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CLINICAL STUDY OF COLORECTAL CANCER IN AL NAJAF AL ASHRAF GOVERNORATE

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Abstract
Background: Colorectal cancer is a type of large intestine cancer that affects many individuals causing significant mortality rate worldwide, including Iraq.
Objective: Determine the clinical and epidemiological characteristics of colorectal cancer patients that are addressed in Al Najaf governorate and assess of factors associated with colorectal cancer
Patients and methods: a sample of 180 patients who had been diagnosed by an oncologist at the Middle Euphrates Cancer Center in al-Najaf, Iraq. The method of collecting data by direct interview technique (face-to-face) with patients using the questionnaire format designed for this purpose. Data collection lasted six months, from December 2022 to May 2023. The data were analyzed using Statistical Package for the Social Sciences (SPSS-29), and Chi-square tests were used to assess the association between numerous variables.

Results: Mean±SD age of study sample was 55.3±14.5 years old. Of all patients, 59.4% had colon cancer, 54.8% had grade II cancer, majority of patients 65.7% were presented at T3 stage according to TNM staging. Lymph node involvement in patients was 52.2%, and 68.9% of them did not have metastatic cancer. History of gallstones and cholecystectomy were 10% and 14.4%, respectively. Diabetes and hypertension were prevalent in 20% and 28.9% of participants, respectively. 39.4% of patients had been exposed to radiation from a uranium-depleted bomb, while 25.6% of patients were current or former smokers. The majority of patients, 87.2%, had cramping, 83.3% weight loss, 70% constipation, 75.6% weakness, and 67.2% bleeding as signs and symptoms. The majority of patients (76%) used colonoscopy as a diagnostic method. The treatment method for the majority of patients (50.6%) was postoperative chemotherapy.

Conclusions: high percentage of study sample presented with colon cancer followed by rectal cancer with grade II and metastasis in 31%.

Recommendation: Colorectal cancer prevention requires the implementation of countrywide screening programs beginning at the age of 50. The early detection of cancer allows for complete recovery. Lifestyle choices appear to be an important component of community prevention efforts. Health education programs that explain the significance of exposed to risk factors in the development or prevention of CRC.

Keywords: cancer, staging, metastasis, colonoscopy, chemotherapy.

1. Introduction

One of the most important cancers is colorectal cancer (CRC). Colorectal cancer is third in terms of recognition (6.1%) and second in terms of mortality (9.2%) (Sawicki et al., 2021). In Iraq CRC is likewise the third most common cancer, (Farhad,et al., 2023) the overall (males and females) CRC incidence proportion(CIP) increased from 2.28 to 6.18 per 100,000 population in 2000 and 2019, respectively, with an annual percentage change (APC) of 5.11% (Ibrahem et al., 2022). Age is one of the most significant risk factors for colorectal cancer, incidence rates increasing about 94% in adults 50 years or older

(Davidson et al., 2021). The existence of a family history of colorectal cancer in first-degree relatives increases the risk of colorectal cancer development even in the absence of the previous history. When there is a history of colorectal cancer in first-degree relatives, the risk exceeds two times when compared to the other individuals. (Thanikachalam and Khan, 2019). Obesity and physical inactivity are the most significant behavioral factors to CRC development. According to studies , persons who engage in regular physical activity had a 25% lower risk of acquiring CRC (Rawla et al., 2019). Early detection by screening, removal of adenomatous polyps, and identification of early-stage disease are important factors in treating colorectal cancer (Araghi et al., 2019).

2. Patients and method:

A sample of 180 patients was collected for six months from December 6, 2022, to May 25, 2023, at the Middle Euphrates Oncology Center through a pre-prepared questionnaire that was reviewed by experts. The sample size was determined using EPI-Info (version 6.0) (Al-Sarray 2019). The researcher used the face-to-face interview method with patients because a large percentage of them are illiterate. The questionnaire form contained several parts, the most important of which were the patient's demographic characteristics, cancer-related information, cancer metastasis, and body mass index (BMI). Furthermore, information were obtained about patients' comorbidities and their exposure to a group of risk factors, such as smoking and exposure to medical radiation.

3. Statistical analysis

Analysis of data were carried out using the available statistical package of SPSS-28 (Statistical Packages for Social Sciences- version 28). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of difference of different means (quantitative data) were tested using Students-t-test for difference between two independent means or Paired-t-test for difference of paired observations (or two dependent means), or ANOVA test for difference among more than two independent means. The significance of difference of different percentages (qualitative data) were tested using Pearson Chi-square test (χ^2-test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was equal or less than 0.05.

4. The results

Tables (1) shows some of the demographic characteristics of the study sample. The most afflicted age groups were 60-69 by 25.6%, while the majority of patients were equal to or older than 50 years old. Males comprised 55% of the sample population. According to the findings, urban patients made up 76.1% of all patients.

Table (1) demographic characteristics of study sample

		No	%
Age (years)	20---29	9	5.0
	30---39	20	11.1
	40---49	33	18.3
	50---59	42	23.3
	60---69	46	25.6
	70---79	23	12.8
	80---89	7	3.9
Age (years)	<50years	62	34.4
	≥50years	118	65.6
	Mean±SD (Range)	55.3±14.5 (20-89)	
Gender	Male	99	55.0
	Female	81	45.0
Residence	Urban	137	76.1
	Rural	43	23.9

In table (2) the results revealed cancer-related information: The colon was the most common site of malignancy in most patients (59.4%). Of all patients, 54.8% had grade II. According to TNM staging, 65.7% of patients had T3 stage, and the majority of patients (68.9%) had no metastatic malignancy. The percentage of patients with lymph node involvement was 52.2%. The majority of patients (42.2%) were diagnosed in 2023.

Table (2) Cancer information of study samples

		No	%
Cancer site	Colon	107	59.4
	Rectum	73	40.6
Cancer grade	Grade I	53	42.7
	Grade II	68	54.8
	Grade III	3	2.4
TNM staging	T1	3	2.9
	T2	15	14.3
	T3	69	65.7
	T4	18	17.1
Date of diagnosis	≤2019	9	5.1
	2020	13	7.2
	2021	28	15.6
	2022	54	30.0
	2023	76	42.2
Metastasis	Yes	56	31.1
	No	124	68.9
Lymph nodes involvement	Yes	94	52.2
	No	86	47.8

According to previous medical history, the results in table (3) indicate that 10% of patients had a history of cholecystectomy, whereas 14.4% of patients had gallstones. Only 20%, 28.9%, 8.9%, and 6.1%, respectively, of patients had diabetes mellitus, hypertension, coronary artery disease, and hypercholesterolemia. The percentage of patients with a positive family history of colorectal cancer was 17.8%, and the family history of other cancers was 25%. The percentage of non-smokers was 74.4%. The previous history of exposure to radiation from depleted uranium during the war was 39.4%, while most patients were not exposed to therapeutic radiation.

Table (3) shows co-morbidity, risk factors of study sample

		No	%
Cholecystectomy	Yes	18	10.0
	No	162	90.0
Gall stone	Yes	26	14.4
	No	154	85.6
Diabetes mellitus	Yes	36	20.0
	No	144	80.0
Hypertension	Yes	52	28.9
	No	128	71.1
Coronary artery disease	Yes	16	8.9
	No	164	91.1
Hypercholesterolemia	Yes	11	6.1
	No	169	93.9
Family history of colorectal cancer	Yes	32	17.8
	No	148	82.2
Family history of other cancer	Yes	45	25.0
	No	135	75.0
Smoking	Current smoker	10	5.6
	Ex-smoker	36	20.0
	Non-smoker	134	74.4
Radiation(depleted uranium) exposure	Yes	71	39.4
	No	109	60.6
Radiation therapy exposure	Yes	2	1.1
	No	178	98.9

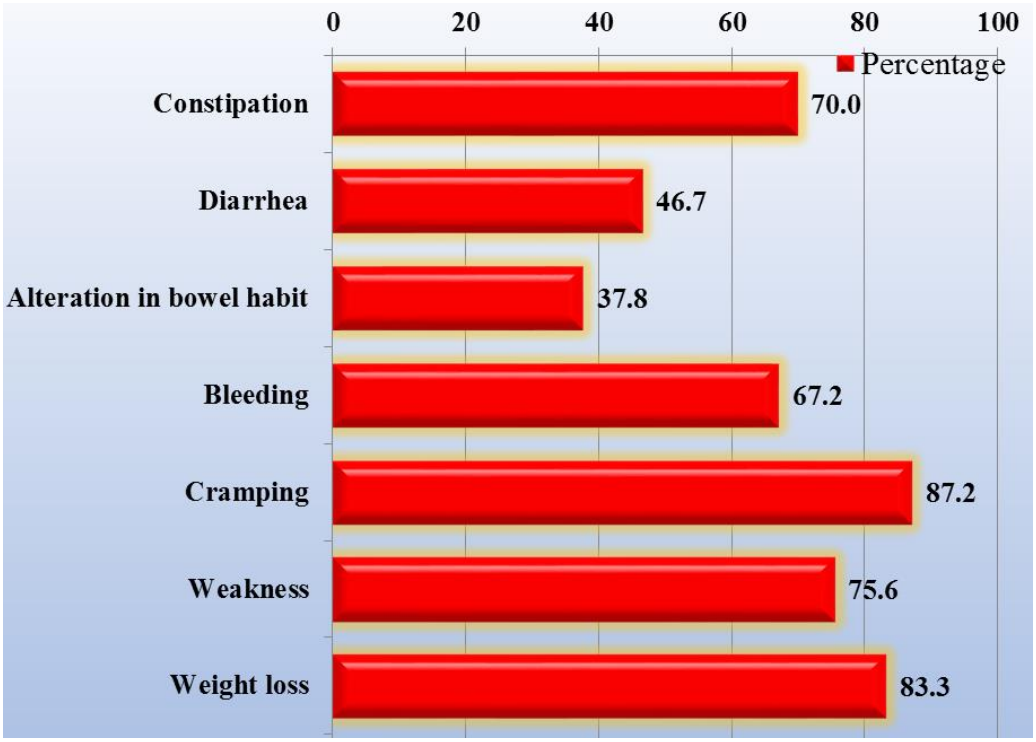

Figure 1: Signs and symptoms of patients of study sample

The results of the clinical presentation of colorectal cancer in figure (1) indicate that 70% of patients had constipation, 46% had diarrhea, and 37.8% had a change in bowel habits. The data show that (67.2, 87.2, 75.6, and 83.3%) respectively, of the participants had bleeding, cramping, weakness, and weight loss.

In the current study, table 4 showed that the most common method used to diagnose colorectal cancer was colonoscopy (76.7%), and 50.6% of patients underwent postoperative chemotherapy.

Table (4) Diagnostic and treatment methods of study sample

		No	%
Diagnosis method	Colonoscopy	138	76.7
	Sigmoidoscopy	1	0.6
	CT scan	-	-
	Histopathology	41	22.7
Treatment method	Radiotherapy	11	6.1
	Chemotherapy	65	36.1
	Postoperative chemotherapy	104	57.8

Table 4 revealed a highly significant association between cancer site and residence at a level of P value 0.002, and there is no association with age, gender, or marital status.

Table (5) Association between cancer site, demographic variables of study sample

Ca by type		Cancer site				P value
		Colon (n=107)		Rectum (n=73)		
		No	%	No	%	
Age (years)	<50years	38	35.5	24	32.9	0.715
	≥50years	69	64.5	49	67.1	
Gender	Male	57	53.3	42	57.5	0.572

	Female	50	46.7	31	42.5	
Residence	Urban	90	84.1	47	64.4	0.002*
	Rural	17	15.9	26	35.6	
Marital status	Single	2	1.9	4	5.5	0.412
	Married	98	91.6	62	84.9	
	Widowed	5	4.7	6	8.2	
	Divorced	2	1.9	1	1.4	
	Separated	-	-	-	-	
*Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.						

In Table 6, the result showed no association between cancer site and cancer-related information: cancer grade, TNM staging, metastasis, and lymph node involvement.

Table (6) Association between cancer site, and cancer information of study sample

Cancer by site		Cancer site				P value
		Colon (n=107)		Rectum (n=73)		
		No	%	No	%	
Cancer grade	Grade I	30	38.5	23	50.0	0.455
	Grade II	46	59.0	22	47.8	
	Grade III	2	2.6	1	2.2	
TNM staging	T1	2	2.7	1	3.2	0.893
	T2	10	13.5	5	16.1	
	T3	48	64.9	21	67.7	
	T4	14	18.9	4	12.9	
Metastasis	Yes	38	35.5	18	24.7	0.122
	No	69	64.5	55	75.3	
Lymph nodes	Yes	59	55.1	35	47.9	0.343
	No	48	44.9	38	52.1	
*Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.						

In the table 7, the results showed a significant association between lymph nodes involvement and type of treatment at a p value of 0.047.

Table (7) Association between lymph node involvement and treatment methods

		Lymph nodes involvement				P value
		Yes (n=94)		No (n=86)		
		No	%	No	%	
Treatment	Radiotherapy	2	2.1	9	10.5	0.047*
	Chemotherapy	38	40.4	27	31.4	
	Postop. chemotherapy	54	57.5	50	58.1	
*Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05 level.						

5. Discussion:

Colorectal cancer is a form of gastrointestinal cancer that can develop in either the colon or the rectum. They are often combined due to the many biological and clinical similarities between them, although they may be classified as colon or rectal cancers depending upon their origin (Mattiuzzi et al., 2019). Unfortunately, colorectal cancer can go unnoticed for a long period in many people, at least until it grows and spreads extensively, badly impacting the prognosis. In symptomatic patients, the disease may cause changes in bowel motility (such as constipation or diarrhea), a persistent urge to urinate, occult or visible colorectal bleeding, abdominal pain, cramping, unexplained weight loss, weakness, and fatigue, among other signs and symptoms, particularly in patients with advanced stages of cancer. (Araghi et al., 2019) This study aims to determine the clinical features of patients with CRC and to assess the risk factors of this disease in AL Najaf governorate, including non-modifiable factors such as age, gender, family history, and smoking.

In this study, the findings indicate that the median age was 55.3±14.5; this result is similar to other reported studies: a study in Baghdad by (Farhad et al. 2023), and a study in Korea by (Dhawan et al., 2021). While this result is not in line with the study in

Poland by (Lewandowska et al., 2022) who found the mean age of patients was 64.53 ± 8.86. 34% of patients, were below 50 years old this result is similar to a study in Baghdad (Farhad et al., 2023). It is clear that colorectal cancer cases among young patients in Iraq are on the rise, and this trend may be attribute to first-degree relative history, sporadic mutation, and genetic predisposition (Syed et al., 2019).

The study results revealed that 55% of cases were male, perfectly matching the result of a study by (Alkarboly, 2015) in Kurdistan, also agrees to other reported studies by (Soliman and Mohamad, 2022) in Baghdad, and a study by (Schneider et al. 2018) in Switzerland. This could be due to the fact that men are more likely than women to smoke or drink. Men are also more likely than women to accumulate visceral fat, which is linked to an elevated risk of CRC (White et al., 2018).

Regarding the effects of environmental and social conditions, in the current study, the results showed that 76.1% of cases resided in urban areas. This is similar to other reported studies: a study by (Shiraz Ali Mahmood, 2023) in Sulaymaniyah who found that majority of patient residences were in urban areas. As with the study by (Charles R. Rogers et al., 2020) in USA. This may be due to The influence of social and environmental conditions on health behaviors and outcomes merits further exploration (Charles R Rogers et al., 2020).

The most commonly observed location of CRC in this study is colon 59.4%. This is similar to other reported studies: a study in Colombia by (Bohorquez et al., 2016), who found 56.2% of cancers were in the colon. As a study in Netherlands by (van der Sijp et al. 2016). This may be due to the fact that the colon and rectum are anatomically quite different in terms of location, blood supply, drainage, and innervation. These variations result in differences in the initial tumor's invasive growth (van der Sijp et al., 2016).

Regarding the histopathological examination of the tumor biopsy, this study reported that 54.8% of patients had grade II cancer. This agrees with a study in Finland that indicated most patients 58.5% had grade II cancer. (Väyrynen et al., 2018). While this result differs from a previous reported study in Al Najaf, by (Al-jubori, 2015) who found that 28% of the study sample were in grade II; this may be related to the difference in the sample size. The result found the percentage of T3 according to TNM staging was 65.7%, (that means tumor invasion of the subserosal and perirectal tissue of the subperitoneal organ). This is inconsistent with other reported studies: a study by (Bohorquez et al. 2016) in Colombia who found that (79.8%) of the cases were in the same stage and from a study by (Altintas and Bayrak 2019) in Turkey who found that 87.6% of patients in the same stage. To explain this the T (tumor), N (node), and M (metastasis) staging systems are used to explain disease extent, define prognosis, and eventually guide the treatment module. The outcome of patients with CRC cancer may vary considerably, even within the same tumor stage (Puppa et al., 2010). Metastasis occurred in 31.1% of patients; this agrees with a study in Saudi Arabia who found one third (30%) of patients had distant metastasis (Alyabsi et al., 2020) This may be due to the development of screening and treatment of this type of cancer.

Also the histopathological examination reported that, 52.2% of patients had lymph node involvement. This is similar to other reported study in Turkey by (Altintas and Bayrak, 2019) who found 53.8% of patients had lymph node involvement, but not in line with a study in Colombia who found 63.7% of patients had lymph node involvement (Bohorquez et al., 2016) . This may be due to the fact that most patients in this study were in different grade and stage of tumor.

In terms of cholecystectomy history, 10.0% of patients had cholecystectomy. This result agrees with other published study by (Polychronidis et al., 2021) in the USA who found 10% of all patients had cholecystectomy. However a study in China found that only 5% had cholecystectomy (Qin et al., 2022). In this study, 14.4% had a history of gallstones. This is similar to other reported study conducted in Europe by (Ward et al., 2019). But it is different from a study in India who found 33% of patients had previous gall bladder disease (Gosavi et al., 2017). for the explanation that excessive production of bile acid during the inflammatory process in the gall bladder and bile duct played an important role in colorectal carcinogenesis.(Gosavi et al., 2017).

Regarding chronic diseases associated with colorectal cancer, the current study reported that the percentage of patients with diabetes mellitus was 20%; this similar to other reported study by (Boustany et al., 2023) in the USA who found 17.04% of patients had diabetes. While the percentage of patients with diabetes in a study by (Demb et al., 2019) in the USA was 28%. CRC is detected in diabetic patients more frequently than would be expected by chance, however the relationship between diabetes and CRC is not entirely understood. There are potential biochemical linkages between these disorders, including hyperinsulinemia, probably hyperglycemia, and inflammation, that have been supported by research. Furthermore, diabetes, particularly T2D, and colorectal cancer have many risk factors such as lower abdominal obesity, systemic inflammation, a lack of physical exercise, and diet, making it biologically likely that they frequently coexist (Hirsz, 2021). The patients with hypertension were 28.9%; this result differ from other reported studies: a study by (Ahmadi et al., 2014) in Iran who found 13.38% had hypertension. And a study in the UK by (Schneider et al., 2018) who reported that 44% of patients had hypertension. This may be due to the fact that hypertension is affected by many factors among the populations, such as age, male sex, sedentary

lifestyle, and obesity. Patients with hypercholesterolemia in current study were 6.1%. This disagrees with other reported studies conducted by (Brown et al., 2019) in North America who found 49% of patients had hypercholesterolemia and with a study by (Boustany et al., 2023) in the USA who found 30.61% had hyperlipidemia. This difference may be due to the fact that the differences in race and ethnicity lead to differences in the etiology and biology of hyperlipidemia between the Iraqi and American populations (Hsu et al., 2022).

In term of family history effects, this study showed that 17.8% of patients had a positive family history of colorectal cancer. This is similar to other reported study by (Li et al., 2022) in Germany who found 15% of patients had a positive family history of colorectal cancer, but not agrees with a study by (Alhilfi et al., 2019) in Misan, Iraq, who found 42.3% of patients had a positive family history. People who had a family history of CRC or adenomatous polyps were considered to have a higher risk for CRC. Possible explanations included inherited risks, environmental factors, or a combination of both (CS Wong et al., 2019). The percentage of other cancer family history was 20.8%, which agrees with a study in Baghdad that found 24.9% had a positive family history of other cancer (Bahir, 2021).

In the context of smoking habits, the current study showed that the total of current smokers and ex-smokers in patients was 25.6%; this result is similar to other reported studies: a study by (Shiraz Ali Mahmood, 2023) in Sulaymaniyah who found 22% had tobacco habits, and the study by (Simonian et al., 2018) in Iran. While the result of the study in Spain was 45% (Jakszyn et al., 2020). This may be due to the variations in cigarette smoking by sociodemographic characteristics (age, race/ethnicity, region, and sex) (Garrett et al., 2019).

In reference to the effect of radiation from depleted uranium bombs, the present study results revealed that 39.4% of patients were exposed to radiation resulting from depleted uranium bombs that had been used in the first and second Gulf Wars in 1990 and 2003. Although there are no previous studies linking colorectal cancer with exposure to bombs containing depleted uranium, there is a study by (Esraa Aldujaily., 2012) in the Middle Euphrates region linking the effect of depleted uranium on the occurrence of cancers in general.

In the observed clinical presentation, this study showed that cramping is the most common sign in patients (87.2%). This result is similar to other reported studies by (Hamilton et al., 2009) in the UK, a study by (Al-Bayati and Jasim, 2018) in Baghdad, and a study in Misan by (Alhilfi et al. 2019). The percentage of weight loss was 83.3%. This result is consistent with a result in Brazil who found the majority of patients had weight loss, while disagrees with other reported studies : a study in Baghdad by (Alrubaie et al., 2019), a study in Sudan who found 32.5% of patients had weight loss (Khougali et al., 2019). This might be a result of the fact that the majority of the study participants had chemotherapy treatments, which had weight loss as one of their side effects.

The result in this study showed that the prevalence of constipation in patients was 70%. This result differs from other reported studies: a study by (Al-Saigh et al., 2019) in Baghdad who found 75.8% of patients had constipation, and a study by (De Mello et al., 2020) in Brazil that found 29.60% had constipation. The percentage of patients with diarrhea was 46.7%, which is in disagreement with a study by (Al-Saigh et al., 2019) who found 14.5% of patients suffered from diarrhea. 37.8% of patients suffered from an alteration in their bowel habits; this result is differ from a study by (D. Zemenfes, 2015) in Ethiopia who found 48% of patients had an alteration in their bowel habits. The result of current study showed 67.2% of patients had bleeding; this disagrees with other reported studies: a study by (Alrubaie et al., 2019) in Baghdad who found 76.2 patients had bleeding per rectum, as well as a study by (Al-Saigh et al., 2019) in Baghdad. The result revealed 75.6% of patients had weakness. This result disagrees with a study in Brazil (De Mello et al., 2020). Differences in the clinical presentation of colorectal cancer may be due to the fact that the prevalence of symptoms varies with changes in the age and stage of the disease. Or it may be due to recall bias (Rasmussen et al., 2015).

In the current study, the results showed that the majority of patients (76%) used colonoscopy as a diagnostic method, which is the golden choice of diagnosis in colorectal cancer (Thanikachalam and Khan, 2019). Sensitivity and specificity of endoscopy for polyps and extended CRC recognition are 92–97% (Świderska et al., 2014).Most patients undergo postoperative chemotherapy (50.6%), which is the most effective method of colorectal cancer treatment (Simillis et al., 2020). Type of treatment depend on stage and grade of cancer.

The study results showed there is no association between cancer site in the large intestine with age or gender. This agrees with a study by (Li et al., 2008) in China. while inconsistence with a study by (Ristescu et al., 2019) in Romania who found a significant association between cancer site and age. This difference may be due to some etiological and biological differences between colorectal cancer anatomical sites (Lee et al., 2017).

In this study, the results showed no significant association between cancer site and cancer-related information. This result is not in line with a study by

(Ghazi et al., 2012) in Sweden who found significant association between cancer site with T (tumor size). This may be due to different in age, grade and staging of cancer (WHO, 2019). The results in current study showed a significant association between lymph nodes involvement and type of treatment at a p value of 0.047. This is the first study to discuss relationship between lymph nodes involvement and type of treatment. There is no similarity to other reported studies.

6. Conclusions:

The majority of cases occur in males, after the age of 50 years for both males and females, in those who live in urban areas. The most common site of cancer were in the colon; the most prevalent grade was grade II, and the frequent stage was T3 according to TNM staging. The majority of patients had no metastatic cancer, while most of them had lymph node involvement. The predominant signs and symptoms of colorectal cancer patients were cramping, weakness, constipation, weight loss, and bleeding. The most common chronic disease in the patient was hypertension, followed by diabetes mellitus. The majority of patients used colonoscopy as a diagnostic method. There is a significant association between cancer site and residence, and there is a significant association between lymph node involvement and type of treatment.

Limitations of the Study: The researcher faced some difficulties through period of study such as resources were limited which have a great deal of impact on the study such as absent of isolation room and data collection time for conducting the research.

Ethical considerations

All participants obtained full details of the research (background, objectives, methods, use of data), and they were informed that participation is voluntary. The participants were guaranteed confidentiality and anonymity, and they were informed that they could withdraw at any time without giving an explanation.

Conflict of interest

The authors declare no conflicts of interest.

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Recommendation: More research are still needed to evaluate the risk factors of colorectal cancer in Iraqi families, as well as larger patient samples and longer follow-up times. Researchers can benefit from this study to conduct further research to learn more about this type of cancer

Data sharing statement

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

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