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Original Research Article

A STUDY ON ULTRASOUND AND COLOUR DOPPLER IN OVARIAN MASSES AND ITS CORRELATION WITH CA-125

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Abstract

Background: To study the spectrum and sonographic patterns of ovarian masses in female patients presented at our centre and to correlate the findings of ovarian masses on gray scale imaging and colour Doppler study with the CA-125 in the same cases. **Materials and Methods:** The present study was conducted at the department of Radio-diagnosis, Mata Gujri Memorial Medical College And Lions Seva Kendra Hospital, Kishanganj, Bihar between December 2020 to November 2022. Out of 98 patients who presented with adnexal masses, 60 patients were found to be eligible for the study based upon the selection criteria. **Result:** Out of the selected 60 patients, 33 (55%) patients were found to have benign disease after final (histopathological) diagnosis while other 27 (45%) patients had malignant disease. Malignant tumours were more common in 41-60 yrs age group as well as in 20-40 yrs age group. On USG of ovarian tumour, most of the predominantly cystic lesions were benign (90%) white most of predominantly solid lesions were malignant (76.19%). Mixed tumours were almost equally distributed among benign & malignant. Cystadenoma was the most common benigntumour. Haemorrhagic corpus luteal cyst & endometrioma were other common tumours. Cystadenocarcinoma was the most common malignanttumour and was also the most common single histopathology of all the ovarian tumours. Tumour with Serum Ca 125value less than 35 U/ml were interpreted as benign while those with serum CA125 value more than 35U/ml were interpreted as malignant. **Conclusion:** The present study demonstrate significant increase in the sensitivity, specificity, positive predictive value and negative predictive value in establishing the preoperative diagnosis of ovarian masses in terms of benign and malignant nature, when using the B mode USG in combination with colour and spectral Doppler as compared to B mode USG alone.Although there is some overlap between the USG appearance of both benign and malignant ovarian masses, certain USG features are helpful in differentiating between the two. Adding serum CA125 to the gray scale and colour Doppler findings further increases the sensitivity and negative predictive value.

INTRODUCTION

Among all the gynaecologic cancers, ovarian malignancies represent the greatest clinical challenge. Although majority of the ovarian masses are benign, malignancy is always a possibility. Ovarian cancer is the fifth leading cause of cancer death in women, the second most commonly diagnosed gynaecological malignancy but the leading cause of death from these malignancies.

Gray scale USG is a non-invasive, cheaper, easily available and omnipresent modality. According to Sutton's text book of radiology, it is advocated as the first investigation to start with. Transabdominal USG, transvaginal USG, or both should be performed for the evaluation of adnexal masses. It does not only determine the organ of origin of pelvic mass but also suggest nature of the mass, its extra-ovarian spread, its operability, and amount of free intra-peritoneal fluid.

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Colour Doppler studies have provided new dimensions in ovarian tumour diagnosis. This is based on "Folkman's theory of neovascularisation" according to which tumour cells elaborate tumour angiogenesis factor (TAF) that promote neovascularisation and is mitogenic to endothelial cells as well. Although 92% of malignant tumours show blood flow, it is the absence of blood flow which is more important that suggest benign nature of the tumour.

In such scenario, present study has been done to compare the results of gray scale and colour Doppler imaging with that of CA-125. It is also be probed that whether CA-125 study along with USG and Colour Doppler study may constitute and provide a good screening strategy in establishing an early and definite diagnosis of ovarian malignancy.

MATERIALS AND METHODS

The present study was conducted at the department of Radiodiagnosis, Mata Gujri Memorial Medical College And Lions Seva Kendra Hospital, Kishanganj, Bihar between December 2020 to November 2022. This comparative study was carried out on patients, referred to our department from various other departments of our hospital and from outside, for the diagnostic evaluation of a clinically suspected or palpable adnexal mass with symptoms suggestive of ovarian tumour like pain, irregular cycles & fullness of abdomen or incidentally detected ovarian mass. Before enrolment, informed consent was taken from each subject. According to a fixed protocol, each patient was undergone a detailed history, clinical examination and lab investigations including Sr. CA 125 followed by Ultrasonography, Colour Doppler. Histopathological diagnosis following surgery obtained as gold standard. Results of USG, USG and Colour Doppler, Sr. CA-125 were compared with the histopathological diagnosis and with each other.

Selection of cases and exclusion criteria:

All patients with adnexal masses of an extra-ovarian origin, determined during any stage of diagnosis, were excluded from the study. Also, patients with anechoic unilocular cyst in ovary that resolved or reduced substantially in follow up USG were not taken in the study. Apart from these, any patients who did not undergo anyone of the diagnostic tests in the decided protocol, or died in between the study or did not completed the study, or did not undergone surgery and histopathological examination or lost in follow up or did not given consent, were not considered for the study.

Ultrasonography:

Real time B –mode ultrasonography was carried out on agray scale imaging unit (GE Healthcare Voluson S10 Ultrasound system & GE Healthcare Voluson P8 Ultrasound System) having colour Doppler and TVS probe facility.

Transabdominal sonography (TAS) of pelvis and upper abdomen was done with 3.5 MHz curved transducer in supine position, and transvaginal examination with a wide band 5 to 9 MHz intracavitary transducer in dorsal position with an empty bladder. Evaluation was limited to transabdominal sonography of pelvis in three virginal patients and 15 other patients who refused transvaginal sonography (TVS). Moreover, transabdominal sonography was helpful in patients with large masses when the maximum field of view for transvaginal transducer was exceeded.

Gray scale findings were evaluated under various headings i.e. Size, Consistency, Septation, Papillary projections/Mural nodules, Laterality, and associated ascites.

- Masses assigned as malignant tumour included those that were complex cystic with solid mural nodules, complex cystic with thick septations, or predominantly solid with few cystic areas.
- Masses that considered as benign were completely cystic with no internal echoes, cystic with thin smooth septation(<3mm) or complex cystic with internal echoes compatible with hemorrhagic cysts, endometrioma,or cystic teratoma.

Colour Doppler

Following the morphologic assessment of tumour by gray scale imaging, colour flow Doppler studies were performed. Colour Doppler parameters were standardized, and for all the subjects, the same presets were used for acquisition. The study was done at high sensitivity settings and lowest pulse repetition frequency possible, without aliasing.

The parameters which were used in this study included blood flow and vascularity(present or absent), blood flow location(central or peripheral), Resistance index(RI),Peak systolic velocity(PSV),Pulsatility index(PI)and Diastolic notch.Vessels detected on colour Doppler studies were evaluated further with spectral Doppler imaging.When present, internal vessels were evaluated in preference to peripheral vessels.PI and RI were calculated and the lowest values were recorded when a reproducible series of waveforms was obtained.The masses were classified as suggestive of malignancy when the lowest calculated PIwas less than 1 or lowest RI was less than 0.4.

Serum CA 125

Peripheral venous samples were obtained to measure Serum CA 125 by radioimmune assay in each subject before surgery. A level greater than 35U/ml was considered abnormal.

Histopathology

The histology of surgically removed ovarian tissues was the final endpoint of the study.

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RESULTS

Out of the selected 60 patients, 33 (55%) patients were found to have benign disease after final (histopathological) diagnosis while other 27 (45%) patients had malignant disease. [Table 1]

Table 1: Distribution of ovarian masses after (Final (Histopathological) diagnosis)

Type of mass	No. of cases	Percentage distribution
Benign	33	55%
Malignant	27	45%
Total	60	100%

Table 2: Age distribution of cases with ovarian tumour.

Age group (Yrs)	No. of cases	Benign	Malignant
Up to 20	03	02	1
21 – 40	19	9	10
41 – 60	31	19	12
> 60	7	3	4
Total	60	33	27

The maximum no. of cases was found in the age group 40-60 yrs and minimum in up to 20 year age group. The youngest patient was of 16 years. Malignant tumours were more common in 41-60 yrs age group as well as in 20-40 yrs age group.

Table 3: Distribution of presenting sides

Laterality	Benign	Malignant
Rt.	18	10
Lt.	15	14
B/L	0	3
Distribution of tumours according to size		
< 10 cm	27 (81.82%)	07 (25.93%)
> 10 cm	6 (18.18%)	20 (74.07%)
Association of ascites with ovarian tumour on USG studies		
Present	09	21
Absent	24	06
Ovarian tumours according to their margin on USG study		
Well defined	28 (84.84%)	9 (33.34%)
Ill defined	05 (15.16%)	18 (66.66%)
Ovarian tumours according to their internal consistency on USG study		
Predominantly cystic	20 (90%)	02 (10%)
Predominantly solid	5 (24%)	16 (76%)
Mixed (both solid & cystic)	08 (47%)	09 (53%)

Tumours were almost equally distributed on either side. All three cases of B/L tumours were of malignant pathology. Most of the malignant tumours (74.07%) were more than 10 cm in diameter while most of the benign tumours (81.82%) were less than 10 cm in diameter. Few cystadenomas& dermoid cysts(3 each) were larger than 10 cm. Ascites was present in half of the patient of ovarian tumour and most of the patient with ascites (70%) had malignancy. 84.84% of benign tumours had well margin while 66.66% of malignant tumours had ill defined margin. Out of 6 dermoid cyst, 3 (50%) had ill defined margin. On USG of ovarian tumour, most of the predominantly cystic lesions were benign (90%) white most of predominantly solid lesions were malignant (76.19%). Mixed tumours were almost equally distributed among benign & malignant.

Table 4: Distribution of ovarian tumours showing neovascularity

Type of lesion	Presence of neovascularity	Absence of neovascularity
Benign	14 (42.24%)	19 (57.76%)
Malignant	25 (22.59%)	2 (7.11%)

92.59% malignant tumours were showing neovascularityon colour Doppler while only 42.24% of benign tumours were showing neovascularity.

Table 5: Characterization of solid ovarian tumour according to vessel location

Solid tumour type	No. of solid tumour	Vessel location	
		Central	Peripheral
Benign	4	1 (25%)	3 (75%)
Malignant	17	13 (76.47%)	4 (23.53%)

Most of benign solid tumours (75%) had peripheral vascularity whereas most of the malignant solid tumours (76.47%) had central vascularity. Mixed lesions with both cystic & solid component had equal propensity of septal and mural vascularity in both benign & malignant ovarian tumours.

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Table 6: Distribution of tumours with neovascularity according to their peak systolic velocity

Tumour type	No. of vasculartumour	Peak systolic velocity	
		Low (<15cm/sec)	High (>15cm/sec)
Benign	14	12 (85.72%)	2 (14.28%)
Malignant	25	3 (12%)	22 (88%)

Most of benign solid tumours (85.72%) had peak systolic velocity less than 15cm/sec while most of malignant tumours (88%) had high (>15cm/sec) peak systolic velocity.

Table 7: Distribution of ovarian tumours with neovascularity, according to their Pulsatility index (PI)

Solid tumour type	No. Of tumour showing neovascularity	Pulsatility index(PI)		
		PI<0.8	PI=8-10	P>1.0
Benign	14	02	03	09
Malignant	25	24	01	0

All of the malignant tumours showing neovascularity, had pulsatility index <1.00 while most of the benign tumors showing neovascularity, had pulsatility index >1.00.

Table 8: Mean & range of Pulsatility index (PI) in benign & malignant ovarian tumours with neovascularity.

Tumour type	Mean	Range
Benign	1.09	0.6 – 1.5
Malignant	0.62	0.5 – 0.9

Table 9: Distribution of ovarian tumours with neovascularity, according to their Resistive Index (RI)

Solid tumour type	No. of tumour	Resistitive index		
		RI<0.4	RI=0.4-0.6	RI>0.6
Benign	14	0	03	11
Malignant	25	08	17	0

Most of the benign vasculartumours had RI>0.6 while none of had RI<0.4. In comparison most of the malignant vasculartumours had a Resistive Index <0.6.

Table 10: Distribution of ovarian tumours with neovascularity according to presence or absence of diastolic notch

Tumour type	No. of vascular tumour	Diastolic present	Notch absent
Benign	14	12 (86%)	02 (14%)
Malignant	25	03 (12%)	22 (85%)

Most of the benign tumour shown presence of diastolic notch while most of the malignant tumour shown its absence.

Table 11: Comparing diagnostic result of B mode USG alone and in combination with colour and spectral Doppler in differentiating benign & malignant ovarian tumour

Tumour type	Diagnosis on histopathology	Diagnosis on B Mode USG alone	Diagnosis on B mode USG &colour and spectral Doppler combination
Benign	33	25	31
Malignant	27	14	22
Total	60	39	53

31 out of 33 benign tumours and 22 out of 27 malignant tumours were correctly diagnosed by the combination of B mode USG and colour and spectral Doppler as benign & malignancy respectively.

Table 12: Relative sensitivity, specificity, positive predictive value and negative predictive value of B mode USG alone and in combination with colour Doppler & spectral Doppler in differentiating benign and malignant ovarian tumour

Diagnostic modality	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
B mode USG alone	51.85	75.75	63.63	65.78	65.00
B mode USG + colour & spectral Doppler	81.48	93.93	91.66	86.11	88.33

On adding colour& spectral Doppler to the B mode USG, each diagnostic indexincreases significantly (pvalue <0.05).

Table 13: Distribution of various benign ovarian tumour on histopathology

Tumour histology	No. of cases	Percentage
Cystadenoma	9	15.00
Haemorragic corpus luteum cyst	8	13.33
Endometrioma	7	11.66
Dermoid cyst	6	10.00

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Fibroma	3	5.00
Total	33	55.00

Cystadenoma was the most common benigntumour. Haemorrhagic corpus luteal cyst & endometrioma were other common tumours.

Table 14: Distribution of various malignant tumour on histopathology

Tumour histology	No. of cases	Percentage
Cystadenocarcinoma	19	31.66
Endometroid adenocarcinoma	01	1.66
Clear cell carcinoma	01	1.66
Sertolicell- leydig cell tumour	01	1.66
Dysgerminoma	01	1.66
Metastases	04	6.60
Total	27	45

Cystadenocarcinoma was the most common malignanttumour and was also the most common single histopathology of all the ovarian tumours.

Table 15: Comparing the diagnostic result of the combination of B mode USG and spectral Doppler with Serum Ca 125 interpretation in ovarian tumours.

Tumour type	Histopathological diagnosis	Diagnosis on B mode USG, colour & Spectral Doppler	Sr. CA 125 interpretation
Benign	33	31	26
Malignant	27	22	21

Tumour with Serum Ca 125value less than 35 U/ml were interpreted as benign while those with serum CA125 value more than 35U/ml were interpreted as malignant

Table 16: Relative sensitivity, specificity, positive predictive value and negative predictive value and accuracy of the combination of B mode USG and colour& spectral Doppler study and Sr. CA 125 estimation

Diagnostic modality	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
B mode USG + colour& spectral Doppler study	81.48	93.93	91.66	86.11	88.33
Sr. Ca 125	77.78	78.78	75.00	81.25	78.33

All the diagnostic indexes of the combination of B mode USG &colour Doppler study were superior to that of Serum Ca 125 estimation alone and this was statistically significant. (p value <0.05)

However, two False positive cases on USG &Colour Doppler study which were actually benign (one Teratoma & one Haemorrhagic corpus luteum cyst each) were correctly interpreted as benign with Sr. Ca 125 estimation thus when considered a modality in diagnosis of ovarian tumour along with USG &colour and spectral Doppler study, Sr. Ca 125 estimation checks the False positive cases and consequently improves specificity & positive predictive value of USG and colour Doppler study.

DISCUSSION

In the current study, total 60 subjects with ovarian masses were evaluated, in which 33(55%) were benign lesions and 27(45%) were malignant. In a study of 170 adnexal masses Stein et al, (1995) reported majority (123) as benign (72.35%) and 47 as malignant (27.64%).[1] In a similar study by Lerner et al, (1994) majority (88%) of ovarian masses were benign ones; with malignancy occurred in only a few cases.[2]

In the current study subjects falling in different age groups were also evaluated. The age of the patients age was ranged between 12 to 85 years with maximum patients were between51 to 60. Mean age for the benign tumours was 40.81years while it was 44.66years in malignant tumours. 72.7 %(24) of benign tumours and 74.07% (20) of malignant tumours were over 40 years.

In the current study, among 28 patients of cystic or mixed solid with cystic benign tumours, only3(10.7 %) had thick septations, on the other hand as many as 7 (63.6 %) such malignant tumours (11) had thick septations. In a study of 101 patients with adnexal masses, Mousavi et al,(2006) found thick septations were present in 20.8% and 92.5% of cases in benign and malignant ovarian tumours, respectively.[3] Meire et al,(1978) also found that multicystictumour with thick septa carry an increase chance of malignancy.[4] However Granberg S et al,(1989) reported that thickness of septa do not correlate with malignancy.[5]

In the current study, papillary projection is present in 21.4 %of patient in benign tumours, whereas malignant ovarian tumours contain papillary projection in 81.8 % cases. Presence of papillary projection on the cyst wall had been claimed to be related to incidence of malignancy. Granberg et al, (1989) in their study reported 93% of tumours that had papillary projection on their cyst wall, were malignant.[5]

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Presence of ascites usually indicates that the tumour has extended beyond its capsule and implanted on peritoneal, diaphragmatic or omental surfaces. Ascites was present in 77.8% and 27.3% of malignant and benign tumours, respectively in the current study and this was comparable to previous study by Mousavi et al,(2006) ascitis was present in 8.3%of benign tumours and 64.2% of malignant tumours.[3]

Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of gray scale ultrasound in detecting malignancy in ovarian masses in the current study was calculated to be 51.85%, 75.75%, 63.63%, 65.78% and 65% respectively.

In the reported literature so far, in the evaluation of ovarian masses with Gray scale ultrasound, wide variations in diagnostic values have been noted Sassone et al, (1991),[6] primarily due to intra observer variations, variability in patient and cohort groups (parity and menopause status) and manner of evaluation (trans abdominal vs trans vaginal) Coleman et al (1988).[7]

Pulsatility index forms an important criterion in colour Doppler study. Malignant neoplasm offered lower resistance to blood flow due to presence of aberrant tumour vessels. In the present study, a pre established cut off criteria of PI < 1.00 and RI < 0.4 was used, as used by Kurjak et al,(1990) though Carter et al, (1994) used a cut off criteria of PI < 0.8 and RI < 0.6 to optimize the study in terms of sensitivity and specificity.[8,9] In the present study,92.59 %(25) malignant tumours had PI < 1.00 in contrast to 15.15% (05) benign tumours. On the other hand, 29.62 % malignant tumours and none of the benign tumours showed RI < 0.4. When the data of present study was extrapolated using the criteria of PI < 0.8 and RI < 0.6 as proposed by Carter et al, (1994), 88.89% (24) malignant tumours had PI < 0.8 in contrast to only 6.06 % (2) benign tumours. Similarly, 92.59 % (25) malignant tumours showed RI < 0.6 in contrast to only 9.09% (3) benign tumours.

In the present study, the prediction of benignity of tumour was more reliable with B mode USG combined with colour Doppler and spectral Doppler as only 6.06% of benign tumours were incorrectly diagnosed in contrast to 18.51% of malignant tumour. Two benign lesions which were incorrectly diagnosed as malignant were dermoid cyst and hemorrhagic corpus luteum cyst which show false positivity ofcolour Doppler finding in these lesions and decrease the sensitivity and specificity of colour Doppler in premenopausal age group. These features correlate well with the results of Stein et al, (1995).[1]

The present study showed the significant increase in the sensitivity, specificity, positive predictive value and negative predictive value in establishing the preoperative diagnosis of adnexal masses/ ovarian masses especially in term of benign and malignant; when using B mode USG in combination with colour and spectral Doppler as compared to B mode USG alone and it is in harmony with other studies Buy et al,(1996) and Taori et al,(2002).[10,11] This isalso supported in a recent multicenter European study, performed as a collaborative work at 3 European university departments of Obstetrics and Gynaecology; a total of 826 complex pelvic mases on which TVS and colour Doppler sonography was performed; they concluded that colour Doppler evaluation was more accurate in the diagnosis of adnexal malignancies in comparison with gray scale sonography, because of significantly higher specificity(0.94 versus 0.84;P<0.01) Guerrieo et al (2001).[12]

By combining gray scale and colour Doppler finding, present study was able to distinguish between benign and malignant tumours with a sensitivity of 81.48%, specificity of 93.93%. Positive predictive value of 91% and negative predictive value of 86.11%. Carter et al,(1994) too, reported the similar results(sensitivity 83% and specificity 95%,positive predictive value of 91% and negative predictive value of 90%.) as in the current study.[9] However, current study was unable to reproduce the extraordinary results published by Kurjak et al, (1992) as they found colour Doppler sensitivity of 97.3% and specificity of 100%.[13] However, in the studies of Weiner et al,(1992) and Chou et al,(1994), colour Doppler added limited or no value in comparison with adnexal morphology evaluation ,or that it slightly increased the specificity of gray scale imaging.[14,15]

Mousavi et al,(2006) in their study of 101 patients with adnexal masses ,found average CA125 level in benign tumours was 29.52 U/ml, whereas in malignant tumours had an average CA- 125 level of 3741 U/ml.[3] In this study, a serum value of below 35 Unit/ml was taken as a benign representation while value above this considered as malignant. When serum CA 125 level evaluated as a sole diagnostic method taking reference value of more than 35 U as malignant, in the current study its sensitivity, specificity, positive predictive value and negative predictive value in differentiating malignant from benign ovarian tumour was 77%,78.78%,75.00%,81.25%, respectively. This was significantly less than that of gray scale combined with colour Doppler results. This was in harmony with the study by Van Calster et al, (2007)who concluded that Pattern recognition was superior to serum CA 125 for discrimination between benign and malignant adnexal masses.[16]

In current study, serum CA 125 was elevated in 90.47% of epithelial ovarian malignancy. This was comparable to the study of Hossain et al, (2010) who reported tumour marker CA 125 is elevated in 80-85% of patients with epithelial ovarian cancer with levels over 35U/ml suggestive of malignancy.[17]

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CONCLUSION

The present study demonstrate significant increase in the sensitivity, specificity, positive predictive value and negative predictive value in establishing the preoperative diagnosis of ovarian masses in terms of benign and malignant nature, when using the B mode USG in combination with colourandspectral Doppler as compared to B mode USG alone.Although there is some overlap between the USG appearance of both benign and malignant ovarian masses, certain USG features are helpful in differentiating between the two. Featuressuggestive of malignancy on gray scale includeill defined, large, solid masses with thick septations and papillary projections.On colour Doppler study central neovascularity, PSV>15cm/sec, PI<1, RI<0.4 and absent diastolic notch favor malignancy.In combination, these features may lead to a diagnosis of malignancy or may provide a clue for a suspicious malignant mass that need further investigations. Adding serum CA125 to the gray scale and colour Doppler findings further increases the sensitivity and negative predictive value.

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