Ten-Year Retrospective Study of Gastric and Gastroesophageal Cancers in South-East Nigeria: Insights into Demographics and Tumour Characteristics

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ABSTRACT

Background: Gastric and gastro-oesophageal junction cancers remain major contributors to global cancer mortality. In Nigeria, late diagnosis is common, and this pattern continues to drive high cancer-related deaths.

Materials and Methods: *Clinico-pathological data were retrieved from four major histopathology laboratories in Anambra State, southeast Nigeria. Statistical analysis was conducted using the Chi-square test in SPSS version 25 to assess differences in proportions.*

Results: *Gastric and gastro-oesophageal junction cancers were most frequently diagnosed in individuals in their sixth and seventh decades of life, with a median age of 56.7 years. There was no clear sex predilection in the study population. The pylorus and antrum were the most common tumour locations, and intestinal-type adenocarcinoma was the predominant histological subtype. Most cases presented at advanced stages, with the majority staged as T3 or T4.*

Conclusion: *Gastric and gastro-oesophageal junction cancers in this setting are characterised by late presentation and are predominantly antral adenocarcinomas. These findings highlight the need for a regional screening initiative aimed at earlier detection and improved outcomes.*

Keywords: Gastric cancer, gastro oesophageal junction cancer, adenocarcinoma, late presentation, Anambra State, Nigeria, histopathology, screening programme

INTRODUCTION

Cancer is the second leading cause of death globally after cardiovascular diseases. Upper gastrointestinal cancers, including gastric and GEJ cancers, are among the most common cancers. Despite the decline in gastric cancer rates in recent decades, it is still a major cause of cancer mortality. It has been shown that 6.8% of global cancer deaths are due to gastric cancer.[1] It is estimated that in 2022, gastric cancer accounted for 768,793 deaths worldwide.[1]

The incidence of gastric and GEJ cancers show wide geographical variation. The high-risk areas are East Asia and Eastern Europe. The low-risk areas are Southern Asia, North and East Africa, and North America.[1] Gastric cancer has a low prevalence in sub-Saharan Africa with the lowest incidence rates in Western Africa.[1,8,10] In Nigeria, gastric cancer accounts for 1.1-6.0% of all cancers and the mean age of diagnosis is 56 years.[2-6,8]

Gastric adenocarcinoma is the most common type of gastric cancer, originating from the glandular tissues of the stomach. Other types of gastric cancers are lymphomas and sarcomas which originate in lymphoid and connective tissue respectively.[7]

MATERIALS AND METHOD

This is a retrospective study of all gastric and GEJ biopsies and gastrectomy specimens diagnosed as cancers at the four major histopathology laboratories in Anambra state. These are: histopathology laboratories of Nnamdi Azikiwe University Teaching Hospital Nnewi, Chukwuemeka Odumegwu Ojukwu University Teaching Hospital Awka, Pathocon Specialist Clinic and Research Institute Nnewi and Nkeoma Specialist Hospital Onitsha, over 10-years, from January 1st 2011 to December 31st 2020. The cases were diagnosed using hematoxylin and eosin stains.

Inclusion and Exclusion Criteria

Inclusion criteria encompassed all well-preserved tissue blocks with adequate data and tissue remaining for sectioning.

Exclusion criteria: All cases with incomplete biodata and missing tissue blocks.

1. Collection of Biographical data

Relevant data such as age, sex, tumour location, etc were extracted from the request forms. However, the names of the patients were excluded in order to protect their identities.

2. Histopathological Examination and WHO Classification.

The histological slides and paraffin blocks of all gastric and GEJ biopsies, and gastrectomy specimens diagnosed as cancers in the facilities mentioned between January 2011 to December 2020 were retrieved from the archives. Fresh sections were cut from paraffin blocks and stained with hematoxylin and eosin for cases with lost or poor-quality slides (mountant breakdown, broken slides, faded stains). All slides were examined, histologically classified, graded and T-staged using the most recent WHO Classification of Gastric Tumours, 2019, for uniformity.

Data was analyzed using simple descriptive statistics such as Chi-square test, which was used to measure associations with level of significance p less than 0.05.

The above analysis was done using Statistical Package for Social Sciences (SPSS version 25)® IBMInc Chicago.

Ethical approval for the study was obtained from the Ethics Committee of NAUTH Nnewi.

RESULTS

During the period of study, a total of 112 gastric and gastroesophageal junction malignant tumours were received at the four laboratories under study. Nineteen cases were excluded after failing to meet the inclusion criteria. Of the 93 included cases, 17 (18%) were gastrectomy specimens while 76 (82%) were biopsies.

The mean age at diagnosis was 56.65yrs (SD±14.4) and their ages ranged from 26 to 85 years. These tumours are most common in the sixth and seventh decades of life, but are uncommon at the extremes of life.

The gender distribution of the 93 cases of gastric & GEJ cancers show that 51.6% (48 cases) of the patients are female while 48.4% (45 cases) are males, revealing a male-female ratio of 0.94:1. The mean age for male patients is 58.2± 12.9years while that of females is 55.2± 12.7years.

TUMOUR HISTOLOGICAL TYPE

The majority of the 93 cancers studied are carcinomas (67 cases, 72.0%). Mesenchymal tumours are the second commonest group of cancers making up 21.5% (20 cases) of the gastric and GEJ cancers. The rest of the tumours were four cases (4.3%) of lymphomas and two cases (2.2%) of neuroendocrine tumours. There was no record of metastatic tumours. (Fig 1)
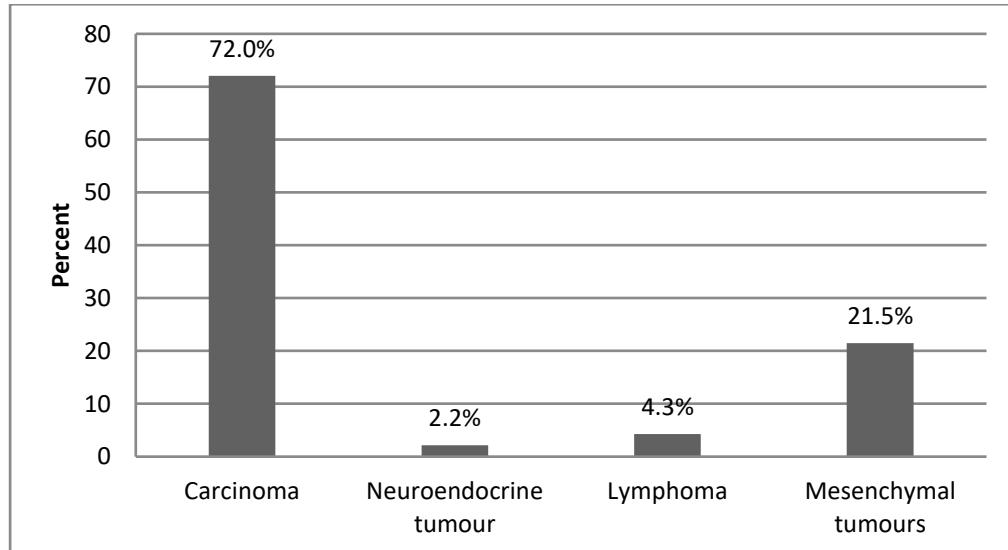

Fig 1: Bar chart showing tumour histological type of 93 gastric and GEJ cancers

Gastrointestinal stromal tumours make up the bulk of mesenchymal tumours (90.0%). A case each of leiomyosarcoma (5.0%) and angiosarcoma (5.0%) completes the rest of this group of tumours. (Fig 2)
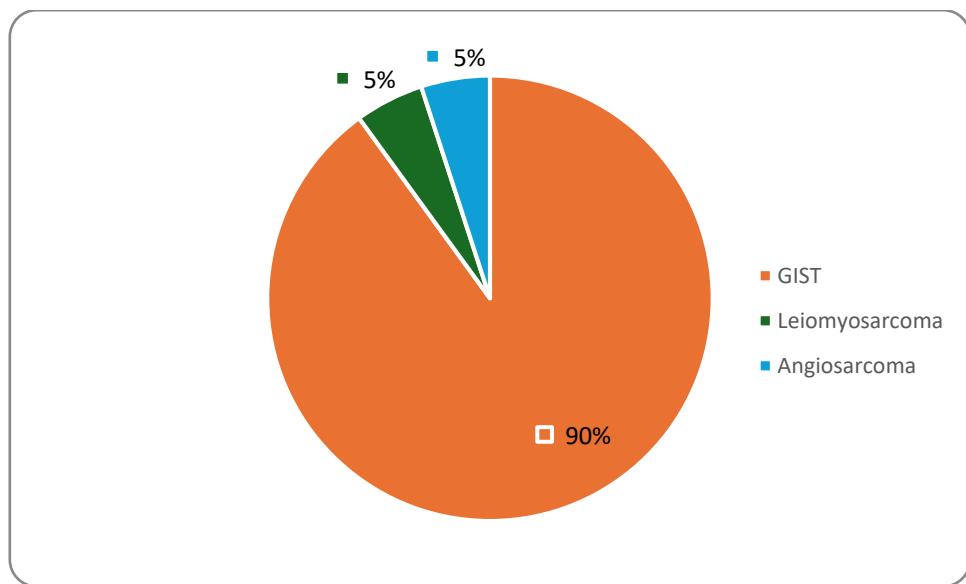
Fig 2: Pie chart showing distribution of mesenchymal tumours.

Table 1 shows the cross-tabulation of tumour histological type and age range in years. There is no significant statistical association between the variables (P=0.314).

Table 1: Age range distribution of various tumour types

		Tumour Type				
		Carcinoma	Neuroendocrine tumour	Lymphoma	Mesenchymal tumours	Total
Age range in years	20-29(% within tumour type)	0(0.0%)	0(0.0%)	0(0.0%)	2(10.0%)	2(2.2%)
	30-39 (% within tumour type)	9(13.4%)	0(0.0%)	1(25.0%)	2(10.0%)	12(12.9%)
	40-49 (% within tumour type)	10(14.9%)	0(0.0%)	1(25.0%)	3(15.0%)	14(15.1%)
	50-59(% within tumour type)	11(16.4%)	2(100.0%)	1(25.0%)	6(30.0%)	20(21.5%)
	60-69 (% within tumour type)	22(32.8%)	0(0.0%)	0(0.0%)	5(25.0%)	27(29.0%)
	70-79(% within tumour type)	11(16.4%)	0(0.0%)	1(25.0%)	2(10.0%)	14(15.1%)
	>79(% within tumour type)	4(6.0%)	0(0.0%)	0(0.0%)	0(0.0%)	4(4.3%)
Total(% within tumour type)		67(100.0%)	2(100.0%)	4(100.0%)	20(100.0%)	93(100.0%)

P=0.314

TUMOUR LOCATION

The location of 67 gastric and GEJ cancers with known tumour topography is shown in Table 2 (26 cases do not have information available on the parts of the stomach the biopsies were taken). The pyloric antrum is the most common location of gastric cancers accounting for 35 of the 67 cases (52.2%). The cardia/fundus is the next most common location, 20.9%. GEJ cancers were found to be 12 cases of 67 (17.9%), while the body of the stomach presented the least cancers, 9%.

Table 2 Tumour location of 67 cases of gastric and GEJ cancers

Tumour location		Frequency	Valid Percent
Valid	pylorus/antrum	35	52.2%
	cardia/fundus	14	20.9%
	gastroesophageal junction	12	17.9%
	body	6	9%
	total	67	100.0%
	missing	26	
Total		93	

Cross-tabulations of tumour location against tumour histological type, age and gender revealed no significant statistical associations between the variables, however most carcinomas occurred in the pylorus while most mesenchymal tumours occurred in the body of the stomach.

CLASSIFICATION OF CARCINOMAS

Using the WHO classification scheme, the tubular adenocarcinoma is the most common tumour histological type, accounting for 31 cases (46%) of the 67 carcinomas. The poorly cohesive carcinomas which encompass signet ring cell type, (8 cases, 11.9%) and other types (13 cases, 19.4%) together accounted for 21 of the 67 carcinomas. There were also four cases of squamous cell carcinoma (6%) and 2 (3%) cases each of papillary and mucinous adenocarcinoma.

Table 3: Histological types of gastric and GEJ junction carcinomas (WHO Classification)

		Count	Percent %
Carcinoma Histological Type (WHO)	Tubular Adenocarcinoma	31	46.3%
	Poorly Cohesive Carcinoma; Other Subtypes	13	19.4%
	Poorly Cohesive Carcinoma; Signet Ring Cell Type	8	11.9%
	Mixed Adenocarcinoma	5	7,5%
	Squamous Cell Carcinoma	4	6.0%

	Mucinous Adenocarcinoma	2	3.0%
	Papillary Adenocarcinoma	2	3%
	Other Histologic Subtypes	2	3.0%
	Total	67	100.0%

Classification of carcinoma types using the Lauren Classification Scheme show that the majority of tumours are of the intestinal type (37 cases, 55.2%). The rest consists of 21 cases (31.3%) of diffuse type, 5 cases (7.5%) of mixed type and 4 indeterminate cases (6%) (Fig 3).

Cross-tabulations of histological type of carcinomas (Lauren Classification) against patients' age & gender. There are no significant statistical associations between the variables.
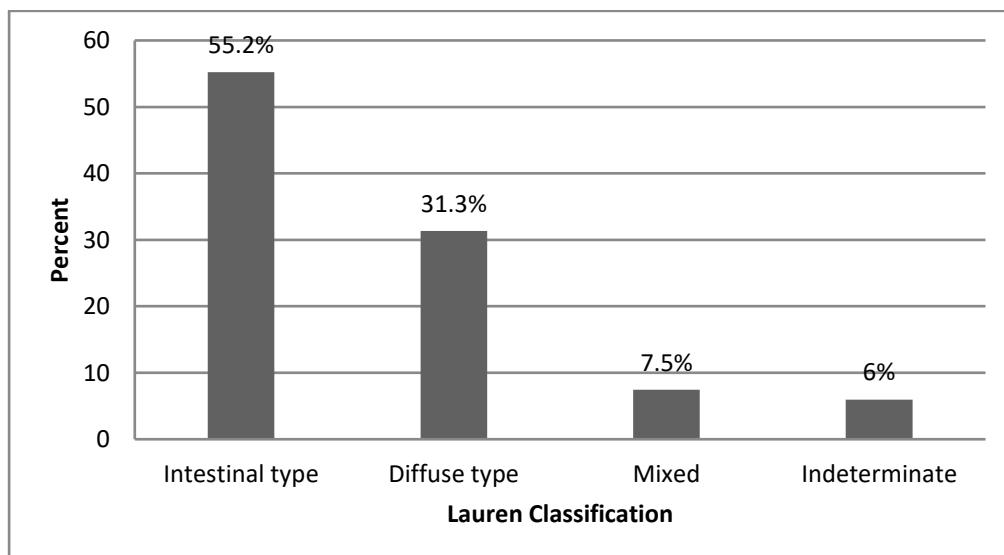

Fig 3: Lauren classification of carcinomas

TUMOUR GRADE OF CARCINOMA

According to the most recent WHO Classification system, only tubular and papillary adenocarcinomas are to be graded into a two-tier system: well differentiated (previously well differentiated and moderately differentiated cancers) and poorly differentiated cancers. 25 of the 33 cases (76%) were well differentiated while 8 of the 32 cases (25%) are poorly differentiated. (Fig 4).

Cross-tabulations of tumour grade against patients' age and gender respectively showed no statistically significant associations between the variables.
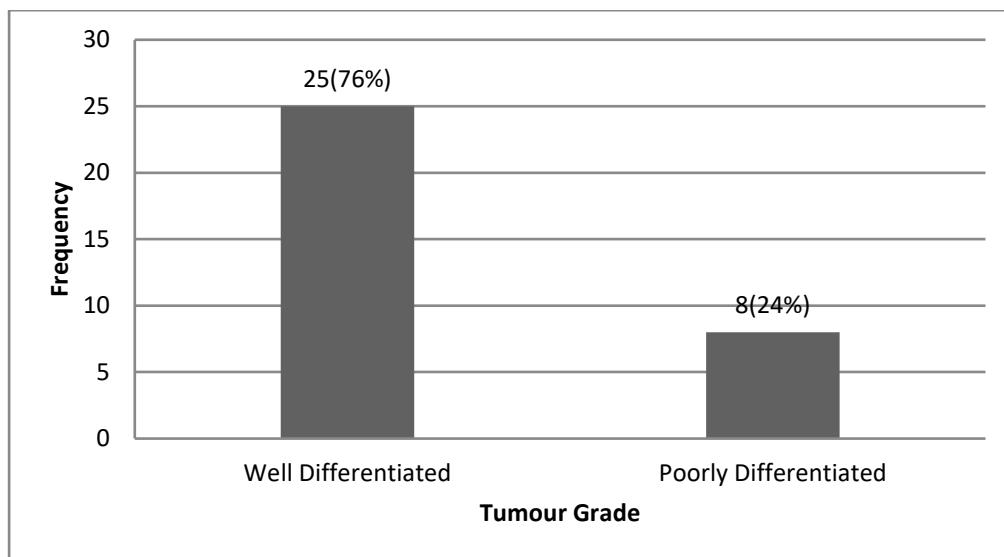
Fig 4: Bar Chart showing tumour grade of carcinomas

TUMOUR STAGE OF CARCINOMA

17 of 67 cases of gastric and GEJ carcinomas were gastrectomies. Their tumour stages were assessed. 11 cases (64.7%) were stage T4. Stages T3 and T2 accounted for 4 cases (23.5%) and 2 cases (11.8%) respectively. There was no stage I tumour. (Fig 5)

Cross-tabulations of tumour stage against patients' gender, age and their tumour histological types showed no statistically significant associations between the variables.
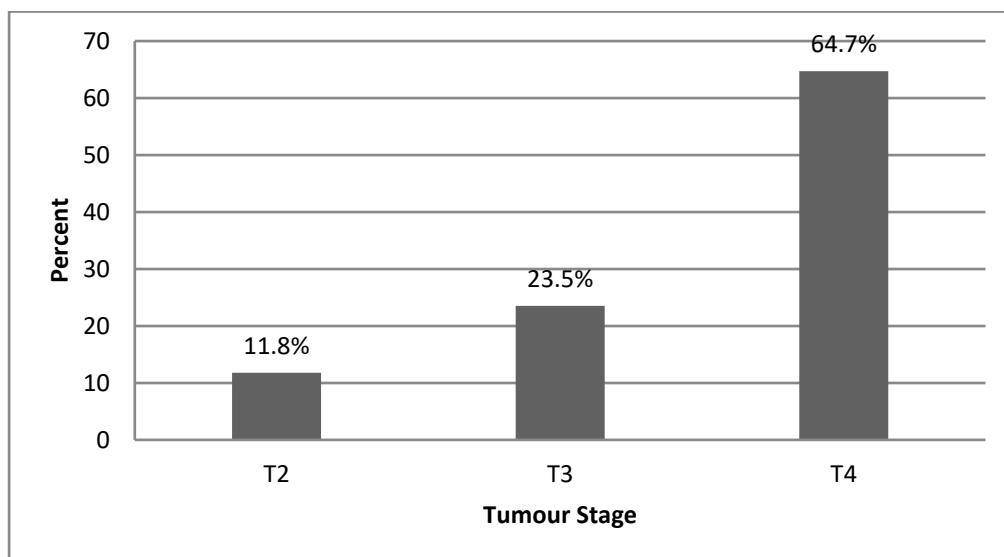

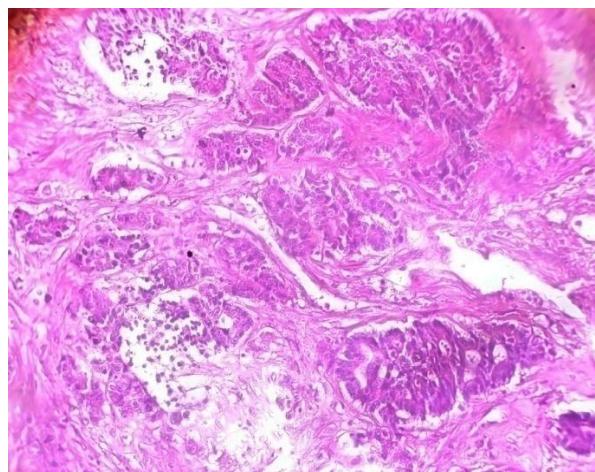**Fig 5:** Bar chart showing tumour stage of gastrectomies

Fig 6: Tubular adenocarcinoma showing fused tubules forming cribriform structures (H&E x200)
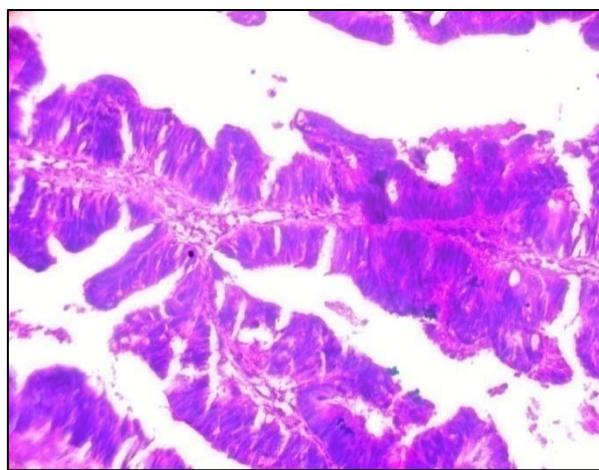

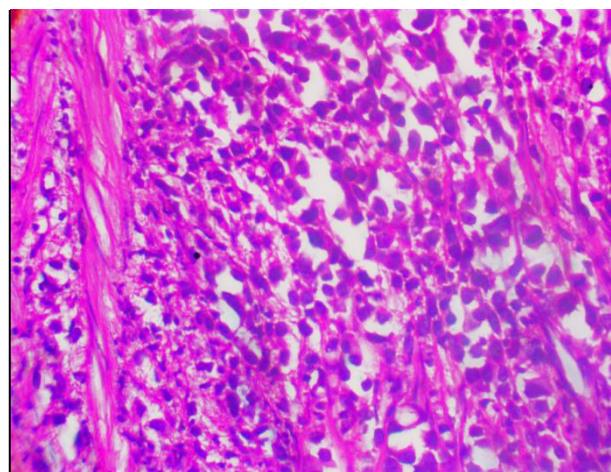**Fig 7:** Papillary adenocarcinoma exhibiting branching papillae (H&E x400)

Fig 8: Poorly cohesive carcinoma showing isolated and small clusters of neoplastic cells without well-formed glands (H&E x 400)
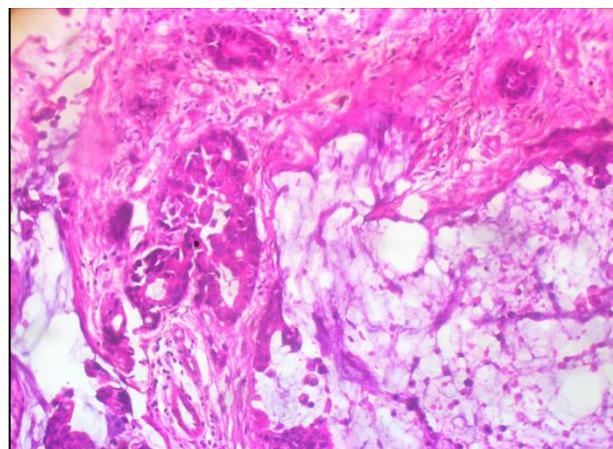
Fig 9: Mucinous carcinoma showing malignant glands surrounded by pools of mucin (H&E x 400).
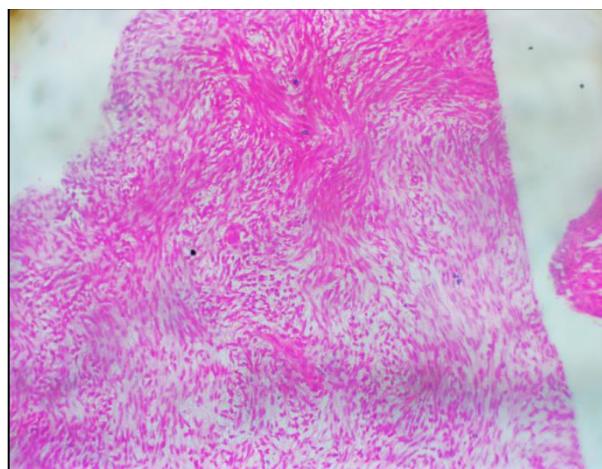

Fig 10: Gastrointessinal stromal tumour with spindle cells disposed loosely in interlacing fascicles (H&E x200)

DISCUSSION

There was a predominance of carcinomas amongst all gastric and GEJ cancers in this study (74.2%). This preponderance of epithelial tumours is in agreement with other previous studies in Nigeria. Abdulkareem et al reported 95.3% carcinomas in Lagos[6], while Bakari et al in Bornu and Mandong et al in Plateau, both in northern Nigeria, reported 90.3% and 96% respectively.[5,9]

The 20 cases of mesenchymal tumours in this study constitute 21.5% of all cancers and most of these tumours are gastrointestinal stromal tumours. Studies from other parts of the country recorded lower incidence of gastric mesenchymal cancers, Abdulkareem et al found 7.6% gastric cancers to be of mesenchymal origin[6] while 9.1% of gastric cancers were mesenchymal tumours in a Jos study by Kwaghe et al.[11] Since there have not been any previous studies examining prevalence of various cancers of the stomach in the southeast region, further studies will be necessary to investigate the mesenchymal

tumour preponderance from this study including immunohistochemical characterization of those mesenchymal tumours.

Gastric lymphomas are much less common cancers than epithelial and mesenchymal tumours. This study found only 4 cases (4.3%) of gastric lymphoma. Three of these lymphomas are extranodal marginal zone of mucosal associated lymphoid tissue (MALT lymphoma) and one case of diffuse large B cell lymphoma. This is consistent with the global incidence of approximately 5% of gastric malignancies.[15] Studies from other parts of Nigeria reported similar results; Mandong et al found 2.4% of gastric cancers to be lymphomas, while Abdulkareem et al from the western part of Nigeria found an even more modest 1.9%.[9,6]

Tubular adenocarcinomas were the most common carcinoma histiotype in this study, accounting for about half of all carcinomas (46.2%). This result is similar to other previous studies in Nigeria; Kwaghe et al in

Northcentral Nigeria, found 52.2% of carcinomas in their study to be tubular adenocarcinoma while Komolafe et al reported 49% in Southwestern Nigeria.[11,14] Studies from other countries in Africa also show tubular-type adenocarcinoma preponderance.[12] These reports from other parts of the world support the evidence that tubular adenocarcinomas are the most common histological subtype of gastric carcinoma according to the WHO classification scheme.[16]

The Lauren Classification Scheme of gastric carcinomas still gathers a wide appeal amongst pathologists evidently because of its brevity. This study found most of carcinomas to be of the intestinal type, 55.2%. This is in agreement with studies carried out in other parts of the country. Kwaghe et al and Mandong et al, both in northern Nigeria, reported 79% and 51.2% of carcinomas as intestinal-type respectively.[11,9] The intestinal-type carcinomas are also the most common histological type of gastric carcinoma globally.[16]

Many studies have shown that the pyloric antrum is the commonest site for gastric cancer to occur. As many as 90% of pyloric antrum gastric cancers are attributable to *H.pylori* infection.[56] Previous studies from northern and south-western parts of Nigeria reported a wide range of percentage of gastric cancers located in the pylorus antrum (44% to 95%).[3,14] This study found 52.2% gastric cancers to be located at the pylorus antrum. As with Nigeria, in the East/Central Asia and Eastern Europe, non-cardia gastric cancer is the predominant anatomic subtype. Conversely, in the North America and Western Europe, cardia cancer is the predominant subtype due to the decline of non-cardia cancers. Success in eradicating *H.pylori* explains this decrease in non-cardia gastric cancer in the developed world. The United States and United Kingdom have the highest proportion of cardia relative to non-cardia gastric cancers possibly as a result of almost complete absence of the *H.pylori* bacterium.[17,18] These findings buttress the importance of scrutiny of the pyloric antrum in this environment during endoscopy of stomach as most gastric cancers are located there.

The average age of gastric cancer diagnosis seen in this study is 56.7years. This is comparable to the mean age of 54.6years reported by Kwaghe et al in Northern Nigeria and 55.3years reported by Abdulkareem et al in Southwestern Nigeria.[11,6] Outside the country, Mabula et al reported an average age of 52.0 years in Tanzania. These median ages of gastric cancer diagnosis in Africa is evidently lower than the average age of diagnosis in

most western countries. In the United States for example, the median age of diagnosis is 69.0years. Six of every ten diagnosis of gastric cancer are made in patients ≥65.0years in that country.[17]

This lower average age of diagnosis in African countries compared to western countries can be attributed to differences in epidemiology and healthcare access. *Helicobacter pylori* infection, which is a major risk factor in Africa, is associated with early age exposure leading to earlier onset of gastric pathology and potentially earlier development of gastric cancer. Also, more advanced screening programs and healthcare systems in western countries lead to earlier detection of precancerous conditions potentially altering the age distribution of diagnosed cases. In Africa, cancers might only be detected once symptoms become severe, potentially skewing age data.[10]

The peak age range of diagnosis from this study is the seventh decade of life. Similarly, various other studies from Nigeria reported the seventh decade of life to be the peak age range of diagnosis, while a few others found the sixth decade to be the most significant decade.[11,13,14]

Gastric cancer is rare in patients less than 30years, and this age group accounted for only 2.2% gastric cancers from this study. Similar low incidence of 1.3%- 4.7% was reported by other studies in Nigeria for the same age group.[11-14]

The male to female ratio from this study show a slight female preponderance of 0.94:1. This ratio contrasts reports from other parts of Nigeria with varying degrees of male predominance ranging from 1.2:1 to 2.4:1.[3,9,14] Across various continents the incidence rates are 2 to 3 times higher for males than females.[18] Further epidemiological studies might be necessary in other ethnically related southeastern states of Nigeria to scrutinize and possibly confirm the lack of clear sex predilection for this region as evident from this study.

Most patients in this study presented with advanced gastric cancer. Late presentation is the norm in countries with no instituted routine screening for gastric cancer. Using the TNM staging system, about 90% of the gastrectomy specimens studied and staged in this population were stages T4 and T3. These tumours have at least penetrated the subserosal connective tissue.

Uncannily no case is staged T1. These findings are similar to other reports from Nigeria. Kwaghe et al and Bakari et al, both in Northern Nigeria, reported that more

than 80% of gastric cancers diagnosed in that region are late stages T3 & T4.[11,5] Diagnostic challenges including lack of effective screening program in the country is to be blamed for no data of early detection of gastric cancers in this study. Gastric cancers are notorious for presentation with nonspecific symptoms that can be easily overlooked or attributed to less serious conditions. By the time more severe symptoms appear, the cancer may already be at an advanced stage.

Some of the eastern Asian countries where the disease burden for gastric cancer is high have instituted national screening protocols for early detection of these tumours. In contrast to Nigeria, 73% of gastric cancers diagnosed in South Korea were confined to the mucosa and submucosa (stage T1). A national gastric cancer screening protocol involving endoscopy with histologic diagnosis has been ongoing in South Korea since 2002.[19]

Most recently, the WHO Classification of tumours recommends a two-tier grading system for gastric carcinoma, reserving this classification for only the tubular and papillary adenocarcinomas. In this study, three quarters of the tumours graded were well differentiated and the rest were poorly differentiated. Komolafe et al also reported that most gastric carcinomas they studied in southwestern Nigeria were well differentiated.[14]

CONCLUSION

This report has spotlighted the similarities and dissimilarities between gastric and GEJ cancers in Southeast Nigerian patients and those in other parts of the world. Due to late diagnosis these cancers remain a significant burden on cancer mortality in this region and early detection will prove useful in curbing the scourge.

AUTHOR CONTRIBUTION

All authors contributed meaningfully to the development of this study. K.G.I. led the conception and design of the work, while data collection across the four participating histopathology laboratories was coordinated jointly by K.G.I. and the collaborating authors. Tissue retrieval, slide review, and histopathological classification were undertaken collectively, with K.G.I. providing oversight and all authors participating in diagnostic verification and consensus review of challenging cases. Data extraction, organisation, and statistical analysis were performed by the full author team. K.O.O., C.O., and C.E.E. prepared the initial manuscript draft, and all co-authors contributed to critical revision of the text,

interpretation of findings, and refinement of the final manuscript. All authors approved the final version and accept responsibility for the accuracy and integrity of the work.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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