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HISTOPATHOLOGICAL EVALUATION OF H. PYLORI ASSOCIATED GASTRIC LESIONS IN BENIN CITY, NIGERIA
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# HISTOPATHOLOGICAL EVALUATION OF H. PYLORI ASSOCIATED GASTRIC LESIONS IN BENIN CITY, NIGERIA

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## ABSTRACT

***Background*: Endoscopic biopsy of the gastric mucosa allows early diagnosis, grading, staging and classification of gastric diseases. Helicobacter pylori, has been recognized as a major aetiologic factor for chronic gastritis, benign gastric ulcers and gastric adenocarcinoma and lymphoma. The loco-regional variability in the prevalence of Helicobacter pylori and associated diseases in Nigeria, emphasise the need for evaluation of subsets of a heterogeneous population like ours**

***Objective*: To determine the frequency of helicobacter pylori in gastric endoscopic biopsies and document the pathology of gastric lesions commonly associated with Helicobacter pylori infection.**

***Design:* Retrospective descriptive study.**

***Settings*: University of Benin Teaching Hospital (UBTH), and Biogenics Histopathology Laboratory (a private Histopathology Laboratory), both based in Benin City, Niger Delta region of Nigeria.**

***Subjects*: Endoscopic gastric biopsies recorded in the surgical pathology register of the department from 2005-2009 were studied and relevant demographic and clinical information extracted from the registers, original request cards and patient case files. The clinical data and slides processed from paraffin embedded tissue blocks of endoscopic biopsies of gastric lesions seen from year 2005 to 2009 were studied, analyzed and statistically presented.**

***Results*: Total number of specimens studied was 142. Chronic gastritis was present in 117(82.39%) specimens; 9(6.34%) were benign gastric ulcers; 3(2.11%) were gastric polyps; and 11(7.75%) were gastric malignancies. Helicobacter pylori, was demonstrated in 55.6% of all specimens. The peak age for Chronic Gastritis and Gastric Cancer is the 6th decade. Amongst patients with chronic gastritis, inflammatory activity was present in 65%; atrophy in 53%; and intestinal metaplasia in 16.6%. All gastric malignancies seen were intestinal type adenocarcinomas.**

***Conclusion*: The spectrum of lesions diagnosed in gastric endoscopic biopsy specimens in Benin, their frequency and associations are largely comparable to what has been described elsewhere in Nigeria and Africa.**

***Key words*: Helicobacter Pylori; Gastric lesions; Endoscopic biopsies.**

## INTRODUCTION

Helicobacter Pylori is associated with approximately 80%-90% of cases of chronic gastritis worldwide1. H. Pylori gastritis confers a 15%-20% lifetime risk of developing peptic ulcer disease. It is found in 95% of duodenal ulcers and 70-80% of gastric ulcers2. Helicobacter pylori, was named a group 1 (definite) carcinogen in 1994 by the International Agency for Research on cancer (IARC). Forty three to eighty three percent of gastric carcinoma biopsies and approximately 90% of Mucosa Associated Lymphoid Tissue (MALT) lymphoma biopsies have been found to be positive for Helicobacter pylori3.

The prevalence of H. Pylori infection in adults approaches 90% in developing countries, particularly in the tropics where exposure occurs relatively early in life. In industrialized nations exposure tends to occur later in life with lower percentage of infected adults (20%-30% by age 50). The prevalence has been steadily declining in industrialized and emerging countries

probably due to increased sanitary conditions. However, despite declining rates of the infection in general the prevalence rates of H. Pylori in patients who undergo endoscopy remain significant (4).

In Japan, Sepulveda and Coelho prospectively studied 1526 cases. One thousand two hundred and forty-six patients were found to be H pylori positive. Out of these, 36 (2.9%) developed carcinoma over a mean follow up period of 7.8 years. Twenty-three were intestinal type cancers, 13 were diffuse5. None of the 280 H pylori negative patients developed cancer.

Caputo et al did a 10 year review of 60 biopsies with diagnoses of gastric adenocarcinoma. H pylori was found in 35 (58%) of the analyzed biopsies. Twenty-four of the 35 H pylori positive cases were of intestinal type, 9 were diffuse adenocarcinoma, and, 2 were mixed (6).

In a series of 31 MALTomas, Bouzourene et al, recorded 18(58%), Helicobacter pylori positive cases7. Wotherspoon et al (United Kingdom) and Stolle et al (Germany) demonstrated stronger associations. They found histologic evidence of H pylori infection in 92% and 98% respectively amongst patients with gastric lymphomas8, (9).

Although, some work has been done in Nigeria in some of our tertiary health / academic institutions, there is a need for continued evaluation of subsets of a heterogeneous population like ours. With increasing availability of endoscopic services in Nigeria, data collection and evaluation has become imperative, to provide a basis for the adoption of recommended diagnostic, prognostic and therapeutic guidelines for the management of H. pylori associated lesions and gastric diseases in general.

## MATERIALS AND METHODS

This is a five year (January, 2005-December, 2009) retrospective, descriptive study of gastric lesions reported in the Department of Morbid Anatomy, University of Benin Teaching Hospital (UBTH), and Biogenics histopathology Laboratory(a private Histopathology Laboratory based in Benin) .

Endoscopic gastric biopsies recorded in the surgical pathology register of the department from 2005-2009 were studied and relevant demographic and clinical information extracted from the registers, original request cards and patient case files.

Original slides were retrieved and reviewed. All available formalin fixed and paraffin embedded tissue blocks of gastric endoscopic biopsies within this period were resectioned at 2-3$\mu$m and stained with Haematoxylin and Eosin. Modified Giemsa stain, and Alcian blue / PAS stain were used for verification of Helicobacter pylori and demonstration of intestinal metaplasia respectively. All biopsies with missing blocks were excluded.

Biopsies were classified using the Updated Sydney system of classification of gastritis10 and the WHO and Lauren classification of gastric cancers11, 12. The pathological reports and diagnoses of all cases studied were reviewed, and all cases reconfirmed, classified and graded.

Statistical analysis was done with SPSS11.0for windows. Results were presented in simple frequencies and a $P < 0.05$ was considered statistically significant.

## RESULTS

A total of 13,255 biopsies were received at the Morbid Anatomy Department of the University of Benin Teaching Hospital (UBTH) and The Biogenics Histopathology Laboratory over the five year period of this study. The total gastrointestinal specimen was 2,554 out of which 292 were of gastric origin. Out of the 292 gastric specimens, 238 were endoscopic biopsies, of these, only 142 cases had tissue blocks and clinical data available, these constituted our study population.

Of the 142 patients, 74 were males (52.1%) and 68 were females (47.9%). The male female ratio was 1.1:1.The ages of this study population (Table I and Figure I), range between 15 and 86 years. The modal age group was 50 – 59 years. The mean age is 48.6 years +1.52 SD). the mean age for males and females are 47.4 years+ 1.46 SD and 49.9 years +1.58 SD respectively. p-value =0.123.

The cases with histological diagnosis of Chronic Gastritis were 117 (82.39%), other non cancerous Gastric Lesions were 12 (8.45%), normal Gastric biopsies were 2 (1.41%) and gastric Malignancies were 11 (7.75%).

The overall rate of Helicobacter pylori is 79(55.6%) out of 142 patients.

For the 117 patients with chronic gastritis, the age range was between 15 and 86 years, mean was 48.6 years+1.56 SD and modal age group was 50-59 years (Table I and Figure 1). There were 60 males and 57 females. Male to female ratio was 1.05:1.

Seventy four (63.2%) of the patients with chronic gastritis had antral biopsies only, 26(22.2%) had corporal biopsies only, while 17(14.5%) cases has both antral and corporal biopsies. Analysis of all biopsies showed a total of 91 antral biopsies and 43 corporal biopsies. Further analyses of the 17 cases with both antral and corporal biopsies showed, pangastritis in 15(88.2%) cases, while 2(11.8%) cases had gastritis restricted to the antrum. Chronic Inflammation was mild in 10 cases (8.5%); moderate in 56 cases (47.9%); and marked in 51 cases (43.6%).

The frequency of Helicobacter pylori positivity in patients with Chronic Gastritis was 69(59.0%). Density of H. pylori was mild in 21(17.9%), moderate in 30(25.65%), and marked in 18(15.4%) of cases (Table II). The 69 patients with H. pylori positive biopsies

were made up of 38 males (64.4%) and 31 females (35. 6%). H. Pylori colonization is not recorded in the 0-9 year age group. Thereafter it steadily rises, peaks in the 40-49years age group (a decade before the modal age for chronic gastritis and gastric malignancies), then slowly declines (Figure II).

Neutrophil infiltrates (activity) were present in 76 cases (65%) while 41 cases (35%) were non active. Glandular atrophy was present in 62cases (53%), while 55 patients had non-atrophic chronic gastritis. Only 19 (16.3%) patients had intestinal metaplasia (Table II).

Other Gastric Lesions seen are 9 cases of Gastric Ulcers and 3 cases of Gastric Hyperplastic Polyps making up 12 cases (9.16% of all lesions seen - Table I). There were 6 Males and 6 Females. Age range was 15years to 72years. The ulcer edge biopsies were antral biopsies in 6 cases and corporal biopsies in 3 cases. They were from 4 males and 5 females. All showed some degree of atrophy, and 6 cases had varying densities of H. pylori colonization. The three polyps were from 2 males and 1 female. 2 were antral polyps, and 1 was a polyp from the corpus which showed mild H. pylori colonisation.

There are 11 cases of gastric cancers seen in this study consisting of 7 males and 4 females with a M: F ratio of 1.75:1. The age range is 40- 72years with a mean of 52.7years and peak age group being 50-59years (Figure I).

All cases were intestinal type adenocarcinoma. They were six cases of tubular adenocarcinomas (54.5%); two papillary adenocarcinomas (18.2%); two solid-type adenocarcinomas (18.2%) and one mucinous adenocarcinoma (9.1%). Seven of the tumours were from the antrum while four were from the corpus.

**Table 1**
*Age distribution of patients*

| Age Group | Ghronic Gastritis | Other Lesions (Ulcers And Polyps) | Gastric Cancer. | Normal Biopsies | Total |
|---|---|---|---|---|---|
| 0-9 | - | - | - | - | - |
| 10-19 | 1 | 1 | - | - | 2(1.4%) |
| 20-29 | 8 | 1 | - | - | 9(6.3%) |
| 30-39 | 12 | 1 | - | - | 13(9.2%) |
| 40-49 | 25 | 3 | 2 | 1 | 31(21.8%) |
| 50-59 | 32 | 2 | 5 | 1 | 40(28.2%) |
| 60-69 | 22 | 2 | 3 | - | 27(19.0%) |
| 70-79 | 12 | 2 | 1 | - | 15(10.6%) |
| 80-89 | 5 | - | - | - | 5(3.5%) |
| Total | 117(82.39%) | 12(8.45%) | 11 (7.75%) | 2(1.41%) | 142(100%) |

**Table 2**
*Frequency analyses of graded variables in chronic gastritis*

| Variable | None | Mild | Moderate | Marked | Total |
|---|---|---|---|---|---|
| Chronic Inflammation | 0(0%) | 10(8.5%) | 56(47.9%) | 51(43.6%) | 117(100%) |
| Activity | 41(35.1%) | 30(25.6%) | 28(23.9%) | 18(15.4%) | 117(100%) |
| Atrophy | 55(47.0%) | 20(17.1%) | 40(34.2%) | 2(1.7%) | 117(100%) |
| Intestinal Metaplasia | 96(83.8%) | 5(4.3%) | 9(7.7%) | 5(4.3%) | 117(100%) |
| Helicobacter Pylori | 48(41.0%) | 21(17.9%) | 30(25.6%) | 18(15.4%) | 117(100%) |

**Figure 1**
*Age distribution chart*

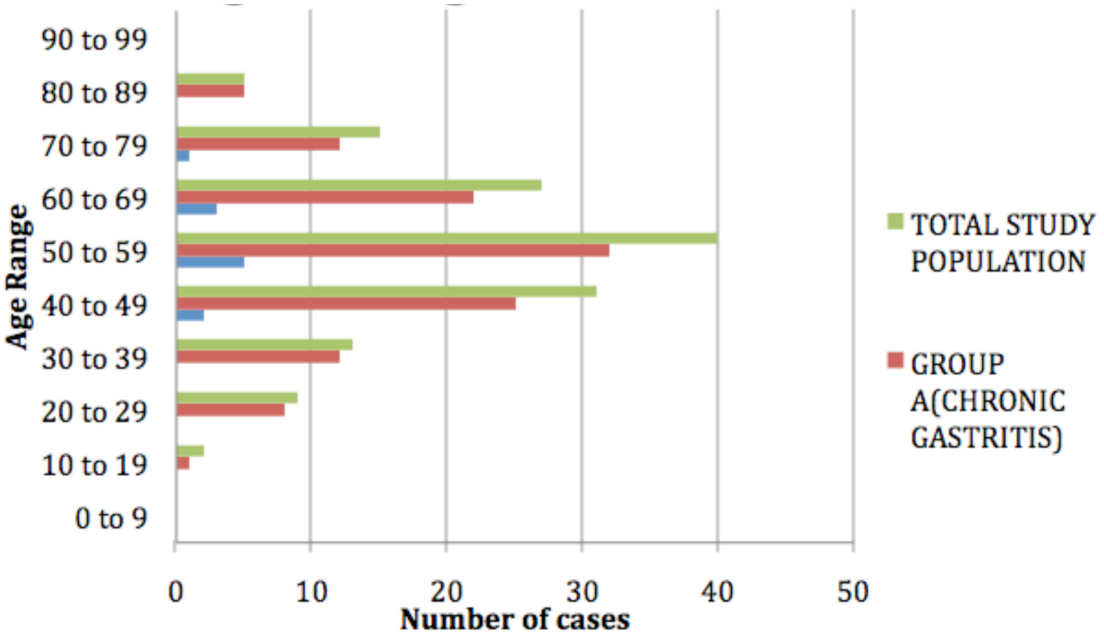
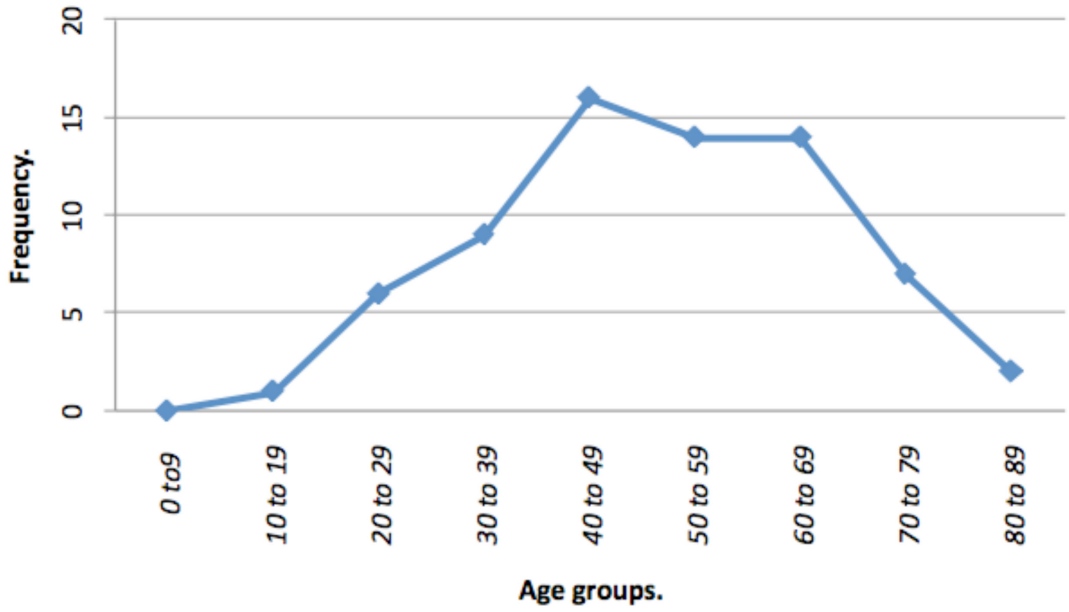



**Figure 2**
*Age distribution of H.pylori positive chronic gastritis patients*




## DISCUSSION

This study evaluates the histopathological features of H. Pylori associated gastric lesions as seen in gastric endoscopic biopsies taken in Benin City.

A total of 142 specimens were seen; 117 (82.39%) had a diagnosis of chronic gastritis; 9(6.34%) were gastric ulcer biopsies; 3(2.1%) were polyps; 11(7.75%) were gastric adenocarcinoma; and 2(1.4%) were normal biopsies.

The ages of the 117 patients with chronic gastritis ranged between 15 and 75 years. The mean age was 48.6 years and the modal age group was 50-59 years. This mean age is similar to that recorded by Awolola in Lagos13 and Oluwasola in Ibadan14, Nigeria who reported mean ages of 48.9 years and 44.4 years respectively. The modal age group in this study is 50-59years, the same age group reported by Oluwasola in Ibadan14, which is a decade later than that reported by Awolola in Lagos13. Chronic

gastritis was first noticed in the 2nd decade peaking in the 6th decade and tailing off in the 8th decade, this pattern is the same observed by Awolola and Oluwasola13, 14. This age distribution is mirrored in the Helicobacter pylori positive patients, though the peak age is a decade earlier. Studies from Europe and Japan showed that chronic gastritis is uncommon in children and young adults; this suggests a later age at acquisition of infection, but a higher percentage (approx. 90%) of persons, 60 years and above has some form of gastritis (15).

The prevalence of Helicobacter Pylori amongst all patients in this study is 55.6%. It is slightly higher amongst patients with Chronic Gastritis (59%). This figure is high when compared to 42.1% recorded in the study of 114 patients by Awolola in Lagos south west Nigeria13; the 22.4% prevalence in the study by Oluwasola in Ibadan south west Nigeria14; or 25% in the Ugandan study by Warbinger16. However, the latter two studies were in smaller sample populations (85 and 56 patients respectively). Higher prevalence rates have been recorded in other studies from Nigeria and parts of Africa, Holcombe recorded 84% rate of Helicobacter pylori infection in M aiduguri17, while Diomande et.al in Cote d' Ivore recorded 91.3%18. These findings show the wide variability in H. pylori prevalence recorded in different regions.

The prevalence rate of Helicobacter pylori in, different studies is subject to, the accuracy of biopsy techniques. Taking into consideration, the sometimes patchy nature of gastritis, multiple biopsies are recommended to improve the yield. The usefulness of this recommendation is reflected in this study by the fact that patients with dual biopsies (antral and corpus) had a higher prevalence of Helicobacter pylori -64.7% amongst 17 patients. Awolola also recorded a higher prevalence of 47.8% amongst 23 patients with dual biopsies compared to 42.1% in total study population of 11 413.

Most of our Helicobacter pylori positive patients had moderate to marked chronic inflammation; however a statistically significant relationship was not demonstrated between the density of Helicobacter pylori infection and the grade of chronic inflammation. This contrasts with the findings of Awolola in Lagos, and Oluwasola and Ogunbiyi in Ibadan13, 14. However, it is known that in some specimens, Helicobacter pylori may be found in the mucus or close to the mucosal cells with little or no inflammation though a repeat biopsy or multiple sampling will reveal inflammation and mucosal damage19. Furthermore possible recent use of antimicrobial therapy -which cannot be ruled out- often eradicates or decreases helicobacter pylori density, without immediate concomitant or commensurate disappearance of chronic inflammation10. These factors may cause a relative discordance between the density of Helicobacter pylori and the grade of chronic inflammation.

The association between Helicobacter pylori infection and the presence of chronic inflammation in the mucosa is reflected in the age distribution of patients with chronic gastritis and that of the Helicobacter pylori infection population (Figure 1 and 2). A general population based study, rather than a study based on dyspeptic/ symptomatic patients may better demonstrate statistically the significance / strength of association.

Other gastric lesions seen were nine cases of gastric ulcer biopsies (6.34%), and 3 gastric hyperplastic polyps (2.11%). Out of 9 ulcers, 6 (66.67%) were positive for Helicobacter pylori. Kidd et al. documented a 7% rate for gastric ulcer, 75% of these were H. Pylori positive in a series of 2286 cases (20).

Gastric polyps are commonly encountered during upper gastrointestinal endoscopy. In this series there were 3 polyps out of 142 specimens, all were hyperplastic polyps, and one was positive for Helicobacter pylori. Hyperplastic polyps usually represent about 75% of gastric epithelial polyps and the frequency increases with age (21).

There are 11 cases of gastric cancers seen in this study consisting of 7 males and 4 females with a M: F ratio of 1.75:1. This sex distribution agrees with other studies that have documented that gastric cancer has a male predilection (20-22).

The age range of patients was 40 years to 72 years. The mean age is 52.7 years and peak age was the 6th decade. Nine (81.8%) out of 11 patients were 50 years and above (Table I). These are similar to Awolola's findings in Lagos. He documented mean age of 58.4 years; and a modal age group of 50-59 years13. Oluwasola and Ogunbiyi in Ibadan also recorded a mean age of 55.8 years (14).

All gastric cancers seen in this study were intestinal-type adenocarcinoma. Adenocarcinomas constitute approximately 90% of gastric cancers seen in most studies, and about 30% of adenocarcinomas usually are of the diffuse type23. Studies from the southwest and northern zones of Nigeria have reported that 56-73.3% of gastric malignancies are intestinal adenocarcinomas, and 22-25% are diffuse type13, 14, 24. The fact that only intestinal-type adenocarcinomas were seen in this study may be because of the small sample size (only 11 cases out of 20 endoscopically diagnosed tumours had blocks available for review.

Out of the eleven cases seen, there were two papillary adenocarcinomas (18.2%), two solid-type adenocarcinomas (118.2%) and one mucinous adenocarcinoma (9.1%); the remaining six showed predominantly tubular pattern of growth with some having focal papillary or solid differentiation.

Topographic distribution of the tumours is mainly antral. Seven tumours were from the antrum

while four tumours were from the corpus. Local studies show that 60-80% of gastric cancers in Nigeria are located in the antrum 24, 25, however, Awolola13 and Obekpa et al26, documented a predominance of corporal tumours.

Intestinal Adenocarcinomas are known to have almost 100% association with Helicobacter pylori. Evaluation of seven specimens that had non-cancerous adjacent mucosa showed three cases (42.8%) were positive for Helicobacter pylori. Although, our small sample may not well reflect the larger population, these rates are similar to what has been recorded in other parts of the country (13-14).

## CONCLUSION

The spectrum of lesions diagnosed in gastric endoscopic biopsy specimens in Benin City, Nigeria, their frequency and associations are largely comparable to what has been described elsewhere in Nigeria and Africa.

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