ORIGINAL ARTICLE

THE FREQUENCY AND CLINICAL USEFULNESS OF CA 19-9 IN THE WORK UP OF OVARIAN MALIGNANCY

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ABSTRACT

Objectives: To assess the frequency and clinical usefulness of CA 19-9 in the workup of ovarian malignancy.

Material and Methods: This cross sectional study included 30 patients with histologically confirmed ovarian adenocarcinomas, was conducted in the departments of medicine, surgery and obstetrics & gynecology of Peshawar Institute of Medical Sciences, Peshawar, Pakistan from January 2016 to October 2017. The patients were initially recruited from and then followed up in surgical and gynecological OPD. Each patient underwent a measurement of CA 19-9. The frequency of elevated CA 19-9 was checked and was sub-stratified amongst age group, ethnicity, tumor bulk and smoking status.

Results: Mean age of the participants was 54.30 years ±10.52, mean CA 19-9 was 64.67± 32.65 and the mean tumor size in cm on CT pelvis was 4.83± 1.76. 36.7% (n=11) had extensive disease with distant metastasis while 50% (n=15) were either abusing tobacco or were exposed to passive smoking at home. The frequency of elevated CA 19-9 in patients with ovarian malignancy was 73.3% (n=22).

Conclusion: CA 19-9 is elevated in more than two-thirds of the patients with ovarian cancer.

Key words: Ovaries, Cancer, Tumor markers.

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INTRODUCTION

CA 19-9 is a known tumor marker for different malignancies of the gastrointestinal tract, particularly pancreatic cancer. In these cases it is not only of diagnostic significance but is also a very good prognostic indicator[1-6]. Recent studies have pointed towards a diagnostic and prognostic role of CA 19-9 in extra-gastrointestinal tumors[7-8].

The aim of our study was to assessthe usefulness of CA 19-9 in the diagnosis of ovarian cancer because no comprehensive studies have been done on this in the past[9-10].

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CA 125 has been used for quite some time as an investigation forovarian malignancy as a rule of thumb. Many studies recently have questioned the reliability on CA 125 in suspected ovarian cancer, as CA 125 is often raised in a variety of non-ovarian pathologies like pelvic inflammatory disease, pregnancy and endometriosis. A lot of publications demonstrated that CA125 was not elevated in most primary ovarian mucinous neoplasms. Due to the scientific variability of true reliance on CA 125, many physicians recommend the additional use of CA19-9 as tumor marker in the diagnostic and prognostic workup of an ovarian mass[11-15].

We conducted this cross sectional study to determine the frequency of elevation of CA 19-9 in patients who had a histologically confirmed ovarian adenocarcinoma. The other aim was to find out whether CA 19-9 has any relation with the tumor size, distant metastasis or tobacco abuse.

MATERIAL AND METHODS

This multi departmental cross sectional study including 30 female patients was conducted in the departments of medicine, surgery and obstetrics & gynecology of Peshawar Institute of Medical Sciences, Peshawar, Pakistan between January 2016 and October 2017. The study was conducted after approval from the ethics review board of our hospital (sample anexed). The participants were recruited in the study from their scheduled follow up appointments from surgical OPD and an informed written consent was taken from each participant of the study during such visits.

The inclusion criteria were; 1) female patients 2) age range 18-70 years 3) biopsy proven ovarian cancer. Patients not fulfilling the above mentioned criteria were excluded from the study. Other exclusion criteria included pelvic inflammatory disease (PID), endometriosis and adenomyosis. Also patients with gynecologic tumors other than ovarian masses were excluded along with patients with cancers of the gastrointestinal system, inflammatory bowel disease, liver cirrhosis.

Those who satisfied the inclusion and exclusion criteria were subjected to a detailed clinical evaluation and relevant investigations. A total of 65 patients were assessed; out of which, only 30 fulfilled the strict inclusion/exclusion criteria and were thus included in this study. The study sample of 30 patients had their serum CA 19-9 measured.

A structured questionnaire (as annexed) with closed and open ended questions was designed for data collection including details like demography, clinical findings, histopathology report, and CA 19-9 levels. Data was stored and analyzed by SPSS version 21.

Percentages and frequencies were determined for qualitative variables like ethnic background, smoking status and others. Means and standard deviations were estimated for quantitative variables like age, tumor size and CA 19-9 levels. Frequency of raised CA 19-9 was determined. Elevated CA 19-9 was stratified amongst different confounder's like age group, smoking status, ethnicity, distant metastasis and tumor size. A *p* value of less than 0.05 was considered as standard criterion.

RESULTS

Mean age of all the participants was 54.30 ±10.52, the mean CA 19-9 was 64.67± 32.65 and the mean tumor size (cm) on CT pelvis was 4.83± 1.76. 36.7% (n=11) had distant metastasis while 50% (n=15) were either actively abusing tobacco or had exposureto passive smoking. The frequency of elevated CA 19-9 in patients with ovarian malignancy was 73.3% (n=22). A description of different demographic characteristics is given below (table 1).

CA 19-9 was elevated in 73.3% of the patients. 27.7% of the participants with biopsy proven ovarian cancer; however, had normal CA 19-9 levels. The minimum value of CA 19-9 was 22 U/L against a maximum value of 145 U/L. CT Pelvis was used to measure the diameter of the tumor, ranging from 2cm to 8cm. More details of these variables is given. (table 2).

The frequency of elevated CA 19-9 was stratified amongst different independent variables by using Chi-Square test (table 3), which showed that CA 19-9 was higher in patients with current or ex-tobacco abuse (n=17) rather than those with no tobacco abuse, $p<0.05$. Similarly, those with a tumor more than 5cm size had a higher CA 19-9 levels, $p<0.05$. CA 19-9 was more elevated in patients without distant metastases (n=12) than those with metastases (n=10), however this was not significant, $p>0.05$. A detailed description of these results is given(table 3).

Table 1: Descriptive statistics of different demographic characteristics of patients with biopsy proven ovarian cancer (n=30).

Variable	No of patients & %ages
Pakistani	24(80%)
Afghani	6(20 %)
Active tobacco abuse	15(50%)
Ex-tobacco abuse	5(16.7%)
No tobacco abuse	10(33.3%)
Married	23(76.6%)
Distant Metastases present	11(36.7%)
Elevated CA 19-9	22(73.3%)

Table 1: Descriptive statistics of the numerical variables (n=30).

Variable	Minimum	Maximum	Mean	SD
AGE	33	77	54.30	10.518
CA 19-9 (U/L)	22	145	64.67	32.657
Tumor Size (cm)	2	8	4.83	1.763

Table 1: Stratification of elevation CA 19-9 with respect to different effect modifiers by using Chi-Square test (n=30).

Variable		CA 19-9 elevated		Total (n)	P Value
		Yes	No		
Ethnicity	Pakistani	22	2	30	P <0.05
	Afghani	0	6		
Tumor size	>5cm	16	1	30	P=0.04
	<5cm	6	7		
Distant metastases	Present	10	1	30	P>0.05
	Not present	12	7		
Exposure to Tobacco	Exposed	17	3	30	P<0.05
	Not Exposed	5	5		

DISCUSSION

Gastrointestinal adenocarcinomas are the main cause of raised CA19-9. Nonetheless, it is noteworthy that although, CA19-9 is a diagnostic tumor marker in a number of gastrointestinal malignancies, ovarian tumors have been proposed as one of the causes of its elevation in the blood[10,15].

There are two sub-types ofprimary mucinous tumors of the ovaries. Namely; 1) the intestinal type (more common) and 2) the Müllerian type (the rarer)[10]. As CA 125 is secreted by the rarer of the two, that is, Mullerian type, which shows that the vast majority of ovarian mass lesions are of intestinal type that will not secrete CA 125[16].

As majority of the ovarian tumors are of intestinal type. Therefore, it is understandable that they will secrete CA 19-9 rather than CA 125. Therefore, CA 19-9 will be more reliable and a definite diagnostic marker for these tumors[15-17]. These observations are in accordance with our study where greater than two thirds of the patients with biopsy proven ovarian adenocarcinomas had elevated CA 19-9.

Magnetic resonance imaging (MRI) of the pelvis can aid in identifying the various subtypes of ovarian neoplasm. Similarly,it can precisely point towards the inborn behavior of the tumors. Based on these facts, MRI can assist in categorizing the grade and the aggressiveness of the lesions[18]. However, keeping in view the cost and availability of MRI in a country like Pakistan, CT Scan of pelvis is the preferred initial imaging modality. In our study, we used CT Scan of the abdomen and pelvis to measure the size and extent of the cancerous lesion. Our results showed that size of the lesion was proportional to the levels of the CA 19-9 levels. Our findings are in accordance with other studies which recommended that the best marker of ovarian malignancy is CA 19-9.[19-20].

Emin U et al suggested that, larger the ovarian tumor, higher the serum CA 19-9[21].This is again in accordance with our results. Our study showed that a size of ovarian tumor equal or greater than 5 cm is a strong predictor of elevated CA 19-9 than otherwise. Hence, CA 19-9 can be used as a marker of the likely size and the degree of aggression of the neoplastic lesion. Contrary to our observations, a retrospective study by Paul et al. failed to show a significant relationship between serum CA19-9 elevation and histologic subtype and size of the primary mucinous tumors of the ovary[10].

Considering that there are limited numbers of studies on this topic, we recommend further studies to evaluate the role of CA 19-9, as a marker of diagnosis and prognosis in ovarian malignancy. One limitation of our study was a small sample size. We therefore, recommend larger studies to further ellaborate the usefulness of CA 19-9 in non-gut malignancies especially the ovarian tumors.

CONCLUSION

CA 19-9 is elevated in patients with malignant ovarian tumors. Bigger the size of the ovarian adenocarcinoma, higher the CA 19-9 will be.

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AUTHOR'S CONTRIBUTION

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

Tahir AA: Concept, Design, Drafting, Manuscript

Kamal S: Data Acquisition,Drafting Manuscript, Bibliography

Waheed R: Drafting and proof reading.

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 investigated and resolved.