

## ACCURACY OF CA-125 CONCENTRATION AS PREDICTOR OF PERITONEAL DISSEMINATION OF COLO-RECTAL CARCINOMA

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### ABSTRACT

**Objective:** To determine the association of CA-125 levels with the peritoneal dissemination among the patients of colo-rectal carcinoma at a tertiary care surgical oncology unit of Pakistan

**Study Design:** Observational study.

**Place and Duration of Study:** Department of Surgical Oncology, Combined Military Hospital Rawalpindi. Duration of ten months, from Jan 2018 to Oct 2018.

**Patients and Methods:** A total of 83 cases of colorectal carcinoma were included in the study, which were diagnosed by consultant oncologist after relevant histological and radiological investigations. Peritoneal dissemination was confirmed during the surgery. CA-125 levels were assessed before the surgery and cut off of 35U/mL was used. Relationship of age, gender, raised CA-125, tumor metastasis and tumor differentiation was assessed with the presence of peritoneal dissemination among the patients suffering from colo-rectal cancer.

**Results:** Fifty nine patients were males and 24 were females. Mean age of the patients was 51.17 ( $\pm 3.395$ ). Out of 83 patients of colo-rectal cancer, 37.3% showed the presence of peritoneal dissemination while 62.7% had no peritoneal dissemination at the time of surgery. Forty one patients had raised levels of CA-125 while 42 had levels within the normal range. After applying the logistic regression we found that raised levels of CA-125 and metastatic illness had significant association with the presence of peritoneal dissemination among the patients of colo-rectal cancer.

**Conclusion:** CA-125 concentration emerged as a strong predictor of peritoneal dissemination of colo-rectal cancer in our study analysis. Routine checking of levels of this marker among the patients of Colon cancer may help in early recognition of the advancement of disease and help the surgical oncologists to manage it in a more effective way.

**Keywords:** CA-125, Cancer, Colo-rectal, Peritoneal dissemination.

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### INTRODUCTION

Colorectal cancer is a life threatening illness and despite all the screening and prevention campaigns is on a rise in all parts of the world<sup>1</sup>. Our country is no exception to this and patients of this disease are increasing with each passing day<sup>2</sup>. A number of invasive and noninvasive screening and diagnostic tools are available for early recognition and prediction of course of illness. Still a lot of research is going on to refine the process of screening and diagnosing this devastating illness<sup>3,4</sup>. Carbohydrate antigen 125

(CA-125) has been linked with various malignancies in the past including ovary, fallopian tubes, peritoneum, endometrium and stomach. Gender also has a link with the concentration of this marker. Its use in screening, diagnosing and predicting the course of malignancy is still debatable<sup>5,6</sup>. A lot of work has been done in this regard all over the world in order to assess the link of CA-125 with the dissemination and metastasis of colorectal carcinoma Gao *et al* concluded that CA 125 has been linked with the poorly differentiated and metastatic disease among the patients of colon cancer<sup>7</sup>. In a comparative study done at Taiwan CA 125 emerged as a better predictor of peri-toneal dissemination of colon cancer as compared to CEA<sup>8</sup>. A recent study done in china revealed that CA 125 concentration is

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also associated with liver metastases of colon cancer<sup>9</sup>. Therefore measuring the concentration of CA 125 may give an early alarm regarding the spread of this catastrophic illness which may result in early treatment leading to slow spread. Peritoneal dissemination and metastasis is not an unusual finding among the patients of colorectal cancer. Around 4 to 60 percent patients have disease spread to the peritoneum or other organs at the time of presentation<sup>10,11</sup> Liver, lung or bone metastatic lesions may be picked up on radiological investigations but peritoneal dissemination is usually assessed first at the time of surgery. If any tumor marker could predict it before the surgery, it may be of immense help to the treating surgeon. Local data is insufficient regarding this aspect of peritoneal dissemination of colon carcinoma. Studies are available on the epidemiology of colo-rectal cancer and its screening in Pakistan<sup>2,12</sup> but no study has so far been conducted to evaluate the association of tumor markers with the peritoneal dissemination of colorectal malignancy. This study was planned with the aim to determine the association of CA-125 levels with the peritoneal dissemination among the patients of colo-rectal carcinoma at a tertiary care surgical oncology unit of Pakistan.

### **PATIENTS AND METHODS**

This cross-sectional study was conducted at the department of surgical oncology Combined Military Hospital Rawalpindi from 1<sup>st</sup> January 2018 to 31<sup>st</sup> October 2018. Sample size was calculated by WHO sample size calculator. Non probability consecutive sampling technique was used to gather the sample. All patients between the age of 18 and 80 with the primary colorectal carcinoma diagnosed by a consultant oncologist after relevant histological and radiological investigations were included in the study. Exclusion criteria were the patients with secondary colorectal involvement or those who had received the neo-adjuvant radiotherapy or those who had past or current history of any malignancy other than the colorectal cancer. Patients who did not give consent were also not included in the final analysis. Ethical review board committee of the

hospital was approached to get the ethical approval for this study. Written informed consent was taken from all the potential participants of this study before the start of study after complete description of the study. Patients of colorectal cancer fulfilling the above men-tioned inclusion and exclusion criteria coming to oncology/ surgical OPD at Combined Military Hospital Rawalpindi were included in the study after all the ethical formalities. All the base line biochemical investigations were done as part of preoperative assessment. Histological diagnosis and degree of differentiation was confirmed by a consultant histopathologist. CT scan of chest, abdomen and pelvis was performed along with the colonoscopy. Variables in the study included age, gender, raised CA-125, tumor metastasis and tumor differentiation. Confounding variables were identified and adjusted by detailed history taking, examination and review of all the relevant investigations. Peritoneal dissemination is considered significant if gross seedling of tumor is found on the peritoneum during the surgery or there is omental involvement of the tumor<sup>13</sup>. Concentration of CA 125 was measured in the blood by radioimmunassay within 15 days prior to the surgery. Value of more than 35U/mL in the blood was considered as significantly high and labeled as abnormal<sup>14</sup>. Characteristics of participants and the distribution of the peritoneal dissemination were described by using the descriptive statistics. Participants were resulted by categorical compared by presence and absence of peritoneal dissemination. Chi-square was used to determine between-group variances in categorical correlates. Binary logistic regression analysis was done to evaluate the relationship of age, gender, raised CA-125, tumor metastasis and tumor differentiation with the presence of peritoneal dissemination of the colorectal cancer. All statistical analysis was performed using statistics package for social sciences version 24.0 (SPSS-24.0). Differences between groups were considered significant if *p*-values were less than or equal to 0.05.

## RESULTS

A total 90 patients were approached to participate in this study. Four did not give consent and three were having neo-adjuvant radio therapy. Therefore total 83 patients were included in the final analysis. Fifty nine patients were males and 24 were females. Mean age of the patients was 51.17 ( $\pm 3.395$ ). Out of 83 patients of colo-rectal cancer, 37.3% showed the presence of peritoneal dissemination while 62.7% had no peritoneal dissemination at the time of surgery. Forty one patients had raised levels of CA-125 while 42 had the levels within the normal range. Raised CA 125 and metastatic illness were found related to the presence of peritoneal dissemi-

may be due to peritoneal irritation by the tumor seedling. Exact reason is not known by this time and future research is required to ascertain this phenomenon in the patients suffering from a lethal disease of colorectal cancer. Relationship of peritoneal involvement and rise in the levels of CA 125 is strengthened by the results of studies on diseases involving peritoneum other than colorectal cancer. Peritoneal involvement in gastric cancer has also been linked with raised CA 125 levels<sup>17,18</sup>. Similarly non-cancerous diseases like tuberculosis when invaded peritoneum also causes a rise in the level of this marker<sup>19</sup>. A very interesting study demonstrated that surgical time also affects the level of rise in the CA 125 levels<sup>20</sup>. Longer the surgeon manipulates and

**Table: The correlated factors relating to presence of peritoneal dissemination among the patients of colorectal cancer: the binary logistic regression analysis.**

	<i>p</i> -value	Odds ratio	Confidence interval	
			lower	upper
Age (ref. is 50 years or less)	0.103	0.382	0.121	1.213
Differentiation	0.775	1.219	0.314	4.735
Gender (ref. is male)	0.604	0.732	0.226	2.376
Metastasis (ref. is no metastasis)	0.003	7.886	1.973	31.515
Concentration of CA 125 (ref. is <35U/ml)	<0.001	10.421	3.049	35.621

nation of tumor when chi-square was applied. After applying the logistic regression we found that raised levels of CA-125 and metastatic illness had significant association with the presence of peritoneal dissemination among the patients of colo-rectal cancer (table).

## DISCUSSION

It is the first study of its kind in a developing country like Pakistan assessing the association of a tumor marker with the dissemination of cancer. Various alimentary canal and pelvic cancers have already been associated with the high concentrations of CA 125 in the blood<sup>8,9,15,16</sup>. Our study also supported this association and raised serum CA 125 had a strong association with peritoneal dissemination of colorectal carcinoma. It was in accordance with the similar studies done in other parts of the world on this tumor marker<sup>6-9</sup>. Colon cancer is otherwise linked with CA 125 too but more association with peritoneal dissemination

irritates the peritoneum the more is rise in the CA 125 level. This finding also gives a clue that peritoneal dissemination of any illness is directly associated with production of CA 125 from its lining. This fact if proved in more sophisticated studies can be applied in various peritoneal ailments including the dissemination of colorectal carcinoma. Majority of the patients included in our study were male. Previously an epidemiological study done in Pakistan showed male predominance among the colorectal cancer patients<sup>2</sup>. It was believed that CA 125 is more elevated in females than males and ovaries are a natural source of it but studies have not supported this fact and gender usually has no direct association with raised levels of this marker. It is basically the disease process and peritoneal involvement which causes the rise in levels. In addition to the raised levels of CA 125 peritoneal dissemination was also associated with

the presence of metastatic illness. This finding is in association with the similar studies done in recent past on similar subject<sup>8,9</sup>. It seems quite logical that the cancer which has metastasized may have increased local filtration and it should have seeded I the local peritoneum. Therefore if there is radiological evidence of metastatic illness before the surgery, surgeon should keep his suspicion high regarding the peritoneal dissemination of the colorectal cancer. Our study has few limitations as well. Randomized selection of study subjects from all the colorectal patients was not done. Therefore, the results of the present study cannot be generalized. We used the cross-sectional study method. Therefore, the cause and effect relationships remain unclear and further studies to look into these associations using longitudinal epidemiological data are suggested. The sample was drawn from a tertiary care military oncological set up where usually soldiers and their first degree relatives are treated and referred from all the military hospitals of Pakistan which creates a lot of sampling bias regarding the severity of illness and time for the work up. Therefore longitudinal studies involving more sample size and sophisticated study design are suggested to ascertain the association between CA 125 and the peritoneal dissemination of the colorectal cancer.

## CONCLUSION

CA-125 concentration emerged as a strong predictor of peritoneal dissemination of colorectal cancer in our study analysis. Routine checking of levels of this marker among the patients of colon cancer may help in early recognition of the advancement of disease and help the surgical oncologists to manage it in a more effective way.

## CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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