

# Clinicopathological Features of Colorectal Carcinoma in a Tertiary Care Center of North India – A retrospective study

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## Abstract

Colorectal carcinoma(CRC) is the third most commonly diagnosed cancer in males and second in females,with 1.8million new cases and almost 861,000 deaths in 2018 according to the World Health Organisation,rates being substantially higher in males than in females.In India,it is the fourth most common cause of cancer in males and the third most common cause of cancer in females.In Kashmir region,colorectal carcinoma was fourth most common cancer in males and held a third rank among the female population.CRC is the cancer of old age,mostly occur after fifth decade of life.

**Key words:** Colorectal cancer, Rectal bleeding, Adenocarcinoma

## INTRODUCTION

Colorectal carcinoma is the third most commonly diagnosed cancer in males and second in females, with 1.8 million new cases and almost 861,000 deaths in 2018 according to the World Health Organization, rates being substantially higher in males than in females.<sup>[1]</sup>

In the US, approximately 145,600 new cases of large bowel cancer are diagnosed annually<sup>[2]</sup> out of which approximately 50,630 Americans die of colorectal cancer (CRC), accounting for approximately 8% of all cancer deaths.

Although colorectal carcinoma is thought to be a rare disease in Asia, an increasing trend in its incidence has been observed lately.<sup>[2,3]</sup>

Compared to the Western world, the incidence rates of CRC are low in India; but apart from geographical variations, the incidences are rising rapidly in India.<sup>[4]</sup>

In India, it is the fourth most common cause of cancer in males and the third most common cause of cancer in females.<sup>[2]</sup> The age-standardized rates of CRC in India have been estimated to be 4.2 and 3.2/100,000 for males and females, respectively, compared to 35.3 and 25.7, respectively, in the USA.<sup>[3,4]</sup>

In Kashmir, colorectal carcinoma was fourth most common cancer in males and held a third rank among the female population. It was found overall in 616 (7%) patients, (342 males and 274 females) with a median age of 53 years in males and 50 years for females.<sup>[5]</sup>

CRC is the cancer of old age, mostly occur after the fifth decade of life.<sup>[6]</sup> However, the incidence of CRC is increasing in young age, especially in developing countries, which is mainly contributed by change in lifestyle and food habits.<sup>[7-10]</sup>

In general, colorectal carcinoma is thought to be a malignancy that primarily occurs in patients older than 50 years of age;<sup>[11]</sup> likelihood, the disease is an unusual in patients under 40 years of age. It has been estimated that between 2% and 3% of CRCs occur in patients younger than the age of 40 years.<sup>[12]</sup> However, in the past few years, the incidence in younger adults has been on the rise. Changing lifestyle, obesity, physical inactivity, intake of diet

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rich in processed foods with insufficient amount of fruits and vegetables, as well as the lack of screening in the young may be some reasons for this disturbing trend.<sup>[13]</sup>

CRC is a malignant neoplasm arising from the lining of the mucosa of the colon and rectum. It develops by a multistep process that analyzed can be influenced by hereditary or genetic and environmental or acquired factors. An individual with a history of adenomatous polyps or inflammatory bowel disease has an increased risk of developing CRC compared to an individual with no history of either.<sup>[14,15]</sup>

The treatment, prognosis, and survival rate largely depend on the stage of disease at diagnosis. Treatment for CRC varies by tumor location and stage at diagnosis. Depending on the stage of the disease, the patient undergoes multimodal treatment, surgery, chemotherapy, radiotherapy, and hormonal therapy. Surgical removal of tumor and nearby lymph nodes is mainstay of the treatment for early stage of CRC. However, with a potentially curative surgery alone, up to 50% of patients will ultimately relapse and die of metastatic disease.<sup>[16]</sup>

In this study, we aimed to investigate the clinic pathologic features of CRC patients who presented to a tertiary care hospital in Kashmir region of India. Although exact incidence rate cannot be provided by a hospital-based study, the information would be useful in showing patterns of malignancies in our region. This study is designed to describe the distribution of the colorectal carcinoma while considering age, gender, site of tumor, tumor pathology, and other related diseases in a retrospective fashion.

## METHODS

All cases of CRC presented to the Department of Radiation Oncology, GMC, Srinagar, between January 2012 and December 2018 were retrospectively reviewed. A total of 199 patients were included in the study. CRC patients were identified through RT numbers in hospital records. The files were reviewed for all medical records in the selected period for collecting the required data. Data were analyzed for age, gender, and district where the patients resided, subsite distribution in the colon, symptoms at the time of diagnosis (early symptoms), type of the CRC, histopathological type, stage of the disease and including metastasis, and treatment received in each case.

Data were presented as frequency and mean plus or minus standard deviation was appropriate. Chi-square test and independent samples *t*-test were performed to examine relationship between different categorical and numerical variables. *P* < 0.05 was considered as statistically significant.

## RESULTS

One hundred and ninety-nine cases were included in the present study. One hundred and eleven patients were male (55.8%) and 88 were female (44.2%) with a male-to-female ratio of 1.26:1 [Figure 1]. The youngest and oldest patients were 18 and 83 years old, respectively [Figure 2]. Mean age was  $53.42 \pm 15.52$  years and median was 55 years. The most prevalent age decade was 51–60 years which comprised 26.6% of cases followed by 61–70 years which comprised 25.5% of cases. About 15.1% of patients were in the age group of 41–50 years whereas only 1.5% of cases were below 20 years of age. In our study, 24.6% of patients had age of <40 years and 39.7% of patients had age <50 years, indicating that the percentage of younger colorectal carcinoma patients is rising in this part of India. The exact reasons behind these observations are still not clear. However, it is assumed that the early-onset CRC may be the consequence of genetic mutation. Besides, several other factors such as intake of red

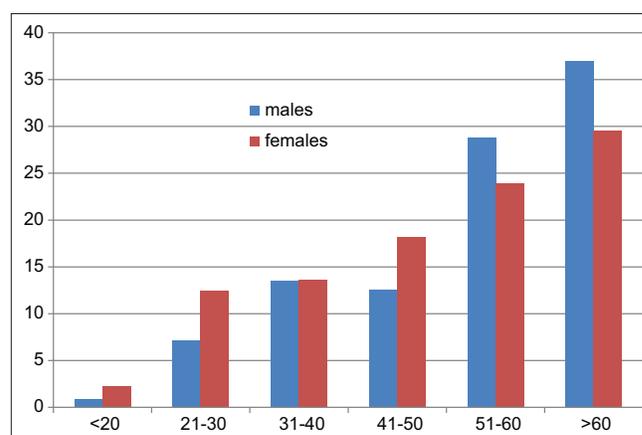


Figure 1: Age distribution of colorectal adenocarcinoma in male and female

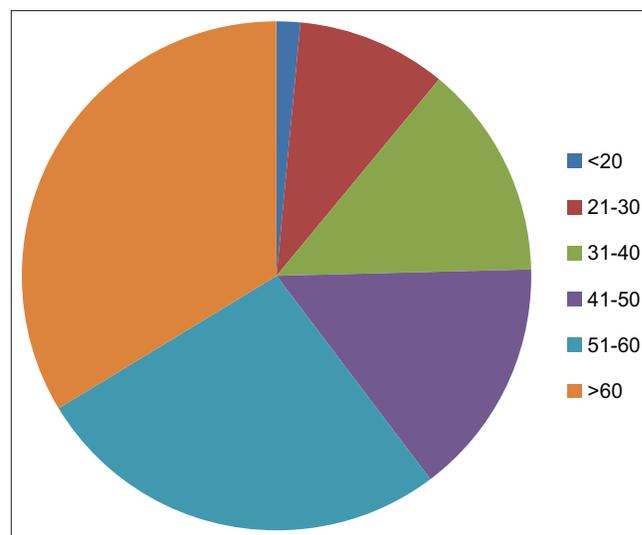


Figure 2: Age distribution of patients

meat, junk foods, uses of tobacco, and lack of exercise have potential risk for such observation.

The clinical presentation was varied including abdominal pain (51.7%), bleeding P/R(50.25%), altered bowel(48.24%), features of intestinal obstruction, weight loss and anaemia. More than one symptom was present in single patient [Figure 3].

Comparison of site and Dukes staging of colorectal cancer in patients below 40 years and above 40 years of age, n (%) is shown in Table 1, whereas location, histology and Dukes staging of colorectal carcinoma according to gender is shown in Table 2. [Tables 1 and 2]. LVI and PNI was available in 178 patients. PNI was positive in 30.7% patients whereas LVI was positive in 42.2% patients.

## DISCUSSION

A total of 196 patients were enrolled in our study. Out of these 111 patients were male (55.8%) and 88 were female

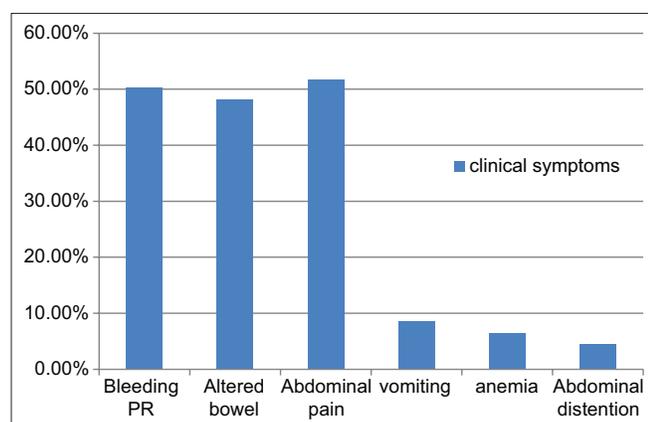


Figure 3: Clinical presentation of patients

**Table 1: Comparison of site and Dukes staging of colorectal cancer in patients below 40 years and above 40 years of age, n (%)**

Patient characteristics	Age<40 years (%)	Age>40 years (%)
<b>SITE</b>	Total – 49 patients	Total – 150 patients
(Total – 199 patients)		
Rectum (69)	24 (49)	45 (30)
Sigmoid (43)	10 (20.4)	33 (22)
Ileocecal (15)	0	15 (10)
Ascending colon and hepatic flexure (47)	11 (22.4)	36 (24)
Transverse colon (12)	3 (6)	9 (6)
Descending colon and splenic flexure (13)	1 (2)	12 (8)
<b>Staging</b>		
Dukes A (24)	4 (8.1)	20 (13.3)
Dukes B (70)	19 (38.7)	51 (34)
Dukes C (69)	14 (28.5)	55 (36.6)
Dukes D (36)	12 (24.4)	24 (16)

(44.2%) with a male-to-female ratio of 1.26:1. Mahmoulou *et al* (17). conducted a study in Iran on 546 patients which coincided with our study, wherein 306 (56%) patients were male and 240 (44%) were female.<sup>[17]</sup> In another study by Aljebreen[18] conducted on a total of 118 patients, 58% of the patients were male and 42% were female. Although in both the studies, there is not a significant difference between the two sexes as compared to the Western study there is significant preponderance of male distribution (male vs. female 2:1).<sup>[19,20]</sup>

In a study by Suryadevara *et al.*<sup>[21]</sup> in Bengaluru, India, conducted on 171 patients, the male-to-female ratio in rectal cancers was 1.26:1<sup>a</sup>, whereas Elzouki *et al.*<sup>[22]</sup> in Libya conducted a study on 152 patients where 84 were male and 68 were female with a male-to-female ratio of 1.2:1.0<sup>e</sup> which coincided with our study.

In our study, the youngest and oldest patients were 18 and 83 years old, respectively. Mean age was 53.42 ± 15.52 years and median was 55 years. The most prevalent age decade was 51–60 years which comprised 26.6% of cases followed by 61–70 years which comprised 25.5% of cases. About 15.1% of patients were in the age group of 41–50 years whereas only 1.5% of cases were below 20 years of age. In our study, 24.6% of patients had age of <40 years and 39.7% of patients had age <50 years, indicating that the percentage of younger colorectal carcinoma patients is rising in this part of India.

In a study by Elzouki *et al.*,<sup>[22]</sup> the ages at diagnosis ranged from 21 to 87 years with a mean age of 57.4 ± 12.92 years. Eighteen (11.8%) patients were below 40 years of age. The

**Table 2: Basic data of CRC according to the gender of patients**

	Total	Males (%)	Females (%)
Number of patients	199	111 (55.8)	88 (44.2)
<b>Location of CRC</b>			
Rectum	69	36 (32.4)	33 (37.5)
Sigmoid colon	43	21 (18.9)	22 (25)
Ileocecal	15	8 (7.2)	7 (7.9)
Ascending colon	47	29 (26)	18 (20)
Transverse colon	12	6 (5.4)	6 (6.8)
Descending colon	13	11 (9.9)	2 (2)
<b>Histology</b>			
Well-differentiated AC	97	52 (46.8)	45 (51)
Moderately differentiated AC	56	36 (32.7)	20 (22.7)
Poorly differentiated AC	28	14 (12.6)	14 (15.9)
Mucinous Ca	13	7 (6.3)	6 (6.8)
Signet-ring cell Ca	5	3 (2.7)	2 (2.2)
<b>Dukes staging</b>			
Dukes A	24	11 (9.9)	13 (14.7)
Dukes B	70	45 (40.5)	25 (28.4)
Dukes C	69	31 (27.9)	38 (43)
Dukes D	36	24 (21.6)	12 (13.6)
Polyps	34	26 (23.4)	8 (9.1) (P=0.008)

CRC: Colorectal cancer

majority of cases (92 patients, 60.5%) were between 50 and 70 years of age.

In another study by Mahmodlou *et al.*,<sup>[17]</sup> the mean age at diagnosis was  $55.2 \pm 11.5$  years old, 33.6% had an age lower than 50, 43.4% were between 50 and 69 years, and 22.9% had an age higher than 70-years-old. About 23% of patients had an age lower than 40 years old.<sup>1</sup>

In a study by Hajmanoochehri *et al.*,<sup>[23]</sup> the youngest and oldest patients were 20 and 90 years old, respectively. Mean age was  $57.3 \pm 14.7$  years and median was 58 years. The most prevalent age decade was 50–59 years which comprised 24.1% of cases. About 12% and 29.2% of patients were under 40 and 50 years old, respectively. About 25.2% and 5.2% of patients were higher than 70 and 80 years old, respectively.

On comparing our data with above-said studies, we found that they tally with our study. In our study, most of the patients presented with abdominal pain (51.7%), followed by bleeding P/R (50.25%), altered bowel (48.24%), features of intestinal obstruction, weight loss, and anemia. More than 1 symptom was present in single patient. Aljebreen<sup>[18]</sup> study also coincided with ours where they found that most common clinical presentation was bleeding per rectum (62%), followed by weight loss (55%), constipation (50%), melena (14%), and fever and anemia (6%). In an another study by Mahmodlou *et al.*,<sup>[17]</sup> the presenting symptoms were rectal bleeding (25%), large bowel obstruction (23%), change in bowel habits (14%), weakness and anemia (5%), abdominal mass (4%), and bowel perforation and peritonitis (3%).

In a study by Elzouki *et al.*,<sup>[22]</sup> the most common presenting symptoms were rectal bleeding and abdominal pain in 71% and the most common sign was palpable abdominal mass found in 13.2% followed by intestinal obstruction in 6.6%. Six patients (3.9%) had a documented history of polyps diagnosed previously and only 2 patients (1.3%) had past long history of ulcerative colitis almost coinciding with our study.

We compared the location of CRC with other studies. In our study, the most common site was transverse colon at 69 sites, 36 (32.4%) in males and 33 (37.5%) in females followed by ascending colon in 47 patients, 29 (26%) in males and 18 (20%) in females, sigmoid colon in 43 patients, ileocecal region in 15 patients, descending colon in 13 patients, and finally, transverse colon in 12 patients. In a study by Abdulkareem *et al.*,<sup>[24]</sup> the left-sided (distal colon) tumor 261 (62%) were more common than right sided (proximal) ones 58 (14%). More than half of the cases were located in the rectosigmoid region 246 cases (58.6%)

followed by cecum 34 cases (9%), ascending colon 24 cases (6%), transverse colon 19 cases (4.5%), and descending colon 15 cases (3.6%) each. In 82 cases (19.5%), the specific site was not indicated. In another study by Xu *et al.*,<sup>[25]</sup> out of 8172 lesions, 4434 (54.3%) were located in the rectum and 3738 in the colon.

Histopathological data from all the patients were collected and analyzed. Well-differentiated adenocarcinoma comprised 97 cases of which 52 (46.8%) males and females were 45 (51%), moderately differentiated adenocarcinoma in 56 cases in which 36 (32.7%) were male and 20 (22.7%) were female. Poorly differentiated adenocarcinoma comprised 28 cases equally divided in both sexes. Mucinous carcinoma was identified in 13 cases followed by signet cell carcinoma in 5 patients. Elzouki *et al.*<sup>[22]</sup> while doing a hospital-based study of 152 patients on colorectal carcinoma found that poorly differentiated adenocarcinoma was the most affected site which involved 65 (42.8%) cases of which 29 (42.6%) were male and 36 (42.9%) were female. It was followed by moderately differentiated adenocarcinoma in 52 (34%) of which 23 (3.8%) were female and 29 (34.5%) were male. Well differentiated was seen in 26 (17.1%) followed by undifferentiated carcinoma in 9 (5.9%) patients. Patra *et al.*'s<sup>[26]</sup> study reported more aggressive histology of tumors in younger in younger patients with CRC, most of the tumor encountered adenocarcinoma and they were subdivided into three grades – well differentiated (9.5%), moderately differentiated (18.3%), and poorly differentiated adenocarcinoma (2.9%).

In our study, the site of involvement and histopathological data were further correlated with two different age groups – younger age group (<40 years) and older age group (>40 years) and the data showed that most common site involved in both the younger and older age groups was rectum, whereas least common site in both the age groups was ileocecal region. Fazeli *et al.*<sup>[27]</sup> in Iran reported that 22% of patients <40 years had poorly differentiated tumor compared to 5.9% in patients above 40 years. Kakar *et al.*<sup>[28]</sup> found that all the cancers other than mucinous adenocarcinoma were significantly more prevalent among the middle-aged and older patients and mucinous adenocarcinoma was more prevalent among the young patients. Tumor microsatellite instability has been identified of the genetic basis in most of the younger patients with colorectal carcinoma. The tumor microsatellite instability was suggested for those younger individuals to have a risk for hereditary non-polyposis CRC like mucinous adenocarcinoma.

On staging the tumor according to Duke's classification, majority of patients ( $n = 19$ , 38.7%) < 40 years of age were in Stage B, whereas maximum number of patients

( $n = 55, 36.6\%$ ) > 40 years were in Stage C. Abdulkareem *et al.*'s<sup>[24]</sup> study showed that most of the patients (52%) were in Stage B.

## CONCLUSION

CRC is among the most common malignancies found in this part of the world and percentage of younger patients is rising in this part of the world. Patient still present in advanced stages so the importance of implementing an appropriate screening programme needs to be considered.

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