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Radiological Imaging and CA125 Correlation as Predictive Variables in Ovarian Pathologies

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Introduction: Primary Ovary Neoplasms are the most frequent tumors showing epithelial differentiation. Tumour Marker CA-125, glycoprotein synthesized mainly by neoplastic cells with epithelial differentiation. Serum Level of CA-125 has a biological potential of these lesions. This study is mainly done to evaluate the association between serum CA-125 levels and imaging findings and to predict malignancy in various ovarian lesions.
Objectives: To evaluate the capacity of CA125 and Imaging findings to predict malignancy in various ovarian pathologies.
Materials and Methods: Study area: Department of Radiology, Saveetha Medical College and Hospital, Chennai, Study design: Retrospective study.
Study period: 6months.
Study population: Patients with history and clinical symptoms of ovarian lesions and USG detected ovarian lesions confirmed on Radiological Imaging.
Sampling method: Purposive sampling Sample size: 30.

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Inclusion criteria: Patients with clinically suspected ovarian lesions or indeterminate ovarian lesions on USG who underwent Radiological imaging and CA-125 estimation.
Exclusion criteria: Children less than 12years of age are excluded from this study.
Results: Among 30 cases, 19(63.33%) were benign and 2(6.67%) were borderline and 9(30%) were malignant lesion in the present study. Ovarian pathologies is mostly seen in women of age above 25 yrs(86.67%). In this study Ovarian lesions are more commonly seen in married women(86.67%) and menstruating women(56.67%). Out of 30 Cases, Serum CA-125 level <35IU/ml is seen among 13(43.33%) and level >35IU/ml is seen among 17(56.67%). Out of 17 women with CA-125 level >35IU/ml, 9 had malignant lesions on histopathology while 7 women had benign lesions and 1 women had borderline lesion.
Conclusion: The present study shows significant association of Serum CA-125 levels with mixed solid cystic ovarian lesions ill defined margins (possible Malignant Ovarian lesions) ($p<0.05$) especially in Post-menopausal women.

Keywords: CA-125; ovarian lesions; cystadenoma; cystadenocarcinoma; epithelial neoplasm; serous; mucinous.

1. INTRODUCTION

Primary Ovarian Tumors have a wide range of clinical and histopathological presentations. Primary Ovary Neoplasms are the most frequent tumors showing epithelial differentiation. They can be benign or malignant. Among the malignant epithelial ovarian tumors, Serous cystadenocarcinoma is the most common histological subtype, confirmed in advanced stage of the disease in 75% of Indian population. Tumour Marker CA-125, is a glycoprotein synthesized mainly by neoplastic cells with epithelial differentiation. Serum Level of CA 125 has a role in predicting the biological potential of these lesions.

The Risk of developing Ovarian Cancer is more common in highly industrialized countries [1]. Notably Older women are at high risk. Half of deaths from ovarian cancer occurs in women between age 55 and 74years and one quarter of deaths occurs in women of age group between 35 and 54years [2]. 93% of cases with ovarian cancer, CA-125 levels correlated well with the burden of the tumor. When CA-125 levels were less than 35U/ml it was estimated to be normal [3,4]. It has been suggested as a established prognostic marker for advanced stages of ovarian cancer. Serum CA-125 is marker commonly used both in diagnosis and management of epithelial tumors of ovary.

Elevated CA-125 levels have been reported even in some other malignant conditions like breast cancer, leiomyoma, gastric cancer, leiomyosarcoma of gastrointestinal origin, Non-Hodgkin lymphoma. Even non neoplastic conditions like endometriosis, Congestive heart failure, Pregnancy, Ovulatory cycles, liver diseases as well as tuberculosis shows elevated CA-125 levels [5].

Thus the aim of this study is mainly done to evaluate the association between serum CA-125 levels radiological cross sectional imaging and to predict malignancy in various ovarian lesions.

2. METHODOLOGY

The present Retrospective study was conducted over a period of 6 months from January 2020-June 2020 in the Department of Radiology, Saveetha Medical College and Hospital, Chennai. The information of the patient was collected through pre-designed proforma. After getting clearance from the institutional ethical committee the study was carried out. Total 30 cases were obtained over a period of 6 months which met the inclusion and exclusion criteria.

Patients with clinically suspected ovarian lesions or indeterminate ovarian lesions on sonographic screening who underwent cross sectional Radiological imaging and CA-125 estimation were included.

Magnetic Resonance Imaging with and without i.v contrast (Inj. Gadovist 10 mg bolus) were performed using PHILIPS MULTIVA 1.5 TESLA MRI. The Magnetic Resonance Imaging protocol, were planned using a 3 Plane Localizer, including routine institutional pelvis protocol(T1W, T2W Sagittal, T2W Coronal, T1W, T2W Axial, GRE, T2 SPAIR Axial, MFFE, VISTA, coronal DWI with ADC) and Computed Tomographic evaluation both plain and I.v contrast (Inj. Iohexol 1.2 mg/kg at rate of 3.5 ml/sec) imaging was performed using Philips Ingenuity 128 Slice CT scanner with axial section Acquisition, Reconstruction with 1 mm slice thickness and Multi-planar reformation.

All contrast studies were performed after confirming normal renal function by serum creatinine, BUN and eGFR estimation.

Serum CA 125 levels were obtained using Vitros 5600 Integrated fully automated Analyzer by Chemiluminescence Immunoassay. The results were expressed in U/mL.

Children less than 12years of age were excluded from this study as they don't form the population demogaphic for epithelial ovarian lesions.

Preoperative serum levels of CA-125 were obtained from all patients. Statistical analysis was performed using SPSS Software. Other Statistical analysis like Chi-Square test and fisher's exact test has used now for comparison of data & p-value <0.05 was considered as significant.

3. RESULTS

In the present study among 30 cases, 19(63.33%) were benign and 2(6.67%) were borderline and 9(30%) were malignant lesion. Ovarian pathologies is mostly seen in women of age above 25yrs (86.67%). In this study Ovarian lesions are more commonly seen in married women (86.67%) and menstruating women (56.67%) (Table 1).

Out of 30 Cases, Serum CA-125 level <35IU/ml is seen among 13(43.33%) and level >35IU/ml is seen among 17(56.67%). Out of 17 women with CA-125 level >35IU/ml, 9 had malignant lesions on histopathology while 7 women had benign lesions and 1 women had borderline lesion (Table 2).

Based on the nature, Solid comprises of 4(13.33%), Mixed comprises of 12(40%), Cystic comprises of 14(46.67%) (Table 3).

Based on the margins, Well defined margin is seen among 20(66.67%) and Undefined margin is seen among 10(33.33%) (Table 4).

Histopathological findings and distribution of ovarian mass were categorised as benign,borderline, malignant. Among malignant cases majority of the cases were Serous Cystadenocarcinoma(55.56%) followed by Mucinous Cystadenocarcinoma(22.22%) and Immature teratoma(22.22%). Among all benign lesions, Benign Serous Cystadenoma and Mucinous Cystadenoma(36.84%) showed equal frequency in this study. Likewise Fibroma and Mature teratoma(10.53%) showed equal frequency in this study. Borderline cases constitute only 2 cases, which include Borderline serous tumor and Teratoma with borderline epithelial tumour (Table 5).

Table 1. Sociodemographic data

Components	Malignant potential						total (n=30)		Chi-squ are value	P-value
	Benign		Borderline		Malignant					
	n=19	%	n=2	%	n=9	%	n=30	%		
Age										
<25yrs	4	21.05%	0	0	0	0	4	13.33%	2.67	0.26
>25yrs	15	78.95%	2	100%	9	100%	26	86.67%		
Marital Status										
Married	15	78.95%	2	100%	9	100%	26	86.67%	2.67	0.26
Unmarried	4	21.05%	0	0	0	0	4	13.33%		
Menopauals Tatus										
Menstruating	14	73.68%	0	0	3	33.33%	17	56.67%	6.85	0.03
Post-Menopausal	5	26.32%	2	100%	6	66.67%	13	43.33%		

Table 2. Correlation between malignant potential and Serum CA-125 Value

Malignant Potential	Serum CA-125(U/ml)				Total (n=30)	
	<35		>35			
	n=13	%	n=17	%	n=30	%
Benign	12	92.31%	7	41.18%	19	63.33%
Borderline	1	7.69%	1	5.88%	2	6.67%
Malignant	0	0	9	52.94%	9	30%

Chi-Square Value= 9.95: P-Value=0.007

Table 3. Correlation between malignant potential and nature of tumour

Contents	Malignant Potential						Total	
	Benign		Borderline		Malignant		n=30	%
	n=19	%	n= 2	%	n=9	%		
Solid	3	15.79%	0	0	1	11.11%	4	13.33%
Mixed	3	15.79%	2	100%	7	77.78%	12	40%
Cystic	13	68.42%	0	0	1	11.11%	14	46.67%

Chi-Square Value= 13.48: P-Value= 0.009

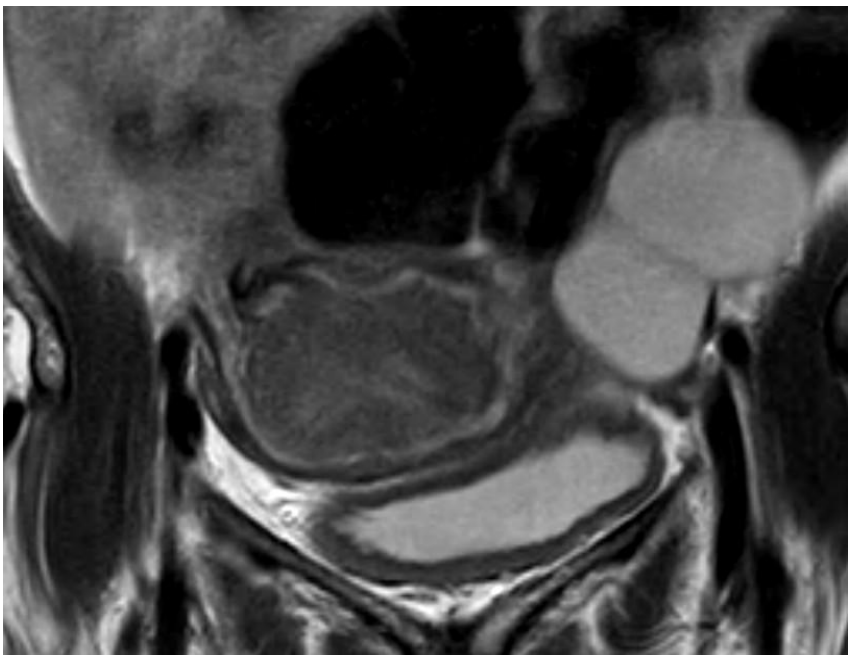
Table 4. Correlation between malignant potential and margins of the lesion

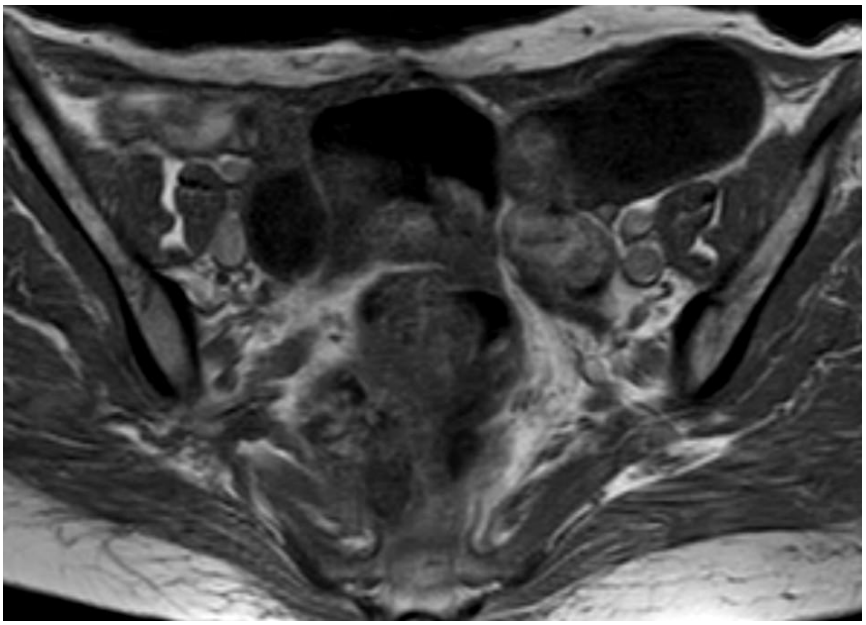
Margins	Malignant Potential						Total	
	Benign		Borderline		Malignant		n=30	%
	n=19	%	n=2	%	n=9	%		
Well defined	18	94.74%	1	50%	1	11.11%	20	66.67%
Undefined	1	5.26%	1	50%	8	88.89%	10	33.33%

Chi-Square Value=19.49: P-Value= 0.00006

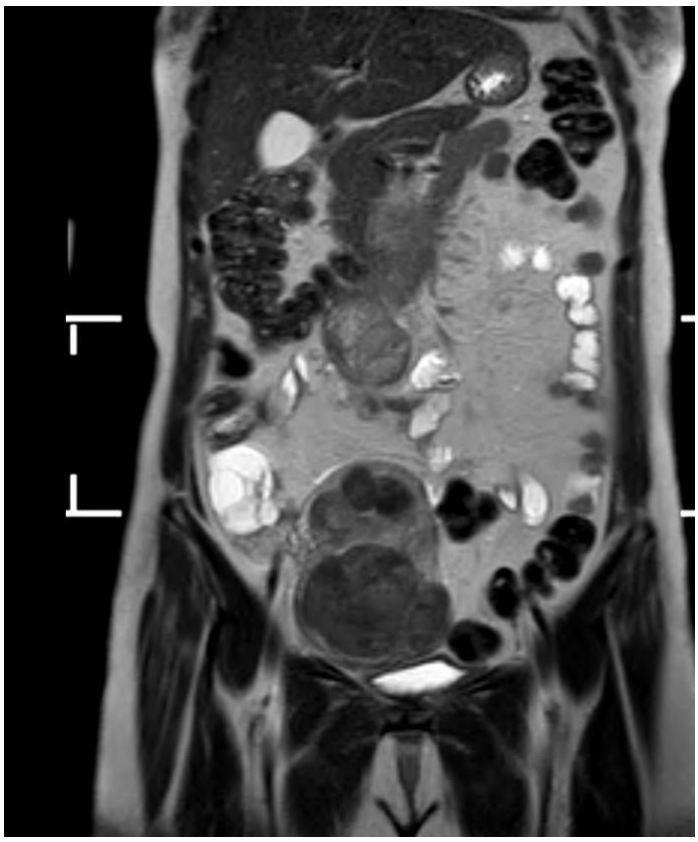
Table 5. Distribution of patients Serum CA-125 and histological findings of malignant potential

Histopathological Findings		Frequency	
		n	%
Benign (n=19)	Fibroma	2	10.53%
	Serous Cystadenoma	7	36.84%
	Mucinous Cystadenoma	7	36.84%
	Benign Cystic Lesion	1	5.26%
	Mature Teratoma	2	10.53%
Borderline (n=2)	Borderline serous tumour	1	50%
	Teratoma with borderline epithelial tumour	1	50%
Malignant (n=9)	Immature Teratoma	2	22.22%
	Mucinous Cystadenocarcinoma	2	22.22%
	Serous Cystadenocarcinoma	5	55.56%

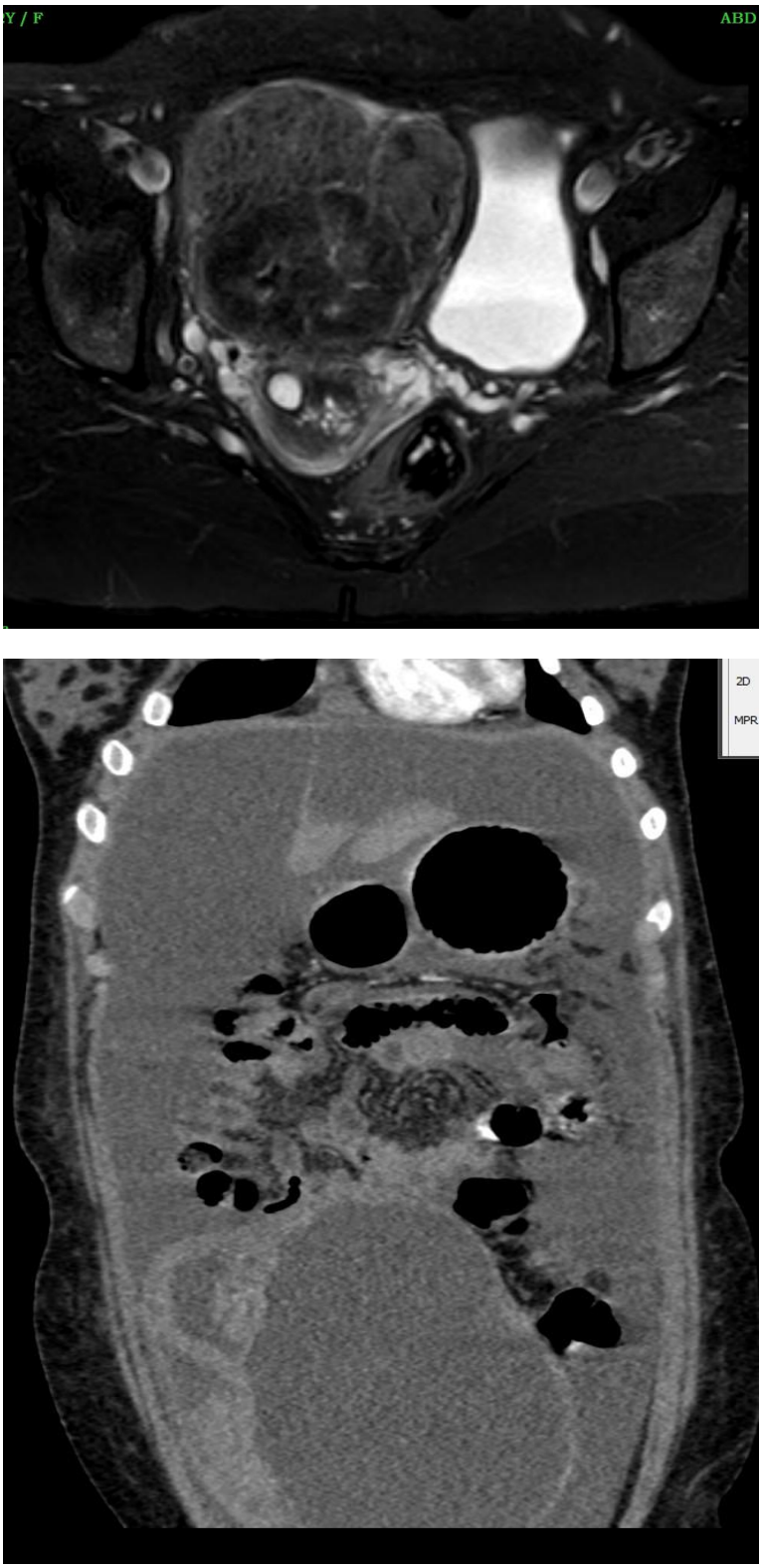




Focal cystic area T1 hypointense seen in the right adnexa (likely epicenter in ovary) central homogenous, peripheral smooth thin margin. T1 Focal bi-loculated hypointense cystic lesion in left adnexa (likely epicenter in ovary) central thin septation



Case 2. T2 – Two Focal moderate heterogenous enhancing iso to mild hypo intense lesions (iso to myometrium) seen in the anterior wall myometrium (fundus), central heterogeneous (likely areas of necrosis), peripheral smooth margins



Case 3. Well defined pelvico-abdominal round to oval shaped intra-peritoneal solid-cystic lesion, predominantly cystic in the supra-pubic, right iliac and umbilical regions of abdomen with severe ascites – Malignant (Complex right ovarian cyst)

4. DISCUSSION

Tumours of mesothelial origin and Epithelial ovarian neoplasms express Carbohydrate antigen–125 which is a high molecular-weight glycoprotein. Besides this, CA -125, glycoprotein is also found in normal tissues which is derived from coelomic epithelium such as pericardium, peritoneum, pleura, endometrium and Fallopian tubes and therefore the levels are raised in benign and malignant conditions which engages these tissues [6].

Some other researches have also shown that levels of Soluble CA-125 are elevated in numerous other malignant conditions such as breast cancer, mesothelioma, Non- Hodgkin lymphoma, leiomyoma, Gastric Cancer and leiomyosarcoma of gastrointestinal origin. Even few benign conditions such as ovulatory cycles, pregnancy, endometriosis, liver diseases and congestive heart failure, infectious condition such as tuberculosis also reveal raised CA-125 levels [5].

Benign epithelial features:

- Component could be – entirely cystic
- Thin wall thickness (< 3 mm)
- No internal components
- No ascites

Borderline:

- Bilateral
- Profuse papillary projections present
- Looks like aggressive but no ascites/ peritoneal metastases

Malignant epithelial features:

- Component : Large soft tissue mass lesion with necrotic areas
- Thick wall thickness
- Evidence of papillary projections
- Peritoneal ascites / adenopathy with implants – represent invasion

In the present study, Out of 30 Cases, Ovarian lesions is mostly seen in women of age above 25yrs(86.67%) which is similar to the study conducted by Dr. Jasbir Kaur Saluja et al. [7] reported in which ovarian lesions mostly seen in age above 25yrs(80%). In the present study Out of 30 cases, Ovarian lesions showed 46.67% cystic lesion while 40% showed mixed lesion followed by 13.33% solid lesions. In the study conducted by Priya et al. [8] reported solid mass only 2.7%, 32.8% mixed mass and 64.5% cystic mass. Another study done by Manoja V et al. [9] also reported 4.2% solid, 24.2% mixed and 71.6% cystic masses in their study.

In the present study out of 30 cases, there was 63.33% benign cases on the basis of histological findings in which Benign Serous Cystadenoma and Mucinous Cystadenoma(36.84%) showed equal frequency.

Among 30 cases, there were 30% malignant lesions among which most common was Serous Cystadenocarcinoma(55.56%) followed by Mucinous Cystadenocarcinoma(22.22%) and Immature teratoma(22.22%).

Borderline cases constitute only 2 case, which include Borderline Serous tumor and Teratoma with borderline epithelial tumour. In the study conducted by Nalini et al. [10] study for 141 tumors, 83.01% were benign, 4.9% were borderline and 12.1% were malignant. The most common benign lesion reported in order as Serous cystadenoma 39.7% and then Mucinous cystadenoma 32.6% in previous studies. Out of the total malignant cases 12.1%, Serous Cystadenocarcinoma(9.22%) was the most common followed by Mucinous Cystadenocarcinoma and one case of endometrioid carcinoma and one case of clear cell carcinoma.

Malignant tumour was more common in postmenopausal women than benign tumour. Out of 30 cases, 9 cases were malignant lesions in which 6(66.67%) were postmenopausal and 3(33.33%) were menstruating. In the benign group, out of 19 patients 5(26.32%) were postmenopausal and 14(73.68%) premenopausal women. This findings is similar with the study conducted by Dr. Sukla Nath et al. [11].

In this study 56.67% of patients with ovarian lesions presented with high CA125 levels of greater than 35 IU/ml. Out of these 52.94% were malignant. In the study conducted by Anurag Prakash et al. [12] report says 76.9% of patients with ovarian lesions presented with high CA125 levels of > 35 IU/ml, 65.4% were malignant.

There was a significant association between malignant potential and Serum CA-125($p<0.05$). This is similar to the study done by Anurag Prakash et al. [13] who also found there is a

significant association between malignant potential and Serum CA-125($p<0.05$). In this study there is a significant association between Post-menopausal women and malignant potential ($p<0.05$).

Even there is significant association between mixed lesion with malignancy($p<0.05$) and significant association between undefined margins and malignancy($p<0.05$). So the result of present study suggests that tumour marker CA-125, seems to be the important biomarker for predicting the Ovarian lesions in these patients.

5. CONCLUSION

To conclude, among 30 cases, 19(63.33%) were benign and 2(6.67%) were borderline and 9(30%) were malignant lesion in the present study. Ovarian pathologies is mostly seen in women of age above 25yrs(86.67%). In this study Ovarian lesions are more commonly seen in married women(86.67%) and menstruating women(56.67%).

Out of 30 Cases, Serum CA-125 level <35IU/ml is seen among 13(43.33%) and level >35IU/ml is seen among 17(56.67%). Out of 17 women with CA-125 level >35IU/ml, 9 had malignant lesions on histopathology while 7 women had benign lesions and 1 women had borderline lesion. So to conclude, the present study shows significant association of Post-menopausal women, Serum CA-125 levels, Mixed lesions, Undefined margins with Malignant Ovarian lesions($p<0.05$).

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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