



### Original Research Article

## Ultrasound Criteria and CA-125 for Evaluation of Adenexal Masses in Developing Countries

Authors

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### Abstract

**Objectives:** Ovarian malignancy being one of the most common among genital malignancy, ascendant importance has to be given to evaluate it pre-operatively with high degree of precision. It is of crowning importance because it helps to tailor neo-adjuvant chemotherapy, chemoradiation, radiotherapy and surgery. This study correlates between the clinical and HPE findings to prove that though USG helps in detection and characterization of adnexal lesion to some extent, its diagnostic ability is further improved by addition of a simple parameter CA-125.

**Methods:** This study is a prospective observational study carried out between January 1, 2016 to 30 June, 2017 in the department of Obs and Gynae, RHP, Patiala. All cases of ovarian masses who underwent USG and CA-125 & were followed with laparotomy, followed by HPE of the specimen, were included in the study.

**Results:** 55 patients were included in the evaluation. The specificity 86% of USG was enhanced to 88% on addition of CA-125 to the study. The specificity increased further to 94% when clinical examination, USG and CA-125 were combined. Sensitivity was 100% with all the three methods.

**Conclusion:** Optimal pre-operative evaluation was achieved with USG. But when combined with clinical features & CA-125, the diagnostic value is extremely high. This aids in planning the management.

**Keywords:** Adenexal masses, Ultrasound, CA-125.

### Introduction

Ovarian masses are common forms of neoplasm in women and form some of the most challenging cases in gynaecology. Ovarian tumours that present in the reproductive age group are mostly benign while about 30% in the postmenopausal

age group are malignant<sup>[1]</sup>. Ovarian tumours also present in a wide spectrum of histopathological patterns. Many ovarian tumors are asymptomatic in the early stages and are unfortunately diagnosed in the advanced stage. The high mortality rate of ovarian cancer is due to its late detection, thus

earning itself the term “Silent Killer”<sup>[2]</sup>. Tumor markers also help in identification of ovarian masses. Adjunctive diagnostic techniques like MRI and CT help further in identifying metastasis of the tumor. Recent statistics in developed countries report better survival rates in patients with ovarian tumours; this being due to early detection and early appropriate treatment<sup>[3]</sup>. Pelvic assessment, tumour markers, and radiological investigations have been proposed in this regard, but all of the parameters when considered separately, are inadequately sensitive or specific. Various combined methods of evaluating ovarian mass have also been proposed. Risk of malignancy index (RMI) is a combined parameter which is simple, practical and highly sensitive, and more specific. RMI is calculated with a simplified regression equation obtained from the product of menopausal status score (M), ultrasonographic score (U), and absolute value of serum CA-125<sup>[4-6]</sup>. Inflammatory diseases or chronic ectopic also mimics adnexal masses, so this study aims to know the accuracy of clinical features combined with USG and CA-125. There is no doubt to the fact that CT and MRI are better modalities to diagnose ovarian masses but in developing countries with limited diagnostic facilities and funds to use CT and MRI, CA-125 serves as a cheap, quick and efficient way to aid in the diagnosis of ovarian tumors.

### Methods

It is a prospective observational study conducted from January 1, 2016 to 30 June, 2017 on a total of 55 patients in the department of Obs and Gynae, RHP, Patiala. Patients in whom ovarian mass was detected during pelvic examination and USG and patients with symptoms of low abdominal pain, dyspepsia, palpable mass, menstrual irregularities and infertility as well as asymptomatic patients who had ovarian masses on USG, were included in this study.

A detailed gynaecological, obstetric and medical history of each patient was taken. A detailed systemic and pelvic examination was done. USG

and CA-125 evaluation of all ovarian masses was done. The mass was predicted as benign or malignant according to the following criteria. The ovarian mass is considered malignant if it has ill-defined border, with ascites, with mixed echogenicity, multiloculated with thick septations and solid components. The mass is considered benign if it is a unilocular cyst which is clear with well defined borders, homogenous echoes, thin septations and no ascites. If one or more malignant features were present in presence of benign features, the mass is classified as malignant. If one or more benign feature is present in absence of malignant features it is benign. If both are present or both are not present, it is inconclusive. After all necessary lab investigations and thorough evaluation, all patients were subjected to surgery. Removal of uterus and ovary depends on the age and fertility requirements of the patient. All specimens were subjected to HPE and were correlated with pre-operative clinical and USG findings and CA-125 values. Analysis was performed, sensitivity, specificity, positive and negative predictive values were calculated.

### Results

In the present study, 38(69.09%) patients presented with abdominal complaints and 7 (12.73%) patients had menstrual irregularity out of which 1(1.82%) presented with postmenopausal bleeding. One (1.82%) patient had infertility. One (1.82%) patient had discharge p/v. Five (9.09%) patients presented with mass abdomen and 2(3.64%) patients were asymptomatic. Sensitivity and specificity in diagnosing the characteristics of ovarian tumours is good clinically but diagnostic accuracy increased when USG along with CA-125 is combined. USG and CA-125 can be used even by a basic examiner to differentiate between benign and malignant tumours which helps us in tailoring further management. Our study of 55 patients with ovarian masses showed various observations. According to clinical features malignancy was

suspected in 15 (27.27%) cases whereas in 40 (72.73%), benign pathology was observed. On the basis of USG 12 (21.82%) cases had malignant pathology and 43(78.19%) found to have benign features. When CA-125 was taken into consideration 15(27.27%) cases were suspected to have malignancy 40(72.73%) cases were again found to be benign. When collectively USG and CA-125 were seen we found 11(20.00%) cases to be malignant and 44 (80.00%) cases with benign pathology. When clinical features, USG, CA-125- all the three parameters together were taken into consideration, 8 (14.55%) were malignant and 47(85.45%) were benign. After laparotomy for ovarian masses we found HPE report as follows, 5 cases of malignant ovarian pathology, 25 with benign ovarian tumours and 25 cases showed other ovarian pathologies as shown in table below. The specificity of 86% with the USG was observed. On addition of CA-125 to the USG, the specificity increased to 88%. After considering all the three parameters of clinical features, USG, & CA-125 in the study the specificity was enhanced to 94%. The sensitivity by all the parameters remained 100%.

**Table No. 1** HPE of 55 women with adenexal masses

Nature of disease	HPE	N	%
Benign	Serous cystadenoma	15	27.27
	Mucinous cystadenoma	5	9.09
	Granulosa cell tumour	5	9.09
Malignant	Mucinous cystadenocarcinoma with	1	1.82

	serous cyst adenoma		
	Serous cyst adenocarcinoma	2	3.64
	Serous papillary cystadenocarcinoma High grade	1	1.82
	Proliferative mucinous tumor with microinvasion	1	1.82
Others	Endometriotic cyst	4	7.27
	Corpus luteal cyst	2	3.64
	Follicular cyst	2	3.64
	Dermoid cyst	5	9.09
	Chronic ectopic	4	7.27
	Endometrioid cyst	1	1.82
	Hemorrhagic cyst	2	3.64
	Fibroid	1	1.82
	Fibroma	1	1.82
	Chronic non specific infections	3	5.45

**Table No. 2** Clinical characteristics of 55 women with adenexal masses

S.No	Clinical features	No.	Percentage
1	Abdominal complaints (postmeal distension loss of appetite, lower abdominal pain)	38	69.09%
2.	Post menopausal bleeding	1	1.82%
3.	Menstrual complaints (including PMB)	7	12.73%
4	Infertility	1	1.82%
5.	PA mass/ lumps	5	9.09%
6.	DPV	1	1.82%
9	No complaint	2	3.64%

**Table No. 3** Distribution according to age

Age group (years)	Benign%	Malignant	Total
<25	9 16.36%	0 0.00%	9 16.36%
25-35	17 30.91%	0 0.00%	17 30.91%
36-45	10 18.18%	2 3.64%	12 21.82%
46-55	8 14.55%	3 5.46%	11 20.01%
56-65	3 5.45%	0 0.00%	3 5.45%
>65	3 5.45%	0 0.00%	3 5.45%
<b>Total</b>	<b>50 90.90%</b>	<b>5 9.10%</b>	<b>55 100%</b>

**Table No. 4** Diagnostic performance of the Criteria evaluated

	Malignant	Malignant	Non-malignant	Non-malignant	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
	No.	Percentage	No.	percentage				
Clinical Features	15	27.27	40	72.73	100	80	33.33	100
USG	12	21.82	43	78.18	100	86	41.67	100
CA125	15	27.27	40	72.73	100	80	33.33	100
USG+ CA125	11	20.00	44	80.00	100	88	45.55	100
Clinical Features+USG+CA125	8	14.55	47	85.45	100	94	62.50	100

**Discussion**

Proper pre-operative description of benign and malignant nature of ovarian mass is the need of the hour. Lack of screening methods is the very

factor that renders the prognosis of ovarian cancers worst among all gynaecological cancers. In our study among ovarian masses, 90.90% were benign and 9.10% were malignant. In the study by

GG Swamy and N Satyanarayana 71.6% were benign, 25% were malignant and 3% were borderline tumours<sup>[7]</sup>. similar to data from western countries where 75-80% tumour were benign<sup>[8]</sup> and also in studies carried out in India by Pilli et al<sup>[9]</sup> and Gupta et al<sup>[10]</sup> which showed approximately similar results of benign ovarian tumours 75.2% and 72.9% respectively. However this figure was only 59.2% in Ahmed et al<sup>[11]</sup> study in Pakistan.

In our study incidence of malignant tumours was 9.10% and all were in the age group of 36-55 years and out of these 60% (3/5 cases) were in the age group of 46-55 years.

There were significant differences of percentage among women with benign or malignant tumours. These findings are in accordance to epidemiological data, which show that the incidence of malignant ovarian carcinomas is higher in older, postmenopausal women<sup>[12,13]</sup>. When analyzing the contribution of age to ovarian tumour discrimination, along with the final ultrasound classification and CA-125 measurement, we noted that age did contribute to diagnostic accuracy.

According to our study out of 15/55 cases CA-125 was >35unit/ml, 10 came out to be benign on HPE providing a specificity of 80% only which was same as for clinical features only (80%).

Differentiating benign from early malignant ovarian disease is important and provides a diagnostic challenge. The combination of pelvic mass and elevated level CA-125 arouses suspicion of a gynaecological malignancy, but other conditions should always be considered in the differential diagnosis, especially in a pre menopausal female. Malkasion<sup>[14]</sup> studied 59 patients with histologically proven benign ovarian cysts. Out of these patients 17 had elevated concentrations of CA-125 (12 > 35 units/ml, 4 > 65 units/ml and 1 > 2000 units/ml). In another study by Dixia<sup>[15]</sup> using 153 patients with benign pelvic masses, 10 patients had CA-125 concentrations >188 units/ml and one patient had a value of more than 400 units/ml. Nolen et al screened 65 biomarkers in patients with adnexal masses and more than half of the biomarkers

differed significantly between benign and malignant masses. CA-125 and HE4 in combination provided the highest discrimination between benign and malignant cases<sup>[16]</sup>. Our study is in concordance with these studies which demonstrate that using CA-125 in isolation has a limited value in differentiating benign from malignant pelvic masses. The patient characteristics and radiological information provides crucial additional information on which to base a diagnosis.

In our study USG provided a specificity of 86% as compared to C/F (80%) and CA-125(80%).

Review of literature from 1990 to 2006 which included 143 studies showed that Ultrasound findings were similar to CT and MRI in differentiation of benign from malignant ovarian masses<sup>[17]</sup>. Currently newer imaging in the form of Positron emission tomography (PET) and CT can be used to judge the extent of the disease and also differentiate between malignant and benign masses<sup>[18]</sup>. As it is evident from above studies all the modalities are complimentary to each other with ultrasound remaining the first diagnostic modality as it is cheap and widely available in all units. Further assessment of the spread of disease can either be made by CT or MRI and PET scanning where facilities exist.

In the present study, USG alone showed 100% sensitivity and 86% specificity and when combined with CA-125, sensitivity was 100% and specificity increased to 88%. When clinical features, USG and CA-125 combined, specificity increased to 94%. Thus according to the present result, use of combined clinical examination with USG and CA-125 is recommended strongly to differentiate between benign and malignant ovarian tumours. According to C.A. Hartman et al<sup>[19]</sup> The majority of tumours were correctly classified using ultrasound criteria. CA-125 alone performed worse than did ultrasound in discriminating malignant from benign adnexal tumours. CA-125 measurement contributed to the diagnosis of malignancy, improving overall specificity, only in sonographically malignant tumours.<sup>[19]</sup>

## Conclusion

Sensitivity and specificity in diagnosing the characteristics of ovarian tumours is good clinically but diagnostic accuracy increased when USG along with CA-125 is combined with clinical examination. So clinical examination, USG and CA-125 can be used even by a basic examiner to differentiate between benign and malignant tumours which helps us in tailoring further management.

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