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PATTERN OF GASTRITIS AND *HELICOBACTER PYLORI* COLONIZATION OF THE STOMACH IN NIGERIAN PATIENTS WITH DYSPEPSIA

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ABSTRACT

Objective: *Helicobacter pylori* infection of the stomach causes chronic active gastritis. The pattern of gastritis is related to the disease outcome. This study aimed to determine the predominant gastritis pattern in Nigerian dyspeptic patients with a view to predicting gastroduodenal disease outcomes.

Methods*:* Patients referred for upper gastrointestinal endoscopy (UGIE) at a tertiary hospital in Nigeria had gastric mucosal biopsies taken and subjected to histopathology using the updated Sydney System. *H. pylori* infection, activity, chronicity and atrophy were categorized into absent (scored 0), mild (scored 1), moderate (scored 2) and severe (scored 3).

Results*:* In all, 726 patients (339 males, 387 females) were studied. There were 705 antral biopsies and 409 corporeal biopsies. *H. pylori* was positive in 487 (69%) and 217 (53%) antral and corporeal biopsies respectively ($P < 0.001$). Intestinal metaplasia (IM) and/or dysplasia was *H. pylori* positive in 131 (64%) of antral biopsies and in 17 (38.6%) of corporeal biopsies ($P < 0.0001$). In the antrum, the total inflammatory score was 3,814 (maximum = 6,336) and in the corpus, the total score was 1,703 (maximum = 3,681) ($P < 0.0001$). There were 61 (8.6%) benign antral gastric ulcers and 19 (2.7%) gastric cancers of which 13 of them (68.4%) were antral lesions.

Conclusions*:* Gastritis, *H. pylori* colonization and gastric ulceration are antrum predominant in Nigerian patients. In spite of a sharp rise in intestinal metaplasia and dysplasia after age 40 and high prevalence of *H. pylori* infection, gastric cancer prevalence appears relatively low.

Keywords: Dyspepsia, Antrum-predominant, Corpus-predominant gastritis, *Helicobacter pylori*, Atrophy, Intestinal metaplasia, Cancer

INTRODUCTION

Helicobacter pylori infection of the stomach is a major cause of chronic active gastritis. The pattern of colonization of the stomach by the organism is known to be associated with disease outcome. While antrum predominant gastritis has been associated with duodenal ulcer (DU) and distal gastric cancer, corpus-predominant gastritis often results in carcinoma of the

gastric body[1,2,3,4,5]. Chronic corpus gastritis has been shown to protect against gastro-esophageal reflux disease (GERD)[6,7,8]. Also, an upper gastrointestinal endoscopy study done in our centre 15 years ago showed DU to be the commonest lesion and a high prevalence of *H. pylori* infection[9]. This study was, therefore, undertaken to determine the predominant pattern of gastritis in Nigerian dyspeptic patients and to see if the widespread use of *H. pylori* eradication therapies and proton pump inhibitors in the last one and a half decade would influence endoscopic findings.

METHODS

This was a retrospective study of patients referred for upper gastrointestinal endoscopy at the Gastrointestinal Endoscopy Centre of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria, between January 2006 and December 2012. This tertiary health institution, located in South-west Nigeria, receives referrals from centres ranging in distances from 30 km to 250 km.

Forward viewing Olympus gastroscope GIF-Q30 and Pentax gastroscope FG-29W were used for the upper gastrointestinal endoscopic examination after overnight fast and informed consent. Topical pharyngeal anaesthesia was achieved with 10% lignocaine and conscious sedation was given with either IV diazepam (2-5mg) or IV midazolam (1-5mg). Duodenal paralysis was achieved with IV hyoscine butylbromide (20mg) just before insertion of the gastroscope. During endoscopic examination, a minimum of 7 biopsies were taken from the stomach (4 from the antrum including 1 from the gastric angle and 3 from the corpus) and subjected to histopathology. Biopsies were fixed overnight in 10% formalin and then embedded in paraffin wax. Thin sections of 3-5µm were stained Haematoxylin and Eosin after which they were examined under light microscope at high magnification. When indicated, Giemsa stain was used to highlight *H. pylori*.

Histopathological appraisal of the gastric mucosa was done using the updated Sydney System[10]. Activity was defined as the density of intra-epithelial neutrophils. Chronicity was diagnosed when more than 5 lymphocytes and/or plasma cells, macrophages were seen in the lamina propria per high power field (HPF). Loss of glandular tissue was diagnosed as atrophy. Each of these parameters (intensity of *H. pylori* infection, activity, chronicity and atrophy) was categorized into absent (scored 0), mild (scored 1), moderate (scored 2) and severe or marked (scored 3). Data collected were entered into SPSS version 16 (SPSS Inc. Chicago, IL, USA) and analyzed using descriptive and chi-square statistics. P value of less than 0.05 was accepted as significant.

RESULTS

In all, 726 patients were studied comprising 339 males and 387 females (M:F = 0.9:1.0). Their ages ranged from 9 years to 100 years with a mean of 48.60 ±SD 16.48 years. The total number of antral biopsies studied was 705 (the results for 21 patients could not be retrieved) while the total number of corporeal biopsies studied was 409 (routine biopsy of the corpus began in our Gastrointestinal Endoscopy Centre about a year into this study).

On endoscopy, antral gastritis was visualized in 254 (35%) patients and corpus gastritis in 23 (3.2%). DU was seen in 134 (18.5%) patients while gastric ulcer (GU) was visualized in 61 (8.4%) patients (all in the antrum). Gastric erosions seen were antral in 73 (10%) patients and corporeal in 2 (0.27%). There were 19 (2.7%) cases of histologically confirmed gastric cancer (males 11, females 8) out of which 13 (68.4%) were antral lesions and 3 (15.8%) were early gastric cancer.

The ages of the gastric cancer patients ranged from 27 years to 81 years with a mean of 50.3 (SD± 17.7) years. Seventy-one patients (9.8%) had normal endoscopic findings. *H. pylori* was positive in 487 (69%) antral biopsies and 217 (53%) corporeal biopsies (Pearson's Chi Square = 28.022, P < 0.001). *H. pylori* was demonstrated in the gastric mucosa of 99 (73.8%) of the DU patients and 42 (68.8%) of the GU patients (table 1).

Table 1: Upper Gastrointestinal endoscopic findings in dyspeptic Patients (n = 726)

Endoscopic Finding	No. (%)
Antral gastritis	254 (35)
Duodenal ulcer	134 (18.5)
Gastric antral erosions	73 (10)
Normal endoscopic findings	71 (9.8)
Gastric ulcer (all antral)	61 (8.4)
Polyps	29* (4.1)
Duodenitis	29 (4.1)
Corporeal gastritis	23 (3.2)
Gastric outlet obstruction	21 (3)
Gastric cancer	19# (2.7)
Erosive GERD	9 (1.3)
Oesophageal varices	5 (0.7)
Gastric corporeal erosions	2 (0.3)

The *H. pylori* infection rate was fairly uniform across all the age groups in both antrum (range: 64% - 75%) and corpus (range: 41% - 60%) (Table 2). The total score for the intensity of *H.* pylori infection for the *H. pylori* positive antral biopsies was 620 out of a maximum obtainable score of 1461 (42.4%) and the total score for the same parameter for the 217 *H. pylori* positive corporeal biopsies was 257 out of 'a maximum obtainable score of 651 (39.5%). Intestinal metaplasia (IM) and/or dysplasia occurred in 205 (162 IM, 43 dysplasia) out of 705 (29%) antral biopsies and of these 205, 131 (64%) were *H. pylori* positive.

Dysplasia and/or IM occurred in 44 (26 IM, 18 dysplasia) out of 409 (10.75%) corporeal biopsies and of these 44, 17 (38.6%) were *H. pylori* positive (c^2 = 47.090, P < 0.0001) (Table 3). In 15 patients (5 males & 10 females), IM and dysplasia occurred together in the antrum while both lesions were seen in the corpus of only 1 male patient. Out of the 162 antral cases of IM, 82 (50.6%) were cases of incomplete IM while 13 (50%) of the 26 corporeal IM were the incomplete type. The prevalence of IM and dysplasia increased with increasing age both in the antrum and the corpus. However, the prevalence of both lesions rose sharply from the age of 40 years and women were more affected than men after the fourth decade of life (Figs. 1 & 2).

The scores for gastric mucosal inflammation and atrophy in the antrum were compared with those of the corpus. In the antrum, the total score for activity, chronicity and atrophy was 3,814 (maximum score obtainable = 6,336). In the corpus, the total score for the same parameters was 1,703 (maximum score obtainable = 3,681) (c^2 = 182.631, P < 0.0001). The total number of cases of non-ulcer dyspepsia (NUD)

Table 2: Number of patients and *Helicobacter pylori* positivity according to the age group and biopsy site

Age Group (Yrs.)	ANTRUM		CORPUS	
	No. of Patients (%)	No. Positive for *H. pylori* (%)	No. of Patients (%)	No. Positive for *H. pylori* (%)
9 – 19	20 (2.8)	13 (65)	9 (2.2)	4 (44)
20 – 29	85 (12)	63 (74)	44 (10.8)	22 (50)
30 – 39	104 (14.8)	78 (75)	63 (15.4)	38 (60)
40 – 49	146 (20.7)	102 (70)	96 (23.5)	56 (58)
50 – 59	156 (22)	100 (64)	85 (20.8)	45 (53)
60 – 69	106 (15)	68 (64)	59 (14.4)	24 (41)
70 - 79	64 (9)	47 (73)	38 (9.3)	20 (53)
80 – 100	24 (3.4)	16 (67)	15 (3.7)	8 (53)
Total	705	487	409	217

Table 3: Association of *Helicobacter pylori* infection with intestinal metaplasia and dysplasia

Gastric Mucosal Lesion	Antrum			Corpus			P value
	H pylori +ve (%)	*H pylori* –ve (%)	Total	*H pylori* +ve (%)	*H pylori* -ve (%)	Total	
Intestinal Metaplasia (IM)	108 (66.7)	54 (33.3)	162	12 (46.15)	14 (53.85)	26	
Dysplasia	23 (53.5)	20 (46.5)	43	5 (27.8)	13 (72.2)	18	
IM + Dysplasia	131 (64)	74 (36)	205	17 (38.6)	27 (61.4)	44	< 0.0001

Table 4: Relationship between *Helicobacter pylori* infection and biopsy site, IM, NUD and gastritis score

Parameter	Antrum (%) *H pylori* +ve	Corpus (%) *H pylori* +ve	P value
Biopsy	487 (69) n=705	217 (53) n=409	< 0.001
IM & Dysplasia	131 (64) n=205	17 (38.6) n=44	< 0.0001
NUD	337 (65.7) n=513	162 (39.6) n=409	= 0.000
Scores for Inflammation & Atrophy	3,814 of 6,336 (60.2)	1,703 of 3,681(46)	< 0.0001

IM = Intestinal Metaplasia *NUD = Non-Ulcer Dyspepsia*

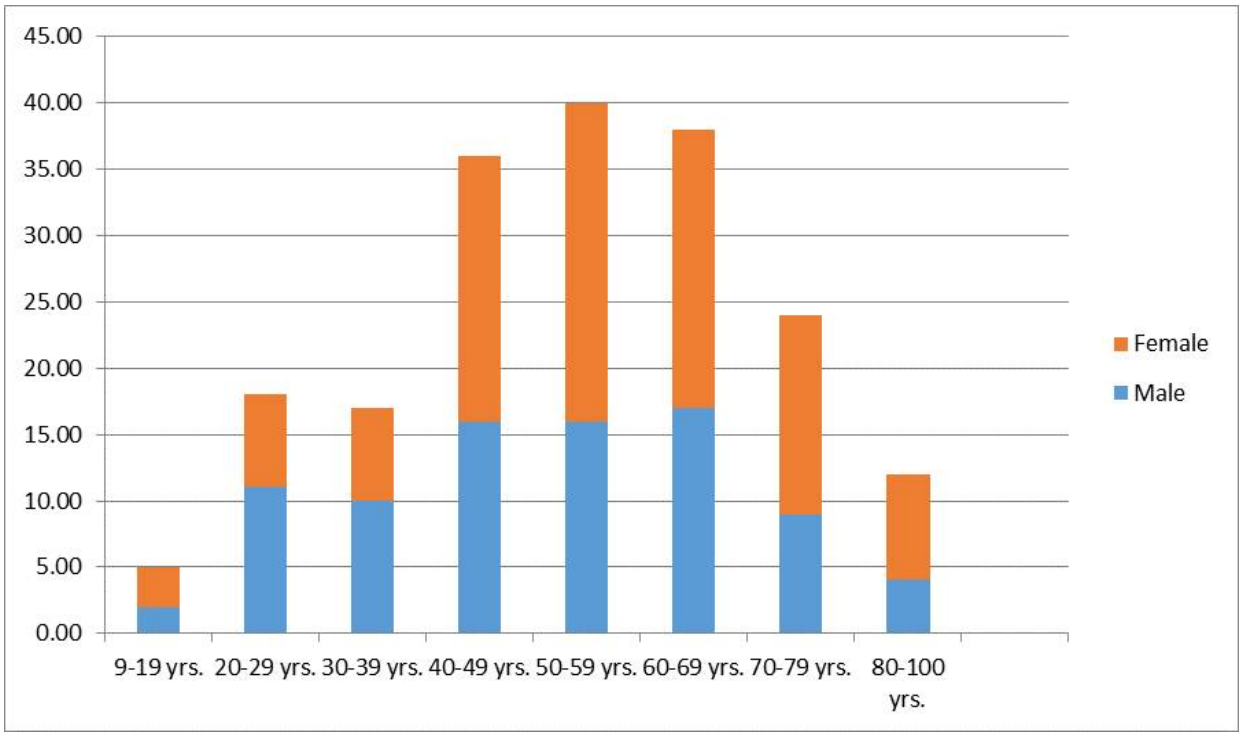

Fig. 1: Age and sex analysis of patients with IM* and dysplasia in the gastric antrum
**IM = Intestinal Metaplasia*

was 513 (70.7%) out of which 337 (65.7%) were positive for *H. pylori* in the antrum. In the corpus, 162 out of the 409 biopsies (39.6%) were *H. pylori* positive among the NUD patients (Pearson's c^2 = 15.421, P = 0.000)(Table 4).

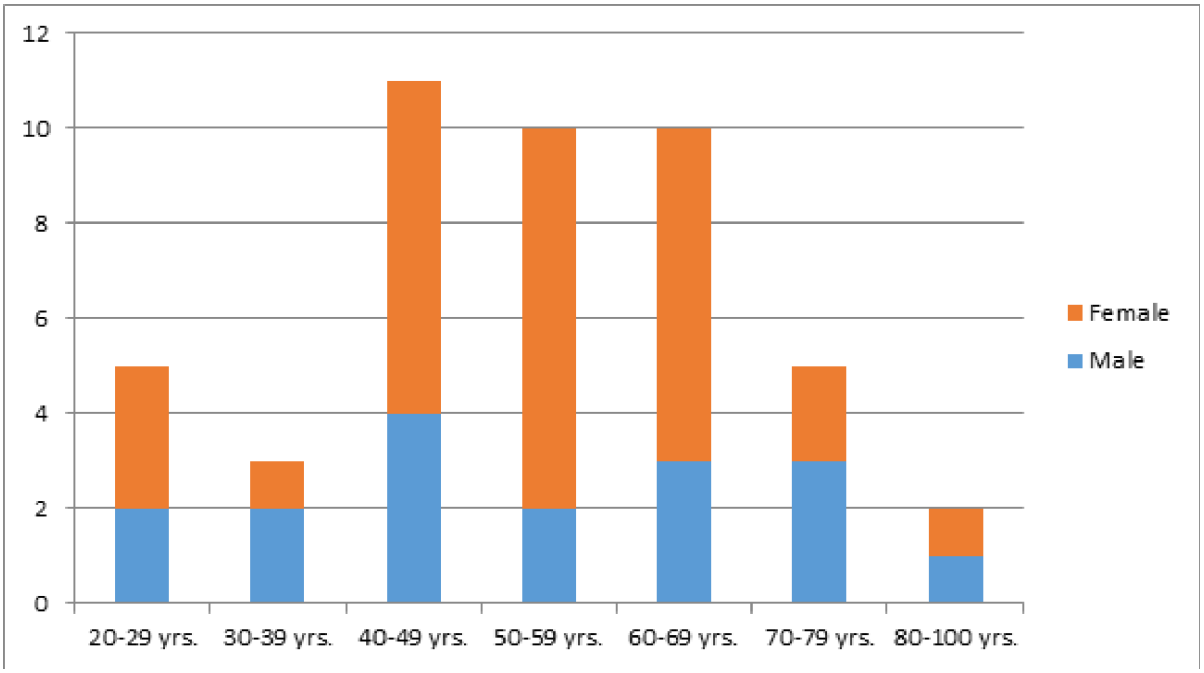

Fig. 2: Age and sex analysis of patients with IM* and dysplasia in the corpus
**IM = Intestinal Metaplasia*

DISCUSSION

Infection with *H. Pylori* is the most predominant cause of chronic active gastritis. The pattern of gastritis is known to determine the gastroduodenal disease outcome. Whereas antrum predominant gastritis has been associated with DU and unusually increased risk of distal gastric cancer, corpus predominant gastritis predisposes patients to mucosal atrophy and increased risk of cancer of the gastric body[1,2,4,5].

Gastric mucosal inflammation, atrophy and *H. pylori* colonization showed more affectation of the antrum than the corpus in our patients. This is comparable to findings from studies in Nepal, Iraq and Iran[11,12, 13]. In those studies, DU and antrum predominant gastritis were common while corpus predominant gastritis and gastric cancer were relatively uncommon. With the DU prevalence of 18.5% obtained in this study, the condition may still be fairly common in our patients. Nevertheless, this result represents a 50% decline in DU prevalence over the past decade in dyspeptic patients seen in our centre (DU prevalence relative to GU has reduced considerably) even though the *H. pylori* infection rate among the DU patients has remained unchanged[9]. Similar declining trends in peptic ulcer hospitalization and prevalence have been recorded in other countries probably reflecting the widespread use of *H. pylori* eradication treatments[14,15].

The development of non-cardia gastric cancer follows a step-wise progression from atrophic gastritis to intestinal metaplasia to dysplasia, the so-called Correa's cascade[16]. Intestinal metaplasia and dysplasia are, therefore, recognised pre-cancerous lesions with the latter showing the highest risk for gastric cancer[5,17]. It was detected in well over half of gastric cancer patients studied in our centre[18]. Intestinal metaplasia has been shown to increase in prevalence with age even in those with normal endoscopy findings[19]. Intestinal metaplasia and/or dysplasia occurred in almost one third of our patients, mainly in the antrum, and this was significantly *H. pylori*-related. The prevalence of intestinal metaplasia alone in the antrum was 23% which is similar to the finding in a recent study from our centre and nearby hospital[20]. Of particular importance was the observed sharp rise in the prevalence of intestinal metaplasia and dysplasia in both males and females from the age of 40 years. It may seem appropriate, therefore, to counsel every Nigerian aged 40 or more years with un-investigated dyspepsia to undergo upper gastrointestinal endoscopy in order to increase the chances of detecting early gastric cancer.

Also, the *H. pylori* infection rate remains high in Nigerian dyspeptic patients with 69% and 73.8% positivity rates in antral biopsies generally and in DU patients respectively. Similar results were obtained in earlier studies done in our centre[9,21]. *H. pylori* has been shown to be responsible for inducing the pre-malignant lesions such as intestinal metaplasia and dysplasia that develop into cancer and in their absence gastric cancer would be extremely rare[22]. It is therefore surprising that in spite of the high prevalence of *H. pylori* infection and the substantial number of cases of intestinal metaplasia and dysplasia, the prevalence of gastric cancer remained relatively low in our patients. Also in Ibadan in the same region as our centre, gastric cancer accounted for only 1.38% of all malignancies seen over a 12-year period[23]. In 1992, Holcombe[24] coined the term "African enigma" to describe this discordance but in a meta-analysis, Agha & Graham[25] found no dissociation between prevalence of *H. pylori* infection and *H. pylori*-related diseases in Africans. However, the study by Hellmig *et al* [26] appeared to support the "African enigma" as it showed genetic diversities of the host immune systems of African and Caucasian populations that may influence clinical outcome.

Our study showed that NUD was diagnosed in over 70% of patients examined and antrum-predominant gastritis was significantly associated with it. A high prevalence of NUD was also obtained in a study from another centre in Nigeria[27]. Antrum-predominant gastritis has been shown to be the most common pattern of gastritis seen in NUD patients in Western populations and appear to carry a high risk of peptic ulcer disease[3, 28]. It would therefore appear that Nigerian NUD patients share a similar pattern of gastritis with their Western counterparts and so are likely to benefit from *H. pylori* eradication as some NUD patients with this gastritis pattern are wont to[29, 30]

In conclusion, this study shows that the pattern of gastritis, *H. pylori* colonization and gastric ulceration in Nigerian dyspeptic patients (including NUD patients) is antrum predominant. There is a low prevalence of gastric cancer in spite of high prevalence of *H. pylori* infection and a sharp rise in the prevalence of intestinal metaplasia and dysplasia after the age of 40 years.

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Conflict of Interest: None declared

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