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RAPID COMMUNICATION

Colorectal carcinoma in Lagos and Sagamu, Southwest Nigeria: A histopathological review

Fatimah Biade Abdulkareem, Emmanuel Kunle Abudu, Nicholas Awodele Awolola, Stephen Olafimihan Elesha, Olorunda Rotimi, Olakanmi Raphael Akinde, Ayoola Oluwole Atoyebi, Adedoyin Adekunle Adesanya, Adetola Olubunmi Daramola, Adekumbiola Aina Fehintola Banjo, Charles Chidozie Anunobi

Fatimah Biade Abdulkareem, Stephen Olafimihan Elesha, Olakanmi Raphael Akinde, Adetola Olubunmi Daramola, Adekumbiola Aina Fehintola Banjo, Charles Chidozie Anunobi, Morbid Anatomy Department, College of Medicine University of Lagos, P.M.B 12003, Surulere, Lagos, Nigeria
Emmanuel Kunle Abudu, Department of Morbid Anatomy, Olabisi Onabanjo University Teaching Hospital, P.M.B 2001, Sagamu, Nigeria
Nicholas Awodele Awolola, Department of Morbid Anatomy, Lagos University Teaching Hospital, P.M.B 12003, Surulere, Lagos, Nigeria
Olorunda Rotimi, Department of Histopathology & Molecular Pathology, St. James University Hospital, LS1 3EX, Leeds, United Kingdom.
Ayoola Oluwole Atoyebi, Adedoyin Adekunle Adesanya, General Surgery Unit, Department of Surgery, College of Medicine University of Lagos, P.M.B 12003, Surulere, Lagos, Nigeria
Author contributions: Abdulkareem FB initiated and designed the research; Abdulkareem FB and Abudu EK reviewed the slides; Awolola NA retrieved tissue blocks from the archives; Banjo AAF and Abudu EK provided the data from Sagamu and reviewed some of the slides with Abdulkareem FB; Abdulkareem FB wrote the initial draft; Rotimi O, Elesha SO and Daramola AO critically reviewed the initial draft; Akinde OR and Anunobi CC retrieved blocks and data from the three private laboratories in Lagos; Atoyebi AO and Adesanya AA reviewed the clinical aspect. Elesha SO assisted with research grant.
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Correspondence to: Dr. Fatimah Biade Abdulkareem, Department of Morbid Anatomy, College of Medicine, University of Lagos, P.M.B. 12003, Surulere, Lagos, Nigeria. biade64@yahoo.co.uk
Telephone: +234-1-8737656 Fax: +234-1-5851432
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Abstract

AIM: To study the frequency, gender and age distribution as well as pathological characteristics of colorectal carcinoma (CRC) in Lagos and Sagamu in SW Nigeria.

METHODS: This is a retrospective pathological review of histologically diagnosed CRC from 5 laboratories in Lagos & Sagamu. The clinical data, such as age, sex and clinical summary were extracted from demographic information. Cases of anal cancer were excluded from this study.

RESULTS: There were 420 cases (237 males and 183 females) of CRC. It peaked in the 60-69 year age group (mean: 50.7; SD: 16.2), M:F ratio 1.3:1 and 23% occurred below 40 years. The majority was well to moderately differentiated adenocarcinoma 321 (76.4%), mucinous carcinoma 45 (10.7%) and signet ring carcinoma 5 (1.2%), and more common in patients under 40 years compared to well differentiated tumors. The recto-sigmoid colon was the most common site (58.6%). About 51% and 34% of cases presented at TNM stages Ⅱ and Ⅲ, respectively.

CONCLUSION: CRC is the commonest malignant gastrointestinal (GIT) tumor most commonly located in the recto-sigmoid region. The age and sex prevalence and histopathological features concur with reports from other parts of the world.

Key words: Colorectal carcinoma; Adenocarcinoma; Pathological staging; Histopathological characteristics

Peer reviewer: Jonathan Terdiman, PhD, Division of Gastroenterology, University of California, San Francisco, Box 1623, San Francisco, CA 94143, United States

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INTRODUCTION

Colorectal carcinoma (CRC) is an important cause of cancer death worldwide, but has variable geographical distribution. In developed countries, it is among the 3 most common cancers with an estimated worldwide incidence of 570 000 new cases per annum[1]. Previous

studies have shown it to be a rare disease in Africans representing 3%-6% of all malignant tumors in most African studies[2-5]. It accounts for 10%-50% of all gastrointestinal (GIT) malignancies in Nigeria[6-8]. Incidences from various parts of the country range between 3.75-6 cases per annum in South South/South-East Nigeria[9,10], 12.5-14.4 cases per annum in the North[11,12] and 26.3 cases per annum in SW regions, respectively[13]. An 81% increase in incidence over a period of two decades was reported from Ibadan SW Nigeria[13]. Several reasons have been adduced for this increase, including an increase in hospital attendance by the populace due to an increasing awareness about cancer and change in dietary habit among others[13]. Major predisposing factors in the etiopathogenesis of CRC include the presence of pre-malignant conditions, such as familial polyposis syndrome, inflammatory bowel disease (IBD) and dietary factors, such as diet rich in refined carbohydrate, diet low in fibre content and fresh vegetables, all of which increase fecal transit time[14]. The low incidence in Africans was attributed to fiber rich diet which is common practice and rarity of the familial polyposis syndrome and IBD[2]. Recent urbanization/civilization has resulted in upsurge of confectionary food outlets in major cities resulting in many Nigerians changing their dietary habit from a fiber rich diet, which was common practice to a highly refined carbohydrate and fat diet.

Molecular studies have characterized 5 subtypes of CRC which have different etio-pathogenetic pathways that correlate with the morphologic and prognostic features[15]. These subtypes are based on DNA microsatellite instability status (MMR) and CpG island methylator phenotype[15]. Hameed, in South Africa using immunohistochemistry to detect expression of hMLH1 & hMSH2 (MMR status) in CRC, found that while 60% had normal expression of both gene products, 40% showed negative expression of either of the two genes[16]. He further observed that CRC with absence MMR (hMLH1 or hMSH2) tended to be right sided, mucinous and poorly differentiated when compared with the tumors that express the gene product. Also, Lanza *et al*, in Italy studying MMR status in CRC reported that 15.9% of CRC studied had abnormal expression of hMLH1 and hMSH2. They also observed that patients whose tumor was MMR negative had better clinical outcome particularly in Stage Ⅱ and Ⅲ tumors[17]. This advantage was more evident in patients with surgery alone than those who had adjuvant chemotherapy.

The present study is aimed at documenting the frequency pattern, age and sex distribution, as well as histopathologic characteristics of CRC in Lagos and Sagamu in SW Nigeria, as a preliminary to immunophenotypic subtyping; which we are currently carrying out in collaboration with the Department of Histopathology & Molecular Biology, Leeds General infirmary, Leeds United Kingdom.

MATERIALS AND METHODS

The paraffin embedded blocks and slides as well as pathology reports of malignant colorectal tumors collected from five laboratories (Morbid Anatomy Departments of the Lagos University Teaching Hospital 1995-2007, Olabisi Onabanjo University Teaching Hospital in Sagamu, Ogun State, as well as the three private histolopathology laboratories in Lagos State between 2002-2007 viz: The Specialist Laboratory, Histolab Diagnostics and Seramoses Laboratory) constituted the materials utilized for this study.

The slides were reviewed to confirm the diagnosis, type and grade of the tumor. The resection samples were further staged using Tumor-Node-Metastases staging system of International Union against Cancer (TNM) and Duke's staging system.

A proforma was used to extract the bio data such as age, sex, clinical symptoms and signs as well as the endoscopic findings when available from the histopathology request forms; some of the patient's case files where available in their various clinics or hospitals.

The clinical biodata and histopathological characteristics were analyzed using Microsoft Excel software and presented as tables.

RESULTS

There were a total of 420 cases of CRC with 237 males and 183 females and a male to female ratio of 1.3:1. CRC was the most common malignant GIT tumor accounting for 59% of all GIT malignancies and representing 87% of all malignant tumors of the colorectal and anal regions. It accounted for 5.8% of all the 7225 malignant lesions diagnosed from the five laboratories during the period.

The youngest patient was 10 years while the oldest was 95 years with a mean age of 50.7 (SD-16.2). CRC peaked in the 60-69 years age group (mode 60 years). About 12% (12.4%) occurred in patients 30 years and below, 23% occurred below 40 years and 16.8% above the age of 60 years.

Left-sided (distal colon) tumor 261 (62%) was more common than right-sided (proximal) ones 58 (14%). More than half of the cases were located in the recto-sigmoid region 246 cases (58.6%) followed by caecum 34 cases (9%), ascending colon 24 cases (6%), transverse 19 cases (4.5%) and descending colon 15 cases (3.6%) each. In 82 cases (19.5%), the specific site was not indicated.

Macroscopically, the right sided tumors were fungating nodular lesions with surface ulcerations while the left sided tumors were flat and infiltrating or constricting. Microscopically, the tumors were adenocarcinoma of varying grades. Majority were well-differentiated adenocarcinoma in 233 (55.5%), 88 (21%) were moderately differentiated and 34 (8%) were poorly differentiated carcinoma. Mucinous and signet ring carcinomas accounted for 45 cases (10.7%) and 5 cases (1.2%), respectively. Fifteen cases (3.6%) were anaplastic (undifferentiated) tumors (Table 1).

Mucinous carcinoma (19%) and signet ring carcinoma (3%) were more common in patients under 40 years; compared to 4% & 0.6% record in patients

Table 1 Site and gender distribution and histological types of CRC in patients 40 yr and above compared with those below 40 yr *n* (%)

	40 yr and above	Below 40 yr
Site		
Cecum	23 (7.14)	11 (11)
Ascending colon	20 (6.21)	4 (4)
Transverse colon	13 (4.04)	6 (6)
Descending colon	13 (4.04)	2 (2)
Recto sigmoid	194 (60.25)	52 (53)
Unspecified	59 (18.32)	23 (23)
Total	322 (100)	98 (100)
Histological grade		
Well differentiated adenocarcinoma	191 (59.3)	42 (43)
Moderately differentiated adenocarcinoma	63 (19.6)	25 (26)
Poorly differentiated adenocarcinoma	38 (11.8)	7 (7)
Mucinous carcinoma	15 (4.7)	19 (19)
Signet Ring carcinoma	2 (0.6)	3 (3)
Undifferentiated	13 (4)	2 (2)
Total	322 (100)	98 (100)
M:F ratio	1.3:1	1.2:1

Table 2 Pathological staging of 123 cases of CRC

Duke's stage	*n* (%)	TNM staging	*n* (%)
A	17 (14)	Stage Ⅰ	17 (14)
B	64 (52)	Stage ⅡA	54 (43)
C	41 (33)	Stage ⅡB	10 (8)
D	1 (1)	Stage ⅢA	13 (11)
		Stage ⅢB	28 (23)
		Stage Ⅳ	1 (1)

above 40 years (Table 1). On the other hand, well differentiated adenocarcinoma was more common in patients above (59%) than those below 40 years (43%). The male to female ratio is also less for younger patients. The cases less than 40 years also tended to be located in the cecum (11%) compared to older patients (7%) (Table 1).

Pathological staging was carried out for 123 cases with colectomy samples using Duke's and TNM staging systems. Of the 123 cases, 14%, 51%, 34% and 1% presented at TNM stages Ⅰ, Ⅱ, Ⅲ and Ⅳ, respectively (Table 2).

The clinical presentation was varied including abdominal pain, abdominal mass, bloody mucoid stool, change in bowel habit, weight loss, anaemia, and/or features of intestinal obstruction.

DISCUSSION

In this study, CRC accounted for 5.8% of all malignancies diagnosed in the five laboratories. This concurs with figures of 3.7%-10% that have been reported from various parts of Nigeria and Africa[2-5,18]. In Libya, it was the 2nd most common malignant tumor accounting for 10% and 9% in males and females, respectively [18]. Ohanaka & Ofoegbu in Benin, South West Nigeria reported CRC to be the 3rd most common cancer[7]. From the surgical biopsy register of Morbid Anatomy Lagos University Teaching Hospital, CRC is the third most common cancer diagnosed after breast and cervix. The annual frequency of this cancer in Lagos as documented in this study, was 32.3, a figure which is higher than 3.76 cases/annum in the South-South, 14.4 in the North-Central and 26.3 recorded in Ibadan South West Nigeria, respectively[9,11,13]. The higher number in this study could be attributed to the wider coverage of all the histopathology laboratories servicing both Lagos and Ogun states in South West, Nigeria.

CRC was the most common malignant GIT tumors, accounting for 59% of all GIT malignancies in this study. This is similar to studies from other parts of Nigeria where it was found to represent between 53%-67% of all malignant GIT tumors[3,7,8]. An earlier study from this center also recorded 56%[19]. Even in the United States of America, it was reported to be the most common GIT cancer and the second leading cause of cancer death[20].

Rising incidence has been reported from various parts of Africa which were considered low incidence areas. Iliyasu reported 81% increase in Ibadan over two decades; a 2.7 fold increase has also been reported from Kenya[13,21]. In the present study, we have also noticed an increase in the number of colorectal cases recorded over the years. Although there has been an increasing awareness resulting in an increased hospital attendance, change in dietary habit of Nigerians is a possible reason for this observation and needs to be further investigated to ascertain its relationship with CRC. A South African study has demonstrated 3-fold higher incidence of MSI-H tumors in African-American patients compared with Caucasian Americans; a difference which the authors suggested may reflect dietary differences or genetic polymorphisms that may be common in the African-American population[22].

African Americans have the highest incidence and mortality rates for colon cancer among ethnic populations in the United States, the incidence being 15% higher and the mortality 40% higher in African-Americans than in Caucasian Americans[20]. The relatively low incidence of CRC in native Africans was associated with high fiber diet. Recent workers have however, affirmed that low prevalence of CRC in black African can no longer be explained by high fiber diet because dietary patterns of Africans has changed and even protective anti-oxidants, such as Vitamins C, E, A and calcium, are low in African diet[23,24]. The most incriminating risk factors for CRC in most studies are the high intake of animal protein and fat[24,25]. O'Keefe *et al*[25] earlier showed that CRC risk is determined by interactions between the external (dietary) and internal (bacterial) environments.

The mean age in this study is 50.7 years which corroborates 44.3, 49.7, 51, and 52.3 years reported from Jos in North-Central Nigeria, Kenya, Egypt and Iran, respectively[12,21,26,27]. The age incidence of CRC in Nigeria is lower compared to developed countries;

about 10 years difference has been reported in many studies[9,28,29]. Peak age reported from Nigeria ranged between 42.9 years to 53 years with a mean of 46[11,12].

There appears to be an increasing number of CRC cases occurring in the young as 23% occurred below age 40 years while 12.4% occurred in patients 30 years and below in this study. Reports from other parts of Nigeria showed that 35%-42% of patients with CRC are below age 40 years[28,30,31]. CRC in younger age has been shown to present a diagnostic and therapeutic problem and prognosis tends to be less favorable[32]. In one study, CRC in young females was reported to have more tendencies to present with a late stage disease and anemia[33]. The reason for increasing incidence may be genetic, thus underscoring the need to study the prevalence of HNPCC associated CRC in our environment. On the other hand, it may be related to dietary factors since the young Africans tend to be more civilized and more likely take Westernized diet. In Nigeria, there has been a shift from the traditional African diet, due to upsurge in the number of fast food outlets, and it has become fashionable particularly among the youths to eat these Westernized food which are high in animal protein and fat.

Similar to previous studies, the sex prevalence is in favor of males with M:F ratio of 1.3:1. Except for the studies from Ife[28] which showed higher ratio of 2:1, other studies from Nigeria had reported ratio ranging between 1.1:1 and 1.6:1[6,9,11-13]. In the Middle East, M:F ratio of 1.1:1 was reported in Iran[27].

In terms of location within the colon, our study concurs with previous studies which have indicated that majority of CRC are located in the distal part of the colon; the rectosigmoid[8-13,28,29,32]. The reason for this may partly be due to the endoscopic practice in Nigeria in which the majority do sigmoidoscopy rather than colonoscopy. For example, in Lagos and Sagamu, only three of the eight endoscopic centers do colonoscopy. This limitation might have caused under-reporting of CRC cases, thus underscoring the need for prospective studies and provision of colonoscopy facilities as well as skilled specialists.

All the CRC cases studied were adenocarcinoma of varying grades. The present study also showed that patients < 40 years tended to have poor prognostic tumors such as mucinous and signet ring carcinoma. This concurs with the finding of Fazeli *et al*[27] in Iran who reported that 22% of patients < 40 years had poorly differentiated tumor compared to 5.9% in patients above 40 years. Mucinous carcinomas have been associated with poor prognosis with poor response to chemotherapy, tend to be located in the proximal colon and associated with micro satellite instability[22]. The majority of CRC in this study presented at TNM stages Ⅱ and Ⅲ or (Duke's Stage B and C), which concurs with most reports from Africa[6,13,21,26,27].

In conclusion, CRC in Lagos and Sagamu is the commonest malignant GIT tumor. The age and sex prevalence, as well as histopathological characteristics, are similar to findings from other parts of the world. However, very little is known about the etio-pathogenetic mechanisms. We have therefore commenced follow-up immunohistochemical study, in Collaboration with the Department of Histopathology & Pathology, St. James University Hospital, Leeds, United Kingdom, to identify the molecular subtypes with a view to ascertaining the specific pathogenetic and prognostic features.

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COMMENTS

Background

Colorectal carcinoma (CRC), the most common gastrointestinal (GIT) cancer, is an important cause of cancer death worldwide, but incidence is lower in Africans representing 3%-6% of all malignant tumors in most African studies.

Research frontiers

Differences exist between the incidence of CRC in Africans and that in developed countries; CRC carcinogenesis is related to development of genetic instability.

Innovations and breakthroughs

The age and sex prevalence, as well as histopathological characteristics of CRC in Lagos & Sagamu SW Nigeria, are similar to findings from other parts of the world. However the incidence is still low compared to Europe and America and very little is known about the immunophenotypic subtypes.

Applications

This study thus underscores the importance of epidemiological study to investigate the immunophenotypic subtypes of CRC in Nigeria respect to the role of dietary factors and genetic factors in the aetiopathogenesis.

Terminology

CRC is a malignant tumor arising from the epithelium of the large bowel; Histopathological characteristics refers to tumor characteristics as seen under the light microscope; Pathological staging means extent of tumor growth and spread based on the size of the primary tumor and extent of lymph node involvement, as well as spread to distant sites (metastasis); Familial Adenomatous Polyposis syndrome is the prototype of polyposis syndrome caused by mutation of adenomatous polyposis coli gene on chromosome 5q21 and characterized by presence of multiple polyps in the GIT tract; Immunophenotypes mean subtypes of CRC based on DNA microsatellite instability status (MMR) and cpG island methylator phenotype.

Peer review

This report on the histopathological characteristics of colorectal cancer in Lagos, Sagamu and southwest Nigeria is of interest as this is a region considered historically to be a low prevalence region for CRC and reports regarding the characteristics of CRC in the region are not great in number. The data reported here are reasonably novel and the presentation is fairly clear and concise.

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