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Colorectal Cancer in Nigeria: Changing Trends and Clinical Phenotype

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Abstract

Background: Colorectal cancer, a disease that was once said to be rare among Nigerians and Africans, now has a rapidly growing incidence in Nigeria. In this review, factors that may be accounting for this trend are looked at, as well as the peculiarities of the disease in Nigeria. Colorectal cancer in Nigeria comes with its peculiarities such as; increasing adoption of disease risk factors such as unhealthy diets and lifestyle such as, consumption of high fat and low fiber diet, tobacco smoking and reduced physical activity and, late disease presentation. The aim of this article is to review theses changing trends and the clinical phenotype of Colorectal Cancer among Nigerians.

Methods: An electronic search of published literature was conducted via MEDLINE, PubMED and Google Scholar using a variety of search items such as 'Colorectal Cancer in Nigeria', 'CRC in Nigeria', 'Risk Factors for Colorectal Cancer in Nigeria' to find related articles. Bibliographies of retrieved papers were further examined for publications of interest. Articles that reported clinically significant findings and research reports using related to Colorectal Cancer were reviewed in detail. Data on the relative frequency of cancers in Nigeria in 1960 was gotten from the Ibadan Cancer Registry, while the 2018 data was gotten from the Globocan Cancer Statistics of 2018.

Results: The results of this review shows an upward trend in the prevalence of Colorectal Cancer. Colorectal Cancer as at 1960, was the 10th most common cancer among Nigerians men and women respectively, and the 12th most common cancer in both sexes in Nigeria. As at 2018, Colorectal Cancer was the 2nd most common cancer among Nigerian men, and 3rd most common cancer among Nigerian women, and the 4th most common cancer in both sexes in Nigeria.

Conclusion: Colorectal cancer, which was once uncommon in Nigeria, has now become the 4th most common cancer in both men and men in Nigeria. This is a call on the government and people to take necessary action in controlling this disease through screening, prompt treatment and adoption of preventive measures such as increased dietary fiber intake.

Keywords: Colorectal cancer; Unhealthy diets; Screening; Gastrointestinal cancer

Introduction

Colorectal cancer is the most common type of gastrointestinal cancer in Nigeria [1]. Colorectal cancer was once described as rare among Nigerians in the 1960s [1], but at present, the incidence of colorectal cancer is rapidly growing in Nigeria. The increasing occurrence of colorectal cancer in Nigeria has been linked to both environmental and hereditary factors, with environmental factors playing a more significant role in Nigeria, due to economic development and changes in dietary and lifestyles preferences [2].

In this review, the changing trends of colorectal cancer in Nigeria are explored. An attempt is also made to explore the factors that may account for this rise in disease incidence. The clinical phenotype and peculiarities of the disease in Nigeria are also reviewed, highlighting disease pathogenesis, clinical presentation, histologic subtypes, risk factors and treatment modalities. Some screening tools, as well as preventive and control measures are also highlighted.

Literature Review

An electronic search of published literature was conducted via MEDLINE, PubMED and Google Scholar using a variety of search items such as 'Colorectal Cancer in Nigeria', 'CRC in Nigeria', 'Risk Factors for Colorectal Cancer in Nigeria' to find related articles. Bibliographies of retrieved papers were further examined for publications of interest. Articles that reported clinically significant findings and research reports using related to Colorectal Cancer were reviewed in detail. Data on the relative frequency of cancers in Nigeria in 1960 was gotten from the Ibadan Cancer Registry, while the 2018 data was gotten from the Globocan Cancer Statistics of 2018.

Results and Discussion

The results of this review shows an upward trend in the prevalence of Colorectal Cancer. Colorectal cancer as at 2018, was the 4th most common cancer in both men and women in Nigeria, the 2nd most common cancer in Nigerian men, and the 3rd most common cancer in Nigerian women. Colorectal Cancer as at 1960, was the 10th most common cancer among Nigerians men and women respectively, and the 12th most common cancer. These are all shown in the tables below (Tables 1-4).

Colorectal cancer in typical descriptions, was reported to be uncommon among native Africans [1]. It was the 10th most common malignancy among men and women respectively in 1960, and as at 2018, holds as the 2nd most common cancer in men and the 3rd most common cancer in women in Nigeria. This points to an increasing disease prevalence. Reports estimate that about 6 to 25 patients present annually in Nigerian tertiary health care centers [3-9]. Due to the poor access to healthcare facilities in Nigeria, most patient with colorectal center present late, at a point where disease cure is usually not achievable.

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Males		Females		
1.	Liver	1.	Cervix	
2.	Non-Hodgkin Lymphoma	2.	Breast	
3.	Burkitt Lymphoma	3.	Liver	
4.	Connective Tissue	4.	Non-Hodgkin Lymphoma	
5.	Stomach	5.	Burkitt Lymphoma	
6.	Skin	6.	Connective Tissue	
7.	Hodgkin Lymphoma	7.	Stomach	
8.	Prostate	8.	Skin	
9.	Bone and Adamantinoma	9.	Bone and Adamantinoma	
10.	Colorectum	10.	Colorectum	
		-		

*Due to the absence of exact figures, the relative frequency of each cancer as a percentage is not available.

Table 1: Relative frequency of the most common cancers in Nigeria in males and females respectively as of 1960 [42].

S/N	Cancer
1.	Cervix
2.	Liver
3.	Breast
4.	Non-Hodgkin Lymphoma
5.	Burkitt Lymphoma
6.	Connective Tissue
7.	Stomach
8.	Skin
9.	Hodgkin Lymphoma
10.	Prostate
11.	Bone and Adamantinoma
12.	Colorectum

Table 2: Overall frequency of cancers in Nigeria for both sexes as at 2018 [42].

S/N	Cancer	%
1.	Breast	22.7%
2.	Cervix	12.9%
3.	Prostate	11.3%
4.	Colorectum	5.8%
5.	Non-Hodgkin Lymphoma	4.6%
6.	Others	42.7%

Table 3: Relative frequency of the most common cancers in Nigeria in males and females respectively as at 2018 [43].

S/N	Males	%	S/N	Females	%
	Prostate	29.1%		Breast	37%
	Colorectum	7.9%		Cervix	21%
	Non-Hodgkin Lymphoma	7.3%		Colorectum	4.4%
	Liver	6.9%		Ovary	3.9%
	Stomach	3.5%		Non-Hodgkin Lymphoma	2.9%
	Other cancers	45.2%		Other cancers	30.7%

 Table 4: Overall frequency of cancers in Nigeria for both Sexes as at 2018 [43].

In contrast to developed countries, there is a paucity of polyposis coli syndromes [10]. In Nigeria only four cases of adenomatous polyposis have been reported in the last thirty-five years [11-14]. The mean age incidence of colon carcinoma in Nigeria is 41 years, [2] with an incidence rate of 3.4/100,000 [15,16]. This increasing incidence may be attributed to an increasing adoption of unhealthy diets and lifestyle, increasing life expectancy; due to an improving access to better health care.

In view of an increasing colorectal cancer incidence in Nigeria, the disease pathogenesis, clinical presentation, histologic subtypes, disease risk factors and modes of treatment are explored in this review, while highlighting changing trends and peculiarities of the disease in Nigeria [17].

Pathogenesis

The carcinogenesis of colorectal cancer among Nigerians is somewhat controversial. The typical adenoma-carcinoma sequence seems unlikely among Nigerians [4,15,18,19]. This is supported by the fact that studies show that it takes fifteen to twenty years for malignant change to occur in an adenoma, [9,20] making it unlikely in Nigerians since the age incidence of clinical disease is relatively commoner among the younger age group. The microsatellite instability theory holds true more commonly for hereditary nonpolyposis colorectal carcinoma, [21] which is rare among Africans. This makes it more likely that most cases of colorectal cancer in Nigeria occur sporadically, with an adequate environmental influence.

Clinical presentation

The clinical presentation depends on the site affected. The most common site of occurrence among Nigerians is the rectum/sigmoid colon [10], which may present as an abdominal mass [17]. In right sided disease, presentation is usually that of an iron deficiency anemia, due to chronic blood loss, while in left sided disease, the features are obstructive such as a change in bowel habit and chronic constipation. In the transverse colon, the features are determined by the proximity to either the right or left side of the abdomen, such that if the lesion is closer to the right, features are similar to right sided disease and if close to the left, features are similar to those of left sided disease. Bleeding per rectum, hemorrhoids due to obstruction of the superior rectal vein [17] and tenesmus may also occur.

In Nigeria, most patients present with advanced disease, after non-orthodox and traditional means are sought before seeking hospital presentation, causing most patients to present with disease that is not curable by conventional means. Most times, palliative care is offered with chemoradiotherapy. In this group of patients, the clinical features may include; weight loss due to elaboration of cachexin (Tumour Necrosis Factor alpha, TNF alpha), malignant peritonitis following perforation of a malignant colon segment or seeding of malignant deposits into the peritoneal cavity, colo-vesical fistula, colo-vaginal fistula and a host of other features due to local invasion, tumor infiltration and distant metastasis.

Histologic subtypes and mode of spread

The mucin-producing adenocarcinoma has a higher proportion among native Africans compared to Caucasians, such that among native Africans it occurs in 13-20% of cases; compared to Caucasians where is occurs in a 4-6% of cases [10]. Mucin-producing adenocarcinomas carry a poor prognosis [10]. A mucin-producing adenocarcinoma is defined as a tumor displaying extracellular mucin in more than 50% of the tumor volume [22]. New evidence is showing that mucinproducing adenocarcinoma may have a distinct biological and genetic identity compared with non-mucinous adenocarcinoma [23,24]. Patients with mucin-producing adenocarcinoma are typically younger [25,26] under which most Nigerian cases fall into, due to average life span demographics in Nigeria. In addition, these tumors may have distinct mutations and cytogenic abnormalities [23,27] and may be less likely to respond to cytotoxic chemotherapy [28-30]. These mucinproducing adenocarcinomas are commonly right sided [31-33] and associated with advanced disease [24,25,31,32].

Spread of colon carcinomas is usually by one of the following means:

- Direct infiltration, usually by a transverse means to encircle the bowel wall. Microscopically it does not spread beyond 5 cm of the macroscopic edge longitudinally [17]. Thus the affected segment must be resected at least 5 cm beyond the tumor edge [17].
- Lymphatic spread first to the paracolic lymph nodes and through the intermediate nodes to the inferior and superior mesenteric lymph nodes [17]. The frequency of lymph node metastases is directly related to the degree of penetration of the intestinal wall and the histologic grade of the malignancy and not necessarily the size of the primary lesion [17].
- Spread hematologically is usually through the inferior or superior mesenteric veins, and the portal vein; to the liver (33%), less frequently to the lungs (22%), adrenals (11%), kidneys and bone (11%) and the brain [17].
- Transperitoneal spread which may result in malignant ascites [17].

Disease risk factors

The role of diet in the epidemiology of colon carcinoma is one that has been extensively studied in the etiopathogenesis of Colon Carcinoma [33,34]. The increasing incidence of colon carcinoma may be linked to adoption of diets high in fat and low in fiber due to increasing affluence [35,36]. Diets rich in fat content and low in fiber content have been consistently been implicated as a risk factor for colon carcinoma [37,38]. Intake of fruits and vegetables is reducing among Nigerians, with a concomitant reduction in the intake of minerals, vitamins, antioxidants and fiber in these fruits and vegetables, which are Colon Carcinoma protective [34].

The increasing adoption of tobacco smoking among Nigerians may also account for an increasing incidence of colon carcinoma [39].

Excessive alcohol intake has also been shown to be a risk factor for colon carcinoma and gastro-intestinal cancers generally, thought to be due to production of acetaldehyde, a known carcinogen [35,36]. Due to increasing affluence among Nigerians, alcohol consumption is on the increase. Adoption of sedentary lifestyles with reduced physical activity is a risk factor for obesity. Obesity has link in the etiology of colon carcinoma [37,38]. Sedentary lifestyles are associated with less sunlight exposure, with a concomitant reduction in vitamin D stores in the body, increasing colon carcinoma risk, as vitamin D is known to be colon carcinoma protective (Figures 1-3) [34].

Treatment options

The modality of treatment to be used in treating Colon Carcinoma governed mainly by the stage of presentation and site affected.

Surgical treatment

- Involvement of the caecum, ascending colon and hepatic flexure: Right hemi-colectomy. This entails resection of the last 15 cm of the terminal ileum, ascending colon and proximal thirds of the transverse colon with ileo-transverse anastomosis.
- **Involvement of the transverse colon:** Resection of the transverse colon and both flexures- transverse colectomy
- **Splenic flexure:** Left hemi-colectomy. This entails the resection of the distal colon and distal two-thirds of the transverse colon.
- Descending colon: same as the splenic flexure, but a more radical resection with removal of the pelvic colon is preferable.

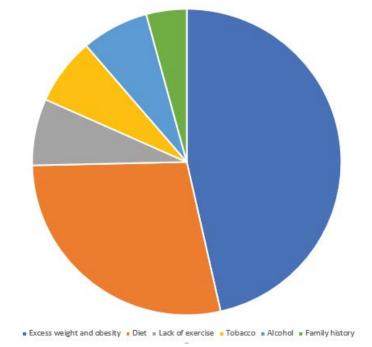


Figure 1: Relative frequency of the most common risk factors for colon carcinoma [40].

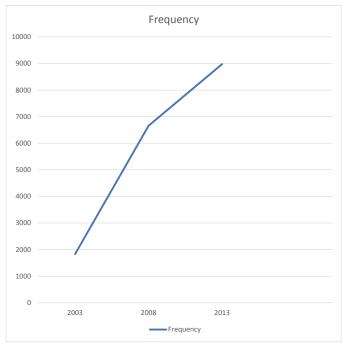


Figure 2: Prevalence and time trends in overweight and obesity among urban women in Nigeria [41] Unit of verical axis: Number of women per 100,000 population, Unit of the horizontal axis: Year; shows an increasing number of Nigerian women over the years, who are either overweight or obese. Being overweight or obese is an important risk factor for the development of colorectal cancer.

• **Sigmoid colon:** Pelvic colectomy with or without left hemicolectomy or resection of the sigmoid colon and rectum.

Treatment is most commonly by open abdominal surgery using diathermy, stiches and staples.

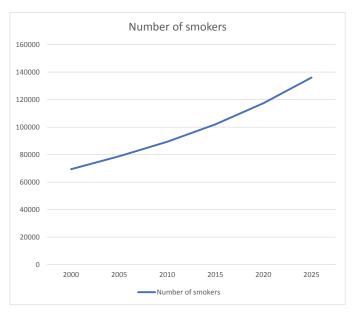


Figure 3: WHO global report on prevalence of Tobacco Smoking [42], Unit of verical axis: Number of smokers per 1,000,000 population, Unit of the horizontal axis: Year; , show an increasing number of people taking up tobacco smoking, which is a very important risk factor for the development of colorectal cancer, with projections showing an increase in the near future.

The role of adjuvant or neo-adjuvant radiotherapy

It is given preoperatively if the tumor is tethered or with evidence of extra-peritoneal spread and/or positive lymph nodes or post-operatively if a tumor turns out to be Dukes' B2 or C [17]. Radiotherapy may also be offered as a palliative measure in advanced disease.

Chemotherapy

5-fluorouracil, an antimetabolite cancer chemotherapeutic agent is the major agent used, with leucovorin usually added as an adjunct due to the associated risk of bone marrow suppression which may cause severe neutropenia [17]. Other agents which may be used in combination with 5-flouro uracil, include the platinum based chemotherapeutic agent, oxaliplatin and irinotecan, a topoisomerase 1 inhibitor. Bevacizumab is a humanized monoclonal IgG antibody which binds and neutralizes vascular endothelial growth factor (VEGF), which has shown so much promise with its use in developed countries, but with limited use in Nigeria due to cost implications [17].

Screening

The long natural history of colorectal cancer as it evolves from an adenomatous polyp in most cases to invasive cancer provides an opportunity for detection of adenomas and excision prior to the development of colorectal cancer [17].

- Colonoscopy
- Sigmoidoscopy
- Fecal Immunochemical Testing (FIT)
- Guaiac Fecal Occult Blood Testing (gFOBT)

Colonoscopy is likely to be at least effective as sigmoidoscopy, since it reaches the whole large bowel, whereas sigmoidoscopy reaches only the distal part of the large bowel [40-43]. Fecal immunochemical testing (FIT) is likely to be at least as effective as gFOBT, since both tests detect

blood in stools, and FIT demonstrates higher sensitivity and specificity [44]. It is important to note that facilities are not widely available in healthcare settings for screening for colorectal cancer, due to poor healthcare funding.

Control and preventive measures

Migration studies demonstrate a higher lifetime incidence of colorectal cancer among immigrants to high-incidence, industrialized countries compared to residents remaining in their native, low-incidence countries [45]. These data demonstrate the importance of environmental influences on colorectal carcinogenesis [46], making the prevention of these environmental influences the most cost-effective way of preventing colorectal cancer. Some of these preventive and control measures include:

- Regular physical activity
- Reduced intake of red meat and fat-rich food
- Intake of high fiber diets
- Intake of fruits, vegetables and fiber
- Intake of vitamins, antioxidants and other micronutrients
- Moderate intake of alcohol
- Cessation of tobacco smoking

Conclusion

Colorectal cancer is a major cause of cancer-related morbidity and mortality in developed climes and has emerged as one of the most common cancers in developing countries like Nigeria, where it was previously uncommon. This has been attributed mainly to increasing adoption of unhealthy diets and lifestyle due to increasing affluence from economic development. Control and preventive measures must be put in place as suggested in the last part of this review, to stem this growing problem, which has the potential to take its toll on Nigeria.

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