

Research Article**Presentations and Management of Colorectal Cancer in under 40 Years of Age in the Sub-Saharan Africa: A Multi-Centre Study****Abubakar Alhaji. Bakari^{1,5}, Haruna Nggada², Abubakar Sadiq Adamu^{3,4}, Mbata Gali¹, Usman Babayo Deba^{1,4}, Usman Nganjwa¹**¹Departments of Surgery, College of Medical Sciences, University of Maiduguri, Maiduguri, Borno State, Nigeria²Histopathology, College of Medical Sciences, University of Maiduguri, Maiduguri, Borno State, Nigeria³Anaesthesia, College of Medical Sciences, University of Maiduguri, Maiduguri, Borno State, Nigeria⁴Federal Teaching Hospital, Gombe, Nigeria⁵Department of Surgery, Federal Medical Centre Yola, North-eastern, Nigeria***Corresponding author**

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Abstract: Colorectal cancer in young adults is commoner in Black Africans and is one of the leading causes of cancer - related death in this race. The aim of the study was to identify the presentation pattern and management of colorectal cancer in young adults in the sub-Saharan Africa. It is a prospective study of 262 patients with 80 out of 102 patients less than or equal to 40 years of age that were managed with colorectal cancer between 2005 and 2011 in the sub-region. Their records were retrieved and analyzed for demographic data, clinico-pathological pattern and interventions. The records of 22 patients were incomplete and hence they were excluded from the study. There were no gender difference and the peak age was in the 3th decade of life. Majority were rural farmers. The average duration of symptoms was 16 months. The major clinical features were documented. Majority of the patients (88.7%) presented with features of acute abdomen and at laparotomy found to have advanced colorectal tumour. Histology showed 37.5% were poorly differentiated adenocarcinoma out of which 20% were mucinous and 40% signet ring subtypes. Thirty three per cent declined any treatment. High index of suspicion, aggressive management would reduce the rate of morbidity and mortality of this disease.**Keywords:** Presentations, Management, Colorectal Cancer, young adults, Sub – Sahara Africa

INTRODUCTION

Colorectal cancer is a disease of the elderly in the western world and with the increase in the life expectancy in the population of the Sub – Saharan and West African sub regions, the incidence of colorectal cancer has increased [1]. The American Cancer Society estimates that 136,830 people will be diagnosed with colorectal cancer and 50,310 people will die from the disease in 2014 [2]. In general, the incidence of colorectal cancer has increased in countries where overall risk is low, especially in the young age group but in high – risk regions the incidence is either stabilized or decreased [3]. Black race has the highest rates of non – hereditary colorectal cancer, likely to be diagnosed at a younger age and is among the leading cause of cancer – related deaths among this race in the United States [4-6].

This is a multicentre study to identify the patterns of presentation and management of colorectal cancer in the younger age group and to suggest ways to reduce the prevalence of the disease in the sub-Saharan Africa.

MATERIALS AND METHODS

This was a prospective cohort study of consecutive of 262 patients with 80 out of 102 patients were less than or equal to 40 years of age; and those above 40 years of age act as control that have being managed with colorectal cancer between 2005 and 2011 at University of Maiduguri Teaching Hospital, Federal Teaching Hospital, Gombe and Federal Medical Centre, Yola were retrieved and analyzed. The protocol for the study was approved by the Ethical committees of all the hospitals. An informed consent was obtained from the patients or their relatives, that to be part of the study is optional and refusal to take part in the study will not affect his or her management. The proforma questionnaire was administered to each patient by self following consent taken.

Some data were collected from medical records department, operation ledger of the theatre and records in the histopathology department of these centres. Each patient record was reviewed in detail and data retrieved for analysis included socio-demographic (age, gender,

occupation), duration of clinical features, tumour location, the type of surgery performed, histopathologic type and grading of the tumour. The histology of each patient was reviewed to determine histological subtypes and stage of tumour. The tumours were classified according to Dukes' staging. Right sided tumours were classified as tumours of right colon and caecum, transverse colon includes hepatic and splenic flexures, then left colon, sigmoid colon, rectal and anorectal tumours and the type of adjuvant cancer chemotherapy.

Follow-up was by direct communication with patients or relatives in the surgical outpatient clinic. Patient was considered lost to follow-up if the patient had failed to present at the surgical outpatient clinic. Records of the patients' history and physical examination, including digital rectal examination, chest X-ray and abdomino-pelvic ultrasound scan during follow up were reviewed. The records of 28 patients were incomplete; hence they were excluded from the study.

Results were expressed as numbers, percentages, mean standard deviation (SD) and median where

appropriate. Comparisons of the clinical characteristics of colorectal cancer patients were performed using Student's t test. A P-value of less than 0.05 was considered statistically significant. Data were recorded and analyzed using SPSS 20.0 (Statistical Program for Social Sciences, Inc. Standard version 2011).

RESULTS

Total of 262 cases with 80 cases of under 40 years were analysed, 56 were males and 24 females. Male to female ratio was 2.33: 1 ($\chi^2 = 25.6$, $p=0.001$) and a median age of 28 ± 3.45 years. The peak age was in the 3rd decade of life as shown in Table 1. The duration of symptoms prior to presentation ranges from 6 months to 4 years with a mean average of 16 months and the major clinical features were abdominal pain/rectal bleeding (77%), change in bowel habits (80%), weight loss (86.2%), anorexia (92.5%), anaemia (90%) and abdominal mass/distention (55%) as shown in Table 2. Majority of the patients presented with advanced colorectal cancer and about 37% were poorly differentiated adenocarcinoma out of which 20% were mucinous and 40% signet ring subtypes.

Table 1: Age and genders distribution of patients

Ages (yrs)	Males	Females	Total	(%)
0-10	1	-	1	0.38
11-20	3	1	4	1.53
21-30	24	12	36	13.74
31-40	28	11	39	14.89
>40	99	83	182	69.47
Total	155(59.16%)	107(40.84%)	262	100

One patient was found to have stage C moderately differentiated adenocarcinoma tumour at the recto-sigmoid colon at second trimester of her pregnancy. She presented with colicky abdominal pains and constipation. She had complete resection of the tumour with colostomy which was reversed after spontaneous vaginal delivery of the baby and had adjuvant chemotherapy of 5-Fluorouracil (5-FU) and

Levamisole. The second pregnant patient presented at third trimester. She was found to have stage C signet ring subtype tumour. She had the tumour resection and caesarean section to deliver a healthy baby. She had adjuvant therapy of 5-FU and Levamisole. However, she died from liver metastasis nine months after the surgery.

Tables 2: Shows the clinical presentations of Colon Cancer

Clinical parameters	Frequency	Percentages
Duration of symptoms (months)		
0-5	5	6.2
6-10	21	26.2
11-15	23	28.8
16-20	18	22.5
21-25	8	10
>35	5	6.2
Total	80	100
Symptoms/signs		
GIT Bleeding	62	77.5
Change in bowel habits	64	80
Abdominal mass/ distention	40	55
Anorexia	74	92.5
Weight loss	69	86.2
Anaemia	72	90

A 9 years old male presented with features of acute abdomen and at laparotomy found to have obstructing sigmo-rectal tumour with carcinomous peritonei. He had resection of the tumour and colostomy. Histology revealed mucinous signet ring subtype tumour. The patient died one month after the surgery. The commonest site of tumour in this study was anorectum as shown in Table 3. About 71.4% of the patients had

surgical resections out of which 28.8% had abdomino-perineal resection of the rectum and permanent colostomy, and 8.8% had colostomy alone as shown in the Table 4. The rest declined for any treatment. The overall hospital stay was 7 to 30 days with a median stay of 2 weeks. Patients who had abdomino-perineal resection had a longer hospital stay.

Table 3: shows the cross- tabulations of sites of tumours and Duke’s staging

Rt. Colon with Caecum	1	4	1	2	8	10
Transverse colon	1	1	-	-	2	2.5
Lt. Colon	1	4	2	1	8	10
Sigmoid Colon	-	8	4	-	12	15
Rectum	-	4	16	-	20	25
Ano-rectal	-	17	10	3	30	37.5
Total (%)	3(3.75)	38(47.50)	33(41.25)	6(7.50)	80(100)	100

Table 4: Types of surgical procedures performed in 80 patients with Colorectal Cancer

Types of operation	Frequency	Percentage
AP Resection	23	28.8
Right Hemicolectomy	8	10
Left Hemicolectomy	10	12.5
Anterior Resection	10	12.5
Sigmoid Resection	3	3.8
Transverse Colectomy	3	3.8
Colostomy only	7	8.8
No surgical interventions	16	20
Total	80	100

Table 5: Frequency of histological types of cancers in 80 patients with Colorectal Cancer

Histological type	Frequency	Percentage
Adenocarcinoma		
- Well differentiated	19	23.8
- Moderately differentiated	22	27
- Poorly differentiated	30	37
Non- Hodgkin’s Lymphoma	3	3.8
Malignant Carcinoid	4	5.0
Unspecified	2	2.4
Total	80	100

DISCUSSION

The prevalence of colorectal cancer especially in the young below 40 years of age is on the increase in our sub region. Within 6 years over 80 patients younger than 40 years of age were treated of colorectal cancer at these three referral centres in the sub – Saharan region of Africa. The prevalence is comparable with the earlier study in our sub region, Egypt and Saudi Arabia but much higher than most other reports from Asia, the West and the United States [1, 3, 7-9] The mean age is 28 years and gender ratio of the patients in this study was almost equal, not different from other reports [8].

In this study the colorectal cancer seen in the younger age group is more aggressive as shown in tables 3 and is also seen among rural dwellers and majority are farmers [1]. The specific cause of colorectal cancer is still not known but a number of genetic and

environmental factors have been associated with the disease [10].

Although there is scanty report on cancer risk occurrence due to chemical fertilizers and pesticides exposure in developing countries, this may explain the reason why high prevalence of colorectal cancer was found among the farmers in this sub-region [1, 11, 12]. Extensive and continuous use of chemical fertilizers results in high concentrations of toxic substances in the ground water which may be used for drinking. It may also result in loss of natural humus of the soil; consequently, the roots do not get oxygen and cannot absorb the salts effectively. The unabsorbed nitrates are washed away in to the rivers and lakes and when the top fertile soil gets destroyed, the dry lands can be ultimately converted in to deserts and the excessive nitrates in the soil can raise the level of free nitrates in

the food plants causing risks to development of cancer. The extent of such risk can be reduced by use of less dissolvable chemical fertilizers and natural fertilizers [11]. There is need for further research on the impact of these chemical fertilizers on prevalence of colorectal cancer in this sub region.

Early colorectal cancer often has no symptom that is why screening is very important. The duration of symptoms in young patients is not different from the older patients [1, 8]. The major challenges in our environment are ignorance on the part of the patient because of low standard of education and awareness, and lack of index of suspicion, by referring to the physicians, of colorectal cancer in this young age group which delays the diagnosis of the disease at earlier stage [13]. Majority of the patients presented late with the features of advance disease as shown in Tables 2. Therefore, it is important to investigate patients in this young age group presenting with general abdominal discomfort, anorexia and weight loss without apparent cause, for colorectal cancer.

The challenges of low socio-economic status, few doctors in suburban areas, poor or lack of facilities to clinical diagnosis and few pathologists in the sub region also preclude adequate investigations and access to current treatment options. [1, 14-16]. The diagnosis of colorectal cancer in our centres is done on the basis of digital rectal examination, barium enema and proctosigmoidoscopy or colonoscopy but majority of patients in this age group were referred late and the diagnosis was done during emergency laparotomy for other complications such as intestinal obstruction, intussusceptions, bowel perforation and abdominal mass. This is a common diagnostic method in most African centers. [14]. Studies have shown that colonoscopy is the most sensitive method for the diagnosis of adenomatous polyps or colorectal cancer [17]. Barium enema with air contrast radiological examination of the colon and computed tomographic colonography are also used to detect invasive colorectal cancer and polyps [17, 18]. Screening is the most important method of prevention of colorectal cancer through the detection and removal of precancerous growths, and diagnosis of cancers at an early treatable stage reduces the rate of mortality [2]. To achieve this goal, examinations that are designed to detect both early cancer and pre-cancerous polyps should be encouraged if the resources are available and patients are willing to undergo invasive test. The tests that are more likely to detect cancer and adenomatous polyps are flexible sigmoidoscopy, colonoscopy, barium enema with air contrast and Computed tomographic colonoscopy (CTC), and those primarily detect cancer are Fecal occult blood test (FOBT) and Stool DNA (SDNA) test.

Colonoscopy is the most sensitive technique to detect colorectal cancers and adenomatous polyps hence has advantage to allow screening, diagnosis, removal of

polyps and has the longest rescreening interval of all form of testing [17]. If the test is normal it can be repeated after 10 years. The American Cancer Society, the US Multi – Society Task Force on colorectal cancer, and the American College of Radiology recommended for colorectal cancer screening in men and women aged 50 years and older at average [18]. However, in our sub-region the incidence of colorectal cancer in men and women younger than the age of 40years is on the increase, we suggest the screening should include the age of 20 years and above (Table 1). The challenges here are limited resources and unwillingness of the patients to undergo these tests. There are few adequately trained radiologists to perform Barium enema with air contrast in the sub region.

Colorectal cancer management involves multidisciplinary team management and often includes Surgeon, Anaesthetist, Gastroenterologist, Pathologist, Medical Oncologist and Radiation Oncologist. Treatment decisions are made by the patients with their management team after considering the best options available for the stage and location of the cancer, as well as benefits and risks associated with each. Only one Teaching hospital in the sub region has such team. It is important for surgeons to recognize the potential aggressiveness of colorectal cancer in young patients and to take an aggressive approach to the diagnosis and early treatment for the disease. The goal of surgery is a wide resection of the involved segment of bowel, with at least 5cm segment on either side of the tumour, together with removal of its lymphatic drainage [3]. Majority of the cases had advanced anorectal cancer (Table 3) either well or moderately differentiated adenocarcinoma, 23.8% and 27% respectively. Sigmoid and rectal tumour were more advanced and poorly differentiated and presented with obstructive symptoms or complications as observed in other studies [8, 9].

Obstructive colorectal cancers can be treated in one or two stages [3]. Two stage procedures can include colostomy first followed by colonic resection, or Hartmann's procedure first followed by colostomy closure and anastomosis. An alternative is a one stage procedure with either subtotal colectomy with ileo-rectal anastomosis or in selected cases, segmental resection after intra-operative colonic lavage. Endoscopic stenting can be used to relieve obstructive recto-sigmoid cancer and allow subsequent one – stage resection. Obstructive right sided cancers can be treated by right hemicolectomy. About 68. 9% of our patients had one stage procedure, 2.5% patients, who were pregnant women, presented with obstructive colorectal cancer, had two – stage procedure and 7% had colostomy alone because the tumour was so advanced with obstructive complications. Sixteen percent of our patient declined surgery either because of lack of funds or did not want colostomy.

Cancer Chemotherapy protocol is poorly adhered to either due to the paucity of its availability or its attendant complications in this sub region. Cancer chemotherapy drugs currently used in treatment of colorectal cancers are fluorouracil (5-FU, Adrucil), capecitabine (Xeloda), irinotecan (Camptosar), oxaliplatin (Eloxatin), bevacizumab (Avastin), cetuximab (Erbix), and panitumumab (Vectibix). Bevacizumab, an anti – angiogenesis and cetuximab and panitumumab an anti – Epidermal growth factor inhibitors are monoclonal antibodies found to retard the rate of tumour growth and hence prolong survival period when combined with chemotherapy. These therapies are suitable for our patients in this region but unfortunately are not readily available and expensive. Because of the nature of presentation majority of these patients were not placed on neo-adjuvant therapy. Ninety percent of adjuvant chemotherapy given was 5 – fluorouracil in combination with levamisole as immunotherapy. Radiotherapy has been used in the treatment of colorectal cancers as adjuvant or neo-adjuvant especially rectal cancers with low rate of tumour recurrence [2]. Radiation therapy can be given, in case of locally advanced disease as intraoperative radiotherapy, brachytherapy using SIR – Spheres, a tiny amount of yttrium – 90, to inject in to liver metastatic lesions or in combination with chemotherapy. In our study, the patients were unable to receive such treatment because there was no radiotherapy centre in this sub region and were reluctant to travel far for such treatment. It is pertinent to establish radiotherapy centre in this sub region. The overall mortality rate in this study was 30% which may be attributed to the fact that most of patients presented late in advanced stage and poorer differentiated and grade tumours [3, 8]. The follow up of patients in this sub region was still generally poor and data on long term survival were not available [1, 14].

CONCLUSION

The increasing prevalence of colorectal cancers, in the ages younger than 40 years among rural dwellers, peasant farmers and the aggressiveness of the tumour, pose serious surgical challenge in this sub region. The use of chemical farming is very common among farmers in our environment. There is a need to critically look into the use of chemicals and follow up these farmers. Institution of adequate screening protocol involving those in this age group and encourage the use of less dissolvable chemical and natural fertilizer by the farmers would control the prevalence of the disease. Setting up well equipped oncological centres in this sub region, high index of suspicion, aggressive management of the tumour would reduce the rate of morbidity and mortality of this disease.

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