



Original Research Article

A comparative study on the clinico-pathological characteristics of early versus late onset colorectal carcinoma cases in a tertiary care centre in central Kerala

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ABSTRACT

Introduction: The incidence of colorectal cancers is rising in the young adult population. To understand its pathogenesis we compared the clinical and pathological characteristics of early and late onset colorectal cancers.

Materials and Methods: Sixty seven consecutive histopathologically confirmed cases who were diagnosed at the centre from April 2018 and March 2019 were studied. The study subjects were divided into two age-groups, the early onset group with subjects younger than 45 years and the late onset group with subjects older than 45 years. The clinico-pathological characteristics of colorectal carcinoma cases were compared using an analytical cross-sectional design.

Results: Majority of patients in both groups presented with bleeding rectum followed by pain abdomen and constipation. Weight loss was significantly higher among early onset group (p value <0.041). A significantly higher proportion of subjects with type 2 diabetes mellitus were observed in the late onset group (p value = 0.008). A predominance of distal colon and rectal site cancers were seen in both groups. Early onset patients had a significantly higher frequency of mucinous tumours (p=0.018). A statistically significant difference was observed between the two groups in the stage wise comparison with majority of early onset subjects presenting in Stage I and II (p value=0.015). Analysis of CEA and Hemoglobin levels also revealed key distinctions.

Conclusion: This study emphasizes the existence of some salient differences between early and late onset colorectal carcinomas with regard to the clinicopathological profile. Further studies are warranted to uncover the molecular features of early onset colorectal cancer.

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1. Introduction

Worldwide colorectal carcinoma (CRC) represents 9.4% of all incident cancers in men and 10.1% in women. In countries with westernised lifestyle colorectal cancer represents 12.6% of all incident cancers in men and 14.1% in women. Colorectal cancer is the second commonest cause of death from any cancer in men in the European Union.¹ According to National Population based Cancer Registry programme, Colorectal carcinoma is the fourth most common cause of cancer in males and third most common cause of cancer in females in India.² The age

standardised incidence rates of colorectal carcinoma in India which has been estimated to be 4.2 per 1 lakh for males and 3.2 per 1 lakh for females is relatively lesser as compared to the global age standardised incidence rates which is 7.7 per 1 lakh for males and 6.5 per 1 lakh for females.^{2,3} The incidence of colorectal malignancies in India is recently showing an age shift from old age to the younger age which is accelerated by urbanisation and change in dietary habits.⁴ The commonly described symptoms of colorectal carcinoma are rectal bleeding, change in bowel habit, loss of weight, anaemia and abdominal discomfort.⁵ The varying symptomatology may be attributed to the anatomic location and aggressiveness of the neoplasm.⁶

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Globally the incidence of early onset colorectal carcinoma is found to be increasing.^{7,8} Studies from India also indicates an increase in the incidence of colorectal carcinoma in young adults.⁹ Early onset colorectal carcinoma always raises the suspicion of hereditary colorectal cancer syndromes but these syndromes represent only a small proportion of young onset cases.¹⁰ Many reports have shown that subjects with young onset colorectal carcinoma have distinguishing pathological characteristics and anatomic location of tumour.⁷ Young onset Colorectal carcinoma tends to occur in the recto-sigmoid and the rectum.⁸ Most research done in early onset colorectal cancers are from the west and there is a paucity of reports from the Indian subcontinent especially South India. With this background we undertook this study to compare the clinicopathologic features of early onset colorectal carcinoma cases with that of the late onset group.

2. Materials and Methods

This was a cross sectional study using a database of malignancies maintained by the clinical epidemiology unit of community medicine department and department of pathology from April 2018 to April 2019. The department of pathology received a total of 104 consecutive specimens of diagnosed or suspected colorectal tumours during this time period. Patients with hereditary syndromes and inflammatory bowel diseases were excluded and sixty seven histo-pathologically confirmed cases were included for the study.

The resected specimens were fixed in 10% formol saline overnight. Detailed gross examination was done on the next day and tissue bits were taken from representative areas. The tissues were then processed using an automated tissue processor followed by paraffin embedding. The sections were cut at five microns size and stained using standard hematoxyllin and eosin staining protocol and were studied under light microscopy.

The socio-demographic details, clinical history, basic laboratory investigations, stage at diagnosis and the details of biomarkers were obtained from the database. We divided the patients into two groups a) The early onset group with subjects upto the age of 45 years and b) the late onset group with subjects above the age of 45 years. The stage wise distribution and analysis was done according to the AJCC cancer staging manual seventh edition.¹¹ All statistical analysis was done using IBM SPSS, version 25. Chi-square test, Fishers exact test and Independent samples t test were used as applicable.

3. Results

We included 67 patients with colorectal cancers using the epidemiological database from April 2018 to April 2019. The age of the subjects in this study ranged from 28 to 75

years with a mean age of 54.94 ± 11.05 with a slightly higher preponderance of female patients (52.2%). A comparison of clinical and pathological characteristics of the early onset and late onset patient groups revealed several differences.

The majority of the patients in the early onset group and the late onset groups presented with bleeding per rectum, followed by pain abdomen and constipation. A comparison of clinical features in the early onset to the late onset group is given in Table 2. Weight loss as a presenting symptom was significantly higher among the early onset CRC group (p value=0.041). The mean duration of presenting symptom was approximately 4 months in the early onset group and 6 months in the late onset group. No significant difference was observed between the early onset group and late onset group in terms of socio-demographic factors like gender distribution, education, socio-economic status and behavioural risk factors like smoking and alcoholism. The clinical attribute distinguishing the late onset group was a significantly higher proportion of subjects with type 2 Diabetes (48% vs 11%, p value = 0.008).

The pathological characteristics of the study population are outlined in Table 3. An assessment of the anatomical location of the tumour revealed a predominance of the distal colon and rectum in both patient groups (58.1% and 53.1%). On histo-pathological examination, majority in the late onset group were having well differentiated tumours (40%) and the majority in the early onset group had moderately differentiated tumours (47.1%). The proportion of undifferentiated tumours in the early onset group and late onset group was 7.1% and 14.3% respectively. There was no statistically significant difference between the two groups on the basis of tumour grade. Early onset patients had a significantly higher frequency of mucinous tumours (17.7% vs 2%, p=0.018). With regard to the stage of disease, the early onset group had 64.7% of the subjects either in stage I or stage II disease compared to 57.1% of the subjects in the late onset group belonging to either stage III or stage IV as shown in Table 3. A statistically significant difference (p value=0.015) was observed between the two groups in the stage wise comparison. There were 3 subjects with distant metastasis in the late onset group and none in the early onset group (6% vs 0%, p value =0.724). The site of metastasis in the late onset group was peritoneum and liver.

The relationship between the Carcinoembryonic Antigen (CEA) levels and the age group of the study subjects is given in Table 4. A significantly higher proportion of subjects among the late onset group had elevated CEA levels (78% vs 41.2%, p value=0.004).

The analysis of haemoglobin levels among the study population is given in Table 5. The mean Hb values were 12.94 ± 1.33 in the early onset CRC group and 9.91 ± 2.33 in the late onset CRC group with values among early onset subjects being significantly higher (p=0.007)

Table 1: Comparison of the symptoms of CRC in the early and late onset groups

Symptom	<45 years, n(%)	>45 years, n(%)	P value
Bleeding per rectum	6(35.2%)	23(46%)	0.441
Abdominal pain	4(23.5%)	22(44%)	0.134
Constipation	4(23.5%)	15(30%)	0.609
Weight loss	4(23.5%)	3(6%)	0.041
Diarrhoea	1(5.9%)	5(10%)	0.520
Fatigue	2(11.7%)	2(4%)	0.264
Tenesmus	0(0%)	1(2%)	0.746

Table 2: Comparison of the study groups based on gender, behavioural factors and co-morbidities

Variables	Category	<45 years, n(%)	>45 years, n(%)	p Value
Gender	Male	8(47.1%)	24(48%)	0.946
	Female	9(52.9%)	26(52%)	
Alcohol use	Yes	2(11.8%)	7(%)	0.815
	No	15(88.2%)	43(%)	
Tobacco use	Yes	2(11.2%)	3(%)	0.434
	No	15(88.2%)	47(%)	
Comorbidity	Diabetes	2(11.8%)	24(48%)	0.008
	Hypertension	2(11.8%)	17(34%)	0.078
	Dyslipidemia	0(0%)	7(14%)	0.177
Gynecologic disorders	Yes	4(%)	11(%)	0.911
	No	5(%)	15(%)	
BMI	Mean±SD	21.74±1.94	23.36±3.75	0.128

Table 3: Comparison of the Pathologic Characteristics between two age groups

Characteristics	Total N(%)	<45 years n(%)	>45 years n(%)	p value	
No of subjects	67	17(25.3%)	50(74.7%)		
Anatomic location	Colon	19(28.4%)	4(23.5%)	15(30%)	0.714
	Rectosigmoid	12(17.9%)	3(17.6%)	9(18.4%)	
	Rectum	36(53.7%)	10(58.8%)	26(53.1%)	
Tumour stage	Stage I	11(16.4%)	7(41.2.3%)	4(8.2%)	0.015
	Stage II	21(31.3%)	4(23.5%)	17(34.7%)	
	Stage III	32(47.8%)	6(35.3%)	25(51%)	
	Stage IV	3(4.5%)	0(0%)	3(6.1%)	
Tumour histological grade	Well Differentiated	24(35.8%)	4(23.5%)	20(40%)	0.556
	Moderately Differentiated	25(37.3%)	8(47.1%)	17(34.7%)	
	Poorly Differentiated	5(7.5%)	1(7.1%)	4(8.2%)	
	Undifferentiated	8(11.9%)	1(7.1%)	7(14.3%)	
Tumour type	Adenocarcinoma	63(94.1%)	14(82.3%)	49(98%)	0.018
	Mucinous histology	4(5.9%)	3(17.7%)	1(2%)	
Metastasis	Present	64(95.5%)	0(0%)	3(6%)	0.724
	Absent	3(4.5%)	17(100%)	47(94%)	

Table 4: CEA levels and age group

Lab parameter	<45 Years n(%)	>45 years n(%)		
CEA	Normal	10(58.8%)	11(22%)	0.004
	Elevated	7(41.2%)	39(78%)	

Table 5: Mean Haemoglobin values and age group

Lab parameter	<45 Years	>45 years		
Hemoglobin Levels	Mean±SD	12.94±1.33	9.91±2.33	0.007

4. Discussion

Numerous studies have reported a male predominance in both early onset and late onset cancers.^{12–14} However in the present study we have a female predominance with a male to female ratio of 1:1.25 in early onset and 1:1.08 in the late onset group.

The clinical characteristics of our study population with respect to the presenting symptoms were similar to those found in literature already published. In our study rectal bleeding and abdominal pain were the most common presenting symptoms in both age groups. Astin et al reported in a systematic review of 55 papers that rectal bleeding and abdominal pain are the principal presenting symptoms in CRC.⁶ A major finding in this study was the significant association of the presenting symptom, loss of weight, with early onset CRC. Low et al reports that weight loss is a potential early clinical finding that could be associated with early onset CRC.¹⁵ The present study reveals that the patients belonging to the late onset CRC group have a significantly higher prevalence of type 2 Diabetes as a comorbidity compared to early onset CRC. This finding confirms the results of a metaanalysis investigating the association of diabetes with colorectal cancer.¹⁶ Many observational studies link early onset CRC with Smoking and Alcoholism.^{17–19} But we did not observe any significant difference in the frequency of tobacco smoking and alcohol intake between the early onset and late onset CRC subjects.

In the present study, early onset patients have a predilection for the left side of the colon namely rectum and rectosigmoid areas. This finding of predominantly left sided lesions is consistent with the findings of investigators from the Indian subcontinent.^{12,14} Numerous reports on CRC from elsewhere in young patients describes tumour localisation in the right colon.^{20,21} We found a significantly higher prevalence of mucinous differentiation among the early onset CRC group. This finding concurs with the patterns observed in studies by Minardi et al and O'Connell et al.^{21,22}

Our findings regarding the stage at diagnosis is in sharp contrast to multiple studies that examined the association with early onset CRC and stage at diagnosis.²³ Majority of the global studies report that advanced stage cancers are more diagnosed in young patients.^{9,24,25} Several studies from India also reported more advanced stage and poor prognosis in early onset patients.^{12,14} Our finding of early stage cancers in early onset CRC patients underlines the need for heightened clinical suspicion when treating young patients.

The association of CRC and iron deficiency anemia is well established. In the current study anemia was found to be significantly higher in the older age group. This observation was found to be in accordance with two studies by Sotaro Sadahiro et al and Chao Hung Ho et al and in contrast to a study by Hamilton W et al which states that

anemia has a strong association in younger patients.^{5,26,27} A systematic review by Astin et al observed that the investigation of rectal bleeding and anaemia in primary care patients can be used as a screening tool, irrespective of whether other symptoms are present.⁶ Anemia is a sign for primary care physicians to consider the possibility of GI cancer and also have an important role in identifying older individuals for screening and timely evaluation of CRC risk. In the present study the late onset group was characterised by a higher proportion of subjects with elevated CEA marker. This may be due to the confounding effect of advanced tumour stage in the late onset group. Sensitivity of CEA in detecting colorectal cancer increases with increasing stage of the disease.^{28,29}

5. Conclusion

Our study indicates that weight loss and abdominal pain in young adults with no predisposing genetic risk factors demand evaluation with a colonoscopy. Based on our data colorectal cancers of the young age occur predominantly in the rectum and rectosigmoid and are less advanced at the time of presentation compared to the elderly population. This study makes it known that early onset CRC vary by stage of the disease, presence of co-morbidities like Diabetes and lab parameters like CEA and haemoglobin. Physicians should be made aware of the increasing incidence of early onset CRC and the importance of recommending early screening. Further research should be undertaken to unveil the pathogenic mechanisms underlying early onset colorectal carcinoma and to evaluate the effectiveness of strategies to screen populations younger than 45 years.

6. Source of funding

None.

7. Conflict of interest

None.

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