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Aim: To characterize the clinico-pathologic features of gastric endoscopic biopsies seen in Port Harcourt.

Methodology: This is a retrospective study of gastric endoscopic biopsies seen in a private pathology referral practice in Port Harcourt between 1st January 2014 and 31st December 2018. The relevant clinical and demographic information were obtained from patients' laboratory request forms. The gastric biopsies were fixed in 10% neutral buffered formalin, processed, and stained with hematoxylin and eosin for general morphology. Modified Giemsa stain was used for Helicobacter pylori identification. The slides were reported using the updated Sydney classification.

Keywords: *gastric biopsy, gastritis, helicobacter pylori, chronic atrophic gastritis (CAG), dyspepsia.*

GJMR-C Classification: *NLMC Code: QY 4*



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Clinicopathologic Profile of Gastric Endoscopic Biopsies in Port Harcourt, Nigeria

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Results: A total of 227 cases were seen. The youngest patient was a seven-year- old female and, the oldest a 99-year-old male, mean age was 48.46 ±16.10. The male to female ratio was 1.1:1. Age group 40-49 years accounted for most cases (25.6%). The main symptom at presentation was epigastric pain (40.5%), distantly followed by a feeling of indigestion (8.4%).The main histological diagnoses were chronic gastritis (62.6%) and chronic active gastritis (22.5%). Malignant lesions were seen in 13.5% of cases. H pylori were seen in 31% of cases. Chronic atrophic gastritis (CAG) was seen in 4.1%, intestinal metaplasia (IM); 4.6%, and dysplasia 7.1%.

Conclusion: Gastric carcinoma is not rare in our environment.

Keywords: gastric biopsy, gastritis, helicobacter pylori, chronic atrophic gastritis (CAG), dyspepsia.

I. Introduction

Common gastric lesions are gastritis and its complications (gastric ulcers, mucosal atrophy (MA), intestinal metaplasia (IM) and dysplasia), and gastric polyps and tumors[1]. Gastritis (which could be active or chronic) is a mucosal inflammatory process, which could be asymptomatic or symptomatic. Common symptoms of gastritis include: / variable degrees of epigastric pain, nausea, vomiting, hematemesis, melena stool, and rarely massive blood loss.[1]Based on pathogenesis; there are two broad types of gastritis - gastritis associated with Helicobacter pylori (H pylori) infection and gastritis without H pylori infection. In the latter group are autoimmune gastritis, granulomatous gastritis, chemically induced reactive gastritis, ex-H pylori gastritis, Crohns gastritis, eosinophilic gastritis, lymphocytic gastritis, collagenous gastritis and Helicobacter heilmanniigastritis.[2] Most of the non-H pylori-associated gastritis are of unknown etiology or due to infection with opportunistic organisms, the use of non steroidal anti-inflammatory drugs (NSAIDs) or auto immunereactions.[2,3]H pylori have been identified globally as the main cause of chronic gastritis (CG).[2-5] H pylori infection is usually acquired during childhood and is mostly associated with poor socio-economic living conditions.[4-6]The global prevalence of H. pylori infection in humans is estimated to be 50%, with a prevalence of about 70-90% in developing countries and 20-30% in developed countries. Developing countries especially in Sub Saharan Africa, and some parts of Asia have the highest prevalence, and it is said to be endemic in such countries.[5,7-9] The sequelae of H pylori CG may include: (MA, IM, dysplasia and adenocarcinoma) is well documented, but fortunately, in SSA the incidence rate of gastric adenocarcinoma is reportedly low, despite the high prevalence rate which has led to the use of the terminology "African Enigma".[7] Due to the wide prevalence in SSA, at times H pylori is seen in persons with normal gastric endoscopic pictures.[10]Diagnostic endoscopy, though an invasive procedure has been proven to be a simple, safe, and well-tolerated procedure.[11] Histologic evaluation of the biopsies obtained at gastric endoscopies is the gold standard for the investigation of patients with complaints of dyspepsia. The histopathology results obtained give the definitive diagnosis that determines the treatment options and prognosis.[12]This study shows the histologic pattern of gastric endoscopic biopsies seen in a private referral pathology diagnostic center in Port Harcourt.

II. Materials and Methods

This is a retrospective case-controlled study of gastric endoscopic biopsies evaluated by the authors in a Port Harcourt based referral pathology diagnostic center – Cedar Pathology and Forensic Services Ltd.

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Port Harcourt is the capital of Rivers state of Nigeria and the epicenter of the oil-rich Niger Delta region, noted for the widely acclaimed environmental oil pollution that resulted from the poorly regulated activities of oil and gas companies operating in the area. Gastric endoscopy biopsy specimens are received from different private and general gastroenterology practitioners in Port Harcourt. Endoscopic biopsies processed in the center within a five years- 1st January 2014 to 31stDecember 2018 were selected for the study. For each case, the relevant clinical information and demographic data were obtained from the laboratory request forms of the patients. Following endoscopy, biopsy specimens were fixed in 10% neutral buffered formalin and processed with automated tissue processor and embedded in paraffin wax with special caution taken to orient the tissue appropriately. The obtained paraffin-embedded tissue blocks were serially sectioned into 2-4μm thick ribbons that were subsequently floated onto clean, transparent glass slides. The mounted sections were then stained with hematoxylin and eosin, for general light microscopic evaluation, while modified Giemsa-stained sections were used to check for the presence of Helicobacter pylori. The latter appears as light blue to grayish colored short rods in the luminal mucin or epithelial crypts. The slides were read by the authors using the Updated Sydney classification system[2]. Due consideration to adequacy of the tissue section based on the presence of components of the surface epithelium and muscular is mucosa was given in the biopsy reporting. For each case, the surface and glandular epithelial cells were assessed for mucin depletion, nuclear pseudo stratification with or without pencillate appearance and hyperchromasia, increased mitotic figures as well as a loss of polarity. These features, when present, depicted dysplasia. Gastric glandular atrophy was evaluated for, based on the adequacy of glands in terms of number, distribution, and architecture, while neutrophilic activity was assessed on the presence of intraepithelial neutrophils. The presence of intestinal epithelium with mucin-producing goblet cells was also sought to ascertain intestinal metaplasia. The data were analyzed using the statistical package for social sciences (SPSS) version 20.

Three cases without stated age and sex were excluded, while 10 cases without stated ages only and 2 cases without stated sexes only were included.

III. Results

A total of 227 cases were seen. The youngest patient was a seven-year-old female, and the oldest a99-year-old male, mean age was 48.46 ±16.10. The male to female ratio was 1.1:1. Table 1, shows the age and sex distribution of cases, with age group 40-49 years accounting for most cases (25.6%) and age group 0-9 years accounting for the least. In 10 patients, the ages were not stated, while in 2 patients, their sexes were not stated, however in all 227 cases, the diagnoses were mentioned.

Table 2 shows the main symptom at presentation. Epigastric pain was the commonest indication for endoscopy (40.5%), distantly followed by the feeling of indigestion (8.4%).

Chronic gastritis (62.6%) and chronic active gastritis (22.5%) were the main histological diagnoses, as shown in table 3.

Table 4 shows the different complications of gastritis seen in the series, and the frequency of detection of H pylori in the cases seen. H pylori were seen in 26.9% of cases. A comparison of the index study with some similar studies from Nigeria, other African countries, Asia and there public of Georgia is shown in Table 5.

Table 1: Age and sex distribution of cases

Age group	Male	Female	Total	Percentage (%)
0-9	-	1	1	0.5
10-19	3	-	3	1.3
20-29	8	9	17	7.9
30-39	29	15	44	20.5
40-49	31	27	58	27
50-59	16	19	35	16.3
60-69	11	22	33	15.3
70-79	11	6	17	7.9
80-89	4	2	6	2.8
≥ 90	1	-	1	0.5
Total	114	101	215	100

Table 2: Symptoms of patients at presentation (indications for endoscopy)

Symptom	Frequency	Percentage (%)
Epigastric pain	92	40.5
Feeling of indigestion	19	8.4
Massive rectal bleeding with upper abdominal pain	10	4.4
Dysphagia	7	3.1
Epigastric pain with anaemia and weight loss	5	2.5
Hematemesis	5	2.2
Persistent vomiting	5	2.2
Melena stool	4	1.8
Heart burn	4	1.8
Abdominal pain with weight loss	4	1.8
Others	33	14.5
Not stated	44	19.4

Others include 3 cases each of the following: Easy satiety, abdominal discomfort, abdominal mass, a combination of epigastric pain and retrosternal pain, epigastric pain with anemia and weight loss, dyspepsia

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with weight loss. Others also include 2 cases each of the following symptoms: excessive belching, persistent throat discomfort, regurgitation, and a combination of persistent vomiting and abdominal pain. A case of each of the following symptoms was also seen: upper abdominal pain with swelling and constipation, hematemes is with weight loss, epigastric pain with blood in saliva, heart burn with dysphagia and feeling of indigestion, feeling of indigestion with throat pain and recurrent vomiting.

Table 3: Pattern of histologic diagnoses

Diagnosis	Frequency	Percentage
Chronic gastritis	142	62.6
Chronic active gastritis	51	22.5
Hyperplastic polyp	2	0.9
Chemical gastritis	1	0.4
Adenocarcinoma	28	12.3
Squamous cell carcinoma	1	0.4
Carcinoid tumor	1	0.4
Maltoma	1	0.4
Total	227	100

Table 4: Frequency of H pylori and complications of gastritis

Histologic features	Chronic gastritis	Chronic-active gastritis	Total (%)
H Pylori	39	22	61 (26.9)
Atrophy	7	1	8 (3.5)
IM	9	-	9(4)
IM with dysplasia	12	2	14(6.2)

IM = Intestinal Metaplasia

Table 5: Comparison of the index study with similar studies from Nigeria, Africa, and Asia

Para Meters	Index study	Jos Nig[13]	Ibadan Nig[10]	Ilorin Nig[14]	Nair obi; Kenya[15]	Maputo; Mozam Bique[16]	Lalitpur; Nepal[17]	Rawal Pindi; Pakistan[18]	Srinager; India[19]	Georgia[20]
Duration of study (months)	66	7	11	6	4	10	6	24	26	36
No of cases	227	100	86	125	71	109	1020	787	196	90
M:F ratio	1.1:1	1:1	1:1.2	1:1.6	1:1	-	1:1.2	6:1	1.9:1	1.1:1
Mean age yrs	48.46	39.6	49.19	35.3	43	37	41.7	-	-	62
CG (%)	62.6	95	64	-	-	90.8	57.3	85.9	31.5	87
H pylori Presence (%)	26.9	79	52.35	-	91	62.4	68.1	70	20.5	72
Activity (%)	22.5	83	-	-	-	-	42.1	68.8	-	90
Atrophy (%)	3.5	38	-	-	57	8.3	2.4	10	-	16
IM (%)	4	28	-	-	11	8.3	3	10	-	35
IM with dysplasia	6.2	-	-	-	-	-	-	-	-	-
Cancer (%)	13.5	3	3.5	-	-	0.9	0.5	5.7	35.4	16

Nig = Nigeria

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IV. Discussion

This study is timely considering the paucity of gastric biopsy-based studies in Port Harcourt. A decade ago, endoscopic biopsies were not carried out in Port Harcourt largely because of a lack of technical expertise. Besides, generally across the globe, gastritis was at a time considered a more or less useful histological finding but not a disease and therefore the need for biopsy- based diagnostic workup of patients was questioned until the discovery of *Helicobacter pylori* by Warren and Marshall in 1983[13]. This erstwhile relegation of biopsy-based diagnosis of gastritis may have contributed to the very slow progress in the training and development of endoscopy skills by physicians in our environment. This, in turn, may explain the slow pace of endoscopy practice and the virtual absence of histological evaluation of endoscopic specimens in our environment. This study portends hope and a bright future for the practice of gastroenterology in Port Harcourt as endoscopies have come to stay.

The updated Sydney system of classification of gastritis, which was worked out at the *H pylori* congress of 1994stipulated that two biopsies each from the corpus and antrum, and another from incisuraangularis be taken during endoscopy, to minimize sampling errors. However, the compliance by our gastroenterology physicians to the tenets of the updated Sydney classification is lacking in the area of strict topography based biopsy. Biopsy specimens received in our Pathology laboratory often come as one or two tiny piece(s) of tissues, lacking in topographic labeling. This practice needs to be improved upon considering the importance of topographic information in the classification of gastritis. Similarly, most of the studies available to us and cited in this work used the updated Sydney classification in their methodology, but a critical review shows that they did not comply strictly with the set standards especially in the area of taking multiple biopsies and topographically identifying them. Most of the studies were based on specimens taken from the gastric antrum only [10,12,15,17,19,21]. Gastroenterologists should strive to obtain specimens from the various topographic sites recommended by the updated Sydney classification scheme.

The mean age of 48.46 years noted in this study is within the mean age range of 35.3 and 49.1 years observed in similar previous African and Asian studies but less than 62 years observed in the Republic of Georgia. Symptomatic manifestation of CG usually arises in later decades of life, despite being acquired in childhood, and tend to arise in subjects with advanced stages of the lesion[22,23]. The implication of the age involvement is that patients are at the prime of their productive family, economic and social life. Thus the associated morbidity will constitute some truncation of productivity with negative socioeconomic consequences to the families and the nation at large.

We observed a slight male preponderance which is different from other Nigerian studies that observed slight female preponderance.[10,15] Studies from India and Pakistan reported significant male preponderance in their series, though no reasons were given.

Chronic gastritis was the predominant histologic diagnosis in this series, which is similar to observations in other studies except in Srinagar India, where gastric hyper plastic polyps were the commonest[10, 12-21]. There were only two cases of hyper plastic polyp in our case. The relatively low rate of chronic active gastritis may be due to antibiotic abuse, which is rife in our environment. Antibiotics, especially the broad-spectrum ones commonly abused by Nigerians, cause the disappearance of neutrophil infiltrate with the persistence of other chronic inflammatory cells like lymphocytes and plasma cells[35,36].

H pylori positivity or presence in the index study is low compared to other studies and this may be due to recent intake of proton pump inhibitors (in an attempt to take anti-ulcer drugs which are easily purchased off the counter in Nigeria), and some level of subjectivity of evaluating pathologists in the recognition and detection of H pylori in tissue specimens. Also, inadequate sampling or sampling errors or taking of specimens only from the antrum, which has been proven to give a low yield of H pylori compared to corpus, especially after treatment, may be accountable.[12,19,24]Other factors include the size of the gastric biopsies, method of staining, and level of experience of the examing pathologist.[25]Gastric biopsies from complete IM sites are also known not to contain H pylori.[26]False positive H pylori CG can also occur when the equipment is not properly cleaned and used on another patient.[27]Other non-histologic ways to confirm the presence of H pylori are the use of Polymer Chain Reaction (PCR), rapid urease test, serological detection of an anti H pylori antibody, 13Carbon-hydrogen urea breath test, or stool antigen testing.[9,10,17,28]Unfortunately these other investigations are expensive and are not routinely available in developing countries like in the setting where the index study was conducted.[9]Antibiotic abuse is also a possible contributing factor to the reduced rate of H.pylori positivity in this work [35].

Chronic atrophic gastritis (CAG) was seen in only 3.5% of cases. This is less than the findings in previous studies but greater than 2.4% observed in Lalitpur; Nepal, while studies in Ibadan and Ilorin Nigeria, did not mention CAG [10,12-20]. CAG is usually a sequelae of a life-long and aggressive inflammation resulting in destruction of gastric mucosa with time.[4] With the passage of time, CAG leads to dysfunction of stomach mucosa, which ultimately manifests as acid-free stomach. Severe CAG and acid-free stomach are

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the highest known risk factors for gastric cancer.[4]The chances of gastric cancer developing due to CGrises exponentially with the progression of H. pylori gastritis from a non-atrophic gastritis form to CAG form[29].

IM occurs as a result of the replacement of the lost gastric mucosal glands due to atrophy. IM comprises of immature small or large intestinal type of epithelium[4]. Although patients with IM run a risk of gastric cancer, it is low compared to adenocarcinoma arising in patients with Barrett esophagus[30]. IM in this series is only greater than the rate seen in Nepal but less than rates observed in Jos, North Central Nigeria, Kenya, Mozambique, Pakistan, and Georgia.[14,16-19,21]

Low-grade dysplasia was seen in 7.1% of cases and in association with IM. The other studies available to us did not make mention of dysplasia in their findings[10,13-21]. Looking out for dysplastic features in endoscopy biopsy is fundamental as its diagnosis may portend adjustment inpatients' treatment protocol, including undertaking surgical resection in high-grade dysplasia.[31]Gastric IM is linked to gastric dysplasia and research has shown that in up to 20% of individuals with IM, concurrent dysplasia is present[32.] Gastric epithelial dysplasia is associated with some risk of gastric cancer development. Since IM and dysplasia are individual risk factors for carcinoma development, the coexistence of both will most likely have a multiplier effect in carcinogenesis [33]. Thus our patients would have been followed up, which unfortunately did not happen. Surgeons and pathologists need closer synergy for optimization of patient treatment outcomes, including instituting patient follow up where necessary as in this case.

Compared to previous Nigerian and African studies, this study, unfortunately, observed a relatively high rate of gastric malignant lesions. The reason/s for this cannot be readily explained. Cancer is the most serious disease linked to H pylori gastritis[34]. There will be the need for a population based study in Port Harcourt to know if the so called 'African Enigma" (high rate of H pylori infection and low rate of gastric cancer in Africans) does not apply in this environment and to know factors responsible for a higher rate of gastric cancers.

The major limitations of this study include: the relatively small sample size (in respect to the long duration of study) and non-availability or use of other ancillary tests that could help in determining the presence of H pylori organisms. Also, the standard five specimen's collection from different parts of the stomach was not routinely done.

V. Conclusion

The histologic patterns of gastric endoscopic biopsies seen in Port Harcourt is different from findings in other parts of Nigeria, especially concerning the low prevalence of H. pylori in tissue specimens and the relatively high rate of gastric carcinomas observed. The current efforts at performing endoscopic biopsies and histologically examining them needs not only to be sustained but improved upon, for better patient treatment outcomes.

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