

## Histopathological Analysis of Gastric Cancers in University of Ilorin Teaching Hospital: A 20-Year Review

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### ABSTRACT

Gastric cancer is a relatively common malignancy in Nigeria. Gastric cancer varies from region, being 4th to 20th in proportion to other malignancies. The symptom and signs are often non-specific with the early stages of the disease. This may be responsible for late presentation and poor prognosis. This is a 20-year retrospective analysis of 107 histopathologically confirmed gastric cancers in the department of pathology. This study aimed to analyze the Histopathological patterns of all the gastric cancer cases diagnosed in U.I.T.H Ilorin, over a twenty-year period. Gastric cancers were classified according to WHO 2010 and Lauren classification of gastric cancers. A total of 107 cases of gastric cancers diagnosed, that met the inclusion criteria, were analyzed with male: female ratio of 1.3:1 out of which epithelial malignancy accounted for 93.5% with tubular adenocarcinoma representing the commonest epithelial subtype. Epithelial malignancy is the commonest histological type in this area. Therefore, it is recommended that patients above 40 years with dyspepsia and other alarm features should undergo routine endoscopic screening.

**Keywords:** Gastric cancer, Epithelial malignancy, Histopathological, Poor prognosis.

### INTRODUCTION

Gastric cancer is malignant neoplasm that arises in the stomach. It still remains a major health burden globally despite its declining incidence.<sup>1</sup> It is the fourth commonest cancer in the world with 985,600 new cases diagnosed annually and about 738,000 patients died yearly from the disease making it the second commonest

cause of cancer related death.<sup>2</sup> Gastric cancers is a heterogeneous disease with various histopathological and epidemiological characteristics. Epithelial malignancy is the commonest histological type in about 95% of cases and there is interplay between the genetics and environmental factors in the pathogenesis of the

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gastric cancer.<sup>3</sup> Most patients present late because of the non-specific nature of its symptoms and signs and the prognosis is fatal in most cases.<sup>4</sup> Metastatic tumour to the stomach is rare although lung and breast are the commonest primary sites and lymphatic spread is more favoured over haematogenous route.<sup>5</sup>

Gastric cancer is the fourth commonest cancer in the western world after cancers of the lungs, breast and colorectal.<sup>6</sup> Worldwide, it is the second most common cancer of the gastro-intestinal tract, following adenocarcinoma of the colon.<sup>7</sup> It is relatively low in the developing world, Nigeria inclusive.<sup>6</sup> In Nigeria, there is a regional variation in prevalence of gastric cancers.<sup>8</sup> In Ibadan, it is ranked fourteenth commonest cancers whereas in Ilorin, it occupied eleventh position of all cancers cases diagnosed.<sup>9,10</sup> However in Zaria, using data from the cancer registry, gastric cancer is the twentieth commonest cancers,<sup>11</sup> while in Calabar it is the fourth commonest cancer.<sup>12</sup>

Gastric cancer usually occurs in adults but most commonly diagnosed at age 50 years and above.<sup>13</sup> Though gastric Cancer is rare in children and adolescent, it has been reported in Ile-Ife in a 7-year-old child.<sup>14</sup> The malignancy occurs in both sexes though males are more affected than females.<sup>7,13</sup> Male to Female ratio is usually in the range of 1.2:1 to 2:1.<sup>8,15,16</sup>

Carcinoma is the commonest histological type of gastric cancer accounting for over 90% of gastric cancer cases,<sup>7,16</sup> while mesenchymal tumour, non-Hodgkin's lymphoma and carcinoid tumour represent 7.6%, 1% and 1% respectively in some study.<sup>16</sup>

Most patients with gastric cancers present late because the symptoms of early gastric cancer is non-specific and lack of routine endoscopic screening and biopsy also contribute to the late presentation.<sup>8,17</sup> Furthermore, endoscopic diagnosis of early cancers are more difficult because it usually shows subtle features of gastritis.<sup>18</sup> The endoscopic findings of advanced gastric cancer includes, a well demarcated lesion, irregularity in colour and surface patterns and microvascular pattern with demarcation lines.<sup>18</sup>

The prognosis of gastric cancer remains poor worldwide with overall five-year survival rate of all patients diagnosed with gastric cancer between 4% and 13%.<sup>7,8,19,20</sup> However, the prognosis of early gastric cancer is fair with five-year survival of about 80% or more.<sup>21</sup>

## MATERIALS METHODS

The study was a retrospective descriptive type conducted in the pathology department of University of Ilorin teaching hospital assessing data from 1991 to 2010.

Records of all cases of gastric cancers within the study period were retrieved from the surgical pathology bench register. The demographic characteristics such as age and sex of all patients were extracted from the histopathology register and request forms. The Haemotoxylin and Eosin (H&E) stained slides of the corresponding cases were retrieved and reviewed. Fresh sections were cut for faded, broken and lost slides from the retrieved paraffin-embedded tissue blocks and were stained with H and E stains. Histochemical stains like modified Giemsa stain for *H.pylori*, periodic acid Schiff diastase for mucin, reticulin stain for lymphomas, Phosphotungstic Acid-Haemotoxylin (PTAH) for skeletal muscle, and Mason trichrome, to differentiate fibrocollagenous tumour (e.g. fibrosarcoma) from muscle fibres, were used accordingly. Immunohistochemistry on malignant lymphoma and *H.pylori* could not be conducted because the facilities are just being developed in our centre.

### Sample size

The study was a retrospective work over a 20-year period. There were 115 cases of gastric cancer diagnosed within the study period of which 107 met the inclusion criteria and were reviewed for the study.

### Inclusion criteria

All registered cases of gastric cancers, with the

necessary data for this study, diagnosed histologically in the Department during the study period were included in the study.

### Exclusion criteria

Cases where either the slides, paraffin-embedded tissue blocks nor the pathology request forms could not be found were all excluded from this study.

### Data analysis

Data obtained were analysed using the computer software statistical package for social sciences (SPSS) version 20. Gastric cancers were classified according to WHO 2010 classification and Lauren's classification of gastric cancers. Data obtained in this study were presented in prose, tables, charts and photomicrographs of representative neoplasms are presented in some cases.

### Ethical consideration

The approval of the hospital ethical committee was obtained before the commencement of this study.

## RESULTS

Out of the total 516 gastric samples received over the period of study, 115 (22.3%) were histologically diagnosed as gastric cancers. During the same period of study, 3,806 cancer cases were histologically diagnosed at our centre out of which gastric cancers accounted for 3% with 115 cancer cases (Figure 1).

Out of the 107 cases of gastric cancers analysed, there were 61 (57%) males and 46 (43%) females giving a Male to Female ratio 1.3:1. The age of the patients with gastric cancers ranged from 20 years to 85 years, and modal age range of 51-60 years with a total of 24 (22.4%) cases (table 1).

Out of the total 107 cases of gastric cancers under review, epithelial malignancies topped the list and accounted for 100 (93.5%) cases, malignant lymphoma represented 4 (3.7%) cases while mesenchymal malignancy accounted for 3 (2.8%) cases. There was no case of metastatic cancer

seen in this study (table 2).

Mesenchymal malignancies accounted for 3 (2.8%) cases of total gastric cancers and all were Leiomyosarcoma.

Using Lauren's criteria, there were 63 cases of intestinal type of gastric carcinoma with 36% cases and 27% cases diagnosed in males and females respectively. The diffuse type was reported in 30 patients with 17% cases in males and 3% cases in females while indeterminate variants accounted for 7 cases with 4% and 3% in males and females respectively (table 3).

Using the number grading system there were 52 gastric cancers cases that could be graded. There were 11 cases of grade 1 (well differentiated adenocarcinoma) accounting for 21.2% of the cases. Grade 2 (moderately differentiated adenocarcinoma) was the commonest with 28 (53.8%) cases while Grade 3 (poorly differentiated adenocarcinoma) represent 13 (25%) cases. Hence both moderate and poorly differentiated adenocarcinoma (Grade 2 and 3) constituted about 80% of all the cases.

**Table 1: socio-demographic characteristics of Patients with Gastric Cancer at U.I.T.H Ilorin**

Age	Frequency		Total	Percentage (%)
	Male	Female		
<10	-	-	-	-
11- 20	1	-	1	0.9
21- 30	1	3	4	3.7
31- 40	11	9	20	18.9
41- 50	12	10	22	20.6
51- 60	16	8	24	22.4
61- 70	14	9	23	21.5
71- 80	6	5	11	10.3
>81	-	2	2	1.9
Total	61	46	107	100

**Table 3: Showing Lauren's classification of Gastric cancer**

Histologic type	Male	Female	Total	Percentage
Intestinal type	36(36%)	27(27%)	63	63%
Diffuse type	17(17%)	13(13%)	30	30%
Indeterminate type	4(4%)	3(3%)	7	7%

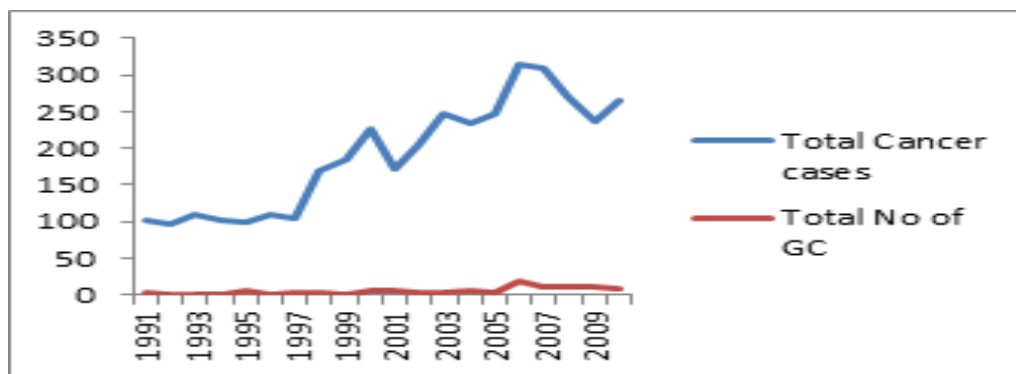
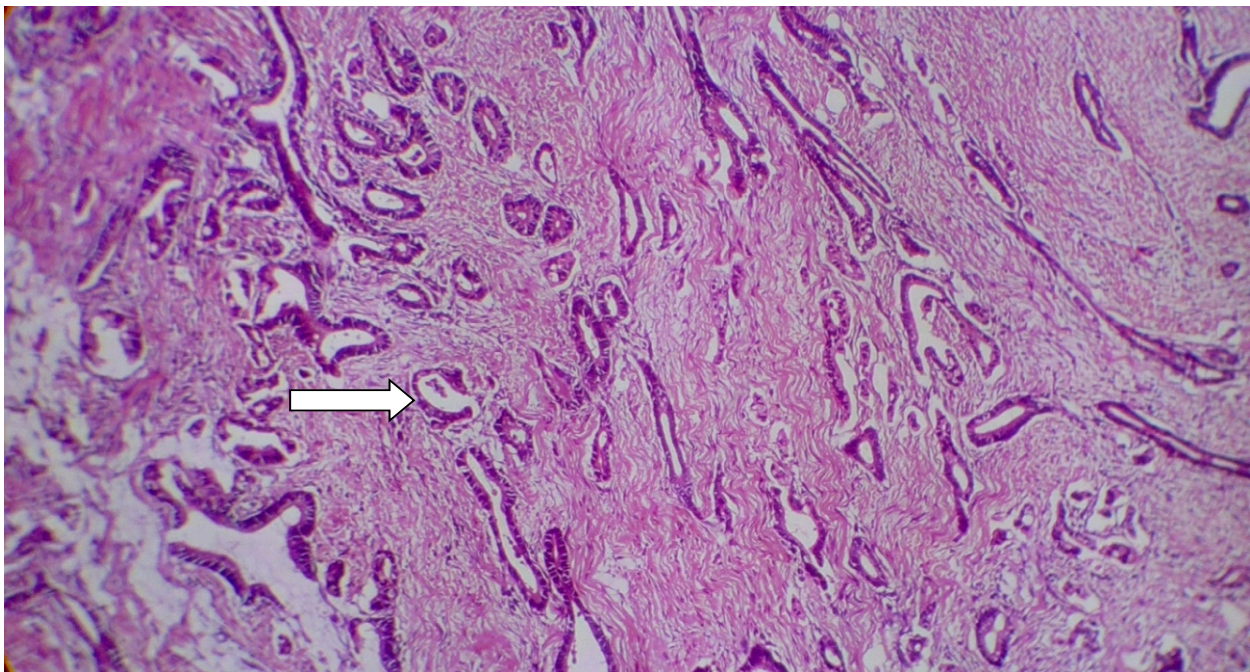
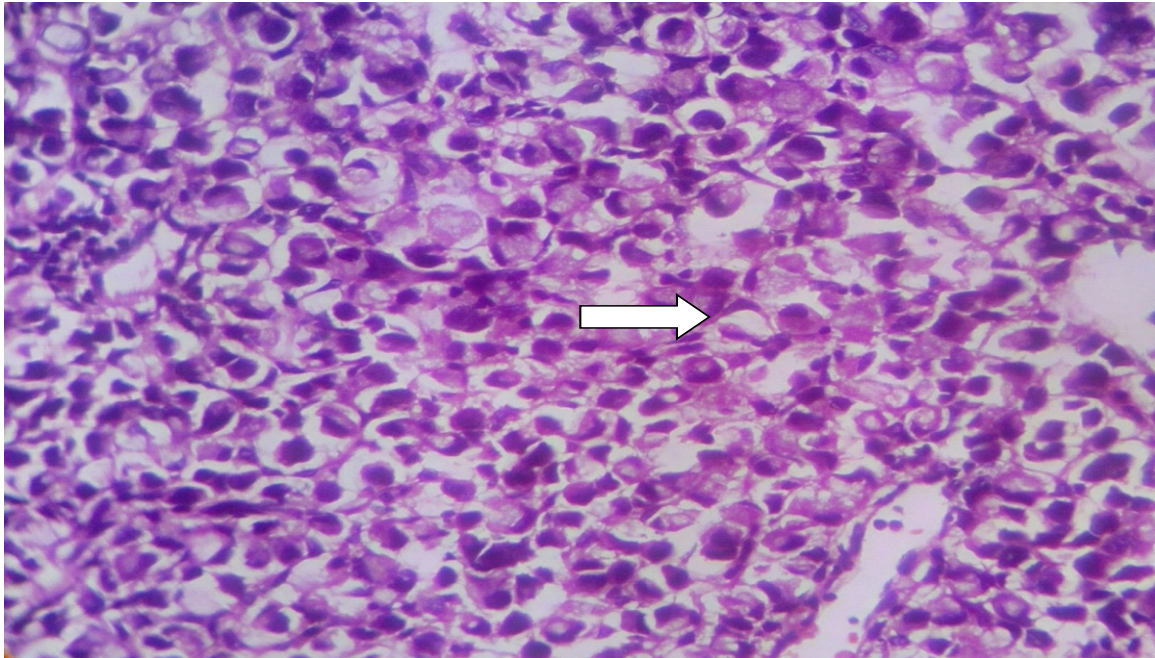
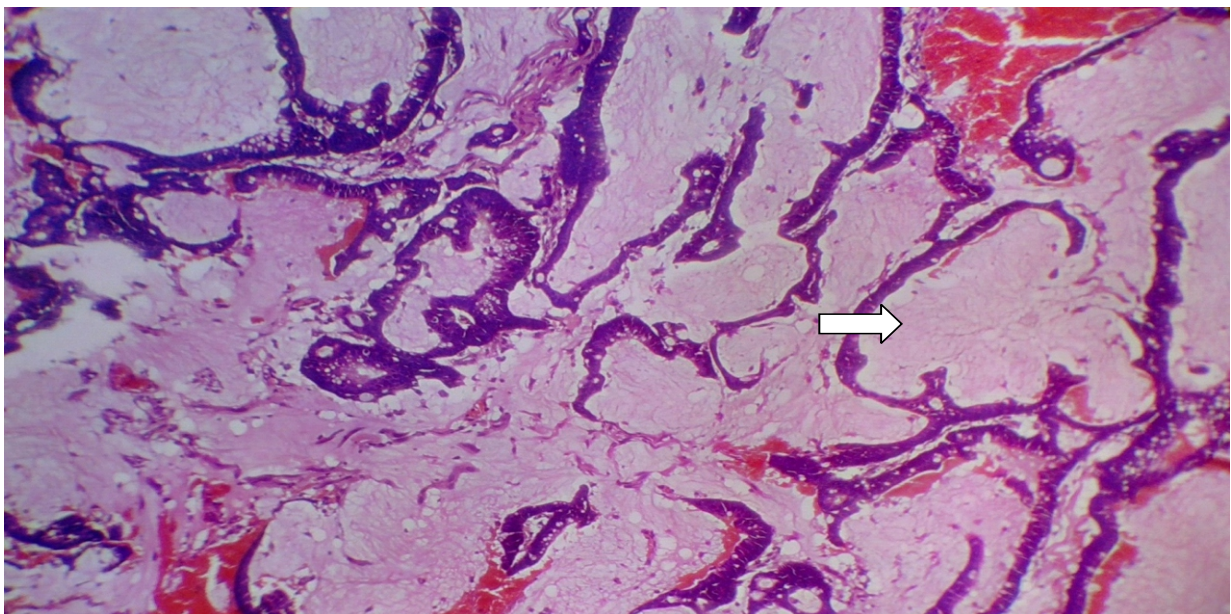
**Figure 1: Line graph showing the yearly occurrence of gastric cancer at U.I.T.H Ilorin.****Figure 2. Gastric biopsy showing Tubular Adenocarcinoma with neoplastic cells arranged in tubular patterns (arrow). H&E X 150.**

Table 2: Showing Histological types and Gender distribution of Gastric Cancers at U.I.T.H Ilorin

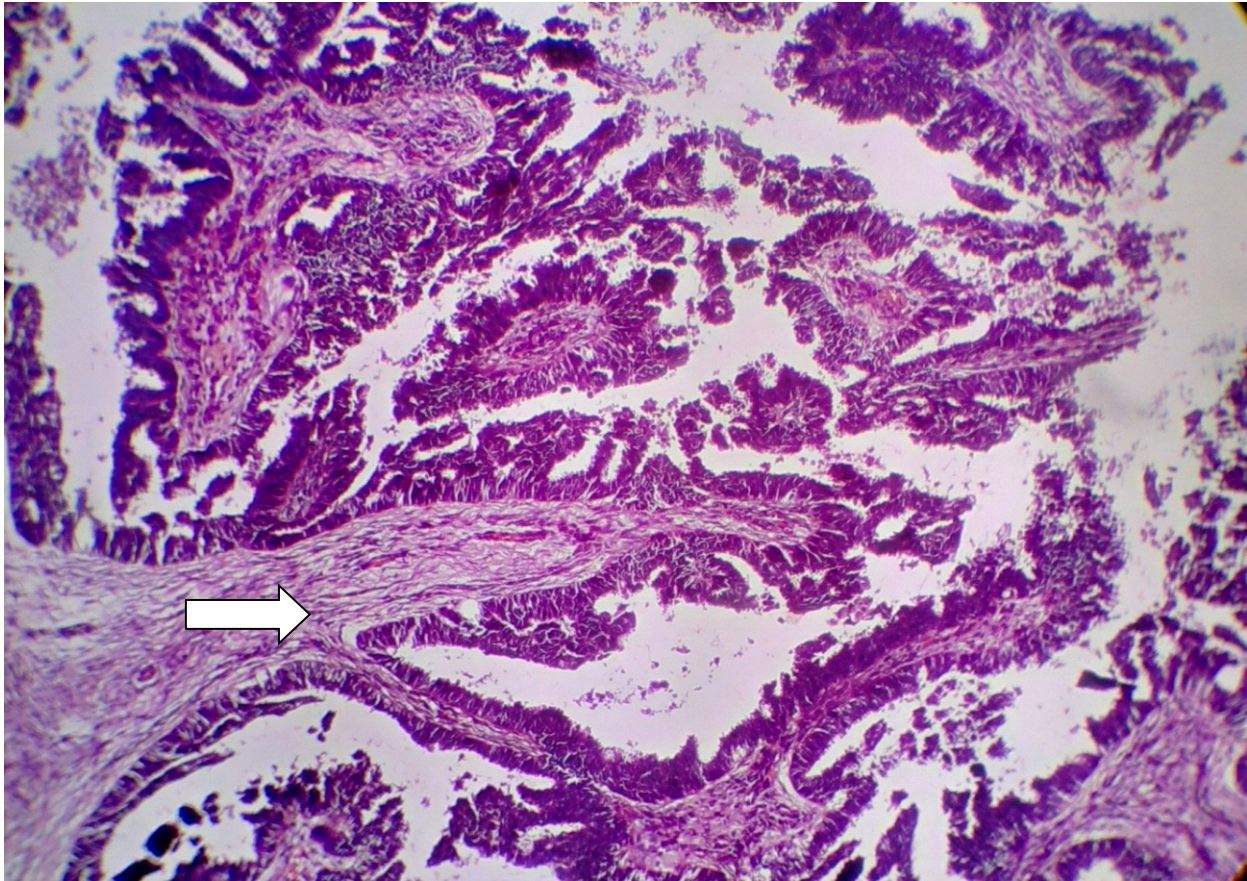
Histological type	Frequency		Total	Percentage (%)
	Male (%)	Female (%)		
<b>Epithelial type</b>				
Tubular adenocarcinoma	30 (28)	20 (18.7)	50	46.7
Signet ring Adenocarcinoma	17 (15.9)	13(12.2)	30	28.1
Mucinous Adenocarcinoma	6 (5.6)	5(4.7)	11	10.3
Carcinosarcoma	1 (0.9)	2(1.9)	3	2.8
Undifferentiated carcinoma	2 (1.9)	1(0.9)	3	2.8
Papillary Adenocarcinoma	---	2 (1.9)	2	---
carcinoid	1 (0.9)	---	1.9	0.9
Others e.g Hepatoid	57 (53.2)	43(40.3)	100	93.5
<b>Lymphoma</b>				
Lymphoma (NHL)	1 (0.9)	1 (0.9)	2	1.8
Lymphoblastic lymphoma	1 (0.9)	-	1	0.9
Small cell lymphoma	--	1 (0.9)	1	0.9
Diffuse large cell lymphoma	---	---	---	---
Others e.g Burkitt	2 (1.8)	2 (1.8)	4	3.6
<b>Subtotal Mesenchymal</b>	2 (1.8)	1 (0.9)	3	2.8
Leiomyosarcoma	--	----	---	---
Other fibrosarcoma	2 (1.9)	1 (0.9)	3	2.8
Subtotal metastasis	-----	-----	----	----
<b>Total</b>	<b>61</b>	<b>46</b>	<b>107</b>	<b>100</b>



**Figure 3. Gastric biopsy showing Signet Ring Adenocarcinoma with sheets of signet ring cells (arrow). H&E X150**



**Figure 4 Mucinous Adenocarcinoma of stomach showing neoplastic cells floating in the lakes of extracellular mucin (arrow) H&E X200**



**Figure 5. Papillary adenocarcinoma of the stomach showing papillary fronds with fibrovascular core (arrow). Gastric biopsy H&E X 200**

## DISCUSSION

In this study, average of 5 cases of gastric cancer were recorded per annum. This is comparable to an average of 4 and 8 cases per annum reported in Maiduguri and Lagos.<sup>8,16</sup> Reports from other African countries and developed countries shows higher annual cases of 20-31 and 67-120 per annum respectively.<sup>22-26</sup> The reason for this disparity may be partly attributable to geographical variation and availability of facilities for the screening and diagnosing of gastric cancer. Gastric cancers accounted for 3% of all 3,806 cancers

diagnosed within the 20 year period of study corroborating the 2.2% obtained in an earlier study in our Centre,<sup>10</sup> and 2% obtained in Maiduguri.<sup>8</sup> This study is also in concordance with 3.6% reported in Jos,<sup>27</sup> In contrast, gastric cancer represented 1.1% in Zaria and 4.1% each in Ibadan and Ife-Ijesha respectively.<sup>11,15,28</sup> The highest frequency of gastric cancer was 8.4% recorded in Calabar.<sup>12</sup> There is a slight male preponderance in this study with M:F ratio of 1.3:1. This is comparable to 1.4:1 each in

Zaria, and Ibadan and 1.2:1 each in Maiduguri, and Ile-Ife respectively.<sup>8,19,14,29</sup> In contrast, there is a slightly high ratio of 2:1 in Lagos, and 2.4: 1 in Jos.<sup>16,27</sup>

The youngest age at diagnosing gastric cancer in this study is 20 years, this is in tandem with 22 years recorded in Maiduguri.<sup>8</sup> Gastric cancers are very rare in young age and the occurrence of cancer at this age is most likely as a result of genetic predisposition of the affected individuals.<sup>30</sup> The rarity of gastric cancer before age 20 is also supported by findings obtained in studies conducted in Middle East and United States with 0.1% of cases occurring before the age of 20 years.<sup>31,32</sup>

The oldest age of gastric cancer in this study was 85 years, this is in agreement with 80 years obtained in a study in Ile-Ife.<sup>14</sup> Gastric cancer is very rare in the elderly people and this assertion was supported by the fact that 2 cases were reported in the age 80 years and above in this study, the finding which is similar to the finding in Ile-Ife in which only 2 cases were reported above 80 years.<sup>14</sup> The modal age of the disease in this study is 6<sup>th</sup> decade in which 22.4% cases of gastric cancers were diagnosed. This is similar to findings by Komolafe et al,<sup>14</sup> and Bakari et al,<sup>8</sup> where modal age of diagnosing gastric cancer was 6<sup>th</sup> decades. In United State the peak age was found to be 7<sup>th</sup> decade and 6<sup>th</sup> decades in both Japan and China which accounted for more than half of the global burden of the disease.<sup>33-35</sup>

The finding in this study that epithelial malignancy, carcinoma is the commonest histologic gastric cancer concurs with findings in other previous studies from Nigeria.<sup>8,14,16</sup> In this study epithelial malignancy accounted for 93.5% of all the total gastric malignancy. Komolafe et al,<sup>14</sup> reported that 93.5% were carcinoma while Abdulkareem et al, Bakari et al, and Irabor et al, reported carcinomas in 90%, 90.3% and 91.9% of all gastric cancers from Lagos, Maiduguri and Ibadan respectively.<sup>8,16,29</sup> Similarly carcinomas represented 78%, 90% and 95.3% of all gastric cancer cases reported from Tanzania, Morocco and Senegal respectively.<sup>36-38</sup> Also studies from Asia, Europe and America reported that adenocarcinomas are seen in more than 90% of gastric cancers studied.<sup>21,33,39,40</sup> It is therefore clear that gastric

carcinoma is the commonest histologic type of gastric malignancy worldwide.

There is paucity of information locally on the histopathological patterns of gastric cancers as majority of studies on gastric malignancies are mainly clinical based.

Out of the 100 cases of epithelial malignancy, 50% were tubular adenocarcinoma subtype and accounted for the commonest epithelial subtype in this series (figure 2). This is similar to the findings in Ile-Ife where tubular adenocarcinoma was the commonest histological subtype and second most common histological subtypes in a study done in Tanzania.<sup>14,36</sup> Our finding corroborate the report from Iraq and New York in which tubular adenocarcinoma was reported in 54.9% and 42% respectively.<sup>41,42</sup>

Signet ring carcinoma accounted for 28.1% of epithelial subtypes in this study (figure 3). Our figure is higher compared to reports from other studies. In Ile-Ife signet ring carcinoma was reported in 8.8%, in Tanzania it was 9% and 18% in Japan.<sup>14,36,40</sup> However in a study by Alaa et al in Iraq,<sup>41</sup> signet ring carcinoma accounted for 25.8% , a figure comparable to the finding in this study while a higher value of 37% was recorded in New York.<sup>42</sup> Mucinous adenocarcinoma represents 10.3% of all gastric malignancies reported (figure 4) and is lower than 21.3% obtained in Ile-Ife.<sup>14</sup> The finding in this study is about four times lower than 46.2% obtained in Tanzania and almost four to five times higher than 2% and 3% obtained in Iraq and Japan.<sup>36,40,41</sup> The variation in the values may be as a result of different geographical location of studies. Carcinosarcoma accounted for 2.8% of all epithelial subtype. This value is greater than 0.4% obtained by in Ibadan,<sup>29</sup> and 0.9% by Ikeda et al.<sup>55</sup> Undifferentiated carcinoma subtype represents 2.8% of cases in this study which is lower than 15.4% obtained in Tanzania.<sup>36</sup> Papillary adenocarcinoma accounted for 1.9% of cases (figure 5). The value obtained is lower than findings in Ile-Ife, Tanzania and Japan where 13.7%, 13.6% and 6% cases of papillary adenocarcinoma were reported respectively.<sup>14,36,40</sup>



Uefuchi et al and Hirota et al, reported 6% and 11% respectively which are also higher than 1.9% reported in this study.<sup>44,45</sup> Carcinoid tumour subtype represents 0.9% of the total epithelial malignancies. The finding in this study is in agreement with findings in Lagos,<sup>16</sup> and Tanzani,<sup>36</sup> and about three times lower than 2.5% obtained in Ibadan.<sup>29</sup> The malignant lymphomas in this study accounted for 3.7% of all gastric malignancies and all the cases are of Non-Hodgkin lymphoma. In the literature the highest frequency was reported from Ibadan with 6.1% while in Lagos Non-Hodgkin Lymphoma accounted for 1% of all gastric cancers which is almost four times lower than the value obtained in this study.<sup>16,46</sup> Histologically, the Non-Hodgkin Lymphoma in this study is comprising of lymphoblastic lymphoma 1.8%, small cell lymphoma 0.9% and diffuse large cell lymphoma 0.9%. A higher value of 5.8% of diffuse large cell lymphoma was obtained in a study by Alaa *et al* in Iraq.<sup>41</sup>

Mesenchymal malignancy represents 2.8% of all the gastric malignancies studied. This value tallies with 3.7% obtained in a study conducted in Ibadan,<sup>29</sup> and 2.8% obtained in Ile-Ife.<sup>14</sup> In Lagos 7.6% of the cases studied were mesenchymal tumours while malignant stromal tumours accounted for 6.1% of all gastric malignancies cases seen in Ibadan.<sup>16,46</sup> In Mali and Morocco 0.9% and 3.2% of their cases were mesenchymal malignancy respectively.<sup>37,47</sup> All the mesenchymal malignancies seen in this study were leiomyosarcoma and represents 2.8% of all gastric malignancies. This value is in agreement with 3% obtained in Ibadan and higher than 1% obtained in India.<sup>29,48</sup>

There is no case of secondary malignancy to the stomach in all the cases seen in this study. This finding is also common in most of the studies done in other centres.<sup>14,16,29,36</sup> The implication of this is that stomach is not a common site for metastasis.

## CONCLUSION

This study has shown that gastric cancer is a relatively common malignancy in Nigeria; they are mostly of

moderately and poorly differentiated adenocarcinoma. The disease is characterized by non-specific gastrointestinal symptoms with late clinical presentation often in an advanced stage. Epithelial malignancy is the commonest histological type.

## Recommendations

In order to reduce the mortality and morbidity of gastric cancer, early detection of gastric cancer is therefore recommended. This is because gastric cancer is characterized by non-specific symptoms hence its late clinical presentation, it is therefore recommended that patients above 40 years with dyspepsia and other alarm features should undergo routine endoscopic screening.

**Conflict of interest:** There is no conflict of interest whatsoever in this work.

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