

Prevalence and Gastric Location of *Helicobacter pylori* in Patients with Intestinal Atrophy and Metaplasia in a Tertiary Care Institution in Colombia

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Citation:

Corso C, Aponte DM, Preciado A, Medina-Parra J, Sabbagh LC. Prevalence and Gastric Location of *Helicobacter pylori* in Patients with Intestinal Atrophy and Metaplasia in a Tertiary Care Institution in Colombia. *Rev Colomb Gastroenterol.* 2022;37(3):289-295. <https://doi.org/10.22516/25007440.858>

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Received: 09/12/2021
Accepted: 01/03/2022



Abstract

Introduction: *Helicobacter pylori* infection plays a critical role in the carcinogenesis cascade of intestinal gastric cancer. However, its prevalence in preneoplastic conditions generating changes in the gastric mucosa is unclear. Currently, endoscopic surveillance using the Sydney protocol is suggested every 2 to 3 years, but the presence of *H. pylori* infection in the subcardial region and gastric fundus is ill-defined. **Objective:** to determine the prevalence and gastric location of *H. pylori* infection in patients with preneoplastic conditions. **Materials and methods:** a cross-sectional study in adults with a previous diagnosis of atrophy or intestinal metaplasia who entered control endoscopy and were antrum, body, incisura *angularis*, subcardial region, and gastric fundus biopsied. A descriptive analysis of the results by gastric regions was performed. **Results:** data from 160 patients with a prevalence of *H. pylori* of 37.5% were collected. It increased from proximal to distal, starting with a 12.5% prevalence in the subcardial region to a 30.6% prevalence in the antrum. In addition, there was a similar pattern in the prevalence of preneoplastic lesions. Furthermore, advanced lesions (dysplasia, carcinoma) were observed in the incisura. **Conclusions:** the prevalence of *H. pylori* in precancerous conditions showed a high presence in the distal regions compared to the proximal ones, and it is more frequent in the antrum and lower in the subcardial region. As for the gastric distribution of atrophy and metaplasia, more involvement was found in the antrum and angular notch and lower in the subcardial region and fundus.

Keywords

Helicobacter pylori, gastric atrophy, intestinal metaplasia, gastric cancer, Operative Link on Gastritis Assessment (OLGA).

INTRODUCTION

Helicobacter pylorus is a gram-negative bacterium that colonizes the gastrointestinal tract and has high implications, especially in the gastric tract, where it is considered a type I carcinogenic agent by the World Health Organization (WHO)⁽¹⁾. Identifying it is critical for gastric carcinoma and public health-related issues since this cancer constitutes the fourth cause of morbidity and the second cause of mortality worldwide⁽²⁾. In Colombia, reports from the National

Cancer Institute have flagged gastric cancer as the first cause of cancer mortality in men and the second in women⁽³⁾. *H. pylori* are characterized by their helical shape and flagella, crucial for its motility and successful colonization. The genes and proteins related to the microorganism's motility in the gastric environment are well documented in the literature⁽⁴⁾.

As described by Dr. Pelayo Correa in his carcinogenesis model for intestinal-type gastric carcinoma, this pathogen activates in people genetically susceptible to the carcinogen cascade, beginning with an inflammatory response and

generating active chronic gastritis that can evolve to atrophic gastritis, intestinal metaplasia, and dysplasia –which will end up causing cellular changes to carcinoma⁽⁵⁾. It is recommended to monitor the patient in preneoplastic conditions (atrophic gastritis and intestinal metaplasia) and preneoplastic lesions (dysplasia) every 2 to 3 years, performing several biopsies on the antrum and gastric body. Additionally, if documented in the patient's histology, a treatment to eradicate *H. pylori* is recommended⁽⁶⁾. The Sydney system is currently the most widely used and recommended biopsy protocol. This system performs biopsies in the antrum (greater and lesser curvature, 2 cm from the pylorus), incisura *angularis*, and body (anterior and posterior wall, 8 cm from the cardia)⁽⁷⁾.

The microorganism migration theory associated with changes in gastric distribution is proposed given the hypothesis of changes in the microenvironment in the gastric mucosa affected by *H. pylori*, as in intestinal atrophy and metaplasia, and considering the motility characteristics of this pathogen. Additionally, current protocols do not involve taking biopsies in the gastric fundus and cardia⁽⁸⁾, which could lead to false negatives identifying *H. pylori* in these patients.

The objective of this study is to identify the distribution patterns of this pathogen in the presence of atrophy and intestinal metaplasia, which will establish a very close value to the actual prevalence and distribution of *H. pylori* in this context.

MATERIALS AND METHODS

Design and population

A descriptive observational cross-sectional study of adult patients diagnosed with intestinal atrophy or metaplasia in a tertiary care institution. Patients with proton pump inhibitor (PPI) use in the last six months, antibiotic use in the last 30 days, patients with a histological diagnosis of gastric cancer, patients with a history of gastric surgery, diagnosis of Zollinger-Ellison syndrome disease or gastric lymphoma, and patients who required emergency surgical management (bleeding, obstruction or perforation) were excluded.

Sampling and sample size

The sample size was calculated based on an estimated prevalence of a 43.3% *H. pylori* presence⁽⁹⁾, with an 8% absolute accuracy and a 95% confidence level for a minimum required sample size of 148 patients.

Procedure

All patients with atrophy and intestinal metaplasia history who entered the gastroenterology unit to undergo upper

gastrointestinal endoscopy (for their pathology check or any upper gastrointestinal symptomatology) were given informed consent. In addition, this study's objectives and the steps for its development were explained in detail in this consent. Likewise, each patient was given a questionnaire about PPI use and *H. pylori* eradication.

Once the clinical history of the previous diagnosis of intestinal atrophy or metaplasia was confirmed and, after ruling out gastrointestinal surgeries, or a history of gastric cancer –the upper endoscopy procedure and biopsy were performed as follows:

- Antrum: 2 and 3 cm from the pylorus in the major and lesser curvature (2 biopsies)
- Incisura *angularis* (1 biopsy)
- Body: 8 cm from the cardia in the anterior and posterior wall (2 biopsies)
- Stomach fundus
- Subcardial region

These biopsies were sent to pathology. Once the results were available, information on the questionnaires and pathologies was collected in a data extraction tool, typed by the same operator, and a double review of the information was made.

Variables

Patient demographic and clinical information was collected, including pre-treatment information for underlying disease (atrophy or intestinal metaplasia) and current or previous use of PPIs. In addition, detailed information was collected on the histological diagnosis of the result of biopsies in the body and antrum, incisura *angularis*, subcardial region, and gastric fundus.

Analysis

The final database was consolidated in the Stata 13 statistic software, and a descriptive analysis of the information was performed. Categorical variables were described as absolute; relative frequencies and quantitative variables were described as measures of central tendency and dispersion depending on the data distribution. The Shapiro-Wilk test evaluated a *p*-value less than 0.05 for statistical significance. An exploratory bivariate analysis was performed comparing the type of initial diagnosis and diagnosis according to the anatomical location.

RESULTS

Of the potential patients in the study, 160 met the inclusion criteria, had no criteria for exclusion, and willingly agreed

to participate. Most of the patients were females (60%), and the median age was 61.5 years (interquartile range [IQR]: 54–71). At the initial patients' diagnosis, 90 (56.3%) were diagnosed with metaplasia and atrophy, 31 (19.4%) were diagnosed with atrophy, and 39 (24.3%) were exclusively diagnosed with metaplasia (**Table 1**).

The histological result highlights that 81.3% of the patients showed some lesion degree (atrophy, metaplasia, dysplasia, or carcinoma), whereas 13 patients (18.7%) did not show any lesion in the biopsies performed. Similarly, a 37.5% prevalence of *H. pylori* was observed in the study population, with a higher prevalence in patients without lesions in the histological results (43.3%) than in patients with lesions (36.2%) (**Table 1**).

Furthermore, among the differences found between patients with and without lesions, there was a striking gender difference. There was a higher proportion of females among patients without lesions (70%) than among patients with lesions (57%). A much subtler disparity in age was also found, with a greater median age in patients with some lesions (62 years) compared to patients without lesions (58.5 years) (**Table 1**).

Of the patients with premalignant lesions, two patients had dysplasia. The first patient was a 72-year-old male. His initial

diagnosis included metaplasia and atrophy. During the pathology result, he was diagnosed with atrophy, metaplasia, and high-grade dysplasia in the incisura, with no evidence of *H. pylori* in any of the biopsies. The second patient was a 61-year-old male. His initial diagnosis was metaplasia and atrophy, showing pathology consistent with high-grade dysplasia in the body, incisura, and antrum. He had atrophy and metaplasia in the antrum with signs of *H. pylori* in the body and incisura.

The histological results also showed a single 60-year-old female patient with carcinoma and an initial diagnosis of metaplasia. Her pathology resulted in carcinoma in the incisura, atrophy, and metaplasia in the antrum with *H. pylori* in the body.

Based on the descriptive geographic analysis, it was possible to see that the prevalence of *H. pylori* increased from proximal to distal, starting with a 12.5% prevalence in the subcardial region and reaching a 30.6% prevalence in the antrum. A similar pattern was observed with the prevalence of preneoplastic lesions, starting with a low prevalence in the subcardial region (16.9%), decreasing at the fundus (11.9%), and with a progressive increase from that point to the antrum (66.2%) (**Figure 1**). In addition, there is a higher presence of advanced lesions (dysplasia, carcinoma) in the incisura (**Table 2**).

Table 1. Characteristics of patients undergoing endoscopic check for premalignant lesions

	No injuries during check (n = 30)		Injuries during check (n = 130)		Total population (n = 160)	
	Frequency	%	Frequency	%	Frequency	%
Age (median/IQR)	58.5	(50-65)	62	(55-71)	61.5	(54-71)
Gender (female)	21	70	75	57	96	60
Initial diagnostic						
- Atrophy	23	76.7	98	75.3	121	75.6
- Metaplasia	23	76.7	106	81.5	129	80.6
Endoscopic check diagnosis						
- <i>H. pylori</i> prevalence	13	43.3	47	36.2	60	37.5
- Atrophy prevalence	0	0	121	93.1	121	75.6
- Metaplasia prevalence	0	0	113	86.9	113	70.6
- Premalignant lesions prevalence					130	81.3
Medical history of PPI treatment	1	3.3	17	13.1	18	11.3
History of antibiotic treatment	12	40	32	24.6	44	27.5

Table 2. Diagnosis prevalence (%) by geographical location

Diagnosis	Subcardial region	Fundus	Body	Incisura	Antrum	Total
<i>H. pylori</i>	12.5	15.6	21.3	27.5	30.6	37.5
Atrophy	14.4	10.6	26.9	50	61.9	75.6
Metaplasia	14.4	8.13	22.5	46.9	55	70.6
Dysplasia	0	0	0.6	1.3	0.6	1.3
Carcinoma	0	0	0	0.6	0	0.6
Neoplastic and pre-neoplastic lesions	16.9	11.9	28.1	55.6	66.2	81.3

In the *H. pylori* intra-gastric distribution analysis with lesions, a higher prevalence of *H. pylori* was observed in all areas of the stomach in patients without lesions compared to patients with at least one lesion, showing a pattern of increasing prevalence from proximal to distal in both groups (Figure 2).

DISCUSSION

The International Agency for Research on Cancer and the WHO classify *H. pylori* as a carcinogen type I⁽¹⁰⁾. Although the involvement of *H. pylori* in the carcinogenesis cascade of intestinal gastric cancer is accepted⁽¹¹⁾, its prevalence in preneoplastic conditions such as intestinal atrophy and metaplasia, causing changes in the mucosal microenvironment –which could alter the gastric distribution of this pathogen, is currently unclear⁽¹²⁾. Currently, many authors recommend surveillance in patients with premalignant conditions through endoscopic monitoring and biopsies of

the antrum, body, and incisura (Sydney protocol) every 2 to 3 years⁽¹³⁾. However, it is unclear whether or not *H. pylori* infection occurs in other gastric regions, which can lead to false negatives in pathogen identification –considering that several authors support the regression theory of these conditions^(8,14), pathogen identification would be critical to start an eradication treatment and, therefore, reduce the risk of gastric adenocarcinoma.

Approximately 50% of the world's population is infected with *H. pylori*, ranging between 40% and 73%, with some variation depending on latitude⁽⁹⁾. In the 2016 study conducted by Dr. Correa in Medellín in a population with dyspeptic symptoms taken to endoscopy, a prevalence of up to 36.4% was found, with male predominance (39.6%) versus female (34%), with an average age of 46.5⁽¹⁵⁾. There was a 36.2% prevalence of *H. pylori* in our population (patients with atrophy and metaplasia).

Although the global prevalence of *H. pylori* and its gastric distribution is known, its distribution in preneoplastic con-

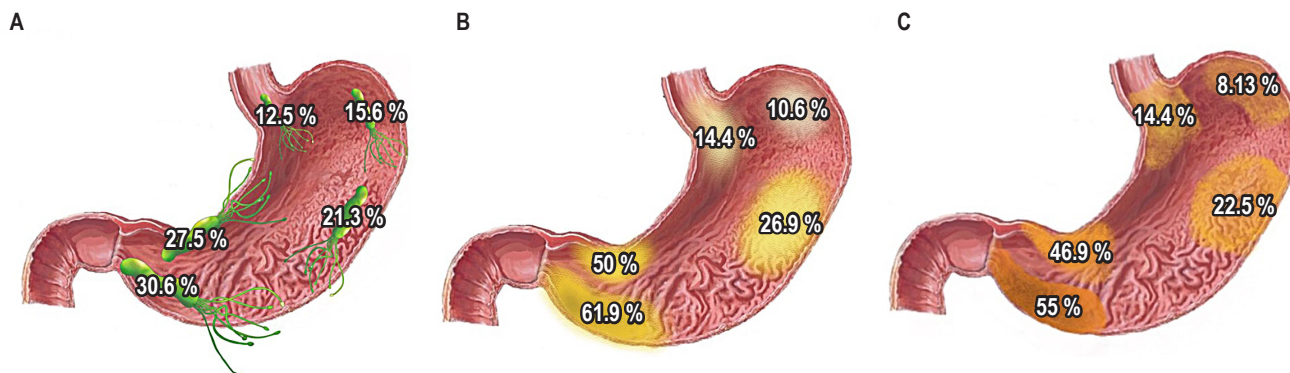


Figure 1. Prevalence and distribution of *H. pylori* (A), atrophy (B), and intestinal metaplasia (C) in patients with a previous diagnosis of preneoplastic conditions in Colombia.

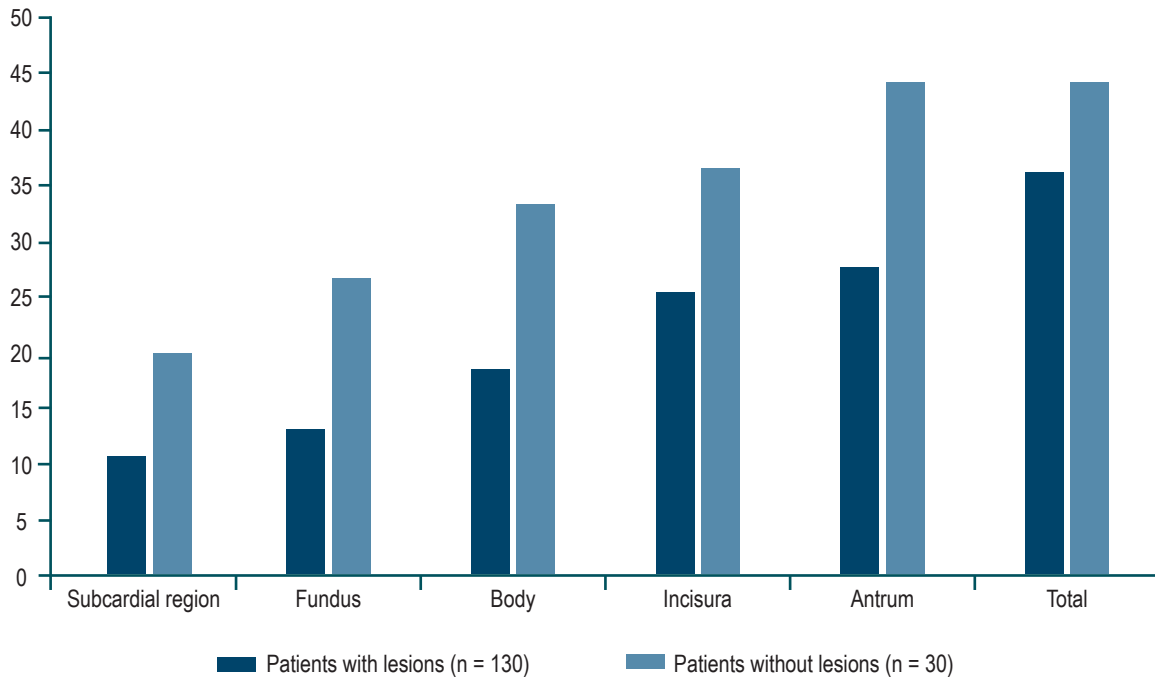


Figure 2. Prevalence (%) of *H. pylori* by presence or absence of lesions.

ditions such as atrophy and intestinal metaplasia is unclear. Therefore, the study was based on this pathogen's location in the different gastric regions and found a higher increase of *H. pylori* in distal regions, which is more frequent in the antral region (30.6%) and lower in the subcardial region, with a 12.5% prevalence. When comparing the distribution of *H. pylori* in patients with atrophy and metaplasia versus patients in whom no premalignant entity was found, the pathogen observed in the latter group had a higher prevalence of the pathogen.

Regarding gastric atrophy prevalence, ranges reported in the literature vary between 9.4% and 63%. On the other hand, for intestinal metaplasia, the ranges reported were between 7.1% and 42.5%⁽¹⁶⁻¹⁸⁾. Park and Kim's extensive review on premalignant entities in gastric cancer reported a 20.1% prevalence of gastric atrophy in the body and 42% in the antrum and a 21.2% prevalence of intestinal metaplasia in the body, and 28% in the antrum⁽¹⁹⁾. Our study found a similar distribution for atrophy and metaplasia in the gastric body (atrophy: 26%, intestinal metaplasia: 22%). However, a higher prevalence was observed in antral regions (atrophy: 61%, intestinal metaplasia: 55%). Notably, a lower prevalence of atrophy and metaplasia was also observed in proximal gastric areas, starting in the subcardial

region (16.9%) and decreasing in the fundus (11.9 %) with a progressive increase up to the antrum (66.2 %).

Furthermore, the study conducted in Colombia in a high-risk population for gastric cancer reported a 39% intestinal metaplasia prevalence. Thus, showing a higher risk of gastric cancer in individuals with incomplete intestinal metaplasia and an extension of the metaplasia to the body and cardia⁽²⁰⁾. Although this study's objective did not include evaluating the risk of adenocarcinoma according to the locations of the atrophy and metaplasia, two cases of patients diagnosed with dysplasia and one with adenocarcinoma were evidenced in the endoscopic check. They showed no *H. pylori* involvement due to atrophy or metaplasia in the gastric fundus or the subcardial region.

Our results suggest a low potential cost-benefit to performing control biopsies in the subcardial region and fundus, supporting the current suggested schemes. Nonetheless, this marginal benefit should be evaluated in longitudinal diagnostic studies to better assess the cost-effectiveness of biopsies in these two regions in patients with atrophy and metaplasia.

Among the strengths of this study is greater *H. pylori* diagnosis accuracy by covering all the anatomical areas of the stomach and a wide heterogeneity of the population as the study was conducted in a referral center in Colombia in a

contributory regime population. Some limitations include the cross-sectional nature of the evaluation, so the times of patients with the disease are not standardized. Likewise, this study's objective was to describe the *H. pylori* map in pre-malignant conditions, so making conclusions beyond the description of the population is not possible with the design.

Based on the evidence generated in this study, works of a longitudinal nature on a larger scale are recommended to measure *H. pylori* infection persistence or appearance impact in patients with preneoplastic entities more accurately. Moreover, studies should be conducted to evaluate the impact of biopsies in the fundus and subcardial region to establish control protocols in this population.

CONCLUSIONS

H. pylori prevalence in premalignant conditions was 36.2%, with a higher presence in distal than proximal regions. It is more frequent in the antral region and less in the subcardial region, which does not support the upward migration theory of *H. pylori* in these premalignant conditions.

As for the gastric distribution of atrophy and metaplasia, more involvement was found in the antrum and incisura and lower in the subcardial region and the fundus.

In Colombia, this is the first study that shows a complete mapping of the prevalence of atrophy, metaplasia, and *H. pylori* in a population with gastric premalignant entities.

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