Original Research

Preoperative Serum CA-125 Levels in Patients with Ovarian Cancer

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Abstract

Introduction: A noteworthy proportion of patients with stage I disease have usual preoperative serum levels, and not all cell types rapid the antigen. Our aim of this study was to predict preoperative serum CA-125 levels in patients with ovarian cancer. **Material & Methods:** This cross-sectional study was carried out at the Department of Gynecological Oncology, Department of Gynae & Obstetric, Ashiyan Medical College Hospital, Barua Khilkhet, Dhaka, Bangladesh during the period from January 2015 to December 2015. A total of 100 patients were selected using purposive sampling technique for this study. Data were collected and documented on a preformed and pretested structured questionnaire. Clinical examination and relevant investigation were done and recorded accordingly. Data were processed and analyzed with the help of computer software SPSS 22. **Results:** Mean age of the study subjects was 45.7 ± 15.2 years with a range of 13-75 years. Table II shows education status of the study subjects. It was observed that half of the study subjects had education up to primary level, 26% had studied up to secondary level, 19% up to higher secondary level and only 5% were graduate. Mean BMI was 23.3± 3.0 kg/m2, mean age of marriage was 16.1± 2.8years and mean CA-125 level was 547.02± 478.74. Maximum study subjects had stage III (44.0%) followed by stage II (24.0%), stage I (21. 0%) and stage IV (11.0%). Also, most of the study subjects had serous tumors (70.0%) followed by mucinous tumors (11.0%), endometrioid adenocarcinoma (8.0%), clear cell tumors (4.0%), malignant tertoma (5.0%), Brenner (1.0%) and dysgerminoma (1.0%). Endometrioid adenocarcinoma was found in elderly study subjects and clear cell tumor was found in young aged study subjects. Histopathological type according to grading of ovarian tumor describes, all stage IV tumors were serous, all clear cell and Brenner tumors were stage I, and all endometrioid adenocarcinoma tumors were stage III. Serum CA-125 was elevated at the advanced stage of ovarian cancer. **Conclusion:** Serum CA-125 had significant positive correlation with surgical stage of ovarian cancer in epithelial cancer patients of this study. But in case of germ cell ovarian cancer, it showed a negative correlation

INTRODUCTION

CA125 level were also correlated to responsiveness to chemotherapy[1]. Patients with elevated serum CA125 had a 3.5-fold higher risk to die compared to patients with low serum CA125.[2] Serum CA-125 has shown a valuable indicator for nursing the treatment of patients with radical disease subsequent debulking surgery in both malignancies.[3] Also, it has comparable limitations in patients with both ovarian epithelial and uterine carcinomas. A noteworthy proportion of patients with stage I disease have usual preoperative serum levels,[4] and not all cell types rapid the antigen. In guiding the early treatment of patients with radical ovarian cancer, models predicting the primary debulking surgical exposing are essential. Insufficient primary debulking surgery (PDS) may upsurge perioperative morbidity, because it does not recover the prediction.[5,6] Repeated high- grade ovarian cancer is typically related to short term survival.[7] Disease stage at diagnosis is a resilient prognostic variable for predicting patient outcome in ovarian cancer. Patients with International Federation of Gynaecology and obstetrics (FIGO) stage II ovarian cancer, representing tumor dissemination and seeding of the peritoneal lining outside of the pelvis, have s 5 – years survival rate of

around 35%. This survival rate reduction to less than 10 % in patients detected with stage IV ovarian cancer, where disease had spread to aloof metastasis.[8] Consequently, initial exposure and suitable administration inhibit the fetal outcome of ovarian cancer. Ovarian carcinomas linked to highest death rate in gynecological malignancies as a lack of indicators shield the disease in the primary stage. Existing evidences have been devoted to determining initial operative screening mechanism before the onset of clinical symptoms. Hence, biomarkers are the significant tools that are skilled of fight against this deadly disease.[9] Unconventional ovarian cancer patients with older age, improved comorbidities, and with an advanced disease load who cannot accomplish core optimal surgical debulking can gain the alike general existence rates and lesser postoperative opposing events related to patients with optimal cytoreduction after they select neoadjuvant as chemotherapy.[5,10] Noteworthy capriciousness in the level of primary optimal surgical cytoreduction for unconventional ovarian cancer, extending from 25 to 90%, happens among institutes.[11] The importance of thorough surgical staging cannot be over emphasized because subsequent treatment will be determined by the stage of the disease. Therefore, we have investigated the histological characteristics and stage of ovarian cancer and have correlated with preoperative level of serum CA -125. We also tried to find out role of CA-125 in identifying different stages of ovarian cancer.

METHODS

This cross-sectional study was carried out *at the Department of Gynecological Oncology, Department of Gynae & Obstetric, Ashiyan Medical College Hospital, Barua Khilkhet, Dhaka, Bangladesh during the period from January 2015 to December 2015*. A total of 100 patients were selected using purposive sampling technique for this study. The aim of this study was to investigate the histological characteristics and stage of ovarian cancer and to correlate with preoperative level of serum CA -125. Data were collected and documented on a preformed and pretested structured questionnaire. Clinical examination and relevant investigation were done and recorded accordingly. Data were processed and analyzed with the help of computer software SPSS 22. P value <0.05 was considered as statistically significant. Patients' blood sample was drawn from the antecubital vein. 5 milliliters blood was drawn with proper aseptic precautions. The blood sample was transferred into a clean, dry test tube and taken to the laboratory. Blood sample was centrifuged for 10 minutes at a rate of 4000rmp. The ARCHITECT CA125 II assay is a two-step immunoassay for the quantitative determination of OC 125 defined antigen in human serum or plasma using CMIA technology, with flexible assay protocols, referred to as Chemi-flex. Sample and OC 125 coated paramagnetic micro particles are combined. The OC125 defined antigen present in the sample binds to the OC 125 coated micro particles. After washing M11 acridinium labelled conjugated is added to create a reaction mixture. Following another wash cycle pre-Trigger and Trigger solution are added to the reaction mixture. The resulting chemiluminesent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of OC125 defined antigen in the sample and the RLUs detected by the ARCHITECT system optics. Under all aseptic precautions after cleaning and draping of the patient, the abdomen was opened through a midline incision to allow adequate access to the upper abdomen. Any free fluid is heparinized and submitted for cytological evaluation. If there is none, peritoneal wash is taken with 50 -100ml of heparinized saline from each of the following sites: the pouch of Douglas, the paracolic gutters and the sub diaphragmatic spaces. For the last a rubber catheter attached to a bulb syringe is used. All intra-abdominal viscera and surfaces are explored systematically that is the caecum, ascending colon, paracolic gutter, right kidney, liver, gall bladder, right hemi diaphragm, transverse colon, left hemi diaphragm, left paracolic gutters, descending colon, sigmoid colon, the small intestine and its mesentery. Biopsies are taken from suspicious areas and adhesions. If there are none, multiple random biopsies are taken from the peritoneum of the pouch of Douglas, both paracolic gutters, over the bladder and intestinal mesentery. Biopsies from the diaphragmatic surface can be taken with the aid of a laparoscope or the surface can be scrapped with a tongue depressor and the sample sent for cytological evaluation. The retro peritoneal spaces are explored to evaluated the pelvic and para-aortic lymph nodes and all enlarged lymph nodes are resected. An infra-omentectomy is performed. Ovarian tumors should preferably be removed intact and all specimens are sent for histopathological examination.

RESULT

This was a cross sectional study which was carried out in inpatient Department of Gynaecology oncology to find out the correlation of pre-operative level of serum CA 125 with

the surgical stage (FIGO -2014) of ovarian cancer. Table I shows age distribution of the study subjects. Maximum (33%) study subjects were ≤30 years old followed by age group 41- 50 years (27%), 31- 40 years (24%) and >50 years (14%). Mean age of the study subjects was 45.7 ± 15.2 years with a range of 13-75 years. Table 2 shows education status of the study subjects. It was observed that half of the study subjects had education up to primary level, 26% had studied up to secondary level, 19% up to higher secondary level and only 5% were graduate. Table 3 shows occupation of study subjects. Maximum study subjects were housewife (68%), followed by 17% teacher, 8% service holder, 4% student and 3% tailor. Table 4 shows that Mean BMI was 23.3± 3.0 kg/m2, mean age of marriage was 16.1± 2.8years and mean CA-125 level was 547.02± 478.74. Table 5 shows surgical stages of ovarian cancer of the study subjects. Maximum study subjects had stage III (44.0%) followed by stage II (24.0%), stage I (21. 0%) and stage IV (11.0%). Table 6 shows histopathological finding of the tumors. Maximum study subjects had serous tumors (70.0%) followed by mucinous tumors (11.0%), endometrioid adenocarcinoma (8.0%), clear cell tumors (4.0%), malignant tertoma (5.0%), Brenner (1.0%) and dysgerminoma (1.0%). Table 7 shows association of age with histopathological findings. Endometrioid adenocarcinoma was found in elderly study subjects and clear cell tumor was found in young aged study subjects. Table 8 shows histopathological type according to grading of ovarian tumor that describes, all stage IV tumors were serous, all clear cell and Brenner tumors were stage I, and all endometrioid adenocarcinoma tumors were stage III. Table 9 shows preoperative serum CA-125 level at different surgical stage of ovarian cancer among the study subjects. Serum CA-125 was elevated at the advanced stage of ovarian cancer.

Table 1: Age distribution of the study subjects (n= 100).

Age (years)	Frequency (%)
≤30	34(34.0)
31-40	24(24.0)
41- 50	28(28.0)
>50	14(14.0)
Mean ± SD	45.7± 15.2 (13-75)

Table 2: Distribution of education status of study subjects. (n= 100)

Education	Frequency (%)
Primary	50(50.0)
Secondary	26(26.0)
Higher Secondary	19(19.0)
Graduate	05(05.0)

Table 3: Distribution of occupational status of study subjects. (n= 100)

Occupation	Frequency (%)
Housewife	68(68.0)
Teacher	17(17.0)
Service holder	08(08.0)
Student	04(04.0)
Tailor	03(03.0)

Table 4: BMI, age of marriage and mean CA-125 level of the study subjects (n=100).

Parameters	Mean ± SD	Min – max
BMI (kg/m^2)	23.3± 3.0	17-28.4
Age of marriage (years)	16.1± 2.8	12-15
CA-125	547.02± 478.74	24-1600

Table 5: Distribution of study subjects according to surgical stage of ovarian cancer. (n=100).

Surgical stages of ovarian Cancer	Frequency (%)
I	21 (21.0)
II	24 (24.0)
III	44 (44.0)
IV	11 (11.0)

Table 6: Distribution of study subjects by histopathological type of ovarian cancer. (n=100)

Type of tumor	Frequency (%)
Epithelial	
Mucinous tumors	11 (11.0)
Serous tumor	70 (70.0)
Clear cell tumors	04 (04.0)
Endrometrioid adenocarcinoma	08 (08.0)
Brenner	01 (01.0)
Germ cell	
Dygerminoma	01 (01.0)
Malignant teratoma	05 (05.0)

Table 7: Histopathological type of ovarian cancer with their mean age of study subjects. (n= 100)

Histopathological tumor	Stage I n (%)	Stage II	Stage III	Stage IV
Epithelial				
Mucinous tumors	04(18.8)	04(16.67)	03(6.6)	00(0.0)
Serous tumor	08(38.9)	20(83.33)	31(70.4)	11(100.0)
Clear cell tumors	04(18.8)	00(0.0)	00(0.0)	00(0.0)
Endrometrioid adenocarcinoma	00(0.0)	00(0.0)	08(18.0)	00(0.0)
Brenner	01(4.5)	00(0.0)	00(0.0)	00(0.0)
Germ cell				
Dygerminoma	00(0.0)	00(0.0)	01(2.5)	00(0.0)
Malignant teratoma	04(18.8)	00(0.0)	01(2.5)	00(0.0)

Table 8: Distribution of study subjects by histopathological findings and relation with stage of ovarian cancer. (n=100)

Histopathological tumor	Stage I	Stage II	Stage III	Stage IV
	N (%)			
Epithelial				
Mucinous tumors	04(18.8)	04(16.67)	03(6.6)	00(0.0)
Serous tumor	08(38.9)	20(83.33)	31(70.4)	11(100.0)
Clear cell tumors	04(18.8)	00(0.0)	00(0.0)	00(0.0)
Endrometrioid adenocarcinoma	00(0.0)	00(0.0)	08(18.0)	00(0.0)
Brenner	0	00(0.0)	00(0.0)	00(0.0)
Germ cell				
Dygerminoma	00(0.0)	00(0.0)	01(2.5)	00(0.0)
Malignant teratoma	04(18.8)	00(0.0)	01(2.5)	00(0.0)

Table 9: Preoperative serum CA -125b level of different surgical stages of ovarian cancer among the study subjects(n=100).

Surgical stage of cancer	Serum CA-125(mean ±SD)	P
I	247.18 ±149.28	<0.001
II	449.26 ± 79.33	
III	505.97 ±481.40	
IV	1484.00 ±101.34	

DISCUSSION

CA 125 antigen is a cell membrane glycoprotein expressed by various types of epithelial cells and it is present in patients with a variety of cancers namely breast, endometrium, gastrointestinal tract, and lung in addition to the ovarian cancer (OC) as well as in benign diseases of the uterus, liver, and gastrointestinal tract and benign tumors of the ovary and uterus.[12] In present study, maximum (34%) study subject was ≤ 30 years old followed by age group 41-50 years (28%), 31-40 years (24%), and >50 years (14%). Mean age of study subjects was almost similar in the study of Nayak et al.[13] found mean age 47.5 ± 10.2 year. Bai et al.[14] found mean age of the ovarian clear cell carcinoma patients was 50.8 ±10.7% years with range of 23- 85 years. Present study showed almost half of this study population having primary education and maximum study subjects were housewife (68%). Mean BMI was 23.3 ±3.0 kg/m^2 and mean age of marriage was 16.1 ±2.8 years. There is evidence that have established obesity to be associated with enhanced ovarian cancer risk through a hormonal mechanism.[15] In present study, maximum study subjects had stage III (44%) followed by stage II (24%), stage I (21%) and stage IV (11%). Previous study done by Nayak et al.[13] showed similar result like (46.2%) had stage III disease. In the study of Bai et al.[14] stage I was 45.0%, stage II was11.5%, stage III was 35.2% and stage IV was 5.3%. Furrer et al.[16] also found maximum stage III Patients (61.0%) followed by stage I (21.0%), stage II (12.0%) and stage IV (6.0%). In another study, preoperative CA-125 was >35 U/ml in 73(90.1%) cases. Preoperative CA-125 was elevated (>35 U/ml) in majority (78.9%) of patients.[14] Jiang et al.[17] suggested a cut-off point of 25 IU/ml for preoperative CA-125 serum levels, whereas Choi et al.[18] recommended a cut-off point of 30 IU/ml for extra-uterine disease and 50 IU/ml for lymph node metastasis, respectively. Hsieh et al.[19] established that raised CA-125 levels preoperatively had noteworthy correlation with lymph node metastasis, unconventional stage, complexity of assault and cervical invasion with a cut-off point of 40 IU/ml, and can be well thought-out for full pelvic lymphadenectomy. Serum CA -125 was elevated at the advanced stage of ovarian cancer. Similar finding also observed in the study of Furrer et al.[16] Patients who have high preoperative serum CA 125 levels may be candidates for comprehensive surgical staging of endometrial cancer as well as lymphadenectomy.[20-22] Surgical methods range from hysterectomy single-handedly for all patients, hysterectomy with lymphadenectomy reliant on the surgeon's criteria for threat of nodal metastasis based on preoperative grading or intraoperative assessment, hysterectomy with limited lymphadenectomy, or hysterectomy with full pelvic and para-aortic lymphadenectomy for all patients.[23] Present study showed histopathological distribution of the ovarian cancers, like serous tumors (70.0%), mucinous tumors (11.0%), endometrioid adenocarcinoma (8.0%), malignant teratoma (5.0%) and clear cell tumors (4.0%). Furrer et al.[16] found serous tumors (65.0%), clear cell tumors (12.0%), Endometrioid tumors (13.0%), mucinous tumors (5.0%), undifferentiated carcinoma (2.0%) and mixed malignant mullerian tumors (3.0%). In the study of Morimoto et al.[24] serous was 79.0%, Adenocarcinoma was 50.0%, carcinoma was 4.0%, endometrioid was 2.0% and mucinous was 1.0%. Most common tumor was serous adenocarcinoma (23.0%) in the study of Nayak et al.[14] Present study Serum CA-125 had significant positive correlation with surgical stage of ovarian cancer in epithelial cancer patients. But in case of germ cell ovarian cancer it showed a negative correlation. unlike our study, Nayak et al.[14] did not find any correlation of CA -125 with stages of ovarian cancer. This could be because he did the correlation for all histopathological tumour together. Preoperative serum tumor marker CA-125 levels are a useful indication of the disease.[25]

LIMITATIONS OF THE STUDY

The present study was conducted at a very short period of time. For being a study in a single community with comparatively small number of sample size, the study result may not reflect the exact scenarios of the mass people.

CONCLUSION

A preoperative dimension of serum CA 125 is essential for women with endometrial cancer since it can be cast-off in preoperative choices concerning the level of surgery and the usage of adjuvant treatment to offer the optimal consequence. In our study, serum CA-125 had significant positive correlation with surgical stage of ovarian cancer in epithelial cancer patients. But in case of germ cell ovarian cancer, it showed a negative correlation. However, multicenter study should be done with large sample size for a longer duration. Moreover, other cofactors which might have an influence on stage of ovarian cancer should be evaluated.

RECOMMENDATION

This study was conducted in a single institute with a small sample size and time frame. For better statistics, the study needs to be conducted with a larger sample size and wide demographics. The knowledge of COVID-19 is still being filtered, and this played a role in the proper knowledge levels of the participants.

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