

ORIGINAL ARTICLE

Histopathological evaluation of chronic gastritis with and without *Helicobacter pylori* colonization: a study from Iran

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Abstract

Chronic gastritis is defined as the presence of chronic mucosal inflammatory changes leading eventually to mucosal atrophy and epithelial metaplasia. It is notable for distinct causal subgroups and for patterns of histological alterations that vary in different parts of the world. By far the most important aetiological association is chronic infection by the bacillus *Helicobacter pylori* (Hp). The organism is a worldwide pathogen that has the highest infection rates in developing countries including Iran.

In this study, samples confirmed for the diagnosis of chronic gastritis from 100 Hp-positive and 36 Hp-negative patients, were reevaluated histopathologically to determine the severity of inflammation, the presence of active gastritis, lymphoid follicle(s), glandular atrophy and intestinal metaplasia. Seventy-five percent of the samples showed mild inflammation, whilst moderate and severe inflammation was seen respectively in 24% and about 1% of the cases. Among the evaluated variables, only activity and intestinal metaplasia had statistically significant associations with Hp ($p < 0.05$) in this survey.

Keywords: Chronic gastritis, *Helicobacter pylori*, glandular atrophy, active gastritis, intestinal metaplasia, lymphoid follicle

INTRODUCTION

Chronic gastritis is defined as the presence of chronic mucosal inflammatory changes leading eventually to mucosal atrophy and epithelial metaplasia. It is notable for distinct casual subgroups and for patterns of histological alterations that vary in different parts of the world. In the Western world, the prevalence of histological changes indicative of chronic gastritis exceeds 50% in the later decades of adult life. By far the most important aetiological association is chronic infection by the bacillus *Helicobacter pylori* (Hp).

Helicobacter pylori is a spiral-shaped Gram-negative bacterium that colonizes the stomach in about 50% of all humans. In 1982, when this bacterium was discovered by Marshall and Warren, stress and lifestyle were considered the major causes of peptic ulcer disease. It is now firmly established that *Helicobacter pylori* causes more than 80% of duodenal ulcers and up to 60% of gastric ulcers. The link between *Helicobacter pylori* infection and subsequent gastritis and

peptic ulcer disease has been established through studies of human volunteers, antibiotic treatment studies and epidemiological studies. In some individuals, *Helicobacter pylori* also infects the corpus region of the stomach. This results in a more widespread inflammation that predisposes not only to ulcer in the corpus region, but also to stomach cancer. This cancer has decreased in incidence in many countries during the last half-century but still ranks as number two in the world in terms of cancer deaths. Inflammation in the stomach mucosa is also a risk factor for a special type of lymphatic neoplasm in the stomach, MALT (mucosa-associated lymphoid tissue) lymphoma. Since such lymphomas may regress when *Helicobacter pylori* is eradicated by antibiotics, the bacterium plays an important role in perpetuating this tumour.

The prevalence of *H pylori*, a worldwide infection, varies greatly among countries and among population groups within the same country.¹ In the United States and Canada, as well as in Northern and Western Europe, 5-

15% of children and 10-60% of adults harbor *Helicobacter pylori*. Hp is highly prevalent in developing countries. For example, in the Middle East 40-65% of children and 80-95% of adults are infected.^{2,3,4} Once acquired in childhood, this bacterium is able to establish a life-long relationship with its host.⁵ Hp infection is also common in 57-91% of Iranian population.⁶⁻¹¹ However, studies regarding *H pylori* prevalence in different regions of Iran, a country with a variable climate, are limited.

The aim of this study was to evaluate biopsy samples of chronic gastritis, histopathologically in order to determine the differences between Hp-positive and Hp-negative patients.

MATERIALS AND METHODS

This cross-sectional study was performed in the Pathology Division, Amir ol-momenin Hospital– Azad Medical University, Tehran-Iran in the first quarter of the year 2007. Biopsy samples confirmed for the diagnosis of chronic gastritis were reevaluated histopathologically to determine the severity of inflammation and to detect the presence of Hp, activity, lymphoid follicle(s), atrophy, and intestinal metaplasia. Patients known to have peptic ulcer disease or any gastrointestinal malignancy, diagnosed endoscopically and/or pathologically, were excluded. One hundred specimens with Hp infection were included in Group A. Group B comprised thirty-six patients without evidence of Hp infection. Written informed consent had been obtained for all upper endoscopy and biopsy procedures.

During endoscopy, at least two biopsies had been taken from the antrum/antropyloric region and corpus. Biopsy specimens were fixed in 40 g/L neutral-buffered formaldehyde and embedded in paraffin. Five-micron thick sections were cut from each paraffin block and stained with haematoxylin and eosin for routine histology, and also stained with Giemsa. The diagnosis of *H pylori* infection was made by direct light microscopy observation of the organism with Giemsa staining. For histopathological analysis, one pathologist blinded to the clinical information of subjects, assessed the histopathological changes. The degree of inflammation was scaled from negative (absent) to 3+ (severe), based on the amount of inflammatory cells (lymphocytes, plasma cells, and granulocytes) and according to updated Sydney System. Being active was signified by the presence of neutrophils within the glandular and surface epithelial layer. Glandular

atrophy was identified when the gastric glands were correspondingly decreased in amount and/or widely separated.

Statistical analysis

Statistical analysis was performed using t-test, Chi-square, and Fisher's exact test as appropriate with significance considered at $p < 0.05$.

RESULTS

One hundred and thirty-six cases of chronic gastritis were enrolled (59 men and 77 women, mean age: 47.3 ± 19.4 years, range: 13-82 years). 75% (n=102) had mild, 24% (n=32) moderate, and 1% (n=2) severe inflammation. Lymphoid follicles were observed in 46% (n=63) of the samples. Activity, atrophy, and intestinal metaplasia were present in 49% (n=67), 18% (n=24), and 10% (n=14) respectively.

The mean age of patients in Groups A and B was 45.7 ± 18.6 and 51.5 ± 21.2 years, respectively ($p=0.1$). Since the number of patients with moderate and severe inflammation was small, the association between the degree of inflammation and the presence of Hp was analyzed in two groups (mild and moderate/severe). The rate of mild and moderate/severe inflammation among Hp-positive patients was 71% (n=71) and 29% (n=29), whilst it was 86.1% (n=31) and 13.9% (n=5) in the Hp-negative group ($p=0.07$). Lymphoid follicle(s) was (were) seen in 50% (n=50) of Group A and 33.3% (n=12) of Group B ($P_v=0.08$). The presence of activity was significantly higher in the Hp infected patients comparing to non-Hp infected ones (56%, n=56 vs. 30.6%, n=11; $p=0.009$). Seventeen percent (n=17) of patients in Group A and 19.4% (n=7) of those in Group B showed atrophy ($P_v=0.7$). Intestinal metaplasia was detected in only 6% (n=6) of Group A, whereas 22.2% (n=8) of Group B exhibited this histological change ($p=0.006$). These findings are depicted in Table 1 in detail.

DISCUSSION

Chronic gastritis, one of the most common chronic conditions of humankind, is now known in many cases to be the result of specific and nonspecific responses mounted by the gastric mucosa against *H pylori* infection.^{12,13} *H pylori* infection is associated with most duodenal and gastric ulcers and with almost all primary gastric MALT lymphomas. Furthermore, certain extragastric conditions, including systemic

TABLE 1: Comparison of gastric histopathological changes in Hp-positive and Hp-negative patients

	Hp-positive (n=100)	Hp-negative (n=36)	P value
Lymphoid follicle Activity	50% (n=50)	33.3% (n=12)	0.08
Atrophy	56% (n=56)	30.6% (n=11)	0.009
Intestinal metaplasia	17% (n=17)	19.4% (n=7)	0.74
	6% (n=6)	22.2% (n=8)	0.006

autoimmune diseases, atherosclerosis, urticaria and migraine have been linked, albeit tenuously, to *H pylori* infection.¹⁴ Thus, the importance of *H pylori* extends into the realm of numerous major diseases that may have gastritis as their common denominator. *H pylori* occupies a unique niche, extremely acidic environment. The urease of *H pylori* is essential for its colonization and survival at extremely low pH, to ensure cytoplasmic homeostasis during large pH changes that occur during feeding. *H pylori* can use molecular hydrogen as energy source; thus, its growth depends to some extent on the hydrogen excreted. *H pylori* infected gastric mucosa evolves through stages of chronic gastritis, intestinal metaplasia, glandular atrophy, and dysplasia before carcinoma develops. As it is mentioned in previous studies, gastric cancer is one of the leading causes of cancer death in Iran.⁶

Yan *et al.*,¹⁵ studied 173 patients with chronic gastritis including 99 Hp-positive and 74 Hp-negative patients. In contrast to our study, they found intestinal metaplasia in antral mucosa was significantly more common in Hp-positive patients. Similarly, the results of Mysorekar *et al.*,¹⁶ shows the association between *H pylori* colonisation with more intestinal metaplasia in acid peptic disease patients. In the latter study, apart from Giemsa staining, Rapid Urease Test (RUT) was done for *H pylori* detection. In our study, the prevalence of intestinal metaplasia was lower in the Hp-positive group. Although intestinal metaplasia is a virtually constant component of atrophic gastritis, and is found more frequently in the stomach of patients with *H pylori* gastritis,^{17,18} in patients with extensive antral intestinal metaplasia, a type of epithelium to which *H pylori* rarely adheres,¹⁹ the infection is virtually confined to the nonmetaplastic areas of the corpus. This is also the case in many patients who regularly use proton pump inhibitors (PPIs). Our study population was

patients with confirmed chronic gastritis, so long term consumption of PPIs was highly probable. In addition, the evidence of *H pylori* infection in the present study was direct observation of the microorganism by microscopy. Considering these facts, the lower prevalence of intestinal metaplasia might appear reasonable.

This study revealed that the frequency of active gastritis among our patients was 51%, very close to the rate reported by Zhang *et al.* (56.2%),²⁰ who studied about 4100 patients with chronic gastritis. On the other hand, active gastritis was markedly higher in Hp-positive patients. This is in accordance with the findings by Yan *et al.*¹⁵ in chronic gastritis patients and Mysorekar *et al.*¹⁶ in acid peptic disease patients.

Although we found no significant difference in the severity of inflammation and development of atrophy between Hp infected and non-Hp infected patients, previous studies showed an increase in the proportion of high grade gastritis with an increase in Hp density.^{15,16,21} There are two possible explanations for our distinctive results: firstly, the majority (75%) of patients studied had mild chronic gastritis and consequently were less probable to reflect atrophy. Secondly, in clinical practice, the most common sampling consists of one specimen from the antrum and one from the corpus –like what we performed– which is insufficient to establish the presence and extent of atrophy. Even when extensive biopsy protocols are used, inevitable sampling errors may affect the documentation of the atrophic foci, which are frequently patchy.²²

In this survey, lymphoid follicles were present in 50% of the Hp infected chronic gastritis patients, quite different from the report by Chen.²³ In contrast to some studies on gastric diseases,^{16,21,23} significant difference in the presence of lymphoid follicles between Hp-positive and Hp-negative patients could not be confirmed. Using an extensive biopsy protocol can lead to more reliable results.

This is one of few studies in Iran that have focused on histopathological changes in patients with chronic gastritis. Although some of our findings were in agreement with previous studies performed in other countries, especially Eastern Asia, complementary studies with larger sample sizes, using extensive biopsy protocols, other diagnostic tools for detecting *H pylori* (e.g. RUT), and determining Hp density will promote the validity of the results. Furthermore, evaluating different geographical and socioeconomical determinants that can affect identified risk factors is invaluable.

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