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CLINICO-PATHOLOGICAL PROFILE OF COLORECTAL CANCER: AN OBSERVATIONAL STUDY

Dr. Rajeev Sharma[1], Dr. Priyanka Tiwari[2], Amitabh Misra[3]

1 Assistant Professor, Dept. of Medicine, Ananta Institute of Medical Sciences & Research Centre, Udaipur, Rajasthan, India

2 Assistant Professor, Dept. of Pathology, American International Institute of Medical Science, Udaipur, Rajasthan, India

3 MBBS student, Kasturba Medical College, Manipal, Karnataka, India

Corresponding author- Dr. Rajeev Sharma, Assistant Professor, Dept. of Medicine, Ananta Institute of Medical Sciences & Research Centre, Udaipur, Rajasthan, India, Email- dr.rajeevsharma.mdmedicine@gmail.com, ph-7795216400

Abstract

Aim: The aim of this study was to evaluate the clinico-pathological profile of colorectal cancer patients in our tertiary care hospital.

Material and methods: This prospective as well as retrospective study was conducted in Gastroenterology division of Department of General Medicine at Ananta Institute of Medical Sciences & Research Center, Udaipur, Rajasthan, India. Total 174 patients presenting with colorectal cancer (CRC) from August 2019 to July 2022 were included in the study. Study tools were Study-questionnaire, investigations [routine blood tests, CEA, Colonoscopy, USG, CECT and MRI] and histopathological reports. Parameters studied were age, sex, site of lesion, clinical presentations and histopathology of the lesion.

Results: We observed that overall proliferative type was the most common type of tumor in our patients (n=75; 43.10%) with p value of <0.0001, followed by infiltrative (n=59; 33.91%), ulcerative (n=36; 20.69%) and ulcero-infiltrative (n=4; 2.29%). History of colorectal cancer in family was present in 45 (25.86%) of patients; with statistically significant p value of <0.0001. Out of 174 patients, 81 (46.55%) were smokers (p value 0.544). The most common clinical presentation of the patients in our study was change in bowel habits (n=136; 78.16%) followed by bleeding per rectum (PR) (n=117; 67.24%), abdominal pain (n=102; 58.20%) and generalized weakness (n=78; 44.83%). Most common site of involvement was rectum (n=78; 44.83%) followed by right colon (ascending colon and

ceacum) (n=5531;61%), descending colon (n=18; 10.34%), sigmoid (n=16; 9.19%) and transverse colon (n=7;(4.02%). Together rectosigmoid comprise about 54.02% of total CRC. In our study we found elevated preoperative CEA levels (≥ 5.1 ng/ ml) in 80 (45.98%) patients, not elevated (≤ 5.0 ng/ml) in 36(20.69%) patients and not taken/unknown in 58 (33.33%) patients.

Conclusion: The incidence of CRC is increasing in younger age group and younger patients present at advanced stage. Lack of awareness about CRC in general population and lack of screening programs are responsible for advanced stage of CRC at presentation. Public awareness through mass-media, screening of high-risk populations, early diagnosis, cost-effective multi-modality treatment and regular follow-up is the call of the time for limiting the morbidity and mortality associated with colorectal cancer.

Keywords: Cancer; Colorectal; Colon; Rectum

Introduction

Colorectal cancer (CRC) is a common cancer worldwide. 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. There is a geographical variation in the incidence rates with more than half of the cases of CRC occurring in developed countries. However, mortality is higher in the less developed countries who have limited resources and inadequate health infrastructure[1.] According to the Globocan report 2018, this contributes 9.2% amongst all major cancer incidence worldwide. There were over 1.8 million new cases in the year 2018. It is the third most common cancer in males with 746,000 new cases and second in females with 614,000 new cases. The variations in the incidence are also present across the world. The highest rates are in Australia, New Zealand and the lowest in western Africa and Southcentral Asia. These geographic differences could be attributable to differences in dietary and environmental exposures.[2] However, a gradual decline in the incidence has been observed, which reflects the increase of early detection by colonoscopy with removal of precancerous lesions in adults from 50 to 75 years of age.[3,4] It is currently the most prevalent malignant cancer of the gastrointestinal tract, accounting for 13% of all malignant tumours. It is also the second most common cause of cancer-related death worldwide, affecting both men and women equally in developed and underdeveloped nations, and it is predicted to surpass heart disease mortality in the coming years.[4-6] The development of flexible endoscopes has led to the great increase

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in the examination and mucosal biopsy evaluation of all portions of the large intestine and rectum.[7] It is a prevalent disease in those aged 65-74, with a higher prevalence in women.[8] Due to risk factors such obesity, sedentarism, poor eating habits (rich in fats and proteins), smoking, and population ageing, this condition is, nevertheless, identified more commonly in younger individuals. The clinical presentation in patients with colorectal cancer varies on the tumor's size, location, and whether or not it has metastasized. Anorexia, abdominal distension, altered chronic bowel habits, altered bowel movements, nausea, vomiting, malaise, and involuntary weight loss are among the symptoms that characterise the clinical presentation.[5] A malignant tumour that develops from the mucosa lining of the colon and rectum is called colorectal cancer. Mutations in specific genes can lead to the onset of colorectal cancer, as happens in other types of cancer. Those mutations can appear in oncogenes, tumour suppressor genes and genes related to DNA repair mechanisms.[8] It develops through a multistep process that can be impacted by acquired, inherited, hereditary, and environmental variables.[9,10] A person who has this type of cancer cells may in the long run metastasize to regional lymph nodes and later to more distant lymph nodes and in the other organs. The treatment, prognosis and survival rate largely depend on the stage of disease at diagnosis. Screening for colorectal cancer is particularly effective. Screening can prevent cancer from occurring as it can detect adenomatous polyps that can be successfully removed.[11] Treatment for colorectal cancer varies by tumor location and stage at diagnosis. Depending upon 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 treatment for early stage of colorectal cancer. However, with a potentially curative surgery alone, up to 50% patients will ultimately relapse and die of metastatic disease.[12] The aim of this study was to evaluate the clinico-pathological profile of colorectal cancer patients in our tertiary care hospital.

Materials and Methods

This prospective as well as retrospective study was conducted in Gastroenterology division of Department of General Medicine at Ananta Institute of Medical Sciences & Research Centre, Udaipur, Rajasthan, India.

Methodology

Total 174 patients presenting with colorectal cancer from August 2019 to July 2022 were included in the study. All patients were evaluated with respect to detailed history and physical examination and were investigated to confirm the diagnosis and stage of disease.

Data collection

Study tools were study-questionnaire, investigations [routine blood tests, CEA, Colonoscopy, USG, CECT and MRI] and histopathological reports.

Parameters studied were age, sex, site of lesion, clinical presentations and histopathology of the lesion.

Results

We observed that overall proliferative type was the most common type of tumor in our patients (n=75; 43.10%) with p value of <0.0001, followed by infiltrative (n=59; 33.91%), ulcerative (n=36; 20.69%) and ulcero- infiltrative (n=4; 2.29%). However, the most common type of tumor in youngest age group (15 to 25 years) was infiltrative; all the 4 tumors seen in this group were infiltrative (Table 1). Again, proliferative type was most common type of tumor in both males and females (41.7% and 41.1% respectively), in both rural and urban patients, in both vegetarians and non-vegetarians and in both smokers and non- smokers.

Table 1: Correlation between tumor morphology and age

Age-group (In years)	**No. of Cases (% age)**				**Total No. of cases (% age)**
	Proliferative	**Ulcerative**	**Infiltrative**	**Ulcero-infiltrative**	
Below -25	0 (0.00)	0 (0.00)	8 (100.00)	0 (0.00)	8(4.59)
25-35	16(59.27)	0 (0.00)	9 (33.33)	2(7.40)	27(15.52)
35-45	10 (50)	6 (30)	4(20)	0 (0.00)	20 (11.49)
45-55	13 (43.33)	9 (30)	8(26.67)	0 (0.00)	30 (17.24)
55-65	22 (48.89)	8 (17.78)	13 (28.89)	2(4.44)	45 (25.86)
65-75	13 (38.23)	9 (26.47)	12 (35.29)	0 (0.00)	34(19.54)
Above 75	1(10)	4 (40)	5 (50)	0 (0.00)	10(5.75)
Total	75 (43.10)	36 (20.69)	59 (33.91)	4 (2.29)	174 (100)
p-value	<0.0001	<0.0001	<0.0001	-	<0.0001

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Total of 174 patients were included in this prospective as well as retrospective study. 105 (60.34**%**) and 69 (39.66**%**) female (p-value 0.012). We had patients from all age groups; from adolescents to elderly. The minimum age of a patient observed was 16 years and the maximum age observed was 78 years. Colorectal cancer was most common in the age group of 55 to 65 years accounting for 25.86% (n=45) of cases followed by 65 to 75 years (n=34; 17.54%), 45 to 55 years (n=30; 17.24%) and 35 to 45 years (n=20; 11.49%). About 20.11% (n=35) of patients were below the age of 35 years while as only 10 (5.75%) patients presented after 75 years of age. Majority of the patients were from rural areas (n=115; 66.10%) as compared from urban areas (n=59; 33.90%) (p value 0.014). History of colorectal cancer in family was present in 45 (25.86%) of patients; with statistically significant p value of <0.0001. Out of 174 patients, 81 (46.55%) were smokers (p value 0.544). Regarding dietary habit we observed that majority (n=161; 92.53%) of our patients were non-vegetarian.

Table 2. Clinical presentation

Clinical presentation	No. of patients	Percentage
Bowel habits	136	78.16
Bleeding PR	117	67.24
Abdominal pain	102	58.20
Generalized weakness	78	44.83
Intestinal obstruction	8	4.59
Abdominal swelling	25	14.37

Table 2: In most of the patients, symptoms did overlap. However, the most common clinical presentation of the patients in our study was change in bowel habits (n=136; 78.16%) followed by bleeding per rectum (PR) (n=117; 67.24%), abdominal pain (n=102; 58.20%) and generalized weakness (n=78; 44.83%). However, 8 (4.59%) patients presented with intestinal obstruction and 25(14.37%) patients had abdominal swelling.

Table 3. Site of involvement

Site of involvement	No. of patients	Percentage
Rectum	78	44.83
Ascending colon and ceacum	55	31.61
Descending colon	18	10.33

Sigmoid	16	9.19
Transverse colon	7	4.02

Table 3: Most common site of involvement was rectum (n=78; 44.83%) followed by right colon (ascending colon and ceacum) (n=5531.61%), descending colon (n=18; 10.34%), sigmoid (n=16; 9.19%) and transverse colon (n=7; 4.02%). Together rectosigmoid comprise about 54.02% of total CRC in our study.

Table 4. Histologically most of the patients

Histology of the patients	**No of patients**	**Percentage**
Adenocarcinoma	172	98.85
Non-Hodgkin lymphoma	1	0.057
Small cell carcinoma	1	0.057
Adenocarcinomas (N=172)		
Well differentiated	87	50.58
Moderately differentiated	57	33.14
Poorly differentiated	28	16.28

Histologically most of the patients (n=172; 98.85%) had adenocarcinoma while as non-Hodgkin lymphoma was in 1 patients and small cell carcinoma in 1 patients. Among 172 adenocarcinomas, 50.58% (n=87) were well differentiated, 33.14% (n=57) moderately differentiated and 16.28% (n=28) poorly differentiated.

Out of 174 patients, 93 (53.45%) had pallor and anemia. Pallor was seen in all patients (100%) of ulcero infiltrative lesions. Also, pallor in patients with proliferative lesions was in 66.67%, with ulcerative lesions in 44.44% and with infiltrative lesions in 42.37% patients.

Overall, the most common type of tumor leading to pallor was proliferative (50%) followed by infiltrative and ulcerative. Overall Bleeding PR was seen in 67.24% patients. Most of the patients (n=47; 40.17%) with bleeding PR had infiltrative tumors closely followed by proliferative 34(29.06%) and ulcerative tumors 32(27.35%). All patients 4(100%) with ulcero infiltrative lesions had bleeding PR and it was present in 92% of ulcerative tumors which was statistically significant (p value =0.014).

In our study we found elevated preoperative CEA levels (≥ 5.1 ng/ ml) in 80 (45.98%) patients, not elevated (≤ 5.0 ng/ml) in 36 patients (20.69%) and not taken/unknown in 58 (33.33%) patients. Out of 80 cases having elevated CEA levels, 66 (82.5%) patients had CEA levels in the range of 5 ng/ml to 10 ng/ml. In our study of 174 patients most (n=89; 51.15%) of the patients presented in stage III followed by stage I (n=39; 22.41%), stage II (n=33; 18.97%) and stage IV (n=13; 7.47%).

Discussion

Colorectal Cancer (CRC) has become one of the commonest malignancies and a major health concern worldwide. It is the third most common cancer in men and the second in women worldwide According to the reports, every 9 minutes, someone dies from CRC.[13] The incidence is highest in developed countries and low in Asia, Middle East, South America, and Africa.[14] Incidence starts to increase after 35 years of age and rises rapidly after 50 years of age, peaking in seventh decade. More than 90% cancers occur after 50 years of age. However, cases have been reported in young children and adolescents. In our study the most common age group of colorectal cancer was 55 to 65 (25.86%) followed by 65 to 75 (17.54%) which was consistent with studies of Al-Samawi et al.[15]

Majority of the patients were from rural areas (n=115; 66.10%) as compared from urban areas (n=59; 33.90%). (p value 0.014). As we have already mentioned that the incidence of colorectal cancer is related to western dietary habits, which is more prevalent in urban population and this paradoxically higher number of patients from rural areas. We noticed higher incidence of colorectal cancer in males (60.34%) as compared to female (39.66%) which is consistent with the available data.[15,16]

Epidemiologic studies have linked increased risk of colorectal cancer with a diet high in red meat and animal fat, low-fiber diet and low overall intake of fruits and vegetables. In our study majority (92.53%) of the patients were non-vegetarian, taking meat regularly in their diet in the form of chicken, mutton and beef. This is in consistent with studies of Chan et al.[17] Larson et al.[18] Sandhu et al.[19] and Cross et al.[20] Dietary modifications along with secondary prevention measures may have an impact on reducing the mortality from colorectal cancer.[21,22]

In our study of 174 patients 81 (46.55%) were smokers which is consistent with findings of various studies in which life style choices such as alcohol and tobacco consumption, obesity and sedentary life style have been associated with increased risk for colorectal cancer.[23]

Family history of colorectal cancer was present in 25.86% of patients. In around 10 to 15% of all colorectal cancer cases, a positive family history of Colorectal Cancer (CRC) is observed.[24] It is probable that dietary and other environmental risk factors, acting solely or in concert with genetic factors, influence the aggregation of the disease.[25] The risk associated with a family history of CRC depends on the number of affected relatives and the age at diagnosis.[26] Subjects with one First-Degree Relative (FDR) with CRC diagnosed at age >50 years, have a relative risk (RR) of 2 to 3.15 for developing CRC. Subjects with two (or more) FDRs, with CRC diagnosed at any age, or with one FDR with CRC diagnosed before the age of 50 years, have a relative risk of 4 to 6 for developing colorectal cancer.[27] A study by Safaee et al.[28] reported a positive family history in 36.4% of the cases. Charles et al.[29] reported that a family history of colorectal cancer is associated with an increased risk of the disease, especially among the young people. Higher frequency of any cancer among family members in the present study is also in agreement with the findings of some other authors.

In our study we found that the most predominant type was adenocarcinoma (n=172; 98.85%). Our results are in agreement with studies of Al-Samawi et al.[15] Kumar Halder et al.[27] and others. Adenocarcinomas compromise the vast majority of colon and rectal cancer (98%). Other rare forms include small cell carcinoma, squamous cell carcinoma, carcinoid, lymphoma and sarcoma. Squamous cell carcinomas may develop in the transition area from the rectum to the anal verge and are considered anal carcinomas. Very rare forms of squamous cell carcinomas of the rectum have been reported.[30] In our study we found Non-Hodgkin lymphoma in 1 cases and small cell carcinoma in 1 cases these results are consistent with other studies.[15]

Most common site of involvement was rectum (n=78; 44.83%) followed by right colon (ascending colon and ceacum) (n=5531; 61%), descending colon (n=18; 10.34%), sigmoid (n=16; 9.19%) and transverse colon (n=7; 4.02%). This frequency of tumor distribution in colon and rectum is consistent with the studies of Morson and Dawson.[31] Halder et al.[27] and other studies.[15] Our results are slightly different as compared to results of Giovannucci et al.[32] who had documented approximately 20% of colon cancers in caecum, another 20% in rectum, and an additional 20% in rectosigmoid junction. Kumar et al.[33] revealed that rectum was involved in 29.6%, sigmoid colon in 26.5%, ascending Colon in 21%, descending Colon in 17.9% and transverse Colon in 4.9%. In a study by Eisenhardt et al.[34] rectum was involved in 34.6% and colon in 65.4%. Waldron et al.[35] found that 23% of colorectal cancers were right

sided (defined as tumors arising from the caecum, ascending colon and hepatic flexure) during their 10-year study period in Birmingham. A 30-year study in Dublin by Crenad et al.[36] revealed that approximately 28% of colorectal cancers were right sided which is comparable to our study.

In our study the most common tumor in young age group (15 to 25 yrs) is infiltrative whereas it is proliferative in older age group (55 to 65 yrs). Overall proliferative is the most common type of tumor in our patients (43.10%). Our findings are consistent with the study by Falterman KW et al.[37] The most common type of tumor in both males and females is proliferative followed by infiltrative and ulcerative. Bleeding PR is most common in ulcerative tumors (92%) followed by infiltrative and proliferative tumors. Pallor was seen in all patients (100%) of ulceroinfiltrative lesions. Also pallor in patients with proliferative lesions was in 66.67%, with ulcerative lesions in 44.44% and with infiltrative lesions in 42.37% patients. This corresponds to the study by Posner MC et al.[38]

The mode of presentation of CRC depends upon the site of cancer. Right colon cancers present with weight loss, anemia, fecal occult blood loss, mass in right iliac fossa and the disease more likely to be advanced at presentation. Left colon cancers present with rectal bleeding, change in bowel habits, bowel obstruction, colicky pain and relatively lesser advanced disease at presentation. Overall, the most common presenting symptoms are bleeding PR and change in bowel habits. It is believed that increased detection of earlier stage colorectal cancer can only be achieved by screening asymptomatic individuals. In our study, the most common mode of presentation was change in bowel habits (78.16%) followed by bleeding PR (67.24%) and abdominal pain (58.20%). Our results were consistent with the study of Smith et al.[39] However our results were slightly different as compared to results of Lynch et al.[40] in which most common mode of presentation of CRC was bleeding PR followed by change in bowel habits and pain abdomen.

In our study among adenocarcinomas, the well differentiated adenocarcinoma accounted for 50.58%, moderately differentiated adenocarcinoma for 33.14% while poorly differentiated adenocarcinoma for 16.28%. These results are consistent with the study of Al-Samawi et al.[15] and Yoshida et al.[41] However, our results were different from those of Halder et al.[27] and Eisenhardt et al.[34] in which the most common pathology was moderately differentiated adenocarcinoma followed by well differentiated adenocarcinoma and poorly differentiated adenocarcinoma.

In our study of 174 patients most (n=89; 51.15%) of the patients presented in stage III followed by stage I (n=39; 22.41%), stage II (n=33; 18.97%) and stage IV (n=13; 7.47%). These results were slightly different from studies of Kumar et al.[33] in which 5.3% of patients presented in stage I, 14.9% in stage II, 40.4% in stage III and 36.8% in stage IV in case of colon cancers while in case of rectal cancers 6.3% presented in stage I, 22.9% in stage II, 47.9% in stage III and 22.9% in stage IV. Eisenhardt et al.[34] reported 40% of patients presented in stage IV, 24.6% in stage III and 32.4% in stage II. Amin et al.[42] found 36% of patients presented in stage IV, 23% in stage III, 30% in stage II, and 11% in stage I. In a study by Chalya et al.[43] 3.3% of cases presented in stage I, 41.6% in stage II, 30.4% in stage III and 24.7% in stage IV. In our study we found elevated preoperative CEA levels (≥ 5.1 ng/ ml) in 80 (45.98%) patients, not elevated (≤ 5.0 ng/ml) in 36patients (20.69%) and not taken/unknown in 58 (33.33%) patients. Out of 80 cases having elevated CEA levels, 66 (82.5%) patients had CEA levels in the range of 5 ng/ml to 10 ng/ml. These results were in agreement with other studies.[34] Serum Carcino Embryonic Antigen (CEA) is not recommended as a screening test, but it might be ordered preoperatively to monitor for any recurrence of disease postoperatively. However, the data is insufficient to support the use of CEA to determine whether to treat the patient with adjuvant therapy or not.[44]

Conclusion

We came to the conclusion that younger age groups are experiencing an increase in CRC incidence, and younger patients are presenting at advanced stage. The general public's lack of knowledge of CRC and the absence of screening programmes are to blame for the advanced state of CRC that is present at presentation. In view of the significant increase in number of young patients presenting with CRC, clinicians should be trained to understand the importance of a detailed family history. Nutritional assessment and therapy should also be included in the management plan as most CRC patients are malnourished. Dietary modifications along with secondary prevention measures may have an impact on reducing the mortality from colorectal cancer. Colorectal carcinoma in young adults is usually locally advanced or metastatic. Therefore, the diagnosis of CRC should be done at early and curable stage. As survival data compilation and will give us a better picture of the ground reality of CRC in India, change in bowel habits and Bleeding per rectum in a younger age group should not be ignored but must be properly evaluated. For colorectal cancer morbidity and mortality to be kept to a minimum, increased public awareness through the media, screening of high-

risk groups, early detection, cost-effective multi-modality therapy, and routine follow-up are all urgently needed.

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