Histo morphology of Helicobacter positive gastric biopsies - Libyan study of 607 cases

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Abstract

Helicobacter pylori (H. pylori), a microaerophilic, flagellated, curved or spiral, gram-negative bacterium, selectively colonizes the human stomach. Its infection affected more than half of the world's population. It is assumed that the sequence of events in gastric cancer is as follows: chronic gastritis, atrophy, intestinal metaplasia (IM), dysplasia, and carcinoma. It is also known that H. pylori can be involved in the chain of these chronic phenomena.
Aim: To know the local incidence and histomorphological pattern of Helicobacter gastritis, especially its association with intestinal metaplasia, dysplasia and malignancy in gastric biopsies.

Methods: Gastric biopsy cases were selected from database of Tripoli medical center from 2002 to 2008. The biopsies were assessed for the parameters as per revised Sydney System. The age, gender and the microscopic findings in the gastric biopsies were tabulated and analysed.
Conclusion: Based on these results, H. pylori is a known common associated agent for chronic gastritis with the progression of atrophy, metaplasia and dysplasia and the high bacterial load possibly results in lymphoid proliferation.
Key wards: H. pylori, chronic gastritis, gastric carcinoma

Introduction

Gastric cancer is the second commonest fatal malignancy in the world with a high incidence in China. H. pyloriinfection is an important factor in the pathogenesis of many gastrointestinal diseases including gastric cancer and even in some extraintestinal disorders. The clinical outcome of this disease is dependent on many variables, including H. pylori genotype, innate host physiology, genetic predisposition and environmental factors [1,2]. The studies showed that eradication of H. pyloriinfection, especially at the early stage, is effective in preventing H.pylori-related gastric carcinogenesis and this strategy is more useful in patients without atrophic gastritis or intestinal metaplasia [3].The infection is widespread throughout the world, and is present in about 50% of the global humanpopulation; with 80% in developing countries and 20% in industrialized countries[4]. It is the major cause of chronic gastritis that plays a key role in the etiology of peptic ulcer,but there are controversial reports regarding its pathogenesis in intestinal metaplasia,dysplasia and malignancy [5, 6, 7]. The prevalence of Helicobacter gastritis in Libya remains unknown.The current study is aimed to know the local incidence and histomorphological pattern of Helicobacter gastritis, especially its association with intestinal metaplasia, dysplasia and malignancy in gastric biopsies.

Methods

We selected all gastric biopsy cases from database of department of anatomical pathology, Tripoli Medical Centre referred during January 2002 to December 2008. This retrospective review consists of only those patients demonstrating the H. pylori bacteria in their gastric endoscopic biopsies, who presented with clinical features of gastritis. Gastric biopsies were paraffin embedded, sectioned at 4 μm and stained with haematoxylin and eosin. The bacteria was identified with its spiral/ curved morphology either in H&E stained sections or in modified Giemsa sections.These biopsies were scored semiquantitatively according to the updated Sydney classification [8]. The following histological features were examined on each slide: type of gastritis, density of inflammation, density of *H pylori* infection, eosinophil count, lymphoid aggregates, intestinal metaplasia and dysplasia. The age, gender, presence, site of ulcer and the microscopic findings in the gastric biopsies were tabulated and analysed.

Sydney classification:

Feature	Definition	Grading guidelines
Chronic inflammation	Increased lymphocytes & plasma cells in lamina propria	Mild, moderate, or severe increase in density
Activity	Neutrophilic infiltrates of lamina propria, pits, or surface epithelium	Mild: Less than 1/3 of pits & surface infiltrated. Moderate; 1/3 to 2/3. Severe: more than 2/3.
H.pylori density	H.pylori density	Mild colonization: Scattered organisms covering less than 1/3 of the surface.Severe: large clusters or a continuous layer over 2/3 of surface. Intermediate numbers: moderate colonization
Intestinal metaplasia	Intestinal metaplasia of surface epithelium	Mild: less than 1/3 of mucosa involved. Moderate: 1/3 to 2/3. Severe: more than 2/3

Results

H. pylori were detected histologically in a total of 607 patient's gastric biopsies,out of 1256 patients who underwent endoscopic gastric biopsy, during this seven years period, constituting 48.3%.

The age&sex distribution

There were 275 male (45.3%) & 332 female (54.7) cases. In male, the maximum cases were seen in 7th decade (18.2%) and in female the maximum cases were seen in 3rd decade (23.2%). Minimum age was a boy with 10 years old and the maximum age was a female with 88 years old (Chart 1).

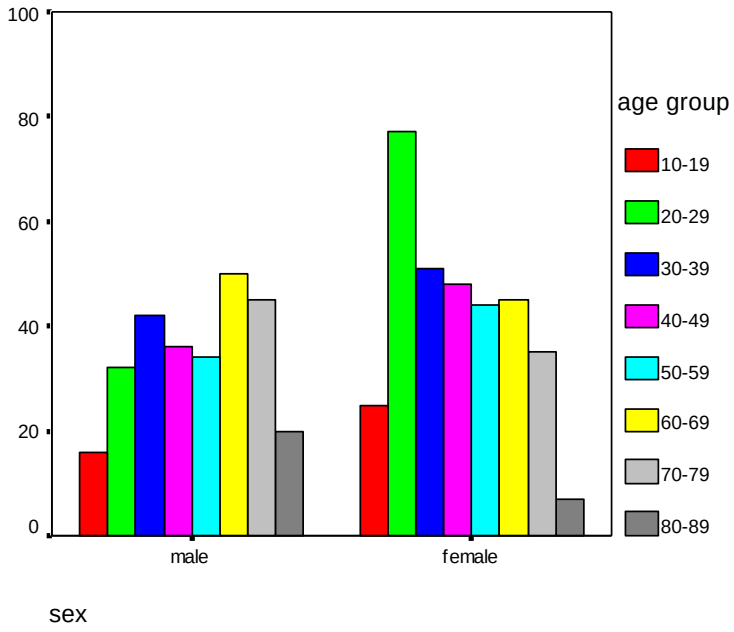

Chart 1: The age & sex distribution in helicobacter associated gastritis.

The presence and the site of ulcer

There were 137 cases (22.6%) of helicobacter gastritis with ulcer and 470 cases (77.4%) without ulcer.The ulcer was in gastric corpus in 5 cases (3.6%), 31 cases (22.6%) in antrum and in 101cases (73.7%), the information about site was not mentioned. There were no cases with perforation of ulcer. The ulcer size was varied from 0.5-2.0 cm in maximum dimension, majority (71%) less than 1.2 cm.

The type of gastritis

The majority of cases are of non-atrophic gastritis, which was noted in 529 (87.4%) cases. Atrophic gastritis was found in 78 cases (12.6%).

The density of inflammation

There were 85 cases (14%) of mild inflammation, 220 cases (36.4%) of moderate inflammation and 300 cases (49.6%) of severe inflammation (Chart 2). The inflammatory cells were mainly lymphocytes, plasma cellsand polymorphonuclear infiltrate in active inflammation (Figure 1). Two cases did not show significant inflammatory cell infiltrate.

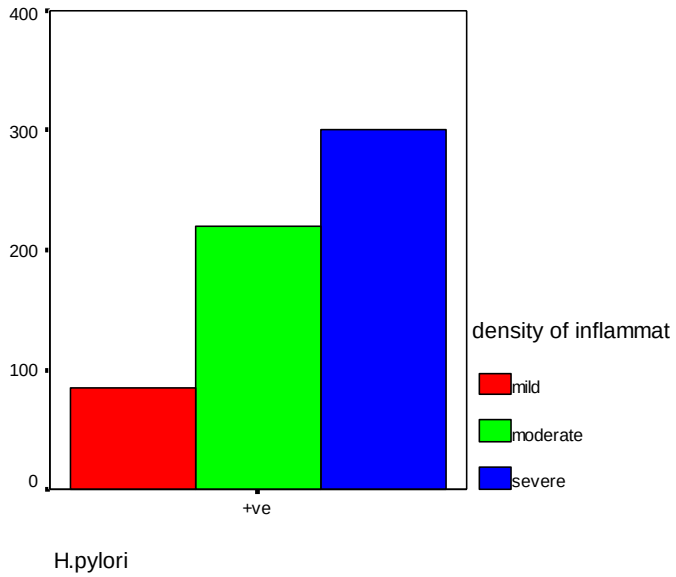

Chart 2: The density of inflammation in helicobacter associated gastritis.

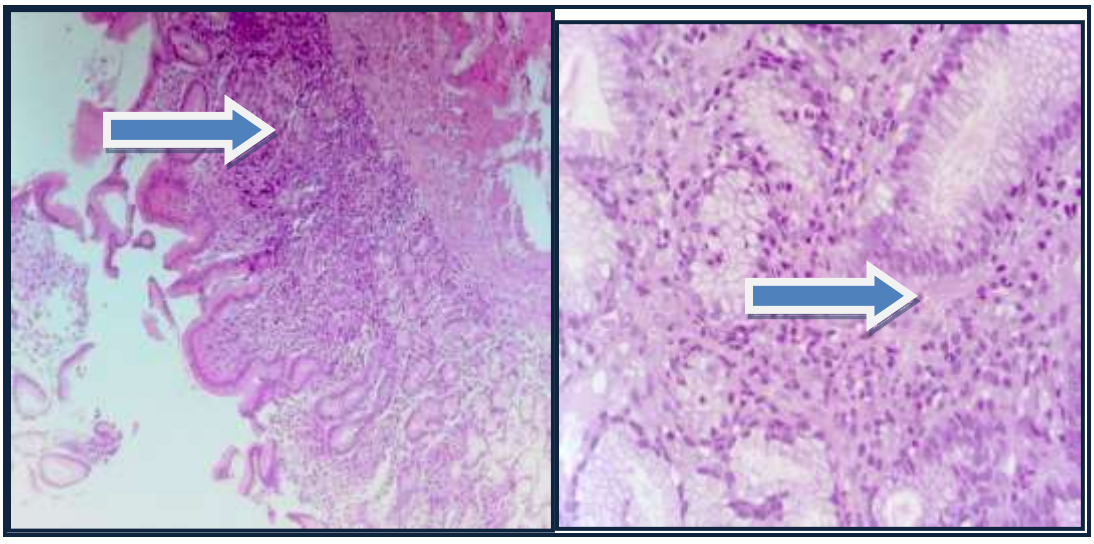

Figure 1: Photomicrograph reveals chronic active gastritis with dense inflammatory cells (x5 & x10 power) (H & E stain).

The density of helicobacter infection

There were 170 cases(28%) with mild density,268 cases (44.2%)with moderate and169 cases (27.8%) of severe density (Chart 3). The bacteria were seen as spiral or curved shaped mainly on the surface epithelium and in some cases in gastric pits (Figure 1).

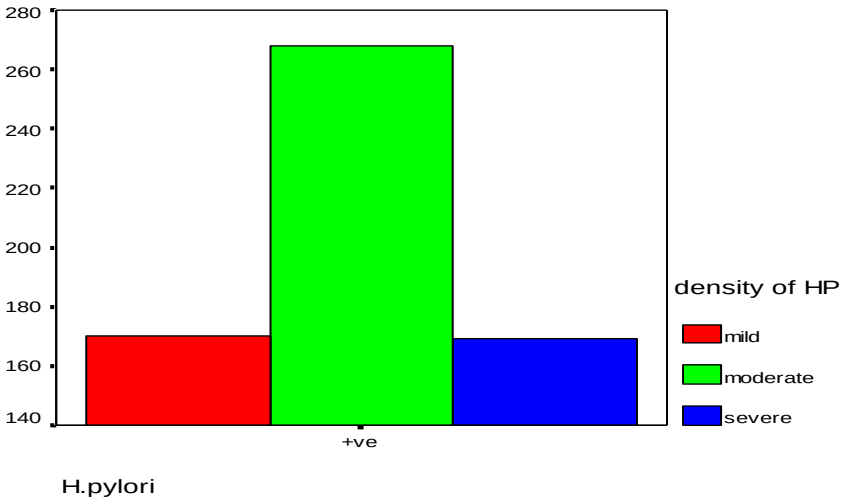

Chart 3: The density of helicobacter infectionin helicobacter associated gastritis

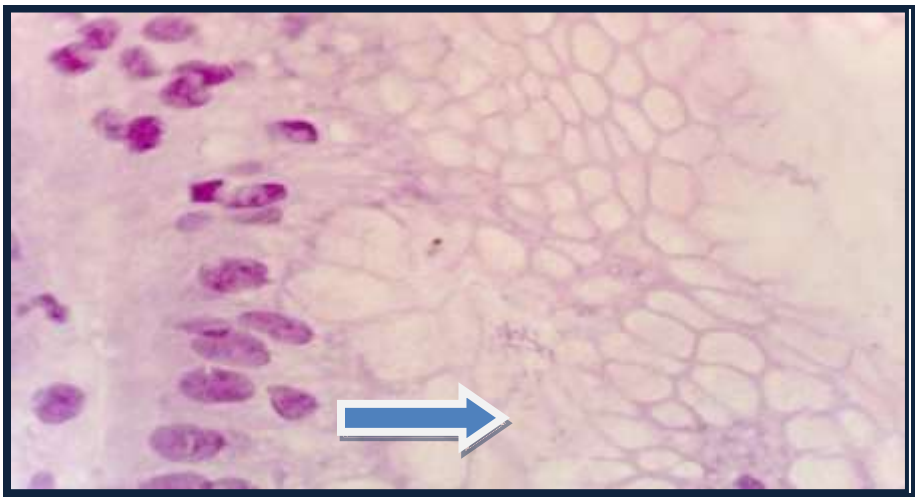

Figure 2: Photomicrograph reveals H. pylori spiral organism (arrow) (x40 power) (H & E stain).

Distribution of H.pylori & inflammation

In cases with mild density of bacteria, 70 cases (41.1%) showed moderate inflammation,62 cases (36.5%) with mild inflammation and 38 cases (22.4%) with marked inflammation. Among biopsies with moderate density of bacteria, 13 cases (4.9%) showed mild inflammation, 116 cases (43.3%) showed moderate inflammation and 139 cases (51.9%) showed severe inflammation. In severe density of bacteria, ten cases (5.9%) showed mild inflammation, 34 cases (20.1%) showed moderate inflammation and 125 (74%) cases showed severe inflammation (Chart 4).

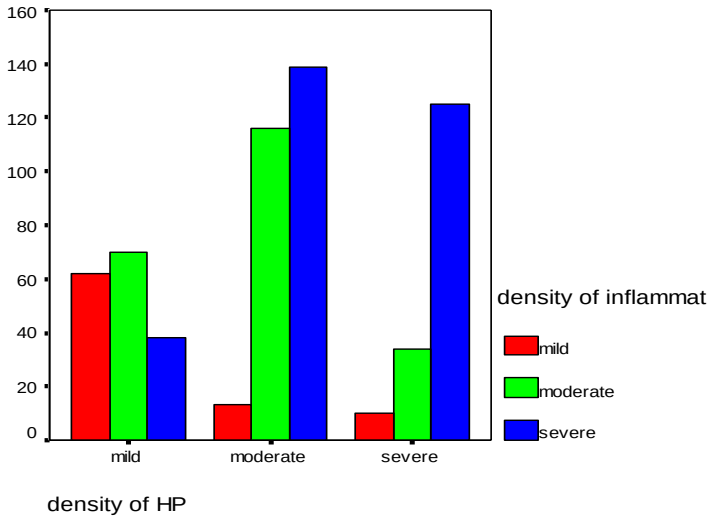

Chart 4:Distribution of H. pylori & inflammationin helicobacter associated gastritis.

Eosinophil count and lymphoid aggregate density in helicobacter gastritis

Eosinophil infiltrate were noted in 32 biopsies. Occasional eosinophils were found in 4 cases (0.7%), few eosinophils found in 18 cases (3%) and many eosinophils found in 10 cases (1.6%) whereas the majority was negative for eosinophils (575) cases (94.7%). The gastric biopsies of 260 cases revealed lymphoid aggregates (Figure 3). Occasional lymphoid aggregate was found in 30 cases (4.9%), few lymphoid aggregate in 82 cases (13.5%), many lymphoid aggregate was found in 148 cases (24.4%) and 347 cases (57.2%) were negative.

Among the cases with lymphoid aggregates, severe lymphoid aggregates appeared to show marked density of bacteria, moderate lymphoid aggregates in majority of cases appeared to show marked bacteria and about one third cases with mild to moderate bacteria. Even majority of cases with mild lymphoid aggregates, also revealed severe bacterial density (Chart 5).

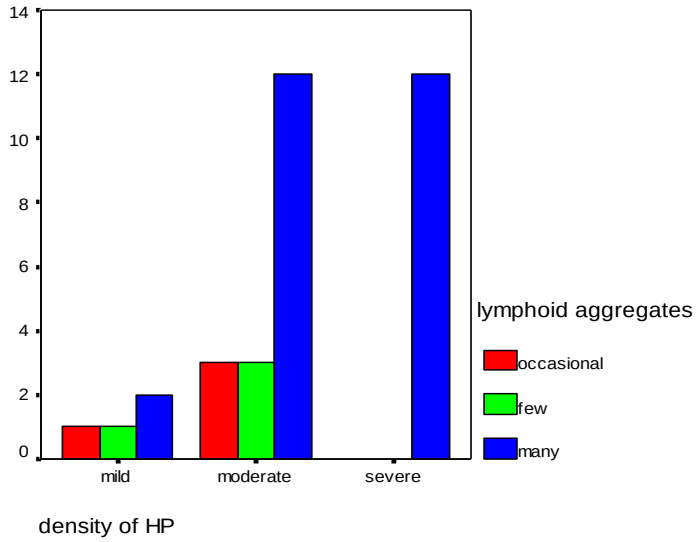

Chart 5: The relation of the density of lymphoid aggregate with the density ofH.pylori.

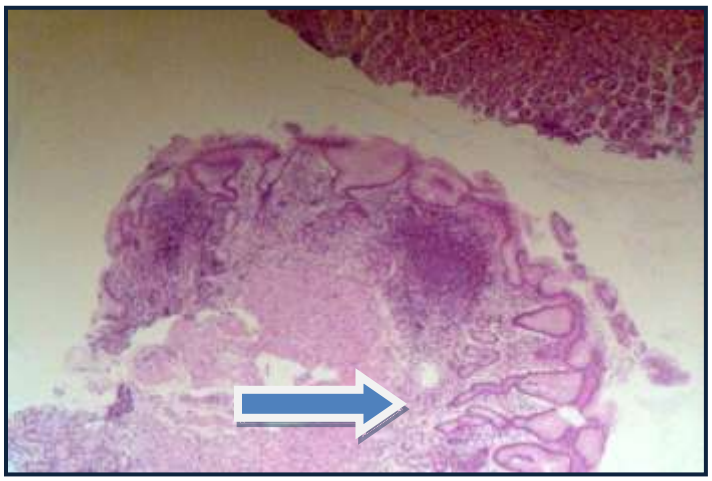

Figure 3: Photomicrograph reveals lymphoid aggregate (x5 power) (H & E stain).

The presence of intestinal metaplasia in helicobacter gastritis

56 cases (9.2%) showed intestinal metaplasia (Figure 4). Incomplete metaplasia was found in 53 cases (94.6%) whereas complete metaplasia was rare and detected in 3 cases only (5.4%) and 551 cases (90.8%) was negative. Twocases of metaplasia was in the body, 10 cases was in the antrum and 44 cases the site was not mentioned (Chart 6).

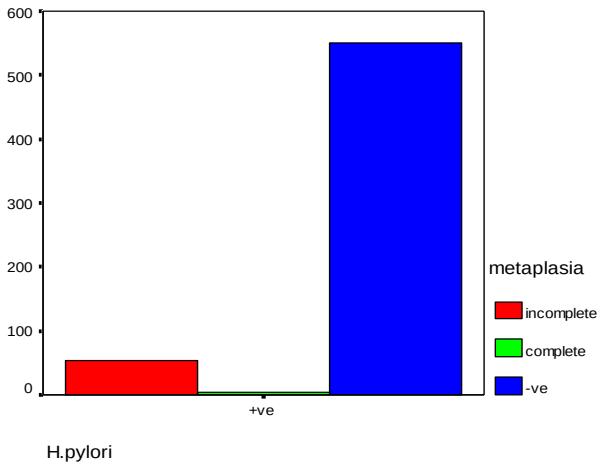

Chart 6: Intestinal metaplasia in helicobacter gastritis

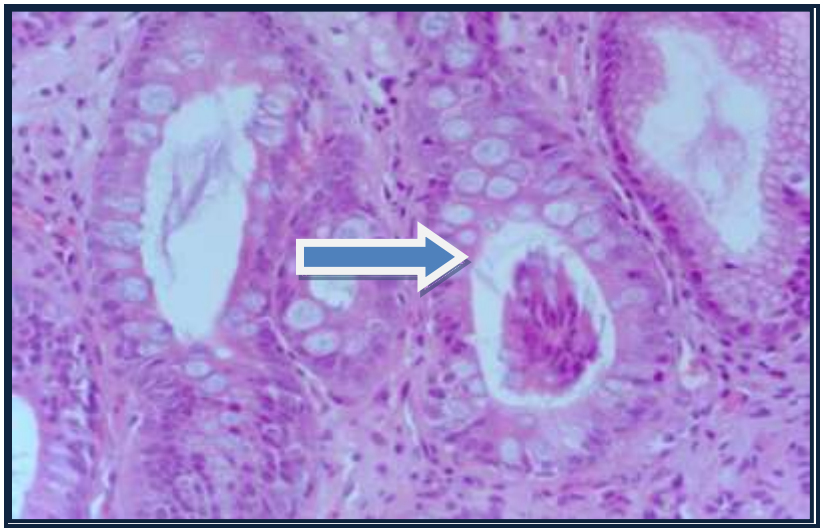

Figure 4: Photomicrograph reveals intestinal metaplasia (power x10) (H & E stain).

The presence of dysplasia in helicobacter gastritis

Twenty one (3.5%) of gastritis cases showed gastric dysplasia.Low grade dysplasia was found in 14 cases (66.7%) and high grade dysplasia was found in seven cases only(33.3%). Among these, eleven cases of low grade dysplasia and 3 cases of high grade showed associated incomplete metaplasia.

Discussion

Since the discovery of H. pylori in 1983 by Warren and Marshall, there were several reports stating the prevalence and various lesions associated with the bacteria. In current gastric biopsy based study, we demonstrated H. pylori in 48.3% of gastric biopsies. This incidence appears less than other North and West African countries. Jemilohun and his coworkers [9] showed H.pylori in 63.5% of 52 gastritis patients with dyspepsia and in Dooley study [10] H. pylori wasdetected in 85.7% of 42 asymptomatic gastritis cases. The prevalence of H. pylori infection appears to vary in different countries, though in general higher in children than in adults, Mohammad and his colleagues [11]noted the prevalence of H.pylori of 72.3% among Egyptian school children, possibly due to lower standards of personal hygiene in younger populations [12].The prevalence of H. pylori in Israel,Algeria,Saudi Arabia, turkey with a high level of infection in childhood

(40-70 %), which increases with age to 85-90 % [13]. Prevalence of gastritis increased significantly in advancing age with maximum(47%) in 7th decade [10]. We basically studied H.pylori in symptomatic patients who underwent endoscopic biopsy. Adults who currently harbour the organism are more likely to have been infected in childhood.

Sultan and Li[14]noted the infection rate similar in male and female and the prevalence rate is less than 10% among children less than 12years, 20% in less than 30years and above 50% in aged more than 60. In current study, in male, the maximum cases were seen in 7th decade (18.2%) and in female the maximum cases were seen in 3rd decade (23.2%). We noted higher incidence among female(54.7%) than male; similar to Jemilohun study [9]. On the otherhandZhang and his co-workers [15] reported the prevalence of H. pylori infection among males higher than that among females.

Ramshoo and his colleagues [16] found a high significant association between H. pylori infection with chronic gastritis both in peptic ulcer patients and healthy volunteers.He noticed 90% association of H. pylori infection and chronic gastritis in peptic ulcer patients.Colonization of the gastric mucosa with H. pyloriresulted in the development of chronic gastritis in all cases of Kandinskystudy [2]. Our study revealed histological frank chronic gastritis in all except two cases (with minimal inflammatory cells) among 607 patients and chronic ulcer was noted in 22.6% of these patients.The ulcer incidence appears to be high comparing to Nigerian study revealing 6.4% [17]. MostH pyloriinfected individuals show antral predominant gastritis, which predisposes them to duodenal ulcers, but rarely causes gastric cancer. On the contrary, patients with corpus-predominant gastritis are likely to develop gastric ulcers, gastric atrophy, intestinal metaplasia and eventually gastric cancer [18]. In our study the ulcer was in gastric corpus in 5 cases (3.6%) and 31 cases (22.6%) in antrum and in 101cases (73.7%), the information about site was not mentioned. Zhang and his coworkers [15]identified glandular atrophy and intestinal metaplasia in 40.3% and 39.9% respectively among antral biopsy, and 14.1% and 13.6% among corpus biopsy. We observed atrophic gastritis and intestinal metaplasia in 12.6% and 9.2% of Helicobacter positive cases respectively. The intestinal metaplasia is mainly seen in antral biopsies(93.3%).Incidence of intestinal metaplasia is similar to Naeem's study [19]

(9.52%), which also noted severe inflammation in 47.6% cases, eosinophil infiltrate in 33.3% cases and lymphoid infiltrate in 23.8% cases.We also found severe chronic inflammation in 49.6% cases, but noted lymphoid aggregates in 42.8% cases and eosinophils only in 5.3%cases.Carilho and his colleagues [20] noted gastric atrophy in 8.3%and intestinal metaplasia in 8.3%.While eosinophils have been observed to comprise part of the inflammatory reaction in acute H. pylori gastritis, the role of the eosinophil in the pathogenesis of chronic gastritis is unknown. In McGovern study[21] the severity of chronic gastritis was significantly correlated with the eosinophil score. There was an increase of H. pylori infection and mucosal lymphoid aggregates rates in parallel with the increasing age of patients noted in the histological assessment of the mucosal sample[22]. We obsevered the presence of lymphoid aggregates as the better marker for the presence and the density of Helicobacter bacteria as the majority of cases with lymphoid follicles show high density of H. pylori. In our study, severe density of H. pylori bacteria is usually associated with severe inflammation(74%), or moderate inflammation(20.1%). Topal and coworkers [23] investigated the relation of H. pyloriwith chronic atrophic gastritis, intestinal metaplasia, and bcl-2 in 52 cases. They found that more the H. pylori intensity, the greater the degree of chronic gastritis, activity and atrophy. The majority of our cases are of non-atrophic gastritis(87.4%) cases. Though several cases were with high density of bacteria, cases going for glandular atrophy were relatively less.Follow-up study among 3433 adults in China, a region with very high rates of gastric cancer demonstrate that *H. pylori* was associated with significant increased risk of progression to dysplasia or gastric cancer with odd ratio 1.8%[24]. Gastric cancer developed in 36 (2.9%) of 1526 Japanese H. pylori-infected patients, especially those with severe gastric atrophy and intestinal metaplasia[25]. Our study showed twenty one (3.5%) of gastritis cases with gastric dysplasia,which is very low in comparison to other study.Naeem [19] from Pakistan detected 19%and Yeh[7]from malaysia noted 31.2%. Low grade dysplasia was found in 14 cases (66.7%) and high grade dysplasia was found in seven cases only (33.3%). Among these, eleven cases of low grade dysplasia and 3 cases of high grade showed associated incomplete metaplasia.In conclusion, our findings acknowledges the global fact that H. pylori is a known common associated agent for chronic gastritis and appear to follow Correa cascade[26] progression of atrophy,metaplasia and dysplasia. The high bacterial load possibly results in lymphoid proliferation. The prevalence of atrophy and intestinal metaplasia is in accordance with some other African countries and that of dysplasia is very low, indicating the further study of CagA genotyping of H. pylori in this region. But the dysplasia is strikingly associated with incomplete dysplasia, which warrants the need of endoscopic surveillance. The possible role of other dietary, environmental and genetic cofactorsfor gastric oncogenesis remainsto beelucidated.

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