

OVARIAN CANCER;

The role of CA-125 as a tumor marker. An institutional based descriptive & prospective study.

Dr. Naseer Ahmed Shaikh, Dr. Rukhsana Parveen Samo, Dr. M. Qasim Memon

ABSTRACT.. Object: 1). To analyze of serum tumor marker CA-125 in patients with ovarian malignant tumors. 2). To correlate between the serum levels of tumor marker with histological types of ovarian malignant tumors. **Study Design:** Institution based descriptive and prospective study. **Place & Duration:** Department of Pathology, Liaquat University of Medical & Health Sciences, Jamshoro from January 2009 to June 2011. **Material & Methods:** One hundred cases, diagnosed as ovarian malignant tumor on H&E staining were selected for study & measure serum CA-125 preoperatively and postoperatively in each case. **Results:** Out of 100 cases diagnosed as on H&E stain were 33 serous cystadenocarcinoma, 24 mucinous adenocarcinoma, 10 germ cell tumors and 08 sex-cord stromal tumors. On serum analysis increased level of CA-125 was seen preoperatively in 33/33 cases of serous cystadenocarcinoma and 24/29 cases of mucinous adenocarcinoma. Serum tumor marker value was declined following appropriate therapy of the tumors. **Conclusions:** Serum tumor markers CA-125 is useful and important for the detection of ovarian tumors. It is most significant for serous cystadenocarcinoma. It may also help in prognosis and specific treatment of ovarian malignancies relating to histological type.

Key words: Serum tumor marker CA-125, cystadenocarcinoma

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INTRODUCTION

CA-125 is a routine investigation in the management of ovarian cancers. It is often considered as. "Gold standard"⁴. CA -125 levels of <35 U/mL are accepted as normal. Elevated levels were found in more than 90% of advanced ovarian cancer but only 50% with stage 1 disease, where additional clinical examination and ultrasonography increased the sensitivity to almost 100%.

CA-125 was first identified by Bast, Knapp and colleagues in 1981. It is a high molecular weight glycoprotein, which is expressed by a large proportion of epithelial ovarian cancer. CA-125 is powerful index of risk of ovarian cancer in asymptomatic post menopausal women⁹. It is more associated with serous tumors rather mucinous. In embryonic life CA-125 is expressed on amniotic and coelomic epithelia and in adult; tissues derived from coelomic and mullarian epithelium.

Ovarian cancer is on fourth of the malignancies of female genital tract. It is group of heterogenous malignancies, arising from epithelial cells,

mesenchymal cells and germ cells. About 70% of epithelial ovarian cancer occurs in women over 50 years⁸ and more than one-half were diagnosed with advanced disease. The cause of ovarian cancer is unknown although low parity, infertility, early menarche and late menopause have been considered risk factors. Traditionally ovarian cancer is known as "silent killer" which does not produce symptoms until advanced stage⁵. At the time of diagnoses ovarian cancer already invade deeper tissue in pelvis and frequent peritoneal seedlings. Metastasis as a result of natural history of malignant ovarian tumors prevents early diagnosis of disease.

Several tumor markers have been detected in association with early diagnosis of ovarian carcinomas, and of these CA-125 proved the most clinical promise to date⁶. It is an early marker of ovarian cancer and is quite useful and non invasive laboratory aid. CA 125 is a sensitive and specific means of monitoring patients with ovarian carcinoma¹². Although a statistically significant association between outcome and CA125 level was observed¹⁰, but it is not sufficient for diagnosis of

ovarian cancer⁷. The sensitivity and specificity increased to almost 100% in association with clinical examination and ultrasonography. CA125 also have potential benefit in monitoring therapy of ovarian cancer¹¹.

The aim of present study was to assess CA-125 as a marker of ovarian cancer and its co-relation in our part of world; as such types of study was not conducted in the department of pathology Liaquat University of Medical and Health Sciences (LUMHS) at Jamshoro Sindh.

MATERIAL AND METHOD

We selected the patients who were diagnosed as ovarian cancer on clinical and radiological grounds. One day before surgery we collected 5cc of blood with BD syringe and serum were separated by centrifuged at 3000 rpm for 10 minutes and transfer 500ul serum in aliquots for storage at -20c. Another sample was collected during first week after surgery.

We selected only those samples which were morphological proven ovarian cancer of all histological types. 100 cases were examined for CA125 levels for preoperative and post operative status.

CA-125 was estimated by solid phase sandwich elecsys method by using commercially available kits (Roche).

Method is used as follows:

1. Total duration of assay: 18 minutes

- 1st incubation: Required sample, a biotinylated monoclonal specific antibody, and a monoclonal specific antibody labeled with a ruthenium complex form a sandwich complex.
- 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin.

- The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.
- Results are determined via a calibration curve which is instrument-specifically generated by 2-point calibration and a master curve provided via the reagent barcode.

Calculations

The analyzer automatically calculates the CA-125 concentration of each sample in U/ml.

For quality control we used Elecsys precicontrol tumor marker 1 & 2.

RESULTS

A total number of 100 patients with histologically confirmed malignant ovarian tumors were included in this study. The age of the patients ranges from 6-70 years with a mean age of 39.53 ± 12.83 years. The age range was wide. The minimum age was 6 years and the maximum age was 70 years. Majority of the patients (56%) were of rural areas. The statistically breakdown of 100 included histologically diagnosed ovarian malignant tumors were serous cystadenocarcinoma (33%), mucinous cystadenocarcinoma (29%), germ cell tumors (19%), sex-cord stromal tumors (15%) and other tumors (4%).

In this study the preoperative and postoperative analysis of serum of 100 included cases for CA-125 were carried out. In our study marker CA-125 was seen increased preoperatively in 33/33 cases of serous cystadenocarcinoma, 24/29 cases of mucinous cystadenocarcinoma, 10/19 cases of germ cell tumors, 8/15 sex-cord stroma tumors and negative in Brenner tumor, endometrioid tumor, clear

cell carcinoma and NHL. While postoperatively, CA-125 level found decreased (below the level of 50 IU/ml) in 33/33 of serous cystadenocarcinoma, 23/24 of mucinous cystadenocarcinoma, 10/10 germ cell tumor and 8/8 in sex-cord stromal tumors.

The results indicate significance in serous cystadenocarcinoma (Table-I & II). Postoperatively

decline in levels of tumor marker is observed significantly following surgical removal / debulking and other treatment.

In this study CA-125 is seen more specific tumor marker for serous cystadenocarcinoma because of increased level in 100% cases.

Type of malignant ovarian tumor	More than 35.0	More than 50.0	More than 100	More than 200	More than 300	More than 400	Total
Surface epithelial tumors Serous cystadenocarcinoma	1	5	10	9	3	5	33
Brenner Tumor	-	-	-	-	-	-	-
Endometroid carcinoma	-	-	-	-	-	-	-
Clear cell carcinoma	-	-	-	-	-	-	-
Mucinous adenocarcinoma	1	9	11	2	1	-	24
Germ cell tumor	4	3	2	1	-	-	10
Sex-cord stromal tumor	5	3	-	-	-	-	8
Others NHL	-	-	-	-	-	-	-

Table-I. Results of preoperative CA-125 level in each histological type of malignant ovarian tumors (N=100). (Normal range upto 35.0 IU/ml)

Type of malignant ovarian tumor	More than 35.0	More than 50.0	More than 100	More than 200	More than 300	More than 400	Total
Surface epithelial tumors Serous cystadenocarcinoma	-	-	-	-	-	-	-
Brenner Tumor	-	-	-	-	-	-	-
Endometroid carcinoma	-	-	-	-	-	-	-
Clear cell carcinoma	-	-	-	-	-	-	-
Mucinous adenocarcinoma	1	-	-	-	-	-	1
Germ cell tumor	-	-	-	-	-	-	-
Sex-cord stromal tumor	-	-	-	-	-	-	-
Others NHL	-	-	-	-	-	-	-

Table-II. Results of postoperative CA-125 level in each histological type of malignant ovarian tumors (N=100). (Normal range upto 35.0 IU/ml)

DISCUSSION

This study is an update on subject, which correlate the histological diagnosis of ovarian tumors with results of serological tumor marker. Ovarian cancers were one of the most common and most lethal diseases in women throughout the world; its incidence is even high in developed countries of world³.

Surface epithelial malignant ovarian tumors were the commonest category followed by germ cell tumors and sex-cord stromal tumors. Among the surface epithelial tumors, serous cystadenocarcinoma were predominant followed by border line serous tumors. A similar distribution of these tumors has been reported by Malik I.A².

Serum tumor markers CA-125 was important indicators of the clinical progress of women with ovarian cancers. Similar studies reported by Mani, R etal⁶.

CA-125 was useful tumor marker in serous cystadenocarcinoma. Similar findings were observed in the study of Mehboob etal¹. The next common group of malignancies included mucinous tumors; they were also associated with marked elevations in serum CA-125 values, as also reported by Mehboob etal¹.

This is the first study in this institution correlating the serum tumor marker with the diagnosis and treatment of malignant ovarian tumors. The value of the tumor marker dropped significantly following appropriate treatment. In this way it is proved to be having a good significance in early diagnosis as well as prognostic significance.

In this study we have further observed the increased serum CA-125 level is not only raised in epithelial ovarian cancers, but also in germ cell & sex cord/stromal tumors.

CONCLUSIONS

Ovarian malignancy is a serious disease, affecting women of all age group. Majority of the patients present in advance stage of disease, therefore prognosis is poor and mortality rate is high. Early detection and appropriate investigation may help to reduce the morbidity and mortality. Clinical, Histological examination and serum ovarian tumor marker may help in the diagnosis, prognosis and treatment of ovarian malignancies.

SUGGESTION

Patients diagnosed as ovarian malignancies either as clinical or histological basis are strongly recommended for serum ovarian tumor marker, such as cancer antigen (CA-125), for diagnosis of bulk of ovarian tumors. This tumor marker may help oncologist / clinicians for diagnosis, prognosis and treatment of patients.

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AUTHOR(S):

1. **DR. NASEER AHMED SHAIKH**
Assistant Professor,
LUMHS Jamshoro.
2. **DR. RUKHSANA PARVEEN SAMO**
Senior Lecturer,
LUMHS Jamshoro.
3. **DR. M. QASIM MEMON**
Assistant Professor,
LUMHS Jamshoro.

Correspondence Address:

Dr. Naseer Ahmed Shaikh
D/44, 2179, Bachal Shah Incline
Hyderabad. Sindh.
naseershaikh1@hotmail.com

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Knowledge speaks, but wisdom listens.

Jimi Hendrix