ISSN 2692-5877
DOI: 10.46998/IJCMCR.2024.44.001078

International Journal of
Clinical Studies & Medical Case Reports

Research Article

Clinical &Pathological Presentation of Colorectal Cancer Among Young Sudanese Adults in Khartoum State Hospitals (2019-2021)

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Received: August 12, 2024 **Published:** October 22, 2024

Abstract

Background: Colorectal cancer is one of the most common cancers worldwide and its incidence is reported to be increasing in resource-limited countries, probably due to the acquisition of western lifestyle.

Objectives: The study aimed to identify the clinical and pathological presentation of colorectal cancer among Sudanese adults aged 50 years and below versus those above 50 years of age.

Methods: A prospective and retrospective comparative study of histological confirmed cases of colorectal cancer. Retrospective from June/ 2019 to November/ 2020 and prospective from December/2020 to December/2021. The study was multicenter conducted within the main three colorectal services units in Khartoum state; Ibrahim Malik teaching hospital, Ibn Sina hospital, and Soba university hospital. Data had been collected by the researcher using administered questionnaire which included all the variables. Either by direct interview or through phone call with the colorectal cancer confirmed patients. Consents were obtained from all patients included in the study. It was cross-sectional collection and age independent. Prospective follow up for three to six months has been conducted for the new cases that presented during 2020-2021. The patients who presented during 2019 had been contacted by the researcher and their data and history of presentation were documented retrospectively. The total numbers of cases include in this study were 120 cases. They had been divided into two groups, group A (50 years and below) and group B (>50 years).

Results: A total of 120 colorectal cancer patients were enrolled in the study. The mean age of patients at presentation was 51.2 years (SD=15). Sixty-one cases (50.8%) belonged to age group B (>50 years) and 59 cases (49.2%) belonged to group A (50 years and below). Male: female ratio in group A was 1.5:1 and in group B was 1.3:1. A significant number; 65 patients (54.3%) presented with rectal cancer, 35 patients (60%) were young adults and 30 patients (54.2%) were elderly. CRC was most frequently misdiagnosed with dysentery which counted 25 young patients (42.4%) and 17 elderly patients (27.9%). The most dominating presenting symptom among young adults was bleeding per rectum which occurred in 48 patients (81.4%), while weight loss was the most common presenting symptom in elderly which was found in 48 patients (78.8%).
The adenocarcinoma was the most common histopathological type reported in 115 patients (95.8%). Both groups at presentation had advance radiological stage. Stage IIIB was reported in 13 patients (29.5%) among group A and in 14 patients (32.6%) of group B. The commonest postoperative histopathological TNM stage in group A was IIA which was reported in 15 cases (34.9%). In group B Stage IIIB and IIA were reported in 13 cases (26.5%). One hundred and six patients (88.3%) underwent surgical procedures for colorectal cancer. Eighty-nine patients (84%) underwent elective curative resections after preoperative full workup and staging. Five patients (4.7%) underwent emergency resections and 12 patients (11.3%) had palliative procedures. Postoperative complications and morbidity rates were 64.6% and 58.2% for group A and B respectively. One hundred and five out of 120 were alive (96.6%) and available for follow-up at the end of 2 years. Cancer recurrence was reported in 3 cases from group B (2.9%) and metachronous tumor also was detected in two cases from group B.

Conclusion: In this study we identified that young Sudanese adults has different remarkable presentations. They presented

mainly with lower GIT symptoms. Rectal followed by left side CRC was the most common site among young adults, in contrast to older where rectal followed by right side. Molecular and genetic studies are increasing the understanding of the pathobiology of colorectal cancer and may ultimately allow at-risk patients to be identified at an earlier stage.

Keywords: Colorectal Cancer; Colonic Cancer; Rectal Cancer; Early-Onset Colorectal Cancer; lower GIT symptoms

Abbreviations: AJCC: American Joint Committee on Cancer; CCa: Colon Cancer; CEA: Carcino Embryonic Antigen; CRC: ColoRectal Cancer; CT: Computed Tomography; ER: Endoscopic Resection; GIT: Gastro Intestinal Tract; HNPCC: Hereditary Nonpolyposis Colorectal Cancer; M/F: Male /Female; MDT: Multi-Disciplinary Team; PCQ: Patient Consultation Questionnaire; PET: Positron Emission Tomography; SEER: Surveillance Epidemiology and End Results; SLE: Systemic Lupus Erythematosus; SMSB: Sudan Medical Specialization Board; SPSS: Statistical Package for Social Sciences; UK: United Kingdom; USPSTF: United States Preventive Services Task Force

Introduction

As the third most common malignancy and the second deadliest cancer, Colorectal Cancer (CRC) estimated 1.9 million cases per year and 0.9 million deaths worldwide in 2020.The global new CRC cases is predicted to reach 3.2 million in 2040 [1].

Of interest, while we have witnessed a declining incidence trend over the past few decades in the older population, young-onset CRC has been increasing steadily [2]. According to recent statistic that has been done in US, the incidence rate increased by approximately 2% annually among those aged less than 50 [3]. Furthermore, an overview of 8695 articles with applying of their inclusion criteria, they identified 40 studies from 12 countries across five continents. The systematic review highlights increasing young-onset CRC risk in North America and Australia driven by rising rectal cancers in younger adults over the past two decades [4].

In Africa a prospective analysis in South Africa including demographics, clinical presentation, site, staging, and grading of colorectal cancer was done. A total of 2232 patients were included during 18-year period with a different race. The proportion of young patients (< 40 years old) was 28%, 7%, 9% and 3% among Africans, Indian, Colored, and White patients respectively. In conclusion of that study African patients were the youngest compared to the other race groups. Mucinous differentiation predominated in Africans and young adults [5].

In Sudan two descriptive studies were conducted in Ibn Sina Hospital. In one study, seventy-three patients of colorectal cancer who presented in the period between January 2010 to December 2012 were included. More than 17 % of the study population were below the age of 40 years, and 43.84% were below 50 years [6]. The second study was done between 2010 -2012; the sample size was 63 patients and the median age reported was 50 years [7].

Moreover, a retrospective study was conducted in Khartoum Teaching Hospital in Sudan. Two hundred and seventy-seven patients who presented in the period between the 1st January 2000 to the 31st December 2006 were enrolled. One hundred (34.5%) of the study population (n=277) were below the age of 40 years, and 17.3% were below 30 years. The male to female ratio was 1.5:1. Intestinal obstruction was the commonest cause of emergency presentation of colorectal cancer (94%) [8].

Background

Risk Factors

Increasing age is the most important risk factor for most cancers. Other risk factors for colorectal cancer include the following:

- Family history of colorectal cancer in a first-degree relative.
- Personal history of colorectal adenomas, colorectal cancer, or ovarian cancer.
- Hereditary conditions, including familial adenomatous polyposis (FAP) and Lynch syndrome (Hereditary Nonpolyposis Colorectal Cancer [HNPCC]).

- Personal history of long-standing chronic ulcerative colitis or Crohn's colitis.
- Excessive alcohol use.
- Cigarette smoking.
- Race/ethnicity: African American.
- Obesity

Colon cancer could present as sporadic (70%), familial clustering (20%) and inherited syndromes (10%) [10].

Prognosis:

The prognosis of patients with colon cancer is clearly related to the following:

- The degree of penetration of the tumor through the bowel wall.
- The presence or absence of nodal involvement.
- The presence or absence of distant metastases.

These three characteristics form the basis for all staging systems developed for this disease.

Other prognostic factors include the following:

- Bowel obstruction and bowel perforation are indicators of poor prognosis.
- Elevated pretreatment serum levels of carcinoembryonic antigen (CEA) have a negative prognostic significance.

Symptoms and signs:

The colorectal cancer may present with symptoms related to the tumor site

Right side

- Abdominal mass
- Anemia
- Melena
- diarrhea
- Change in bowel habits

Left side
- Constipation
- Bleeding per rectum
- Abdominal distention
- Abdominal mass
- Sense of incomplete evacuation
- Anal mass

Systemic symptoms which include
- Weight loss
- Fatigability
- Loss of appetite.etc

The tumor, node, metastasis (TNM) staging 8th edition system of the American Joint Committee on Cancer/Union for International Cancer Control (AJCC/UICC) 2017 is the preferred staging system for CRC. This was adopted in this study **(Table 1)**.

Diagnosis and treatment [11]

American cancer society recommendation for colorectal cancer diagnosis and treatment as follows:

1. An assessment of disease-specific symptoms, past medical and family history, physical examination, and serum CEA level should typically be evaluated in patients with colon cancer
2. When possible, patients with presumed or proven colon cancer should undergo a full colonic evaluation with histological assessment of the colonic lesion before treatment.
3. Preoperative radiologic staging with a chest/abdomen/pelvis CT should typically be performed.
4. Positron emission tomography/CT (PET/CT) is generally not recommended for routine colon cancer staging.
5. Colon cancer staging should be performed according to the American Joint Committee on Cancer (AJCC)/ TNM system and include an assessment of the completeness of surgical resection designated by the residual tumor code “R”.
6. A thorough surgical exploration should be performed and the findings documented in the operative report.
7. The extent of resection of the colon should correspond to the lymphovascular drainage of the site of the colon cancer.
8. Routine performance of extended lymphadenectomy is not recommended.
9. Resection of adherent or grossly involved adjacent organs should be en bloc.
10. Synchronous colon cancers may be treated by 2 separate resections or subtotal colectomy.
11. Sentinel lymph node mapping for colon cancer does not replace standard lymphadenectomy.
12. When expertise is available, a minimally invasive approach to elective colectomy for colon cancer is preferred.
13. Hand-assisted laparoscopic and robotic surgical techniques for right colon cancer result in oncologic outcomes that are equivalent to open or straight laparoscopic techniques.
14. Treatment of the malignant polyp is determined by the morphology and histology of the polyp.
15. Management of Stage IV Disease patients, presenting with synchronous or metachcronous colon cancer should be individualized and guided by a multidisciplinary team.

Literature Review

Early-onset Colorectal Cancer

Davis et al, evaluated the rates of change in CRC incidence within the Surveillance Epidemiology and End Results (SEER) database (1987-2006). They reported that people older than 50 years had decreasing incidences. They also noted a higher incidence across age groups 20-49 years in 2006 than in 1987. Most significantly, the highest increase (67%) occurred in age 40-44 (from a low of 10.7 per 100,000 in 1988 to 17.9 per 100,000 in 2006) [12].

In a retrospective study using data from the Surveillance Epidemiology and End Results (SEER) Cancer Registry, Meyer et al, identified 7,661 colon and rectal cancer patients under age 40 years between 1973 and 2005. After calculating the change in incidence over time for colon and rectal cancers, the researchers described that while colon cancer rates remained flat, rectal cancer rates have been increasing. Between 1984 and 2005, rectal cancer rate rose by 3.8% per year. This finding led the authors’ state that "in young people presenting with rectal bleeding or other common signs of rectal cancer, endoscopic evaluation should be considered in order to rule out a malignancy". They also suggested that more frequent endoscopic evaluation could decrease the documented delay in diagnosis among young people. But, as the overall incidence of rectal cancer is relatively low, the authors did not advocate for a change in screening guidelines [13].

Another study in Tunisia aim to provide an updated overview on clinicopathological features, treatment, and outcome of colorectal cancer in young adults under the age of 40. In a retrospective study, they covered 32 cases of colorectal cancer in adults aged less than 40 years that were diagnosed at the pathology department of Mongi Slim hospital over a fifteen-year period (April 2000 - November 2014). They included 13 males and 19 females (M/F ratio = 0,68). Their age ranged between 17 and 39 years of age (mean = 31.25 years). The presenting clinical symptoms were dominated by altered bowel habits (n=17), followed by bleeding per rectum (n=16). Histopathological examination of the surgical and biopsy specimens established the diagnosis of mucinous adenocarcinoma in nine cases. They were well-differentiated adenocarcinoma in 11 cases, moderately differentiated adenocarcinoma in six cases, poorly differentiated adenocarcinoma in four cases, and signet ring cell carcinoma in two cases. The tumors were classified after surgery as stage I (n = 2) (6%), stage IIA (n = 7) (22%), stage IIB (n=4) (13%), stage IIC (n=1) (3%), stage IIIB (n=8) (25%), stage IIIC (n= 4) (12%), stage IVA (n=4) (13%) and stage IVB (n=2) (6%). During the follow-up period which ranged between one month and 9 years, local recurrence of the tumor occurred in six cases, seven patients had hepatic metastases and seven patients died after a mean follow-up period of seven months [14].

In an effort to detect the disease at early stages, the United State Preventive Services Task Force (USPSTF) recommended CRC screening in adults aged 45–49 years with a grade “B” recommendation. While the recommendation recognizes the aggressive nature of early-onset CRC, it also reflects the implications of early-onset CRC in terms of the choice of therapies and prognosis [15].

In an interesting retrospective study, O'Connell et al collected data on 6425 patients from 55 manuscripts in the literature. While the majority of articles (n=37) defined "young" those patients under 40 years of age, four articles (7%) focused attention on patients younger than 35 years, 14 articles (25%) looked at patients before 30 years and only one article looked at patients before 25 [16].

According to the literature, research evaluating genetic and molecular differences as well as environmental triggers for early-onset CRCs should provide a clearer understanding to inform targeted screening for pre-symptomatic at risk younger individuals [17].

Furthermore, recent publications have documented that young CRC patients are mostly symptomatic. Advanced disease at presentation could be caused by a delay in investigating these patients. Colonoscopy should be offered early to young patients presenting with warning symptoms. [18].

Attempts to describe clinical, pathological and molecular features in young patients have reached controversial conclusions regarding tumor grade and disease stage at diagnosis. So far, there is no consensus if age should be considered an adverse independent prognostic factor if other features such as topography and staging are considered together. However, it is commonly accepted that diagnosis in young patients is always difficult, because both patient and the doctor usually don't give credit to the presenting symptoms, leading to a frequent unfavorable outcome of the disease [19].

Tumor tissues were prospectively collected from patients from two tertiary hospitals in the Philippines. Patients of age ≤ 45 years with resected adenocarcinoma of the colon or rectum were recruited. Seventy-seven out of 124 patients had tumor samples sent for immunohistochemistry. Of these, 61 samples (79%) were found to have proficient status while 16 samples (21%) had deficient status. Mismatch repair protein deficiencies, when present, more commonly involved MSH2 and MSH6 (9%) rather than MLH1 and PMS2 (5%). The deficient group had a mean age of 37.1 years and a female preponderance (56.25%), presenting as locally advanced ascending or descending colon tumors with mucinous histology in half of the population. The mismatch repair proficient group presented as locally advanced rectal and sigmoid tumors but with fewer mucinous adenocarcinomas (26.2%) compared to the deficient group. In both the mismatch repair proficient and deficient patients with family history reports, most did not have any known relative with cancer (75.4% and 68.75%, respectively) [20].

Sporadic colorectal cancer (CRC) amongst adolescents and young adults is increasing in incidence. The reasons for this trend are not well understood. A systematic literature search was conducted and a total of 17 studies were included from 2010 to 2019. Overall, young adults with CRC tend to present with non-specific symptoms. The majority of these patients have a delayed diagnosis and more advanced disease at presentation, with a rise in prevalence of distal colon and rectal cancers. They tend to have poorly differentiated tumors and are managed more aggressively. Overall 5-year survival varies between studies [21, 22].

In order to improve early detection rate in UK another study was done in 2286 patient with low colorectal symptoms. Patient Consultation Questionnaire (PCQ) linked to a computerized record were used. They detected only 95 cases with early stage CRC. In conclusion, patient consultation questionnaire depends on history alone in conjunction with the weighted numerical score can be used as an accurate system for prediction of symptomatic colorectal cancer [23].

However, in 2021, given the rising incidence in younger adults, the United States Preventive Services Task Force (USPSTF), has aligned with the American Cancer Society and issued an updated recommendation to initiate screening at age 45 in all adults [15].

Investigation tools:

The appropriateness and diagnostic yield of colonoscopy referrals in an African setting using the American Society of Gastrointestinal Endoscopy guidelines was investigated by a prospective, descriptive, cross-sectional hospital-based study in Sudan. In under developed countries where the screening program is not implemented; colonoscopy is mandatory among patient older than 50 years who present with lower GIT symptoms [24].

In almost all patients, a diagnostic or screening colonoscopy is required for tissue biopsy pathological confirmation of colon carcinoma. Baseline Computed Tomography (CT) of the chest, abdomen, and pelvis with contrast and Carcinoembryonic Antigen (CEA) are the preferred cost-effective, colon cancer staging studies done before surgical resection. Initial evaluation and diagnosis may involve barium enema or CT colonography if available, but ultimately a colonoscopy is required for tissue biopsy. Colonoscopy sensitivity is about 94.7% and may miss from 2% to 6% of cases, mostly right-sided, depending on preparation quality and hands experience [25].

Colon cancer management:

Surgical resection is the main treatment modality for localized non-metastatic stage colorectal cancer at any age with acceptable performance status and optimized comorbidities. Endoscopic resection (ER) is reserved for selected favorable risk and early stage colon carcinomas found in a polyp (cT0-1 [25]. Neoadjuvant therapy is not standard of care for colorectal cancer and reserved for advanced disease surgical conversion intend. Adjuvant therapy is recommended for all colorectal cancer stage III (node-positive) and individualized by stage II with high-risk features [25]. Surgery in conjunction with chemotherapy may provide a curative option on oligo-metastatic lung and liver disease. Palliative systemic chemotherapy is offered to non-surgical candidates with unresectable locally advanced disease or high metastatic burden to improved quality of life and prolong life expectancy. Individualized local recurrent disease patients may achieve cure with further multimodality therapy [25].

In the literature there was a study that reflected a decreased mortality from advanced colorectal cancer in the era of modern combination chemotherapy in younger and older patients. Younger age, non-right-sided tumors, and absence of signet ring histology significantly were associate with better survival. Younger patients had a greater proportion of negative clinicopathological features (male sex, African American ethnicity, and signet ring or mucinous histology). In multivariate analysis, older age, male sex, African American ethnicity, right-sided tumors, and signet ring histology were associated with higher mortality risk. Younger patients had improved survival (hazard ratio 0.72; 95% confidence interval: 0.70-0.75) compared with older patients, whereas all patients experienced increased 2-year survival by joinpoint analysis beginning in 1999-2000 [26].

Problems statement:

Colorectal cancer incidence has been rapidly rising in those

under the age of 50 years over the last 20 years. They tend to have a different spectrum of clinical and pathologic presentation compared to CRC diagnosed in older individuals.

Justifications:

- Although there were pervious descriptive studies that showed rising in CRC among young Sudanese, but still no study had covered CRC presentations among young Sudanese adults.
- The burden of young adult's colorectal cancer in Sudan is unknown
- Assessment of the disease behavior in different groups will lead to remap the treatment strategies

Objectives

General objectives:

To identify the clinical and pathological presentation of colorectal cancer among Sudanese adults aged below 50 years (group A) versus those above 50 years (group B) of age.

Specific objectives:

I. To identify the early and more common symptoms and signs in both groups.
II. To identify the most common histological types of colorectal cancer among both groups.
III. To identify the most common colorectal cancer sites among both groups.
IV. To assess the most common misdiagnosis before confirmation.
V. To study the management practice of colorectal cancer among both groups in Sudan.

Patients and Methods

Data collections:

Data has been collected by the researcher using administered questionnaire which included all the variables; either by direct interview or through phone calls with the colorectal cancer confirmed patients. Consents were obtained from all patients included in the study or their relatives. The data was collected cross -sectional and age independent.

A prospective follow up has been conducted for the new cases that presented during 2020-2021. The patients who presented during 2019 had been contacted by the researcher and their data were collected directly from them as they were still on regular follow up. The total number of patients included were120. The familial history was taken for all cases. Lynch syndrome had been assessed according to Amsterdam's Criteria I. The FAP cases which were included had malignant changes on histopathology.

The radiological staging and TNM staging were taken according to AJCC 8th Edition. Clavien-Dindo classification had been applied to assess the postoperative complications in patients who underwent curative surgeries.

Study design:

A prospective and retrospective comparative study of histological confirmed cases of colorectal cancer. Retrospective from June/ 2019 to November/ 2020. And prospective from December/2020 to December/2021.The cases had been divided into two groups according to age, group A (50 years and below) and group B (>50 years).

Study area:

It was multicenter that conducted in colorectal cancer services units in Khartoum state:

- Ibrahim malik teaching hospital
- Ibn sina hospital
- Soba university hospital

Study populations:

Inclusion criteria

- All patients who had histological confirmed colorectal cancer during the study period and were managed within the study centers
- Patient's whose contacts and medical record were available.

Exclusion criteria:

- Patient's whose contacts and follow up were lost.
- Patient who refused to be enrolled in the study.

Sampling: The sample size is total coverage bound to study duration.

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Study variables:

A-Background variables:

- Personal data
- Family background.

1-FAP
2-Lynch syndrome
3-Family history with similar condition.

- Misdiagnosed diseases
- Comorbid diseases

Clavien–Dindo classification of surgical complications.

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions
	Allowed therapeutic regimens are: drugs as antiemetics, antipyretics, analgetics, diuretics, electrolytes, and physiotherapy. This grade also includes wound infections opened at the bedside
Grade II	Requiring pharmacological treatment with drugs other than such allowed for grade I complications
	Blood transfusions and total parenteral nutrition are also included
Grade III	Requiring surgical, endoscopic or radiological intervention
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication (including CNS complications)* requiring IC/ICU management
IVa	Single organ dysfunction (including dialysis)
IVb	Multiorgan dysfunction
Grade V	Death of a patient

The American Joint Committee on Cancer Staging for Colorectal Cancer (8th Edition)

AJCC stage [2]	TNM stage [2]	TNM stage criteria [2]
Stage 0	Tis N0 M0	Tis: Tumor confined to mucosa; cancer-in-situ
Stage I	T1 N0 M0	T1: Tumor invades submucosa
	T2 N0 M0	T2: Tumor invades muscularispropria
Stage II-A	T3 N0 M0	T3: Tumor invades subserosa or beyond (without other organs involved)
Stage II-B	T4a N0 M0	T4a: Tumor perforates the visceral peritoneum
Stage II-C	T4b N0 M0	T4b: Tumor invades adjacent organs
Stage III-A	· T1-2 N1 M0 or	· N1: Tumor cells in 1 to 3 regional lymph nodes. T1 or T2.
	· T1, N2a, M0	· N2a: Tumor cells in 4 to 6 regional lymph nodes. T1
Stage III-B	· T3-4a, N1 M0 or	· N1: Tumor cells in 1 to 3 regional lymph nodes. T3 or T4
	· T2-3, N2a, M0 or	· N2a: Tumor cells in 4 to 6 regional lymph nodes. T2 or T3
	· T1-2 N2b M0	· N2b: Tumor cells in 7 or more regional lymph nodes. T1 or 2
Stage III-C	· T4a N2a M0 or	· N2a: Tumor cells in 4 to 6 regional lymph nodes. T4a
	· T3-4a N2b M0 or	· N2b: Tumor cells in 7 or more regional lymph nodes. T3-4a
	· T4b N1-2, M0	· N1-2: Tumor cells in at least one regional lymph node. T4b
Stage Iva	any T, any N, M1a	M1a: Metastasis to 1 other part of the body beyond the colon, rectum or regional lymph nodes. Any T, any N.
Stage IVb	any T, any N, M1b	M1b: Metastasis to more than 1 other part of the body beyond the colon, rectum or regional lymph nodes. Any T, any N.
Stage IVc	any T, any N, M1c	M1c: Metastasis to the peritoneal surface. Any T, any N.

B-Independent variables:
- Diagnostic tools
- Management
- Outcome of treatment

C-Dependent variables:
- Age
- Clinical Presentation
- Radiological and histopathology TNM staging.

Data management:
Data has been processed and sorted in relevant master sheet. Analysis was done by SPSS version 25.

Ethical considerations
- All patients were consented verbally and by written consent.
- Ethical clearance was obtained from the ethical committee in Sudan medical specialization board (SMSB).
- Hospital permissions were obtained.
- The data confidentiality was maintained and well secured.

Results

Socio-demographic characteristics of patients
A total of 120 patients were included. They were divided in two groups according to age, group A (50 years and below) and group B (more than 50 years). Fifty-nine patients (49.2%) belong to group A and 61 patients (50.8%) were group B **(Figure 1,2)**.

The mean age was 51.2 (SD=15.2). There were no significant differences in male to female ratio in both groups. In group A male: female ratio was 1.5:1, male=35(59.2%), female=24(40.8%). In group B it was 1.3:1. male=35(57.3%), female=26(42.6%).

Presentation:
Rectal cancer was reported as the commonest CRC in both age groups. In group A rectal cancer was reported in 35 patients (60 %), followed by left side CRC in 12 patients (20.3%). In group B rectal cancer was reported in 30 patients (49.2%) followed by right site CRC in 15 patients (24.6%). However, synchronous tumors were detected in three cases in group A one of them is FAP and two cases from group
B. There were 3 (4.9%) metachronouse tumors among elderly while one (1.8%) case among younger **(Figure 3)**.

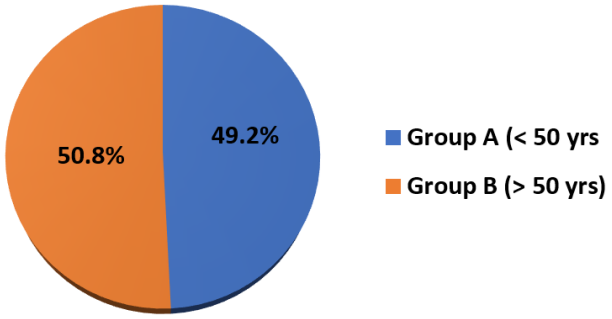

Figure 1: Age distribution among the 120 CRC cases who presented during 2019-2021in Khartoum state GIT units.

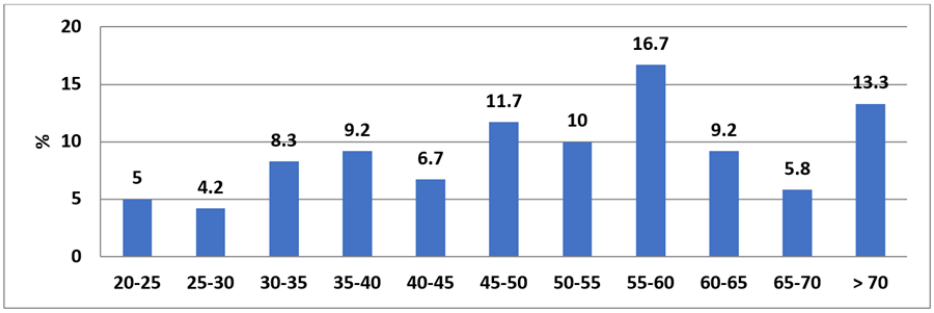

Figure 2: Age categories distributions among the 120 CRC cases presented during 2019-2021in Khartoum state GIT units.

The most dominating presenting symptoms:

The most dominating symptoms among young adults were bleeding per rectum which occurred in 48 patients (81.4%), followed by weight loss in 42 patients (71.2%), and abdominal pain which occurred in 38 patients (64.4%). On the other hand, weight loss was the most common presenting symptom in group B which was reported in 48 patients (78.8%), followed by bleeding per rectum in 42 patients (68.9%), and constipation in 26 patients (42.6%) **(Figure 4,5)**.

Familial backgrounds:

The highest incidence was for the Sporadic CRC without any familial background. Sporadic CRC among group A was 46 patients (78%) and 50 patients (85%) in group B.

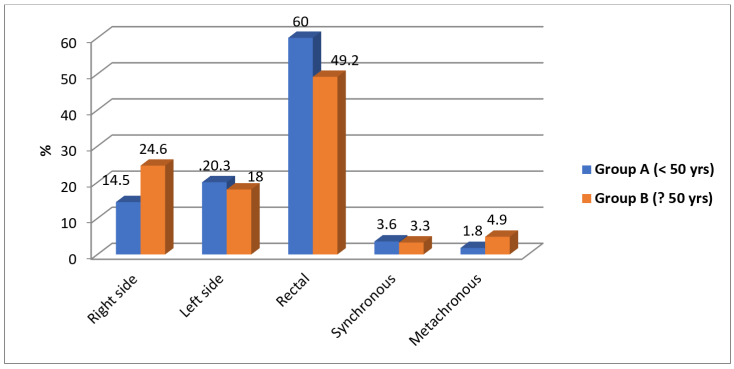

Figure 3: Tumor site distribution among the 120 CRC cases who presented during 2019-2021in Khartoum state GIT units.

In group A there were 13 patients (22%) with a positive family history. There were two patients with FAP and one patient with Lynch syndrome who met the Amsterdam I criteria. In group B; 11 patients (18%) had familial background, seven with first degree relatives and four with second degree relatives **(Table 1)**.

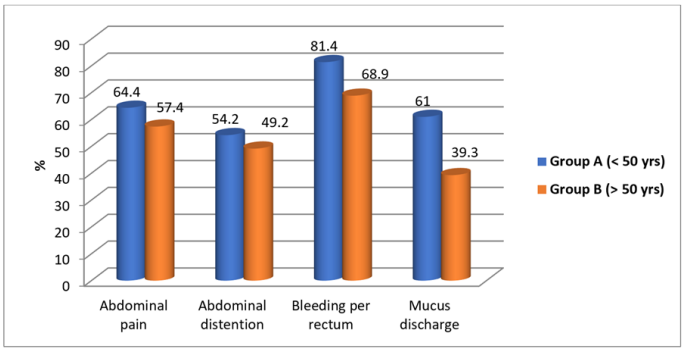

Figure 4: Distribution of presenting symptoms by age among the 120 CRC cases who presented during 2019- 2021in Khartoum state GIT units.

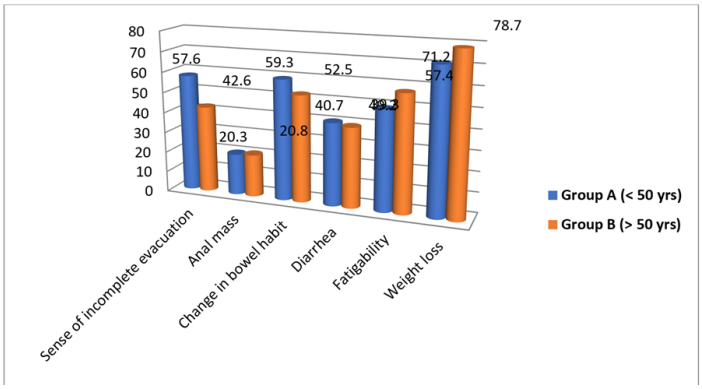

Figure 5: Distribution of presenting symptoms by age among the 120 CRC cases who presented during 2019- 2021in Khartoum state GIT units.

Table 1: Distribution of age group by similar condition in family among the 120 CRC cases during 2019-2021 in Khartoum state GIT units.

Similar condition in family		Age group		Total
		Group A (< 50 yrs)	Group B (> 50 yrs)	
Yes	n	13	11	24
	%	22.0%	18.0%	20.0%
No	n	46	50	96
	%	78.0%	82.0%	80.0%
Total	n	59	61	120
	%	100.0%	100.0%	100.0%

$\chi 2$ =.300; DF=1; P-value= . 375 (Not significant)

In this study CRC was most frequently misdiagnosed with dysentery which was reported in 25 patients (42.4%) among younger and 17 patients (27.9%) among elderly. On the other hand, benign anorectal diseases were the commonest misdiagnosis in elderly and were reported in 20 patients (32.8%). However, fifteen cases (25.4%) from both groups were mistakenly diagnosed with irritable bowel syndrome (IBS).

Comorbid diseases: Ten cases from group A and six cases from group B recalled a history of GIT belharziases. However, diabetes mellitus was reported among 13 cases (21.3%) from group B and seven cases (11.9%) from group A.

Methods of diagnosis: In our study CRC cases were investigated according to presentation suggestive of CRC in both groups; 78% and 68.9% for group A and B respectively. No one in group A had been enrolled in a screening program. Only two cases from group B were diagnosed with CRC during self-screening. There were patients of the study population had been diagnosed as CRC during investigations for other diseases; 9 patients (7.5%) from group A and 12 patients (10%) from group B. Those who came with emergency presentations among group A were three cases; one case with appendicitis and two cases with intestinal obstruction. Six patients (5%) from group B had emergency presentations; one case with right side iliac fossa abscess and 5 cases with intestinal obstruction.

The radiological staging: The preoperative radiological staging was examined in 44 patients (36.6%) from group A and 43 patients (35%) from group B. CT abdomen was not done in two cases from group A and four cases from group B. The radiological staging was deficient in 20 patients (16%) from group A and 26 patients (21%) from group B. In group A there were 13 patients (29.5%) with stage IIIB ,10 patients (22.7%) stage IIA and 5 patients (11.4%) stage IIIC. In group B 14 patients (32.6%) presented with stage IIIB ,8 patients (18.6%) stage IIIC and 6 patients (14%) stage IIA. There was no significant difference regarding the stage of presentation in the two groups (p value=0.235) **(Figure 6)**.

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Histological TNM Stage: In the patients who were operated the histopathological TNM stage revealed that the most common stage in group A was stage IIA which was reported in 15 patients (34.9%) followed by stage IIIB in 9 patients (20.9%). However, in group B stage IIIB and IIA were reported in 13 patients (26.5%). There was no significant difference (p value=0.157).

Histological finding: Adenocarcinoma was the commonest

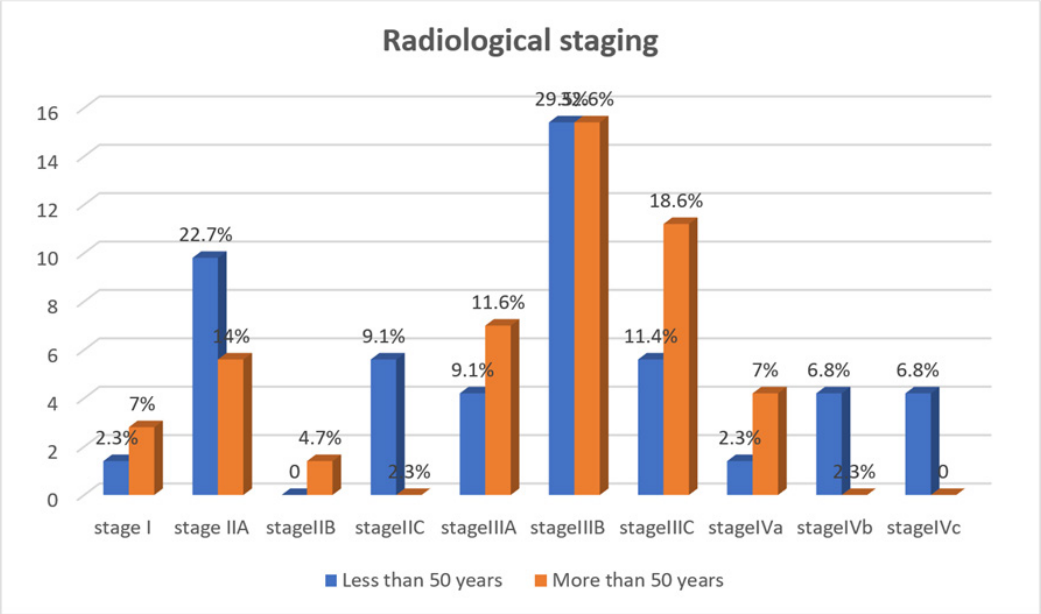

Figure 6: Radiological staging by age groups according to AJCC 8th edition among the 120 CRC cases from 2019-2021 in Khartoum state GIT units.

encountered histological type of colorectal cancer among both groups which included 96.9% and 95.1% for group A and B respectively. Furthermore, grade II adenocarcinoma was the commonest one in both groups, reported in 27 patients and 36 patients for A and B respectively. There was one case reported with anorectal squamous cell carcinoma in each group.

In group A, five cases (4.1%) were reported as mucinous adenocarcinoma and in two cases (1.6%) signet ring cells were detected. In group B, there were three case (2.5%) reported with mucinous adenocarcinoma and in one case signet ring cell was detected.

Table 2: Histological TNM stage by age groups among the 120 CRC cases from 2019-2021 in Khartoum state GIT units.

		Age group		Total	P-value
		Group A (< 50 yrs)	Group B (> 50 yrs)		
Stage 0	n	3	2	5	.157
	%	7.0%	4.1%	5.4%	
Stage I	n	2	13	15	
	%	4.7%	26.5%	16.3%	
Stage IIA	n	15	13	28	
	%	34.9%	26.5%	30.4%	
StageIIB	n	2	1	3	
	%	4.7%	2.0%	3.3%	
StageIIC	n	0	1	1	
	%	.0%	2.0%	1.1%	
StageIIIA	n	3	1	4	
	%	7.0%	2.0%	4.3%	
StageIIIB	n	9	13	22	
	%	20.9%	26.5%	23.9%	
StageIIIC	n	6	3	9	
	%	14.0%	6.1%	9.8%	
Stage IVa	n	2	2	4	
	%	4.7%	4.1%	4.3%	
Stage IVC	n	1	0	1	
	%	2.3%	.0%	1.1%	
Total	n	43	49	92	
	%	100.0%	100.0%	100.0%	

*P-value considered significant at less than 0.05 levels

Surgical treatment and outcome: The total number of patients who underwent surgery were 49 (83%) from group A and 57 (93.4%) from group B. Forty-four patients (89.7%) of group A and 50 patients (86%) from group B were considered curative procedures. Palliative surgeries were done in 7 patients from group A and 5 from group B **(Table 4)**.

According to Clavien Dindo classifications which was applied for curative surgeries only, most of the patients experienced grade I complications which occurred in 29 patients out of 44 (65.9%) from group A and 30 patients out of 50 (60.0%) from group B (p=.706) **(Table 5)**.

Table 3: Distribution of age group by histological type among the 120 CRC cases from 2019-2021 in Khartoum state GIT units.

Histological type		Age group		Total	P-value
		GroupA (< 50 yrs)	Group B (> 50 yrs)		
Adenocarcinoma	n	57	58	115	.807
	%	96.6%	95.1%	95.8%	
Neuroendocrine tumor	n	1	1	2	
	%	1.7%	1.6%	1.7%	
lymphoma	n	0	1	1	
	%	.0%	1.6%	.8%	
Squamous cell carcinoma	n	1	1	2	
	%	1.7%	1.6%	1.7%	
Total	n	59	61	120	
	%	100.0%	100.0%	100.0%	

*P-value considered significant at less than 0.05 levels

Two patients from group A died before surgery and two died after. In group B deaths were reported in six patients; five after surgery and one death before surgery. No recurrences or metachronous tumor had been reported among group A. There were three cases with recurrent CRC and two metachronous tumor documented among group B **(Table 6)**.

Table 4: Surgical procedure aim among both groups of the 120 CRC cases during 2019-2021 in Khartoum state GIT units.

Surgical procedure		Age group		Total
		Group A (< 50 yrs	Group B (> 50 yrs)	
Curative	n	44	50	94
	%	89.7%	86.0%	88.0%
Palliative	n	5	7	12
	%	10.2%	12.3%	11.3%
Total	n	49	57	106
	%	100.0%	100.0%	100.0%

Table 5: Calvien Dindo classifications grade of surgical complications among both groups of the 120 CRC cases during 2019-2021 in Khartoum state GIT units.

Complication After Surgery		Age group		Total	P-value
		Group A (< 50 yrs	Group B (> 50 yrs)		
Grad 1	n	29	30	59	.514
	%	65.9%	60.0%	62.8%	
Grade ii	n	5	7	12	
	%	11.4%	14.0%	12.8%	
Grade iii-a	n	0	2	2	
	%	.0%	4.0%	2.1%	
Grade iii-b	n	1	1	2	
	%	2.3%	2.0%	2.1%	
Grade IV-a	n	0	1	1	
	%	.0%	2.0%	1.1%	
Grade V	n	2	0	2	
	%	4.5%	.0%	2.1%	
No complications	n	7	9	16	
	%	15.9%	18.0%	17.0%	
Total	n	44	50	94	
	%	100.0%	100.0%	100.0%	

*P-value considered significant at less than 0.05 levels

Table 6: Distribution of age groups by short term outcome among the 120 CRC cases during 2019-2021 in Khartoum state GIT units.

short term outcome		Age group		Total	P-value
		Group A (< 50 yrs	Group B (> 50 yrs)		
Alive	n	55	50	105	..222
	%	93.2%	81.9%	87.5%	
Death before surgery	n	2	1	3	
	%	3.3%	1.6%	2.5%	
Death after surgery	n	2	5	7	
	%	3.3%	8.1%	5.8%	
Metachronous tumour.	n	0	2	2	
	%	.0%	3.3%	1.7%	
Recurrence	n	0	3	3	
	%	.0%	4.9%	2.5%	
Total	n	59	61	120	
	%	100.0%	100.0%	100.0%	

*P-value considered significant at less than 0.05 levels

Discussion

Colorectal cancer among young adults or early-onset CRC still being considered as international challenging issue. In this study the age 50 years was used, as the age recommended by most of the international screening programs, despite the recent recommendation by US Preventive Services Task to reduce the age to 45 for low-risk patients [15]. In Sudan the colorectal cancer screening is not well established with deficiency in information background and adoption of other countries guidelines.

One hundred and twenty patients were enrolled in the study from the three main GIT surgical units in Khartoum state which are providing colorectal cancer services. The patients had been collected randomly to identify the pattern of the early-onset CRC among Sudanese population. Patients aged 50 years were added to group A as they have long interval between complains and hospital presentations which ranged between 4-10 months.

The young adults CRC incidence in the study was 59 patients (49.2%) and most of them were between 45-50 years of age (23.7%). This may support the US preventive task recommendation [15] to reduce the screening age to 45 years. In group B the most common age group found was 50-64 years (31%) which goes with the 2020 colorectal cancer statistics which reported that CRC increases among population aged between 50-64 years annually by 1% [27- 29].

According to statistics in US Sporadic CRC among young adults incidence is about 50% [29,30]. However, it reached 78% in our study. This finding is similar to a study which was done in US, that revealed African Americans have higher CRC incidence and mortality than Whites [31].

A significant proportion of group A experienced rectal cancer (57%). These results had been detected by several previous international studies and figures [32,33] that revealed rectal cancer is the most predominating site among all ages. In our study left side CRC in younger group was the second most detected tumor, which resembles the finding of a study done in South Africa [5]. Also, in UK by reviewing 17 international papers an overall young adult with CRC has a rising prevalence of distal colon and rectal cancers. Early-onset CRC tend to have poorly differentiated tumors and were managed more aggressively [30]. Bleeding per rectum was the most reported symptom among young because rectal and left side CRC are common. On the other hand, rectal cancer followed by right side colon cancer among elderly was commonly detected in our study with the dominating symptoms of weight loss. Patients with right side colon cancer were more often older, females, with advanced stage and high grade [35,36].

Infectious diseases are common in Sudan. Dysentery is always diagnosed clinically by history of abdominal pain and bleeding per rectum; that is why in our series most of CRC were misdiagnosed with dysentery. Gastrointestinal Schistosomiasis and Amebiasis are uncommon in the western world, while such infections are frequent in the African community. M Waku et, in Uganda (Mulago and Arua hospitals) and Luisa Guidotti Hospital in Zimbabwe investigated the risk of cancer onset in sub-Saharan Africans affected with chronic gastrointestinal parasitic diseases. In 950 patients, they found a total of 45 tumors. In 34 patients the tumor was in the colorectal region, in 3 patients in the stomach, in 4 patients in the esophagus and 1 patient had cancer in the small bowel. But this hypothesis needs more investigations and researches [37]. In our study also 10 patients (8.3%) had schistosomiases chronic infection among young group and 6 patients (5%) from group B. There was one case reported in Soba university hospital in Sudan; that showed association between schistosomiasis and colon cancer in a young adult aged 35 years with the tumor site loaded with Schistosoma ova which was documented during histopathology [38].

Accurate preoperative radiological staging was done in 87 cases. It wasn't done in the rest, either because they present in an emergency situation or the CT was unremarkable. Stage IIIB was counted as the most detected radiological stage among both groups. In contrasts to postoperative histopathological staging (TNM AJCC 8th edition), where stage IIA occurred more frequently than stage IIIB in group A. Among older group stage IIIB was the commonest post-operative histopathological stage. That might be explained by, the remarkable response to neoadjuvant therapy with good down staging, as most of the cases were rectal cancer. Second reason that the radiological stage over estimated their condition or the lymph nodes which were detected by radiological imaging appeared negative in histopathology. On the other side, for those who presented with early radiological stage and appeared more advanced postoperatively this may relate to the long interval between the presentations and surgeries.

In our case series, adenocarcinoma was the commonest histological type reported. This finding is similar to international statistics [39]. Mucinous and signet ring type more detected among group A which has poorer prognosis [40]. Pure squamous cell carcinoma was detected in two cases one from each group who presented with anorectal CRC. The grade is moderately differentiated among most of the cases 63 (30%) and no significant differences between both groups; 27 (42%) in group A and 29 (46%) in group B.

The neoadjuvant therapy was noticed to be given more in group A (29)24.1%, because rectal cancer had high incidence among young group. In general, 84% of the cases who received neoadjuvant therapy are still alive with good treatment response. Adjuvant therapy was given in almost equal cases (33 cases vs. 31 cases) from both groups. Metachronous tumors were reported in 2 cases above 50. According to literature, the occurrence of metachronous advanced neoplasia in young adults is similar to older adults [41].

Intention curative related to procedures that adopted to resect the primary tumor without need for accurate oncological resection which occurred in an emergency setting. Palliative surgeries for those who presented with unrespectable tumor and need diversion colostomy. In this study curative procedures had been undertaken more frequent in 50(81.9%) of group B and only 44(74.6%) from group A. The rest of the patients in the study whom not operated either they are taking neoadjuvant therapy about 10(16.9%) in group A and 4 cases from group B (6.7%) or died before surgery. Two cases from group A refused the surgery and preferred traditional treatments.

The short term outcome of surgeries had been assessed during the study by applying the Calvien-Dindo classification, which was used to rank the severity of postoperative complications within 30 days after surgery. Grade I complication was the commonest grade among both groups. Two deaths were reported among group A with massive pulmonary embolism as the cause of death. Only one death was reported in group B.

Conclusion and Recommendations

Conclusion:

Based on the study objectives it can be concluded that:

In this study we identify that bleeding per rectum was the most frequent symptoms of CRC among young Sudanese adults aged 50 years and below followed by weight loss.

In patients aged above 50 years, weight loss was the commonest presenting symptoms followed by bleeding per rectum then constipations.

Rectal cancer was the commonest CRC site among both age groups. It was followed by left site colonic cancer among young population. However, right site colonic cancer was the second dominating site among elderly which explained their presenting symptoms.

The delay in diagnosis of colorectal cancer in young Sudanese adults appeared clearly to be due to misdiagnosis with other infectious diseases like dysentery. Which was used to be diagnosed clinically by history of abdominal pain, tenesmus, mucous discharge, and bleeding per rectum.

There are no significant differences in the histological types among both groups.

There are no significant differences in the radiological and postoperative pathological staging of CRC among both groups.

Preoperative radiological staging was not available in some cases because of reports deficiency that need more focus from radiologist and need to increase their level of practice.

Recommendations:

This study provides an overview on clinical symptoms, radiological features, histopathological features, treatment, and outcome of colorectal cancer in young adults (< 50 years) adult and elderly patients (> 50 years).

Molecular genetic studies are increasing the understanding of the pathobiology of colorectal cancer and may ultimately allow at-risk patients to be identified at an earlier stage.

Future interventions tailored to this young population may help achieve improvements in their overall prognosis.

In terms of the management practice of colorectal cancer among both groups in Sudan, the early detection of CRC followed by a sufficient oncologic treatment is crucial regardless of age.

More frequent endoscopic evaluation could decrease the delay in diagnosis among young people.

Outcome of young patients could be improved if patients with alarming symptoms are investigated early to exclude colorectal cancer to diagnose tumors at an early stage.

We recommend to do colonoscopy or at least sigmoidoscopy for patients aged 50 years or below who present with lower GIT symptoms especially per rectal bleeding.

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