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Original Article

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Prevalence of *Helicobacter pylori* Infection in Samples of Gastric Biopsies

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Abstract

Background: *Helicobacter pylori* (*H. pylori*) infection affects about 50% of the world population and its association with environmental factors and host properties is involved in gastric carcinogenesis. The study aimed to estimate the prevalence of *H. pylori* in samples of gastric mucosa biopsies, correlate the presence of the bacteria in the sample with the variables age, sex and origin, to identify the types of lesions found in patients with *H. pylori*, and to evaluate the association of the lesions with the region of the gastric mucosa.

Methods: A cross-sectional, retrospective study was carried out in Aracaju, Sergipe, Brazil, from January 2013 to December 2015. A total of 45,206 gastric mucosal biopsies were obtained from patients submitted to upper gastrointestinal endoscopy. Of the reports evaluated, 12,909 met the inclusion criteria since they presented the patient's demographic data as well as the histopathological characteristics of gastric mucosal regions and positivity for *H. pylori*. Data were analyzed by IBM SPSS Statistic 20 and subjected to descriptive analyses (categorical variables) and inferential (Pearson's Qui-square and linear association tests) and multiple correspondence analyses. Significance level adopted 5%.

Results: Of the total of 12,909 (28.6%) reports evaluated, 67% (8,647) came from urban areas and 64.5% (8,320) were female. The mean age (standard deviation (SD)) was 43 years, ranging from 8 to 100 years, prevailing between 21 and 60 years. Among the types of gastric mucosa analyzed, 95.5% (12,322) were of the antral mucosa. The absence of glandular atrophy, the mild infection intensity for *H. pylori*, the absence of metaplasia, the presence of foveolar hyperplasia and lymphoid follicles were statistically significant ($P < 0.001$) in this region. In the fundic region, the evidence of fibrinoleucocytic crust and lymphoid follicles was significant ($P < 0.001$). There was no evidence of associated ulcerated lesions or significant relationship with intestinal metaplasia in the antral mucosa, whereas the fundic mucosa had a strong association with lymphoid follicles. The prevalence of active *H. pylori* infection in this study was 30.93%.

Conclusion: Detection rate of *H. pylori* and its association with acute and chronic inflammation should be taken into account. The antral region has shown higher incidence and the presence of *H. pylori* was strongly associated with foveolar hyperplasia and lymphoid follicles.

Keywords: *Helicobacter pylori*; Gastric mucosa; Prevalence of *Helicobacter pylori*; Atrophy; Intestinal metaplasia

Introduction

For over 100 years, micro-organisms have been observed in the gastric tissue, and its association with gastritis has been known since the 1970s. In 1982, Marshall and Warren identified and cultivated *Campylobacter pyloridis*, later called *Helicobacter pylori* (*H. pylori*) [1].

H. pylori is a spiral-shaped gram-negative and microaerophilic [2]. Its ability to proliferate and survive in the gastric environment is due to factors such as the production of urease by the microorganism, its motility and ability to adhere to the gastric epithelium. The way through which the infection occurs remains unknown. However, person to person transmission appears to be the most likely one, either through fecal-oral or oral-oral exposure [3].

Conservative approaches to this issue suggest that 50% of the population is affected by *H. pylori* and it is considered the commonest bacterial infection in humans [4]. Genetic sequencing analysis suggests that humans have been infected with *H. pylori* since their first migration from Africa some 58,000 years ago [5]. Once acquired, the infection persists and may or may not produce gastroduodenal disease [3]. The prevalence of the infection varies according to age, socioeconomic status and ethnicity. Socioeconomic status is also an important determinant and inversely correlated to *H. pylori* infection [6]. Furthermore, within any age range, the infection appears to be more common amongst blacks and Hispanics compared to whites [7].

In developing countries, where most children are infected

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before the age of 10, the prevalence in adults reaches more than 80% before aged 50. In developed countries, like the United States, the evidence of the infection among children is very unlikely to happen, but it becomes more common during adulthood [7]. The increase in the prevalence of infection with age was initially thought to represent a continuous rate of acquisition of the bacterium throughout the life. However, new epidemiological evidence indicates that most infections are acquired during childhood, even in developed countries [7].

Recent studies [6] suggest that, in developing countries, such as Iran, hygiene practices in childhood and family education determine the prevalence of the infection. In Japan, from 1950 on, there was a rapid decline of the infection rate attributed to the economic progress of the post-war period and improved sanitation [8]. The quality of life and socioeconomic conditions should be considered risk factors to acquire *H. pylori* infection [9].

The chronic inflammation induced by *H. pylori* interferes with the normal physiology of the gastric acid secretion in different degrees, thus leading to chronic gastritis, which, in most individuals, remains asymptomatic and does not progress. However, in some cases, altered gastric secretion, associated with tissue injury, induces the development of peptic ulcer, whereas in other cases, gastritis progresses to atrophy, intestinal metaplasia, and eventually to gastric carcinoma or rarely to gastric lymphoma, due to the persistent immune stimulation of the lymphoid tissue [10].

The gastritis can be classified based on the severity of the mucosal lesion as erosive or non-erosive, according to the site of gastric involvement (cardia, body and antrum) and histologically, as acute or chronic based on the type of inflammatory cell. However, no classification scheme fits perfectly into pathophysiology, and the evolution of gastric atrophy involves different clinical and pathophysiological consequences. Gastric gland atrophy may be present in several lesions, especially gastritis, which can progress to the multifocal gastritis associated with the bacterium *H. pylori* and atrophic gastritis of the body, not dependent on the presence of the bacterium [11].

In view of the above, it is necessary to identify the prevalence with *H. pillory* infection, independently of associated lesions, in order to discuss these aspects with the purpose of contributing to their reduction. The study aimed to: 1) determine the prevalence of *H. pylori* in samples of gastric mucosa biopsies (antrum, body, cardia and fundus), obtained through upper digestive endoscopy and original reports of surgical pathology in a pathology laboratory Aracaju, Sergipe, Brazil; 2) correlate the presence of *H. pylori* in gastric biopsy material with the variables such as age, region (urban versus rural) and sex; 3) identify the types of lesions found in gastric mucosa with *H. pylori* positive; and 4) evaluate the association of the lesions found with the biopsied gastric mucosal region.

Methodology

Between January 2013 and December 2015, a cross-sectional, retrospective study was performed at the Laboratory of Pathological Anatomy Dra. Monica Araujo (LAPMA), in Aracaju, Sergipe, based on the analysis of gastric mucosa reports obtained through biopsies of gastric mucosa from body, antrum, cardia and fundus, with *H. pylori* infection, regardless of whether through endoscopy and/or specimens of surgical resection. Reports from specimens of surgical resection were excluded because they presented incomplete information. During the research period, 45,206 biopsies were performed for the study of *H. pylori* from endoscopic gastric mucosa biopsy. Of this total, 13,986 reports were evaluated because they presented a positive result for the bacterium, and 1,077 were excluded because they did not meet the inclusion criteria, i.e., all reports should present the patients' demographic data, histopathological characteristics of the biopsied regions of the gastric mucosa and positivity for *H. pylori*. The final sample consisted of 12,909 biopsy reports.

A questionnaire was used as a data collection tool to identify the anatomopathological profile of the mucosa, which consisted of a tab with multiple-choice and short-text questions, elaborated by the researchers, having as dependent variable, the existence of *H. pylori* and independent variables: the patients' demographic characteristics (name, age, urban vs. rural region and sex); the histopathological characteristics of the antrum, fundus, cardia and body regions of the gastric mucosa such as the presence of chronic inflammation and inflammatory activity; glandular atrophy; intestinal metaplasia; evidence of ulcerated lesion; presence of fibrinoleukocytic crust, foveolar hyperplasia, lymphoid follicles, granulomas and other alterations, and the intensity of *H. pylori* colonization. The degree of intestinal metaplasia, classification of glandular atrophy and intensity of *H. pylori* colonization were performed according to the Sydney System [11]. The histological diagnosis of gastritis with and without *H. pylori* infection based on the Sydney System allowed to classify it histologically and to identify its topographic distribution from gastric biopsy.

As for the methodology used for the staining of the gastric biopsy fragments, for the histological examination, the fragments were deposited in bottles identified topographically, containing 10% formalin solution and led to a routine histological process, then subjected to 5 μm cuts and stained with hematoxylin-eosin and Giemsa.

To analyze the data, descriptive and inferential analyses were performed. In the descriptive ones, the categorical variables were presented by means of simple frequency and percentage, as for the continuous ones, through mean and standard deviation (SD). In the inferential analysis, Pearson's Chi-square association and line tests were used. In order to evaluate the histopathological profile of the biopsied regions of the gastric mucosa, the perceptual map was constructed from the multiple correspondence analyses. The significance level adopted was 5% and the software used for the analysis was IBM SPSS Statistics 20.0. The study was approved by the Committee of Ethics and Research of the Universidade Tiradentes-CEP/UNIT (CAAE: 49195515.4.0000.5371).

Results

Endoscopic gastric biopsies totaled a sample of 45,206 biop-

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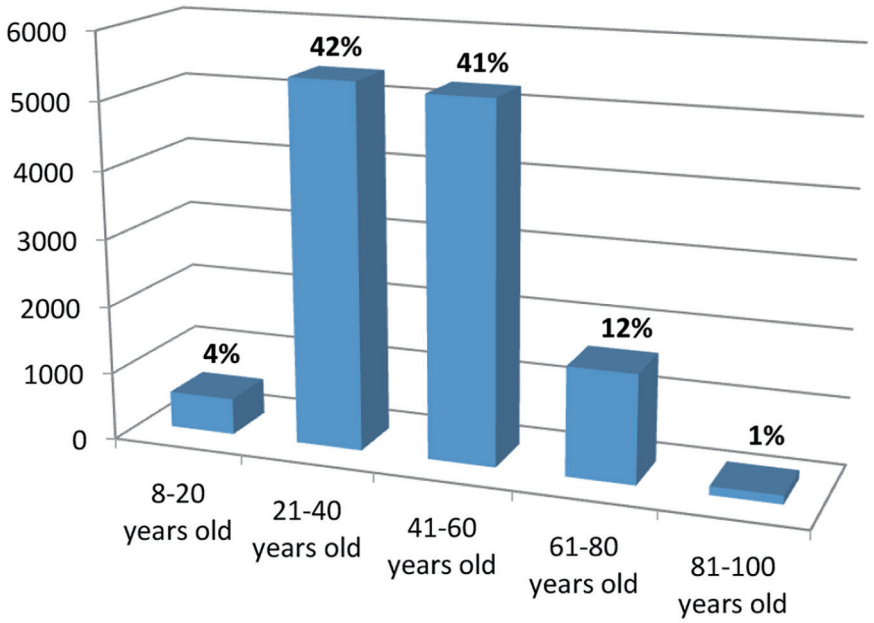

Figure 1. Age group of patients with positive *H. pylori* infection.

sies. Of the total sample, 13,986 were *H. pylori* positive, which translates into a prevalence of 30.93% (45,206). For data analysis, 12,909 reports met the inclusion criteria. Regarding sociodemographic variables, 8,320 (64.5%) of the samples were female and 4,589 (35.5%) were male. Of the samples, 8,647 (72.3%) were from urban areas. The mean age (SD) was 43 years (14.5%), and the age range of the sample varied from 8 to 100 years, being more prevalent between 21 and 60 years (Fig. 1).

As for the prevalence of gastric mucosa types and levels of infection, the antral mucosa was stated to appear the most representative fragment, corresponding to 95.5% (12,322) of the samples. It was also observed that 45.4% (5,857) of them had mild infection and 43.3% (5,587) presented moderate infection levels (Table 1).

The lesions were characterized as: glandular atrophy, intestinal metaplasia (specialized glands of the gastric body are replaced by intestinal type cells), ulcerations (gastric and duodenal ulcers), fibrinoleucocytic crust, foveolar hyperplasia, lymphoid follicles, granulomas, in addition to chronic inflammation and evidence of inflammatory activity. The absence of glandular atrophy was observed in 93.2% (12,033) of the biopsies. The mild type level of angular atrophy appeared in 6.1% (793) of the samples. In this study, 89.5% (11,548) of the cases had no intestinal metaplasia. In the 10.5% of cases with intestinal metaplasia, focal type was the most frequent when compared to diffuse and multifocal metaplasia. Some of the histologic features examined in this study were shown in Figures 2 and 3.

The presence of lymphoid follicles was more often observed compared to other alterations found (gastric and duodenal ulceration, fibrinoleucocytic crust, presence of foveolar hyperplasia and granulomas) (Table 2).

Regarding the relationship between the inflammatory process and the biopsied regions of the gastric mucosa, in all the regions evaluated, there was predominance of moderate degree, both in chronic inflammation and in the presence of inflammatory activity (Table 3).

Comparing the histopathological findings between the antrum and other regions of the stomach, the antral region has a higher rate ($P < 0.001$) of glandular atrophy, *H. pylori* infection level, presence of foveolar hyperplasia and lymphoid follicles (Table 4).

In the fundic region, an evidence of fibrinoleucocytic crust and lymphoid follicles were significant ($P < 0.001$) when compared to other regions of the gastric mucosa (Table 5).

Through the multiple correspondence analyses, the anato-

Table 1. Prevalence of Gastric Mucosa Types Represented in the Study and Levels of *H. pylori* Infection

	N	%
Mucosa type		
Antrum	12,322	95.5
Fundus	6,058	46.9
Antrum and fundus	5,504	42.6
Cardia	3	0.02
Body	62	0.5
Antral-fundic transition	75	0.6
H. pylori infection levels		
Mild	5,857	45.4
Moderate	5,587	43.3
Severe	1,465	11.3

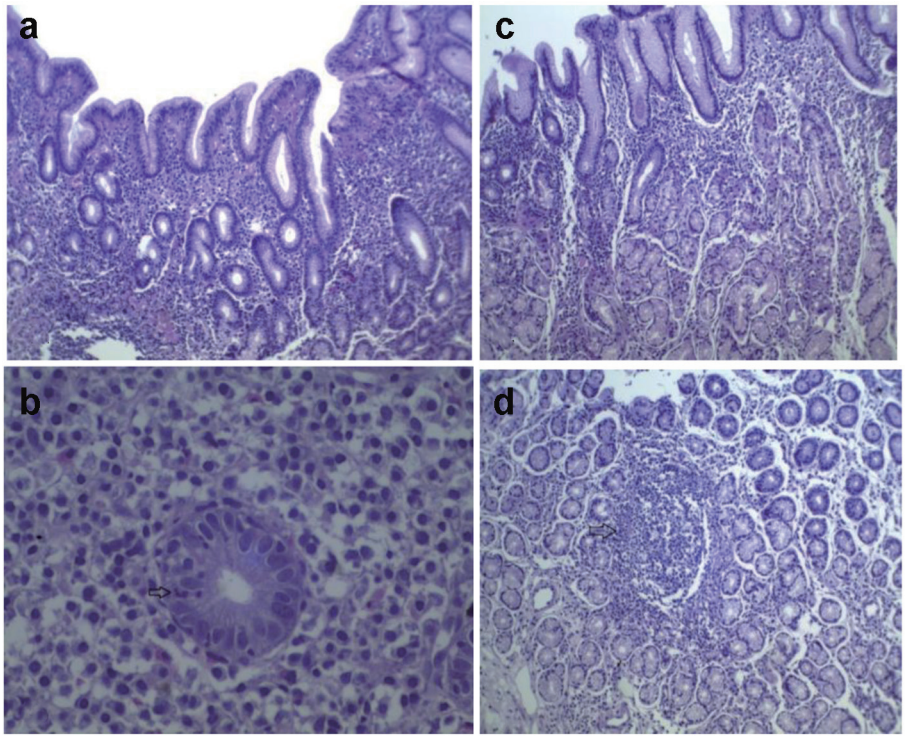

Figure 2. Histological section of gastric mucosa with *H. pylori* chronic gastritis. (A) Gastritis. (B) Inflammatory activity. (C) Oxyntic mucosal gastritis. (D) Lymphoid follicle (arrow) (H&E, × 100).

mopathological profile of the antral and fundic mucosa was observed due to the proximity between the objects. In the antral mucosa, in addition to the presence of *H. pylori* degrees of mild to moderate, there was significant relationship with the absence of glandular atrophy, absence of associated ulcerated lesions and absence of intestinal metaplasia (Fig. 4).

Fundic mucosa displayed a strong association with the lymphoid follicles, partially linked to the mild and moderate levels of *H. pylori* infection, partially associated with the absence of glandular atrophy and absence of foveolar hyperplasia (Fig. 5).

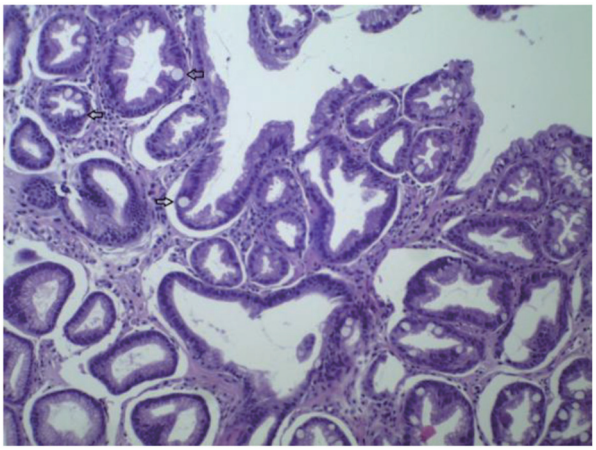

Figure 3. Antral mucosa with intestinal metaplasia (H&E, × 100).

Discussion

Evidence estimates that 50% of the world population is affected by *H. pylori*. It is considered the commonest bacterial

Table 2. Histopathologic Findings of the Gastric Mucosa in Patients With Positive *H. pylori* Infection

	N	%
Glandular atrophy		
Absent	12,033	93.23
Mild	793	6.14
Moderate	75	0.58
Severe	5	0.04
Metaplasia classification		
Absent	11,548	89.5
Focal	939	7.3
Multifocal	310	2.4
Diffuse	112	0.9
Evidence of ulcerated injury	538	4.2
Fibrinoleukocytic crust	289	2.2
Foveolar hyperplasia	2,033	15.7
Lymphoid follicles	8,001	62
Granulomas	23	0.2

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Table 3. Correlation Between Inflammation and Biopsied Gastric Regions in Patients With Positive *H. pylori* Infection

	Antral		Fundus		Cardia		Body		Antral-fundic transition	
	N	%	N	%	N	%	N	%	N	%
Chronic inflammation										
Absent	5	0.04	91	1.5	0	0	1	1.6	0	0
Mild	1,599	12.97	1,324	21.9	0	0	20	31.7	2	2.7
Moderate	8,335	67.64	3,875	64	2	66.7	41	65.1	56	74.7
Severe	2,383	19.33	768	12.7	1	33.3	1	1.6	17	22.7
Inflammatory activity										
Absent	506	4.1	514	8.5	0	0	6	9.7	7	9.3
Mild	4,934	40	2,495	41.2	1	33.3	25	40.3	31	41.3
Moderate	6,024	48.9	2,809	46.3	1	33.3	30	48.4	32	42.7
Severe	858	7.0	240	4	1	33.3	1	1.6	5	6.7

infection in humans [12, 13]. The prevalence of infection varies from age to age, ethnicity and especially socioeconomic status which is an important determinant and inversely correlated with the infection [4, 6].

The present study displayed a *H. pylori* infection prevalence of 30.93%. Previous studies [14-16] ranged from 26.91% to 76% in prevalence putting the present study close to the lower range point. Although the literature points out that *H. pylori* serum-prevalence is equally distributed in men and women, in this study, females had a higher prevalence, and the mean age

Table 4. Correlation Between Histopathological Findings of Antral Region and Other Locations of the Gastric Mucosa in *H. pylori* Positive Patients

	Antral		Others regions		X^2 (P-value)
	N	%	N	%	
Glandular atrophy					
Absent	11,453	92.97	580	98.8	25.8 (< 0.001)*
Mild	788	6.40	5	0.9	
Moderate	73	0.59	2	0.3	
Severe	5	0.04	0	0	
H. pylori search					
Mild (+/3+)	5,539	45	318	54.1	27.4 (< 0.001)*
Moderate (++/3+)	5,353	43.4	234	39.9	
Severe (+++/3)	1,430	11.6	35	6	
Metaplastic classification					
Absent	10,975	89.1	573	97,6	43.5 (< 0.001)
Focal	111	0.9	1	0.2	
Multifocal	928	7.5	11	1.9	
Diffuse	308	2.5	2	0.3	
Evidence of ulcerated injury	528	4.3	10	1.7	9.3 (0.002)
Fibrinoleucocytic crust	279	2.3	10	1.7	0.80 (0.370)
Foveolar hyperplasia	1,997	16.2	36	6.1	42.8 (< 0.001)
Lymphoid follicles	7,780	63.1	221	37.6	154 (< 0.001)
Granulomas	22	0.02	1	0.02	0.002 (0.963)

X^2: Chi-square test. *Linear association.

Table 5. Correlation Between Histopathological Findings of Fundus and Other Locations of the Gastric Mucosa in *H. pylori* Positive Patients

	Fundus		Other regions		X^2 (P-value)
	N	%	N	%	
Glandular atrophy					
Absent	5,688	93.92	6,345	92.63	9.6 (0.002)*
Mild	339	5.60	454	6.63	
Moderate	27	0.45	48	0.7	
Severe	2	0.03	3	0.04	
H. pylori infection levels					
Mild (+/3+)	2,807	46.3	3,050	44.5	5.6 (0.018)*
Moderate (++/3+)	2,595	42.8	2,992	43.7	
Severe (+++/3+)	656	10.8	809	11.8	
Metaplastic classification					
Absent	5,451	90	6,097	89	5.7 (0.127)
Focal	55	0.9	57	0.8	
Multifocal	424	7	515	7.5	
Diffuse	128	2.1	182	2.7	
Evidence of ulcerated injury	257	4.2	281	4.1	0.16 (0.690)
Fibrinoleucocytic crust	97	1.6	192	2.8	21.2 (< 0.001)
Foveolar hyperplasia	1,015	16.8	1,018	14.5	8.7 (0.003)
Lymphoid follicles	3,984	65.8	4,017	58.6	69.3 (< 0.001)
Granulomas	15	0.2	8	0.1	3.09 (0.079)

X^2: Chi-square test. *Linear association.

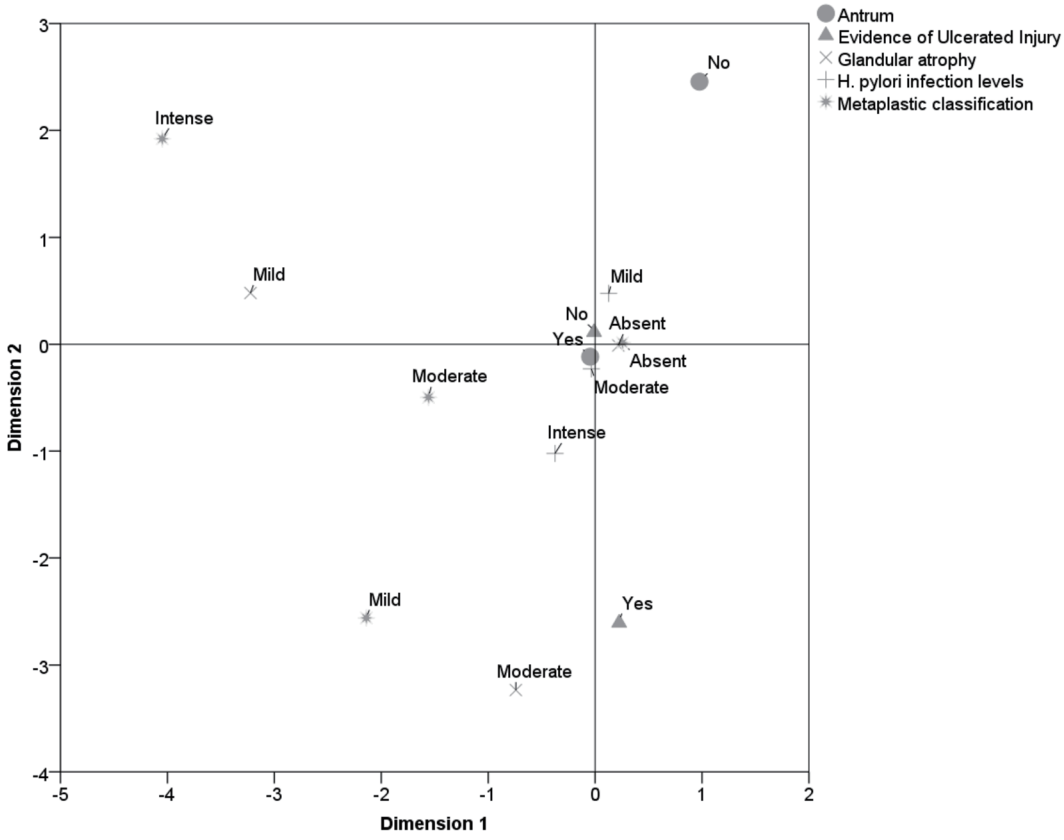

Figure 4. Pathological profile of the antral mucosa.

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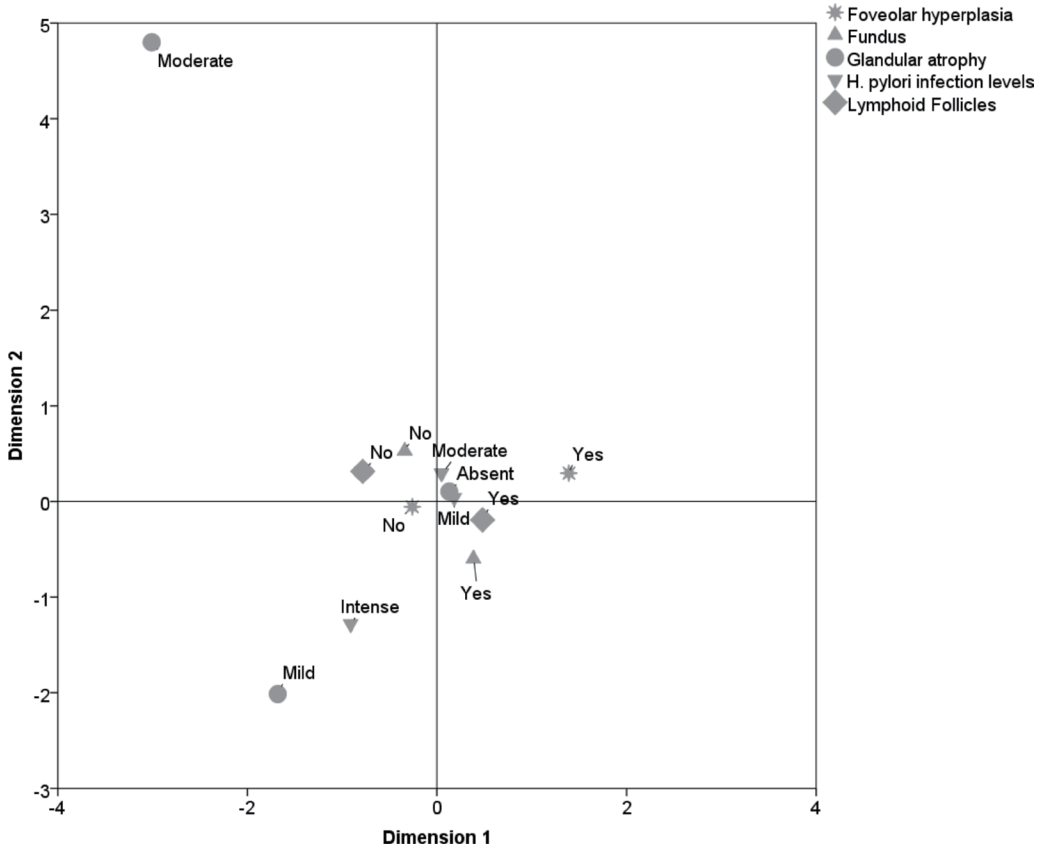

Figure 5. Pathological profile of the fundic mucosa.

of the infected was 43 years [13, 17]. The predominant age group ranged from 21 to 60 years (83%), whereas in developed countries, such as the United States, serologic values ??of *H. pylori* are rarely found before the age of 10. Between the age of 18 and 30, these values reach 10% and increase to 50% in people over 60 [4]. In developing nations, where most children are infected before the age of 10, the prevalence in adults reaches more than 80% before the age of 50 [4]. In Brazil, Bedoya et al [18] made a comparison with several diagnostic tests and reported a prevalence of 34% in children and young people up to 18 years old, increasing significantly over aging process.

Evaluating the level of intensity regarding the presence of *H. pylori* in the biopsied material, it was found that the mild and moderate levels predominated in all gastric regions. No studies supporting these findings could be found in literature.

The pathological profile of the gastric mucosa displayed presence of chronic inflammation and inflammatory activity in a moderated level in almost all biopsied regions, except for the region of the cardia, in relation to the inflammatory activity. According to Hagymasi et al [19], *H. pylori*-induced continuous inflammation, usually confined to the antrum, alters the physiology of gastric acid secretion to varying degrees, leading to chronic gastritis, which in most individuals does not further evolve.

Evidence points out that chronic gastritis induced by *H. pylori* affects the stomach's antrum and body mucosa in most of the cases [20, 21]. A study conducted in Brazil by Alvares et al [22] identified a prevalence of 88.4% of chronic gastritis in *H. pylori* positive patients, with significantly more inflammation in the antrum and angular incisure than in the gastric body. In the present study, evidence of ulcerated lesions was found in 4.2% of the *H. pylori* positive samples evaluated. Antral and fundic regions presented similar results, with a prevalence of 4.3% and 4.2%, respectively.

Odze and Goldblum [23] stated that although *H. pylori* infects more than half of the world's population, only 1-3% of the patients infected develop gastric adenocarcinoma. Therefore, a prevalence of glandular atrophy and intestinal metaplasia in the samples was evaluated. Glandular atrophy was absent in 93.2% of the *H. pylori* positive samples. Gastric intestinal metaplasia defined as the replacement of the surface, foveolar and glandular epithelium in the oxyntic or antral mucosa by the intestinal epithelium was absent in 89.5% of the samples.

Lymphoid follicles appear within a week after the onset of acute *H. pylori* infection, and are unusual on healthy/uninfected gastric mucosa [24]. Histopathological changes like foveolar hyperplasia and lymphoid follicles have shown, in the analyzed samples, a significant association with *H. pylori*. However, the evidence of ulcerated lesions in the antral region and fundic region did not support the idea that the presence of *H. pylori* represents significant development of either type of ulcerated lesion. The data showed that the lymphoid follicles were evidenced in 62% of the *H. pylori* positive gastric

biopsy samples, evidenced the hypothesis of an important link between lymphoid follicles and infection [25]. The presence of foveolar hyperplasia in the gastric mucosa occurs in patients with normal histological presentation of gastric mucosa. It may, however, be a consequence of chronic inflammation and its association with *H. pylori* [26]. This finding had significant value ($P < 0.001$) in both the antrum and fundic regions.

It is known that *H. pylori* infection is characterized by a transient increase in acid secretion and hypochlorhydria, being a precursor for the development of active chronic gastritis, with a dense cellular infiltrate in the mucosa, which due to its persistence can cause serious damage to the gastric mucosa, which can progress to atrophic gastritis, glandular atrophy and intestinal metaplasia. The infection by the micro-organism is characterized by chronicity, which predisposes its participation in the pathogenesis of chronic gastritis, peptic ulcers (gastric and duodenal), adenocarcinoma, gastric lymphoma and recurrent abdominal pain.

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Conflicts of Interest

None.

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