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# CA125 and Ovarian Neoplasm, do they Tally in the Rally: Study in Eastern India

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**ABSTRACT**
Cancer antigen 125 (CA125), a transmembrane glycoprotein detectable and measurable in the blood is found on most malignant ovarian cells. Although it may be a good indicator of ovarian tumors, it is raised in physiologic and non-malignant conditions. CA125 is still superior and popular to other novel biomarkers in detecting ovarian tumors and an indicator of response to treatment. In this study, various histological types of ovarian neoplasm were evaluated histopathologically along with their respective pre-operative CA 125 level. All female patients presented with pelvic mass and raised CA125 levels posted for surgery, were included in the study. 122 cases were examined. The data was recorded and appropriate statistical analysis plan was applied. Majority of the patients belonged to 41-50 years of age group. Serous cystadenoma constituted major proportions (28.7%). Of the 77 women with normal CA-125 level, 98.7% had benign neoplasm. 45 women had raised CA-125, of which 17.8%, 37.8% and 44.4% had benign, borderline and malignant neoplasm respectively. Hence concluding, pre-operative high levels are usually related to clinically advanced ovarian neoplasm, thus helping in stratification of ovarian neoplasm thereby planning the further treatment course.

## INTRODUCTION

Cancer antigen 125 (CA 125), a transmembrane glycoprotein, is a major component of mucus lining surface of viscera like peritoneum, pleura, pericardium and ovaries[1]. It is coded by the homonymous MUC16 gene[2]. CA 125 is a thoroughly studied and validated biomarker in epithelial ovarian malignancies and is a well acknowledged marker for follow up. However, CA 125 has clinical limitations. It is raised in benign conditions like endometriosis, pelvic inflammatory conditions, normal physiological menstruation, pregnancy period, peritonitis and previous abdominal surgery[2-4]. CA 125 levels are often used to assess treatment response in patients diagnosed with epithelial ovarian malignancy. CA 125 level of =35 U/ml is a useful preoperative test for predicting the benign or malignant nature of pelvic masses. The accuracy of CA 125 in the diagnosis of ovarian tumors is high and very important in helping the specialist plan the surgery[5].

The approaches used for the evaluation of women with suspected adnexal masses are physical examination, ultrasound and determination of serum CA 125 levels[6]. CA 125 is an antigenic determinant of a high molecular-weight glycoprotein recognized by a monoclonal antibody. This is expressed by epithelial ovarian tumors as well as by other tissues of Müllerian origin (peritoneum, pleura, and pericardium). A CA 125 level =35 U/ml is considered to indicate suspected malignancy[7]. Despite the identification of numerous new biomarkers, CA125 is still superior to the majority of novel biomarkers in postmenopausal women. In addition to its role as a diagnostic marker for recurrent ovarian cancer, CA125 is also used as an indicator of tumor burden and response to treatment.

**Objective:** In this study various histological types of ovarian neoplasm were evaluated along with their respective pre-operative CA 125 level so as to estimate the pattern of histopathological features with the rising titers of CA125, thereby helping in the decision making of treatment protocol.

## MATERIALS AND METHODS

An institutional-based descriptive type of study was conducted in the Department of Pathology in collaboration with the Department of Obstetrics and Gynecology for a period of 2 years. All female patients presented with pelvic mass and raised CA125 levels posted for surgery were included in the study. A total of 122 cases were examined after obtaining their informed consent along with the approval of the Institutional Ethics Committee. The specimen of the tissues was sent to the Department of Pathology with requisition forms encompassing patient particulars and relevant information. These specimens were histologically evaluated and correlated with their pre-operative serum CA 125 levels. The data were recorded and an appropriate statistical analysis plan was applied. Data were analyzed using SPSS version 22.0 (Statistical Product for Services Solutions).

## RESULTS AND DISCUSSIONS

A total of 122 patients were studied. The majority of the study population belonged to the 41-50 years of age group (34.4%). The mean age was 43.8±11.1 years (Table 1). In this study, 43.4% of subjects (majority) had tumor size of 5-10 cm (Table 2). 67.2% of the tumors (Table 3) were cystic in nature followed by solid-cystic and solid (20.5 and 12.3% respectively). The majority (68.9%) of the ovarian tumors were benign trailed by malignant tumors (16.3%). The remaining 14.8% were

**Table 1: Frequency Distribution Table Showing Distribution of Ovarian Neoplasm among Different Age Groups**

| Age Group (Years) | Frequency (n = 122) | Percentage |
|---|---|---|
| <30 | 12 | 9.8 |
| 30-40 | 36 | 29.5 |
| 41-50 | 42 | 34.4 |
| 51-60 | 27 | 22.1 |
| >60 | 5 | 4.1 |
| Total | 122 | 100.0 |

**Table 2: Frequency Distribution Table Showing Distribution of Ovarian Neoplasm According to Size of Tumour**

| Size of Tumor (IN CM) | Frequency (n=122) | Percentage |
|---|---|---|
| < 5 | 16 | 13.1 |
| 5-10 | 53 | 43.4 |
| 11-15 | 35 | 28.7 |
| 16-20 | 13 | 10.7 |
| 21-25 | 5 | 4.1 |
| Total | 122 | 100.0 |

**Table 3: Frequency Distribution Table Showing Distribution of Ovarian Neoplasm According to Gross Features of the Tumour**

| Gross Features | Frequency (n=122) | Percentage |
|---|---|---|
| Cystic | 82 | 67.2 |
| Solid | 15 | 12.3 |
| Solid-cystic | 25 | 20.5 |
| Total | 122 | 100.0 |

**Table 4: Frequency Distribution Table Showing Distribution of Ovarian Neoplasm According to Nature of the Tumour**

| Nature of Tumour | Frequency (n=122) | Percentage |
|---|---|---|
| Benign | 84 | 68.9 |
| Borderline | 18 | 14.8 |
| Malignant | 20 | 16.3 |
| Total | 122 | 100.0 |

**Table 5: Frequency Distribution Table Showing Distribution of Ovarian Neoplasm According to Histomorphological Types**

| Histomorphological Types | Frequency (n=122) | Percentage |
|---|---|---|
| Fibroma 6 | 5.0 | |
| Mature cystic Teratoma | 18 | 14.8 |
| Brenner tumor | 2 | 1.6 |
| Carcinosarcoma ovary | 1 | .8 |
| Clear cell carcinoma | 2 | 1.6 |
| Endometrioid carcinoma | 3 | 2.5 |
| Endometrioid cystadenoma | 4 | 3.3 |
| High grade serous carcinoma | 4 | 3.3 |
| Low grade serous carcinoma | 6 | 4.9 |
| Mucinious borderline tumor | 9 | 7.3 |
| Mucinous Carcinoma | 4 | 3.2 |
| Mucinous cystadeno fibroma | 2 | 1.6 |
| Mucinous cystadenoma | 13 | 10.7 |
| Serous borderline Tumor | 9 | 7.4 |
| Serous cyst adenofibroma | 2 | 1.6 |
| Serous cystadenoma | 35 | 28.7 |
| Thecoma | 2 | 1.6 |
| Total 122 | 100.0 | |

**Table 6: Frequency Distribution Table Showing Age Distribution of Major Histopathological Subtypes**

| | Major Histopathological Subtypes (%) | | | |
|---|---|---|---|---|
| A ge Group (in years) | Epithelial Tumours | Germ cell Tumours | Sex cord stromal tumours | Total (%) (n=122) |
| <30 | 7(58.3) | 5(41.7) | 0(0.0) | 12(100.0) |
| 30-40 | 25(69.4) | 11(30.6) | 0(0.0) | 36(100.0) |
| 41-50 | 37(88.1) | 2(4.8) | 3(7.1) | 42(100.0) |
| 51-60 | 25(92.6) | 0(0.0) | 2(7.4) | 27(100.0) |
| >60 | 2(40.0) | 0(0.0) | 3(60.0) | 5(100.0) |
| Total | 96(78.7) | 18(14.8) | 8(6.6) | 122(100.0) |

**Table 7: Tumour Marker (CA-125) and Ovarian Neoplasm**

| | Nature of Tumour (Frequency) | | | |
|---|---|---|---|---|
| CA-125 Level | Benign | Borderline | Malignant | Total (%)(n=122) |
| Normal | 76(98.7) | 1(1.3) | 0(0.0) | 77(100.0) |
| Raised | 8(17.8) | 17(37.8) | 20(44.4) | 45(100.0) |
| Total | 84(68.9) | 18(14.8) | 20(16.4) | 122(100.0) |

Pearson Chi-Square value=86.8, df=2, p=.000

**Table 8: Comparison of Age Group in this Study with Other Relevant Studies**

| Age Group | Present Study (%) | Kumari A, *et al.,* | Patel A.S. *et al.,* | Chandra K *et al.,* |
|---|---|---|---|---|
| <30 | 9.8 | 33.8 | 30.2 | 27.9 |
| 30-40 | 29.5 | 28 | 29.1 | 26.7 |
| 41-50 | 34.4 | 26.4 | 23.5 | 23.2 |
| 51-60 | 22.1 | 10.2 | 11.6 % | 12.7 |
| >60 | 4.1 | 1.4 | 3.1 | 9.1 |
| Total | 100.0 | 100.0 | 100 | 100 |

**Table 9: Comparison of Gross Features of Present Study with Other Studies**

| Gross Features | Current Study | Priyadarshika M *et al.,* | Patel A.S. *et al.,* | Thakkar N N *et al.,* | Jayadhar K *et al.,* |
|---|---|---|---|---|---|
| Cystic | 67.2 | 37.5 | 68.5% | 58.1 | 48 |
| Solid | 12.3 | 8.9 | 6.2% | 13.2 | 10 |
| Solid-cystic | 20.5 | 53.6 | 25.3 | 28.7 | 42 |

**Table 10: Histopathological Subtypes Comparision with Other Studies**

| Major Histopathological subtypes | Current study (%) | Thakkar NN *et al.,* | Patel A S *et al.,* | Pachori G *et al.,* | Jayadhar K *et al.,* |
|---|---|---|---|---|---|
| Surface Epithelial tumor | 78.7 | 73.8 | 77.7 | 65.2 | 72.35 |
| Germ cell tumor | 14.8 | 17.8 | 18.5 | 23.9 | 19.51 |
| Sex cord stromal tumor | 6.6 | 6.1 | 3.8 | 7.4 | 4.87 |

borderline in nature (Table 4). Serous cystadenoma (Table 5) constituted major proportions (28.7%) followed by Teratoma (14.8%) and Mucinous cystadenoma (10.7%). 92.6% of the epithelial tumors belonged to 51-60 years of age group (Table 6). 41.7% of the germ cell tumors were in <30 years of age group and 60% of the sex cord stromal tumors were in above 60 years of age group. 77 women with normal CA-125 level, of which 98.7% had benign neoplasm. 45 women had raised CA-125, of which 17.8, 37.8 and 44.4% had benign, borderline and malignant neoplasm respectively (Table 7). The differences between the groups were found to be statistically significant (p<.05). Ovaries are complex organs from which develop a wide range of neoplasms. Symptoms like pain abdomen, mass per abdomen, ascites, changes in menstrual pattern are persistent, should raise the suspicion of ovarian neoplasm and further evaluation and investigations should be done.

Identification of various histological patterns of ovarian tumors is important in diagnosis, prognosis and treatment of ovarian cancers. In this study 122 female patients were included and analysis of various histopathological types of ovarian neoplasms was done along with clinical and biochemical profile to help the clinician for planning the treatment modality. Ovarian tumors are prevalent in all age groups. The majority of the study subjects belonged to 30-60 years of age group. Mean age 43.8±11.1 years. These findings were similar to studies done by Kumari *et al*., Patel *et al*., Chandra *et al*.,[8,9,10](Table 8).

In present study majority of cases 43.4% of the study subjects had tumour size of 5-10 cm which is consistent with study by Priyadarshika M et al., where 73.2% of lesions were less than 10cm in size [11]. In the present study shows 67.2% of the tumour was cystic in nature followed by solid-cystic and solid (20.5% and 12.3% respectively). These findings were similar to the gross features of ovarian tumor in studies conducted by Priyadarshika *et al*., Patel *et al*., Thakkar NN ET and Jayadhar *et al*.,[9,11,12,13] (Table 9). In the present study 68.9% of the tumour were benign in nature followed by 16.3% of malignant tumors. Rest 14.8% belong to borderline in nature. Findings of study conducted by Deshmukh *et al*., were similar to present study[14]. In this study WHO classification was implemented to classify the tumors. Various studies including present study show surface epithelial ovarian tumors as the most common histological subtype encountered. Germ cell tumor had the prevalence of 14.8% in the present study, similar findings were noted in studies conducted by Thakkar *et al*., Patel *et al*., Pachori *et al* and Jayadhar *et al*.,[9,12,13,15] (Table 10).

CA125 is a useful test for ovarian cancer detection in primary care, particularly in women ≥50 years old. In current study majority of malignant tumor showed

raised CA-125(35 U/ml as normal) and was also elevated in 17% of benign tumors. The difference in levels of CA125 in benign and malignant tumors were statistically significant ($p<0.05$). Similar findings were observed in study by Agarwal *et al*.,[16]. Borderline ovarian epithelial tumors are noninvasive neoplasms which show intermediate behavior between benign cystadenomas and invasive carcinomas. The prevalence of borderline ovarian tumors was 14% which is similar to study by Deshmukh *et al*.,[14](14%). In the current study 44% patients with BOT were younger than 40 years which was higher than study by Nayyar *et al*.,[17](33%). There are no sonographic features strongly suggestive of borderline histology. Sonographic appearance ranges from unilocular cysts to solid-cystic. Out of 45 women with raised CA-125, proportion of people who had borderline tumor were 37.8% where as in study Kumari *et al*., by CA 125 was raised >35 U/ml in only 46 (61%) of ovarian tumor. Commonly seen BOT are usually serous and mucinous, in current study constitute approximately 40%. In study by Kumari *et al*., mucinous BOT were more common (48%) women followed by serous (46%). The diagnosis of these neoplasms is based upon histopathologic examination strictly. Borderline tumors have an excellent prognosis (stage I five-year survival is 99 percent). The risk of malignant transformation is unclear[17,18].

## CONCLUSION

So to conclude, pre-operative high levels of CA 125 are generally well related to clinically advanced ovarian neoplasm. Women belonging to 41-50 years of age group are at risk as per this study. The patients presenting with pelvic masses should routinely be evaluated for serum CA 125 levels, thus, helping in the risk stratification of ovarian neoplasm thereby planning the further treatment course.

**Ethics Statement:** This study was approved by the institutional review board. Informed consent was sought from each participating patient.

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