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Review article

Factors that influence *Helicobacter pylori* infection and the occurrence of gastric cancer: a systematic review

Fatores que influenciam a infecção por *Helicobacter pylori* e a ocorrência de câncer gástrico: uma revisão sistemática

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RESUMO: Introdução: Dentre os fatores de risco para o câncer gástrico se destaca a infecção por *H. pylori*. Assim, objetiva-se compilar essa relação e os fatores que a influenciam de maneira sistemática para facilitar seu acesso e entendimento. **Material e métodos:** Trata-se de uma revisão sistemática. As buscas ocorreram nas bases de dados PubMed, LILACS e SciELO. **Resultados:** Verificou-se a investigação de 6 fatores que influenciam a relação entre a infecção por *H. pylori* e o desenvolvimento de câncer gástrico, sendo eles: parâmetros de cinética do ferro dentro da normalidade e tratamento farmacológico contra *H. pylori*, os quais diminuem o risco de ocorrência de câncer gástrico; diabetes mellitus tipo 2, consumo de álcool, de tabaco, e positividade para cepas e antígenos específicos de *H. pylori* enquanto fatores que elevam esse risco. Já a soropositividade para o antígeno CAGM possui efeito inverso para o desenvolvimento do adenocarcinoma gástrico não localizado na cárdia. **Discussão:** Há alta associação *H. pylori* e a carcinogênese gástrica, a partir da influência dos fatores anteriormente citados nessa relação. **Conclusão:** Portanto, a infecção por *H. pylori* associada a alguns fatores se caracteriza como instrumento de desencadeamento e progressão do câncer gástrico não situado na cárdia.

PALAVRAS-CHAVE: *Helicobacter pylori*; Neoplasias Gástricas; Fatores de Risco.

ABSTRACT: Introduction: Among the risk factors for the occurrence of gastric cancer, *H. pylori* infection stands out. Therefore, the objective of this study is to compile evidence on this relationship and the factors that influence it to facilitate its access and understanding. **Materials and methods:** This is a systematic review. Searches were conducted in the PubMed, LILACS and SciELO databases. **Results:** Six factors that influence the relationship between *H. pylori* infection and gastric cancer were investigated: normal iron kinetics and pharmacological treatment against *H. pylori*, as factors that reduce the risk of gastric cancer; type 2 diabetes mellitus, alcohol and tobacco consumption, and positivity for specific strains and antigens of *H. pylori* as factors that increase this risk. However, CAGM antigen seropositivity has an inverse effect for gastric noncardia adenocarcinoma. **Discussion:** There is a significant association between *H. pylori* and gastric carcinogenesis, and the previously mentioned factors influence this relationship. **Conclusion:** *H. pylori* infection associated with some factors can trigger and enhance the development of non-cardia gastric cancer.

KEYWORDS: *Helicobacter pylori*; Stomach Neoplasms; Risk Factors.

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INTRODUCTION

Gastric cancer is a disease with high incidence and mortality rates worldwide. In 2020, it was the fifth most incident cancer and the fourth cancer-related cause of death in the world. Incidence rates are higher in Eastern Asia, Eastern Europe and South America[1] and lower in Northern America, Northern Europe and in a large part of the African continent[1,2]. Furthermore, the incidence is twice as high in men compared to women[1]. In Brazil, in the three-year period 2020-2022, stomach cancer was the sixth most common form of cancer (21,000 new cases), being the fifth in the male population (5.9% of new cases) and the seventh in the female population (3.5% of new cases)[3].

Although there was a decline in these variables in the last century, the disease is still a concern, as the overall population is aging[4]. Furthermore, in high-income countries, the incidence in the younger population has increased[5].

The factors responsible for the decline in gastric cancer rates include improvement in sanitary conditions, use of refrigerators, increased consumption of fresh fruits and vegetables, which reduces the use of salt, disease screening and, mainly, increased search for treatment for *Helicobacter pylori* infection[6,7].

The *Helicobacter pylori* bacterium is responsible for the development of noncardia gastric cancer and, therefore, does not influence cardia cancer, whose incidence tends to remain constant or increase in Western countries[8,9]. Therefore, the risk factors for noncardia gastric cancer involve infection by *Helicobacter pylori*, advanced age, low-socioeconomic status, smoking and alcohol consumption, family predisposition, previous gastric surgery, pernicious anemia, and being part of a high-risk population[10–12]. As for cancer of the gastric cardia, reports indicate it is associated with obesity [13] and gastroesophageal reflux[14,15].

Therefore, it is extremely important to study the relationship between *Helicobacter pylori* infection and occurrence of gastric cancer, as well as the factors that influence this relationship, in order to contribute to the reduction of its incidence, as *Helicobacter pylori* infection is one of the main risk factors for gastric cancer. Therefore, the present study aims to systematically identify scientific articles on the study topic, aiming to facilitate their access, provide understanding, and contribute to evidence-based medicine.

METHODS

The present study is a systematic literature review following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (PRISMA 2020). The search was conducted in the databases PubMed, Latin American & Caribbean Health Sciences Literature (LILACS) and Scientific Electronic Library Online (SciELO).

The descriptors used were mostly in the Health Sciences Descriptors (DeCS) and Medical Subject Heading Terms (MeSH) dictionaries and were organized with Boolean operators to form the following search strategies: in PubMed, "GASTRIC CANCER" AND "RISK FACTORS"; in SciELO and LILACS, "*CÂNCER GÁSTRICO*" AND "*FATORES DE RISCO*" were applied. As for filters, "Free full text", "Full text", "Books and Documents", "Clinical Trials", "Randomized Controlled Trial" were used in the PubMed search; no search filters were used in the databases SciELO and LILACS.

Original articles in English, Portuguese and Spanish, published until July 2021, and addressing the relationship between H. pylori infection and the occurrence of gastric cancer were included.

Review articles, letters and editorials were excluded. After reading the titles and abstracts, studies that were not clear, did not address the studied topic, did not present one of the stipulated methodological designs, were not open access, or were duplicates were also excluded.

Three reviewers were necessary for data collection and analysis, and all applied the same criteria and performed their functions independently. After this step, to reinforce the relevance of the primary analysis, the reviewers exchanged the articles and performed the process again in a judicious manner, and then reached the same conclusions.

As the present work is a systematic literature review and did not involve data collection with human beings, appreciation by a research ethics committee was not necessary.

RESULTS

Selection of studies

The database search with the previously described filters revealed 121 studies in Pubmed, of which 120 were open access. After reading the title and abstract, only 24 were included, and after a complete analysis of the articles, 22 remained. In LILACS, a total of 81 studies were found, of which 80 were available in full and for free. After excluding 1 duplicate, 79 articles were read. After analyzing the title and abstract, 18 were included and, after evaluating the full text, 9 remained. Finally, in SciELO, 38 studies were found, of which all were open access. After the exclusion of duplicates, 35 remained for further analysis. After reading the title and abstract, 14 were included and, after considering the complete study, only 8 remained. Due to the presence of a duplicate study in the LILACS and SciELO databases, 1 of them was excluded.

Therefore, a total of 7 articles from SciELO were included. The reasons for exclusion were, for the most part, not addressing the theme, using methodological designs that were not in the inclusion criteria and being a duplicate. Of the 38 selected articles, which report several risk factors, only 15 are part of this research, as they address the relationship between *H. pylori* infection and the occurrence of gastric cancer (Figure 1).

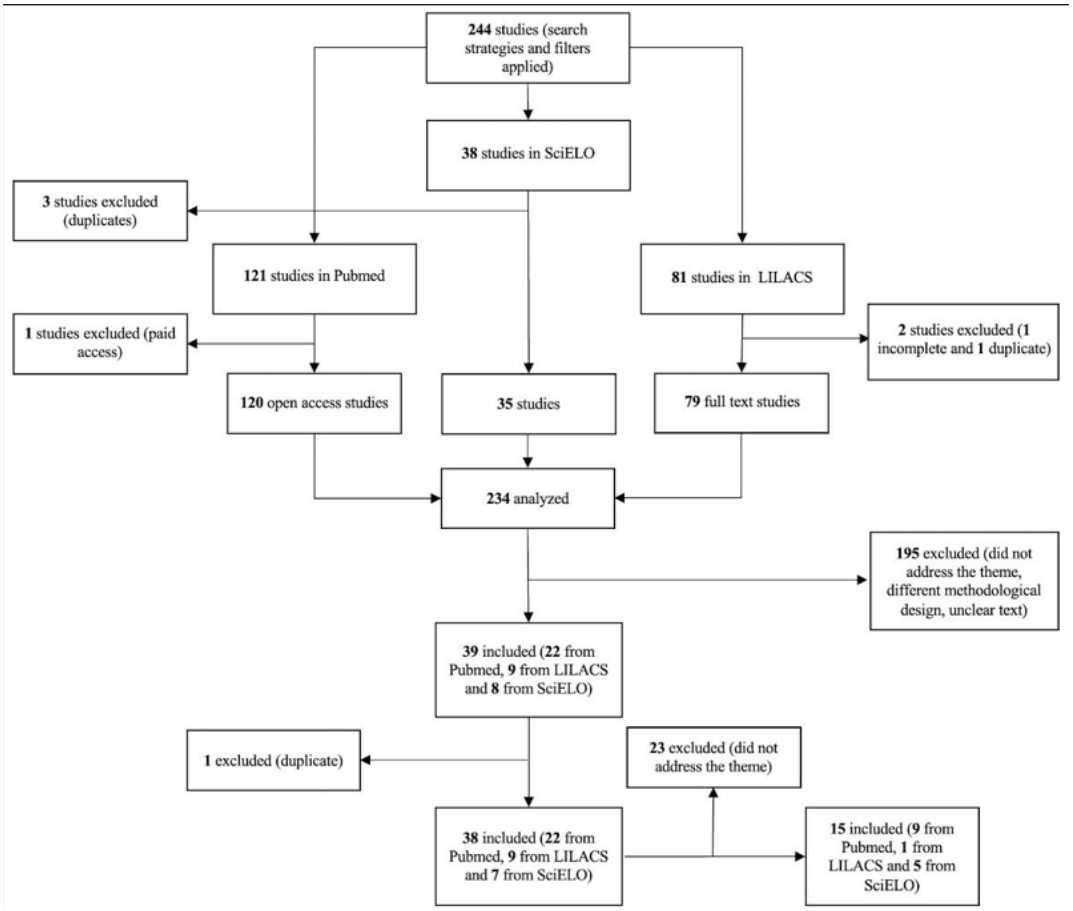

Figure 1 - Flowchart of the phases of the systematic review to obtain articles relevant to the study.
Source: elaborated by the authors (2023).

Characteristics of the studies

A total of six factors that influence the relationship between *H. pylori* infection and the development of gastric cancer were investigated in a more consensual way in the 15 included studies, and are described in the findings of the present study. Factors such as normal iron kinetics, listed 2 times, and pharmacological treatment against *H. pylori*, listed 1 time, reduce the risk of gastric cancer. The presence of type 2 diabetes mellitus, cited 1 time, alcohol consumption, cited in 1 study, smoking, addressed in 2 articles, and specific strains and antigens of *H. pylori*, cited 4 times, are factors that increase the risk of gastric cancer. However, the presence of the CAGM antigen of the cagM strain has an inverse effect on the development of gastric noncardia adenocarcinoma. Results regarding the influence of garlic and vitamin supplementation on the risk of the disease differ in the literature. In addition, age, sex and gender do not have a clear role in this context.

Regarding the methodological designs, case-control studies predominated, with 5 studies out of the 15 selected. The exceptions were: Cook et al.[16], Ley et al.[17] and Li et al.[18], which were randomized, double-blind, placebo-controlled clinical trials; Webb et al.[19], a multicenter clinical trial on the relationships between plasma levels of vitamin C and mortality or incidence of gastric cancer; Noto et al.[20], a clinical trial that addressed the role of bacterial virulence determinants in *H. pylori*-induced gastric carcinogenesis within the context of iron deficiency; Guo et al.[21], in which an unplanned secondary analysis of the Shandong Intervention Trial (SIT) was conducted to evaluate the effects of *H. pylori* treatment for 2 weeks and vitamin and garlic supplementation for 7.3 years on the progression of precancerous gastric lesions and occurrence of gastric cancer; Rodrigues et al.[22] and Muller et al.[23], a retrospective study assessing the association between *H. pylori*

infection and the prevalence of intestinal metaplasia and a retrospective study of gastric biopsies from corpus and antrum of patients who underwent upper gastrointestinal endoscopy, respectively; Miranda et al.[24], a cross-sectional study on the association between predetermined risk factors (e.g. gender, age, endoscopic findings, urease and *H. pylori*); and Borges et al.[25], a cohort study aimed at investigating the prevalence of *H. pylori* infection is dyspeptic patients and determining the link between clinical infection and risk factors for the development of gastric cancer.

Presentation of studies

Table 1 - Characterization of the studies included.

Author/year	Qualis	Objectives	Main results
Rodrigues et al., 2019[22]	B1	To evaluate the prevalence of *H. pylori* infection in patients undergoing upper digestive endoscopy, as well as the prevalence of intestinal metaplasia, atrophy and chronic inflammation and their association with *H. pylori* infection .	In the sample composed of 4,604 patients, the prevalence of *H. pylori* was 31.7%, and the percentage of infection was significantly higher in patients from the public health service (42%) compared to patients from the private health service (25.6%). Furthermore, higher percentages of intestinal metaplasia and glandular atrophy were observed in patients with *H. pylori* when compared to those *H. pylori* (-). Among the *H. pylori (+)* patients, 38.5% had metaplasia and chronic inflammation, 38.3% had atrophy and chronic inflammation, and 23.2% had metaplasia, atrophy, and chronic inflammation simultaneously.
Guo et al., 2020[21]	C	To evaluate how lifestyle factors, including smoking, alcohol intake, and diet, may change the risk of gastric cancer incidence and mortality and whether the effects of vitamin and garlic supplementation on gastric cancer are associated with major lifestyle factors.	Smoking was associated with an increased risk of gastric cancer incidence (odds ratio, 1.72; 95% CI, 1.003-2.93) and mortality (hazard ratio, 2.01; 95% CI, 1.01-3.98). These associations were significant only among participants with *H. pylori*. The protective effect of garlic supplementation on gastric cancer mortality was seen particularly among those who did not drink alcohol. No significant interactions between vitamin supplementation and lifestyle factors were found.
Ley et al., 2004[17]	A1	To determine whether *H. pylori* eradication is associated with regression of gastric preneoplastic conditions over 1 year.	Worst diagnoses in *helicobacter pylori* placebo and treatment subjects were similar over the study period. In contrast, in the same interval, the mean index stomach score in the primary analyses of intention-to-treat and per-eradication-protocol of two pathologists decreased significantly more in the treatment than in the placebo group.
Li et al., 2019 [18]	A1	To assess the effects of *Helicobacter pylori* treatment, vitamin supplementation and garlic supplementation in the prevention of gastric cancer.	A protective effect of *H. pylori* treatment on gastric cancer incidence persisted 22 years post-intervention. Incidence decreased significantly with vitamin supplementation, but not with garlic supplementation. The effects of *H. pylori* treatment on gastric cancer incidence and mortality and of vitamin supplementation on gastric cancer mortality appeared early, but the effects of vitamin supplementation on gastric cancer incidence and of garlic supplementation became apparent only after 8 and 12 years, respectively. No statistically significant associations were found between the proposed interventions and other cancers or cardiovascular diseases.
Borges et al., 2019 [25]	B1	To investigate the prevalence of *H. pylori* infection in dyspeptic patients and to evaluate the association of clinical risk factors and development of gastric adenocarcinoma.	The prevalence of gastric adenocarcinoma in this study was 1.3% and, among the infected patients, six (8.2%) were at high risk and 67 (91.8%) at low risk of developing this type of cancer. (P<0.05).

continue

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Author/year	Qualis	Objectives	Main results
Muller et al., 2007 [23]	B1	To estimate the prevalence of *H. pylori* infection and precancerous gastric lesions and their relationship in patients undergoing upper gastrointestinal endoscopy in a reference center in the central region of the State of Rio Grande do Sul.	Normal mucosa, chronic non-atrophic gastritis, atrophic gastritis and intestinal metaplasia were diagnosed in 5%, 77%, 3% and 15% of the biopsies, respectively. Infection by *H. pylori* was associated with a 10-fold greater odd (95% CI: 6.50 - 17%) of finding some degree of histological alteration in the gastric mucosa. In addition, the odds ratio for *H. pylori*-infected patients to have chronic non-atrophic gastritis was 3 (95% CI: 2.2 - 3.4), and the odds ratio for infected patients to have atrophic gastritis (95%CI: 0.5-1.4) and intestinal metaplasia (95% CI: 0.5-0.8) was less than 1. Therefore, patients infected with *H. pylori* are 3 times more likely to develop non-atrophic chronic gastritis.
Favacho et al., 2013 [26]	B1	To identify the epidemiological aspects of patients diagnosed with T4b gastric adenocarcinoma.	Risk factors for the development of T4b adenocarcinoma were smoking (n=11; 40.7%), family history of gastric cancer (n=3; 11.1%), previous surgery (n=2; 7.4%) and *H. pylori* infection (n=1; 3.7%). No risk factors were found in 48.1% (n=13) of the patients. Most individuals were male (n=22; 81.5%), the mean age of the people affected was 58.78 years and the time to access the health service varied from 1 to 120 months, with a mean of 12.5 months.
Palli et al., 2006 [27]	A1	To evaluate the association between *H. pylori* infection and gastric cancer risk in a prospective design, taking into account the effect of serologically defined severe chronic atrophic gastritis and the role of dietary and other environmental factors in gastric carcinogenesis.	Overall, *H. pylori* seropositivity was associated with gastric cancer risk. However, subjects showing only antibodies anti-*H. pylori* were not at an increased risk, while those with antiCagA antibodies had a 3.4-fold increased risk. Furthermore, the odds ratio associated with severe chronic atrophic gastritis was 3.3 (95% CI 2.2-5.2) and the risk of noncardia gastric cancer associated with seropositivity showed a further increase (OR 6 .5; 95% CI 3.3-12.6). On the other hand, a ten-fold increased risk of cardia gastric cancer was associated with severe chronic atrophic gastritis (OR 11.0; 95% CI 3.0-40.9). These results support the causal relationship between *H. pylori* Cag A+ strains infection and gastric cancer.
Murphy et al., 2015 [28]	A1	To use multiplex serology including 15 *H. pylori* antigens to determine whether seropositivity is associated with the development of non-cardia gastric cancer in Linxian, China.	*H. pylori* multiplex seropositivity was associated with a significant increase in risk of gastric non-cardia adenocarcinoma at an early time point in the survey (OR: 3.44, 95% CI: 1.91, 6.19). In the combination of data from both analyzed timepoints (baseline and 5.25 years post intervention with combinations of vitamins and minerals), *H. pylori* multiplex seropositivity was also associated with an increased risk of gastric non-cardia adenocarcinoma, as were six individual antigens: GroEL, HP0305, VacA, HcpC and Omp. CagM, in turn, was inversely associated with risk of gastric noncardia adenocarcinoma.
Noto et al., 2013 [20]	A1	To define the role of bacterial virulence determinants in *H. pylori*-induced gastric carcinogenesis within the context of iron deficiency, using an animal model of *H. pylori* infection and cancer that resembles human disease.	In rodents, iron depletion accelerated the development of *H.* pylori-induced premalignant or malignant lesions in a cagA-dependent manner. However, regardless of iron status, seroprevalence of CagA played a crucial role in gastric inflammation and carcinogenesis, as its absence significantly attenuated the development of inflammation (p-value < 0.0001), dysplasia (0 cases out of 64 rodents) and adenocarcinoma (0 cases out of 64 rodents). Furthermore, *H. pylori* strains that grew in iron-depleted organisms exhibited enhanced virulence and more significant induction of inflammatory factors. In humans participating in the study, *H. pylori* strains isolated from individuals with lower ferritin levels induced more robust proinflammatory responses compared with strains isolated from individuals with higher ferritin levels.
Miranda et al., 2019 [24]	B1	To observe the correlation between gender, age, gastritis and *H. pylori* in patients from Belém, Pará, Brazil.	There were no statistically relevant associations between gender, age, endoscopic findings, urease and *H. pylori* seropositivity or between these factors and the prevalence of gastric cancer in the region.

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Author/year	Qualis	Objectives	Main results
Yang et al., 2017[29]	A2	To conduct a large-scale comparison between patients with type 2 diabetes mellitus who had dyspeptic symptoms to investigate whether type 2 diabetes mellitus predisposes patients to a higher rate of precancerous lesions, more advanced gastritis or gastric intestinal metaplasia state, or a higher rate of gastritis, to predict the risk of gastric cancer after *H. pylori* infection.	Patients with type 2 diabetes mellitus and *H. pylori* infection had more severe gastric inflammation measured by the gastric body gastritis (CGI) index than non-diabetic patients. Moreover, male patients and non-insulin users were predisposed to have corpus-predominant gastritis after *H. pylori* infection.
Meine et al., 2011[30]	B1	To investigate the association between cagA-positive *H. pylori* and gastric cancer, using polymerase chain reaction (PCR) for the detection of this bacterial strain.	The rate of cagA-positive *H. pylori* infection was significantly higher in the group of patients with gastric cancer when compared with the control group, occurring in 62.1% and 29.3%, respectively (OR=3.95; 95% CI 1.543-10.096).
Webb et al., 1997[19]	A1	To investigate the relationships between plasma levels of vitamin C and gastric cancer rates, markers of gastritis and other socio-demographic variables.	There was no association between average plasma vitamin C levels and *H. pylori* infection. Furthermore, the study evaluated the association between mean fasting plasma vitamin C levels and gastritis markers, and found lower levels of vitamin C in *H. pylori*-seropositive subjects and higher levels of vitamin C in individuals with very low serum PgA levels and detectable DNA adducts (both statistically insignificant factors).
Cook et al., 2012[16]	A1	To assess whether iron metrics from previous studies were associated with gastric cardia cancer and gastric noncardia cancer.	Serum iron metrics were not associated with gastric cardia cancer, except for a potential 'n'-shaped relationship with total iron-binding capacity (TIBC) (global p=0.038). Gastric noncardia cancer was inversely associated with serum ferritin (global p=0.024), serum iron (overall p=0.060) and, possibly, transferrin saturation. TIBC appeared to share a 'u'-shaped relationship with noncardia gastric cancer (global p=0.033). Dietary iron exposure was not associated with either subsite. Adjustment for *H. pylori* and gastric atrophy had little effect on observed associations.

Source: elaborated by the authors (2023).

DISCUSSION

It is important to highlight the relationship between *H. pylori* infection and a higher risk of developing gastric cancer. In the study by Favacho et al.[26], this microorganism was identified as one of the risk factors for the occurrence of this disease. Other authors also reinforce and demonstrate this relationship, such as Meine et al.[30], who pointed out that *H. pylori* infection, especially with the cagA-positive strain, has a strong relationship with gastric cancer. Furthermore, Murphy et al.[28] demonstrated that *H. pylori* seropostivity was associated with a 2.95-fold increase in the risk of developing noncardia gastric cancer; in addition, five antigens, as well as the cagA strain already mentioned by other studies, were found, corroborating this increased risk. On the other hand, antilysate *H. pylori* antibodies[27], as well as the cagM strain and CAGM antigens, are not associated with a high risk, and the latter is inversely correlated to gastric cancer[28]. Furthermore, Palli et al.[27] found that a 6-fold increased risk of developing gastric cancer emerged with cagA seropositivity, and that *H. pylori* seropositivy was more strongly associated with noncardia gastric cancer compared to cardia gastric cancer. *H. pylori* treatment with amoxicillin and omeprazole was inversely associated with the risk of developing gastric cancer[18]. Thus, there is a significant association between *Helicobacter pylori* seropositivity, mainly with the *cag*A strain, and the occurrence of gastric cancer, mostly not in the cardia.

H. pylori infection intensifies the histological alterations in the gastric mucosa, increasing the risk of developing gastric cancer. According to Rodrigues et al.[22], the chances of developing intestinal metaplasia, atrophy and chronic inflammation were increased in *H. pylori* (+)

patients. Some authors also point to an improvement in the mean stomach index score during *H. pylori* treatment, indicating a tendency towards regression of gastric mucosal lesions[17]. The relationship between these lesions, enhanced by this infection, and the occurrence of gastric cancer was outlined in the study by Palli et al.[27], which revealed that the prevalence of severe chronic atrophic gastritis was higher among *H. pylori* (+) patients, as well as among people with gastric cancer, compared to those without cancer. On the other hand, some authors, such as Miranda et al.[24], did not identify a significant relationship between endoscopic findings and gastric cancer.

Studies had conflicting results regarding the association between age, sex and gender and *H. pylori* infection and, consequently, gastric cancer. In the study by Miranda et al.[24], the gender factor did not have a statistically significant relationship with both *H. pylori* infection and the development of gastric cancer. On the other hand, studies by Muller et al.[23] and Palli et al.[27] found that the effect of the cagA-positive *H. pylori* on the development of gastric cancer was stronger in younger people, identifying age as a risk factor exclusive to this strain. However, when comparing age and gender to *H. pylori* infection without a determined strain, with a higher risk of gastric cancer, there was a predominance of individuals over 52±15 years old and females[23,27]. Therefore, studies present different results regarding the relationships between these factors and gastric cancer.

Some studies analyzed dyspeptic patients, such as the study conducted by Borges et al.[25], which found that the risk of developing gastric adenocarcinoma is higher among patients infected with *H. pylori* and dyspeptic patients compared to those without *H. pylori* infection. Furthermore, the study by Muller et al.[23] also had a sample composed of people with dyspepsia and concluded that *H. pylori* (+) patients had a 10 times greater odds of presenting lesions in the stomach mucosa. Thus, patients with dyspepsia are also predisposed to gastric cancer when infected with *Helicobacter pylori*.

Studies also identified relationships between type 2 diabetes mellitus, *H. pylori* infection and gastric cancer. The study by Yang et al.[29] demonstrated that male patients and non-insulin users were independent risk factors for the development of corpus-predominant gastric inflammation in *H. pylori* (+) patients with type 2 diabetes mellitus. A meta-analysis by Yoon et al.[31] corroborated these findings, concluding that diabetic patients have an increased risk for gastric cancer and, in *H. pylori* (+) cases, the risk was 2 times higher. Thus, diabetes is also a contributing factor to histological alterations associated with the development of gastric cancer.

In the study by Noto et al.[20], iron depletion associated with *H. pylori* infection was identified as a risk factor for gastric cancer. In the rodent population, iron deficiency accelerated the development of malignant and premalignant lesions associated with *H. pylori* infection, especially the cagA strain. Furthermore, iron deficiency allowed the development of *H. pylori* strains with greater virulence, enhancing the induction of inflammatory factors. In humans, the results were similar: the lowest ferritin levels induced more robust proinflammatory responses caused by *H. pylori*. Cook et al.[16] also addressed this relationship in humans, presenting similar but more modest results. Thus, adequate levels of iron were identified as important factors to avoid enhancing *H. pylori* virulence.

Some lifestyle habits associated with *H. pylori* infection may also influence the risk of gastric cancer. Guo et al.[21] found that, in *H. pylori (+)* patients, smoking was associated with a higher gastric cancer incidence and mortality. Alcohol intake and dietary factors were not associated with gastric cancer. Furthermore, relationships between alcohol intake, garlic supplementation and a reduction on gastric cancer mortality were found among H. pylori (+) patients who never drank alcohol. In *H. pylori* (–) patients, there was an association between vitamin supplementation, consumption of vegetables and fruits and progression of gastric lesions. Thus, the presence or absence of *H. pylori* infection interferes with lifestyle habits associated with gastric cancer risk. In addition, the study by Li et al.[18] found that in *H. pylori (+)* individuals the incidence of gastric cancer decreased with vitamin supplementation, but not with garlic supplementation. However, both supplementations led to a decrease in mortality after 12 years. On this subject, Webb et al.[19] also showed an inverse relationship between vitamin C levels and *H. pylori* infection. Thus, lifestyle habits can affect gastric cancer incidence and mortality, but studies disagree on some of the studied factors.

CONCLUSION

The results obtained showed that the risk of the disease was correlated to the effect of this bacterium on the histological alterations in the gastric mucosa, leading to the development of gastric cancer. The relationship between *H. pylori* infection and increased risk of gastric cancer has been observed mainly with the cagA strain. However, proper treatment against *H. pylori* with amoxicillin and omeprazole was inversely associated with a negative prognosis of the disease. Moreover, when this infection is associated with factors such as age, sex and gender, studies find conflicting results, pointing to correlation with or independence from the increased risk of the disease. However, studies that analyzed dyspeptic patients and *Helicobacter pylori* infection revealed an increased predisposition. Type 2 diabetes mellitus has also been associated with this infection and gastric cancer, being a possible risk factor for gastric inflammation in people with *H. pylori*.

In another analysis, iron depletion associated with

H. pylori infection was also identified as a risk factor for gastric cancer, demonstrating that this deficiency is associated with *H. pylori* strains with greater virulence and induction of risk factors, that is, adequate levels of iron are protective factors against enhanced *H. pylori* virulence. Finally, regarding *H. pylori* infection and its relationship with gastric cancer, some lifestyle habits increase the risk of gastric cancer, such as smoking and drinking alcohol, while others, such as garlic and vitamin supplementation, have diverging results regarding its relevance in reducing the risk of disease.

Studies like the present one are important sources of information that can support evidence-based medicine. The systematic gathering of data from the scientific literature revealed the importance of carrying out primary and secondary studies on the topic addressed. Thus, it is important to compile more evidence in systematic reviews, so that these data can increasingly guide medical conduct, contributing to the reduction of gastric cancer associated with H. pylori *infection*.

Contribution of the authors: *Aranha MFAC*: elaboration of the theme and objective, research, project writing, data analysis and critical review. *Silva ABD* and *Souza INTC*: research, project writing, data analysis and critical review. *de Oliveira RCS*: guidance and critical review.

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