is 97.05%.
If only postmenopausal women with a cut-off value 30 U/ml was taken, out of 13 tumours 4 had CA125 > 30 U/ml and 9 cases had CA125 < 30 U/ml. out of 4 cases with CA125 >30 U/ml, 3 cases were malignant and 1 was benign. All the 9 cases with CA125 < 30 U/ml are benign. Sensitivity is 100%, Specificity 90%, PPV is 75% and NPV is 90%. This correlated with the studies of RCOG Oct 2003 (5).

**DISCUSSION:** In any case of suspicious ovarian tumor differentiating whether it is benign or malignant pre-operatively is helpful in proper planning of management. Apart from age, family history, tumor markers, morphological examination of ovarian tumors by grey scale ultrasound can aid in differentiating benign from malignant ovarian tumors. Current evidence is that the combination of ovarian morphology and colour Doppler, ultrasound is best way of predicting the nature of ovarian tumors.(4,6)
CORELATION OF B-MODE WITH HPE: The present study group comprised of 57 patients with neoplastic ovarian masses with a mean age of 45.5 years. A morphological assessment was initially made by B-mode using the morphological criteria described earlier followed by Duplex Doppler analysis. Comparison of preoperative diagnosis based on morphology and final pathological diagnosis revealed a correct sonographic diagnosis in 49 (85.96%) of the 57 cases, which correlated with the study of Benacerraf et al (68%). In addition sonography correctly identified a benign condition in 43 of 44 cases (97.72%) and malignant in 6 out of 13 cases (46.15%). Sonography was frankly misleading in 8 cases (14.03%). These findings correlated with Benacerraf et al (15%). Benign tumours mistaken to malignancy on grey scale due to haemorrhage, organized mucin, in torsion (thin septae look thick), clots and endometriomas.

The identification of ovarian malignancy was correct in 6 out of 13 cases that were proven malignant (Sens 85.7%). The specificity for correctly diagnosing a malignant condition was 89.7%. The positive Predictive Value was 46.15% and the Negative Predictive Value for excluding malignancy was 97.72%.

These values correlated with the study of Benacerraf et al, Mukund Joshi, but did not correlate with the studies of Bromley et al, Stein et al, Sassone, and Depriest.

| Study            | Sensitivity | Specificity | PPV   | NPV   |
|------------------|-------------|-------------|-------|-------|
| Present          | 85.7        | 86          | 46.15 | 97.72 |
| Benacerraf et al | 80          | 87          | 73    | 91    |
| Bromley et al    | 91          | 52          |       |       |
| Stein et al      | 98          | 62          | 99    | 50    |
| Sassone          | 89.1        | 65          | 70    | 86.67 |
| Deutinger        | 88.9        | 50          | 61.54 | 83.3  |
| Mukund Joshi     | 88 to 100%  | 62 to 96%   |       |       |

Table 6

The morphological criteria for internal consistency correlated with the study of Carter et al, stacy et al, Obwegeser R et al.

Malignant tumours were more likely to have a solid or mixed pattern (100%) of the cases as correlated with the study by Carter et al. Similarly most of the benign tumours were cystic as given by Stacy et al, Obwegser R et al.

| Morphology | Percentage |
|------------|------------|
| Benign     |            |
| Cystic     | 100%       |
| Mixed      | 70%        |
| Solid      | -          |
| Malignant  |            |
| Cystic     | -          |
| Mixed      | 30%        |
| Solid      | 100%       |

Table 7
The presence of ascites was found in 6 cases, out of which 4 were proven malignant (66.66%). Thus, the presence of associated findings on B-mode sonography was highly suggestive of malignancy lesions as stated by Fleischer et al.

The other benign conditions showing minimal free fluid are due to torsion and pelvic congestion.

SUPPLEMENTARY VALUE OF COLOUR AND POWER DOPPLER:

Presence of Neovascularization: The incidence of neovascularization was higher in malignant tumours. 85.71% of the malignant tumours and 42% of benign tumours had neovascularisation, which correlated with the study of Sawicki et al.,(11) who had similar findings (malignant 98.6% and benign 74.5%) and with the study of Alcazzar et al.(10) (100% of malignant masses and 74.6% in benign masses). In our study, we noticed that most of the tumours that lacked blood flow were proved to be benign except for one malignant tumour. The benign tumours that lacked neovascularisation accounted for 58% of all benign tumours. These findings are in accordance with the study by Carter et al.(9,10) and Caruso et al.,(12) Taori et al.,(13) who found absent color flow more commonly in benign tumours.

Pattern of Neovascularisation: In benign tumours, peripheral and superficial (Mural, Mural and Septal) vascularity was found in 95.23% of the cases, which correlated with 82.7% found in the study by Sawicki et al.,(11) 88.6% in the study by J.L. Alcazar.(10)

In malignant tumours, central vascularity was found in 83.33% and central and peripheral in 16.6%. These observations coincided with J. L. Alcazar(10) (central in 90%), Sim Kurjak et al.,(14) Taori et al.,(13) where central vascularity was seen in majority of the cases. From the above discussion we conclude that the presence and pattern of neovascularisation also plays a significant and substantial role in differentiating benign from malignant lesions.

Spectral Doppler: It is known that malignant neoplasms offer lower resistance to blood flow, therefore the PI and RI values tend to be lower in malignant ovarian tumours. These indices cannot reliably differentiate between tumours because some benign tumours have flow patterns similar to that found in ovarian malignancies. For this reason pulse Doppler cannot be used as an independent indicator of malignancy but it may provide supplementary information useful for differentiating benign from malignant lesions.

The present study used a pre-established cutoff criterian of PI < 0.8 and RI < 0.6 as used by Carter et al,(9) and PI < 1 and RI < 0.4 by Stein et al,(8) and Kurjak et al.(15) The calculated PI and RI were lower in patients with malignant tumours compared with those of benign tumours. Malignant PI 0.69 + 0.129; Malignant RI 0.40 + 0.138; benign PI 1.28 + 0.489; Benign RI 0.62 + 0.25. (The standard error of difference between two means is 0.03 for PI. The actual difference between two means is 0.5841, which is more than twice the standard error between means, therefore statistically significant. The standard error of difference between two means is 0.074 for RI the actual difference between two means is 0.215 so which is more than twice the standard error between means, therefore significant) (SPM Park 19th Edition Page No. 704).
The sensitivity and specificity in our study correlated with that of KB Taori 31.

| PI < 1 | Spec                  | PPV | NPV     | Sens       | Spec       | PPV       | NPV     |
|--------|-----------------------|-----|---------|------------|------------|-----------|---------|
| 100%   | 71.42%                | 50% | 100%    | 100%       | 85%        | 86.95%    | 100%    |
| PI < 0.8 | 83.33%            | 90.47% | 71.42% | 95%       | 96.29%     | 93.94%    | 94.07%  | 96.20% |
| RI < 0.6 | 83.33%            | 80.95% | 55.55% | 94.44%    | 92.59%     | 90.91%    | 91.06%  | 92.46% |
| RI < 0.4 | 33.33%            | 90.47% | 50%    | 33.33%    | 29.62%     | 85%       | 29.62%  | 58.69% |

Table 8

When the data of present study was explored using the criteria PI <1 and RI <0.4 proposed by Kurjak et al (15) and Jean Noel Buy et al, 100% of malignant tumours and 28.57% of benign tumours showed PI <1, while only 33.33% malignant tumours and 9.52% benign tumours showed RI <0.4%. Though Kurjak et al used cut-off criteria of PI <1 and RI <0.4 and achieved high sensitivity score, it was in post-menopausal women. Present study comprised all groups of women. Thus present data was rendered slightly more specific and less sensitive with RI <0.4 and slightly more sensitive and less specific with PI <1, thus established that PI <0.8 and RI <0.6 as the better choice for the threshold values, in terms of optimizing sensitivity and specificity. The present study yielded fairly good specificity and sensitivity with PI and RI <0.8 and <0.6 respectively, despite some overlap in the values between benign and malignant lesions.

**ROLE OF B-MODE IN COMBINATION WITH COLOUR DOPPLER AND SPECTRAL ANALYSIS:** Comparison of pre-surgical sonographic diagnosis based on B-mode with Duplex sonography and final pathological diagnosis revealed a correct diagnosis in 54 out of 57 cases (94.73%). In addition, B-mode with Duplex Doppler sonography correctly identified a benign condition in 48 out of 49 cases (97.95%) and malignant in 6 out of 7 cases (85.7%). When compared to B-mode alone, the addition of Doppler increased the specificity in diagnosing malignant tumours. This correlated with the studies of Caruso et al, (12) Leeners et al, (16) Fleisher et al, Taori et al, (13) Singh Uma, Anuradha Khanna. (17)

Using B-mode with Duplex Doppler sonography, the identification of ovarian malignancy was correct in 6 of the 7 cases that were proven malignant (Sensitivity 85.7%). The specificity for correctly diagnosing a malignant was 96%. The positive predictive value of sonographic diagnosis of ovarian malignancy was 75% and negative predictive value for excluding malignancy was 97.95%.

**SUMMARY:** The purpose of the study was to evaluate prospectively the relative usefulness of grey scale sonography, color/power Doppler and spectral Doppler in differentiating benign from malignant ovarian tumors.

After B-mode sonography, a conventional color/power Doppler was performed before pulsed Doppler evaluation.
A total of 57 cases were classified prospectively as suggestive of benign or malignant tumors on basis of grey scale morphology, presence and pattern of neovascularisation and spectral Doppler findings.

On grey scale analysis 6 out of 13 (46.15%), tumors characterised as malignant were proven malignant, while 43 of 44 (97.2%) tumors characterized as benign were proven benign. Therefore grey scale was found reliable in tumor differentiation.

When internal consistency was analysed tumors having a solid or mixed pattern were likely to be malignant, while predominantly cystic were almost always benign.

Presence of internal color flow was found to be a helpful adjunct of prediction of malignancy, while lack of vascularization favoured benignity.

Pattern of neovascularization was also helpful with superficial and peripheral vascularity favouring benignity and central vascularity in malignant tumors.

The calculated PI and RI values were lower with malignant tumors compared with benign tumors (Mean PI 0.69+0.489 and mean RI 0.40+0.138) for malignant tumors, (Mean PI 1.28+0.489 and mean RI 0.62+0.25), which was statistically significant, because the actual difference between two means is more than twice the standard error between two means. Spectral Doppler analysis with PI and RI with cut – off values <0.8 and <0.6, yielded fairly good specificity and sensitivity, despite some overlap in the values between benign and malignant lesions. When B-mode ultrasonography in combination with colour and spectral Doppler was used, it increased the specificity and positive predictive value is establishing the pre-operative diagnosis of ovarian tumors in terms of benign or malignant CA 125 levels were not of much value when taken in general in all age groups for prediction of malignancy, but they were very much predictive of malignancy in post – menopausal group.

Triaging the post – menopausal women by risk of malignancy index, helps in proper management of cases as per RCOG guidelines (Whether can be managed by a gynaecologist, in a cancer unit or a cancer centre).

**CONCLUSIONS:** From our study we concluded that, B-mode ultrasonographic assessment of morphological features and associated features was found to be useful in predicting benignity or malignancy of ovarian neoplasms pre-operatively. The presence and pattern of neovascularisation was helpful in differentiation of ovarian masses. The PI, RI indices, when taken as cut – off values as <1 and <0.4, had either high sensitivity or high specificity but not both. But when cut – off values for PI and RI were taken as <0.8 and <0.6, both had good sensitivity and specificity, despite some overlap between benign or malignant ovarian tumors. The present study established a multi – fold increase in the specificity and positive predictive value in establishing the pre-operative diagnosis of ovarian masses, especially in terms of benignity and malignancy, when using B-mode ultrasonography in combination with colour and spectral Doppler as compared to B-mode ultrasound alone. CA 125 levels and triaging post – menopausal women according to RMI was helpful in predicting high risk cases preoperatively. The combination of age, family history, clinical history, Gynaecological examination, tumor markers, morphological examination by B-mode and Duplex Doppler examination helps us in differentiating between benign and malignant ovarian tumors pre operatively.
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