

Pathological Study of Colorectal Carcinoma in Adult Nigerians: A Study of 45 Cases

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ABSTRACT

Background: A 12-year (1st Jan. 1990-31st Dec. 2001) retrospective study of 45 colorectal carcinomas was carried out in University of Port Harcourt Teaching Hospital (UPTH) based on age, sex, clinical presentation, anatomical sites, histological types and clinical stages.

Methods: All the histological slides from surgical specimen obtained from the large intestine and diagnosed as colorectal carcinoma were reviewed in Anatomical Pathology department of UPTH, Port Harcourt. The age, sex, sites and histological types were extracted from the request forms and reports while the clinical presentation and staging were obtained from the case notes.

Results: A total of 34 (75.6%) and 11 (24.4%) occurred in males and females respectively, giving a sex ratio of 3:1. The least age of occurrence was a 22 year old male and the oldest was a 82 year old male. The highest frequency (28.9%) occurred in the age group 50-59 years which is a decade earlier than the Caucasians. Majority of our patients (33.3%) presented with either diarrhoea or constipation (altered bowel habit). The commonest site of this cancer is the rectum and the least occurred in the transverse colon. Most of our patients presented with advanced cancer of stage IV & III of TNM classification (D and C of Astler-Coller System). The tumours were also histologically graded into well moderately and undifferentiated type.

Conclusion: Colorectal carcinoma is one of commonest malignancies that occurs in young and middle aged in this environment. Patients present when the tumour is in an advanced stage hence poorer prognosis and the ages of the patients is about 10 years earlier than that of Caucasians.

KEY WORDS: Colorectal Carcinoma; Symptoms; Types; Classification

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INTRODUCTION

The incidence of colorectal carcinoma is lower in Africans than Caucasians and American Negroes^{1,2}. In Japan, the rate would appear to be increasing as the incidence of gastric cancer decline³. This tumour is considered to originate from benign adenomas that gradually increase in size, in extent of dysplasia and in villous morphology⁴. Non-polypoid early colorectal carcinoma easily progress to advanced carcinoma which is one of the original forms of advanced colorectal carcinoma⁵. An earlier World Health Organization (WHO) classification of this cancer was merely descriptive⁶. Later classification viewed the cancer along the extent of primary mural infiltration, colonic site, degree of differentiation, presence of mucin and lymphovascular invasion⁷. This classification formed the basis of the prognostic-based TNM and Astler-Coller^{8,9} classification of the cancer.

Previous inflammatory bowel diseases, adenomatous polyposis, familial clustering, cancers of the breast, ovary and uterus are high risk factors for colorectal cancers¹⁰⁻¹³. Other factors include old age, high energy intake, obesity, increased fecal transit time and inadequate physical exercise^{11,14}. There is a good correlation between a high animal fat intake in the diet and the risk of colorectal cancer and it has been suggested that this leads to greater production of cholesterol and their active metabolites which may be carcinogenic. Also, faeces from persons in high risk populations have higher counts of certain bacteria such as bacteroides and clostridia which can degrade bile salts with the production of potential carcinogens³. In countries where the incidence of colorectal carcinoma is high, a relatively higher proportion of the tumour occurs in the recto-sigmoid colon whereas in countries

of low incidence, a greater proportion of the cancer is found in the caecum and ascending colon¹⁵.

Studies in a subset of colorectal cancer and hereditary non polyposis colorectal cancer have shown that, microsatellite sequence are generally unstable and susceptible to replication errors^{4,15}. The microsatellite instability appears to be a novel molecular mechanism of colorectal carcinogenesis¹⁵ and also suggests the tumour location to be in the proximal part of the colon¹⁶⁻²⁰. Also resection fragment length polymorphism analysis shows allelic losses of chromosomes 5q, 17p, 18q which were found to be twice as common with the distal colorectal cancer than any other colorectal sites^{15,20}.

The inhibition of apoptosis and the augmentation of proliferative activity of adenoma is also related to colorectal carcinogenesis⁴. This tumour can metastasize to the regional lymph nodes⁷ and the liver²¹. This study aims at analyzing all the colorectal carcinomas with respect to age, sex, sites, clinical presentation and classification of various histological types.

MATERIALS AND METHODS

All the surgical specimens from the large intestine diagnosed as colorectal carcinoma were retrieved and reviewed from the records of the Anatomical Pathology department of the University of Port Harcourt Teaching Hospital (UPTH), Port Harcourt. This study covers the period January 1st 1990 to December 31st 2001 inclusive.

The colorectal carcinomas were histologically classified according to the three recognized staging systems used in different parts of the World based on nodal involvement, nuclear grading, site of metastasis and the extent of large bowel wall infiltration^{8,9,22}. Missing and broken slides were recut from the tissue blocks, processed and stained with hematoxylin and eosin stains. The ages, sex, clinical presentation, anatomical site and histological type of the tumour were extracted from the histology request forms, daybook and patients' case notes. Those with inadequate

documentation and where the slides and/or blocks were missing have been excluded from the study. The results are analyzed in percentages and photomicrograph illustrations are used for some cases. In other cases Alcian blue stain was used to demonstrate mucin produced by the cancer.

RESULTS

A total of 2105 malignant tumours were recorded during the study period. Only 53 of these were large bowel malignancies, representing 2.5% of the total malignancies. Out of the 53 colorectal malignancies, 45 (85%) were colorectal carcinomas, 4(7.5%) were Non Hodgkin's lymphomas, 3(5.7%) carcinoid tumours and 1(1.9%) leiomyosarcoma. There was no diagnosis of Crohn's disease, ulcerative colitis and familial adenomatous polyps which are risk factors for colorectal carcinoma.

Table I shows a total of 34 cancers (75.6%) occurring in males and 11(24.4%) cancers in females; giving a sex ratio of 3:1. The tumour was not recorded in the ages less than 20 years in our study. Only 3(6.7%) of the cancer occurred in the ages 20-29 years of which the youngest was a 22 year old male. Five (11.1%) cases occurred in the age group 30-39 years; 10(22.2%) was recorded in the age group 40-49 year and 13(28.9%) in the age group 50-59 years. The age group 60-69 had 8(17.3%) and ages 70 years and above had 6 (13.3%) of which the oldest was an 82 year old male.

The commonest clinical presentation was altered bowel habit 15(33.3%) (that is diarrhoea or constipation), followed in order of frequency by abdominal mass 10(22.2%), abdominal pains 8(17.8%), large bowel obstruction 7(15.6%), haematochezia 3(6.7%) and faecal incontinence 2(4.4%). In all cases except those who presented with faecal incontinence where both sexes recorded one each, males are more affected in all the clinical presentations of this tumour.

Table II shows the anatomical distribution of colorectal carcinoma in UPTH. A total of 21(46.7%) occurred in the rectosigmoid area of the large bowel (M=16; F=5) of which the rectum had 12 (M=9, F=3) and sigmoid 9 (M=7,

F=2). This is followed in frequency by descending colon 10(22.2%) [M=7; F=3], caecum 8(17.8%) [M=6; F=2], ascending colon 4(8.9%) [M=3; F=1], 2(4.4%) occurred in the transverse colon affecting only males (M=2). None was recorded for the flexures.

In Europe the Duke's system of classification²² is widely used while in America the Astler-Coller System⁹ is used in addition to Duke's, system. Recently a more detailed TNM System^{8,22} was instituted. The Duke's system is the simplest. Stage A are cancers restricted to colorectal wall, those that invade out side the muscularis externa are stage B, those with positive nodes are stage C and those that have distant metastasis are stage D²². The Astler-Coller System is similar, except, that it provides a better distinction between minimally invasive tumours in terms of their nodal status⁹. This was also found to be of disadvantage because the extent of wall invasion and nodal status are independent prognostic factors. Although the TNM system is much more accurate in terms of definition, it suffers the major drawback of being too cumbersome for general use. Table III shows a composite table of the three systems of classification.

Table IV shows the histological types, frequency of occurrence, sex distribution and Astler-Coller classification of colorectal carcinoma in UPTH. Well differentiated adenocarcinoma were 18(40%), [M=12, F = 6] distributed as 1,2,2,4,7 along Astler-Coller classes A,B₂,C₁,C₂,D respectively. Moderately differentiated adenocarcinomas are of two types: moderately well differentiated adenocarcinomas were 4(8.9%), [M=3, F=1] and moderately undifferentiated adenocarcinoma 3(6.7%), [M=2, F=1] distributed as 2,1,1 and 1,2 along Astler-Coller A,B₁,D and C₁,D respectively. Undifferentiated carcinomas were 10(22.2%), [M=8, F=2] distributed 2,5,3 under Astler-Coller C₁,C₂ & D only, papillary carcinoma were 2[M=2, F=0] distributed under Astler-Coller D only. Mucinous adenocarcinoma were 5(11.1%), [M=5, F=0] distributed as 1,2,2 along class C₁,C₂,D respectively while Signet ring carcinoma were 3(6.7%), [M=2, F=1] distributed under class D

only. A total of 3(6.7%), 1(2.2%), 3(6.7%), 5(11.1%), 11(24.4%), 20(44.2%) of the cancer occurred in Astler-Coller classes A,B₁,B₂,C₁,C₂,D respectively.

Figures 1 and 2 show the gross and microscopic appearance of colonic adenocarcinoma.

Table I. Sex, Age and clinical Presentation of Colorectal Carcinoma Patients in UPTH.

Age group in years	Abdominal mass		Abdominal pains		Altered bowel habit		Haematochezia		Large bowel obstruction		Faecal incontinence		Total	%
	M	F	M	F	M	F	M	F	M	F	M	F		
< 20	-	-	-	-	-	-	-	-	-	-	-	-	-	-
20-29	-	-	1	-	1	1	-	-	-	-	-	-	3	(6.7)
30-39	1	-	1	-	2	-	-	-	1	-	-	-	5	(11.1)
40-49	2	-	-	-	4	1	1	-	1	1	-	-	10	(22.2)
50-59	2	2	2	-	1	2	1	-	2	-	-	1	13	(28.9)
60-69	2	-	3	-	1	-	-	1	1	-	-	-	8	(17.8)
70 and above	1	-	1	-	2	-	-	-	1	1	-	-	6	(13.3)
Sub Total	8	2	7	1	11	4	2	1	5	2	1	1	45	(100.0)
Grand Total	10	(22.2%)	8	(17.8%)	15	(33.3%)	3	(6.7%)	7	(15.6%)	2	(4.4%)	45	(100.0)

Table II. Anatomical distribution of Colorectal carcinoma in UPTH

Anatomical Sites of Colorectal carcinoma	Sex		Total	Percentage
	Male	Female		
Rectum	9	3	12	26.7
Descending colon	7	3	10	22.2
Sigmoid	7	2	9	20.0
Caecum	6	2	8	17.8
Ascending colon	3	1	4	8.9
Transverse colon	2	-	2	4.4
Total	34	11	45	100.0

Table III. Staging Criteria of Colorectal Carcinoma as applied by the different Systems

Criteria	Dukes	Astler-Coller	TNM
Tumour invasion restricted to the mucosa	A	A	Tis, No
Tumour restricted to submucosa, node negative	A	B1	T ₁ No
Tumour restricted to the Muscularis	A	B1	T ₂ No
Tumour completely through muscle wall node negative	B	B2	T ₃ No
Tumour involving adjacent organ, node negative	B	B2	T ₄ No
Tumour restricted to submucosa, node positive	C	C1	T ₁ N ₁₋₃₊
Tumour restricted to muscle wall, node positive	C	C2	T ₂ N ₁₋₃₊
Tumour completely through muscle wall, node positives	C	C2	T ₃ N ₁₋₃₊
Tumour involving adjacent organs, node positive	C	C2	T ₄ N ₁₋₃₊
Distant metastasis present irrespective of any other factor	D	D	T ₁₋₄ , N ₀₋₃ M1

Table IV. Sex, frequency distribution of histological types and Astler-Coller classification of Colorectal carcinoma in UPTH.

Histological types	SEX		Astler-Coller Classes							Total	%
	M	F	A	B ₁	B ₂	C ₁	C ₂	D			
Well differentiated adenocarcinoma	12	6	1	-	2	2	4	7	18	40.0	
Moderately well differentiated adenocarcinoma	3	1	2	1	-	-	-	1	4	8.9	
Moderately undifferentiated carcinoma	2	1	-	-	-	1	-	2	3	6.7	
Undifferentiated carcinoma	8	2	-	-	-	2	5	3	10	22.2	
Papillary adenocarcinoma	2	-	-	-	-	-	-	2	2	4.4	
Mucinous adenocarcinoma	5	-	-	-	-	1	2	2	5	11.1	
Signet ring carcinoma	2	1	-	-	-	-	-	3	3	6.7	
Total	34	11	3	1	3	5	11	20	45	100.0	
			(6.7%)	(2.2%)	(6.7%)	(11.1%)	(24.4%)	(44.4%)			



Figure 1
Shows colonic malignancy, measuring 10x6cm with the surrounding soft tissue. The cancer is ulcerated with necrotic and haemorrhagic floor. The ulcer measures 4x3cm.

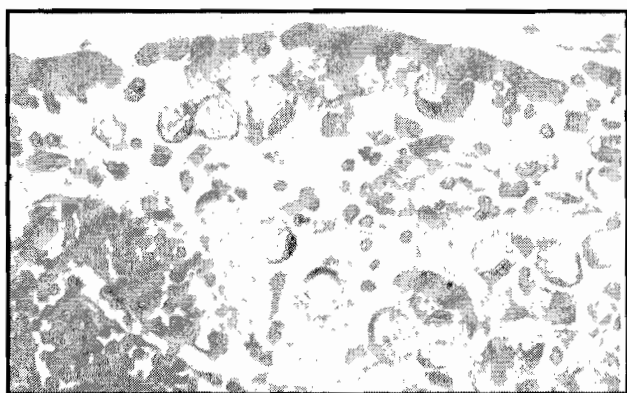


Figure 2
Shows the histology of the Fig 1 displaying infiltrating columns of malignant epithelial cells with copious amount of intracellular mucin displaying the hyperchromatic and pleomorphic nuclei peripherally giving signet ring cell pattern.

DISCUSSION

Colorectal carcinoma is the commonest malignancy of the gastrointestinal tract but this tumour is uncommon in this environment as it accounted for only 2.1% of the total malignancies diagnosed during the study period. The rarity of this tumour was also cited by earlier studies in this country^{1,2}. Majority of our patients, (51.1%) presented at younger ages than the Caucasians. This is in keeping with other local studies^{2,24} but is at variance with other studies outside Nigeria where the tumour is commoner in their sixth decade of life²³. This age variation may not be unconnected with genetic predisposition especially when it occurs in patients below the age of 49 years of age, in addition to the patient's lifestyle and geographical location²³. Males are more affected than females with a ratio of 3:1 in this study which is similar to the report of another Nigerian study²⁴ but is at variance with other reports from advanced and economically affluent countries where females predominate^{3,23}. The male dominance may also be attributed to the rarity of frank cancer of the colon and increase in rectal cancers in males³ which is in consonance with this study.

The predisposing factors like ulcerative colitis, Crohn's disease and familial adenomatous polyps^{2,4,10,11,13} were not seen in our patients as these diseases are uncommon in Africans. The cancer is however seen together with other chronic inflammatory diseases such as amoebiasis and schistosomiasis, villous and tubular adenomas in some patients. None of our patients had multiple cancers as reported in other studies^{11,23}. The rectum is the most frequent site of this tumour which is similar to the reports in advanced countries¹³ and Nigeria^{1,2}. Cancers of the left side (descending colon) appears to be commoner in patients below the age of 50 years and they tend to be more aggressive than tumours at any other site of the colorectal region as reported elsewhere²³ but this was not observed in our patients.

The disease is usually asymptomatic in the early stage, making most of our patients to present late to the clinic when the tumour is in

advanced stage. The delay may not be unconnected with spiritual or socio-cultural belief system in this environment, ignorance and poverty as well as denial. These patients hardly present to the clinics where at least digital rectal examination would have been performed for possible early diagnosis. The practice of regular colonoscopic and sigmoidoscopic examination of the system to detect the disease in its early stage is unavailable at the time of writing. About 33% of our patients presented with altered bowel habit which manifests as either constipation, diarrhoea and bloody stool. This presentation is however at variance with an earlier study in this country which recorded abdominal pain as the commonest symptom² but similar to another study in the same geographical area²⁴. Intestinal obstruction and abdominal mass due to this tumour are commoner in the African population than the Western World, suggesting late presentation of the diseases. Haematochezia is an uncommon presentation in this study probably because, patients do not look at their stool generally. Some of the elderly male and postmenopausal female patients presented with severe anaemia of iron deficiency type probably due to unnoticed haematochezia.

The well differentiated adenocarcinoma is the commonest histological variant in this report which agreed with other studies^{2,23,24}. The undifferentiated carcinoma ranked second in frequency and appears to have very aggressive biological behaviour¹⁰. The moderately differentiated adenocarcinoma are of two types which were not cited by earlier authors in Nigeria^{1,2,24}. The moderately well-differentiated adenocarcinomas fall into Astler-Coller Class A and B while the moderately undifferentiated type was classed under C and D. The prognosis of this cancer depend on the age of the patient at the time of diagnosis, histological variant of the tumour and the Astler-Coller class at the time of presentation^{21,24}. The prognosis is better with patients in classes A and B and worst with C and D.

This report has 17.8% of patients under the better prognosis group while over 82% belong to the poor prognostic category. Signet ring and

mucinous carcinomas have poor prognostic values since the mucin potentiate the spread of the cancer. This is corroborated by this report where majority of these tumour belong to classes C and D of the Astler-Coller classification. The gross feature of one of the specimens show tumour ulceration with haemorrhagic necrosis of the floor. Microscopy shows malignant cells with intracellular mucin, giving a signet pattern. Metastasis to regional lymph nodes, omentum, lungs, liver and the ovaries were seen in over 68% of our patients and this formed the basis for the various classifications of the cancer. Finally, colorectal carcinoma is known to be the most common malignancy of the gastrointestinal system of the young and middle aged in this setting. The patients present when the tumour is in an advanced stage with an attendant bleak prognosis.

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