

Clinicopathological Features and Treatment Outcome of Patients with Gastric Cancer in Lagos: Is the Outlook Getting Better?

Abstract

Background: Gastric cancer (GC) is an important cause of morbidity and mortality in Nigeria. Significant advances in the management of GC in South-West Nigeria occurred in the last three decades. **Patients and Methods:** This was a retrospective comparative study of patients with GC that presented at our tertiary hospital in the last three decades. Information on clinicopathological features and treatment outcome were analysed. Data of two consecutive periods; 1991–2004 (Group I) and 2005–2018 (Group II) were compared. **Results:** Ninety-one patients were studied; Group I (47 patients), Group II (44 patients). The mean age was 56.4 ± 12.7 years and male-to-female ratio was 1.8 to 1.0. The predominant symptoms were epigastric pain in 81(89.0%) (43 vs. 38) and weight loss in 63(69.2%) (32 vs. 31), whereas the signs were epigastric tenderness in 44(46.1%) (24 vs. 20) and epigastric mass in 42(46.1%) (26 vs. 16). The overall mean duration of symptom was 12.3 ± 16.9 months. Barium meal diagnosed GC in 29(61.7%) patients in Group I vs. 4(9.1%) patients in Group II. Conversely, endoscopy diagnosed GC in 23(48.9%) patients in Group I vs. 37(84.1%) patients in Group II. Operations undertaken included palliative subtotal gastrectomy 26(28.6%), potentially curative subtotal gastrectomy 15(16.5%) and non-resectional surgeries in 27(29.7%) patients. The overall incidence of major post-operative complications was 33%. Thirty-nine (42.8%) of the studied patients were lost to follow up. The median postoperative survival for Groups I and II patients was 22 weeks and 58 weeks, $P = 0.012$, respectively. **Conclusion:** The outcome of management of patients with GC at our tertiary hospital has improved modestly in the past three decades. Patients are still presenting late with very advanced disease.

Keywords: Advanced gastric cancer, gastric adenocarcinoma, gastric cancer, gastric cancer in Lagos

Introduction

Gastric cancer (GC) is relatively uncommon in Nigeria but is an important cause of morbidity and mortality. The age-standardized incidence rate for both sexes and all ages in 2018 was 2.4 per 100,000 according to Globocan 2018.^[1] Worldwide, GC accounts for 989,600 new cases and 738,000 deaths annually.^[2] The case-fatality ratio of GC is higher than for commoner malignancies like colon, breast, and prostate cancers.^[2] Essentially GC is still the “Captain of the Men of Death” as it was in the 1930s.^[3] The incidence and mortality are highly variable by region and highly dependent on diet and *Helicobacter pylori* infection.^[4] Incidences are highest in Eastern Asia, Eastern Europe, and South America, whereas the lowest incidences are in North America and parts of Africa.^[5,6]

Helicobacter pylori is an important aetiological factor for the occurrence of non-cardia adenocarcinoma.^[7,8] There is a low incidence of GC in Africa despite a high prevalence of *H. pylori* infection hence the Africa enigma.^[9] The African enigma reflects the interplay of three major etiologic forces; the oncogenic potential of the specific strains of *H. pylori*, the modulation by co-infections of the immune response towards a Th 2 type and the abundance of antioxidant micronutrients in the diet.^[10]

GC is a disease predominantly of middle age and the elderly. In the Far East where the highest prevalence of gastric carcinoma is reported, the peak age incidence is in the seventh decade with an average age of occurrence of 65.2.^[11] In Nigeria studies from the late 1980s to 2014 put the peak age range of occurrence to the 51–60 age group and the average ages of occurrence to be between 51 and 52.3 years.^[12,13]

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Similar to observations elsewhere, patients usually present with either potentially resectable locoregional disease or advanced incurable disease.^[14] Surgically curable early GCs are frequently asymptomatic and are infrequently detected outside a screening programme.^[14] There is no screening programme for GC in Nigeria.

The management of GC patients in our tertiary hospital has evolved over the last three decades from Barium meal for establishing diagnosis in the 1990s to the more regular use of gastrointestinal (GI) endoscopy for diagnosis, clinical staging with Helical computerized tomography (CT) scan of the abdomen and gastric resection with GI staplers in the year 2005. In addition, chemotherapy is now readily available and affordable. These trends constitute considerable progress in diagnostic and therapeutic tools which can improve the outcome of the treatment of GC patients. Based on the foregoing a study to review and compare the clinicopathological features and management outcome of patients with GC seen in the first and second halves of the study period at our tertiary hospital was deemed necessary. Outcomes of GC management following multi-modality treatment have never been reported from this tertiary hospital.

Patients and Methods

This was a retrospective study of patients with GC seen between January 1991 and December 2018. Case notes of patients were retrieved from the Medical records department and relevant data were entered into a proforma designed for the study. Data obtained included demographics, clinical features, findings on barium meal, upper gastrointestinal endoscopy (UGE) CT scan of the abdomen, operations undertaken, intraoperative findings, post-operative complications, histopathological diagnosis and treatment outcomes. The study population was divided into two groups based on the time of presentation for review and comparison. Patients admitted from January 1991 to December 2004 were allocated to group I, whereas those admitted from January 2005 to December 2018 were allocated group II. The patients in each group were subsequently followed-up for 1 year.

Staging for the purpose of the study was based on the tumour (T), node (N), and metastasis (M) for GC of the 8th edition of the American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) tumour, node metastasis (TNM) staging system 8th edition.^[15]

Stage 0	Tis	N0	M0
Stage I:	T1-2	N0	M0
Stage IIA;	T1-2	N1-3	M0
Stage IIB:	T3-4a	N0	M0
Stage III:	T3-4a	N1-3	M0
Stage IVA:	T4b	N1-3	M0
Stage IVB:	any T	any N	M1

Advanced GC was defined as T2-T4b/N0-N3b/M0 according to the AJCC/UICC TNM classification.^[16]

Post-operative survival in weeks (Primary end point) was defined as the duration in weeks the patient survived following post-operative discharge and adjuvant chemotherapy.^[17]

Data were analysed using the Statistical Package for Social Sciences (SPSS) version 21. Categorical data were expressed in proportions. Quantitative variables were expressed in frequencies and percentages. The proportions between categorical variables were compared using chi-square. Statistical significance was set at a p-value of 0.05

Results

Ninety-one patients were managed for GC at our institution during the period reviewed: Group I; 47 patients and Group II; 44 patients. The peak incidence age was in the seventh decade of life with a mean age (SD) of 56.4 (12.7) years. The mean ages (SD) for group I and group II were 55(13.2) years and 57 (12.3) years, respectively, $P = 0.270$. The frequency distribution of the age groups is shown in [Table 1]. The male-to-female ratio was 1.8 to 1.0.

The predominant initial symptom was epigastric pain in 83 (91.2%) patients. Of the patients that had epigastric pain as the initial predominant symptom, only 10 (12.3%) patients presented within 3 months of onset of symptoms, whereas the remaining 71 (87.7%) patients were reviewed more than 3 months after onset of symptoms. The overall mean duration of symptoms was 12.3 ± 16.9 months [Table 1]. There was no statistically significant difference between the groups as regards duration of the initial symptom, $P = 0.514$.

Table 2 depicts the clinical symptoms and signs observed in our patients. The common symptoms were epigastric pain (91.2%), weight loss (69.2%), vomiting (62.6%), nausea (37.4%), constipation (28.7%) and upper GI bleeding (melena and/or hematemesis (27.5%)), whereas the frequent signs were epigastric tenderness (48.3%), anemia (47.2%) epigastric mass (46.1%) and gastric outlet obstruction (GOO) (46.1%). The other symptoms and signs of GC are shown in Table 2. There was no statistically significant difference in the prevalence of clinical symptoms and signs between the two groups except for upper GI bleeding and anemia. Upper GI bleeding (9 vs. 16; $P = 0.005$) and anemia (16 vs. 25; $P = 0.009$) showed statistically significant differences between the two groups.

In the early part of our review (group I) double contrast Barium meal defined the morphological characteristics of GC in 29 (61.7%) patients vs. 4(9.1) patients in Group II. Conversely, UGE defined the morphological characteristics of GC in 23(48.9%) patients in Group I patients vs. 37 (84.1%) in Group II. Pre-operative CT scan was undertaken in 3.4% (6 patients) of group I patients vs. 75% (33 patients) in group II patients.

Seventy-four surgical operations were performed in this review, resectional and non-resectional. Resectional operations included palliative subtotal gastrectomy 26

(28.6%) and potentially curative subtotal gastrectomy 15 (16.5%) and non-resectional operations comprised of exploratory laparotomy 11 (12.1%) and gastrojejunostomy 16 (17.6%). Potentially curative subtotal gastrectomy (D1 lymphadenectomy) was performed in 15 patients. It was performed for advanced disease, stage IIB: 12 patients

(group I:8, group II:4) and stage III: 3 patients (group I:1, group II:2). Contrastingly, palliative subtotal gastrectomy was performed in 26 patients for locally advanced and metastatic; stage III: 11 patients (group I:10, group II:1) stage IVA: 8 patients (group I:4, group II:4) and stage IVB: 7 patients (group I:4, group II:3). The ratios of surgery

Table 1: Patient characteristics

	Total n = 91	Group I n = 47	Group II n = 44	P Value
Number of patients	91	47	44	
Male	59	31	28	
Female	32	16	16	0.817
Male/female ratio	1.8:1	1.9: 1	1.75: 1	
Mean (SD) (years)	56.4 ± 12.7	55.7 ± 13.2	57.2 ± 12.3	0.270
Age distribution n (%)				
31–40		2 (4.3)	1(2.3)	
41–50		5 (10.6)	4 (9.1)	
51–60		10 (21.2)	4 (9.1)	
61–70		14(29.8)	10(22.7)	
71–80		9 (19.1)	14 (31.8)	
81–90		7 (14.9)	6 (13.6)	0.816
Duration of abdominal pain at presentation		81	43 (93.6)	38(88.6)
≤ 1 month	2	1	1	
≤ 3 months	10	6	4	
≤ 6 months	31	18	13	
> 6months	50	25	25	
Mean (SD) (months)	12.3 ± 16.9	13.4 ± 20.2	10.6 ± 12.9	
Median (months)	9	7.2	9	

Table 2: Clinical features (symptoms and signs)

Clinical parameter	Total	Group I n = 47 (%)	Group II n = 44 (%)	P Value
Symptoms				
Epigastric pain	81	43(91.5)	38(86.3)	0.514
Weight loss	63	32(68.0)	31(70.4)	0.82
Vomiting	57	29 (61.7)	28 (63.6)	0.862
Nausea	34	16 (34.0)	18 (40.9)	0.519
Constipation	26	16 (34.0)	10 (22.7)	0.215
Melena/hematemesis	25	7 (14.9)	18 (40.9)	0.005*
Anorexia	22	12 (25.6)	10 (22.7)	0.734
Diarrhoea	7	5 (10.6)	2 (4.5)	0.192
Dysphagia	5	2 (4.3)	3 (6.8)	0.608
Signs				
Epigastric tenderness	44	24 (51.0)	20 (45.4)	0.593
Anaemia	43	16 (34.0)	27 (38.6)	0.009*
Epigastric mass	42	26 (55.3)	16 (36.3)	0.070
GOO	41	24 (51.0)	17 (38.6)	0.234
Ascites	13	8 (17.0)	5 (11.3)	0.441
Jaundice	9	3 (6.4)	6 (13.6)	0.257
Supraclavicular				
Node	7	6 (12.8)	1 (2.3)	0.112
Abdominal distension	6	2 (4.3)	4 (9.1)	0.109
Others	5	0	5	

GOO = gastric outlet obstruction, Others = sister Mary Joseph nodule and Krukenburg

Table 3: Operations performed

Operation	Total n = 91(%)	Group I n = 47(%)	Group II n = 44(%)
Palliative subtotal			
Gastrectomy	26(28.6)	18(38.3)	8(18.2)
Potentially curative			
Subtotal gastrectomy	15(16.5)	6(12.8)	9(20.5)
Gastrojejunostomy	16(17.6)	9(19.1)	7(15.9)
Exploratory			
Laparotomy	11(12.1)	6(12.8)	5(11.4)
Sleeve gastrectomy	1(1.1)	0(0.0)	1(2.3)
Sleeve gastrectomy and excision of omental tumour	1(1.1)	0(0.0)	1(2.3)
Wedge gastrectomy	2(2.2)	1(2.1)	1(2.3)
Feeding jejunostomy	1(1.1)	0(0.0)	1(2.3)
Supraclavicular lymph node biopsy	1(1.1)	1(2.1)	0(0.0)
No Surgery	17(18.7)	6(12.8)	11(25.0)

Table 4: Histopathologic types

Histologic type	Total n = 91(%)	Group I n = 47(%)	Group II n = 44(%)
Adenocarcinoma			
Intestinal type	70(76.9)	39(82.3)	31(70.5)
Signet ring cell (diffuse)	9 (9.8)	3(6.4)	9(13.6)
Others			
GIST	5 (5.4)	0(0.0)	5(11.4)
Mesenchymal	2 (2.1)	2(4.3)	1(2.3)
Lymphoma	1(1.0)	0(0.0)	1(2.3)
Carcinoid	1(1.0)	1(2.1)	0(0.0)
Not known	2(2.1)	2(4.3)	0(0.0)

Adenocarcinoma = intestinal, signet ring cell

with curative intent to palliative resectional surgery for group I and group II were 1:3 and 1.1:1, respectively. Non-resectional operations (gastrojejunostomy and laparotomy) were performed for 27 patients with unresectable locally advanced and metastatic diseases with stages IVA (16 patients) and IVB (11 patients). Other procedures undertaken are shown in Table 3.

Table 4 shows the histopathologic types of the cancers. Adenocarcinomas (Intestinal and Signet ring cell) were the most common identified in 85.7% of our patients. The frequency of other histologic types is shown in Table 4. Staging using the AJCC classification^[15] revealed the following prevalence: stage IIB 13 (14.2%) patients (group I:4, group II:9), stage III 18 (19.8%) patients (group I:13, group II:5), stage IVA 15 (16.5%) (group I:10, group II:5) and stage IVB 43 (47.2%) patients (group I:18, group II:25) and undetermined 2 (2.2%) patients. There were no patients with stages 0, I, or IIA. Overall, 43 (47.2%) patients had metastatic disease (stage IVB) and 46 (50.5%) patients had advanced disease (stages IIA-IVB). There were no patients with early GC.

Using either barium meal, UGI, CT scan of the abdomen or surgery; adenocarcinomas were located in the following

segments of the stomach: antrum 51(64.6%) (group I:27 group II:24), body 26 (32.9%) (group I:14, group II:12), and whole stomach 2 (2.5%) (group I:1, group II:1).

A total of 25 (33.8%) major post-operative complications were noted within 30 postoperative days and these were GOO (9) and GI bleeding (anastomotic) (6), sepsis (4) duodenal fistula (3), pancreatitis (2) and common bile duct stricture (1). Of these two patients required re-operation: conversion of a Billroth II gastrojejunostomy to a Roux-en-Y gastrostomy and repair of a biliary stricture. However, the patients with GOO were managed successfully non-operatively by a combination of prolonged nasogastric tube drainage and parenteral nutrition. Six patients (3 in each group) died in the post-operative period from complications: deep venous thrombosis (1), sepsis (2), malignant ascites (1), hypoproteinemia (1) and duodenal blowout (1). Thirteen patients in Group I had adjuvant chemotherapy, nevertheless developed progressive disease, whereas 20 patients in Group II had chemotherapy.

Thirty-nine patients were lost to follow-up: Group I—22 patients and Group II—17 patients, whereas 22 patients in Group I and 24 patients in Group II were followed up.

Three patients (all in Group II) were still alive at the end of the followed-up period.

Group I patients had a median post-operative survival of 22 weeks vs. 58 weeks for Group II. The difference was statistically significant, $P = 0.012$. Additionally, the mean of the post-operative survival in weeks was 21.8 ± 8.97 in Group I vs. 37.6 ± 26.1 in Group II. Furthermore, the 6-month postoperative survival was 45.5% in Group I vs. 62.5% in Group II including the 3 patients in Group II that were still alive at the end of the follow-up period. The statistical difference in 6-month survival was not significant, $P = 0.547$.

Discussion

Our findings revealed that the incidence of GC increases with age with a peak incidence between 51 and 60 years. In our study, similar to reports from previous studies^[12,13] in Nigeria the mean age for GC in both cohorts was the 6th decade of life. In the Far East where the highest prevalence of gastric carcinoma is reported, the peak age incidence is in the 7th decade with an average age of occurrence of 65.2 years.^[11] Furthermore, a male preponderance (group I; 1.9: 1, group II; 1.75: 1) was found in our patients comparable to what obtains in most parts of the world for noncardia GC.^[18-20] Generally GC rates have been lower in females than in males. A possible explanation is the protective effect offered by oestrogen.^[21,22]

Early diagnosis of GC and tumour resection occurs in Japan and confers five-year survival of 90% and is the only way to improve survival rate.^[23,24] However, early diagnosis is difficult since symptoms appear late. In our study, the commonest initial symptoms were epigastric pain (91.2%) and weight loss (69.2%). This is similar to another study conducted in Morocco, where GC is the most common GI cancer.^[25] Generally, most patients with GC are symptomatic and already have advanced incurable disease at the time of presentation. Symptoms of abdominal pain, vomiting, weight loss and loss of appetite are associated with advanced GC with poor prognosis.^[26,27] These symptoms were identified in most of the patients in our study.

Similarly, physical signs in GC are late events. These signs customarily associated with advanced or metastatic disease were identified in our patients. Invariably when present the patients cannot be offered curative surgery. The presence of a palpable epigastric mass was a common physical finding in our series and generally indicates long-standing advanced disease and invariably associated with poor prognosis.^[28-30] A number of studies that assessed the prognostic value of this sign found a strong association with very low 5-year survival rate (0–20%) and also with a very short life span (<4 months).^[31,32]

Only 48.9% of Group I patients had UGE vs. 84.0% in Group II. The difference was due to the popularity of double

contrast barium meal in the 1990s and thus patients had undergone this before being referred to our tertiary centre. Moreover, endoscopy was not readily available in the 1990s. Only 3 (6.4%) of the Group I patients underwent staging CT scan of the abdomen and it revealed liver metastases in 2. Conversely, 75% of Group II had abdominal CT scan and it revealed evidence of liver metastases, D3 lymph nodes or ascites in 18.1%. The poor utilization of CT scan in the first half of the review were due to low availability and relative high cost of the test.

In our review, advanced disease (stages II, III, and IVA) and metastatic disease (stage IVB) constituted 50.5% and 47.2%, respectively, of the patients. Notably, there were no cases of stage I disease, patients that would otherwise have qualified for curative surgical resection.

Similar to other series,^[33,34] our study revealed that adenocarcinoma was the predominant type of GC accounting for 84.5% of cases. A preponderance of the adenocarcinomas were found to be non-cardiac (antrum 78%, body 16% 9, whole stomach 6%) which is similar to studies^[35] done in other developing countries but, at variant with what obtains in developed countries where gastric cardia is becoming the most common site of GC.^[33,36,37] Intestinal type adenocarcinoma (IT) was the prevalent histologic subtype accounting for 79.0% and this is similar to other reports from Nigeria and most parts of the world.^[29,38]

GC is most often diagnosed in symptomatic patients with advanced disease. It was the case in our series, where advanced and metastatic diseases, represented 50.5% and 47.2% of patients, respectively. This is comparable to other studies worldwide.^[14,29] There were no cases of early GC or stage I disease. This further corroborated the fact that early disease is asymptomatic and rarely diagnosed outside a screening programme as obtained in Japan.

Surgical procedures were performed in 74 patients and manifestly most of these procedures were palliative and only 16.5% of patients underwent potentially curative resection due to the advanced nature of the diseases. Non-resectional palliative procedures (gastrojejunostomy and exploratory laparotomy) were undertaken in 29.7% of the patients on account of unresectable advanced diseases at laparotomy.

The median post-operative survival was short despite the multimodal therapy reflecting the advanced stage of presentation of the patients similar to what obtains in developing and developed countries where there is no screening for GC. Nevertheless, it has improved modestly over the decades as reflected in the statistically significant difference in median post-operative survival between the two groups.

The limitations of the review included the following: it was a single hospital-based study so it could not depict the true incidence of GC in South-west Nigeria. Secondly, a proportion of case notes were not seen, thereby reducing

the number of patients studied. Thirdly, many patients did not come back to the hospital for follow-up after discharge.

Conclusion

The outcome of the management of GC patients at our tertiary hospital has improved modestly in the last 3 decades with the advent of better diagnostic tools, surgery, and chemotherapy. However, late presentation with very advanced disease persists.

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Conflicts of interest

There are no conflicts of interest.

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