

The first Scientific Conference for Medical and Health Sciences 2/20240University of Zawia - 27-28/ المؤتمر العلمي الأول للعلوم الطبية والصحية جامعة الزاوية – 27-284/02/28م



Study of Correlation between H. pylori, Gastric Diseases, and Life Habits among Students of the University of Zawia

Khadija Ali Alkadea¹, Asmahan A Krayem¹, Fawzia Shawesh^{1*}, Hanadi Said¹, Raja Alsharef¹, and Rayan Abdlmola¹

¹Department of Medical Laboratories, Faculty of Medical Technology, University of Zawia, Libya

Corresponding Author*Dr. Fawzia Shawesh, Department of Medical Laboratories, Faculty of Medical Technology, University of Zawia, Libya. Email: fawziashawesh@zu.edu.ly

Abstract

Background: Helicobacter Pylori is one of the main culprits behind gastric diseases. It can be considered multi-factorial and relates to the immune system, genotype, and the habits of the host organism in the development of many clinical outcomes. The bacteria are associated with serious gastrointestinal tract (GIT) diseases, including gastritis, peptic ulcers, mucosa-associated changes to lymphoma, and gastric cancers in adults. Direct contact between people is recognized as the main route of infection transmission, followed by food and water from contaminated sources. Aim: This study aimed to determine the seroprevalence of *H. pylori* among students suffering from GIT disorders at the University of Zawia. Methodology: The study was conducted from 3 July until 1 September 2022. 100 students filled out a questionnaire about their history of tea consumption, smoking intake, fast food, and other different life habits. There was an evaluation of the patients clinically, and gastrointestinal symptoms were recorded.

Students were also given knowledge about the *H. Pylori* infection and its outcome. Venous blood was collected from 100 students from males. Hundred sera samples were collected and performed using a Rapid test to determine *H. pylori* IgG antibodies. All data were analyzed by the SPSS version 25. Results: The population was aged 18 - 30 years old. *H. pylori* antibody was found in 60 students (60 %) of the students examined. The age group (24 - 30) showed a high positive anti- *H. pylori* IgG in 32 (72.7%) subjects. Positive anti- *H. pylori* IgG was 60 % in just males of 100. **Conclusion:** Based on the findings of this study, it may be concluded that University students are seemingly endemic with *H. pylori*. The rate of infection increased with age. This study shows that students with low outcomes and those who drink coffee and tea are more likely to be infected with *H. pylori*.

Keywords:

Seroprevalence, gastric diseases, H. pylori, Zawia

Introduction

Helicobacter Pylori can be considered a small, spiral-shaped, and Gram-negative bacillus and this organism is mainly associated with chronic gastritis, gastric cancer, and ulcers. It was estimated that almost 50% of the population of the world hot affected by this organism (Yang et al., 2021). Studies in Ethiopia show that *H.pylori* is mainly associated with the transmission of poor hygiene and lack of sanitation. It was reported by Boren et al that individuals with the blood group O mainly have a high frequency of developing gastritis (Mezmale et al., 2020).

It was found that various socioeconomic factors were associated with the high risk of *H*. *pylori* as compared to those that are economically strong. Moreover, a family history of *H.Pylori* infection may cause the infections and the source of the drinking water was not the risk factor for causing such a condition. School washrooms are also a risk factor for causing H. Pylori (Monno R et al., 2019).

It is more common in patients of developing countries mainly due to the poor economic status of the individuals. It also shows the increased consumption of fast food and less food and vegetable intake. The diseases that Helicobacter Pylori causes are multi-factorial, in which the host plays a role in many clinical outcomes. Moreover, detecting this bacterium urease test is the most common detection method. In developing countries, the colonization of this bacteria in subjects is almost 70-80%, while in developed countries, this rate is between 13-50% of the population (Wang, et al. 2021).

Due to the infection of Pylori, many nutrients get malabsorbed, which may affect the physiological absorption of metabolic hormones of the intestine, such as leptin which is involved in food intake and mass of the body. The patients that are usually positive for this infection may have low levels of ghrelin, and there is also an inactivation of vitamin C. Diet is involved in the progression and development of H. pylori infection as it may involve in the variation of the gastric environment by taking different types of nutrients. It is very well known that a high-fat diet, processed foods, and low usage of fruits and vegetables may cause obesity, and infection might increase in these patients (Assaad, 2018).

The most important environmental factors associated with gastric cancer are diet and *H*. *Pylori* infection, so any change in lifestyles and dietary habits may help eradicate this infection. Therefore, different investigations were carried out in high and low risks to evaluate the role of diet in both high and low-risk geographical areas. *H. Pylori* is detected in drinking water, vegetables, and foods that have an animal origin, and it may be present in complex foodstuffs such as vegetables, milk, and ready-to-eat food. According to the study, this bacterium is present in artificially contaminated foods such as Sterilized milk, tofu, yogurt, chicken, apple and orange juices, lettuce and carrots, and fermented sausage; these all foods contain the bacterial counts of H. pylori (Log et al., 2018).

Epidemiological surveys show that *H.pylori* can be considered high in those individuals that have poor diet and lifestyle patterns and it mainly ranges from 70% to almost 90% in which different risk factors are present such as dietary habits and the lifestyle of the individuals such as the consumption of coffee is highly associated with the high rate of the infection of *H.pylori* and rising of various symptoms of *H.pylori* in recent literature (Mezmale et al., 2020).

A study from Brazil showed that *H.pylori* infection is mainly associated with a higher number of children associated with poor housing. In addition, poor conditions living are also considered an important factor for the infection of *H.pylori*. Another study conducted in Germany showed positive results associated with the infection *H.pylori* having more than three children in the household, location of the house on the main road, and poor consumption of food and water. This study shows that the prevalence of this infection is not associated with coffee drinking, alcohol consumption, and smoking (Mezmale et al., 2020).

Helicobacter Pylori can be considered the most common factor that has the main role in the canceration of the stomach and in addition, the incidence of gastric cancer and peptic ulcer increases. *H. Pylori* can be considered a carcinogen by the International Agency of Research on Cancer and many scholars consider *H. pylori* present in the prognosis of gastric cancer. It is revealed from the study that cancer can be associated with various kinds of factors such as genes and different stages in the process of interaction which involves smoking, smoked products, and diet factors such as high sugar and salt (Park et al., 2018).

The complexity of the relationship between host and pathogen for humans and *H. pylori* can be considered the genetic diversity caused by this bacterium. The characteristics can be considered evidence for the genome of various kinds of strains. According to the research in Tanzania *H. pylori* seroprevalence can be considered to be 39.1% of dyspeptic patients. Moreover, there is fluctuation seen in the trends of the dyspeptic patients of the observation in Ethiopia and the seroprevalence of the North West regions in the setting of the hospital can be considered 27.5% which also involved the hospital-based studies in which endoscopy and biopsy methods can be considered significant for diagnosis (Jung et al., 2021).

In one of the population-based studies, it was demonstrated that gastrointestinal symptoms were also present in HIV patients. In addition, various studies were obtained from the tertiary hospital of Cameroon regarding the prevalence of *H. pylori* in the primary care setting of the hospitals where it was associated with stomach disease. In developing countries, almost 90% of the population *H. pylori* is mainly acquired in childhood, and proper sanitation, poor diets, and overcrowding can be considered the prevalence of this disease. It is also pronounced by the poor environment and the crowding conditions of the water resources. The majority of research in European adult studies shows no significant difference in the prevalence of the infection of *H. pylori* (Halland et al., 2021).

Previous studies do not show any significant interaction between smoking and the infection of *H. Pylori* that further causes various gastric diseases. One control case study in Asia shows that non-smokers often suffer from *H. pylori* and have a decreased risk of gastric atrophy. Multiple studies are involved in the demonstration of the increased risk of *H.pylori* that is associated with cancer and the case-control study of Japanese showed the high risk of noncardiac cancer in the stomach in the positive group of smokers. Another study of the case-control in Hawaii showed *H. pylori* seropositive smokers and such individuals are at high risk of developing stomach cancer (Wang et al., 2021).

One of the associations between the use of alcohol and chronic gastritis caused by *H. pylori* infection cannot be shown in the cross-sectional studies of only the European infected populations and no analysis was seen in the drinking of alcohol after the unadjusted analysis (Halland et al., 2021). In the Korean cohort studies, no association can be seen between alcohol drinking and stomach diseases. In addition, no years of alcohol drinking, frequency of drinking, or the average dose of drinking were associated with the *H. pylori* infection (Jung et al., 2020).

One of the case-control studies of Portuguese showed an increased risk of gastric disease such as cancer which is mainly associated with *H. pylori* for the total intake of energy. It suggested less use of dairy products but there was no trend of interaction seen in *H. pylori*. One of the

case-control studies of Ekstrom, et al mainly showed higher dietary intake of Vitamin C and beta carotene involved in decreasing the risk of cancer in H. pylori-positive individuals (Nakamura et al., 2020). In general, few studies have been conducted to determine whether there is a connection between *H. pylori* Gastric Diseases, and Life Habits among Students in Arabic countries. Also, particularly, in Libya, neither has been done. Therefore, the main aim of this study is to examine the association between *H. pylori*, life habits, and gastric diseases among students of the University of Zawia.

Methodology

Sample Collection

This study was performed among 100 students (males), aged between 18 to 30 years old. The study was conducted from 3 July until 1 September 2022. There is an evaluation of 100 students surveyed at the University of Zawia who were questioned about their life habits. Venous blood is then taken from the participants which are then placed in a plain tube. These tubes are then centrifuged and stored for later analysis. This analysis is on the antibodies that were released against *H. pylori*. It can be checked by the serum that was separated from the venous blood.

Study Design

A retrospective study was conducted on 100 students (males) and identified the symptoms associated with the disturbance of the gastrointestinal tract, such as vomiting, nausea, bleeding, and abdominal pain. Moreover, there is also a history of alcohol consumption, tea consumption, or smoking intake. In addition, another critical piece of information was also taken using the nonsteroidal anti-inflammatory drugs. There was an evaluation of the patients clinically, and gastrointestinal symptoms were recorded. Students were given knowledge about the *H. Pylori* infection and its outcome.

Laboratory Examination

A blood sample of 5ml was collected from students included in this study. The Samples were allowed to clot and after 20 minutes, serum was collected using centrifugation at 3000 rpm per 5 min. Qualitative detection of *H. pylori* antibodies, IgG and IgM, were identified using a Rapid test cassette and the tests were performed following the manufacturer's guidelines.

Statistical Analysis

Analysis of data can be carried out with the help of SPSS, or chi-squared test. Data analysis and entry were performed by the SPSS having 25 Version. After that, there is a summarization of the result in descriptive form. Moreover, the Chi-square test was used in the evaluation of the difference between different proportions the value of which is less than 0.05 (p<0.05). After that the analysis was on the study of the two student groups one is positive and the other is negative further, it can be run on the Statistical Analysis System.

Results

Figure 1. Prevalence of *H.pylori* infection among University of Zawia Students.

A total of 100 male students were included in this study at the University of Zawia. Nearly 60 students (about 60 %) indicated that this microorganism was present in their gastric mucosa, and the remaining 40 students (40 %) were negative (figure 1).



Figure 1. Prevalence of *H.pylori* infection among University of Zawia Students.

Table.1. Seroprevalence of *H.pylori* according to age group.

Negative	Positive	Total

Age of students	No	%	No	%	No	%
18-20	15	55.5 %	12	44.4 %	27	27 %
21-23	13	44.8 %	16	55.1 %	29	29 %
24-30	12	22.2 %	32	72.7 %	44	44 %
Total	40	40 %	60	60 %	100	100 %

Table 1 shows the prevalence of *H.pylori* infection among University students in Zawia according to age group. The distribution of the results illustrates that among the age groups, the highest infection in the age group (24- 30) with a total of 32 infections (72.7 %), while the age group (21-23) with a total of 16 infections (55.1 %). The lowest rate was among the age group (18-20) with a total of 12 infections (44.4 %).

 Table 2. Assesses the correlation of different lifestyles with *Helicobacter pylori* Infections.

 Though many aspects were taken into consideration, no connection was detected in any of them.

Table 2 - Correlation of different lifestyles with Helicobacter pylori infections.									
	Positive		Negative						
	NO	%	NO	%					
Gastric Symptoms									
Yes	14	37.84 %	19	30.16 %					
No	23	62.16 %	44	69.84 %					
	Count of the family size								
2-5	21	56.76 %	39	61.90 %					
6-9	13	35.14 %	23 36.51						
10-13	3	8.11 %	1	1.59 %					
Smoking									
Yes	15	27.7 %	39	72.2 %					
No	15	42.8 %	20	57.1 %					
		Fast food							
Yes	27	72.97 %	39	61.90 %					
No	10	27.03 %	24	38.10 %					
	D	rinking Tea/ coffe	ee						
Yes	33	89.19 %	55	87.30 %					
No	4	10.81 %	8	12.70 %					
		Monthly Income							
≤ 1000	25	67.57 %	43	68.25 %					
1500-2000	3	8.11 %	7	11.11 %					
≥ 2000	9	24.32 %	13	20.63 %					
		Water Source							
Тар	10	27.03 %	15	23.81 %					
mineral	27	72.97 %	48	76.19 %					
Playing Exercise/Sport									
Always	20	53.6 %	45	41.9 %					
Usually	19	50.35 %	34	57.4 %					
Hand Washing before Eating									
Always	19	51.35 %	36	57.14 %					
Usually	18	48.65 %	27	42.86 %					
Antibiotic/Antiacid Intake									
Yes	21	32 %	18	16 %					
No	40	19 %	21	14 %					
Previous Infection with Covid-19									
Yes	27	57.4 %	22	66.7 %					
No	26	69.4 %	23	68.4 %					

Discussion

H. pylori is a Gram-negative spiral bacteria colonizing the human stomach (Buta et al., 2010). It is linked with various serious GIT disorders, including mucosa-associated changes to lymphoma, and gastric cancers in adults (Parsonnet, 2006). The exact mode of transmission is not yet known. The infection is now considered one of the most frequently encountered human bacterial infections.

Countless studies regarding the subject have been published globally, and numerous have been carried out in Libya. The epidemiology of *H.pylori* infection among the Libyan population is very important for public health investigations because of its high occurrence as well as its association with various other GIT disorders. However, the current study established an overall seroprevalence rate of 60 %. A lower prevalence rate of 20 – 30% was found in healthy individuals in developed countries (Jones DM *et al.*, 1968), where the study was geographically dependent and related to age. Our findings were low compared with other countries like in Iraq, the prevalence of infection was 81 % in Jordan, 82 % in Kuwait, an Turkey 63 % (Tayfun Y et al., 2008). This difference may be due to the design of our study in which we screened only male students aged between 18-30 years old.

Four studies executed in Libya showed varying results. Two of these carried out in Tripoli had similar results to this current study; 35% (I. A. Altayyar *et al.*, 2015) and 56.5% prevalence rates among the general population (Khaled and Ramadhan, 2016). Dissimilarly, two additional studies in Libya found seroprevalence rates of 70.8%, among healthy persons (M. A. Mohammad *et al.*, 2011), and 82%, in those suffering from chronic dyspepsia (Bakka *et al.*, 2009). Still, most of the data available on the prevalence of *H.pylori* are unsatisfactory.

87

As for gender, however, this study is just on the males. These results are in agreement with numerous studies performed in Libya as well as other countries. A study in Tripoli found that the prevalence of H.pylori infections in regards to sex was almost the same, 35.9% (males) and 36% (females), and so, no statistical significance was established (I. A. Altayyar *et al.*, 2015). Additionally, another study also found no relationship between gender and infections as both seemed to be equally susceptible to infection, males 41.6% and 58.4% females (Khaled and Ramadhan, 2016). Further studies also agree with these findings, where no significance was found between gender and H.pylori infections (M. A. Mohammad *et al.*, 2011; Rana M. Abu Mugsieb, 2007; Bakka *et al.*, 2002; Altuglu *et al.*, 2011). Nonetheless, a few studies did find some connections between gender and *H. pylori* infections. A meta-analysis designated that male gender is a factor linked with elevated prevalence for infections, though the researchers admitted limitation by sparse primary data, thus making it difficult to control confounding variables (Drumm B *et al.*, 1990). A review paper also acknowledged the significance of gender and infection (Goodman and Correa, 1995).

In regards to age, this study found the highest of infections, a total of 32 (72.7 %), in the age group (24-30), this may be due to more exposure to this infection. At the same time, infections decreased and remained changed across the remaining age groups. Differently (55.1 %) had a total of 16 infections while the lowest was in the age group (18-20) with the lowest infection at (44.4%) a total of 12 infections so not a similar rate between age groups in this study. An investigation in Tripoli found no significant association between the variables but did conclude a general decrease in infections with advanced age (Khaled and Ramadhan, 2016), agreeing with previous literature in Palestine, Ethiopia, and many others (Rana M. Abu Mugsieb, 2007; Alemayehu A, 2011).

In contrast, various studies have concluded otherwise. For example, a study in Tripoli, Libya, found an increasing trend of infections with progressing age, ranging from (6.3%) in the 9 – 19-year-old to (55%) in the 40-49-year-old, and then dropping drastically to 0% in the 60 - 69 and 80 - 89-year-old groups (I. A. Altayyar *et al.*, 2015). These findings go in line with those found in previous studies (Tadesse *et al.*, 2014). Furthermore, a Kuwaiti study determined a steady positive correlation between age and *H.pylori* infections (Waleed M *et al.*, 2014). The current study was limited by specific age groups that only include students (males) in the University of Zawia, and this may have affected the seroprevalence concerning age, as no samples under the age of 18 nor over the age of 30 were collected.

Low socioeconomic statuses were not associated with the prevalence of *H. pylori* infection in the studied population. Unlike, in this study, it was (67.57%) of students Which were monthly income of less than 1000, have *H.pylori* infection, in agreement with a study conducted in Tripoli (A. Altayyar *et al.*, 2015). The findings of the present study in contrast with results obtained by other authors who found that low socioeconomic status is associated with an increase in the prevalence of *H. pylori* infection (Banatvala *et al.*, 1993; Goldman *et al.*, 2006), which may be due to more sedentary life and bad quality of food. In addition, a Libyan study carried out in Benghazi, also contradicts our findings as they declared that socioeconomic deprivation significantly modifies *H.pylori* prevalence (M. A. Mohammad *et al.*, *al.*, *al.*

2011), approving with another study (Moayedi P et al., 2002).

Family size was also irrelevant in this study, as no correlation was detected, but in this study, the number of people with families is highest infected with *H.pylori* (56.76%). Our findings are similar to those concluded by another research performed in Benghazi, which also found no correlations (Khaled and Ramadhan, 2016). These results are also in line with a Mexican study (Torres J *et al.*, 1998). On the other hand, some studies did find a connection between family size and the prevalence of infection. For example, one that was conducted in

Benghazi stated that the number of siblings was a strong predictor of infection (M. A. Mohammad *et al.*, 2011), which is similar to the results of another study (Galpin *et al.*, 1992).

Stimulants (smoking and consuming tea and coffee) were expected to be a dominant factor in the prevalence of *H.pylori* but showed higher significance in our study. Likewise, many other studies find connections between smokers and *H.pylori* infection. In this study, the rate of student smokers (27.7 %) indicates that smokers are not more likely to be infected than non-smokers. Increased gastric acidity in the stomach through smoking may be a cause of the dose-dependently negative association between H. pylori and smoking. Two studies conducted in Benghazi declared the same findings (Khaled and Ramadhan, 2016; M. A. Mohammad *et al.*, 2011). These findings contradict another study in Tripoli that found a positive correlation between smoking and *H. pylori* infections (I. A. Altayyar *et al.*, 2015), agreeing with the results of many other studies around the world (EUROGAST study group, 1993; Forman D *et al.*, 1993), the smoking cases can increasing stomach bacteria and play an important role in increasing stomach and gastric ulcer and also cigarette prevent the healing in the stomach and increasing their complication that may reach the bleeding in the digestive system.

As for the consumption of tea and coffee, in this study, there was an increasing percentage of *H.pylori* infections among students who were drinking coffee/tea (89.19 %), which is linked to *H.pylori* infection. Likewise, studies detected an increase in the percentage of *H.pylori* infections, reaching 85.8% in those who did consume stimulant beverages in contrast to 14.2% in those who did not (Khaled and Ramadhan, 2016), while another study observed that drinking coffee was not associated with the infections (Khaled and Ramadhan, 2016). Some of the studies where a positive correlation between the consumption of coffee

and *H.pylori* infections and justified this by saying that coffee intake supports the growth of *H.pylori* by suppressing acid production (Alemayehu A. et al., 2011).

The source of drinking water seemed to not affect the level of infection through this study, the percentage of students who drink mineral water, was (72.97%) higher than students who drink tap water. Various studies contrast with our study as they did not find any relation between the water source and infection rates (Khaled and Ramadhan, 2016; Torres J *et al.*, 1998). Conversely, a study in Sudan did find a positive correlation (Abdallah T *et al.*, 2014).

Interestingly, family history also appeared to be not of importance. One study stated that a family history of epigastric pain increased the chance of *H.pylori* harboring (M. A. Mohammad et al., 2011). German research concluded that a history of gastric disease correlated with acquiring the infection (Herbart *et al.*, 2001). It is very unusual for people to know their *H.pylori* status and, thus, it is unlikely that there are systematic biases that threaten the validity of our results. In addition, the students who suffered the infection of Covid do not have any significant association with the prevalence of *H.Pylori*. Although our studied population is small and narrowed, it may be representative of the general population, despite the differences between this group and the general population. A high prevalence of duodenal and gastric ulcers can be seen in patients with the bacterium known as H. Pylori, so it shows that this bacterium correlates with different pathologies. There is also an inverse correlation in which a high proportion of patients who suffered from ulcers have no presence of *H. pylori*. There is also a positive association between ethnic groups and life habits, showing the link between nonsteroidal pills and gastritis. There is logistic regression done to perform the adjustment with different variables. After that, it shows that the relation between the gastric ulcer, peptic ulcer, and duodenal ulcer with H. pylori was confirmed. (Palamides, 2020).

91

In addition, the students who suffered the infection of covid-19 do not have any significant association with H.pylori infection. Likewise, many other studies find no connections between covid-19 and H.pylori infection (Ud Din et al., 2022).

6. Conclusion and Recommendation

In conclusion, Helicobacter Pylori is highly prevalent among University students in our region (Zawia). Life habits (family history, family size, source of water, smoking, as well as gender did not affect the seroprevalence of *H.pylori* infections. However, The seroprevalence of *H.pylori* increases with age and has correlations with consumption of tea/coffee—moreover, higher frequency is found in students from low-income social status. There should be consideration of the isolated food items as the link between H. Pylori with nutrient interactions. These studies are helpful for clinicians to make better decisions depending on the patient's dietary and lifestyle habits. Moreover, specific health-related education interventions should promote healthy eating patterns instead of the intake of a particular food.

References

- 1. Assaad, S., Chaaban, R., Tannous, F., & Costanian, C. (2018). Dietary habits and Helicobacter pylori infection: a cross-sectional study at a Lebanese hospital. *BMC gastroenterology*, *18*(1), 1-13.
- 2. Bordin, D. S., Voynovan, I. N., Andreev, D. N., & Maev, I. V. (2021). Current Helicobacter pylori diagnostics. *Diagnostics*, *11*(8), 1458.
- 3. Dash, N. R., Khoder, G., Nada, A. M., & Al Bataineh, M. T. (2019). We are exploring the impact of Helicobacter pylori on gut microbiome composition. *PloS one*, *14*(6), e0218274.

- 4. Ding, S. Z., Du, Y. Q., Lu, H., Wang, W. H., Cheng, H., Chen, S. Y., ... & Li, Z. S. (2022). Chinese consensus report on family-based Helicobacter pylori infection control and management (2021 edition). *Gut*, *71*(2), 238-253.
- 5. Dore, M. P., & Pes, G. M. (2021). What is new in Helicobacter pylori diagnosis? An overview. *Journal of Clinical Medicine*, *10*(10), 2091.
- 6. Emerenini, F. C., Nwolisa, E. C., Iregbu, F. U., Eke, C. B., & Ikefuna, A. N. (2021). Prevalence and risk factors for helicobacter pylori infection among children in Owerri, Nigeria. *Nigerian Journal of Clinical Practice*, *24*(8), 1188-1188.
- Everhart, J. E., Kruszon-Moran, D., Perez-Perez, G. I., Tralka, T. S., & McQuillan, G. (2000). Seroprevalence and ethnic differences in Helicobacter pylori infection among adults in the United States. *The Journal of infectious diseases*, *181*(4), 1359-1363.
- 8. Halland, M., Haque, R., Langhorst, J., Boone, J. H., & Petri, W. A. (2021). Clinical performance of the H. PYLORI QUIK CHEK[™] and H. PYLORI CHEK[™] assays, novel stool antigen tests for diagnosis of Helicobacter pylori. *European Journal of Clinical Microbiology* & *Infectious Diseases*, *40*(5), 1023-1028.
- 9. Georgopoulos, S., & Papastergiou, V. (2021). An update on current and advancing pharmacotherapy options for treating H. pylori infection. *Expert Opinion on Pharmacotherapy*, 22(6), 729-741.
- Handa, O., Naito, Y., Osawa, M., Murao, T., Matsumoto, H., Umegaki, E., & Shiotani,
 A. (2020). Nutrients and probiotics: current trends in their use to eradicate Helicobacter
 pylori. *Journal of Clinical Biochemistry and Nutrition*, 67(1), 26-28.
- Jung, H. K., Kang, S. J., Lee, Y. C., Yang, H. J., Park, S. Y., Shin, C. M., ... & Research,
 U. G. (2021). Evidence-based guidelines for the treatment of Helicobacter pylori infection in
 Korea 2020. *Gut and liver*, *15*(2), 168.

- Kawakatsu, Y., Koyanagi, Y. N., Oze, I., Kasugai, Y., Morioka, H., Yamaguchi, R., ...
 & Matsuo, K. (2020). Association between socioeconomic status and digestive tract cancers: a case-control study. *Cancers*, *12*(11), 3258.
- 13. Liu, Q., Meng, X., Li, Y., Zhao, C. N., Tang, G. Y., Li, S., ... & Li, H. B. (2018). Natural products for the prevention and management of Helicobacter pylori infection. *Comprehensive reviews in food science and food safety*, *17*(4), 937-952.
- 14. Li, S., Wu, D., Cao, M., Yu, Z., Wu, M., Liu, Y., ... & Zhao, J. (2020). Effects of choline supplementation on liver biology, gut microbiota, and inflammation in Helicobacter pylori-infected mice. *Life Sciences*, *259*, 118200.
- 15. Loh, J. T., Beckett, A. C., Scholz, M. B., & Cover, T. L. (2018). High-salt conditions alter the transcription of Helicobacter pylori genes encoding outer membrane proteins. *Infection and immunity*, 86(3), e00626-17.
- Lu, T. L., Zhang, J. M., Li, S. R., & Chen, C. W. (2022). Spatial-temporal Distribution and Influencing Factors of Helicobacter pylori Infection in Chinese Mainland, 2001-2020: A Systematic Review and Meta-Analysis. *Journal of Clinical Gastroenterology*, 56(5), e273e282.
- 17. McNicholl, A. G., Bordin, D. S., Lucendo, A., Fadeenko, G., Fernandez, M. C., Voynovan, I., ... & Gisbert, J. P. (2020). A combination of bismuth and standard triple therapy eradicates Helicobacter pylori infection in more than 90% of patients. *Clinical Gastroenterology and Hepatology*, *18*(1), 89-98.
- 18. Mezmale, L., Coelho, L. G., Bordin, D., & Leja, M. (2020). Epidemiology of Helicobacter pylori. *Helicobacter*, 25, e12734.
- Monno, R., De Laurentiis, V., Trerotoli, P., Roselli, A. M., Ierardi, E., & Portincasa, P. (2019). Helicobacter pylori infection: association with dietary habits and socioeconomic conditions. *Clinics and research in hepatology and gastroenterology*, *43*(5), 603-607.

- 20. Nakamura, M., Øverby, A., Michimae, H., Matsui, H., Takahashi, S., Mabe, K., ... & Yamagata Murayama, S. (2020). PCR analysis and specific immunohistochemistry revealing a high prevalence of non-Helicobacter pylori Helicobacters in Helicobacter pylori-negative gastric disease patients in Japan: High susceptibility to a Hp eradication regimen. *Helicobacter*, *25*(5), e12700.
- 21. O'Connor, A., Furuta, T., Gisbert, J. P., & O'Morain, C. (2020). Review-treatment of Helicobacter pylori infection 2020. *Helicobacter*, *25*, e12743.
- 22. Oster, P., Vaillant, L., Riva, E., McMillan, B., Belka, C., Truntzer, C., ... & Velin, D. (2022). Helicobacter pylori infection has a detrimental impact on the efficacy of cancer immunotherapies. *Gut*, *71*(3), 457-466.
- 23. Palamides, Pia, Tolulope Jolaiya, Ayodeji Idowu, Eva Lowell, Charles Onyekwere, Rose Ugiagbe, Ifeanyi Agbo, et al. "Helicobacter pylori patient isolates from South Africa and Nigeria differ in virulence factor pathogenicity profile and associated gastric disease outcome." *Scientific Reports* 10, no. 1 (2020): 1-13.
- Park, J. Y., Forman, D., Waskito, L. A., Yamaoka, Y., & Crabtree, J. E. (2018).
 Epidemiology of Helicobacter pylori and CagA-positive infections and global variations in gastric cancer. *Toxins*, 10(4), 163.
- 25. Pellicano, R., Ianiro, G., Fagoonee, S., Settanni, C. R., & Gasbarrini, A. (2020). Extragastric diseases and Helicobacter pylori. *Helicobacter*, 25, e12741.
- 26. Quaglia, N. C., & Dambrosio, A. (2018). Helicobacter pylori: A foodborne pathogen. *World journal of gastroenterology*, *24*(31), 3472.
- Rueda-Robles, A., Rubio-Tomás, T., Plaza-Diaz, J., & Álvarez-Mercado, A. I. (2021).
 Impact of Dietary Patterns on H. pylori Infection and the Modulation of Microbiota to Counteract Its Effect. A Narrative Review. *Pathogens*, *10*(7), 875.

- 28. Smith, S. I., Ajayi, A., Jolaiya, T., Onyekwere, C., Setshedi, M., Schulz, C., ... & Arigbabu, A. (2022). Helicobacter pylori infection in Africa: update of the current situation and challenges. *Digestive Diseases*, *40*(4), 535-544.
- 29. Testerman, T. L., Semino-Mora, C., Cann, J. A., Qiang, B., Peña, E. A., Liu, H., ... & Dubois, A. (2019). Both diet and Helicobacter pylori infection contribute to atherosclerosis in pre-and postmenopausal cynomolgus monkeys. *PloS one*, *14*(9), e0222001.
- 30. Toh, J. W., & Wilson, R. B. (2020). Pathways of gastric carcinogenesis, Helicobacter pylori virulence and interactions with antioxidant systems, vitamin C and phytochemicals. *International Journal of Molecular Sciences*, *21*(17), 6451.
- 31. Ud Din, Rafi, Ahmed, Asma, Abdullah, Imran, Khan, Hasan Akbar, Sheikh, Shaheer Mujahid, Shafqat, Fauzia Azra (2022). A Study to Investigate The Impact Of Helicobacter Pylori On The Victims Of Covid-19. World Health Organization, 19(3):226-231, 2022.
- 32. Wang, X., Shu, X., Li, Q., Li, Y., Chen, Z., Wang, Y., ... & Zhou, Y. (2021). Prevalence and risk factors of Helicobacter pylori infection in Wuwei, a high-risk area for gastric cancer in northwest China: An all-ages population-based cross-sectional study. *Helicobacter*, *26*(4), e12810..
- 33. Yang, H., & Hu, B. (2021). Diagnosis of Helicobacter pylori infection and recent advances. *Diagnostics*, *11*(8), 1305.