ORIGINAL ARTICLE

# Gastric Histopathological Findings In Mucosal Biopsies Of Symptomatic Patients In Jos Central Nigeria

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## *Abstract*

***Background:*** *Dyspepsia is a common disease worldwide. It is a cause of great absenteeism from work with a lot of economic loss. In Jos, it is one of the most common complaints encountered in both general outpatient and specialist clinics.*

***Aim:*** *To evaluate the histopathological changes in gastric mucosa of patients presenting with symptoms of dyspepsia.*

***Methods:*** *Cross sectional study. Gastric endoscopic biopsy specimens from 100 consecutive patients with symptoms of dyspepsia were histologically evaluated using the criteria of the updated Sydney system.*

***Results:*** *There were 50 males and 50 females. Their overall mean age was 39.6 ± 12.2 (S.D).*

*The prevalence of Helicobacter pylori colonization was 79%. Males were 53.2% and females 46.8% respectively giving a sex ratio of 1.4:1.*

*Gastritis, neutrophil activity, glandular atrophy and intestinal metaplasia were observed in 95%, 83%, 38% and 28% respectively. Gastric carcinoma was found in 3% of the patients.*

***Conclusion:*** *From our study, we conclude that the majority of our patients with dyspeptic symptoms have significant histopathological changes in their gastric mucosa with implications for the development of further gastric lesions, and that the most common cause of dyspepsia in our environment is Helicobacter pylori infection.*

**Keywords:** Dyspepsia, *Helicobacter pylori,* Gastritis, Jos

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## INTRODUCTION

Dyspepsia is a common disease worldwide. It is a cause of great absenteeism from work with a lot of economic loss.[1] In Jos, it is one of the most common complaints encountered in both general out patient and specialists' clinics. The exact diagnosis of the causes of dyspepsia may not be made on history alone.

In some earlier reports by authors working in tropical countries, data on the epidemiology of various gastrointestinal diseases have been incomplete or unreliable since inaccurate methods of investigations were commonly employed[2.] Indeed, some authors had reported a low prevalence of gastric atrophy and high prevalence of chronic gastritis in African adults and children; the so-called "African enigma"[2.] Others have reported a high prevalence of *Helicobacter pylori* infection but low incidence of peptic ulcer disease, intestinal metaplasia and gastric cancer in the savannah regions of Africa [2,3.] These conclusions were based mainly on anecdotal observations of doctors working in rural mission hospitals and a few studies relying only on clinical or single contrast radiological diagnoses. However, more recent observations most of which were based on endoscopic features alone do not all support these hypotheses[4,5,6.]

In this study, we present the histopathological findings in gastric mucosal biopsies of one hundred patients who presented with dyspeptic symptoms at the Jos University Teaching Hospital in central Nigeria.

## PATIENTS AND METHODS

One hundred consecutive Nigerian patients seen at the Jos University Teaching Hospital with dyspepsia, who were referred for upper gastrointestinal endoscopy between the months of February and August, 2003 were studied. The patients were referred either by consultants in the teaching hospital or general practitioners in the town. None of the patients had *Helicobacter pylori* eradication therapy in the past nor did any have previous endoscopy or gastric surgery. Informed consent for biopsy was obtained from those patients in whom biopsy was not necessary as judged by the gastroenterologist. Ethical clearance was obtained from the hospital's ethics committee.

After an overnight fast, they had a pharyngeal spray of 4% xylocaine and were examined by endoscopy using wide channel Olympus GIF-P30 endoscope and the fenestrated biopsy forceps Olympus FB-21k-1 was used to take the biopsies. The topographic mapping of biopsy sites followed the recommendation of the updated Sydney system[7] which recommends that biopsies be taken as follows:

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- 2 from the corpus, 8cm from the pyloric ring; one each from the lesser and greater curvatures.
- 2 from the antrum, 2cm from the pyloric ring; one each from the lesser and greater curvatures and
- 1 from the incisura angularis.

The tissues were then fixed immediately in 10% buffered formalin in separate containers and labeled appropriately. They were then transported to the histopathology laboratory and subjected to routine procedures of tissue processing. Sections of 3mm thick were made from paraffin embedded blocks and deparaffinized by heating at 60$^{o}$C for ten minutes and then rehydrated in graded alcohol concentrations. They were stained with haematoxylin and eosin. Giemsa stain and Periodic Acid Schiff/Alcian Blue were employed for *Helicobacter pylori* and intestinal metaplasia where it was necessary. Endoscopic biopsy specimens from the gastric mucosae of 100 consecutive patients with dyspepsia were histologically evaluated for the intensity of *H. pylori* colonization, the degrees of inflammatory activity (presence of intramucosal neutrophils), chronic inflammation (presence of lympocytes and plasma cells with or without lymphoid follicles), gastric atrophy and intestinal metaplasia.

The Gimenez technique which is of comparable sensitivity to the Giemsa stain was not employed in this study because it was not readily available.

All the slides were independently evaluated under light microscope by two pathologists using the criteria of the updated Sydney system. Where there was interobserver variation, group review was done until a general consensus was arrived at. All the morphologic variables were graded using the visual analogue scale of the updated Sydney system into four semi-quantitative parameters as follows: normal (nil), mild, moderate and marked with corresponding scores of 0-3, according to the degree of mucosal involvement.

Where

*0 = normal (nil)*
*1 = mild*
*2 = moderate*
*3 = marked*

The graded variables included *H. pylori* colonization density, neutrophil (inflammatory) activity, chronic inflammation, glandular atrophy and intestinal metaplasia.

Other histologic features which are non graded variables were also assessed.

These included reactive changes (reactive gastropathy), epithelial dysplasia and early gastric cancer (EGC).

The results were analyzed using simple statistical tables

*Table 1. The updated Sydney system*

| ***Histologic Feature*** | ***Definition*** | ***Grade*** mild | moderate | marked |
|---|---|---|---|---|
| *H. pylori* | H.p intensity in Epithelium | + | ++ | +++ |
| Activity | Neutrophil infiltration In lamina propria or Superficial epithelium | <1/3 | 1/3-2/3 | >2/3 |
| Chronic inf. | Lymphocytes & plasma Cells in the lamina propria | + | ++ | +++ |
| Gland atrophy | Loss of corpus and antral Glands | + | ++ | +++ |
| I. M | I.M in mucosal epithelium | <1/3 | 1/3-2/3 | >2/3 |

H. p = *Helicobacter pylori*
I. M = Intestinal metaplasia

## RESULTS

### Age and sex distribution

There were 50 (50%) males and 50 (50%) females. The mean of the ages of females and males were 36 ± 11.5 (S.D) and 42 ± 12.8 (S.D) respectively. The age distribution showed that, the females were significantly younger than the males (p= 0.0078).

### *H. pylori* colonization density (gastritis)

*Helicobacter pylori colonization* was found in 79(79%) of the biopsies. Of these, 42(53.2%) were males while

37(46.8%) were females. This gives a *H. pylori* sex colonization ratio of 1.4: 1. No significant statistical difference was found when colonization rates were related to sex suggesting that *H. pylori* infection does not have more predilections for any sex.

*Table II: Distribution of the study population by sex and Age groups.*

| AGE GROUP | MALE | FEMALE | TOTAL |
|---|---|---|---|
| 11-20 | 0(0%) | 2(4%) | 2 |
| 21-30 | 11(22%) | 17(34%) | 28 |
| 31-40 | 14(28%) | 17(34%) | 31 |
| 41-50 | 10(20%) | 10(20%) | 20 |
| 51-60 | 12(24%) | 2(4%) | 14 |
| 61-70 | 2(4%) | 2(4%) | 4 |
| 71-80 | 1(2%) | 0(0%) | 1 |
| **TOTAL** | **50(100%)** | **50(100%)** | **100** |

Mean of age distribution: male = 42.9 ±12.8,
Female = 36.3 ±11.5
(T statistics = 2.72, P< 0.0078)

Of the 42 males with mucosal colonization, 15(35.7%) had mild, 23(54.8%) moderate and 4(9.5%) marked colonization respectively while among the 37 females with mucosal colonization, 22(59.5%) had mild, 11(29.7%) had moderate and 4(10.8%) had marked colonization respectively. Higher prevalence of *H. pylori* colonization was found in the 3rd and 4th decades with peak age prevalence at 31-40 years representing 31% of the study population. However, there was no statistical significant correlation between the degree of *H. pylori* colonization and the age groups of the study population (table III, Fig. 1).

**Inflammatory activity**

Of the 100 biopsies evaluated, 83 (83%) showed the presence of neutrophils activity in their mucosae ranging from sprinkles of neutrophils in the lamina propria to pit abscesses.

All the 79 cases with *H. pylori* gastritis were associated with polymorphonuclear neutrophils activity in their gastric mucosae. Twenty five (31.6%) had mild neutrophil activity; 42 (53.2%) moderate and 12(15.2%) had marked activity respectively. The neutrophil activity correlated well with the presence of *H. pylori.* However, the presence of *H. pylori* could not be demonstrated in the remaining 4 patients with active gastritis. It might be that these patients had taken antisecretory medications (proton pump inhibitors), and the information was not volunteered or that sampling error had occurred. Three of them were males and one was a female all in their 4th decades.

**Chronic gastritis**

Ninety-five (95%) of the biopsies evaluated showed chronic gastritis. Eighty-three were chronic active gastritis, and 79 were associated with *H. pylori.* The topography of active chronic gastritis was found to be predominantly antral in 53(56%) patients while diffuse corpus and antral gastritis were 23 (24%). Corpus predominant gastritis was found in 19 (20%) of the patients in this study. All the chronic *H. pylori* gastritis showed mucosal changes ranging from lamina propria oedema to erosive and/or haemorrhagic gastritis with focal areas of mucosal denudation, fibrinous inflammation and cellular debris forming pit abscesses in some glands. Sixty- three of the 79 *H. pylori* gastritis (79.7%) showed moderate to marked colonization; 28 were females and 35 were males all in their 4th decades.

*Table III: Distribution of Helicobacter pylori colonization density by age groups of the study population.*

| AGE GROUP | NONE | MILD | MODERATE | MAKRED | TOTAL |
|---|---|---|---|---|---|
| 11 - 20 | 1(4.8%) | 1(2.7%) | 0(0%) | 0(0%) | 2 |
| 21 - 30 | 6(28.6%) | 10(27%) | 8(23.5%) | 4(50%) | 28 |
| 31 - 40 | 5(23.8%) | 14(37.8%) | 8(23.5%) | 4(50%) | 31 |
| 41 - 50 | 4(19%) | 7(19%) | 9(26.5%) | 0(0%) | 20 |
| 51 - 60 | 5(23.8%) | 1(2.7%) | 8(23.5%) | 0(0%) | 14 |
| 61 - 70 | 0(0%) | 4(10.8%) | 0(0%) | 0(0%) | 4 |
| 71 - 80 | 0(0%) | 0(0%) | 1(3%) | 0(0%) | 1 |
| **TOTAL** | **21(100%)** | **37(100%)** | **34(100%)** | **8(100%)** | **100** |

($x^2$ = 7.26, P $\leq$ 0.30)

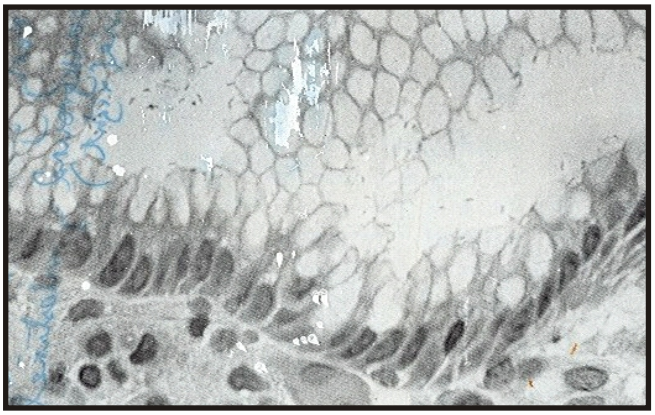

*Figure 1: Helicobacter pylori in gastric mucosa (H & E stain x400)*

**Glandular atrophy**

Thirty-eight patients (38%) had atrophic changes in their gastric mucosae. Of these, 23(60.5%) were males and 15(39.5%) were females; giving a male: female ratio of 1.5: 1. When atrophy was related to *H. pylori* colonization, 31 patients with *H. pylori* colonization had atrophy representing 82% of the 38 patients with atrophic changes. Of the 38 patients with atrophy, 23 (29%) were males and 15 (19%) were females. Thirteen (34%) patients had mild atrophy, 22(58%) had moderate and 3(8%) had marked atrophy respectively. All the patients were in their 4$^{th}$ decades. The remaining 7 cases had no *H. pylori* colonization; 3 were females and 4 males all in their 4$^{th}$ decades. There were 4 mild, 2 moderate and 1 marked atrophy. When the category of mild atrophy was removed, the incidence dropped from 38% to 24%. Twenty of these were associated with *H. pylori* infection (83.3%). Minor degrees of atrophy are sometimes difficult to differentiate from inflammatory damage to the glands. Moreover, many studies have shown that there is poor interobserver agreement between different pathologists in the assessment of mild atrophy[8]. So moderate and marked categories of atrophy might be the true incidence in this study (table IV, Fig. 2).

*Table IV: Distribution of glandular atrophy by age groups of the study population*

| AGE GROUP | NONE | MILD | MODERATE | MARKED | TOTAL |
|---|---|---|---|---|---|
| 11 - 20 | 2(3.2%) | 0(0%) | 0(0%) | 0(0%) | 2 |
| 21 - 30 | 19(30.6%) | 3(23%) | 5(22.73%) | 1(33.33%) | 28 |
| 31 - 40 | 21(33.9%) | 3(23%) | 7(31.82%) | 0(0%) | 31 |
| 41 -50 | 10(16.1%) | 4(31%) | 5(22.73%) | 1(33.33%) | 20 |
| 51 - 60 | 5(8.1%) | 3(23%) | 5(22.73%) | 1(33.33%) | 14 |
| 61 - 70 | 4(6.5%) | 0(0%) | 0(0%) | 0(0%) | 4 |
| 71 - 80 | 1(1.6%) | 0(0%) | 0(0%) | 0(0%) | 1 |
| **TOTAL** | **62(100%)** | **13(100%)** | **22(100%)** | **3(100%)** | **100** |

($X^2$ = 12.06, P = 0.84).

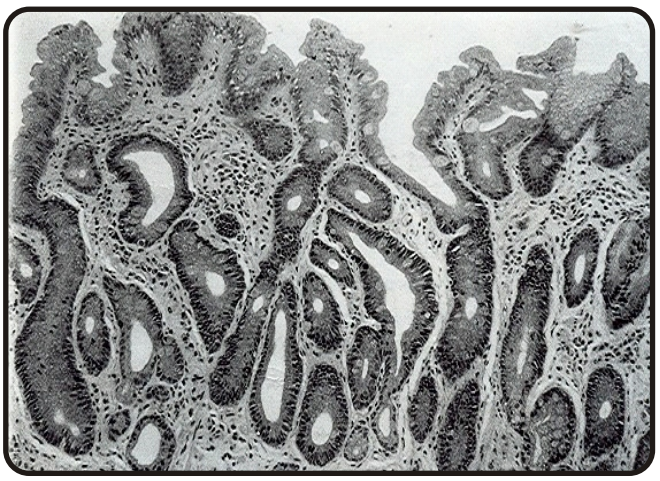

*Figure 2: Multifocal chronic atrophic gastritis, intestinal metaplasia and low-grade epithelial dysplasia ( H & E stain x 200)*

**Intestinal metaplasia**

Twenty-eight (28%) of the patients had intestinal metaplasia. Eighteen (64.3%) were males while 10(35.7%) were females. Male: female ratio was 1.8:1. Seventy-two (72%) patients did not show intestinal metaplasia in their mucosae. Of the 28 with intestinal metaplasia, 13 (46%) was mild, 10 (36%) moderate and 5 (18%) marked intestinal metaplasia respectively. When intestinal metaplasia was related to specific age categories, no significant statistical difference was found suggesting that the incidence of intestinal metaplasia was independent of patient age in this study (table v ).

*Table V: Distribution of intestinal metaplasia by age groups of the study population*

| AGE GROUP | NONE | MILD | MODERATE | MARKED | TOTAL |
|---|---|---|---|---|---|
| 11 - 20 | 2(2.8%) | 0(0%) | 0(0%) | 0(0%) | 2 |
| 1 - 30 | 27(37.5%) | 0(0%) | 1(10%) | 0(0%) | 28 |
| 31 - 40 | 20(27.8%) | 9(69.2%) | 2(20%) | 0(0%) | 31 |
| 41 - 50 | 13(18%) | 3(23.1%) | 4(40%) | 2(40%) | 22 |
| 51 - 60 | 7(9.7%) | 1(7.7%) | 3(30%) | 3(60%) | 14 |
| 61 - 70 | 2(2.8%) | 0(0%) | 0(0%) | 0(0%) | 2 |
| 71 - 80 | 1(1.4%) | 0(0%) | 0(0%) | 0(0%) | 1 |
| **TOTAL** | **72(100%)** | **13(100%)** | **10(100%)** | **5(100%)** | **100** |

($X^2$ = 15.02, P =0.24)

**NON- GRADED VARIABLES**

**Reactive gastropathy**

Out of the 100 consecutive patients, 7 (7%) showed reactive gastropathy which was demonstrated by the presence of elongated and tortuous foveolae with luminal serrations, mucin depletion and reactive cytological atypia. Smooth muscle proliferation was also evident in the lamina propria. Inflammatory cells infiltrate were either very mild or conspicuously absent. Two were males and 5 were females. Three in their 3rd decades, 2 in their 4th decades and 1 each in their 5th and 6th decades.

**Epithelial dysplasia**

Two patients (2%), one male and one female each had epithelial dysplasia of low- and high-grades respectively. The two patients were in their 4th and 5th decades respectively.

**Gastric carcinoma**

Three patients (3%) had gastric carcinoma of the intestinal type. All the three patients were males in their 6th decades. Background moderate chronic gastritis and intestinal metaplasia were observed in these patients. When only those 40 years and above were considered, 18 patients were found in this category. The prevalence of gastric carcinoma based on this age category was found to be 16.7%. This suggests that the incidence of gastric carcinoma increases with age and therefore the need for greater surveillance with age (Fig. 3)

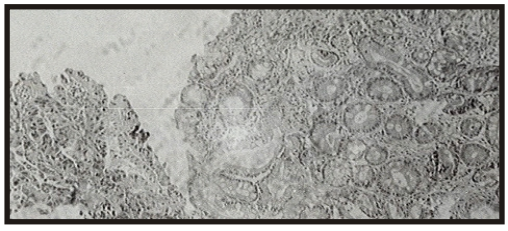

*Figure 3: Early gastric cancer (left) on a background of intestinal metaplasia (right) (H & E x200).*

**DISCUSSION**

This study observed central Nigeria to be a region of high prevalence of *Helicobacter pylori* infection, similar to other reports in this environment and other parts of Nigeria[8, 9, 10]. The present knowledge about *H. pylori* and its relation to gastric pathology makes one wonders why an area of high prevalence of *H. pylori* infection could be reported as having low incidence of gastroduodenal diseases. Several explanations have been proposed by these authors such as genetic differences in *H. pylori* strain, differences in the virulence factors of the organism, differences in initiating and/or promoting factors and shorter life expectancy of Africans who die of other diseases before they have had time to develop those associated with *H. Pylori.*[6]

The 38% glandular atrophy, 28% intestinal metaplasia, 20% peptic ulcer disease and 3% gastric carcinoma in our study suggest that the prevalence of diseases associated with *H. pylori* infection is not low in central Nigeria as was previously reported[1]. We believe that the conclusion of previous authors was premised only on anecdotal observations and single contrast radiological diagnosis. The use of fibreoptic upper gastrointestinal endoscopy and biopsy is gradually bringing to light the true picture of diseases associated with *H. pylori* in our environment.

It is assumed that the sequence of events in gastric cancer is as follows: chronic gastritis, atrophy, intestinal metaplasia, dysplasia and gastric cancer, and that *Helicobacter pylori* may be involved in the chain of this chronic phenomenon at least early in its evolution. However, due to its rarity or complete absence in metaplastic gastric epithelium, it is not certain whether its continuous presence is necessary for the development of cancer. The current view is that *H. pylori* serves as an initiating factor in the process of gastric

carcinogenesis and once precancerous lesions (atrophy and intestinal metaplasia) are established, its presence is not necessary for progression to cancer[8]. It has also been observed that the intestinal type of gastric cancer is more associated with *H. pylori* infection than any other histological type.

We found intestinal metaplasia in 28% of our series. A previous study in this area had reported a prevalence of 25%[8]. The prevalence of gastric cancer in this study was 3%. Previous studies from Ibadan had reported that the prevalence of gastric cancer in Nigeria ranged from 2% in northern Nigeria to 4% in southwestern Nigeria[11, 12]. The incidence of 3% gastric cancer is also similar to 2.9% reported in *H. pylori* infected Japanese population over a 7 to 8-year period[13].

Our opinion is that, with the use of modern diagnostic equipment and gastric biopsy of *H. pylori* infected patients, the incidence of gastric cancer might not be as low as was once thought in our population. For instance, none of the gastric cancers was diagnosed at endoscopy. They were all early gastric cancers (EGC) that were diagnosed histologically.

Although the number of patients in this study is small and conclusions may be limited, the results suggest that *H. pylori* may be the most important cause of dyspepsia and that the same spectrum of *H. pylori* related gastroduodenal diseases are found in our patients as in other parts of the world. Earlier reports which came to a contrary conclusion used relatively crude methods of diagnosis. More studies will be required to draw definite conclusions.

## References


1. Barton C. J., Cockshott WP. Post-bulbar duodenal ulceration in Nigeria. Br J Radiol 1961; **34**: 216-220.
2. Campbell D. I., Warren B F, Thomas J E, Figura N, Telford J L, Sullivan PB. The African enigma: low prevalence of gastric atrophy, high Prevalence of chronic inflammation in West African adults and children. Helicobacter 2001; **6(4)**: 263-7.
3. Trovey F I, Tunstall M. Duodenal ulcer in black population in Africa south of the sahara. Gut 1975; **16**: 568-575.
4. Konstan P G. Peptic ulcer in West Africa and India. Schweizerische zeitschrift fur pathologie. 1985; **21**: 229-335.
5. Malu A O, Wali S S, Kazmi R, Fakunle Y M. Upper gastrointestinal endoscopy in Zaria, northern Nigeria. West Afr J Med 1990; **9**: 279-284.
6. Ofili O P. Obstructed duodenal ulcer syndrome, observations from Kano, northern Nigeria. Tropical and geographical medicine 1992; **44**: 131-134.
7. Malu A O, Okeke E N, Daniyam C. Gastroduodenal diseases on the Jos plateau, Nigeria. Trans R Soc Trop Med Hyg 1994; **88**: 413-414.
8. Dixon M F, Genta R M, Yardley H, Correa P. Classification and grading of gastritis. The updated Sydney system. Am J Surg Pathol 1996; **10**: 1161-1181.
9. Malu A O. Gastric and duodenal histology of patients undergoing endoscopy at the Jos University Teaching Hospital, Jos, Nigeria. Nigerian Medical Practitioner 1994; **28**: 42-43.
10. Oluwasola A O, Ogunbiyi J O. Chronic gastritis and *Helicobacter pylori* infection in University College Hospital Ibadan, Nigeria- a study of 85 fibreoptic gastric biopsies. Nig J Med 2004; **13(4)**: 372- 378.
11. Agatha A, Malu A O, Bello C S S, Okeke E N, Adisa A O. Comparison of laboratory methods for the detection of *Helicobacter pylori*. Ghana Medical Journal 1998; **32a.**
12. Oluwasola A. O., Ogunbiyi J O. Gastric cancer: aetiological, clinicopathological and management patterns in Nigeria. Nig J Med 2003; **12**: 177-186.
13. Elebute E.A, Ngu V A, Mainwaring A R, . Cancer of the stomach seen at the University College Hospital Ibadan. West Afr med J 1963; **12**: 11-17.
14. Naomi U, Shiro O, Soichiro Y *et al*. *Helicobacter pylori* infection and the development of gastric cancer. N Eng J med 2001; 345(11): 784-789.
15. Aydin O. ***H. pylori* gastritis** and the Sydney system. World J Gastroenterol 2003; 9: 2232-2235.