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Epidemiological profile of infections caused by *Helicobacter pylori* diagnosed through histopathological examinations conducted at a reference University Hospital

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Summary

Introduction: This study analyzed cases of *Helicobacter pylori* infection diagnosed through histopathological examinations. **Aim:** to analyze the results of anatomopathological examinations of gastric mucosa performed in the Pathology Department. **Methods:** It was an epidemiological, retrospective, descriptive and analytical study with a quantitative approach. The sample consisted of all the histopathological examinations of gastric mucosa obtained by upper digestive endoscopy (UDE) carried out at the Alcides Carneiro University Hospital between 01/01/2017 and 31/12/2019, for which there was a suspicion of *H. pylori* infection. **Results:** A total of 2028 reports and their respective requests were analyzed. The year with the highest prevalence of reports was 2018, with 798 (39.3%) tests carried out. The female sex prevailed with 1313 (64.7%) analyzes. The highest concentration of individuals was between 40 and 59 years of age, with 784 (38.7%). The main endoscopic finding presented by the doctor was gastritis, with 801 cases (39.5%). However, positive results proving clinical suspicion of *H. pylori* represented a smaller proportion of the findings, with 686 (33.7%). In addition, positive cases for *H. pylori* were more associated with the 20-59 age group (n=471; 23.2%) and it was found that patients with an endoscopic diagnosis of ulcers were more associated with positive results proving clinical suspicion for *H. pylori* on pathology examination

(n=106; 5.2%). **Conclusion:** We conclude that one third of the population seen at the hospital for EDA with biopsy and who had clinical suspicion of *H. pylori* infection were positive for the bacterium in the anatomopathological study subsequently carried out at the hospital during the period studied, corroborating the bacterial association with inflammatory processes of the gastric mucosa already described in previous studies.

Keywords: Gastric mucosa, Gastritis, Inflammation, *Helicobacter pylori*, Biopsy.

Resumo

Perfil epidemiológico das infecções causadas pelo *Helicobacter pylori* diagnosticadas através de exames histopatológicos realizados em um Hospital Universitário de referência

Introdução: O presente estudo analisou os casos de infecção causada por *Helicobacter pylori* diagnosticados através de exames histopatológicos. **Objetivo:** analisar os resultados dos exames anatomopatológicos da mucosa gástrica realizados no Serviço de Patologia. **Métodos:** Tratou-se de estudo epidemiológico, retrospectivo, descritivo e analítico, com abordagem quantitativa. A amostra foi composta por todos os exames anatomopatológicos de mucosa gástrica obtida por endoscopia digestiva alta (EDA) realizados no Hospital Universitário Alcides Carneiro entre 01/01/2017 e 31/12/2019, cuja solicitação foi apresentada suspeita de infecção por *H. pylori*. **Resultados:** Foram analisados 2028 laudos, com suas respectivas requisições. O ano com maior prevalência de laudos foi 2018, com 798 (39,3%) exames realizados. O sexo feminino prevaleceu com 1313 (64,7%) análises. A maior concentração dos indivíduos foi entre 40 a 59 anos de idade, com 784 (38,7%). O principal achado endoscópico apresentada(o) pelo médico foi gastrite, com 801 casos (39,5%). Contudo, os resultados positivos que comprovam a suspeita clínica para *H. pylori* representaram menor parcela dos achados, com 686 (33,7%). Além disso, os casos positivos para *H. pylori* associam-se mais com a faixa etária de 20 a 59 anos (n=471; 23,2%) e constatou-se que os pacientes com diagnóstico endoscópico de úlcera apresentaram maior associação com resultados positivos que comprovam a suspeita clínica para *H. pylori* ao exame anatomopatológico (n=106; 5,2%). **Conclusão:** Conclui-se que um terço da população atendida no Hospital para realização de EDA com biópsia e que apresentavam suspeita clínica de infecção por *H. pylori* apresentou positividade para a bactéria ao estudo anatomopatológico

subsequentemente realizado no hospital no período estudado, corroborando a associação bacteriana com processos inflamatórios de mucosa gástrica já descrita em estudos anteriores.

Palavras-chave: Mucosa gástrica, Gastrite, Inflamação, *Helicobacter pylori*, Biópsia.

Resumen

Perfil epidemiológico de las infecciones por *Helicobacter pylori* diagnosticadas mediante exámenes histopatológicos realizados en un Hospital Universitario de referencia

Introducción: El presente estudio analizó casos de infección por *Helicobacter pylori* diagnosticados mediante exámenes histopatológicos. **Objetivo:** analizar los resultados de los exámenes anatomopatológicos de la mucosa gástrica realizados en el Servicio de Patología. **Métodos:** Se trató de un estudio epidemiológico, retrospectivo, descriptivo y analítico, con enfoque cuantitativo. La muestra estuvo compuesta por todos los exámenes anatomopatológicos de la mucosa gástrica obtenidos por endoscopia digestiva alta (EDA) realizados en el Hospital Universitário Alcides Carneiro entre el 01/01/2017 y el 31/12/2019, cuya solicitud fue sospechosa de infección por *H. pylori*. **Resultados:** Se analizaron 2028 informes, con sus respectivas solicitudes. El año con mayor prevalencia de reportes fue 2018, con 798 (39,3%) exámenes realizados. Predominaron las mujeres con 1.313 (64,7%) análisis. La mayor concentración de individuos se registró entre 40 y 59 años, con 784 (38,7%). El principal hallazgo endoscópico presentado por el médico fue la gastritis, con 801 casos (39,5%). Sin embargo, los resultados positivos que confirman la sospecha clínica de *H. pylori* representaron una porción menor de los hallazgos, con 686 (33,7%). Además, los casos positivos para *H. pylori* se asocian más con el grupo etario de 20 a 59 años (n=471; 23,2%) y se encontró que los pacientes con diagnóstico endoscópico de úlceras tuvieron una mayor asociación con resultados positivos que confirman sospecha clínica de *H. pylori* en el examen patológico (n=106; 5,2%). **Conclusión:** Se concluye que un tercio de la población atendida en el Hospital por EDA con biopsia y que tuvo sospecha clínica de infección por *H. pylori* resultó positiva a la bacteria en el estudio anatomopatológico realizado posteriormente en el hospital durante el período estudiado, corroborando la asociación bacteriana con procesos inflamatorios de la mucosa gástrica ya descritos en estudios previos.

Palabras clave: Mucosa gastrica, Gastritis, Inflamación, *Helicobacter pylori*, Biopsia.

Introduction

In the world, there are thousands of microorganism species, including fungi, bacteria, and protozoa, but only a small fraction of these species have the potential to be pathogenic to humans [1].

One common bacterial infection worldwide is caused by *Helicobacter pylori*, a Gram-negative bacillus that infects the human stomach and can lead to gastritis, ulcers, and even more serious conditions such as cancer. It is estimated that a portion of the world's population may have this microorganism infecting their gastric mucosa, with the prevalence varying by region, affecting 46.3% of men, with a prevalence of 48.6% in adults compared to children [2].

Histopathological examinations are used in the diagnosis of various infections, including those caused by Helicobacter pylori, enabling the prescription of specific treatment [3].

The present study aimed to analyze the results of anatomopathological examinations of gastric mucosa performed in the Pathology Department of Alcides Carneiro University Hospital (ACUH), using tissue samples obtained via endoscopy, where the request indicated suspicion of *H. pylori* infection. The study is retrospective and includes examinations conducted from 01/01/17 to 31/12/2019, aiming to determine the profile of patients concerning age, gender, clinical hypotheses, endoscopic findings, and biopsy topography.

Materials and methods

The research consisted of an epidemiological, retrospective, descriptive, and analytical study with a quantitative approach [4]. Data collection was carried out in the physical archive of requests and reports from the Pathology Department of HUAC.

To constitute the sample, all anatomopathological examinations of gastric mucosa with tissue samples obtained through endoscopy were included, where there was a suspicion of *H. pylori* infection, while documents with incomplete information or outside the predefined time frame were excluded.

The data selected for analysis included the year of the examination, patient's gender, patient's age, diagnostic hypothesis (+/- endoscopic findings), biopsy topography, and the result of the *H. pylori* investigation.

The collected data were organized into a Microsoft Office Excel 2013 spreadsheet and later processed in the Statistical Package for Social Sciences (SPSS) software version

20.0, obtaining their absolute and relative frequencies and calculating adjusted residuals, considering ≥ 1.96.

Adjusted residuals can be used as a tool for interpreting data displayed in contingency tables. With this statistical tool, it is possible to analyze how the possible values in the tables contribute to the Chi-square value and, consequently, to the associations between the variables analyzed. For a 95% significance level, the adjusted residual with statistical significance is one greater than 1.96 times the standard deviation. When significant residual values are positive, it indicates a tendency of more observed cases than expected in the statistics, while significant residuals [5].

The adjusted residual (R) has a normal distribution with a mean of zero and a standard deviation of 1. Thus, if the adjusted residual is greater than 1.96 in absolute value, it can be said that there is evidence of a significant association between the two categories. The higher the adjusted residual, the stronger the association between the categories, with a 95% confidence interval and a p-value ≤ 0.05, using the Pearson Chi-Square Test. Additionally, the Graphpad Prism program was used to create graphs of the variables under study.

Information such as year, month, gender, age group, type of biopsy (incision, excision, absent when the patient's record did not specify the biopsy type, and others when the patient's record marked "other" as the biopsy type), clinical hypothesis (the diagnostic hypothesis raised by the doctor), positive or negative microorganism, and removal location were collected.

In accordance with Resolution N°. 466 of December 12, 2012, and Resolution N°. 510 of April 7, 2016, this research complied with the guidelines and norms for research involving human subjects. The project was approved by the ethics committee on February 8, 2022, under opinion number 5.231.298, and data collection began shortly thereafter, with due respect to the confidentiality of sensitive patient data and the caution not to harm the Pathology service, the patients it serves, and the research results. Furthermore, the project received approval from the Education and Research Management (ERM) of ACUH under Process N°. 23769.010333/2021-01 SEI N°. 18173742.

Results

Within the analyzed time frame, the Pathology department of HUAC had 10600 anatomopathological reports in its archives, and those that met the objectives of this study were selected, totaling 2028 records (19%).

The year 2018 had the highest number of examinations, with 798 (39.3%). Concerning the months, there were more examinations in the months of August, with 100 (5%), November with 114 (6%), and December with 106 (5%), as shown in Figure 1. Regarding gender, there was a higher number of anatomopathological examinations of gastric mucosa for females, with 1313 (64.7%) exams (Figure 1B). As for age groups, the highest concentration was among individuals aged 40 to 59 years, with 784 (7%), followed by those aged 20 to 39 years, with 495 (24.4%) in anatomopathological examinations of gastric mucosa (Figure 1C).

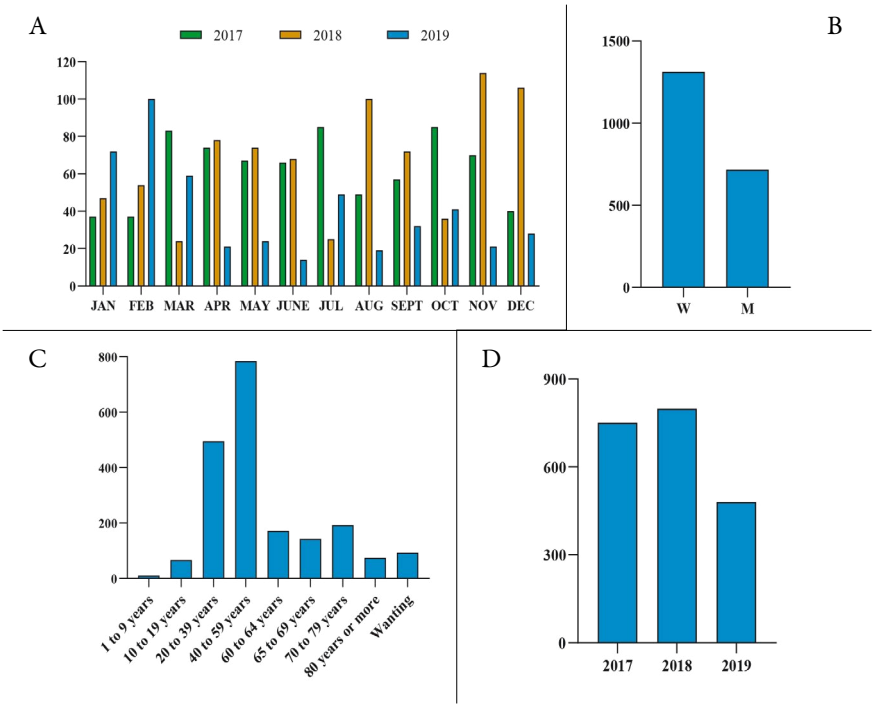

Figure 1. Frequencies of years, months, gender, and age groups of histopathological results for bacteria and fungi performed at ACUH from 2017 to 2019. Fig. 1A - Distribution of histopathological examinations by months and years. Fig. 1B - Frequency by gender. Fig. 1C - Frequency of the study's age groups. Fig. 1D - Analyzed time period. M - Male; W - Women. JAN - January. FEB - February. MAR - March. APR - April. MAY - May. JUNE - June. JUL - July. AUG - August. SEPT - September. OCT - October. NOV - November. DEC - December.

In this study, a greater number of biopsies were performed by incision (n=1,217; 60%), followed by biopsies by excision (n=458; 22.6%) (Figure 2A). Among the examined cases, 686 (33.7%) tested positive for *H. pylori* (Figure 2B). Regarding the diagnostic

hypotheses presented by the requesting physician, pangastritis prevailed (n=801; 39.5%), followed by gastritis (n=510; 25.1%) (Figure 2C). As for the biopsy topography, the body and antrum of the stomach were the most frequent sites (n=1,097; 54.1%), followed by biopsies from the antrum alone (n=610; 30.1%) (Figure 2D).

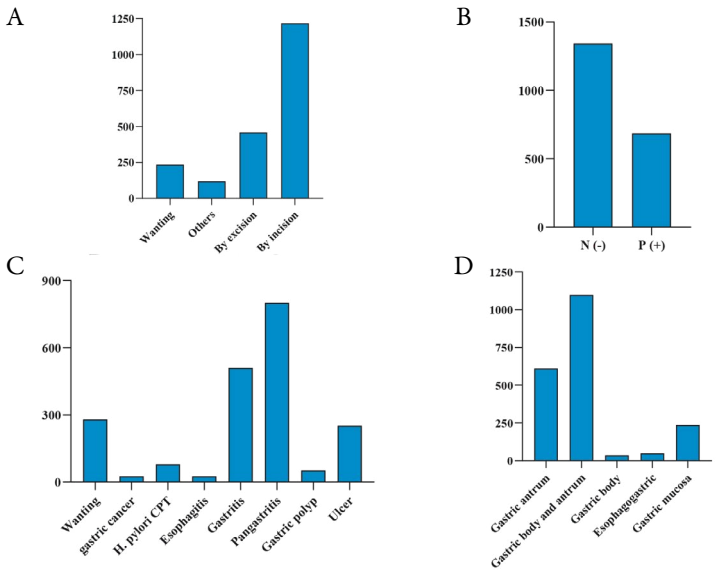

Figure 2. Laboratory Aspects. Fig. 2A - Type of lesion removal for subsequent biopsy. Fig. 2B - Distribution of positive or negative results for *H. pylori*. Fig. 2C - Clinical hypothesis raised by the physician. Fig. 2D - Anatomical locations removed for histopathological examination. N - Negative. P - Positive.

In Table 1, it was observed that the male gender is positively associated with biopsies for *H. pylori* in the esophagogastric region (n=29; 1.4%). Furthermore, it can be noted that patients with endoscopic findings of gastric ulcers had a stronger association with histopathological positivity for *H. pylori* (n=106; 5.2%).

It was found that the age group of 60 years or older is positively associated with excision biopsies (n=145; 7.1%), and the age group of 20 to 59 years is associated with incision biopsies (n=778; 38.4%). Regarding the removal location, the age group of 20 to 59 years was positively associated with removals in the gastric antrum (n=410; 20.2%). Additionally, cases positive for *H. pylori* were more associated with the age group of 20 to 59 years (n=471; 23.2%) (Table 2)

Table 1. Association between the removal site and the patients' sex, as well as between the microorganism and clinical hypothesis.

Removal location	**Sex**						
	Women		**Male**		**TOTAL**		**p**
	N	**%**	**N**	**%**	**N**	**%**	
Gastric antrum	399	19.7	211	10.4	610	30.1	0.008
Gastric body and antrum	716	35.3	381	18.8	1097	54.1	
Gastric body	25	1.2	11	0.5	36	1.8	
Esophagogastric	19	0.9	29+	1.4	48	2.4	
Gastric mucosa	154	7.6	83	4.1	237	11.7	
TOTAL	1313	64.7	715	35.3	2028	100	
Clinical hypothesis	**Positive or negative microorganism**						
	Negative		**Positive**		**TOTAL**		**p**
	N	%	N	%	N	%	
Wanting	211	10.4	69	3.4	280	13.8	0.006
Gastric cancer	19	0.9	7	0.3	26	1.3	
Control after *H. pylori* treatment	49	2.4	31	1.5	80	3.9	
Esophagitis	19	0.8	7	0.3	26	0.8	
Gastritis	344	17	166	8.2	510	25.1	
Pangastritis	518	25.5	283	14	801	39.5	
Gastric polyp	38	1.9	15	0.7	53	2.6	
Ulcer	146	7.2	106+	5.2	252	12.4	
TOTAL	1344	66.3	684	33.7	2028	100	

+ – Adjusted residual; *p* – Pearson's Chi-square test.

Table 2. Association of removal type, removal site, and microorganism (positive or negative) with age group.

Type of Biopsy	**Age range**										
	1-19 years		**20-59 years**		**60 years or more**		**Wanting**		**TOTAL**		**p**
	N	%	N	%	N	%	N	%	N	%	
By excision	16	0.8	293	14.4	146+	7.1	5	0.2	460	22.7	<0.001
By incision	48	2.4	778+	38.4	332	16.4	59	2.9	1217	60	
Wanting	11	0.5	160	7.9	68	3.4	0	0	235	11.9	
Others	1	0	48	2.4	34	1.7	29	1.4	110	5.5	
TOTAL	76	3.7	1279	63.1	580	28.6	93	4.6	2028	100	

(*Continued*)

Type of Biopsy	**Age range**										
	1-19 years		**20-59 years**		**60 years or more**		**Wanting**		**TOTAL**		**p**
	N	%	N	%	N	%	N	%	N	%	
Removal location	Age range										
	1-19 years		20-59 years		60 years or more		Wanting		TOTAL		p
	N	%	N	%	N	%	N	%	N	%	
Gastric antrum	21	1	410+	20.2	175	8.6	4	0.2	610	30.1	<0.001
Gastric body and antrum	44	2.2	675	33.3	307	15.1	71	3.5	1097	54.1	
Gastric body	2	0.1	21	1	13	0.6	0	0	36	1.8	
Esophagogastric	3	0.1	34	1.7	11	0.5	0	0	48	2.4	
Gastric mucosa	6	0.3	139	6.9	74	3.6	18	0.9	237	11.7	
TOTAL	76	3.7	1279	63.1	580	28.6	93	4.6	2028	100	
Positive/ negative microorganism	Age range										
	1-19 years		20-59 years		60 years or more		Wanting		TOTAL		p
	N	%	N	%	N	%	N	%	N	%	
Negative	59+	2.9	808	39.8	419+	20.7	58	2.9	1344	66.3	<0.001
Positive	17	0.8	471+	23.2	161	7.9	35	1.7	684	33.7	
TOTAL	76	3.7	1279	63.1	580	28.6	93	4.6	2028	100	

+ – Adjusted residual; *p* – Pearson's Chi-square test.

Discussion

In the present study, a higher number of anatomopathological examinations of gastric mucosa were observed for females. The lower number of male patients can be justified by social and cultural factors contributing to a reduced utilization of healthcare services by men, potentially leading to delays in diagnosing and treating diseases [6, 7].

Regarding age groups, the predominant group was individuals aged 40 to 59 years, consistent with another study conducted in two reference services in the southern region of Santa Catarina, which showed that individuals undergoing histopathological examinations of stomach tissue had an average age between 40 and 60 years [8].

In the current study, there was a higher number of incision biopsies, followed by excision biopsies. Histopathological biopsies can be classified based on the type of lesion removal, with the most common methods being incision (removing only a part of the lesion), excision (removing the entire lesion, including adjacent cells), puncture (removing part of the material using needles, including Fine Needle Aspiration Biopsy - FNA), scraping (ideal for evaluating small local infections like fungal infections and dermatitis), and surgical specimen (removing organs or parts of them) [9].

The choice of the lesion removal site for biopsy should be based on the region with the highest number of possible alterations detectable in the tissue, while avoiding necrotic tissues. In the incision biopsy format, the removal should be elliptical, in a "V" shape. Excision biopsies are typically performed on theoretically small-sized materials, which are often benign [10].

Histopathological testing for *H. pylori* was positive in 33.7% of suspected cases of infection by the bacterium. Histopathological examinations can assist in diagnosing various infections, including *H. pylori* infections in regions such as the stomach, esophagus, gastroduodenal regions, and esophagogastric regions [3].

Regarding the clinical hypothesis raised by the physician, pangastritis prevailed, followed by gastritis. As for the removal location for *H. pylori* biopsy, the removal of both the body and antrum of the stomach was more frequent, followed by the removal of just the gastric antrum. Gastritis, pangastritis, and ulcers are more common than other clinical hypotheses because a larger number of examinations were conducted to investigate *H. pylori*, a pathogen that can cause the aforementioned diseases. Most removals occurred in the stomach, in the body and antrum region, due to material collection for *H. pylori* research. Typically, two samples are collected from different locations in each region of the body and gastric antrum, depending on the level of inflammation observed in the endoscopy [11]. The treatment of ulcers and diseases acid-peptics, associated the proton pump inhibitors (PPIs) which have fully replaced antacids, parasympatholytics and histamine H2 receptor antagonists. The most effective approach is to administer PPIs in the morning on an empty stomach, in a single daily dose. This therapy is generally considered very safe. However, potential adverse effects of long-term PPI treatment on the efficacy of other medications (such as clopidogrel), bone metabolism, and the development of respiratory infections have been discussed recently. PPIs also play an essential role in the eradication treatment of *H. pylori* infection, as well as in the prevention and treatment of gastropathy induced by nonsteroidal anti-inflammatory drugs. Additionally, they are utilized in relation to some rare hypersecretory conditions [12].

Table 1 showed that the male gender was positively associated with biopsies for *H. pylori* in the esophagogastric region. One of the main characteristics developed when *H. pylori* is present in gastrointestinal regions is gastric atrophy [13]. A study by Chiang *et al.* (2021) [14] that demonstrated the association between *H. pylori* and gastric junction atrophy observed that this atrophy is more strongly associated with the male gender.

In Table 2, it was found that the age group of 60 years or older is positively associated with excision biopsies, and the age group of 20 to 59 years is associated with incision biopsies. In excision, it is important to consider the removal direction in line with local tension to reduce the need for skin grafts and reconstructive skin procedures. Large lesions undergoing excision should be carefully considered, as this procedure can interfere with lymphatic mapping, affecting lymphoscintigraphy accuracy. To mitigate this issue with excision, other techniques such as incision are used; however, incision has some disadvantages, like the potential loss of malignant material in the analyzed lesions [15].

As seen in Table 2, histopathological examinations that were positive for *H. pylori* were associated with the age group of 20 to 59 years, while negative results for *H. pylori* were associated with the age group of 60 years or older. This bacterium has several mechanisms that enhance its mobility, adhesion, and manipulation of the gastric microenvironment, including a variety of virulence factors that increase its pathogenicity, such as the antigen A associated with cytotoxin, vacuolating cytotoxin, A-promoter duodenal ulcer gene protein, and urease, which enables the bacterium to survive in an acidic environment. The host's immune system may react with a polarized Th1-type immune response. Therefore, it is essential to use diagnostic methods for this infection to prevent future health problems [16].

Patients with the presence of *H. pylori*, leading to chronic gastritis, have various factors contributing to this health issue. Foods can affect gastric motility, for example, hot foods can cause gastric mucosa congestion, leading to increased acid secretion. In addition, the consumption of alcoholic beverages also increases gastric acid secretion [17].

Conclusion

With the present study, it was possible to observe that, within the analyzed time frame, the year 2018 had the highest number of histopathological examinations for the diagnosis of *H. pylori* infections, with a predominance of females in the age group of 40 to 59 years. Positive results for the bacterium occurred in a lower proportion, accounting for 33.7% of suspected cases, especially in those with a clinical hypothesis of gastritis and biopsies of the body and antrum of the stomach. Furthermore, in esophagogastric

region removals for investigative *H. pylori* biopsies, males are more likely to undergo these procedures. The age group of 60 years or older is more prone to excision biopsies, while the age group of 20 to 59 years is more associated with incision biopsies and removals in the gastric antrum. Additionally, the age group of 20 to 59 years is more associated with positive results for *H. pylori*, while the age group of 60 years or older is more associated with negative results.

The present study allowed for an epidemiological assessment of histopathological diagnoses of *H. pylori* infections. There is a lack of epidemiological studies related to histopathological diagnosis of *H. pylori* infection. In the current study, there was a higher proportion of males and adults, especially in the age group of 40 to 59 years, with positive results for *H. pylori*, which aligns with studies described in the literature. However, more studies of this nature are still necessary, or the observation that there is a need for better completion of requests for anatomopathological examinations.

Conflict of interest

No potential conflicts of interest were reported by the authors.

Ethics approval

This research was approved by the Research Ethics Committee of the Center for Education and Health at the Federal University of Campina Grande - CES/UFCG, under opinion number 5.231.298.

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