

# Clinical spectrum of colorectal cancer: Experience of 186 patients from Jinnah Postgraduate Medical Centre Karachi

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## ABSTRACT

**Background:** Colorectal cancer (CRC) is a major cause of morbidity and mortality globally and its incidence raising among younger age group in recent years have been observed. The aim of this study was to evaluate the clinical presentation of older (>50 years) and younger (≤50 years) patients with colorectal cancer at tertiary care hospital of Karachi.

**Patients and methods:** It was a cross-sectional study conducted at the Oncology Department of Jinnah Postgraduate Medical College, Karachi Pakistan from March 2017 to July 2018. The non-probability consecutive sampling technique was employed. Total of 186 patients aged 16-80 years of either gender with biopsy proven diagnosis of colorectal cancer were included in the study. Patients presented with other large bowel disease or non-malignant tumors confirmed on histopathology were excluded. Information regarding socio-demographic and clinicopathologic factors and treatments were obtained from all the patients.

**Results:** Total of 186 patients were included in the study. Among them, 144 (77.4%) patients were less than 50 years of age and 42 patients (22.6%) were greater or equal to 50 years of age. In all, most of the subjects presented with abdominal pain (17.7%), followed by change in bowel habit (17.2%), weight loss (15.6%), constipation (13.4%), anorexia (11.8%), bleeding per rectum (12.4%), hematochezia (7.5%) and anemia (4.3%). The rectum was the most frequent site (72.5%) for colorectal cancer, followed by rectosigmoid (8.1%). Microscopically, adenocarcinoma was the most common histopathological tumour in 157 (84.4%) patients followed by mucinous adenocarcinoma (10.8%) and signet ring cell carcinoma (3.8%) and squamous cell carcinoma (2.2%). About 41.9% of the tumors were moderately differentiated. According to the TNM staging of cancer, 42.5% were identified as being in late stages (TNM Stage III & IV) and only 1.6% were in stage I. Among 186 patients, liver was observed as the most frequent site of metastasis (5.4%).

**Conclusion:** In the present study frequency of colorectal cancer was discovered high in ages ≤50 years. It showed colorectal cancer found to influence more Pakistani patients at early age as compared to older patients. There is a great need of awareness about the potential factors and screening decisions for CRC in young adults.

## Keywords:

Colorectal cancer, Age stratification, Treatment modalities, Potential factors, Rectum, Adenocarcinoma, Rectal

## INTRODUCTION

The development of cancer in the areas of large intestine including rectum or colon is known as colorectal cancer (CRC).<sup>1</sup> In United States, CRC is the third most common cancer among males and females. As per “The American Cancer Society” approximately one of every 22 males (4.49%) and one out of 24 females (4.15%) are at risk of developing CRC in their lifetime.<sup>2</sup> It was estimated that 8.8 million deaths occurred due to cancer worldwide in year 2015 among them colorectal cancer causes about 774,000 deaths.<sup>3</sup> The high incidence rate of colorectal cancer has been observed in New Zealand, Australia, US, Canada and Europe, whereas the lowest incidence rate has been

observed in countries including India, China, parts of South America and Africa.<sup>4</sup> Pakistan is considered as a low risk zone for CRC.<sup>5</sup> In an analysis by Bhurji et al, a crude incidence rate of CRC was reported as 3.2 to 4.5%.<sup>6</sup> According to meta-analysis conducted in Pakistan in year 2018, the incidence of CRC is reported as 5-19%.<sup>7</sup>

In US, the incidence of CRC is increasing among individuals aged 20-49 years.<sup>8</sup> By 2030, regardless of increasing age of populace roughly 23% of rectal and 11% of colon malignancies are expected to be diagnosed in patients below the age of 50.<sup>9</sup> In Pakistan 52.1% of the patients were younger and 47.8% were older at the time of diagnosis of CRC.<sup>10</sup> However, the fundamental components and reasons for the raise in the incidence of CRC among younger populace are inadequately comprehended and explained.<sup>11</sup> The differences among the various clinicopathologic and

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sociodemographic features of CRC patients with respect to age may give an essential knowledge into mechanisms that have added to increasing prevalence of CRC in younger populaces.<sup>11</sup>

According to the previous literature in recent years the raise in incidence of CRC among younger age group have been observed. The aim of this study was to evaluate the clinical presentation of older (>50 years) and younger (≤50 years) patients with colorectal cancer at tertiary care hospital of Karachi.

## PATIENTS AND METHODS

It was a cross-sectional study conducted at the Oncology Department of Jinnah Postgraduate Medical College, Karachi Pakistan from March 2017 to July 2018. The ethical review committee approval was sought before the conduct of study. The sample size of 186 patients was obtained by using open epi online sample size calculator. The statistics considered for sample size estimation was 50%<sup>12</sup> patients presented with colorectal cancer under the age of 50 years margin of error as 7.2% and 95% confidence level. The non-probability consecutive sampling technique was employed. All patients aged 16-80 of either gender with biopsy proven diagnosis of colorectal cancer were included in the study. Patients presented with other large bowel disease or non-malignant tumors confirmed on histopathology were excluded. Informed written and verbal consent was taken from all the patients. Information regarding socio-demographic and clinicopathologic factors were obtained from all the patients. Patient's socio-demographics included the data of age, gender, marital status, socio-economic status and residence. Clinicopathologic characteristics included duration of disease, clinical presentation, anatomical site of tumor, histologic type, grade and TNM stage of cancer at the time of diagnosis.

Statistical Package for Social Sciences (SPSS) version 23 was used to perform analysis of data. Descriptive statistics including mean, standard deviation, frequencies and percentages were calculated for quantitative and qualitative variable respectively. Patient's age were categorized into two groups i.e. <50 years and ≥50 years. The clinicopathological pattern were compared between both groups using chi-square test. A p<0.05 was considered as statistically significant.

## RESULTS

Total of 186 patients were included in the study. The mean age of the patients was 37.19±14.61 years ranging from 16-80 years. Majority of the patients (n=144,

Table 1. Socio-demographic factors

Characteristics	n (%)
<i>Age groups</i>	
<50 years	144 (77.4)
≥50 years	42 (22.6)
Mean±SD	37.19±14.61
<i>Gender</i>	
Male	113 (60.8)
Female	73 (39.2)
<i>Marital status</i>	
Married	107 (57.5)
Unmarried	79 (42.5)
<i>Socio-economic status (monthly income)</i>	
Low (<15000 PKR)	98 (52.7)
Middle (15,000-35,000 PKR)	71 (38.2)
High (>35,000 PKR)	17 (9.1)
<i>Smoker</i>	
Yes	12 (6.5)
No	174 (93.5)
<i>Pan/Gutka chewer</i>	
Yes	22 (11.8)
No	164 (88.2)
<i>Family history of malignancy</i>	
Yes	13 (7)
No	173 (93)

77.4%) were less than 50 years of age and 22.6% (n=42) of patients were greater than and equal to 50 years of age. One hundred and 13 patients were males (60.8%) whereas 73 patients (39.2%) were females. Most of them were married (57.5%) and belong to low socioeconomic status (52.7%). Out of 186 cases, 12 (6.5%) were smokers, 22 (11.8%) were pan/gutka consumers and 13 (7%) had family history of malignancy (Table 1).

One hundred and ten patients presented with more than and equal to 1 years of symptoms duration. In all, most of the subjects presented with abdominal pain (17.7%), followed by change in bowel habit (17.2%), weight loss (15.6%), constipation (13.4%), anorexia (11.8%), bleeding per rectum (12.4%), hemochezia (7.5%) and anemia (4.3%). The rectum 135 (72.5%) was the most frequent site for colorectal cancer, followed by rectosigmoid (8.1%). Microscopically, adenocarcinoma was the most common histopathological tumour in 157 (84.4%) patients followed by mucinous adenocarcinoma (n=20, 10.8%) and signet ring cell carcinoma (n=7, 3.8%) and squamous cell carcinoma (n=1, 2.2%). About 78 (41.9%) of the tumors were moderately differentiated. According to the TNM staging of cancer, 79 (42.5%) were identified as being in late stages (TNM Stage III & IV) and only 3 (1.6%) were in stage 1. Among 186 patients, liver was observed as the most frequent site of metastasis (5.4%) (Table 2).

The age was divided into two groups (<50 years and ≥50years) and stratified for clinicopathological

features. The anatomical site of tumor showed statistical difference when compared with age ( $p < 0.05$ ) (Table 3).

**Table 2. Clinicopathologic characteristics**

Characteristics	n (%)
<i>Duration of symptoms</i>	
<1 year	76 (40.9)
≥1 year	110 (59.1)
<i>Clinical presentation</i>	
Constipation	25 (13.4)
Abdominal pain	33 (17.7)
Anorexia	22 (11.8)
Weight loss	29 (15.6)
Change in bowel habit	32 (17.2)
Bleeding per rectum	23 (12.4)
Hematochezia	14 (7.5)
Anaemia	8 (4.3)
<i>Anatomical site of tumor</i>	
Caceum	4 (2.2)
Ascending colon	9 (4.8)
Transverse colon	4 (2.2)
Descending colon	5 (2.7)
Sigmoid colon	8 (4.3)
Rectosigmoid	15 (8.1)
Rectum	106 (57)
Anorectum	17 (9.1)
Anus	11 (5.9)
Multiple sites	7 (3.8)
<i>Histopathological type of cancer</i>	
Adenocarcinoma	157 (84.4)
Mucinous adenocarcinoma	20 (10.8)
Signet ring cell carcinoma	7 (3.8)
Squamous cell carcinoma	2 (1.1)
<i>Tumor grade</i>	
Well differentiated	27 (14.5)
Poorly differentiated	81 (43.5)
Moderately differentiated	78 (41.9)
<i>Stage of cancer</i>	
Stage 1	3 (1.6)
Stage 2	17 (9.1)
Stage 3	79 (42.5)
Stage 4	79 (42.5)
Unknown	8 (4.3)
<i>Localization recurrence/metastasis</i>	
Liver	10 (5.4)
Bone	5 (2.7)
Brain	3 (1.6)
Pulmonary embolism	2 (1.1)
Peritoneal	7 (3.8)
Lung	5 (2.7)
Multiple sites	7 (3.8)
<i>Surgery done</i>	
Yes	85 (45.7)
No	101 (54.3)
<i>Treatment given</i>	
Radiotherapy	11 (5.9)
Chemotherapy	81 (43.5)
Both chemo and radiotherapy	92 (49.5%)

## DISCUSSION

In the current study total 186 patients of colorectal cancer were included with age range of 16-80 years (mean 37.9 years). It has been observed that frequency of colorectal cancer is higher among the age ≤50 years as compared to >50 years in our area. In a recent study conducted at Previous local and international studies have quoted high incidence of CRC among younger patients, which is comparable to findings of this study.<sup>10, 12-15</sup> Usually, risk of CRC increased after the age of 45 years and most of the patients were over the age of 50 years (90%).<sup>16, 17</sup> However, now a days occurrence of CRC among the age group 20-40 years has been increased by 17-20%.<sup>9</sup> Still the actual factors behind these outcomes are unclear. It might be possible that occurrence CRC at early is due to the consequences of genetic mutation, dietary habits, drug addictions or lack of physical activities.

In the present study there were 113 males and 73 females. The proportion of men was significantly higher as compared to females. The ratio of male to female was 1.5:1. Thus the present study showed that males contributed more to CRC than females. The similar observations for male predominance have been reported in many previous studies.<sup>1, 18, 19</sup>

Marital status is an important psychological & prognostic factor for many cancers.<sup>20-23</sup> In the present study the proportion of married CRC patients is higher than unmarried patients. In the study by Liu et al. showed the similar proportion.<sup>24</sup> Many various previous literature showed that being married at the time of diagnosis of CRC is related with a better prognosis as compared to single, widowed, separated or divorced.<sup>22, 23, 25-27</sup>

Low socioeconomic status (SES) background is an individual risk factor for the incidence of CRC.<sup>28, 29</sup> In the present study proportion of low income status (52.7%) is high as compared to middle and high SES. In a previous study from Canada and US, low SES contributed more to the incidence of CRC than high SES groups. The reason behind this might be due to expanse and choice of treatment.<sup>30</sup> In Pakistan the prevalence of CRC is high among middle followed by higher SES.<sup>5</sup>

In the present study, a positive family history of malignancy (CRC) (first degree relative had CRC) was reported among 7% of the cases, this percentage is higher than 4.3% and 5.4% reported in previous studies.<sup>31, 32</sup> However, Kumar and coworkers from Oman reported slightly higher proportion (8.6%) than

Table 3. Comparison of clinicopathological features with respect to age of the patients

Clinicopathological features	Age, n (%)		Total	p-value
	≤50 years	>50 years		
<i>Clinical presentation</i>				
Constipation	22 (15.3)	3 (7.1)	25 (13.4)	0.173
Abdominal pain	23 (16)	10 (23.8)	33 (17.7)	0.24
Anorexia	19 (13.2)	3 (7.1)	22 (11.8)	0.258
Weight loss	21 (14.6)	8 (19)	29 (15.6)	0.48
Change in bowel habit	27 (18.8)	5 (11.9)	32 (17.2)	0.301
Bleeding per rectum	19 (13.2)	4 (9.5)	23 (12.4)	0.52
Hematochezia	8 (5.6)	6 (14.3)	14 (7.5)	0.06
Anaemia	5 (3.5)	3 (7.1)	8 (4.3)	0.302
<i>Stages of cancer</i>				
Stage 1	2 (1.4)	1 (2.4)	3 (1.6)	0.823
Stage 2	13 (9)	4 (9.5)	17 (9.1)	
Stage 3	61 (42.4)	18 (42.9)	79 (42.5)	
Stage 4	63 (43.8)	16 (38.1)	79 (42.5)	
Unknown	5 (3.5)	3 (7.1)	8 (4.3)	
<i>Type of cancer</i>				
Adenocarcinoma	117 (81.3)	40 (95.2)	157 (84.4)	0.158
Mucinous adenocarcinoma	18 (12.5)	2 (4.8)	20 (10.8)	
Signet ring cell carcinoma	7 (4.9)	0	7 (3.8)	
Squamous cell carcinoma	2 (1.4)	0	2 (1.1)	

the present study.<sup>18</sup> This concludes that genetic factors could play an important part in the development of CRC and suggest family screening for genetic mutations. In the present study, majority of the patients presented with abdominal pain, change in bowel habit and weight loss. In a similar study, weight loss, bleeding per rectum & abdominal pain were the most common clinical presentations.<sup>33</sup> In a study from Pakistan, 41% of the patients were presented altered bowel habits, tenesmus and obstructive bowel symptoms.<sup>12</sup> According to previous literature which demonstrated that bleeding per rectum especially when diagnosed in older age and in combination with abdominal pain & change in bowel habits can reasonably predict incidence of CRC.<sup>34, 35</sup> It is recommended that early referral and investigation of colorectal in patients presented with change in bowel habits, rectal bleeding and anemia may improve the outcomes.<sup>32</sup>

Present study showed that majority of the patients had rectum anatomical site of CRC (57%). Similar finding has been observed for rectum in other studies.<sup>15,36</sup> Finding of current study is also supported by the systematic review conducted at Sub Saharan Africa, which reported rectum as major anatomical site (in 46% of the cases).<sup>37</sup> In the present study most of the patients presented with TNM stage 3 and 4 (42.5%). Adenocarcinoma is the most frequent histological type (84.4%) with poorly differentiated tumors accounting for 43.5% of the cases. Chalya and coworker found adenocarcinoma as the most frequent histological type (98.8%) with moderately differentiated tumors

accounting for more than 50% of cases.<sup>32</sup> Another study by Missaoui and coauthors also reported adenocarcinoma among 90.9% of the cases with moderately differentiated tumors accounting for 76.7% of cases.<sup>38</sup> The low standard of education, inadequate diagnosis and therapeutic tool, lack of awareness are the major barriers for the late presentation of CRC patients.

In the present study, the age was divided into two groups for risk stratification with respect to clinicopathological features. Among the age≤50 years majority of the patients were presented with the change in bowel habit (18.8%), adenocarcinoma (81.3%) & stage 4 (43.8%). Among the age>50 years majority of the patients were presented with abdominal pain (23.8%), adenocarcinoma (95.2%) and stage 3 (42.9%).

The outcomes of the present study conducted at Pakistan suggest the requirement for future research on the cost-viability of earlier-age screening policies for CRC with minimal cost and risk fecal testing, and further research on survival care in these young, aggressively treated patients.

## CONCLUSION

CRC is found to influence more patients at an age of 50 years or younger studied in the local patient population represented at JPMC Karachi. Increasing awareness about the potential contributing factors for the disease and appropriate screening programs is emphasized.

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