

# Chronic Gastritis and *Helicobacter pylori*: A Histopathological Study of Gastric Mucosal Biopsies

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## ABSTRACT

The aim of this study was to observe the histological features of chronic gastritis and associated effects due to *Helicobacter pylori* infection in 176 randomly selected antral biopsy specimens of chronic gastritis cases. The specimens were reviewed for the presence or absence of *H.pylori*. The activity (neutrophilic infiltration) of gastritis and the presence or absence of mucosa-associated lymphoid tissue (MALT) were also noted. Chi-square test (Pearson value) was used to analyze categorical variables. *H.pylori* was detected in 110 (62.5%) cases of chronic gastritis. There was a significant association between *H.pylori* infection and activity of chronic gastritis ( $p=0.002$ ). Lymphoid aggregates were significantly more frequently noted in *H.pylori*-positive patients (68.2%) vs. *H.pylori* negative group (47%), ( $p=0.005$ ). It is concluded that *H.pylori* is significantly associated with active chronic gastritis and with formation of mucosa-associated lymphoid tissue (MALT), which may develop into gastric lymphoma (MALT type).

**Key words:** *H.pylori*. Chronic active gastritis. Mucosa-associated lymphoid tissue (MALT). Neutrophilic infiltration activity.

*Helicobacter (H.) pylori* is a spiral shaped, basophilic, gram negative bacillus that resides exclusively in the gastric mucosa. It is found in all parts of the world. It is believed that half of the world's population is infected with *H.pylori*, with the burden of disease being highest in the developing countries.<sup>1</sup> In India, for example, 80% of the population is infected with this bacterium and most of them have been infected since 10 years of age.<sup>2</sup> The infection with this bacterium is related to overcrowding and poor hygienic conditions. Possible modes of transmission generally described are through direct person-to-person contact between family members and also through contaminated food and water.<sup>3</sup>

Chronic gastritis is chronic inflammation of the gastric mucosa. Although a variety of etiological factors are associated with chronic gastritis, *Helicobacter pylori* is the primary cause. The inflammatory infiltrate is usually characterized by an increase in chronic cells (lymphocytes and plasma cells) in the lamina propria.<sup>4</sup> Presence of polymorphonuclear leukocytes indicates an active component.<sup>4</sup> *H.pylori* was the first bacterium observed to behave as a carcinogen. It is implicated as a risk factor/etiologic agent in a variety of other gastrointestinal disorders, including peptic ulcers and cancers like gastric MALTomas and adenocarcinomas.<sup>5,6</sup> Given the importance of this bacterium in causing gastric pathology, this study was undertaken to observe the

histological features of chronic gastritis, with special emphasis on presence or absence of *H.pylori*, activity (neutrophilic infiltration) of gastric mucosa and presence or absence of lymphoid aggregates.

This was a retrospective cohort study conducted at the Aga Khan University Hospital in Pakistan. The record of histopathology laboratory identified 1080 cases of chronic gastritis during a one-year period, of which 176 cases were randomly selected (every sixth case). The endoscopically derived antral biopsy slides of these patients were retrieved. All the slides were hematoxylin and eosin (H&E) stained. The slides were reviewed by the authors for presence or absence of *H.pylori*. The activity of gastritis (neutrophilic infiltration) was graded on a scale of 0–3, as shown in Table I. The data were entered and analyzed in SPSS Windows 11.5. Chi-square test (Pearson value) was used for categorical variables. Student's t-test was used to compare means. A p-value of less than 0.05 was considered statistically significant.

**Table I:** *Helicobacter pylori* infection and activity of chronic gastritis.

	Activity of gastritis*				
	0	1	2	3	
<i>H.pylori</i> positive	21 (11.9%)	13 (7.4%)	60 (34.1%)	16 (9.1%)	110
<i>H.pylori</i> negative	26 (14.8%)	14 (7.9%)	20 (11.4%)	6 (3.4%)	66
Total #	47	27	80	22	176

**\* Activity of Gastritis:**

Activity refers to presence of neutrophils in the lamina propria (LP) (9). The activity was graded on a scale of 0-3 (modified from Bayerdorffer E, et al.) (9).

0: Chronic inflammatory cells with no neutrophilic infiltration (chronic gastritis only).

1: Neutrophils in LP only.

2: Neutrophils in LP and glandular epithelial lining only (cryptitis).

3: Neutrophils in LP, glandular epithelial lining and lumina (cryptitis and crypt abscesses).

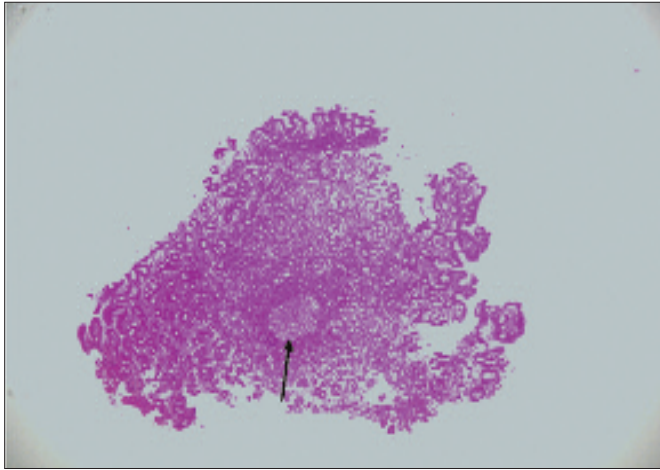
The mean age of the study sample was  $39.6 \pm 15.2$  years ( $n = 173$ , range = 4-76 years). The data on age were missing for 3 cases. The male to female ratio was 1.2:1. *H.pylori* was detected in 110 of 176 (62.5%) cases of chronic gastritis. The mean age of patients in *H.pylori*-

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**Figure 1:** Gastric antral biopsy; low power view showing lymphoid follicle with germinal center 4X.

positive ( $38.9 \pm 15.1$  years, range=4 - 76) and *H.pylori* negative groups ( $40.9 \pm 15.6$ , range=13-74) was not markedly different ( $p=0.4$ ). Sixty (55%) patients with *H.pylori* positivity were males, compared to 36 (54.5%) in the other group ( $p=0.95$ ). Table I shows the activity of gastritis in *H.pylori*-positive and negative groups. *H.Pylori* infection was significantly associated with the activity of gastric inflammation (Pearson  $\chi^2=15.1$ ,  $df=3$ ,  $p=0.002$ ). Lymphoid aggregates were also significantly noted in the *H.pylori* positive cases more frequently, compared to the negative ones (Pearson  $\chi^2=7.8$ ,  $df=1$ ,  $p=0.005$ ). Table I also shows the gastric antral biopsy specimen showing lymphoid follicle with germinal center.

*H.pylori* was detected in 110/176 (62.5%) specimens of chronic gastritis. This is comparable to figures of 50.4% and 66.9% reported in two studies from India.<sup>7,8</sup> The use of histology for detecting *H.pylori*, however, has its own inherent limitations. It may fail to detect organisms because of patchy distribution of bacteria and/or sampling error. Low density infections may, therefore, have been missed. Other specific stains, like Giemsa, for detecting *H.pylori* were not used in this study. Absence of *H.pylori* in histological specimens with chronic gastritis, however, may point towards other causes. It may indicate covert use of non-steroidal anti-inflammatory drug (NSAID) by the patient, when the appropriate history is not available. Presence of granulomas can suggest Crohn's disease. Similarly, lymphocytic gastritis can be associated with gluten enteropathy and eosinophilic gastritis with an allergic condition.

This study showed a significant association between *H.pylori* infection and activity of chronic gastritis. This is in agreement with results of other studies on the topic.<sup>9,10</sup> *H.pylori* may produce gastric epithelial cell damage directly or by stimulating host immune response. Adherence of the organism produces loss of microvilli and irregularity of the luminal border.<sup>4</sup> It is also known to release vacuolating cytotoxins and enzymes, including

urease, which have toxic effects on the epithelium. *H.pylori* induces epithelial cells to release chemokines including GRO- $\alpha$  and IL-8 which are chemotactic for neutrophils.<sup>4</sup> IL-8 also causes neutrophils to produce reactive oxygen radicals (ROR) which cause tissue damage. Other factors released (RANTES and MIP-1 $\alpha$ ) recruit monocytes and lymphocytes which also release pro-inflammatory mediators and act as antigen presenting cells to initiate specific immunity (T-lymphocytes and plasma cells).<sup>4</sup>

Lymphoid aggregates were significantly more frequent in *H.pylori* infected slides. This is in contrast to the result of an Indian study, which failed to show a significant association between *H.pylori* infection and lymphoid aggregates.<sup>11</sup> This study, however, supports the findings of other studies on the subject.<sup>10</sup> The normal human stomach is devoid of organized MALT. *In vitro* studies have demonstrated *H.pylori* specific CD4<sup>+</sup> T-cell clones have been obtained from gastric biopsies of infected patients. These T-lymphocytes extend antigen dependent helper function for B-cell proliferation. The germinal centre is a morphologic indication of lymphocyte response to antigen. The presence of a germinal centre represents a cascade of events that include proliferation of lymphocytes, differentiation of plasma cells, and antibody production. The significant association of *H.pylori* and MALT in this study indicates that the bacterium may induce local humoral and T-cell response in the gastric mucosa. *H.pylori* infection triggers the development of MALT tissue, which can act as a nidus in which a lymphoma might develop.

In conclusion, *H.pylori* is significantly associated with activity of chronic gastritis and mucosa-associated lymphoid tissue. Absence of *H.pylori* in histological specimens may either indicate inappropriate specimen or point towards other causes of chronic gastritis like NSAID use by the patient.

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