

# Positive Predictive Value of Ca125 in Diagnosis of Ovarian Tumors

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## ABSTRACT

**Objectives:** To determine the positive predictive value of CA125 for ovarian masses taking histopathology as gold standard.

**Methods:** 65 patients of all ages with adnexal masses were included in this study. This study was carried out in the department of pathology Fatima Jinnah medical college/ Sir Ganga Ram Hospital Lahore in six months period.

**Results:** Out of 65 patients, 43 patients presents with raised CA 125 levels. Out of these 43 patients 32 have serum CA 125 level between 35U/ml-200U/ml, 14 patients were confirmed to have malignant ovarian tumour and 18 have benign tumour. The positive predictive value is 44%. 11 patients have CA 125 level more than 200U/ml, 10 patients have malignant ovarian tumour and 1 patient was confirmed to have benign ovarian tumour on histopathology. The positive predictive value is 90%. So it is concluded that CA 125 is an important tumour marker to determine the nature of ovarian mass preoperatively as very high levels (more than 200 u/ml) are mostly found in ovarian carcinomas and it helps in further management plan.

## INTRODUCTION

Tumours of the ovary are common form of neoplasia in females<sup>1</sup>. They are the sixth most common female cancer and the fourth leading cause of death<sup>2</sup>. They arise from one of the three ovarian components (1) surface epithelium (2) germ cells (3) sex cords<sup>3</sup>. Of these different types, cancers of epithelial origin are the most common<sup>4</sup>, comprising 90% of all ovarian malignancies<sup>3</sup>.

Most ovarian cancers occur after menopause when the ovaries have no physiological role and consequently abnormal ovarian function causes no symptoms. As a result of this factor, combined with the anatomical location of the ovaries deep in the pelvis, ovarian cancers cause few symptoms until they reach a large size or have disseminated. Patient usually present with pelvic or abdominal pain<sup>5</sup>, increased abdominal size, abnormal vaginal bleeding, backache, nausea, indigestion, bloating<sup>6</sup>, frequency, urgency of urine<sup>7</sup>.

The risk of developing ovarian cancers appears to be affected by several factors. Risk increases with age, nulliparity, family history and genetic factors. Mutation in BRCA1 and BRCA2 increase susceptibility to ovarian cancers<sup>8</sup>. Use of combined oral contraceptives pills is a protective factor. Risk also reduces in women after tubal ligation<sup>9</sup>.

Ovarian cancer is diagnosed by pelvic examination, serum CA 125, ultrasound, and CT

scan but the diagnosis is confirmed by histopathology of a biopsy specimen<sup>4</sup>.

CA125 is used as tumour marker in ovarian cancer and it is raised in approximately 90% of patients with epithelial ovarian tumours. CA125 expression is influenced by the histologic subtype of the ovarian cancer. Mucinous and clear cell tumours exhibit less reactivity as compared to serous adenocarcinomas and low expression is seen in germ cell tumours<sup>8</sup>. The antigen is detected with monoclonal antibody OC 125 that is raised using an ovarian cancer cell line as an immunogen. The normal value of CA125 is >35U/ml<sup>10</sup>.

The purpose of this study is to access preoperatively the nature of the ovarian tumour either benign or malignant which will help in further management of the patient.

## MATERIAL AND METHODS

This study was conducted at the department of pathology Fatima Jinnah medical college/Sir Ganga Ram Hospital Lahore. Patients of all ages having ovarian masses were included in this study, while patients having confirmed diagnosis of endometriosis or with previous history of ovarian malignancy were excluded from the study. All specimens of ovarian masses referred to our department, meeting the inclusion criteria were included. All the cases were recorded for their

demographic features i.e., age etc. Their histopathology was done. The results of CA125 and histopathology were compared.

**RESULTS**

According to this study out of 65 patients, 43 patients present with raised CA 125 and 22 patients had normal CA 125 level (table 1), out of 43 patients who had raised CA125 level 32

patients had level between 35U/ml-200U/ml and 11 patients had serum level of CA 125 more than 200U/ml(table2).

Out of 32 patients who had CA 125 between 35U/ml-200U/ml 14 had malignant ovarian tumour and 18 had benign ovarian tumour on histopathology(table3). The positive predictive value is 44% which is calculated as under:

$$\text{Positive predictive value} = \frac{\text{True positive}}{\text{True positive} + \text{False positive}}$$

$$\text{Positive predictive value} = \frac{14}{14 + 18}$$

$$\text{Positive predictive value} = \frac{14}{32}$$

**Positive predictive value = 44%**

11 patients presents with CA 125 level more than 200U/ml. 10 were confirmed to have malignant ovarian tumour on histopathology and 1 had benign ovarian tumour(table4). The positive predictive value is 90% which is calculated as under:

$$\text{Positive predictive value} = \frac{\text{True positive}}{\text{True positive} + \text{False positive}}$$

$$\text{Positive predictive value} = \frac{10}{10 + 1}$$

$$\text{Positive predictive value} = \frac{10}{11}$$

**Positive predictive value = 90%**

22 patients had normal CA 125 out of these 22 patients 16 had benign ovarian tumour and 6 patients had malignant ovarian tumour on histopathology.

**Table 1:** Distribution of CA 125 in patients with ovarian masses n=65

CA 125	No of patients
Normal CA 125	22
Raised CA 125	43

**Table 2:** Distribution of raised CA 125 in patients n=43

Value of CA 125	No of patients
35U/ml-200U/ml	32
more than 200U/ml	11

**Table 3:** Ratio of benign and malignant tumours in patients having CA 125 between 35U/ml -200U/ml n=32

Nature of tumour	Number of patients
Benign	18
Malignant	14

**Table 4:** Ratio of benign and malignant tumours in patients having CA 125 more than 200U/ml n=11

Nature of tumour	Number of patients
Benign	1
Malignant	10

**DISCUSSION**

Tumours of the ovary are common form of neoplasia in females. They are sixth most common

form of neoplasia in females and fourth leading cause of death. They arise from either surface epithelium, germ cells or sex cords of the ovary. Of these tumours surface epithelial tumours are most common and are further subdivided into serous, mucinous, endometrioid, clear cell, and transitional cell tumours.

CA 125 is used for early detection of ovarian tumours and to distinguish between benign and malignant ovarian masses. Early detection of ovarian cancers improves the survival rate of the women with ovarian tumour. It is also used to monitor response to chemotherapy<sup>11</sup>, recurrence and progression of the disease<sup>12</sup>. Therefore, it should be monitored at regular intervals after treatment. The level of CA 125 decreases after surgery or chemotherapy. If the level decreases it shows that the tumour is responding to treatment. If level increases it indicates the recurrence of the disease or progression of disease.

CA 125 is high molecular weight glycoproteins<sup>13</sup>. It is a tumour associated antigen which is detected by the OC 125 monoclonal antibody. OC 125 antibody is present on the surface of ovarian cancer cells<sup>3</sup> and can be used for recognition of tumour cells by immune system. It is a useful marker for surface epithelial tumours<sup>3</sup> but it is not elevated in all cancer patients, particularly patients with early stage cancer. False positive results have been noted in many medical disorders, both malignant and benign<sup>14</sup>. It can be raised in many benign conditions<sup>15</sup> including pregnancy leiomyoma, ovarian cysts, endometriosis, appendicitis and diverticulosis. It can also be raised in many cancers including uterine, colon, lung and pancreas<sup>16</sup>, but very high level of CA125 more than 200U/ml is usually found in ovarian malignancies especially in surface epithelial tumours.

In this study, 65 females of all ages having ovarian masses are included, out of 65 patients, 43 patients had raised serum CA 125 level and 22 patients had normal CA 125 (table I). Out of 22 patients who have normal CA 125 level 6 patients have malignant ovarian tumour and 16 have benign tumour. The patients having CA 125 less than 35U/ml and proves to be malignant on histopathology have yolk sac tumour, granulosa cell tumour, dysgerminoma, malignant teratoma, sclerosing stromal tumour, krukensberg tumour. As also discussed earlier, that CA 125 is mostly raised in surface epithelial tumours and above mentioned tumours having CA 125 less than 35U/ml and

proves to be malignant on histopathology belong to germ cell tumours and sex cord tumours, therefore, level of CA 125 is not raised in these tumours. Other tumour markers are used to diagnose these tumours, such as alpha fetoproteins in yolk sac tumours<sup>17</sup>. Inhibin is raised in granulosa cell tumour<sup>18</sup>, chorionic gonadotrophin is raised in choriocarcinoma<sup>19</sup>.

## CONCLUSION

CA 125 is an important tumour marker. It is helpful to assess preoperatively the nature of ovarian mass. The value more than 200U/ml is usually found in ovarian carcinomas and to make a management plan accordingly. The value between 35U/ml-200U/ml is found either in benign or malignant ovarian tumours. For the ovarian tumours having value of CA 125 less than 35U/ml other tumour markers such as inhibin, alpha fetoproteins human chorionic gonadotrophins etc should be used.

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