Al-Rafidain J Med Sci. 2023;5:86-91.
DOI: https://doi.org/10.54133/ajms.v5i.158

Research Article

Clinicopathological Features of Colorectal Cancer in the Iraqi Population Focusing on Age and Early-Onset of Malignancy: A Descriptive Cross-Sectional Study

Rand Muthanna Farhad[1]*, Eman Saadi Saleh[2], Ahmed Zuhair Alsammarraie[3]

[1] Department of Clinical Pharmacy, College of Pharmacy, University of Baghdad, Baghdad, Iraq; [2] Department of Clinical Laboratory Sciences, College of Pharmacy, University of Baghdad, Baghdad, Iraq; [3] Oncology Teaching Hospital, Medical City, Baghdad, Iraq

Received: 17 June 2023; Revised: 20 July 2023; Accepted: 25 July 2023

Abstract

Background: Colorectal cancer (CRC) is one of the top ten most common cancers worldwide. There are multiple risk factors for CRC, one of which is aging. However, in recent years, CRC has been reported in children. ***Objective***: To describe the main characteristics and symptoms of CRC as well as highlight pathologic data for early-onset CRC. ***Methods***: 79 CRC patients were recruited from the Oncology Teaching Hospital in the period February–December 2022. A questionnaire was used to collect demographic and clinical data. ***Results***: 25 (31.6%) of patients were below 50 years of age. 52 (65.8%) patients had their tumors in the colon. The most common symptom is bleeding per rectum in both age groups. There was no significant difference in pathologic characteristics between early and late-onset CRC. ***Conclusion***: Although older people are more likely to develop CRC, both age groups can be affected. Younger and older individuals both had roughly similar symptoms and clinicopathologic features.

Keywords: Early-onset CRC, Late-onset CRC, Rectal bleeding, Clinicopathologic features.

السمات السريرية المرضية لسرطان القولون والمستقيم لدى السكان العراقيين مع التركيز على العمر والبداية المبكرة للأورام الخبيثة: دراسة وصفية مقطعية

الخلاصة

الخلفية: سرطان القولون والمستقيم (CRC) هو واحد من أكثر عشرة سرطانات شيوعا في جميع أنحاء العالم. هناك العديد من عوامل الخطر لهذا المرض، أحدها هو الشيخوخة. ومع ذلك ، في السنوات الأخيرة، تم الإبلاغ عن حصول هذا النوع من الأورام لدى الأطفال. **الهدف**: وصف الخصائص والأعراض المرضية لسرطان القولون والمستقيم وكذلك تسليط الضوء على البيانات المرضية لحدوث CRC المبكر لدى المرضى العراقيين. **الطريقة**: تم استدعاء 79 مريضا من مرضى سرطان القولون والمستقيم من مستشفى الأورام التعليمي في بغداد خلال الفترة من فبراير إلى ديسمبر 2022. تم استخدام استبيان لجمع البيانات الديموغرافية والسريرية. **النتائج**: 25 (31.6٪) من المرضى تقل أعمارهم عن 50 عاما. 52 (65.8٪) مريض لديهم أورام في القولون. أكثر الأعراض شيوعا هو النزيف المستقيم في كلتا الفئتين العمريتين. لم يكن هناك فرق كبير في الخصائص المرضية بين بين مرض سرطان القولون والمستقيم المبكر والمتأخر. **الأستنتاج**: على الرغم من أن كبار السن أكثر عرضة للإصابة بسرطان القولون والمستقيم، إلا أن كلتا الفئتين العمريتين يمكن أن تتأثر. كان لدى كل من الأفراد الأصغر سنا والأكبر سنا أعراض وخصائص سريرية مرضية متشابهة تقريبا.

* ***Corresponding author***: Rand M. Farhad, Department of Clinical Pharmacy, College of Pharmacy, University of Baghdad, Baghdad, Iraq; Email: rand.mothana1100e@copharm.uobaghdad.edu.iq

Article citation: Farhad RM, Saleh ES, Alsammarraie AZ. Clinicopathological features of colorectal cancer in the Iraqi population focusing on age and early-onset of malignancy: A descriptive cross-sectional study. *Al-Rafidain J Med Sci*. 2023;5:86-91. doi: https://doi.org/10.54133/ajms.v5i.158

INTRODUCTION

Colorectal cancer (CRC) is the third most prevalent malignancy and the second leading cause of mortality worldwide, with an estimated 1.9 million cases and 0.9 deaths globally in the year 2020 [1]. The epidemiology of CRC differs markedly between multiple countries in the world; it is more common in developed countries than in low- and middle-income countries. However, the incidence is increasing in developing countries due to westernization and changes in environmental factors, and by the year 2030, it is anticipated to rise by 60% [2]. In Iraq, CRC is likewise the third most common cancer, with 2,328 new cases detected in the year 2019 [3]. Like in other developing nations, CRC cases in Iraq in both genders increased significantly after 2007 [4]. As Cancer is linked to aging, most CRC cases arise after the age of 50, and they are more common in males than females, as males seem to be more influenced by environmental factors [5]. Numerous risk factors, which can be further broken down into modifiable (diet and lifestyle) and non-modifiable (age, gender, and ethnicity), most often co-occur and interact to cause CRC [6]. Genetic factors also play a major role in the development of CRC, which mostly involves the activation of proto-oncogenes or the inactivation of tumor suppressor genes [7]. Adenocarcinoma, a malignant tumor that arises from glandular epithelial cells of the colon and rectum, accounts for the vast majority (>90%) of CRCs; other uncommon kinds include squamous cell carcinoma, adenosquamous carcinoma, and undifferentiated carcinoma [8]. Depending on the source of mutation, CRC can be classified as sporadic, which constitutes 70% of cases that occur without the presence of family history; familial due to the existence of family history (25%); and inherited, which compromises 5% due to heredity cancer syndromes such as familial adenomatous polyposis and Lynch syndrome [9]. CRC pathogenesis occurs through three molecular mechanisms: microsatellite instability, chromosomal instability, and the cytosine guanine (CpG) island methylator phenotype [10,11]. Although most CRC cases occur in individuals over 50 years of age, in recent years CRC cases have been reported at younger ages, and it is called early-onset colorectal cancer (EO-CRC). There is no clear definition of EO-CRC in the literature or guidelines. Nonetheless, generally, it includes all CRC malignancies that were diagnosed before the screening age, which is below 50 years [12]. The problem with EO-CRC is that younger patients are more likely to present with later stages of the disease, as physicians do not suspect CRC when young patients present with initial minor symptoms [13]. In a number of cases, CRC tumors begin as very small asymptomatic polyps, and patients do not present with any symptoms in the early stages of the disease; as the symptoms occur, they differ depending on tumor location, lymph node involvement, and metastasis to other organs [14,15]. The aim of this study is to describe the epidemiological and clinical data of CRC cases in a sample of the Iraqi population, highlighting characteristics of EO-CRC with regard to demographics, clinical, and pathologic features.

METHODS

Study design and subjects

This is a descriptive cross-sectional study conducted in the Oncology Teaching Hospital, Medical City, Baghdad, from February to December 2022 that involved 79 CRC patients, with the primary outcome being to highlight their clinicopathologic characteristics.

Inclusion criteria

CRC patients whose diagnosis was confirmed by colonoscopy and histopathological biopsy [16] who are over the age of 18 years.

Exclusion criteria

Patients with other forms of cancer, as well as those with genetic, hematological, or neurological abnormalities, were excluded.

Data collection

A questionnaire was designed to obtain demographic information directly from patients, such as age, BMI, family history, and smoking status. Clinicopathological information from patients' files included TNM classification [17], stage, tumor differentiation, and signs and symptoms. Blood samples were taken to determine the level of Carcino-Embryonic Antigen (CEA), a tumor marker used to determine the diagnosis and severity of the disease.

Ethical considerations

The ethics committee at the University of Baghdad, College of Pharmacy (approval number: RECAUBCP26102021B) accepted the study in compliance with the responsible committee on human experimentation's ethical requirements. Before being included in the study, all subjects provided informed consent.

Statistical analysis

SPSS software version 26 (SPSS® Inc., Chicago, USA) was used to analyze the data. Continuous data were expressed as mean ± standard deviation (SD) and categorical data as count and percentage. For discrete variables, associations between distinct parameters were evaluated using the chi-square or Fisher exact test. For continuous variables, however, an independent

sample t-test was utilized. A p-value less than 0.05 was judged statistically significant.

RESULTS

The present study included 79 confirmed CRC patients; among the studied participants, there were 45 males and 34 females, with a ratio of 1:3. The average age of patients was 55.4±12.5 years. Only 25 (31.6%) subjects were under the age of 50 years; 14 (56%) of them were males, and the male to female ratio was approximately 1:3. Other demographics of CRC patients are illustrated in Table 1, and the age distribution of the study sample is shown in Figure 1.

Table 1: Demographics of CRC patients, (*n*=79)

Parameters	Results
Age (year) (mean±SD)	55.4±12.5
Gender n (%)	
Male	45 (57)
Female	34 (43)
Smoking *n* (%)	
Yes	35 (44.3)
No	44 (55.7)
BMI (kg/m^2) (mean±SD)	26.1±4.02
Family history of CRC *n* (%)	11 (13.9)

BMI: Body Mass Index, SD: standard deviation

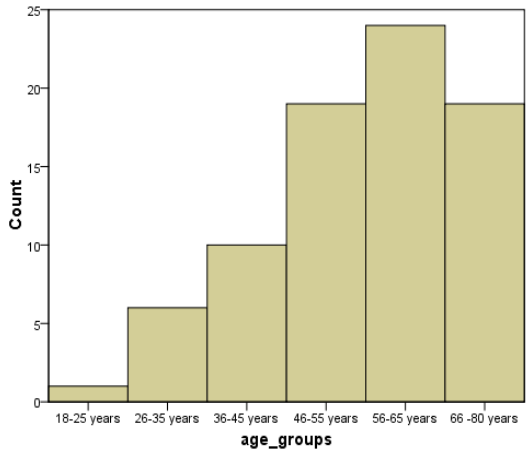

Figure 1: Age distribution of CRC patients

About the clinicopathologic characteristics, the majority of patients had tumors in the colon (65.8%), and most of the tumors were moderately differentiated (62%). None of the patients had stage 1, and the most common stage found was stage II, with a percentage of 43%. The frequency of tumor invasion, lymph node involvement, and level of CEA at diagnosis are found in Table 2.

Table 2: Clinicopathological characteristics of CRC patients, *n* (79)

Parameters	Results *n* (%)
Tumor location	
Colon	52 (65.8)
Rectum	27 (34.2)
Tumor differentiation	
Well	15 (19)
Moderate	49 (62)
Poor	15 (19)
Stage	
II	34 (43)
III	32 (40.5)
IV	13 (16.5)
Tumor invasion	
T1	2 (2.5)
T2	12 (15.2)
T3	44 (55.7)
T4	21 (26.6)
Lymph node involvement	
N0	32 (40.5)
N1	23 (29.1)
N2	24 (30.4)
CEA at diagnosis (mean±SD)	21.8±6.8

CEA: Carcino-embryonic antigen (µg/L), SD: Standard Deviation

Concerning symptoms, the most common symptom reported is bleeding per rectum (35.7%), while the least common is tenesmus (1.8%). In addition, approximately one third of the patients had abdominal pain and altered eating habits (27.7% and 23.2%, respectively). Other symptoms are illustrated in Table 3.

Table 3: Distribution of most common symptoms

Symptoms	*n* (%)
Bleeding per rectum	40 (35.7)
Abdominal pain	31 (27.7)
Alteration in bowl habits	26 (23.2)
Weight loss	9 (8)
Intestinal obstruction	4 (3.6)
Tenesmus	2 (1.8)

Regarding early-onset CRC (below the age of 50 years), the demographics between the two age groups were non-comparable except for smoking. Smokers under the age of 50 constitute 28%. On the other hand, smokers aged 50 years and older are 51.9% (Table 4).

Table 4: Comparison of demographic features based on age

Demographics	EO-CRC (age <50 y) *n*(%)	LO-CRC (age≥50 y) *n*(%)	*p*-value
Age	25 (31.6)	54 (68.4)	<0.0001*
Gender			
Male	14 (56)	31 (57.4)	0.90†
Female	11 (44)	23 (42.6)	
Smoking			
Yes	7 (28)	28 (51.9)	0.04†
No	18 (72)	26 (48.1)	
BMI (kg/m^2) (mean±SD)	27.4± 4.5	25.4±3.6	0.07*
Family history			
Yes	6 (24)	5 (9.3)	0.15†
No	19 (76)	49 (90.7)	

* *t*-test was used, † chi square test was used, EO-CRC: early-onset colorectal cancer, LO-CRC: late-onset colorectal cancer, BMI: Body Mass Index, SD: standard deviation

There was no difference in the distribution of tumor location, tumor differentiation, tumor invasion, lymph node involvement, or metastasis compared to patients who were 50 years of age or older (Table 5).

Table 5: comparison of clinicopathologic characteristics based on age

Parameters	Age<50 y	Age > 50 y	*p*-value
Tumor location *n*(%)			
Colon	13 (25)	39 (75)	
Rectum	12 (44.4)	15 (55.6)	0.078 *
Tumor differentiation *n*(%)			
Well	4 (26.7)	11 (73.3)	
moderate	18 (36.7)	31 (63.3)	0.48†
Severe	3 (20)	12 (80)	
Tumor invasion *n*(%)			
T1 and T2	7 (50)	7 (50)	0.12 †
T3 and T4	18 (27.7)	47 (72.3)	
Lymph node involvement *n*(%)			
Negative lymph node	9 (28.1)	23 (71.9)	0.57 *
Positive lymph node	16 (34)	31 (66)	
Stage *n*(%)			
2	11 (44)	23 (42.6)	0.75 †
3	11 (44)	21 (38.9)	
4	3 (12)	10 (18.5)	
Metastasis *n*(%)			
No	22 (33.8)	43 (66.2)	0.53 †
Yes	3 (23.1)	10 (76.9)	
CEA at time of diagnosis (µg/L)	15.2±31.9	24.7±52.3	0.40 ‡

* chi square was used, † Fisher exact test was used, ‡ independent sample t test was used, CEA: Carcino-Embryonic Antigen

The most frequent reported symptom in patients aged under 50 years is bleeding per rectum. However, the least reported symptom was weight loss. No significant association was found between early-onset CRC and late-onset CRC with regard to symptoms (Table 6).

Table 6: Comparison of symptoms distribution based on age

Symptom	< 50 y	≥ 50 y	*p*-value
Bleeding *n*(%)			
Yes	16 (40)	24 (60)	0.10 *
No	9 (23.1)	30 (76.9)	
Abdominal pain *n*(%)			
Yes	9 (29)	22 (71)	0.80 *
No	16 (33.3)	32 (66.7)	
Altered bowl movement *n*(%)			
Yes	7 (26.9)	19 (73.1)	0.43 *
No	19 (35.2)	35 (64.8)	
Bowel obstruction *n*(%)			
Yes	2 (50)	2 (50)	0.23 †
No	23 (30.3)	53 (69.7)	
Weight loss *n*(%)			
Yes	1 (100)	0 (0)	0.31 †
No	24 (30.8)	54 (69.2)	
Tenesmus *n*(%)			
Yes	2 (66.7)	1 (33.3)	0.23 †
No	23 (30.3)	53 (69.7)	

* chi square test was used, † Fisher exact test was used

DISCUSSION

Colorectal cancer (CRC) is a prevalent cancer that has been associated with the elderly in Western societies. Nonetheless, the trend is turning toward a higher occurrence in low- and middle-income countries as well as in younger individuals due to westernization and globalization [18]. Iraq, as part of the MENA region, has been associated with a lower incidence of CRC (6.12 per 100,000 population), although during the past two decades, it has gradually increased [19]. There have been several studies that have investigated the epidemiology of CRC cases in Iraq [4,16,19-21]. Yet none of them focused on the characteristics of EO-CRC cases. Therefore, the aim of this study was to describe the major characteristics of this tumor concerning age, gender, main symptoms, and clinicopathologic characteristics, as well as shed light on the features of EO-CRC among a sample of Iraqi CRC patients. The present research found that 57% of CRC patients were male and 31.6% of the sample were younger than 50 years, which is consistent with previous research [16,19,20]. It is obvious that there is a trend toward CRC cases in relatively young patients in Iraq, and it could be affiliated with the movement from traditional Iraqi food to westernized fast food loaded with fat and processed meat, which has become popular among these age groups. The most common symptom reported among both age groups of patients is bleeding per rectum. On the other hand, the least frequent symptom is weight loss in patients younger than 50 years, while patients 50 years and older did not report any weight loss, and the least frequent symptom was tenesmus. These findings are in agreement with

research conducted on 63 CRC patients recruited from a gastroenterology and hepatic center in Baghdad [16]. Dhahir and Noaman found that anemia is the most frequent among both age groups, and tenesmus is the least common finding among EO-CRC cases, which is similar to this study [22]. Moreover, bleeding per rectum and iron deficiency anemia were found to be ten times more associated with EO-CRC in a review published in 2021 [23]. Interestingly, the vast majority of EO-CRC cases are diagnosed due to the presence of signs and symptoms, in contrast to late-onset CRC, which in several cases is diagnosed accidentally. There was no statistically significant difference in clinicopathologic characteristics between the two age groups; both age groups had more tumors in the colon, most tumors were moderately differentiated, and most were in stages 3 and 4. Furthermore, there was no statistical difference in the mean CEA at diagnosis. None of the previous studies conducted in Iraq assessed the difference in clinicopathologic features based on age groups [24]. A few studies have investigated the molecular, histologic, and pathologic characteristics of EO-CRC, concluding that it usually presents with later stages, poorly or undifferentiated tumors, mucinous tumors, and a higher count of signet ring cells [25,26]. The limitations of the study include a relatively small number of patients and the fact that recruitment was only from a single center

Conclusion

The present study showed that there is no difference in clinicopathologic characteristics between early-onset and late-onset CRC. Further studies with a larger sample size and from several oncology centers in different Iraqi governorates are warranted.

ACKNOWLEDGMENTS

The authors would like to express appreciation to all subjects whose participation made this study possible.

Conflicts of interest

There are no conflicts of interest.

Funding source

The authors did not receive any source of fund.

Data sharing statement

Supplementary data can be shared with the corresponding author upon reasonable request.

REFERENCES

1. Xi Y, Xu P. Global colorectal cancer burden in 2020 and projections to 2040. *Transl Oncol*. 2021;14(10):101174. doi: 10.1016/j.tranon.2021.101174.

2. Ahmad R, Singh JK, Wunnava A, Al-Obeed O, Abdulla M, Srivastava SK. Emerging trends in colorectal cancer: Dysregulated signaling pathways. *Int J Mol Med*. 2021;47(3):14. doi: 10.3892/ijmm.2021.4847.

3. Al Alwan NA. Cancer control and oncology care in Iraq. *J Contemp Med Sci*. 2022;8(1):82-85. doi: 10.22317/jcms.v8i1.1154.

4. Hussain AM, Lafta RK. Cancer trends in Iraq 2000-2016. *Oman Med J*. 2021;36(1):e219. doi: 10.5001/omj.2021.18.

5. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. *Nat Rev Gastroenterol Hepatol*. 2019;16(12):713-732. doi: 10.1038/s41575-019-0189-8.

6. Dekker E, Tanis PJ, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. *Lancet*. 2019;394(10207):1467-1480. doi: 10.1016/S0140-6736(19)32319-0.

7. Abbood IS, Aziz IH. Genetic variation in BRAF gene among Iraqi colorectal cancer patients. *Iraqi J Biotechnol*. 2018;17(3):78-84.

8. Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: Pathologic aspects. *J Gastrointest Oncol*. 2012;3(3):153-173. doi: 10.3978/j.issn.2078-6891.2012.030.

9. Mármol I, Sánchez-de-Diego C, Pradilla Dieste A, Cerrada E, Rodriguez Yoldi MJ. Colorectal carcinoma: A general overview and future perspectives in colorectal cancer. *Int J Mol Sci*. 2017;18(1):197. doi: 10.3390/ijms18010197.

10. Hanon BM, Al-Mohaimen Mohammad NA, Mahmood AS. CpG island methylator phenotype (CIMP) correlation with clinical and morphological feature of colorectal cancer in Iraqi patients. *Pan Arab J Oncol*. 2015;8(2):6-13.

11. Mahood WS, Nadir MI, Tobal K, Asker BA. Methylation status of p16 gene in Iraqi colorectal cancer patients. *Iraqi J Biotechnol*. 2014;13(2):237-247.

12. Mauri G, Sartore-Bianchi A, Russo AG, Marsoni S, Bardelli A, Siena S. Early-onset colorectal cancer in young individuals. *Mol Oncol*. 2019;13(2):109-131. doi: 10.1002/1878-0261.12417.

13. Khan SA, Morris M, Idrees K, Gimbel MI, Rosenberg S, Zeng Z, et al. Colorectal cancer in the very young: a comparative study of tumor markers, pathology and survival in early onset and adult onset patients. *J Pediatr Surg*. 2016;51(11):1812-1817. doi: 10.1016/j.jpedsurg.2016.07.015.

14. Aljarshawi M, Albadree H, Bahar H, Al-Imam A. Misleading presentation of colorectal cancer in an otherwise healthy patient. *J Faculty Med Baghdad*. 2020;62(4):132-138. doi: 10.32007/jfacmedbagdad.6241800.

15. Mahmood AH, Zeiny SM, Mahmood AS. Serological markers "CEA test & sAPRIL test" in Iraqi patients with colon cancer. *J Faculty Med Baghdad*. 2017;59(4):317-320. doi: 10.32007/jfacmedbagdad.59472.

16. Alrubaie A, Alkhalidi N, Abd-Alhusain S. A clinical study of newly-diagnosed colorectal cancer over 2 years in a gastroenterology center in Iraq. *J Coloproctol (Rio de Janeiro)*. 2019;39:217-222. doi: 10.53350/pjmhs22163328.

17. Weiser MR. AJCC 8th Edition: Colorectal Cancer. *Ann Surg Oncol*. 2018;25:1454-1455. doi: 10.1245/s10434-018-6462-1.

18. Clinton SK, Giovannucci EL, Hursting SD. The world cancer research fund/American institute for cancer research third expert report on diet, nutrition, physical activity, and cancer: Impact and future directions. *J Nutr*. 2020;150(4):663-671. doi: 10.1093/jn/nxz268.

19. Ibrahem S, Ahmed H, Zangana S. Trends in colorectal cancer in Iraq over two decades: incidence, mortality, topography and morphology. *Ann Saudi Med*. 2022;42(4):252-261. doi: 10.5144/0256-4947.2022.252.

20. Al-Saigh TH, Al-Bayati SA, Abdulmawjood SA, Ahmed FA. Descriptive study of colorectal cancer in Iraq, 1999-2016. *Ann Coll Med Mosul*. 2019;41(1):81-85. doi: 10.33899/mmed.2019.161330.

21. Alsafi RA, Metib NJ, Hameedi AD, Alqanbar MF. The clinical and pathological characteristics of colorectal cancer in young age group in Karbala province/ Iraq. *Karb J Med*. 2019;11(2):4025.

22. Dhahir NK, Noaman, A. A. A Comparative study of colorectal cancer based on patient's age. *J Faculty Med Baghdad*. 2021;63(2):70-73. doi: 10.32007/jfacmedbagdad.6321825.

23. Burnett-Hartman AN, Lee JK, Demb J, Gupta S. An update on the epidemiology, molecular characterization, diagnosis, and screening strategies for early-onset colorectal cancer. *Gastroenterology*. 2021;160(4):1041-1049. doi: 10.1053/j.gastro.2020.12.068.

24. Chen FW, Sundaram V, Chew TA, Ladabaum U. Advanced-stage colorectal cancer in persons younger than 50 years not associated with longer duration of symptoms or time to diagnosis. *Clin Gastroenterol Hepatol*. 2017;15(5):728-737. doi: 10.1016/j.cgh.2016.10.038.

25. Patel SG, Ahnen DJ. Colorectal cancer in the young. *Curr Gastroenterol Rep*. 2018;20(4):15. doi: 10.1007/s11894-018-0618-9.

26. Silla IO, Rueda D, Rodríguez Y, García JL, de la Cruz Vigo F, Perea J. Early-onset colorectal cancer: a separate subset of colorectal cancer. *World J Gastroenterol*. 2014;20(46):17288-17296. doi: 10.3748/wjg.v20.i46.17288.