

Prevalence of *Helicobacter pylori* and Histopathological Features in Gastric Biopsies from Patients with Dyspeptic Symptoms at a Referral Center in Medellin

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Abstract

Introduction: *Helicobacter pylori* infection is considered to be the most prevalent chronic infection in the world. It occurs primarily in developing countries. **Objective:** The main objective of this study was to estimate the prevalence of *H. pylori* infections and gastritis in patients with dyspeptic symptoms who underwent upper endoscopy and correlate endoscopic findings with principal histopathological findings. **Methods:** We reviewed 2,708 gastric biopsies from patients who had come to the VID Specialized Diagnostic Clinic of the Congregación Mariana in Medellin because of dyspeptic symptoms in 2012 and 2013. Biopsies were studied in the VID Clinical Laboratory of the Congregación Mariana. Histological variables of the results reported by the pathologist were analyzed with statistical methods. **Results:** The prevalence of *H. pylori* infection was 36.4%, the average age of infected patients was 46.5 years (SD: 17.1) with a peak prevalence in the group between 40 and 49 years. Prevalence decreased after age 49. The amount of *H. pylori* was correlated with the intensity of inflammation and activity. The presence of the bacteria was associated with the presence of metaplasia, lymphoid follicles, atrophy and hyperplastic polyps. The intensity of inflammation was associated with the amount of *H. pylori* and neutrophil activity. **Conclusion:** The prevalence of *H. pylori* infection in our study is low compared with other research and exhibited unusual behavior by age group. The amount of *H. pylori* was correlated with the intensity of inflammation and neutrophil activity.

Keywords

Helicobacter pylori, prevalence, gastritis, gastric atrophy, intestinal metaplasia, dysplasia, gastric cancer.

INTRODUCTION

H. pylori is a gram-negative microaerophilic bacillus with four to six flagella that is associated with acid peptic disease. It was first identified in 1983 by Warren and Marshall. Its prevalence is high, especially in developing countries: it is considered the most common chronic bacterial infection in the world. (1) Prevalence increases with age. *H. pylori* enters the digestive tract presumably by fecal-oral or oral-oral route. The bacteria produce proteases that weaken the mucosal lining of the gastric epithelium. It also expresses urease which breaks down the urea of the gastric lumen into ammonia and carbon dioxide and thereby generates a layer

that provides protection against the acid of the stomach. Through specific proteins they adhere to the membranes of gastric epithelial cells throughout the stomach, but especially in the antrum since no acid is secreted there. (2-5).

By adhering to the epithelium, the bacteria can generate an inflammatory reaction and migration of polymorphonuclear neutrophils and lymphocytes which can lead to the generation of the lymphoid follicles characteristic of this infection.

Factors specific to the bacterium, host, and chronicity of infection contribute to the development of gastric or duodenal ulcers that can be complicated by bleeding or perforation. (5-6)

Other diseases associated with *H. pylori* infections include gastric cancer and mucosa-associated lymphoid

tissue (MALT) for which reason the World Health Organization (WHO) has classified this infection as carcinogenic. (7-9) The extent of the infection has not so far been linked to the development of ulcers or the other diseases mentioned. (7)

The infection is asymptomatic in most cases. However, it may present classic symptoms of acid peptic disease, including epigastric pain, early satiety, feeling of emptiness or “painful hunger”, nausea and vomiting. In cases with bleeding, there may be melena, hematemesis and anemia. (7, 10)

The diagnosis can be confirmed by urea breath tests, blood tests, stool antigen tests, rapid urease tests of biopsy samples, histopathological studies and by cultures. All of these have very good sensitivity and specificity. The goal of treatment is to eradicate the bacteria. (11)

Because of the ease of diagnosis, the effectiveness of therapy and fatal outcomes that can be avoided with the eradication of this bacteria, it is very important to know the prevalence of this infection in our environment.

The objectives of this study are to estimate the prevalence of H. pylori infections, to describe its histopathological features, and to correlate H. pylori infections with histopathological findings from gastric biopsies taken endoscopically from patients with dyspeptic symptoms and analyzed in a referral laboratory in Medellin.

MATERIALS AND METHODS

This is a retrospective study of a population of patients seen in the VID Diagnostic Clinic who had consulted because of dyspeptic symptoms and who had undergone upper gastrointestinal endoscopy and had biopsies taken between May 2012 and April 2013. Patients who had received antimicrobial therapy for H. pylori and those who had received acid suppression therapy were excluded.

The pathology section of the VID Clinical Laboratory analyzed gastric biopsies of these patients. Slides were reinterpreted by the laboratory pathologist, who filled out forms about the histological variables of each case.

The information collected was transcribed into two databases which were then compared in the Microsoft Excel Compare®. When there were inconsistencies between the records of the two databases, they were corrected on the basis of the original histological variables.

Histological variables collected included H. pylori, inflammation, activity of neutrophils, erosion, ulcers, eosinophils, metaplasia, lymphoid follicles, carcinoma, lymphoma and hyperplastic polyps.

H. pylori activity and inflammation due to the bacteria were categorized according to the updated Sydney system: negative, mild, moderate and marked. (12) The remaining histological variables were rated as present or absent.

Pathology specimens were fixed in 10% buffered formalin, dehydrated and embedded in paraffin blocks after 12 hours. Tissues were oriented by placing the mucosa on a surface perpendicular to the plane of the cut. Four micron thick histological sections of each fragment were obtained, mounted on glass slides in multiple groups and stained with hematoxylin and eosin for reading.

Averages and standard deviations were used for statistical description of frequency distributions. Spearman’s rank correlation coefficient was used for correlations between ordinal variables, and the chi-squared test or Fischer’s exact test was used for associations between categorical variables. A p value of 0.01 was used for statistical significance. All analyses were performed with SPSS 18 (IBM, Armonk, New York).

RESULTS

Demographics

A total of 2,708 samples, 1,727 (63.8%) from women and 981 (36.2%) from men were analyzed. The average age of the population was 51.3 years (SD 17.9). The average age of male patients was 50.2 (SD 17.6) years, and the average age of women was 52 (SD: 18.1). The distribution of samples from patients by age group is shown in Table 1.

Table 1. Distribution of H. pylori by age group and sex

Age Group	Sex		Total
	Feminine	Masculine	
Less than 20	26 4.4%	18 4.6%	44 4.5%
20 – 29	99 16.6%	56 14.4%	155 15.7%
30 – 39	85 14.2%	69 17.8%	154 15.6%
40 – 49	113 18.9%	91 23.5%	204 20.7%
50 – 59	111 18.6%	70 18.0%	181 18.4%
60 – 69	103 17.2%	47 12.1%	150 15.2%
70 or older	61 10.2%	37 9.5%	98 9.9%
Total	598	388	986

Prevalence of H. pylori

H. pylori were found in samples from 986 patients (36.4%). In 20.3%, the infections were classified as mild and 16.1% as marked. No moderate cases were found.

H. pylori prevalence was 34.6% among women and 39.6% among men. The average age of patients with H.

Pylori infections was 46.5 (SD: 17.1) years. *H. pylori* distributions by age group and sex are shown in Table 1.

Histopathologic Findings

Inflammation (gastritis): Inflammation was found in 99.9% of cases. Mild inflammation predominated and was found in 2,211 (81.6%) cases, 491 (18.1%) had moderate inflammation (18.1%) and 2 (0.1%) cases had marked inflammation. Four patients had no inflammatory infiltrate. The average age of patients with gastritis was 51.3 years (SD: 17.9)

Neutrophil activity: In total 1,014 (37.4%) patients had neutrophil activity. Of these, 523 (19.3%) were mild, 490 (18.1%) were moderate, and only one case was markedly intense.

Other histological findings: The prevalence of erosions was 2.1%, prevalence of ulcers was 1.3%, prevalence of metaplasia was 13.3%, prevalence of atrophy was 1.7%, prevalence of carcinoma was 0.6%, prevalence of lymphoid follicles was 8.1%, and prevalence of hyperplastic polyps was 3.3%. Only one case of lymphoma was documented.

Correlation and association of *H. pylori* with other variables

The amount of *H. pylori* and intensity of inflammation (categorized as negative, mild, moderate or marked) were correlated: Spearman's rank correlation coefficient was 0.7 ($p < 0.01$). The intensity of neutrophil activity and the amount of *H. pylori* were also correlated: Spearman's rank correlation coefficient was ($p < 0.01$).

There were significant associations between the presence of *H. pylori* and the presence of metaplasia ($p < 0.01$), lymphoid follicles ($p < 0.01$), atrophy ($p < 0.01$) and hyperplastic polyps ($p < 0.01$). There was no significant association between the presence of *H. pylori* and erosion ($p > 0.01$), gastric ulcers ($p > 0.01$), eosinophils ($p > 0.01$) and carcinoma ($p > 0.01$).

Correlation and association of inflammation with other variables

The intensity of inflammation had a positive linear correlation with the intensity of neutrophil activity ($p < 0.01$). No associations between the presence of inflammation and other variables were found.

DISCUSSION

H. pylori infections have been demonstrated worldwide and affect all age groups. It is estimated that 50% of the

world's population is infected. (13) In our study, *H. pylori* was found in 36.4% of the cases.

A comparison shows that the prevalence we found is lower than those found in other studies. The study of *H. pylori* prevalence in Colombia published in 2003 by Bravo et al. estimated the prevalence of infection in 8,652 gastric biopsies from 16 cities to be 69.1%. In that series, the prevalence in Medellin was 65% which is almost twice that found in our series. Other cities with a high prevalences were Tunja (99.1%), Popayan (86.5%) and Manizales (85.5%). (14) A study published by Garg et al. found a prevalence of infection of 43% at a center in India, but other studies from the same country have reported prevalences as high as 78%. (15-17)

It has been reported that over 50% of the population of developing countries is infected at 10 years of age, with a peak prevalence of 80% just before age 50. (13, 18) In contrast, in developed countries only 10% of the population is infected at 10 years of age. (19) This increases from 10% between 18 and 30 years of age up to 50% in those over 60 years of age. (13) We found that in people under 60 years of age, the prevalence of infection was 41.9%, and in those over 60 years of age, the prevalence was 26.1%.

The prevalence of *H. pylori* infections is related to three factors: the acquisition rate (incidence), the rate of curing the infection; and prolonged persistence of bacteria in the gastroduodenal mucosa between infection and eradication. (13) Table 2 shows the prevalence of infections in various studies.

Torres et al. found associations between infection and overcrowded housing (OR = 1.4, 95% CI: 1.23-1.60), low educational level (OR = 2.42, 95% CI: 1.71-3.44) and low socioeconomic status (OR = 1.43, 95% CI: 1.26 -1.63). (18) This may explain, in part, the low prevalence of *H. pylori* found in our series which included primarily middle and upper-middle class patients in the population which comes to our laboratory. Other factors associated with higher rates of infection are the number of children in a family, shared beds and water quality. (20-22) It should be borne in mind that water quality of the city water service of Medellin is classified as high. (23) A study that examined the prevalence of infection in the pre-war and postwar Japan has also proposed that decreasing prevalence of infection parallels improvement of a country's economy. (24) This could explain the decrease in prevalence from the 2003 study of Bravo et al. which found a 65% prevalence in contrast to the 36.4% prevalence found 10 years later in our study.

Classically, the prevalence of infection has been found to increase with age. (1) Pounder et al. conducted a study that evaluated the prevalence of *H. pylori* in several countries. They classified those countries into two groups: Group One countries in which most individuals were infected during childhood and continued to be infected as adults, and Group Two in which only a minority of individuals

Table 2. Prevalence of *Helicobacter pylori* in various studies

Author	Year	Number of patients	Test used by laboratory	Prevalence	Country
Lim SH et al. (26)	2013	19 272	IgG Serology for <i>H. pylori</i>	54.4%	Korea
Bravo LE et al. (14)	2003	8652	Biopsy for histopathology	69.1%	Colombia
Hu D et al. (27)	2013	3995	IgG Serology for <i>H. pylori</i>	44.9%	China
Nakajima S et al. (28)	2010	1246	Biopsy for histopathology	52.7%	Japan
Gill HH et al. (17)	1993	526	Biopsy for histopathology and urease test of biopsy	65%	India
Shiota S et al. (29)	2013	381	IgG Serology for <i>H. pylori</i>	71.1%	Bhutan
Garg B et al. (15)	2012	300	Biopsy for histopathology	43%	India
Krashias G et al. (30)	2013	103	PCR* for <i>H. pylori</i> in tissue sample	39.8%	Cyprus
Bakri MM (31)	2012	70	Culture and PCR* for <i>H. pylori</i> in tissue sample	85.7%	Saudi Arabia

*PCR: polymerase chain reaction

were infected during childhood, but the prevalence of infection increased in proportion to age in adulthood. (13)

The prevalence of infection exhibited unusual behavior in our series. In the general population, and for both sexes, the prevalence was highest in the 40 to 49 year old group and gradually decreased in the following age groups for both the general population and for men and women.

Prevalence was higher among men than among women (39.6% vs. 34.6%) which coincides with the results of Dorji et al. (18, 25)

Gastritis was found in 99.9% of the patients whose average age was 51.3 years. Of these, only 36.4% were found to be infected with *H. pylori*, a result that does not match reports in the literature that this infection is a major cause of gastritis. (2, 10, 31, 32-34) The Bravo et al. study in Colombia found an 83.6% prevalence of gastritis, although the prevalence in the city of Medellin was only 73.7%. (14) The age group with the highest absolute number of cases of gastritis was 50 to 59 years which is similar to that found in the literature. (15)

Glandular atrophy, intestinal metaplasia and dysplasia are of great clinical importance because they are considered to be precursors of malignancy according to the sequence described by Dr. Pelayo Correa. (35) The prevalence of atrophy and dysplasia were very low in our study, 1.7% and 0.1% respectively. However, the prevalence of metaplasia was 13.3% which is considerably higher and which is similar to the 14% prevalence found in India. (15). In the study by Bravo et al., the prevalence of metaplasia was 10.3% for men and 11% for women. (14)

Thirty-four gastric ulcers (1.3% of cases) were found. Eleven of these patients had *H. pylori* infections (32.3%) which is similar to that described in Colombia and elsewhere. (1, 14)

In 1994, the International Agency for Research on Cancer included *H. pylori* in Group I of human carcinogens responsible for gastric adenocarcinoma. (36) The prevalence of gastric cancer in our series was only 0.6% which is considerably lower than the Colombian study of 2003 which found a prevalence of 9.3%. (14)

Several studies have shown an association between *H. pylori* and MALT. It is believed that persistent stimulation of activated B cells by T cells predisposes the development of neoplasia and that development of lymphoid follicles precedes it. (37-39). In our series, there were 219 patients (8.1%) with lymphoid follicles. This is about half of the proportion reported in the literature. (15) We found only one case of MALT.

We found that the amount of *H. pylori* was positively correlated with the intensity of inflammation and activity. This coincides with the findings of Garg and Mysorekar. (15, 40) In addition the presence of the microorganism was associated with metaplasia, lymphoid follicles, atrophy and hyperplastic polyps. It is noteworthy that *H. pylori* does not colonize the metaplastic epithelium, and the positive association between these variables does not reflect the invasion of the metaplastic epithelium by the bacteria, but rather the possibility of finding areas with and without metaplastic invasion in the same sample.

We also observed that as intensity of inflammation increased, the intensity of neutrophil activity increased and the quantity of *H. pylori* grew. This is similar to what has been described elsewhere in the literature. (15)

It should be noted that this is a study of the prevalence of *H. pylori* and histopathological findings in a selected symptomatic population. In addition, presence of *H. pylori* is not always associated with dyspeptic symptoms.

Colonization is possible without any symptoms. However, all patients evaluated in this study had dyspeptic symptoms. We believe it is not possible to attribute the universality of dyspeptic symptoms to *H. pylori*, since we only found the presence of bacteria in 36.4% of these cases.

In conclusion, the prevalence of *H. pylori* infection in our study was lower than in other studies and exhibited unusual behavior by age group. Conversely the prevalence of gastritis is almost universal, while the prevalences of metaplasia and lymphoid follicles are similar to those described in the literature. Some of these changes are correlated with each other, and are precursors of malignancy, especially of adenocarcinomas and MALT which are important causes of morbidity and mortality. Early detection and treatment of precursor lesions could significantly impact these outcomes.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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