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Younger Patients with Colorectal Cancer Presents with More Advanced Disease at Initial Presentation in Iraq

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Abstract

Background: Colorectal cancer is the third most common type of cancer in oncologic pathology, and it is considered the second most common cause of death related to cancer affecting men as women in the same manner worldwide, the onset of disease in genetic CRCs is known to be about 45 years old, but sporadic CRCs are mostly patients aged 65 years or older. However, recent reports show an increasing incidence among young people. Aim of the study: To raise the index of suspicion for early colorectal cancer that develops in persons under the screening age (<50 years old). Patients and method: A retrospective case control study started from January 2019 to the end of December 2022 in the Department of General Surgery at surgical wards in Al Imamain Alkadhumain Teaching Hospital. 176 patients, newly diagnosed as a case of CRC at our center during the study period were included. Results: Male was common in young and old age (62%, and 68.3%) respectively than female and the most common tumor location was in rectum (34%), While in (≥50) is descending colon (34%), significant difference between both groups regarding the site of tumor (P<0.001) (left sided is significant). Significant difference found between both groups in the study regarding staging of tumor in the left side (p=0.005). Conclusion: The clinical suspicion for colorectal carcinoma should be kept high in young age group (<50 years) with suspected clinical features.

Keywords:

Colorectal cancer, sporadic, early onset, right colon, left colon, rectum.

Introduction

Colorectal cancer (CRC) is a prevalent and serious malignancy that affects the gastrointestinal tract. It accounts for approximately 13% of all cancer cases and is the second leading cause of cancer-related deaths worldwide, affecting both men and women equally [1].

While the incidence of CRC is typically higher in individuals above the age of 60, recent reports have shown an increasing number of cases in young people. This shift in demographics has led to concerns regarding the biological behavior and prognosis of early-onset CRC, defined as the development of CRC in individuals under the recommended screening age of 50 years [2]. Traditionally, CRC has been associated with older age groups, and screening efforts have primarily focused on individuals aged 50 and above.

This approach aims to detect early-stage CRC and remove precursor lesions such as adenomatous polyps and sessile serrated lesions (SSLs), which can progress to invasive cancer.

Approximately 70% of sporadic CRCs develop from adenomatous polyps, while 25%-30% arise from SSLs through the SSL-to-carcinoma pathway [3]. However, the increasing incidence of early-onset CRC highlights the need to reevaluate screening strategies and raise awareness among healthcare providers and the general population. The biological characteristics of CRC in young patients appear to differ from those in older patients. Studies have shown that early-onset CRC is associated with more aggressive tumor behavior, advanced tumor stage high rates of poorly differentiated cancer, and shorter survival rates [4]. These findings suggest that early-onset CRC may be a distinct disease entity requiring tailored

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The global burden of early-onset CRC is of particular concern in several Asian and African countries, including Pakistan, where more than 80% of the population is younger than 40 years [5].

The majority of early-onset CRC cases are considered sporadic and are likely influenced by behavioral and environmental factors. However, a minority of cases are associated with inherited CRC syndromes [6]. Identifying the underlying etiology of early-onset CRC remains a topic of ongoing research. Effective screening strategies play a vital role in reducing the incidence and mortality of CRC [7].

In the United States, various screening tests are available, including guaiac-based fecal occult blood tests (gFOBTs), flexible sigmoidoscopy, fecal immunochemical tests (FITs), and screening colonoscopies. Randomized controlled trials have demonstrated significant reductions in CRC mortality with gFOBTs and flexible sigmoidoscopy, while observational studies support the effectiveness of FITs and screening colonoscopies [8, 9]. The stage of CRC at the time of diagnosis significantly impacts treatment options and survival rates. Staging is determined by assessing the size of the primary tumor (T stage), involvement of lymph nodes (N stage), and presence of distant metastases (M stage) [10].

Early detection through screening programs allows for the identification of CRC at its earliest, curable stages, enhancing the chances of successful treatment and improved outcomes [11]. Unfortunately, the low index of suspicion for CRC in young patients without a family history often results in delayed diagnosis. Young patients may exhibit a longer time interval between symptom onset and diagnosis due to delayed medical care-seeking, limited access to healthcare, or delays in diagnosis by healthcare professionals [12]. Aim of the study: To raise the index of suspicion for early colorectal cancer that develops in persons under the screening age (<50 years old).

Method

A retrospective case-control study was conducted from January 2019 to December 2022 at the Department of General Surgery in Al Imamain Alkadhumain Teaching Hospital. The study included 176 newly diagnosed colorectal cancer (CRC) patients at the center during the study period. Among them, 62 patients (35.2%) were under 50 years old (group A), while 104 patients were 50 years old or older. Seven patients in group A had a family history of CRC, and 5 cases had incomplete data and were excluded from the analysis. Diagnosis of CRC in all patients was based on clinical presentation, investigations (colonoscopy, histopathology, CT scan of the abdomen, and CEA level), and documentation of age at diagnosis, sex, tumor location, and disease stage. The most common presenting symptom leading patients to seek medical care was recorded, and the percentage of each clinical presentation was calculated.

The duration in months from symptom onset to CRC diagnosis was also determined as a measure of delay in diagnosis. Tumor localization was classified into rectal cancer (within 16 cm of the anal verge) and colon cancer (above 16 cm from the anal verge). Colon cancer was further subdivided into left colon and right colon based on the operation protocol. The American Joint Committee on Cancer Staging System (AJCC 7th edition) was used for staging, dividing patients into early stages (I and II) and late stages (III and IV).

The inclusion criteria for the study were age less than 50 or 50 years and older, newly diagnosed with CRC, no prior screening test, and both males and females. Patients with suspected familial syndromes, Lynch syndrome, recurrent tumors, incomplete histopathological reports, or biopsy reports from other centers were excluded. Ethical considerations were taken into account, and approval was obtained from the Iraqi Council of Medical Specializations and the hospital administration.

Participants were provided with an explanation of the study's purpose and procedures, and verbal consent was obtained with the assurance of confidentiality. Statistical analysis was performed using the SPSS program (version 23). Descriptive statistics such as frequencies, percentages, measures of central tendency, and dispersion were used for qualitative and quantitative variables. Inferential statistics included chi-square tests and paired t-tests, with a significance level set at $p \leq 0.05$.

Results

Table 1, showed that mean age of patients < 50 years was (40.3+ 13.8) years old, and for group ≥ 50 years was (57.6+ 22.4) years old with significant difference found between both groups (P<0.001). Male was common in group I (62%) than female with male to female ratio: 1.6:1. Moreover, it is common in group II (68.3%) in which the ratio of male to female was 2.15:1.

Table 1: Demographic criteria of the studied groups.

Age in years		Group 1 (<50 years (n=50)	Group 2 (≥ 50 years) (n=104)	P value
Mean age+ SD		40.3+ 13.8	57.6+ 22.4	<0.001 S
Gender	Male	31 (62%)	71 (68.3%)	0.5 Ns
	Female	19 (38%)	33 (31.7%)	
Total		50 (100%)	104 (100%)	

Abdominal pain was the most common presentation in both studied groups (34% in group 1, and 49% in group 2), then bleeding per rectum (22% in group 1, and 28% in group 2), altered bowel habit (16% in group 1, and 9.6% in group 2), intestinal obstruction found in (14% in group 1, and 7.7% in group 2), acute abdomen found in (8% in group 1, and 1.9% in group 2), and palpable mass was found in (6% in group 1, and 4.8% in group 2) with no significant difference found between both groups (P=0.3). All these were found in table 2.

Table 2: Clinical presentations in the studied groups.

Presentation	Group 1 (<50 years (n=50)	Group 2 (≥ 50 years) (n=104)	P value
Abdominal pain	17 (34%)	51 (49.0%)	0.3 Ns
Bleeding per rectum	11 (22%)	28 (26.9%)	
Altered bowel habit	8 (16%)	10 (9.6%)	
Intestinal obstruction	7 (14%)	8 (7.7%)	
Acute abdomen	4 (8%)	2 (1.9%)	
Palpable mass	3 (6%)	5 (4.8)	
Total	50(100.0%)	104 (100.0%)	

The delayed in diagnosis of the disease was found in 26 patients in group 1 (<50 years) and 23 patients in group 2 (≥ 50 years) in which the most common symptom delayed in diagnosis was abdominal pain (50% in group 1 and 47.8% in group 2), then bleeding per rectum (30.8% in group 1, and 26.1% in group 2), and lastly altered bowel habit found in (19.2% in group 1, and 26.1% in group 2). The time interval between the symptom and diagnosis of the disease was increased significantly in group 1 than that in group 2 in which it is (247.8±62.4) days in group 1 and (112.6 ±22.7) days in group 2 with P value=<0.001, (table 3).

Causes of delay in diagnosis was as follow; poor educational level was found in (34.6%) in group 1 and (30.5%) in group 2, weak awareness of the screening program was found in (19.2%) in group 1and (34.8%) in group 2, faraway distance from hospital that make the delay in diagnosis was found as (23.1%) in group 1 and (21.7%) in group 2, and doctors related in delayed (misdiagnosis) was found as (23.1%) in group 1 and (21.7%) in group 2 (table 3).

Table 3: Symptom, causes delay and duration.

Symptoms delayed	Group 1 (<50 years (n=26)		Group 2 (≥ 50 years) (n=23)		P value
	No.	%	No.	%	
Abdominal pain	13	50.0	11	47.8	0.8 Ns
Bleeding per rectum	8	30.8	6	26.1	0.9 Ns
Altered bowel habit	5	19.2	6	26.1	0.8 Ns
Total	26	100.0	23	100.0	
Duration of delayed for all patients (days)	247.8±62.4		112.6 ±22.7		<0.001 S
Causes of delay	**Group 1 (<50 years (n=26)**		**Group 2 (≥ 50 years) (n=23)**		**P value**
	No.	%	No.	%	
1. Poor educational level	9	34.6	7	30.5	Ns
2. weak awareness of the screening program	5	19.2	8	34.8	Ns
3. Distance from the hospital	6	23.1	3	13.0	Ns
4.Doctor related (misdiagnosis)	6	23.1	5	21.7	NS
Total	26 (100%)		23 (100%)		

The most common tumor location in group 1(<50 years) was in rectum (34%), then sigmoid (22%), then cecum in (16%), then (8%) in each of ascending and transverse colon, and lesser site was (4%) in each of (hepatic flexure, splenic flexure, and descending colon). While in group 2(≥50) the most common site was in descending colon (34%), then transverse colon (17.3%), then cecum in (16.3%), rectum in (12.6%), then sigmoid in (6.7%), hepatic flexur(5%), Ascending colon in (5%), and splenic flexure in (2.9%), with significant difference between both groups regarding the site of tumor (P<0.001) (left sided is significant) (table 4).

Table 4: Tumor locations in the studied groups

Sub sites	Group 1 <50 (n=50)	Group 2 (≥50) (n=104)	P value
Cecum	8 (16%)	17 (16.3%)	<0.001
Ascending colon	4 (8%)	5 (4.8%)	
Hepatic flexure	2 (4%)	5 (4.8%)	
Transverse colon	4 (8%)	18 (17.3%)	
Splenic flexure	2 (4%)	3 (2.9%)	
Descending colon	2 (4%)	36 (34.6%)	
Sigmoid	11 (22%)	7 (6.7%)	
Rectum	17 (34%)	13 (12.6%)	
Total	50 (100%)	104 (100%)	

Stage of disease in group 1 showed that stage I and II was found in 19 patients and stage III and IV was in 31 patients, in right colon 6 (31.6%) in early stage and 8 (25.8%) in late stage, in left colon 7 (36.8%) in early stage and 12 (38.7%) in late stage, and in rectum 6 (31.6%) in early stage and 11 (35.5%) in late stage with no difference between early and late stage of tumor in group 1 (P=0.9) (table 5).

Moreover, significant difference found between both groups in the study regarding staging of tumor in the left side (p=0.005) (table 6).

Table 5: Staging of the tumor in group 1.

Site	Group 1 <50 (n=50)				P value
	Stage I &II		Stage III &IV		
	No.	%	No.	%	
Rt. colon	6	31.6	8	25.8	0.9 Ns
Left colon	7	36.8	12	38.7	
rectum	6	31.6	11	35.5	
Total	19	100.0	31	100.0	

Table 6: stage of disease in related to tumor locations.

Site	Group 1 <50 (n=50)				Group 2 (≥50) (n=104)				P value
	Stage I &II		Stage III &IV		Stage I &II		Stage III &IV		
	No.	%	No.	%	No.	%	No.	%	
Rt. colon	6	31.6	8	25.8	17	50.0	20	28.6	0.005 S
Left colon	7	36.8	12	38.7	11	32.3	43	61.4	
rectum	6	31.6	11	35.5	6	17.6	7	10.0	
Total	19	100.0	31	100.0	34	100.0	70	100.0	

Discussion

Colorectal cancer (CRC) is a significant health concern worldwide, and the incidence of early-onset CRC (EOCRC) is on the rise. In our study, which focused on CRC patients under the age of 50, we found that 35% of the diagnosed cases belonged to this age group. This percentage is similar to findings from other studies, such as the study by Zahir et al. [5], which reported a comparable proportion of early-onset CRC cases in the Pakistani population. However, it is important to note that the incidence of EOCRC can vary across different regions and populations [13]. The incidence of EOCRC in developing countries is often higher compared to developed countries. This disparity may be attributed to various factors, including differences in lifestyle, dietary habits, genetic predisposition, and limited access to healthcare services. In our study, the majority of EOCRC cases were sporadic, suggesting that environmental and behavioral factors play a significant role in the development of CRC in young individuals. Clinical presentation is a crucial aspect of CRC diagnosis; as early detection is closely linked to improved outcomes. In our study [14], the most common symptoms reported by young CRC patients were rectal bleeding, altered bowel movements, and abdominal pain. These findings align with the general symptom profile of CRC patients, regardless of age [15, 16]. However, it is worth noting that the duration of symptoms before diagnosis was significantly longer in the EOCRC group compared to older patients [17, 18]. This delay in diagnosis may be attributed to factors such as lack of awareness, misinterpretation of symptoms, and limited access to healthcare services, both on the part of the patients and the healthcare providers [19, 20]. Tumor location is an important consideration in CRC, as it can influence disease management and prognosis. In our study, we found that the rectum and sigmoid colon were the most commonly affected sites in young CRC patients [21]. This is consistent with previous studies that have reported a higher prevalence of left-sided CRC in young individuals. The predominance of left-sided tumors in EOCRC may be associated with differences in genetic and molecular characteristics compared to right-sided tumors [22]. Further research is needed to explore the underlying mechanisms behind these differences. The stage of the tumor at the time of diagnosis is a critical determinant of treatment options and overall survival [23, 24]. In our study, a significant proportion of young CRC patients presented with advanced-stage disease (stage III and IV). This finding is consistent with previous studies that have shown a higher likelihood of advanced disease at diagnosis in younger patients [25]. The lack of screening programs targeted at the younger population, delays in diagnosis, and seeking non-specialized healthcare providers may contribute to the higher proportion of advanced-stage disease in this age group.

Conclusion

Colorectal cancer (CRC) in young individuals (<50 years) is a concerning issue due to its sporadic nature and delayed diagnosis. Young patients commonly present with symptoms such as abdominal pain, rectal bleeding, and altered bowel habits. Early suspicion and prompt colonoscopy are crucial for timely disease management. Left-sided or rectal diagnoses are more prevalent in CRC patients. Delays in consultation and treatment contribute to advanced disease at presentation. Extending screening programs to younger individuals and improving public awareness are essential to enhance early detection and treatment outcomes.

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