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CO Relation between the CA 125 and Staging and Histopathological Type of Ovarian Cancer

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Abstract

Introduction: *This study intends to find the correlation between CA125 and the staging and histopathology of ovarian tumours.*

Methods: *patients with ovarian tumours between January 2009 and January 2014 were included. Serum CA125 levels were noted. Ovarian tumor was staged using the FIGO staging system. The correlation between preoperative CA125 and staging and histopathology were evaluated. Chi square analysis was done and p value <0.05 was considered to be statistically significant.*

Results: *106 ovarian cancer patients were included in the study period. the mean age was 47.5 ± 10.2 years.Preoperative CA125 level did not correlate significantly with the stage of ovarian cancer. Highest levels of CA 125 were found in serous tumours.Mean serum CA125 concentration in papillary serous adenocarcinoma patients (n = 45) was 1456±320 U/ml whereas in mucinous adenocarcinoma (n =24) 756 ±125 U/ml.*

Conclusion: *In our study, preoperative CA125levels does not correlate well with FIGO staging.*

Introduction

Ovarian cancer is the sixth most common cancer and seventh most common cause of death amoung women worldwide(1).In India ovarian cancer is ranked the third most common cancer according to population based study, following the cancer cervix and then the breast cancer. The incidance of ovarian cancer varies between 5.4 – 8.0 per 1,00,000 population in varies parts of the country(2).

The investigation of choice which is often said to be the 'gold standard' is CA125(3).The discovery of OC125, an antibody that recognizes CA125, was made by Bob Bast and his colleagues in 1981.(4) For women with ovarian cancer, CA 125 levels were found to correlate with tumor burden in 93% of cases. (5)CA125 levels is said to be normal when it is of less than 35 U/mL (5,6). It has an established role in monitoring treatment and detecting recurrence of ovarian cancer and has

been advocated as a prognostic marker for advanced ovarian cancer. [7-9]. CA125 is expressed by over 80% of ovarian cancers, and levels at presentation correlate with the risk of malignancy, stage of disease and histology[10].The aim of the present study was to correlate the levels of CA 125 and the various histopathological types of ovarian cancer.

Material and Methods

The study was conducted in Department of Obstetrics and Gynecology, M S Ramaiah hospital. Medical records of all ovarian cancer patients admitted at M S Ramaiah hospitals between January 2009 and January 2014 were reviewed. A total of 106 ovarian cancer patients were admitted over duration of 5 years. The detailed history of all the patients and their demographic data were collected. The surgical findings such as size of the tumour, histopathology and staging of the cancerwere also noted. The tumors were staged according to the 2009 FIGO staging system and histologically defined according to World Health Organization (WHO) classification. The surgical specimens retrieved during laparotomy and the serum CA 125 levels measured were correlated. The statistical analysis of this study was done by chi-square test to verify the association among variables. P value less than 0.05 was considered to be significant.

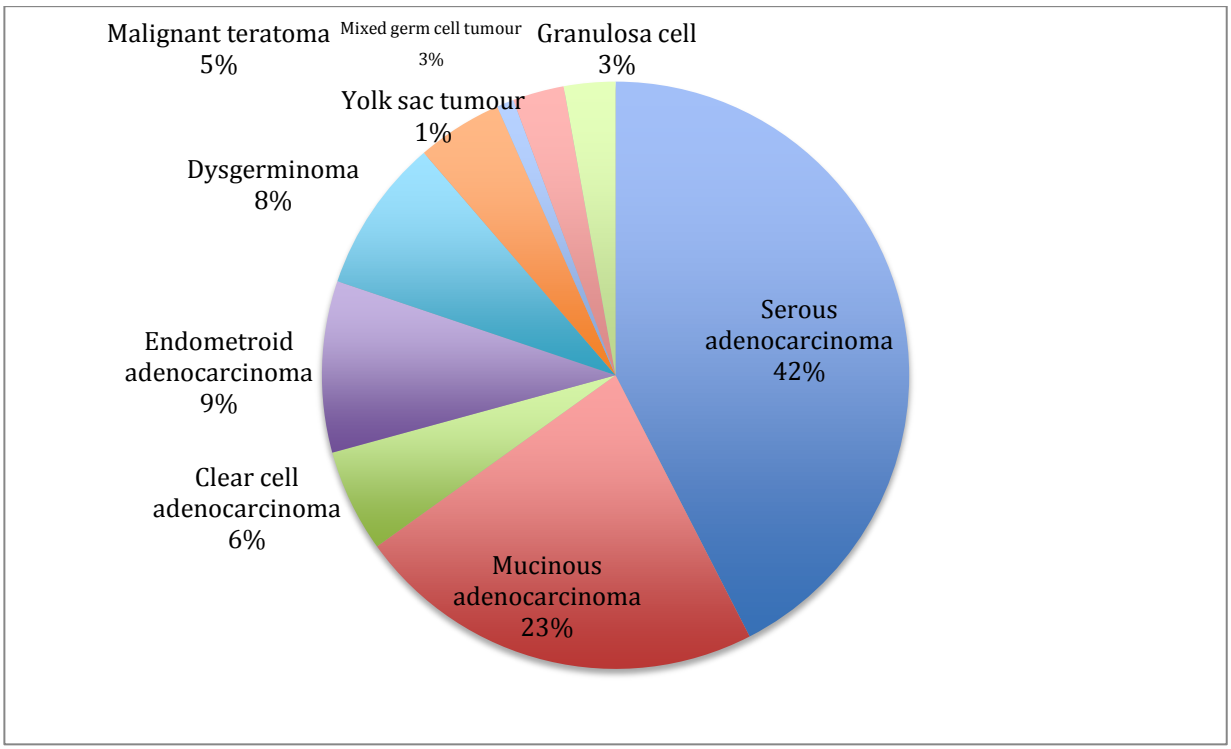
Results

In 106 patients, the mean age was 47.5 ± 10.2 years. Out of 106, 45 patients had papillary serous adenocarcinoma (42%),24 had mucinous adenocarcinoma (22%), 10 had endometrioid carcinoma (9%) and 6 patient was reported to have clear cell carcinoma (0.9%) (Table I). Table 2 shows correlation with the tumor staging was done according to FIGO classification. As shown in table II, out of 106 patients majority of the patients were in stage 3 at the time of admission. 15 had stage I disease (14%), 7 had stage II (6%), 48 had stage III (45%) , 11were with stage IV disease (10%) and 25 had recurrence.

Serum CA125 was determined by streptavidin biotin EIA (M/s Roche diagnostics). The antibodies against serum CA125 were M11 & OC125 (Centocor, melvern, Pa.) which were highly specific for this molecule. The upper limit was taken as 35 U/ml for non-pregnant healthy females.

Table I : HISTOPATHOLOGY TYPE:

Type	Num of patient
Serous adenocarcinoma	45 (42.4%)
Mucinous adenocarcinoma	24(22.6%)
Clear cell adenocarcinoma	6(5.6%)
Endometroid adenocarcinoma	10(9.4%)
Dysgerminoma	9(8.4%)
Malignant teratoma	5 (4.7%)
Yolk sac tumour	1(0.9%)
Mixed germ cell tumour	3(2.8%)
Granulosa cell	3(2.8%)



The distribution of histologic subtypes of ovarian cancers in our study is shown in Figure 2.

Stage of the disease: table 2

CA 125 levels were correlated with the stage of the ovarian cancer.

Staging of ovarian cancer	Number (%)	Serum CA125 levels(IU)
Stage 1	15	4333+/-432
Stage 2	7	1206+/- 123
Stage 3	49	1386+/- 116
Stage 4	10	1432+/- 125
Recrrance/unable to grade	25	2430+/-167

Table 3: correlation of staging and age of the patient-the highest number of patients in stage 1 were in age group 40-49 years, stage 2 and 3 in 50-59 age group and stage 4 in 40-49 years. Recurrence was in 49-59 years age group.

RELATION OF THE CA 125 WITH HISTOPATHOLOGICAL TYPE:

TYPE OF TUMOUR	CA125 levels
Serous adenocarcinoma	1456+/-320
Mucinous adenocarcinoma	756+/- 125
Clear cell adenocarcinoma	123+/-16
Endometroid adenocarcinoma	2654+/-231
Dysgerminoma	74+/-25
Malignant teratoma	65+/-43
Yolk sac tumour	134
Mixed germ cell tumour	324+/-60

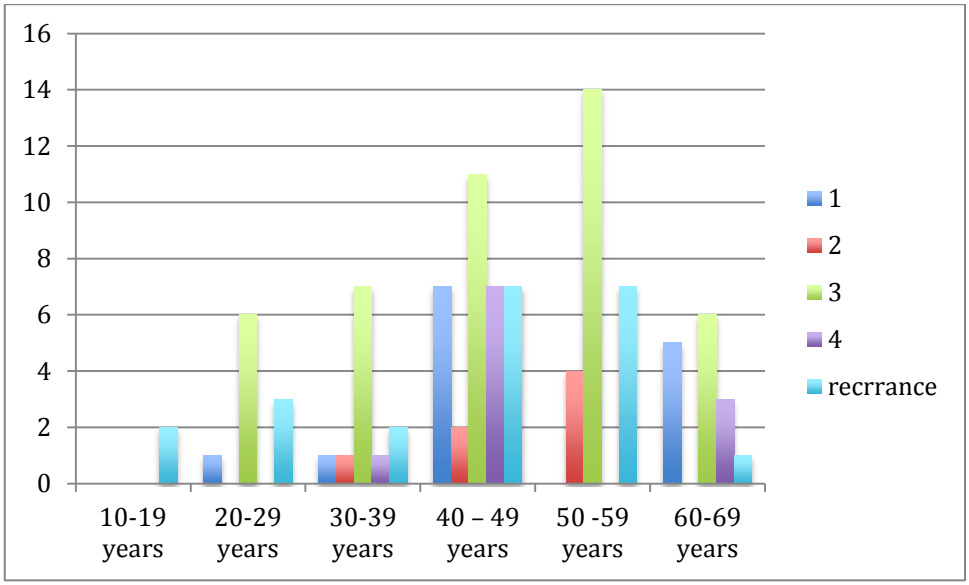
By convensional method there was a statistical significance between the ca 125 serum levels and serous adenocarcinoma and endomertial adenocarcinoma in comparison to the other ovarian tumors.

Table 4: Correlation of CA 125 and the histopathology of the ovarian cancer

The highest levels were found in serous ovarian cancer. Granulosa cell tumour had the least levels. Meanserum CA125 concentration in papillary serous adenocarcinoma patients (n = 45) was 1456±320 U/ml whereas in mucinous adenocarcinoma (n =24) 756 ±125 U/ml.

RELATION BETWEEN THE STAGE AND AGE LEVEL

Stage of tumor	10-19 years	20-29 years	30-39 years	40 – 49 years	50 -59 years	60-69 years	>70 years
1	0	1	1	7	0	5	3
2	0	0	1	2	4	0	0
3	0	6	7	11	14	6	4
4	0	0	1	7	0	3	0
recrrance	2	3	2	7	7	1	1



DISCUSSION

Carbohydrate antigen 125 (CA-125) is a high molecular-weight glycoprotein expressed by epithelial ovarian tumors as well as on the surface of cells of mesothelial origin[(11)]. Cancer antigen 125 (CA 125) is a glycoprotein expressed in normal tissues originally derived from coelomic epithelia such as peritoneum, pleura, pericardium, fallopian tubes and endometrium and hence the levels are elevated in various benign and malignant conditions that involve stimulation of these tissues.[(12)] Many studies have shown that levels of soluble CA125 are elevated in a number of other malignant conditions such as breast cancer, mesothelioma, non-Hodgkin lymphoma (NHL), gastric cancer, and leiomyoma and leiomyosarcoma of gastrointestinal origin and CA125 levels have also been found elevated in benign conditions such as endometriosis, pregnancy, ovulatory cycles, liver diseases and congestive heart failure , as well as in infectious disease such as tuberculosis.[(13)]In the study by Hogdall EV et. Al, elevated levels of CA125 are more strongly associated with serous, rather than mucinous tumors [(14)]In the present study, Serous tumours showed highest levels of CA 125 levels compared to other tumours (1456±320 U/ml).

The CA-125 level is elevated in the combined presence of hydrothorax and ascites in cases with an ovarian tumor.[(15)]In our study CA 125 was elevated in non-epithelial tumours as well such as dysgerminoma, teratoma, yolk sac tumour and granulosa tumour though the levels were >35U/ml it was much lower than the epithelial ovarian

tumours. (75±25, 65±43,134 and40±19 U/ml respectively).The presence of a pelvic mass with a raised CA 125 of 657 units/ml, lymphadenopathy and other associated suspicious features on CT scan suggested an ovarian malignancy[16] rather than levels merely more than 35U/ml.

Kolwijck *et al*. [17] describe that the pre-operative serum CA 125 levels are significantly higher in serous tumors (p < 0,001). In the present study, the mean age of patients was 47.5 ± 10.2 years similar to study by Eduardo Cambruzzi et al[18]in which it was 50.24 ± 11.12 years. The tumor marker CA-125, the most extensively studied molecule for ovarian cancer in the literature, seems to be the most promising biomarker to predict the stage in a given patient.[19]But in the present study there was no correlation between CA 125 and staging as stage 1 showed 4333±432 compared to stage 2 1206±123.This is similar to the study by V.Thakur et al.in which there was no correlation was found between serum CA125 concentration and the FIGO staging of disease.[20]In a similar study by Munstedt et al 1997 [21] have not found any correlation of high FIGO staging &presence of ascitis with serum CA125concentration.In another study by N. Osman et al., preoperative CA125 level did not correlate significantly with stage, tumor grade or Overall Survival (p=0.08. p=0.113 and p=0.847 respectively).[22]

CONCLUSION

Serum CA125 concentration was much higher in serous ovarian cancer. No correlation was obtained between CA 125 and staging of the tumor.

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