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Original Article

Association between Histopathologic Type of Ovarian Cancer and Serum CA-125 Level

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ABSTRACT

Objective: to find an association between the serum CA-125 level and the histopathological type of ovarian tumor.
Study Design: Cross-sectional study.
Place and Duration of Study: Medical Oncology, Jinnah postgraduate Medical Center, Karachi Pakistan from Jan 2018 to Dec 2019.
Methodology: This study included 107 patients presenting with epithelial ovarian cancer. In each case, histological type, pathological stage, degree of differentiation and serum CA-125 was evaluated. The association between preoperative CA-125 and histopathological type of tumor were evaluated.
Result: About 107 ovarian cancer patients were included. The mean age in our study was 50.80±10.16 years. Raised CA-125 level was found in most of the patients with serous histology 46(56.1%).
Conclusion: Serum level CA-125 elevated in most patients with serous histology. A statistically non-significant association was found between raise CA-125 levels and histological types of ovarian cancer.

Keywords: Epithelial ovarian cancer, Histological type, Ovarian cancer, Serum CA-125, Serous histology, Tumor stage, Tumor size.

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INTRODUCTION

Ovarian malignancy is the 6th prevalent malignancy among the women and considered to be the 4th leading cause of death due to cancer in females worldwide.[1] In Pakistan, the ovarian cancer is ranked at eight most common malignancy.[2] Most of the postmenopausal women are being diagnosed with epithelial ovarian carcinomas at the median age of 63 years and over.[3] Primary ovarian neoplasms exhibit a wide range of clinical and histopathological presentations, from an excellent prognosis and high likelihood of cure to rapid progression and poor prognosis.[4] In 90% of cases of ovarian cancer, CA-125 levels were shown to be consistent with tumor burden.[5] The most frequent histological subtype is serous adenocarcinoma among malignant epithelial tumors, which usually present as advance stage disease in approximately 75% of patients.

The ovarian tumors that originate from the stroma or epithelium are either moderately or poorly differentiated. Epithelial ovarian neoplasms and tumors of mesothelial origin express CA-125 which is a high molecular-weight glycoprotein. Besides this, CA-125, a glycoprotein is also found in normal tissues which is originally derived from coelomic epithelium during embryogenesis such as pericardium, peritoneum, fallopian tubes, pleura and endometrium and therefore the levels are raised in several malignant and benign conditions that engage these tissues. CA-125 levels<35 U/ml is normal. Serum CA-125 has been playing significant part in observing, treating and differentiating the recurrence of ovarian cancer and it is a prognostic marker for the advanced stages of ovarian cancers.[6,7] In majority of the ovarian cancers cases, CA-125 was over expressed and its levels at presentation were well correlated with histology.[8,9]

Various studies have reported other malignant conditions such as in mesothelioma, breast cancer, gastric cancer, leiomyoma, non-Hodgkin lymphoma (NHL) and leiomyosarcoma of gastrointestinal origin, correlated with raised CA-125 levels. Many benign conditions such as pregnancy, endometriosis, ovulatory cycles, congestive heart failure, liver diseases, as well as infectious disease like tuberculosis also revealed raised CA-125 levels.[10] Hence, the aim of this study was to find the association between serum CA-125 level and histopathological type of ovarian cancer.

METHDOLOGY

The cross sectional study was carried out from January 2018 till December 2019 at Department of Medical Oncology, Jinnah Postgraduate Medical Center, Karachi. Permission from the ethics review committee (ERC NO. F.2-81-IRB/2019-GENL/18150/

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JPMC) of the hospital was taken prior to conduction of the study. The sampling method for patient inclusion was non-probability purposive technique. The sample size was estimated using Open epi sample size calsulatostatistics of serum-125>35 IU/ml as 65.4% 9 among malignant tumors, margin of error as 9% and 95% confidence level. The estimated sample size was 107.

Inclusion Criteria: Female patients presenting with epithelial ovarian cancer were inlcuded.

Exclusion Criteria: Patients with germ cell, stromal tumors, metastatic malignancy and systemic illness were excluded from the study.

Pretreatment data including demographic data, history of contraceptive use, marital status, occupational status and family income status was collected. Surgical findings such as size of the tumor, histopathology, and staging of the cancer were also noted. The tumors were staged according to the FIGO staging system and histologically defined according to WHO classification. The surgical specimen retrieved during laparotomy and the serum CA-125 level were measured.

Data was analyzed by using SPSS Version 20. Numeric variables were represented as mean and standard deviation whereas categorical variables were presented as frequencies and percentages. Chi-square test was applied to see the association between elevated serum CA-125 levels with histological subtypes. $p \leq 0.05$ was taken as statistically significant.

RESULT

A total of 107 diagnosed patients with epithelial ovarian cancer were enrolled. The average age in our study was 50.80±10.16 years. Most of the patients were of age 20-40 years 81(74.3%).

Patients who presented with epithelial ovarian cancer, 48(44.9%) had history of oral contraceptive use. Furthermore, 22(20.69%) and 85(79.4%) patients were employed and unemployed. Family income showed that 54(50.5%) patients belonged from upper income group (Table-I).

Patients who presented with epithelial ovarian cancer showed that as per histological types, serous tumor was most frequent comprising 61 cases (57%) followed by 26(24.3%), 16(15%) and 4(3.7%) patients having mucinous, endometroid and clear cell histological types. Moreover, 45 patients had well differentiated (42.1%), 24 had moderately differentiated (22.4%), 18 had poorly differentiated (16.8%) and 20 had unknown histological grade (18.7%).

Table-I: Patient Characteristics (n=107)

Patient Characteristics		n(%)
Age	20-40	81(74.3)
	41-60	28(25.7)
History of Oral Contraceptive Use	Yes	48(44.9)
	No	59(55.1)
Marital Status	Married	9(85)
	Unmarried	16(15)
Occupational Status	Yes	22(20.6)
	No	85(79.4)
Family Income Status	Lower	4(3.7)
	Lower middle	8(7.5)
	Middle	14(13.1)
	Upper middle	27(25.2)
	Upper	54(50.5)
Mean±SD		
Age In Years	50.80±10.16	

Staging of the disease was done on the basis of FIGO classification and majority of the cases belonged to stage 3. About 76.6% of the patients had raised CA-125 (Table-II).

Table-II: Epithelial Ovarian Cancer Characteristics (n=107)

Epithelial Ovarian Cancer		n(%)
Histological Type	Serous	61(57)
	Mucinous	26(24.3)
	Endometroid	16(15)
	Clear cell	4(3.7)
Elevated CA-125 Level	Yes	82(76.6)
	No	25(23.4)
Histological Grade	Well	45(42.1)
	Modertaely	24(22.4)
	Poorly	18(16.8)
	Unknown	20(18.7)
Stage	Stage 1	21(19.6)
	Stage 2	18(16.8)
	Stage 3	56(52.3)
	Stage 4	12(11.2)

As Table-III showed that about 46 patients with serous histology (56.1%) had elevated CA-125 level and the relationship between histologic type and elevated CA-125 was statistically insignificant (p=0.64).

Table-III: Stratified of Elevated CA-125 Level According to Histologic Type (n=107)

Histologic type	Elevated CA-125		*p*-value
	Yes	No	
Serous	46(56.1%)	15(60%)	0.64
Mucinous	19(23.2%)	07(28%)	
Endometroid	13(15.9%)	03(12%)	
Clear Cell	04(4.9%)	00(00%)	

DISCUSSION

The present study findings showed that most common age for ovarian cancer is between 20-40 years

whereas the mean age is 50 years. According to ovarian cancer statistics, it has been suggested that there is 0.1 percent probability of developing ovarian cancer in 40 years of age.[11] The most common subtype of ovarian cancer found in the present study is serous ovarian cancer followed by mucinous ovarian cancer. The incidence of epithelial ovarian cancer in Pakistan is comparable to developed countries. The findings of the present study are in concurrence with other studies.[12-14] In another study, it was found that prevalence of serous ovarian cancer was very high in European population followed by American then Asian population.[15] Most of the patients belonged to middle or upper socioeconomic class, were married and were homemakers. Histopathologically, serous: 75.4%, mucinous: 23.2%, endometroid: 15.9%, clear cell: 4.9% had elevated CA-125 level. Hogdall EV *et al*, in their study showed that raised CA-125 levels were more strongly related with serous, as compared to mucinous tumors.[16] Kolwijck *et al*. showed that the pre-operative serum CA-125 levels were significantly elevated in advanced stage and in serous tumors.[17] Most of the patients in the present study had stage three ovarian cancer. The staging of cancer determines prognosis of the disease and measure survival rate of the patient. The results reflect late diagnosis and rapid progression of the tumor. This explains the need to implement screening for ovarian cancer among women of all ages which is also emphasized in other study.[18]

The study is focused on finding CA-125 levels among different subtypes of ovarian cancer in Pakistan. In KPK province, the levels of CA-125 had been determined and it was found that fifty two percent patients had elevated CA-125 levels.[13] In comparison with the present study, three fourth of the patients had raised CA-125. Previously in Karachi, CA-125 levels among ovarian cancer have not been demonstrated. The elevated CA-125 levels in present study are in agreement with Dewan R *et al*. Kardag *et al*. and Green *et al*.[19-21]

In another study, it was evident that CA-125 levels decreased post treatment. The study further concluded that CA-125 levels is also important to determine the recurrence of epithelial ovarian cancer.[22] However, in the present study, the recurrence is not determined. The CA-125 level among different subtypes of ovarian cancer varies in the present study. the present study revealed that serous ovarian cancer presented with most elevated levels of CA-125. However, the study showed no impact of different subtypes with CA-125 level.

CONCLUSION

Serum level CA-125 elevated in most patients with serous histology. A statistically non-significant association was found between raise CA-125 levels and histological types of ovarian cancer.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

HP: & GH: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

PK: & SZ: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

KM: & PM: Conception, study design, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investi-gated and resolved.

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