Gastric Carcinoma: A Review of the Histopathological Features of Cases Seen at Ile-Ife, Nigeria

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Abstract

Aim: *To describe the histopathological features of gastric carcinoma as seen in a tertiary institution in Nigeria and compare these with those of other populations.*

Methods: *This is a retrospective study in which gastric surgical and endoscopic biopsies specimens seen over a 10 year period were reviewed with respect to age, sex and histopathological characteristics. Statistical analysis was performed for differences in proportion using Chi square by SPSS version 13.*

Results: *Ninety-seven cases consisting of 37 gastrectomy specimens, 10 open biopsies and 50 endoscopic biopsies were studied. There was a slight male preponderance with a male to female ratio of 1.2:1. The peak age of occurrence was the 6th decade of life (mean age was 52.8 years). Most cases were located in the antro-pyloric region. Majority of the tumours were either fungating or excavated. The vast majority of cases were intestinal-type carcinomas. There were 40 well-differentiated, 30 moderately-differentiated and 27poorly-differentiated tumours. More than 90% of the tumours were advanced carcinomas with majority showing evidence of metastatic spread most commonly to peri-gastric lymph nodes. Majority of the tumours were associated with chronic gastritis and H. pylori infection.*

Conclusion: *This report highlights fundamental differences between the histopathological features of gastric carcinoma in Nigerians and those in other parts of the world, suggesting possible differences in their pathogenetic mechanisms and biologic behavior. It will be instructive to further investigate these differences.*

Keywords: *Gastric carcinoma, histopathological features, Nigeria*

Introduction

Gastric carcinoma, a worldwide disease, has been reported to be the commonest malignant tumour of the stomach, accounting for more than 90% of cases.[1] It is a disease that shows wide variations in its epidemiological and histopathological characteristics both within and between countries.[2,3] A good understanding of these characteristics is very important in elucidating the pathogenetic mechanisms of gastric cancer. This has strong implications on cancer prevention and treatment strategies. Environmental factors are known to be the most important in its

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pathogenesis (especially the intestinal type), although genetic as well as a number of other host factors also play a role.[1]

There is a growing awareness that gastric carcinoma is rapidly becoming a larger problem in developing countries with increasing incidence rates and a predilection for urban and low socioeconomic groups.[4] In Nigeria, the world's most populous homogenous black population, it has been shown by various authors to constitute a significant proportion of cancer-related hospital admissions.[5'66].

The prognosis for gastric carcinomas in many parts of the world remains disappointingly poor as it does also in Nigeria[9'10].

It, therefore, becomes imperative for us to study in great detail the peculiar features of this disease in our environment and compare these with those of high-risk countries. This may help improve our understanding of gastric cancer in Nigeria and also assist in developing rational preventive and treatment strategies, as has been done in high-risk regions with good results. This paper, therefore, seeks to give a detailed description of the histopathological features of gastric carcinoma as seen in a university teaching hospital in Nigeria over a 10-year period.

Materials and Methods

Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria is a tertiary health institution with 576 beds. It serves a population of about 1,333,603 people with a slight female predominance (1991 census) in the Ife-Ijesa zone of Osun State, Nigeria.

Surgical specimens of patients diagnosed with gastric carcinoma in the histopathology laboratory of the hospital between 1995 and 2004 were selected for the study.

The original request cards of the patients were scrutinized and the demographic data extracted. The surgical pathology reports of gastrectomy specimens were scrutinized for the tumour topography while the macroscopic growth patterns were reviewed and classified according to Borrmann's scheme[11]. The endoscopy reports of biopsy specimens were also retrieved and reviewed for the topography and macroscopic growth patterns.

The appropriate slides were retrieved, reviewed and new sections cut in some cases. The tumors were reclassified histologically using the Lauren scheme of 1965[1]. Tumour depth was assessed in sections of gastrectomy specimens and open biopsy specimens that included the muscularis propria and classified either as early or advanced gastric carcinoma. The tumours were histologically graded as well, moderately or poorly differentiated. Sections containing surrounding tumour-free gastric tissue were scrutinized for the presence of chronic gastritis, gastric glandular atrophy and intestinal metaplasia. These were graded using the modified Sydney System[12]. Modified Giemsa stain was used to identify *H. pylori* in such sections.

Slides of lymph nodes and other tissues submitted along with the gastric tissue were assessed for the presence or absence of metastasis.

TMN staging was impracticable due to the shortfalls in the clinical and pathological assessment of the gastric tissues, lymph nodes and distant metastasis.

Statistical analysis was performed for differences in proportion using Chi square (p is significant at <0.05) by SPSS version 13. The mean was also calculated where applicable.

Results

There were 97 cases consisting of 37 gastrectomy specimens, 10 open biopsies and 50 endoscopic biopsies.

Biodata of patients

Figure 1 show that there were 53 males (54.6%) and 44 females (45.4%). The overall male to

female ratio was 1.2: 1. The age range was 25-85 years while the mean age was 52.8 years. The peak age frequency was in the 50-59 year age-group with 29 cases (29.9%). Eighty-three patients (85.6%) were aged 40 years and older while 14.4% were younger than 40 years.

Topographical Characteristics

Topographically, 81 cases (83.5%) were located within the antropyloric region, 4 cases (4.1%) in the cardia and 12 cases (12.4%) in the gastric body.

Table 1.

Some pathological characteristics of gastric carcinoma

Parameters		Histological Pattern (%)			Tumour Depth (%)	
		Intestinal	Diffuse	Mixed	Superficial	Advanced
Total No.		86(88.7)	10(10.3)	1(1.0)	4(8.5)	43(91.5)
Mean Age		55.0 yrs	55.8 yrs	50 yrs	53 yrs	55ys
Histologic Grade	Well Differentiated	40(46.5)	0(0.0)	0(0.0)	3(75.0)	16(37.2)
	Moderately Differentiated	29(33.7)	0(0.0)	1(100.0)	1(25.0)	13(30.2)
	Poorly Differentiated	17(19.8)	10(100.0)	0(0.0)	0(0.0)	4(32.6)

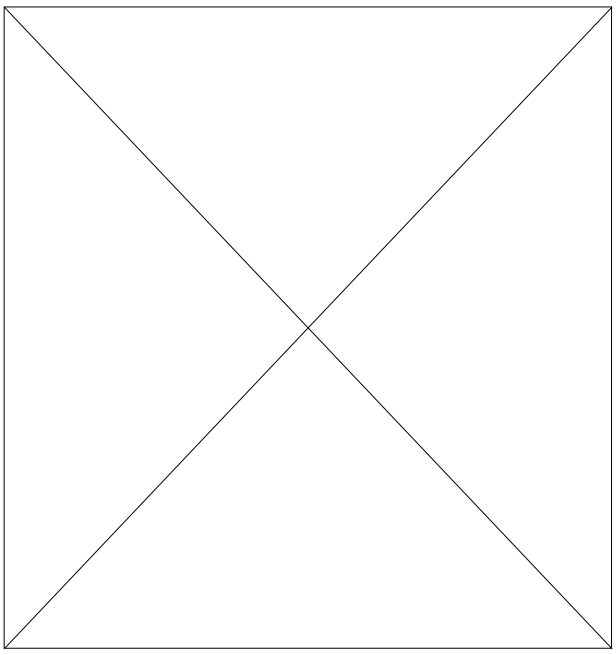

Fig: Age-group key: 1(20-29 years); 2(30-39 years); 3(40-49 years); 4(50-59 years); 5(60-69 years); 6(70-79 years); 7(80-89 years)

Gross growth pattern

There were 58 cases (59.8%) of fungating/ polypoid tumours, 30 (30.9%) excavated tumours, 6 cases (6.2%) of ulcerative/ infiltrative and 3 cases (3.1%) of diffusely infiltrating tumours. Although majority (65.4%) of antropyloric tumours were fungating while 50% and 55.7% respectively of cardiac and corporal tumours were excavated, the association between topography and growth pattern was statistically insignificant (p=0.056).

Histological patterns

There were 10 cases (10.3%) of the diffuse carcinomas, 86 cases (88.7%) of intestinal-type carcinomas and 1 case (1.0%) with a mixed histological pattern (Table 1). The mean age was 55.8 years for the diffuse carcinomas and 55.0 years for the intestinal-type carcinomas. While 90.0% of all cases were seen between 50 and 69 years, only 1 case (10.0%) of the diffuse carcinoma and 14.0% of intestinal-type carcinomas occurred below the age of 40 years. The peak age group for the intestinal-type

tumours was the 50-59 years (27.9%). Intestinal-type tumours showed a male to female ratio of 1.2:1 while the diffuse-type tumours showed an equal sex distribution.

The fungating growth pattern was most common with both histological types (70% of the diffuse and 58.1% of the intestinal-type carcinomas). Majority of cases (90% of diffuse-type and 82.6% of intestinal-type tumours) were located in the antro-pyloric region.

Histological grade

There were forty (41.3%) well-differentiated, 30 (30.9%) moderately-differentiated and 27 (27.8%) poorly-differentiated carcinomas (Table 1). Among patients younger than 40 years, 47.4%, 21.1% and 31.5% were respectively well, moderately and poorly differentiated carcinomas. On the other hand, among patients older than 40 years, 39.7%, 33.3% and 26.9% were well, moderately and poorly differentiated.

Among female patients, 53.5% were well differentiated while 23.3% each were moderately and poorly differentiated. In males, however, 36.5% were well differentiated while 37.0% and 36.5% were respectively moderately and poorly differentiated tumours.

Table 2.
Pattern of metastasis according to depth of tumour invasion

Location	Depth		Total (%)
	Superficial (%)	Advanced (%)	
Absent	1(25.0)	12(36.4)	13(35.1)
Liver	0(0.0)	1(3.0)	1(2.7)
Lymphnode	3(75.0)	18(54.5)	21(56.8)
Omentum	0(0.0)	2(6.0)	2(5.4)
Total	4(10.8)	33(89.2)	37(100.0)

P=0.860

Tumour depth

Overall, 43 (91.5%) of the 47 cases studied were advanced carcinomas while only 4 (8.5%) were early carcinomas (Table 1). The mean age was 53 years for early carcinomas and 55 years for advanced carcinomas.

With regards to the growth pattern, majority of fungating (96%) and excavated (87.5%) tumours were advanced carcinomas. The only ulcerative tumour was an early carcinoma. All the 3 cases of diffusely infiltrating carcinoma were advanced carcinomas.

Histologically, all the diffuse carcinomas and 87.2% of intestinal-type carcinomas were advanced carcinomas. There were 3 (75.0%) well-differentiated and 1 (25.0%) moderately-differentiated early carcinomas while 37.2%, 30.2% and 32.6% of advanced carcinomas were well, moderately and poorly differentiated respectively.

Patterns of metastasis

Table 2 shows that metastasis to lymph nodes occurred in 21 of the 37 cases reviewed. Other sites included omentum(2), liver(1) and umbilicus(1). There was no evidence of metastasis in 13 cases.

Neither the specific group nor the total number of lymph nodes involved in each case could be verified. A total of 21(63.6%) advanced carcinomas showed evidence of metastatic spread as opposed to 3 (75.0%) of early carcinomas with 18(54.5%) advanced carcinomas showing metastasis to the peri-gastric lymph nodes and 3(9.08%) to the omentum and 1(3.03%) to the liver (Table 3). All early carcinomas metastasized to the peri-gastric lymph nodes. The depth of the tumour with umbilical metastasis could not be determined as the biopsy was a superficial one.

Associated incidental findings

Table 3 shows that a total of 79(81.4%) of the 97 cases showed evidence of associated chronic gastritis. *H. pylori* was detected in 43(54.4%) of these cases. *H. pylori* was seen in all age groups (33.3% were younger than 40 years). It

was also seen in 60% of patients with diffuse carcinoma, 41.9% of patients with intestinal-type carcinoma as well as in the antro-pylorus (45.7%), cardia (25.0%) and corpus (41.67%).

Table 3.

Associated incidental findings

Parameters	HLO		Glandular Atrophy		Intestinal Metaplasia	
	Present (%)	Absent (%)	Present (%)	Absent (%)	Present (%)	Absent (%)
Age						
< 40years	6(33.3)	12(66.7)	0(0.0)	18(100.0)	2(11.1)	16(88.9)
> 40 years0	37(46.8)	42(53.2)	17(21.5)	62(78.5)	36(45.6)	43(54.4)
Histology						
Diffuse	6(60.0)	4(40.0)	0(0.0)	10(100.0)	3(30.0)	7(70.0)
Intestina	36(41.9)	50(58.1)	17(19.8)	69(80.2)	35(40.7)	51(59.3)
lMixed	1(100.0)	0(0.0)	0(0.0)	1(100.0)	0(0.0)	1(100.0)
Topography						
Antrum	37(45.7)	44(54.3)	16(19.8)	65(80.2)	33(40.7)	48(59.3)
Cardia	1(25.0)	3(75.0)	0(0.0)	4(100.0)	0(0.0)	4(100.0)
Corpus	5(41.67)	7(58.33)	1(9.09)	11(90.91)	5(41.67)	7(58.33)
Gastritis						
Present	43(54.4)	36(45.6)	17(21.5)	62(78.5)	37(46.8)	42(53.2)
Absent	0.(0.0)	18(100.0)	0(0.0)	18(100.0)	1(5.6)	17(94.4)

Gastric atrophy was seen in 17(21.5%) patients who were all older than 40 years (p=0.03). Atrophy was mild (1 case), moderate (11 cases) and severe (5 cases).

Intestinal metaplasia was present in 38(56.7%) patients, 2(11.1%) of which were younger than 40 years (p=0.007). It was found in only 30% of diffuse carcinomas and 40.7% of intestinal-type tumours (p=0.582).

Discussion

The age range and sex distribution seen in this study are similar to those of previous Nigerian studies.[5,8,9,1,2] However, patients in this study are relatively younger when compared with British, Iranian, Israeli, Japanese and American (including African-Americans and Hispanic-Americans) patients who all show higher mean ages.[2,3,4,5,6] These populations also show much higher male predominance.

Our study corroborates the fact that the antro-pylorus is the commonest location for gastric carcinoma among Nigerians.[5,8,9,13,14] Cardiac and corporal cases on the other hand are uncommon. This is in sharp contrast to Japanese and Western populations in whom cardiac and corporal cases constitute a major proportion as documented by Murayama et al and Hawley *et al*.[15,16] Although the high incidence of cardiac and corporal cases in these populations is thought to be the result of the increasing influence of chronic reflux disease and hiatus hernia, it may just be related to the significant reduction in gastric antral cases due to proper control of *H. pylori*-associated chronic antral gastritis in these environments.[1] Our study also shows (in contrast to the aforementioned populations) that linitis plastic is a relatively rare entity among Nigerians.[2] Fuchs and Meyer, who acknowledged a steady rise

in the frequency of proximal gastric carcinomas over the years, especially in Americans and Europeans, suggested that genetic factors may play very significant roles in their pathogenesis.[1] Although Iranians and Israelis show a higher proportion of gastric cardiac disease, the antropyloric region still constitutes the majority of cases.[17'18]

Exophytic tumours formed the majority of cases in our study. Mabogunje and Lawrie (who worked in other regions of Nigeria), on the other hand, found majority of cases in their study to be diffusely infiltrating tumours.[5] Caucasian and Oriental populations again show contrasting features with reports of much lower frequencies of exophytic tumours and interestingly, higher numbers of excavated and ulcerating tumours. [15'16,]

Lauren in 1965 reported the preponderance of intestinal-type carcinomas in Finland, which has one of the highest incidences of gastric carcinoma in the world. He found that the intestinal type predominated in high risk areas while the diffuse type predominated in low risk areas, findings corroborated by other workers. [1'17] This, however, contrasts with our study conducted in a low-risk area with intestinal-type carcinomas predominating.

The diffuse-type carcinomas are known to show approximately equal male to female sex ratio while the intestinal-type tumours are twice as common in males.[7] Our study agrees with this fact. We also found out that both histologic types showed similar mean ages at presentation in contrast to other populations where diffuse carcinomas occur at a younger mean age than intestinal-type carcinomas.

A large proportion of cases in our series were well differentiated carcinomas, irrespective of the patient's age. Much higher percentages of poorly differentiated gastric carcinomas have, however, been reported in other populations. [15,16] Murayama also reported that poorly differentiated tumours were more predominant under the age of 55 years in Americans and Japanese.

The low frequency of early gastric carcinomas in Western populations is well known. [1'15,16] This was also demonstrated in this study. The Japanese, who show far much higher numbers of early carcinomas, are known to have well developed mass endoscopy based screening programmes which detect these tumours in the early stages.

Abdi-Rad *et al* in Iran found a significant difference between the tumour locations and the degree of invasion (serosal invasion was higher in carcinomas of upper and middle third of the stomach in their series).[17] We, however, did not find any association between tumour location and the depth of gastric wall invasion. Our study supports the widely held view that the degree of tumour differentiation is closely related to the depth of invasion of the gastric wall, with poorer differentiation evident in submucosal and advanced cancers than in mucosal lesions. It is known that tumours progressively acquire aggressive characteristics as growth progresses through the gastric wall although they may be poorly differentiated ab-initio.

We found evidence of regional metastasis in our series. The peri-gastric lymph nodes constituted the majority. Both superficial and advanced carcinomas showed very high frequencies of metastasis at the time of presentation to hospital. While American and Japanese populations show high metastatic rates in advanced cancers, only few superficial carcinomas showed evidence of metastasis.[15]
A little over half of the cases of gastric carcinoma in our study were found to be associated with *H. pylori* induced chronic gastritis, with gastric glandular atrophy and intestinal metaplasia occurring in only 21.5% and 46.8% of cases respectively. Diffuse-type carcinomas on the

other hand were not associated with gastric atrophy. Uemura *et al* showed that intestinal-type tumours only developed in Japanese patients with *H. pylori* infection especially when associated with severe atrophy and intestinal metaplasia. [8] He also found an association between diffuse-type gastric carcinoma and atrophic gastritis. There is virtually no doubt that *H pylori* is a very strong factor in the genesis of a large proportion of gastric carcinomas worldwide. However, the high prevalence of *H. pylori* infection in our environment sharply contrasts with the low incidence of gastric glandular atrophy and intestinal metaplasia as well that of gastric carcinoma. It is thought that this may be due to the fact that the appropriate genetic and environmental profile needed to complement the effect of *H. pylori*-induced gastritis to further transform into cancer is lacking in this environment.[13]

This report has highlighted fundamental differences between gastric carcinoma in Nigerian patients and those in other parts of the world. These differences may be significant and seem to suggest possible differences in the pathogenetic mechanisms and biologic behavior of gastric carcinoma between these populations. It will be instructive to further investigate these differences as they may have important consequences on therapeutic measures and disease prevention.

References

1. Fuchs CS. and Mayer RJ: Gastric carcinoma. N Engl J Med 1995; 333: 32-41.
1. Yao JC, Tseng JF, Worah S, Hess KR, Mansfield PF, Crane CH *et al.* Clinicopathologic behaviour of gastric adenocarcinomas in Hispanic patients. Analysis of a single institution's experience over 15 years. J Clin Onco. 2005; 23: 3094-3103.
2. Boring CC, Squires TS and Heath CW Jr: Cancer statistics for African Americans. CA Cancer J Clin. 1992; 42: 7–17.
3. Howson CP., Hiyamu T. and Wynder EL.: The decline in gastric cancer: Epidemiology of an unplanned triumph. Epidmiol Rev 1986; 8: 1-27.
4. Mabogunje OA, Subbuswamy SG and Lawrie JH. The two Histological types of gastric carcinoma in Northern Nigeria. Gut 1978; 19: 425-429.
5. Abioye AA, Hendrickse M and Junaid TA. Ibadan Cancer Registry. 1970-1976 in Parkin DM. Cancer Occurrence in Developing Countries. International Agency for Research on Cancer 1986; 67-71.
6. Cederquist R and Attah EB. Zaria Cancer Registry. 1976-1978 in Parkin DM. Cancer Occurrence in Developing Countries. International Agency for Research on Cancer 1986; 68-73.
7. Elebute EA, Ngu VA, Mainwaring AR and Eruchalu RC. Cancer of the stomach seen at University College Hospital, Ibadan. W. Afr. Med. Jour 1963; Feb:11-17.
8. Arigbabu AO. Gastric Cancer in Nigeria. Tropical Doctor 1988; 18: 13-15.
9. Pagnini CA and Rugge M. Advanced gastric cancer and prognosis. Virchows Arch (Pathol Anat) 1985; 406: 213-221.
10. Borrman R: Tumours of the Stomach and Duodenum. In: Manual of Special Anatomic and Histologic Pathology. Henske F, Lubarsch O (Eds): Julius Springer. Berlin. 1926.
11. Dickson NS, Genta RM, Yaigmey JH and Correa P. Classification and grading of gastritis. The updated Sydney Sysytem. Amr. J. Surg Path 1996; 20(10): 1161-1181.
12. Oluwasola AO and Ogunbiyi JO. Gastric Carcinoma: Aetiological, Clinicopathological and Management Patterns in Nigeria. Nig. J. Med 2003; 12: 177-186.
13. Obekpa PO, Onuminya JE, Nwana EJC, Anteyi EA, Malu AO and Momoh JT. A Clinicopathological review of gastric malignancies in the middle belt of Nigeria. Nig. Med. Pract 1994; 27: 6: 69-72.

14. Murayama M, Takeshita K, Endo M, Deakin M and Moosa AR. Clinicopathological study of gastric carcinoma in high- and low-mortality countries: comparison between Japan and the United States. Gastric Cancer 1998; 1: 64-70.
15. Hawley PR, Westerholm P and Morson BC. Pathology and prognosis of carcinoma of the stomach. Brit. J. Surg 1970; 57: 877-883.
16. Abdi-Rad A, Ghaderi-sohi S, Nadimi-Barfroosh H and Emami S. Trend in incidence of gastric adenocarcinoma by tumor location from 1969–2004: a study in one referral center in Iran. Diag Pathol 2006; 1-5.
17. Antonioli DA and Goldman H: Changes in the location and type of gastric adenocarcinoma. Cancer 1982; 50: 775-781.
18 Liu C and Crawford JM. The Gastrointestinal Tract. *In:* Robbins and Cotran Pathologic Basis of Disease. 7th ed. Kumar V, Abbas AK, Fausto N (Eds). Elsevier. Pennsylvania. 2005; 822-826.
19. Uemura N, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Taniyama K, Sasaki N, Schlemper J. helicobacter pylori infection and the development of gastric cancer. N. Engl. J. Med 2001; 345: 784-789.