Original article

Patterns of serum CEA levels in different clinico-pathological variables of colorectal cancer

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ABSTRACT

Background: Globally, colorectal malignancy is the 3rd most frequent cancer and the 2nd major cause of mortality. Serum carcinoembryonic antigen (CEA) is a simple tumor marker for the diagnosis, predicting response to therapy and survival and identifying the recurrence of colorectal cancer. Therefore, the aim was to evaluate the pattern of serum CEA levels in patients with colorectal cancer presenting at a tertiary care hospital in Karachi

Patients and methods: It was a cross-sectional study conducted at the Department of Medical Oncology of Jinnah Postgraduate Medical Center, Karachi from January till August 2019. One ninety-nine patients of 12-80 years age and either gender diagnosed with colorectal cancer (biopsy-proven) were included. Data on demographics, clinical and pathological findings were recorded in the pre-designed proforma. The serum CEA levels in colorectal cancer patients were assessed using an ELISA kit. CEA levels higher than 5.0 ng/mL were deemed as elevated CEA levels in colorectal patients. Data were analyzed using SPSS version 23.

Results: A total of 191 colorectal cancer patients were included. The mean age of the patients was 42.81±15.22 years. Most of the patients (61.3%) were male. Out of 191 colorectal cancer patients, 60 (31.4%) had CEA level 0-0.3 ng/ml, whereas 79 (41.4%) had elevated serum CEA level (>10 ng/ml). The CEA levels were stratified with respect to effect modifiers. The size of the tumor, TNM staging and localization and metastasis of cancer showed a statistically significant difference between levels of CEA ($p<0.05$).

Conclusion: The raised CEA levels are associated with clinically progressive or presence of residual and recurrent disease. For patients with progressive tumors, particularly colorectal carcinoma, CEA assays are an important guide to assess the burden of the tumor, hence clinicians and surgeons ought to monitor antigen levels. It is recommended to enhance the clinical efficacy of the CEA levels.

Keywords:

Colorectal cancer; CEA levels; Serum carcinoembryonic antigen; TNM staging

INTRODUCTION

Globally, colorectal malignancy is the 3rd most frequent cancer and the 2nd major cause of mortality. In 2018, according to WHO approximately 180,0000 cases of colorectal cancer have happened resulting in 862,000 fatalities. It is the 3rd and 2nd most commonly occurring cancer in males and females respectively.[1,2] The odds of having colorectal cancer is one in twenty males (4.5%) and one in twenty-four females (4.2%), this shows males are slightly more affected by it than females.[3] Large disparities in the rate of occurrence have been noted, the highest incidence has been observed in western Europe, Australia, North America and New Zealand, whereas the lowest in districts of South Central Asia and Central Africa.[4] In Pakistan, colorectal cancer is the most frequent malignancy among adults and the highest incidence has been reported for both genders as 5335 per 148,041 cases (3.6%).[5] According to a recent meta-analysis, the pooled prevalence of colorectal cancer is reported as 5% (range 4-6%) in the Pakistani population.[6] Serum carcinoembryonic antigen (CEA) is a simple tumor marker for the diagnosis, predicting response to therapy and survival and identifying the recurrence of colorectal cancer. CEA was first identified in extracts of human colon carcinoma. It plays a significant part as a ligand in the dissemination of cancer.[7-10] Approximately seventeen to forty-seven percent of colorectal cancer patients have raised serum CEA levels.[11, 12] Objective of this study was to evaluate the pattern of serum CEA levels in patients with colorectal cancer presenting at tertiary care hospital of Karachi, Pakistan. As this tumor marker is cost-effective and simple to use therefore it could be helpful for an oncologist in lessening the unnecessary and more costly diagnostic investigations.

Competing interests: The author declares no competing interests exist.

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PATIENTS AND METHODS

It was a cross-sectional study conducted at the Department of Medical Oncology of Jinnah Postgraduate medical center, Karachi from January till August 2019. The sample size of 191 colorectal cancer patients was estimated using the WHO sample size calculator by taking the statistics of high CEA level as 59.1%[13], margin of error as 7% and 95% confidence level. All the patients of age 12-80 years of either gender diagnosed with colorectal cancer (biopsy-proven) were included in the study. Patients with malignancy other than colorectal cancer, neoplastic and renal disorder, lung and liver diseases and pregnant females were excluded from the study. The non-probability consecutive sampling technique was applied to select the patients.

The study was undertaken after approval from the institutional ethical review committee. Informed consent from all the eligible patients was obtained before data collection. Data on demographics, clinical and pathological findings were recorded in the pre-designed proforma by the researcher. The grading of the tumor was assessed by cellular differentiation of tumor cells from normal cells, i.e. (G 1 Low grade to G4 Anaplastic), whereas the size of the tumor was assessed using radiological methods, i.e. CT Scan and MRI. The tumor stage was evaluated using AJCC, TNM system.

The serum CEA levels in colorectal cancer patients were assessed using an ELISA kit. CEA levels higher than 5.0 ng/mL were deemed as elevated CEA levels in colorectal patients. Data were analyzed using SPSS version 23. The numeric variables were presented as mean and standard deviation whereas nominal and categorical variables were presented as frequency and percentage. A chi-square test was applied to assess the relationship between potential effect modifiers and elevated serum CEA levels. A p-value of ≤ 0.05 was taken as statistically significant.

RESULTS

A total of 191 colorectal cancer patients were included in the study. The mean age of the patients was 42.81±15.22 years. One seventeen patients were males (61.3%) whereas 38.7% were females. Almost 63 patients had education till primary (33%) and 68.6% belonged from the middle socio-economic background. Out of 191, 167 (87.4%) of the colorectal cancer patients were married (Table 1).

Most patients had symptoms duration of less than 1 year (53.4%). The rectum was the most common site for tumor (33.5%), followed by the sigmoid colon (20.9%) and rectosigmoid (11.5%). Over half of the patients had a tumor of size >5 cm (58.6%). About 100 (52.4%) tumors were moderately differentiated.

Table 1. Demographic characteristics of the study participants

Characteristics	*n*	%
Gender		
Male	117	61.3
Female	74	38.7
Educational status		
Illiterate	30	15.7
Primary	63	33.0
Matric	62	32.5
Intermediate	24	12.6
Graduate	12	6.3
Socio-economic status		
Low (<15,000 rupees)	45	23.6
Middle (15,000-30,000 rupees)	131	68.6
High (>30,000 rupees)	15	7.9
Marital status		
Single	20	10.5
Married	167	87.4
Widow	4	2.1

Table 2. Clinico-pathological characteristics of the study participants

Characteristics	*n*	%
Duration of symptoms		
<1 year	102	53.4
=>1 year	89	46.6
Anatomical site		
Recto sigmoid	22	11.5
Sigmoid colon	40	20.9
Caecum	17	8.9
Rectum	64	33.5
Ascending colon	12	6.3
Splenic flexure	4	2.1
Descending colon	12	6.3
Transverse colon	10	5.2
Multiple sites	4	2.1
Anorectum	3	1.6
Hepatic	3	1.6
Tumor size		
<5	79	41.4
>5	112	58.6
Grade		
Unknown	5	2.6
Well-differentiated; Grade I	48	25.1
Moderately differentiated; Grade II	100	52.4
Poorly differentiated; Grade III	33	17.3
Undifferentiated; anaplastic; Grade IV	5	2.6
TNM Stage		
1	1	0.5
2	40	20.9
3	62	32.5
4	88	46.1
Localization recurrence/metastatic		
Localized	101	52.9
Recurrence/Residual	18	9.4
Metastatic	72	37.7
Site of metastasis		
Liver	34	17.8
Nodal	4	2.1
Peritoneal	17	8.9
Lung	13	6.8
Bone	3	1.6
Multiples site	1	0.5

Table 3. Comparison of clinicopathological characteristics with CEA levels

Characteristics	CEA levels				p-value
Duration of symptoms	**0-0.3 ng/ml**	**3.1-5.0 ng/ml**	**5.1-10.0 ng/ml**	**>10 ng/ml**	
<1 year	33	22	8	39	0.77
=>1 year	27	15	7	40	
Tumor size					
<5 cm	30	24	3	22	0.001
=>5 cm	30	13	12	57	
Grade					
Unknown	1	2	0	2	
Well differentiated; Grade I	16	12	2	19	0.838
Moderately differentiated; Grade II	34	15	9	41	
Poorly differentiated; Grade III	7	7	4	15	
Undifferentiated; anaplastic; Grade IV	2	1	0	2	
TNM staging					
1	1	0	0	0	
2	22	10	2	6	0.001
3	24	16	3	19	
4	13	11	10	54	
Localization recurrence/metastatic					
Localized	45	27	6	23	
Recurrence/Residual	6	2	0	10	0.001
Metastatic	9	8	9	46	

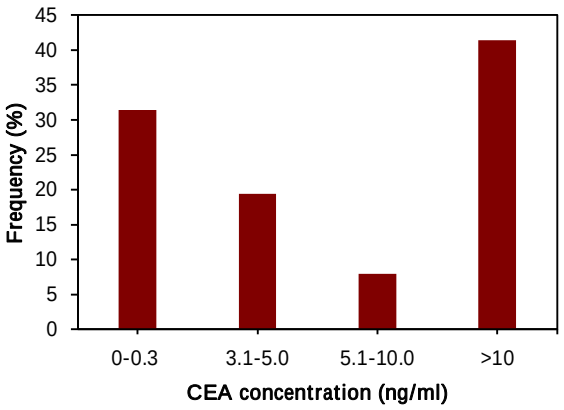

Figure 1. Frequency distribution of CEA levels

According to TNM staging, the majority of them presented in late stages of cancer, 46.1% of the patients had stage 4 followed by stage 3 (32.5%). In 37.7% of cases, metastasis was identified and among them, the liver was the most prevalent metastasis location (17.8%) (Table 2). Out of 191 colorectal cancer patients, 60(31.4%) had CEA level 0-0.3 ng/ml, whereas 79 (41.4%) had elevated serum CEA level (>10 ng/ml). The other categories of the CEA levels are displayed in Figure 1. The CEA levels were stratified with respect to effect modifiers. The size of the tumor, TNM staging and localization and metastasis of cancer showed a statistically significant difference between levels of CEA ($p<0.05$) (Table 3).

DISCUSSION

According to the National Institutes of Health (NIH), serum carcinoembryonic antigen (CEA) is one of the significant prognostic factors and a tumor marker in diagnosing colorectal cancer. The elevated levels of carcinoembryonic antigen (CEA) are highly associated with increased risk of different malignancies in ovaries, gastrointestinal tract, or lungs. Therefore, the present study has been conducted to determine the presence of CEA levels in the plasma in patients who were diagnosed with colorectal cancer.[14] Conferring to the present study, the patients of colorectal cancer had a mean age of 42.81±15.22 years with male preponderance (61.3%). However, the International Agency for Research on Cancer has reported that females are more likely at risk of developing colorectal cancer with a higher mortality rate in older ages.[15] On the contrary, researches have shown that the male gender is more likely to be associated with the prevalence of colorectal cancer among the Asian population. The surveys conducted in Korea, Japan, China, and Hong Kong have reported that the majority of the patients were males which are in agreement with the current study findings.[16-18] The anatomical distribution of colorectal cancer varies from patient to patient. In accordance with the present study, the majority of patients had cancer in the rectum, followed by a sigmoid colon. This explains that cancer cells can be certainly multiplied in this two anatomical distribution. In a study in Kenya, colorectal cancer was

disseminated uniformly across the anatomy nevertheless, the rectum and colon showed increased symptoms of obstruction and profuse bleeding.[16] The current study showed that 31.4% of patients had a CEA level between 0-0.3 ng/ml whereas 41.4% of patients had elevated serum CEA level >10 ng/ml. The identification of tumor biomarkers facilitates with survival rate. In a study, CEA levels showed a positive impact on the survival rate of the patients.17-19 In another local study conducted from Peshawar, CEA analysis was carried out between stomach and colon cancer patients. it was found that the CEA level was much higher in colon cancer. Moreover, CEA was fairly greater in patients having moderately differentiated histology as compare to well and poorly differentiated tumors.[13] Hence, the results were analogous to the present study. Comparable results have also been found out in previous studies. Moreover, in a comparative study sensitivity of CEA Levels in colorectal cancer patients was found high.[18] In an Iranian study, CEA levels were detected in more than 60% of patients and was found to be significantly associated with gastric cancer ($p = <0.05$). The CEA levels were also detected in patients having initial stage tumors however the majority of patients showed CEA levels in advanced stage.[19]

CONCLUSIONS

Carcinoembryonic antigen (CEA) is a sensitive serum marker for the detection of metastatic and recurrent colorectal cancer. The raised CEA levels are associated with clinically progressing or presence of the disease. The gradual rise in CEA levels is suggestive of local recurrence. The patients with progressive tumors, particularly colorectal carcinoma, CEA assays are the only guide to assess the burden of the tumor.

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