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Research Article

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Clinical Features of Colorectal Carcinoma at the Jinnah Postgraduate Medical Centre, Karachi, Pakistan: A Cross-Sectional Study

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Abstract

Introduction; Colorectal carcinoma is the third most common cancer worldwide. The risk factors for colon carcinoma include age, family history, obesity, dietary factors etc. Incidence of rectal carcinoma has been found to vary in different geographic. The current study was aimed to evaluate the clinical features, pathological features, association of age, gender, marital status, CEA level with lymph node involvement, metastasis and grading in colorectal carcinoma patients treated at Jinnah Post-graduate Medical Centre, Karachi.

Methods; This was an observational retrospective study conducted at the Oncology department of Jinnah Post-graduate Medical Centre Karachi. All the patients diagnosed with colorectal carcinoma whether having synchronous, metachronous or recurrent rectal carcinoma were included. Binary and mutinominal logistic regression model was implied to assess the association of lymph node involvement, metastatic disease at presentation and tumour grading with different covariants. IBM SPSS V.20 was used for statistical analysis.

Result; A total of 174 patients were included. Majority of the patients were males 112 (64.4%). The mean age of the patients was 44.43±14.02 years. Urdu speaking people made the greater part of study population 65 (34.5%). Sigmoid colon was the site involved in majority 65 (34.5%) of the cases and Mucinous adenocarcinoma was found in 174 (98.9%) of the patients. People with normal CEA levels were found more prone to have lymph node involvement than patient with raised CEA level (OR-3.727, 95% CI-1.437-9.668). Unmarried people were found to have less chances of a metastatic disease at presentation than married people (OR-0.351, 95% CI-0.126-0.976).

Conclusion: Higher incidence of colorectal carcinoma was observed in younger population in our study. Therefore, measures should be taken to promote screening of young population to detect patients in early phase of the disease and improve survival and decrease morbidity and mortality.

Keywords; Colorectal Neoplasms, Adenocarcinoma, Developing countries. Copyright: © 2021 The Authors. Published by Medical Editor and Educational Research Publishers Ltd. This is an open access article under the CC BY-NC-ND license (https://creativecommons.org/lic enses/by-nc-nd/4.0/).

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Introduction

Colorectal carcinoma (CRC) is the third most common cancer and fourth major cause of death from cancer worldwide.[1] This carcinoma affects both males and females but males being affected more than females.[2] Large bowel distal to splenic flexure is affected in majority of the cases, therefore sigmoidoscopy is the preferred tool for the purpose of screening.[3]

The risk factors for colon carcinoma include age, family history, inflammatory bowel disease (IBD), obesity, sedentary lifestyle, environmental and dietary factors etc. Incidence of rectal carcinoma been found to vary in geographies.[4] Despite being considered an old age disease, higher incidence of CRC has been reported in younger population of developing countries.[3, 5] The most common clinical presentation of colon cancer is hematochezia especially in patients having carcinoma involving recto-sigmoidal area. Young patients usually present with abdominal pain, rectal bleeding and altered bowel habits. Other symptoms can be fever. weight loss, abdominal mass anemia.[2,3,6]

Colorectal carcinoma is the fifth most common malignancy in Pakistan. The mean age of its presentation is approximately 36 years and major histopathological type being adenocarcinoma.[7,8] The most frequent used criteria for staging colorectal carcinoma is Dukes' staging system.[9] Patients can be given adjuvant therapies or clinical trials on the basis of this classification. Dukes' staging is classified into A, B and C depending on the extent of cancer margins whereas histological grading is beneficial in defining prognosis of colorectal cancer.[10]In younger individuals, the prognosis of CRC is poorer than the older ones.[11]

The current study was aimed to evaluate the clinical features, pathological features, risk factors and outcome of colorectal carcinoma patients treated at Jinnah Post-graduate Medical Centre, Karachi. We also tried to find any association of tumor grading, lymph node involvement and metastasis with age, gender, marital status, CEA level and family history.

It was an observational retrospective analysis of the patients diagnosed with colorectal carcinoma and treated in the Oncology department of Jinnah Post-graduate Medical Centre, Karachi. retrospectively evaluated the data of patients treated for colorectal carcinoma from January, 2017 to December, 2019 at Jinnah Post-graduate Medical Centre. All the patients diagnosed with colorectal carcinoma whether having synchronous (Metastatic disease at the time or within 6 months of the original diagnosis) [12], metachronous (Metastatic disease developing after 6 months of original diagnosis) or recurrent rectal carcinoma were included) [12] or recurrent rectal carcinoma were included. All the patients with Familial adenomatous polyposis, Squamous cell carcinoma of anal canal, rectal gastrointestinal stroma cell tumors (GIST) and metastatic tumors were exempted from this review. The data was collected through a self-administered proforma. The data collected included patient's demographic, anatomical site, grading, staging and treatment provided to the patients.

IBM SPSS version 22.0 was used for data analysis. Continuous data was presented in mean and standard deviation. Categorical data was presented in frequencies and percentages. Univariable logistic regression was used to find the association of lvmph node involvement. metastatic disease with age, gender, marital status, family history of colon cancer and CEA levels and presented as unadjusted odds ratios. Further multivariable analysis was used in a step wise manner to assess the association of lymph node involvement and presence of metastasis at presentation with the covariants and presented as adjusted odds ratios. Multi-nominal logistic regression analysis was used to assess the association of tumour grading with the covariants and presented as unadjusted odds ratios. Then covariants were removed in a step wise manner to see their effects and odds were presented as adjusted odds ratios. P-value of <0.05 was considered significant.

All ethical issues were addressed and the study was conducted in accordance with the declaration

Methods:

of Helsinki. IRB approval was also obtained from the institute.

Results:

We retrospectively reviewed the colorectal cancer patients who presented at Oncology department of JPMC from Jan, 2017 till Dec, 2019 and included a total of 174 patients who met our inclusion criteria. The mean age of the patients was 44.43±14.02 years. Majority of the patients were males 112 (64.4%). Most of the patients were married 149 (85.6%) and the rest were unmarried

25 (14.4%). Majority of the patients 119 (68.4%) did not had any co-morbid while in the rest diabetes mellitus was seen in 17 (9.8%), hypertension in 12 (6.9%), hepatitis C in 8 (4.9%), ischemic heart disease in 7 (4%), tuberculosis in 6 (3.4%), and hepatitis B was seen in 5 (2.9%) patients. Only 31 (17.8%) patients had a family history of colorectal cancer. Abdominal pain was the most communal presentation of the patients other presenting symptoms of the patients are presented in **table 1**.

Table 1; Presenting sign and symptoms of patients.

Presenting sign and symptoms	N (%)
Abdominal pain	90 (51.7)
Bleeding per rectum	20 (11.5)
Weight loss	20 (11.5)
Constipation	17 (9.8)
Altered bowel habits	11 (6.3)
Obstruction	10 (5.7)
Lump in abdomen	6 (3.4)

Urdu speaking people made the greater part of study population 60 (34.5%), 51 (29.3%) were Sindhi, 23 (13.2%) were Punjabi, 20 (11.5%) were Pathan/Pashtun, only 5 (2.9%) were Baloch and

15 (8.6%) patients were from other minor ethnic groups.

Sigmoid colon was the site involved in 60 (34.5%) of the cases, other sites involved are shown in **table 2**.

Table 2; Anatomical site involved in colorectal cancer patients.

Site of tumor	N (%)
Rectum	18 (10.3)
Sigmoid Colon	60 (34.5)
Right Colon	38 (21.8)
Left Colon	18 (10.3)
Transverse colon	16 (9.2)
Cecum	15 (8.6)
Splenic flexure	9 (5.2)

When histology of the carcinoma was observed Mucinous adenocarcinoma was found in 172 (98.9%) of the patients and 2 (1.1%) had Signetring cell type. The T3 stage tumor was detected in majority 80 (45.9%) of the patients followed by T4 stage in 70 (40.2%), T2 tumors in 19 (10.9%) and T1 stage tumors in 5 (2.9%) patients. N1 and N2 disease was seen in 78 (44.8%) and 29 (16.7%) patients respectively while the rest 67 (38.5%) had no nodal involvement. Metastatic disease was diagnosed in 60 (34.55%) patients.

Moderately differentiated tumor was detected in 104 (59.8%) cases, poorly differentiated disease was seen in 53 (30.5%) patients and well differentiated tumor was diagnosed in 17 (9.8%) patients. CEA level was normal in 131 (75.3%) cases and elevated in the rest.

Univariable logistic regression analysis was unable to show any association of lymph node

involvement and metastatic disease at presentation with age, gender, marital status and family history

of colon cancer. However after adjusting for other covariants using multi variable logistic regression it was observed that people with normal CEA levels were 3 times more prone to have lymph node involvement than people with elevated CEA level (OR-3.727, CI 95% 1.442-9.768). Similarly unmarried people were found to have less chances of a metastatic disease at presentation than married people (OR-0.351, CI 95% 0.126-0.976). Disease metastasis was not found to be affected by patient's age, gender, marital status, family history and CEA level. Multi-nominal logistic regression showed that patients age, gender, marital status, family history of colon cancer and CEA level did not pose any extra risk to patients for having moderately or poorly differentiated tumours than well differentiated tumour table 3.

Table 3; Odds of lymph node involvement, metastatic disease at presentation and grading of tumour using binary and multinominal logistic regression analysis.

Lymph node	Unadjusted ORs	P-value	Adjusted ORs	P-value
involvement	(CL 95%)		(CL 95%)	
Age	0.514 (0.150.1.505)	0.000	0.402 (0.445.4.600)	0.000
0-40 years	0.514 (0.173-1.525)	0.230	0.482 (0.145-1.600)	0.233
41-60 years	0.758 (0.264-2.172)	0.605	0.640 (0.206-1.983)	0.439
Gender				
Male	0.954 (0.481-1.858)	0.871	0.915 (0.446-1.874)	0.807
Marital status				
Single	0.543 (0.192-1.534)	0.249	0.607 (0.185-1.988)	0.409
Family history				
Positive	1.082 (0.472-2.482)	0.852	0.946 (0.397-2.251)	0.899
CEA level				
Normal	3.337 (1.311-8.494)	0.110	3.752 (1.442-9.768)	0.007
Metastasis presence				
Age				
0-40 years	1.084 (0.336-3.130)	0.881	1.506 (0.470-4.825)	0.491
41-60 years	1.250 (0.437-3.576)	0.677	1.290 (0.430-3.868)	0.649
Gender				
Male	0.709 (0.366-1.373)	0.308	0.670 (0.336-1.334)	0.254
Marital status				
Single	0.452 (0.192-1.064)	0.069	0.351 (0.126-0.976)	0.045
Family history				
Positive	0.906 (0.409-2.004)	0.807	0.813 (0.357-1.851)	0.622
CEA level				
Normal	1.843 (0.913-3.720)	0.088	2.034 (0.982-4.214)	0.056
Well differentiated	Unadjusted ORs (CI 95%)	P-value	Adjusted ORS (CI 95%)	P-value
Age			` ′	
0-40 years	0.538 (0.081-3.569)	0.521	0.647 (0.086-4.8640	0.672
41-60 years	0.609 (0.091-4.056)	0.608	0.486 (0.068-3.463)	0.471
Gender				
Male	1.444 (0.438-4.754)	0.546	1.558 (0.453-5.362)	0.482
Marital status				
Single	0.440 (0.088-2.195)	0.316	0.360 (0.058-2.239)	0.273
Family history				

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0.881 (0.213-3.646)	0.881	0.800 (0.186-3.449)	0.765
2.275 (0.456-11.362)	0.316	2.548 (0.498-13.045)	0.262
0.513 (0.149-1.783)	0.289	0.750 (0.201-2.799)	0.669
0.768 (0.224-2.635)	0.675	0.744 (0.211-2.626)	0.645
1.258 (0.636-2.488)	0.510	1.312 (0.645-2.670)	0.454
0.324 (0.231-0.799)	0.114	0.323 (0.112-0.933)	0.323
0.790 (0.343-1.822)	0.790	0.729 (0.307-1.730)	0.473
0.894 (0.418-1.912)	0.772	0.995 (0.454-2.180)	0.989
	2.275 (0.456-11.362) 0.513 (0.149-1.783) 0.768 (0.224-2.635) 1.258 (0.636-2.488) 0.324 (0.231-0.799) 0.790 (0.343-1.822)	2.275 (0.456-11.362) 0.316 0.513 (0.149-1.783) 0.289 0.768 (0.224-2.635) 0.675 1.258 (0.636-2.488) 0.510 0.324 (0.231-0.799) 0.114 0.790 (0.343-1.822) 0.790	2.275 (0.456-11.362) 0.316 2.548 (0.498-13.045) 0.513 (0.149-1.783) 0.289 0.750 (0.201-2.799) 0.768 (0.224-2.635) 0.675 0.744 (0.211-2.626) 1.258 (0.636-2.488) 0.510 1.312 (0.645-2.670) 0.324 (0.231-0.799) 0.114 0.323 (0.112-0.933) 0.790 (0.343-1.822) 0.790 0.729 (0.307-1.730)

Surgery with adjuvant chemotherapy was the treatment used in 80 (45.9%) of the cases. Other treatment methods used were palliative chemo or radio in 34 (19.5%) cases, surgery alone was used in 17 (9.8%), chemotherapy was given to 14 (8%) patients, palliative care was provided to 24 (13.8%) patients and therapeutic chemo with concurrent radiotherapy was used in 5 (2.9%) patients. On follow up many of the patients 125

(71.8%) were lost. Among the remaining 22 (12.6%) got completely cured, 12 (6.9%) had progressive disease, stable response was noted in 8 (4.6%), partial response was seen in 1 (0.6%) and 6 (3.4%) patient had died during the treatment. Tumor recurrence was seen in only 8 (4.6%) patients.

Discussion:

Colorectal carcinoma is the one top three most prevalent cancers around the world but in Pakistan it is the fifth most common malignancy. Many risk factors have been implicated in its pathogenesis and a positive family history being considered as the major risk factor for this cancer. Although, CRC is considered as the disease of elder group but recent data in our region showed a significant number of young adults being diagnosed with this condition.[1, 2, 7]

In our study 42% of the patients were below 40 years of age. Studies previously conducted in our district have also reported higher incidence of

CRC in young population. Taha et al [13], in his study from Sudan stated that 43.84% of CRC patients were younger than 50 years of age. Saluja et al [14] registered 42% incidence of CRC in people of age below 40 years. A study conducted in Pakistan by Pirzada et al [2] has showed that 43.8% of CRC patients in their study were below 40 years of age. These results illustrate an alarming scenario and require that screening should also be done in younger population so that the disease can be detected early and treatment initiated promptly to improve the outcomes. Our study revealed that males 64.4% were more frequently affected by this cancer than the female

35.6%. This result is similar to a previous study conducted in Pakistan in which 70% of patients were male.[1] Majority 34.5% of patients in our study were Urdu speaking people followed by 29.3% Sindhi speaking ethnic group. This could be due to the reason that our tertiary care hospital is situated in Karachi where bulk of the population is Urdu speaking.

Adenocarcinoma was the most common histological type of CRC in our study with 98.9% of patients having this type of cancer. Our findings aligned to a study of United States in which similar findings (96%) were observed.[15] Another study from Iran had results comparable to ours with 95% of the patients having adenocarcinoma.[16] The most frequent tumor site found in our study was sigmoid colon in 35% of

patients followed by ascending colon in 21%, 11% had rectum involved. These results are alike to a cohort by Schmuck et al [17] which reported sigmoid colon as the most frequent site involved in CRC. Contrary to our study, where only 11% had rectal involvement, a study in Iran conveyed that almost 45% of cases had rectum involved. [16] Majority of patients in our study presented at stage III 47% followed by stage IV 41%. These findings are parallel to the studies conducted in Pakistan where 90.5% of the patients had advance stage disease. [1] Our outcomes are different to an Iranian study where 33% had stage III and 24% had stage IV disease.[16] This contradiction might be due to smaller sample size of our study as compared to Iranian study. Another possibility could be geographical variation. Synchronus carcinoma was observed in 85.6% of cases in our study which is comparable to a study by Ubink et al [18] who reported synchronous colorectal carcinoma in 91.4% cases.

Tumor markers like CEA, CA19-9 and CA 72-4 are beneficial in determining the prognosis and recurrence rate of colorectal carcinoma. A study conducted by Wu et al [19] found a positive association of CEA levels with depth of invasion, TNM stage, lymph node metastasis, recurrence within two years after the operation. In our study, CEA levels were normal in 75.3% of the patients and we were unable to find any association of levels with stage of tumor, tumor CEA differentiation and lymph node metastasis. This finding has raised questions on the efficacy of tumor marker in CRC diagnosis and prognosis. Therefore, we recommend that further studies should be carried out to determine the prognostic value of CEA level in CRC patients in our country.

One of the limitations of the study was its smaller sample size, a study with a bigger sample size would have provide more insight. This is a single centre based and a multi centre study will help to give a more clear image relating to frequency of CRC.

Conclusion:

Unfortunately our study demonstrated that people of young age are being diagnosed with CRC. Therefore, measures should be taken to promote

screening of young generation especially those having positive family history. The patients mostly presented in the late stages of the disease which raise questions on the effectiveness of the screening programs and awareness about the disease among population. Therefore, we recommend that awareness campaigns should be organized to improve people awareness and screening programs should be initiated to detect people in early phase of the disease and improve survival and reduce morbidity.

Conflict of interest: None

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