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Colorectal Cancer in India: An Audit from A Tertiary Care Centre

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Abstract

Background and Aims: *Colorectal cancer (CRC) is a common cancer worldwide with a low reported incidence in India. The presentation pattern and incidence rates vary significantly across the geographical regions. There are a few studies evaluating the clinical profile of CRC among Indian patients.*

Methods: *We retrospectively analyzed the clinical profiles of CRC patients who had presented to Department of Gastroenterology at a tertiary referral center in South India, over a period of four years between December 2017 to December 2021. Demographics, clinicopathological profile, colonoscopy findings along with management and complications were taken into consideration. The aim was to assess the current clinical picture and compare it with those of the reported literature.*

Results: *Two hundred and seventy-six new patients with CRC were seen in our colorectal clinic over a four-year period. The median age group was 60.5 years. 50.7 percent were males. Patients were symptomatic for an average period of three months prior to presentation. The commonest symptoms were loss of weight and appetite (80.7%), bleeding per rectum (60.5%), abdominal pain (55.7%), followed by altered bowel habits (26.4%) and vomiting (15.9%). 20 patients had signet ring tumors. The median CEA (carcinoembryonic antigen) level were 4.96 ng/mL (range 0.2 to 145789 ng/ml). 12.3 percent of the patients had metastatic disease with liver being the commonest site of metastases (55.8%) followed by omentum and mesenteric lymph nodes. 63 patients had received chemotherapy and 15 had received radiotherapy treatment with a curative intent.*

Conclusion: *Colorectal cancer in India differs from that described in the Western countries. We had higher proportion of mucinous adenocarcinomas, and more patients presenting with an advanced stage compared to Western literature. Inadequate access to healthcare and socioeconomic factors may play a role in some of these differences.*

Keywords: *Colorectal cancer, Epidemiology, Mortality, Risk factors, Symptoms, Treatment.*

Introduction

Colorectal cancer (CRC) is a common cancer worldwide. More than fifty percent of cases of CRC occur in developed countries. It is the third most commonly diagnosed cancer in males and the second in females, with more than 1.4 million new cancer cases every year **[**1**]**. The mortality rates are however higher in the less developed countries, due to limited resources and inadequate health infrastructure. In western countries the mortality rates have been decreasing due to early detection owing to regular screening programs, timely surveillance and improved treatment of CRC **[**2**]**. The age standardized rate (ASR) for CRC in India is low at 7.2 per 100,000 population in males and 5.1 per 100,000 population in women **[**3**]**. However, the absolute burden of the people suffering from CRC disease in a country with a population of a billion plus people is large. Five-year survival of CRC in India is less than 40%, one of the lowest in the world. According to the CONCORDE-2 study, five-year survival of rectal cancer in India is actually falling in some registries **[**4**]**. This could be due to lacuna in the diagnostic and treatment pathways for CRC. There is an urgent need to assess the reasons for the poor outcomes and survival.

The spectrum of CRC disease profile among Indian patients varies widely compared to that of western population. Most of the cases of CRC in India present at a younger age, with more advanced-stage disease, more signet ring morphology, and more anorectal as compared to colonic site of primary as compared to that reported worldwide. Published literature on CRC from India is very scarce and these involve a small number of patients **[**5**]**. Moreover, there is a sparsity of data regarding clinical and demographic profile. Hence, we planned an audit of all CRC patients seen at our center over a four-year period.

Methods

Ethics Statement: This study was performed according to the principles of Declaration of Helsinki. The study protocol was approved by the Institutional Ethical Committees (IEC). All participants have been contacted over telephone and followed up in OPD clinics. Written consent has been obtained, providing their willingness for being included in the study.

Study Design: We performed a retrospective audit of all patients who had presented to our hospital from 1st of December 2017 to 1st December 2021 with a biopsy proven diagnosis of colorectal tumors. A total data of 276 patients was analyzed and included in our study. Evaluation was done by a multidisciplinary team of Gastroenterologists, gastrosurgeons, radiologists, medical and radiation

oncologists. Treatment was planned by consensus as per prevailing standards of care. Medical records and hospital health information system was used to retrieve the data of the patients. Nutritional assessment was done for all the patients on admission, which has been retrieved from hospital health information system. If Patients had skipped follow up, they were contacted over telephone and data regarding treatment and general wellbeing was recorded.

Statistical Methods

In our study, we have considered age, side of involvement, CEA levels and duration of symptoms as primary exposure variables, while biopsy report, stage of cancer, CT received were considered as the primary outcome variables.

Descriptive analysis was carried out by frequency and proportion for categorical variables; mean, standard deviation/median, and IQR for quantitative continuous variables. For normally distributed Quantitative parameters, the mean values were compared between respective groups of categorical variable using an independent sample t-test (2 groups). Categorical outcomes were compared between study groups using the Chi-square test. P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis. (IBM Corp. Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

Data Analysis and Interpretation

Results

Among the 276 patients with CRC, 140(50.7%) were males and 136 females (49.2%). The median age group of the patients with CRC was 60.5 years (range 16 years to 98 years). Majority of the patients were between the age group 55- 69 years (40.58%), with 7.97% of patients being in the age group less than 40 years (Table 1).

Age Groups	Frequency	Percentages
<25	3	1.09%
25 to 39	19	6.88%
40 to 54	73	26.45%
55 to 69	112	40.58%
>=70	69	25.00%

Table 1: Descriptive analysis of age groups in the study population (N=276)

In our study left sided tumors (65.8%) were more common than right sided (34.4%). The commonest primary site was rectum (31.88%) followed by ascending colon (17.39%) and recto-sigmoid (13.04%) (Table 2).

Site of Cancer	Frequency	Percentages
Rectum	88	31.88%
Ascending colon	48	17.39%
Rectosigmoid	36	13.04%
Descending colon	27	9.78%
Transverse colon	24	8.70%
Sigmoid colon	22	7.97%
Cecum	18	6.52%
Anorectum	4	1.45%
Hepatic flexure	4	1.45%
Anal canal	2	0.72%
Splenic flexure	2	0.72%
Ileum	1	0.36%

Table 2: Descriptive analysis of site of cancer in the study population (N=276)

Patients with right sided involvement were younger compared to the left sided primaries (Table 3)

Parameter	Side of involvement		P value
	Left (N=181)	Right (N=95)	
Age (years) **(Mean± SD)**	60.46 ± 14.46	57.33 ± 13.85	0.084*

Table 3: Comparison of mean of age (years) between side of involvement(N=276)

***Independent sample t test**

The median duration of symptoms was 3 months (Range-1 to 60 months) in the study population. Most common symptoms with CRC patients being loss of weight and appetite (80.7%), bleeding per rectum (60.5%), abdominal pain (55.7%), followed by altered bowel habits (26.4%) and vomiting (15.9%). Among the patients with CRC in our study, red meat consumption was present in 88.4%, alcohol consumption was seen in 47.4% and smoking was present in 47.1% of patients.

Most patients (79.7%) had ECOG PS-1 (PS-Performance Status). 42 (15.2%) patients had PS-2. Only 11 patients (3.98%) had PS-3, and 3 patients (1.08%) had PS-4. We used the subjective global assessment score (SGA) for staging malnutrition. Most of our patients were malnourished. Only 22 patients (7.97%) had an SGA score of A (none or minimal malnutrition). Two hundred and two (73.1%) were SGA-B (moderate malnutrition), and 52 (18.8%) were SGA-C (severe malnutrition).

All 276 patients had tumor histology revealing an adenocarcinoma. Majority had moderately differentiated tumors (63.41%). 23.9% had poorly differentiated tumors and 12.68% had well-differentiated tumors. Twenty patients (7.24%) had a signet ring cell carcinoma reported, while 43(15.5%) had mucinous carcinoma. Patients younger than 40 years of age had a higher proportion of signet ring positivity as compared to those above 40 years (26.32% vs. 17.05%). (Table 4).

Age Group	Signet Ring Cell Ca		Fisher exact P value
	Yes	No	
<40 Years (N=22)	5 (22.73%)	17 (77.27%)	0.014
>=40 Years (N=254)	15 (5.91%)	239 (94.09%)	

Table 4: Comparison of age group between signet ring cell ca (N=276)

The median CEA levels was 4.96 ng/ml (IQR), ranges between 0.20 to 145789 ng/ml in the study population. Majority of the patients had CEA with normal range (0- 2.5 ng/ml) (Table 5)

CEA Levels	Frequency	Percentages
<2.5	103	37.32%
2.5 to 100	99	35.87%
101 to 1000	40	14.49%
>1000	34	12.32%

Table 5: Descriptive analysis of CEA levels in the study population (N=276)

In our study 34 patients (12.3%) had metastases with most common areas of metastases being liver (19 patients), followed by omentum and mesenteric lymph nodes (7 patients). Four patients had metastases to ovary, two had to lung. One had metastases to urinary bladder and one had to gall bladder. 63 patients had received chemotherapy and 15 patients had received radiotherapy with a curative intent. 29 patients (10.5%) had Intestinal obstruction and three had Caecal perforation. 20

patients succumbed to their illness 20 (7.2%), 13 patients had cardiac arrest, three patients had pulmonary embolism, one had ARDS (acute respiratory distress syndrome), one had aspiration pneumonia, one had peritonitis and one had shock and coagulopathy.

Discussion

Colorectal cancer is a common cancer worldwide with a majority of cases occurring in the developed countries. India has a low prevalence of CRC. The five-year estimated prevalence of CRC in India is 87 per 100,000 population.**[**5**]**

A predominant high fiber diet and patterns of lifestyle are thought to be responsible for this low incidence of CRC in the developing world. Also, prevalence of obesity is more in developed countries which could be a possible risk factor for CRC, compared to the developing world. There is a higher proportion of younger population in the developing countries which could be another reason for low incidence of CRC. Underreporting of the cases is seen in India compared to the Western world, population registries in India cover only 7.45% of the population, while worldwide cancer registries cover 21% of the population **[**6**]**.

However, studies on Indian immigrants from countries with a high prevalence of CRC like the USA and Singapore show that CRC incidence is lower in Indians than in the native population but higher than that observed from the Indian registries **[**7, 8**]**. This points to the possibility that there is an additional component of environmental factors which influence the incidence of CRC along with genetic factors. In the United States, CRC incidence rates and disease-related death rates have declined over the last few decades in subjects above 50 years; however, the incidence rates have been increasing in the under age 50 group **[**9–11**]**. This decrease in the incidence rate could be primarily attributed to the regular screening programs along with detection and removal of adenomatous polyps. Most of these programs target the population above 50 years of age. Trends in most other Western countries have been variable. Incidence rates continue to increase in some low-resource countries of South America and Eastern Europe, possibly secondary to dietary pattern, lifestyle factors like obesity, physical inactivity and smoking **[**1**]**. In India, some registries have shown decreasing trend/stable incidence while others have shown an increasing trend for rectal cancer **[**12, 13**]**. The six population-based registries have shown an increase in the rates of colon cancer **[**13**]**. This pattern could be secondary to urbanization and changing lifestyles, leading to a change in the environmental risk factors. Also, there is no population-based screening program in India.

CRC incidence rates are higher for men in most regions of the world [1]. Sixty-five percent of our patients were male. However, there could be a referral bias here in terms of seeking treatment at a referral center. The mean age of patients in our study was 47.2 years. Thirty-five percent of the patients were below 40 years of age, and 80% were below 60 years. In a study from eastern India on 168 patients with sporadic CRC, the mean age of presentation was 47.01 years, while it was 58.4 years in a retrospective descriptive analysis of 220 cases of CRC diagnosed at colonoscopy over a five-year period [14, 15]. In a study from central India by Hussain et al, on 233 patients over 8 years, the median age at diagnosis was 43 years with 39% of CRC patients being diagnosed at the age of 40 or younger [16]. In a few other studies from India, done on a small number of patients show similar results which elicits the question whether CRC occurs at a younger age in India [17, 18]. This is in contrast to Western data. In the USA, 90% of new CRC cases are above 50 years at diagnosis and 58% of all new CRC cases are above 65 years of age [11]. A higher proportion of younger patients with CRC in Indian patients should be looked at critically. This could possibly be secondary to referral bias, as younger patients are more likely to access healthcare compared to older patients or may be a pointer to a biologically different type of disease. Moreover, India has a larger proportion of young population with a broad-based population pyramid. According to the data from the 2011 census, 29.5% of the population is in the age group 0–14, 62.5% of the proportion is in the age group 15–59 years, and the percentage of elderly population above 60 years is 8.0% [19]. The median age of India's population is around 25 years [20]. The average life expectancy at birth is approximately 68 years. This is unlike Western countries which have a larger elderly population. Hence, the increased incidence of CRC in younger subjects could well be a bias due to a larger proportion of young population in India.

Studies from the US and Europe report an increasing incidence of right-sided colon cancer [21, 22]. This could be partly explained by the fact that screening sigmoidoscopies will mainly target precursor lesions in the left colon which are easily accessible. Poor preparations and incomplete evaluations during colonoscopy will also have a bigger impact on right-sided tumors. So also, fecal occult blood tests, both guaiac- and immunochemical-based, show better diagnostic performance for detecting CRC in the distal colon than in the proximal colon [23]. Thus, commonly used screening tests will be more effective in preventing left-sided than right-sided CRCs; however, there could also be a true increase in incidence of right-sided tumors with a different biology which could also contribute to a shift in distribution of CRC. In our study, most of the tumors were left-sided, the commonest primary site being rectum (31.88%) followed by ascending colon (17.39%), recto-sigmoid (13.04%) and descending colon (9.78%). 34% of our patients had right sided tumor. Similar findings have been reported from other single-center studies in India, especially among younger patients [16, 17, 24]. As

left-sided tumors are more likely to present with abdominal pain and overt bleed per rectum, they are more likely to become symptomatic earlier. It is uncertain whether increased proportion of left-sided tumors is a referral bias or whether rectal cancer is truly more common than colon cancer in India [25].

Majority of the patients with early-stage CRC are asymptomatic, and they may be diagnosed at the time of screening. Symptomatic patients can present with pain, bleeding, or obstructive symptoms, or rarely in an emergency setting with obstruction or perforation. Although screening for bowel cancer is recommended by most major societies in developed countries, the uptake rates are relatively low and most CRC would be diagnosed when symptomatic. In our patients, the median duration of symptoms was 3 months and the commonest symptom was loss of appetite and weight (80.7%), bleeding per rectum (60.5%), abdominal pain (55.7%), followed by altered bowel habits (26.4%) and vomiting (15.9%). Most studies have reported similar common symptoms in patients with CRC [24, 26, 27].

Carcinoembryonic antigen (CEA) is a tumor marker commonly evaluated in CRC and used for prognostication, for post-treatment follow-up, and for monitoring the response of metastatic disease to systemic therapy [28]. However, it has a low diagnostic ability with a pooled sensitivity for diagnosis of CRC being 46% (95% CI 0.45–0.47) and specificity being 89% (95% CI 0.88–0.92) [29]. In our audit, 37.32% of the patients had CEA levels within the normal range (0–2.5 ng/mL). Higher baseline CEA level was associated with increased likelihood of stage IV disease especially those with CEA levels > 1000 ng/mL. Twenty (7.2%) of our patients had signet ring cell carcinomas which are typically associated with poorer prognosis. They were seen more frequently in younger patients (<40 years of age) or advanced stages (stage III/IV). 15.5 percent of patients had mucinous carcinomas in our study. Most Western studies report a prevalence of 5–15% for mucinous tumours and 1% for signet ring tumours [30,31].

Approximately 20% of patients in the United States have distant metastatic disease at the time of presentation [32]. Twelve percent of the patients in our study had metastatic disease. Studies from India show 10–20% prevalence of metastatic disease. The reasons for patients to present at an advanced stage during presentation could be attributed to the lack of population-based screening. Social and economic factors could also influence availability and timely access to healthcare. There is a lesser suspicion of malignancy, especially in younger patients and possibility of misdiagnosis as haemorrhoids/fissures leading to a delay in diagnosis.

There are only few studies evaluating the prevalence of malnutrition in patients with CRC using validated malnutrition screening tools [5].

Almost 92% of our patients were malnourished at presentation. Though nutritional assessment is an important tool in addition to baseline assessment of all cancer patients, it is frequently neglected. Our study highlights the necessity for nutritional assessment to appropriately identify patients with malnutrition who can thereby receive adequate nutritional counselling and treatment.

Our study is a single-center audit of 276 consecutive patients with CRC from a tertiary care hospital in south India, a country with a low prevalence of CRC. There is a possibility of referral bias which would be a limitation of our audit. This audit gave us an idea about the number of patients with CRC at our setup. Approximately one-third of the patients at our center were younger than 40 years of age. As majority of the patients in our audit had left sided tumours, single flexible sigmoidoscopy for screening appears to be an attractive option and can be evaluated for cost–benefit analysis. It also gave us an idea about patients who are likely to be eligible for therapies to downstage tumors, lung or liver metastasectomy, hyperthermic intraperitoneal chemotherapy (HIPEC) with cytoreduction. This can be used for strategic planning for development and budgetary allocation of resources in specialist centers.

Conclusion

Our study shows a difference in demographic and histological features compared to the West (younger age, more left-sided tumors, advanced stage at presentation, more malnourished patients). Younger population pyramid structure of India, referral bias might contribute to the higher number patients with a young age at presentation. In our study, mucinous tumors were more compared to the signet ring tumors just like the Western population. A detailed family history along with regular screening programs is important in India given the significant number of young patients presenting with CRC in our study. Nutritional assessment and therapy should also be included in the management plan as most CRC patients are malnourished, which in turn affects the survival and outcomes. This study gives us a better picture of the ground reality of CRC in India.

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