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Lack of association between *Helicobacter pylori* infection and diabetes mellitus: a cross-sectional study in the Central Brazil region

D.N. Maciel[1], H.A. da Silva[1], F.A.S. Moraes[1], S.B. Santiago[1], L.P. Assunção[2], L.T. Rasmussen[3], R.S. Santos[2] and M.S. Barbosa[1]

[1] Núcleo de Estudos da *Helicobacter pylori*, Departamento de Biociências e Biotecnologia, Instituto de Patologia Tropical e Saúde Pública, Universidade Federal de Goiás, Goiânia, Goiás, Brasil
[2] Laboratório de Patologia Molecular, Departamento de Bioquímica e Biologia Molecular, Instituto de Ciências Biológicas, Universidade Federal de Goiás, Goiânia, Goiás, Brasil
[3] Departamento de Genética, Escola de Medicina de Marília, Marília, SP, Brasil

Corresponding author: M.S. Barbosa
E-mail: santiago@ufg.br

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ABSTRACT. *Helicobacter pylori* is a pathogen that infects approximately half of the world population and is associated with gastroduodenal diseases. Several studies have demonstrated an association with extragastric diseases and metabolic syndromes, mainly diabetes mellitus (DM). Inflammation associated with *H. pylori* can lead to increased insulin resistance, leading to an increased risk of DM among infected individuals. The objective of this study was to investigate the association between *H. pylori* infection and DM. This was done with a cross-sectional study carried out in the central region of Brazil with dyspeptic patients undergoing digestive endoscopy. Gastric biopsies were analyzed using histopathological and molecular techniques. A total of 117 patients were recruited for the research; 45 patients without a report of DM were excluded from the study. A total of 72 dyspeptic patients participated in the study (18 men and 54 women, mean age 49.1 years). Of these, 65% were

infected by *H. pylori* and15% were diabetic. The prevalence of *H. pylori* infection in diabetics was higher among participants with incomplete high school at 83%, non-smokers 64% and non-drinkers 55%, though not significantly different. There was a positive relationship between coffee consumption and *H. pylori* infection. In the two-sample proportion test, a higher proportion of *hpx+* diabetic individuals was found among coffee consumers with 45%, when compared to *hpx–* diabetics (27%), though with no significant difference (p=0.285). In this study, there was no significant association between *H. pylori* infection and DM. New trials with a larger sample size would be useful to elucidate a possible association between *H. pylori* infection and DM, as well as the pathological mechanisms of the bacteria that are involved in the development of DM.

Key words: *Helicobacter pylori*; Gastric diseases; Metabolic syndrome; Diabetes mellitus

INTRODUCTION

Helicobacter pylori infects approximately half of the world's population, but in most cases, infected individuals remain asymptomatic. According to the World Health Organization (WHO), prevalence rates vary according to geography, ethnicity, age and socioeconomic conditions of populations. Host conditions, environmental factors and bacterial characteristics, which are strain-dependent, determine the pathogenesis of *H. pylori* infection. Once permanent infection is established in the stomach, various gastroduodenal complications such as chronic gastritis, peptic ulcer, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue lymphoma can develop (Ansari and Yamaoka, 2019).

The role of *H. pylori* infection in the development of gastroduodenal disorders is well established. However, more recent studies have associated this infection with several extragastric diseases, such as neurological, dermatological, hematological, ocular, cardiovascular, allergic and metabolic diseases, especially diabetes mellitus (DM) (Franceschi, 2015). In fact, infection with *H. pylori* is associated with alterations in glycolipid metabolism, especially in DM, which is characterized by hyperglycemia. Diabetic patients are more susceptible to a variety of infections because of chronic elevated blood glucose levels and impaired immune response. This immunity deficiency is responsible for more frequent and serious infections, such as *H. pylori* (Haj et al., 2017; Wawro, et al., 2019).

Studies have shown divergent results between the association of bacterial infection, insulin levels and fasting serum glucose levels. This can be explained because some strains of *H. pylori* are more virulent, especially the *cagA* positive strains. These are associated with increased production of pro-inflammatory cytokines such as TNF (Tumor Necrosis Factor), C-reactive protein, Ils (Interleukins) 1, 6 and 8, which can alter glycemic control contributing to insulin resistance and incidence of DM, especially type 2. In addition, gastritis resulting from *H. pylori* infection can potentially affect gut-related hormones such

as leptin, ghrelin, gastrin and somatostatin, and, consequently, insulin sensitivity and homeostasis of the glucose, thus increasing the risk of diabetes (Candelli et al., 2003; Maluf et al., 2020).

Currently, diabetes is a major public health concern worldwide. In 2021, it was estimated that there were 537 million people with diabetes aged between 20 and 79 years. In that same period, the total global health expenditure due to diabetes was estimated at US$ 966 billion. It is estimated that the number of people with diabetes will increase to 783 million by 2045 (IDF, 2021). Due to the high rates of *H. pylori* infection in diabetic patients and the scarcity of data in Brazil, it is relevant to investigate the possible association of infection with DM. This is a pioneering study that reinforces the relevance of this research for the population of this region. The study was designed to evaluate the possible relationship between *H. pylori* infection and diabetes mellitus in dyspeptic adults in Central-West Brazil.

MATERIAL AND METHODS

Ethical considerations

This cross-sectional study was submitted and approved by the Research Ethics Committee of the Hospital das Clínicas, Universidade Federal de Goiás (UFG) – Brasil, under opinion 2.519.032 (CAEE: 83422017.7.0000.5078). All patients who agreed to participate in the study were in accordance with the Informed Consent Form.

Study participants

The study was carried out in Goiânia, State of Goiás, located in the Central Brazil region. The patients treated at the Hospital das Clínicas of the UFG were recruited from January 2020 to December 2022. The selection of patients was based on the diagnosis of *H. pylori* infection and on reports of Upper Digestive Endoscopy (UDE). A total of 117 members were included in the study. This value was based on the prevalence of *H. pylori* with a statistical power of 80% and significance level of 0.05. Participants answered a sociodemographic questionnaire with the help of a trained team.

Participants of both sexes, aged 18 years or older and submitted to UDE and who agreed to participate in the study were included. Patients who used antibiotics and immunosuppressants eight weeks before sample collection, use of proton pump inhibitors two weeks before sample collection, pregnancy, lactation, active gastrointestinal bleeding and history of gastrectomy were excluded from the study. Information about the diagnosis of DM was obtained from medical records or self-reports.

Samples

Gastric samples were collected by the gastroenterologist and obtained in accordance with the recommendations of the IV Brazilian Consensus on *H. pylori* infection. At the time of collection, the samples were identified only by the initials of the patients' names. Sociodemographic and clinical data were obtained through questionnaires and medical

records. The anonymity of the patient's identity and data were preserved (Coelho et al., 2018).

Two samples (one from the antrum and the other from the gastric body) were sent to the Clinical Pathology Laboratory at HC/UFG for histopathological analysis. The other two samples were sent to the Núcleo de Estudos da *Helicobacter pylori* (NEHP) of Universidade Federal de Goiás for molecular analysis. Fragments intended for molecular analysis were transported and stored at -20ºC for adequate tissue preservation. Patients who were positive in any of the tests (histopathological and/or molecular) were considered positive.

Histopathological analysis

Gastric mucosa biopsies were fixed in 10% buffered formalin, cut, and stained with hematoxylin-eosin and Giemsa. Histological parameters were classified using the criteria described in the Sydney system (Nevoa et al., 2017).

Molecular detection of *Helicobacter pylori*

DNA extraction from gastric samples was performed at NEHP/UFG according to the instructions of the DNA extraction protocol provided by the KitQIAamp DNA Minikit® (Quiagen, Valencia, CA, USA). The *hpx1* and *hpx2* oligonucleotides of the 16S ribosomal rRNA gene were used for molecular detection of the bacteria by PCR (Polymerase Chain Reaction), as described by Silva, et al. (2021) and Nevoa, et al. (2017).

The gene-specific oligonucleotides (primers), reaction conditions and the sizes of the amplified fragments are described in Table 1.

Table 1. Primer sequences used for detection of *Helicobacter pylori* using 16S rRNA, amplification conditions and fragment sizes.

Gene	Oligonucleotides	Sequence of oligonucleotides (5'-3')	Amplification Conditions	bp	Reference
16S rRNA	*hpx*1	CTGGAGARACTAAGYCCTCC	94ºC 5', 40 cycles 94ºC 1'/ 59ºC 1'/ 72ºC 1' e 72ºC 7'.	150	Luscenti and Gatti (2008)
	*hpx*2	GAGGAATACTCATTGCGAAGGCGA			

To visualize the PCR product, a 2% agarose gel electrophoresis was performed. Samples were stained with BlueGreen nucleic acid stain (Lab Biotechnology). The gel with samples and molecular weight marker (100 bp insert manufacturer) was visualized under ultraviolet light.

Statistical processing and analysis

Data analyses were divided into three non-parametric approaches, the first was the Cohen's Kappa test, in which the Kappa coefficient (K) was calculated to assess the degree of agreement and reproducibility of the results of histopathological and molecular diagnoses. The second approach, Fisher's exact test was performed to verify the association

of *H. pylori* infection status and diabetes with all sociodemographic variables of the study. Finally, the two-sample ratio test was applied to compare DM status in the *H. pylori*-infected population. In all statistical tests, p-value (p) ≤ 0.05 was considered. All analyses and data tabulation were performed in Microsoft Excel 2016 spreadsheets and with the aid of R software version 3.5.3 (Miot, 2016).

RESULTS AND DISCUSSION

Association between *H. pylori* infection and DM with sociodemographic conditions and lifestyle habits

A total of 117 dyspeptic patients participated in this study. Among these, a total of 45 patients were excluded from the study due to lack of DM diagnosis. Seventy-two patients (18 men and 54 women) were included in this study. The prevalence of *H. pylori* infection was 65%, this rate was calculated based on the results of histopathological exams and/or PCR. Among *H. pylori* positive individuals, 23% of the men and 62% of the women were non-diabetic, aged between 21 and 77 years (mean 49.1 years) (Ramos et al., 2020).

The concordance test between the *H. pylori* diagnostic methods showed a Kappa coefficient of 0.68 with a p-value of 0.00003. Thus, the two methodologies (histopathological and molecular) are classified according to Landis and Koch (1977) as "very good". Therefore, these results allow the use of all diagnostic data of the participants considered in the study.

As for education, 65 of 72 dyspeptic individuals had incomplete secondary education. Approximately 36% had a family income between 1 and 2 minimum wages and 31% had an income between 3 and 5 minimum wages. Among the 47 that were infected, 40% had a family income between 1 and 2 minimum wages. All individuals infected with *H. pylori* and diabetics had piped water in their homes and shared rooms with more than three people.

The prevalence of *H. pylori* infection in diabetic patients was higher in females (83%). From this perspective, in the study by Man et al. (2020) it was observed that the subgroup analysis (male and female) indicated an increased risk of diabetes in the female group that were infected by the bacteria. The study by Haj et al. (2017) showed that *H. pylori* infection may be associated with worse glycemic control in men. There is likely to be an interaction between sex hormones and *H. pylori*-induced inflammation. Markle et al. (2013) presented a direct interaction between sex hormones and bacterial exposures, which showed that manipulations of the microbiome can cause a testosterone-dependent effect on inflammation and autoimmunity, which can lead to protection against DM1.

Among diabetics, the present study showed that *H. pylori* infection was prevalent in participants aged ≥ 30 years, although there is no evidence showing that the interaction between *H. pylori* infection and age has an effect on the development of DM. The study by Han et al. (2016) found a significant relationship between these two factors, in which the *H. pylori* positive Chinese population between middle age and old age had a higher prevalence of DM2. In contrast, in the study by Dai et al. (2015) there was a positive association between infection by the bacteria and DM in children and adolescents. As most infections occur during childhood, the long-term cumulative effect and long history of *H. pylori*

infection may help explain why *H. pylori* infection was associated with DM among aged participants ≥ 30 years (Table 2).

Table 2. Prevalence of diabetes according to sociodemographic variables and presence (+) or absence (-) of *H. pylori* infection, from January to December 2018, Goiás, Brazil.

Sociodemografic characteristics		**Status DM**	***H. pylori* +** n	***H. pylori* -** n	***P-value***
Sex	Male	Diabetic	1	0	0.99
		Not diabetic	11	6	0.99
	Female	Diabetic	6	4	0.99
		Not diabetic	29	15	0.99
Age	<30 years	Diabetic	0	0	0.99
		Not diabetic	9	0	0.02
	≥30 years	Diabetic	7	4	0.99
		No diabetic	31	21	0.02
Schooling	Illiterate	Diabetic	2	1	0.99
		Not diabetic	0	0	0.28
	Incomplete high school	Diabetic	5	3	0.99
		Not diabetic	36	21	0.28
	Complete high school	Diabetic	0	0	0.99
		Not diabetic	4	0	0.28
Family income	Up to 1 salaty	Diabetic	0	0	0.81
		Not diabetic	5	1	0.17
	1 to 2 salaries	Diabetic	4	2	0.81
		Not diabetic	15	5	0.17
	3 to 5 salaries	Diabetic	2	1	0.81
		Not diabetic	14	6	0.17
	> 5 salaries	Diabetic	0	1	0.81
		Not diabetic	1	1	0.17
	Uniformed	Diabetic	1	0	0.81
		Not diabetic	5	8	0.17
Items missing from the home (childhood)	Piped water	Diabetic	7	3	0.99
		Not diabetic	27	15	0.54
	Piped water, Sewer; Toilet	Diabetic	0	0	0.99
		Not diabetic	0	0	0.54
	Sewer; Toilet	Diabetic	0	0	0.99
		Not diabetic	2	0	0.54
	Sewer	Diabetic	0	0	0.99
		Not diabetic	0	0	0.54
	Piped water; Sewer	Diabetic	0	0	0.99
		Not diabetic	11	0	0.54
	Uninformed	Diabetic	0	1	0.99
		Not diabetic	0	6	0.54
Number of people sharing the rooms	< 2	Diabetic	0	0	0.36
		Not diabetic	1	3	0.24
	3	Diabetic	0	1	0.36
		Not diabetic	3	1	0.24
	> 3	Diabetic	7	3	0.36
		Not diabetic	36	17	0.24

P-value: Fisher's exact test.

In the our study, the prevalence of *H. pylori* infection in diabetic patients was higher among participants with incomplete high school education, although the difference was not significant. In the study by Wawro et al. (2019) low education was significantly associated with seropositivity for *H. pylori* in the survey, but no association between bacterial infection and DM was demonstrated (Table 2).

With regard to family income, the prevalence was 57% in patients with *H. pylori* infection and diabetics, who had a monthly income of 1 to 2 minimum wages. This relationship is justifiable due to the high prevalence of *H. pylori* infection in a low-income population and because diabetes is one of the NCDs (Chronic Non-Communicable Diseases) that strongly affects low-income groups that are vulnerable to factors of risk, such as being overweight (Schmidt et al., 2011). However, most *H. pylori* positive participants were non-diabetics (40/47). The study by Pereira et al. (2012) also demonstrated a lack of association between *H. pylori* infection and glycemic index and glycemic load in participants with a mean income of 2.18 minimum wages (Table 2).

The prevalence of *H. pylori* infection varies as function of socioeconomic and hygienic conditions, and vertical transmission, especially within the same family, seems to have an influence. In our study, a higher prevalence of infection was obtained in diabetic participants with no running water (100%), as well as in those who shared rooms with more than three people in the household (100%) ($p<0.05$). It is noteworthy that most of the participants for these two variables were non-diabetics (40/47) (Table 2).

Diabetes is one of the most common metabolic disorders and arises secondary to an interaction between genetic, environmental and lifestyle factors. In our study, the combined presence of lifestyle habits, including excessive consumption of tobacco, alcohol and coffee among patients and *H. pylori* infection, were associated with the development of DM (Table 3). However, regarding the consumption of alcohol, tobacco and coffee, a higher prevalence of *H. pylori* infection was observed among non-diabetic patients. It is noteworthy that in the literature there are no associations between these three variables in our study.

Table 3. Prevalence of diabetes according to lifestyle and presence or absence of *Helicobacter pylori* infection, from January to December 2018, Goiás, Brazil.

Life habits		Diabetics				P	Non diabetics				P
		H. pylori +		*H. pylori* -			*H. pylori* +		*H. pylori* -		
		n	%	n	%		n	%	n	%	
Tobacco consumption	No	7	63.6	4	36.4	0.99	36	59.0	19	31.1	0.99
	Yes	0	0	0	0		4	6.6	2	3.3	
Alcohol consumption	No	6	54.5	4	36.4	0.99	26	42.6	17	27.8	0.24
	Yes	1	9.1	0	0		14	22.9	4	6.6	
Coffee consumption	No	2	18.2	1	1	0.99	6	9.8	3	4.9	0.99
	Yes	5	45.4	3	3		34	55.7	18	29.5	

The prevalence of *H. pylori* infection and DM was more common among non-smokers with 64%, though not significant. However, Sliwinska-Masson and Milnerowicz (2017) demonstrated that smoking is a predictor of the progression of glucose intolerance, both in the transition from normoglycemia to the state of low glucose tolerance and in the increased risk of developing DM2. The mechanisms that explain the relationship between smoking and the development of DM are not fully understood, but it is understood that smoking and exposure to nicotine can induce a pro-inflammatory metabolic state that could impact both insulin sensitivity and function of the β cells. In contrast, in Keith et al. (2016) there was no independent association between tobacco use and insulin resistance or the development of incident DM.

In this context, smoking has been designated as a decisive factor in promoting *H. pylori* infection. Smoking is believed to adversely affect the gastric mucosa by increasing acidity in the stomach, and it is a well-established risk factor for peptic ulcer and gastric atrophy that can progress to the development of cancer. In the findings by Brenner et al. (2002) found an association between smoking and *H. pylori* infection in patients with gastric cancer. Shi et al. (2008) reported no association between the prevalence of *H. pylori* and tobacco consumption, as in the present study.

Non-alcoholics had a higher prevalence (55%) among those positive for *H. pylori* infection and diabetics. However, it was shown in the study by Turner et al. (2001) that glycemic control and glucose production are affected by alcohol. There is also some evidence that modest alcohol consumption may have a long-term beneficial impact on the course of diabetes. In the research by Shai et al. (2007) participants with diabetes who drank a glass of wine a day over a three-month period had the lowest fasting plasma glucose level compared to abstainers. However, it is known that patients with DM who drink tend to have low adherence to their treatment, leading to an increase in morbidity and mortality (Engler, 2013).

Some recent studies suggest a protective effect of alcohol against active infection with *H. pylori*, as alcohol can have an antibacterial action and that its concentration and the amount consumed reduce the risk of infection by the bacteria. In the research by Liu et al. (2016) found evidence to suggest that moderate alcohol intake is associated with a 22% reduction in *H. pylori* infection and may facilitate its elimination. Bujanda (2000) demonstrated that alcoholic beverages can stimulate gastric acid secretion, thus lowering the pH of the stomach and making the environment even less favorable for *H. pylori*. But among the alcoholics in the present study, a large part had *H. pylori* infection (15/19). It is believed that alcohol consumption facilitates *H. pylori* infection by damaging the gastric mucosa, which is in agreement with the study by Zhang et al. (2010) who observed an association between alcohol consumption and bacterial infection.

Recent evidence suggests that coffee consumption is associated with a decreased risk of DM, which is in agreement with our findings, in which the prevalence of positive participants for *H. pylori* infection and non-diabetics who consume coffee was of 56%, although not significant. Coffee consumption has been associated with a reduced incidence of impaired glucose tolerance, hyperglycemia, and insulin sensitivity (Bidel and Tuomilehto, 2013). Several mechanisms have been proposed for this protective effect, including effects on incretin release, liver glucose metabolism, and insulin sensitivity. In this perspective, the Dutch study by Van Dam et al. (2006) reported that participants who drank at least seven cups of coffee a day were half as likely to develop DM2 compared to those who did not consume coffee.

A possible relationship between coffee consumption and *H. pylori* infection was identified in our study. In *hpx+* diabetic subjects, approximately 45% consumed coffee and 55% of non-diabetic *hpx+* participants consumed this habit. Brenner et al. (1997) stated that coffee consumption was associated with an increased risk of *H. pylori* infection. However, it is known that caffeine induces gastric acid secretion, as well as

causing negative effects in several diseases of the upper gastrointestinal tract (Shimamoto et al. 2013).

The proportion test (TP) for two samples was performed to evaluate only diabetic participants (7/72) positive (*hpx* +) or negative (*hpx* -) for *H. pylori* infection in relation to gender, age and consumption of tobacco, alcohol, and coffee (Figure 1).

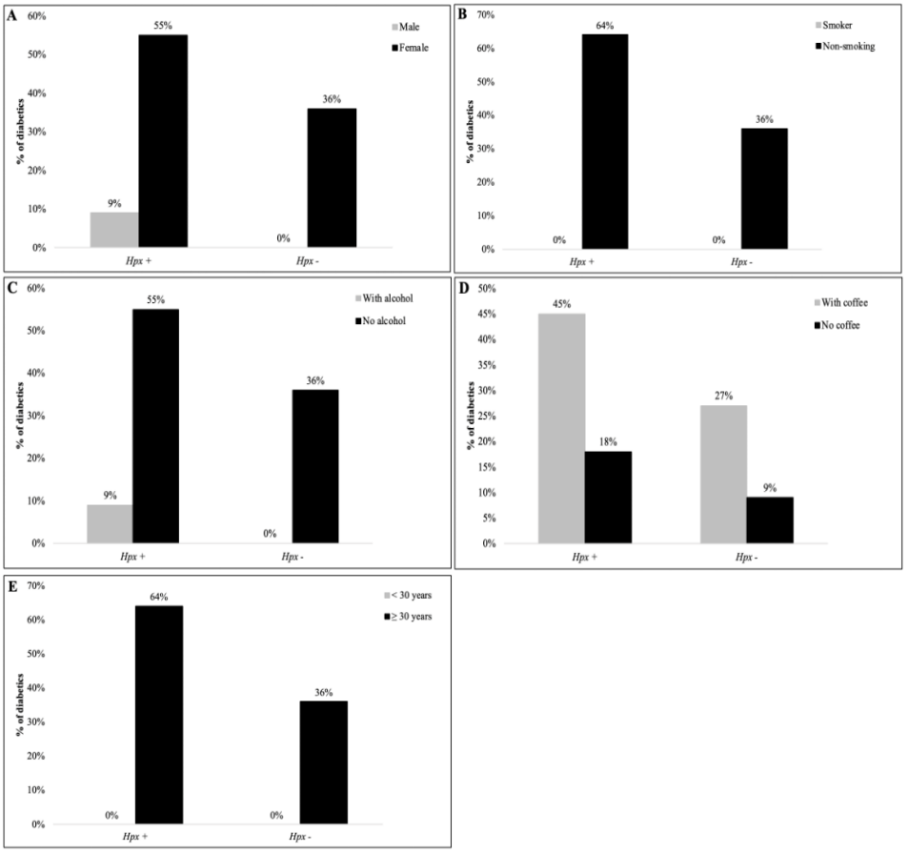

Figure 1. Proportion of positive and negative diabetics for *Helicobacter pylori* infection according to gender, age, smoker or non-smoker status, alcohol consumption and coffee consumption.

The proportion test showed that in females there was a greater number of diabetic patients *hpx*+ with 55% (p=0.0325), when compared to *hpx*– (36%) (Figure 1A). Regarding diabetics and tobacco consumption, there was a proportion of 64% among non-smokers *hpx*+ (p=0.0013), when compared to non-smokers *hpx*– (36%) (Figure 1B). Among non-alcohol consuming participants, there was a proportion of 55% of *hpx*+ diabetics (p=0.0325), when associated with *hpx*– consumers (36%) (Figure 1C). The proportion test showed a higher proportion of diabetics *hpx*+ individuals among coffee consumers with 45%, when compared to *hpx*– (27%) (p=0.285) (Figure 1D). Finally, among diabetics, there was a proportion of 64% among participants aged ≥ 30 years *hpx*+ (p=0.0013), in contrast to *hpx*– (36%) (Figure 1E).

Association between *H. pylori* infection, DM and clinical diagnosis

For clinical analysis of *H. pylori* infection, according to the prevalence of DM and the clinical diagnosis obtained from the patients (endoscopic and histopathological analysis), we classified atrophy, metaplasia and gastric cancer as severe diseases, and gastritis, duodenitis, esophagitis and ulcer gastric disease as non-severe diseases (Table 4).

Table 4. Prevalence of severe and non-severe diseases associated with diabetics or non-diabetics and positive or negative for *Helicobacter pylori* infection, period from January to December 2018, Goiás, Brazil.

Diagnosis	Diabetics				P-value	Non diabetics				P-value
	H. pylori +		*H. pylori* -			*H. pylori* +		*H. pylori* -		
	n	%	n	%		n	%	n	%	
Severe Illnesses	3	27.27	1	9.09	0.99	4	6.56	6	9.84	0.07
Non-severe diseases	4	36.36	3	27.27	0.99	36	59.02	15	24.59	0.07

Despite the low number of serious illnesses (14/72), no significant association was observed between non-diabetic and *H. pylori*-negative participants (p=0.07). In the work by Jmaa et al. (2014) there was no significant difference between diabetics and non-diabetics who had *H. pylori* infection, intestinal metaplasia and gastric atrophy. In the study by Ikeda et al. (2009) it was shown that among hyperglycemic individuals and positive for *H. pylori* infection, the risk of gastric cancer was extremely high (p=0.004). An assay carried out by Kato et al. (2019), revealed that *H. pylori* infection was associated with an increased risk of diabetes, however, the increased risk was observed only among participants with current infection and was not observed among participants after eradication.

It is possible that DM acts synergistically with *H. pylori* infection to increase the risk of gastric cancer. It is known that diabetes is associated with an increased production of reactive oxygen species and greater oxidative damage to DNA, which can lead to mutational changes in oncogenes and tumor suppressor genes and, consequently, to the development of gastric cancer. In this sense, it is also known that *H. pylori* infection contributes to changes in the proliferation of epithelial cells. Therefore, it is noteworthy to state that the increase in reactive damage caused by oxygen to DNA and genetic changes in the gastric mucosa induced by hyperglycemia or hyperinsulinemia, stimulate a pathogenic modifying effect of *H pylori* on epithelial cell proliferation, since this is the step of a cascade that results in the development of gastric cancer. Furthermore, it is possible that hyperglycemia affects the bacterium and its infection status or stimulates its carcinogenic effects (Ikeda et al., 2009).

Among non-severe diseases, the highest prevalence was in non-diabetic patients who are positive for *H. pylori* infection. However, Quatrini et al. (2001) observed in their study a high prevalence of *H. pylori* infection (69%), esophagitis and peptic ulcers (77%) in participants with DM. Anastasios et al. (2002) showed in their research that among patients positive for *H. pylori*, no difference was found between diabetics and non-diabetics in relation to the prevalence of gastritis, with 80% and 72.9%, respectively, or peptic ulcer, with 91.8% and 76%, respectively. A systematic review performed by Gravina et al. (2018)

points out *H. pylori* is associated with various gastropathies such as peptic ulcers, cancer and extragastric manifestations, such as changes in glycolipid metabolism, although the role of *H. pylori* infection in DM is still quite controversial. Mansori (2020), through a systematic review and meta-analysis, involving 41 studies and 9559 individuals, suggest a significant association between *H. pylori* infection and the risk of diabetes (overall OR: 1.27; 95% CI: 1.11–1.45).

Inflammation induced by *H. pylori* and damage to the gastric mucosa may explain the positive associations observed in studies between *H. pylori* infection, non-severe diseases and DM. The infection can also affect the regulation of ghrelin and leptin, important hormones for energy homeostasis, which are secreted by the epithelial cells of the stomach. Ghrelin decreases energy expenditure and encourages weight gain, while leptin reduces appetite and increases energy expenditure. Thus, studies suggest that *H. pylori* can alter gastric physiology, consequently metabolic homeostasis and the risk of DM (Haj et al., 2017; Francois et al., 2011).

The main limitation of this work was the small number of participants involved, due to the various exclusion criteria necessary to carry out the study. In addition, it was difficult to obtain some information, such as the "diabetic" or "non-diabetic" status of the patients, which was the main motivator for the sample reduction. We also did not obtain information on the type of DM that the participants had, which is an important factor to explain some of the associations.

CONCLUSIONS

In this study, there was no significant association between *H. pylori* infection and DM. This correlation remains controversial, as some studies report that individuals with *H. pylori* infection are more prone to insulin resistance, altered glycometabolism, and consequently the development of DM. Nevertheless, more research is needed to investigate this association. Understanding the etiology of *H. pylori* infection in metabolic diseases can help in public policies to eliminate the infection and promote health, with the aim of preventing DM in the population. New investigations with a larger sample size are needed to elucidate the association between *H. pylori* infection and DM, as well as the pathological mechanisms of the bacteria that are involved in the development of DM.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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