Hindawi
Advanced Gut & Microbiome Research
Volume 2023, Article ID 9747027, 9 pages
https://doi.org/10.1155/2023/9747027

AGMR | Hindawi

Review Article

Overview of *Helicobacter pylori* Infection, Prevalence, Risk Factors, and Its Prevention

Samina Khan Bashir[1] **and Muhammad Bashir Khan**[2]

[1]*Doc4U Medical Centre, 110-Watt Common SW, Edmonton, AB, Canada T6X 1X2*
[2]*Department of Biochemistry, Membrane Protein Disease Research Group, University of Alberta, Edmonton, AB, Canada T6G 2R3*

Correspondence should be addressed to Muhammad Bashir Khan; mbk@ualberta.ca

Received 30 December 2022; Revised 13 April 2023; Accepted 26 April 2023; Published 10 May 2023

Academic Editor: Jian Wu

Helicobacter pylori (*H. pylori*) (formerly known as *Campylobacter pyloridis*) has been studied for over a century due to its association with peptic ulcer disease and gastric cancer. Its prevalence has been declining due to improvements in hygienic conditions and effective curative and preventive approaches. However, it is still present in different communities and continues to spread, increasing its global presence in both developing as well as developed countries. Extensive research has been ongoing to eradicate this pathogen, and at present, scientists have discovered different management options. This article highlights the global prevalence of *H. pylori* infection and the factors responsible for its transmission, treatment regimens, and prevention.

1. Introduction

Helicobacter pylori belongs to the family *Helicobacteraceae*. It is a transmissible and pathogenic gram-negative spiral-shaped bacterium thought to be a contaminant of digested food as opposed to being a true colonizer of the gastric mucosa [1]. It was first successfully isolated and discovered by Barry Marshall and Robin Warren in 1980, for which they were awarded the Nobel Prize in 2005 [2]. They intentionally ingested the bacterium and subsequently developed persistent gastritis. Later, it was found that the bacteria are strongly associated with multiple upper gastrointestinal disorders, such as chronic gastritis, peptic ulcer disease, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, and gastric cancer [3–5].

H. pylori is the most common human bacterial infection occurring in ~4.4 billion people, representing over 50% of the world population. The World Health Organization (WHO) now considers it a class 1 carcinogen leading to peptic ulcer disease and gastric cancer [6–8]. The *H. pylori* infection rate is 30–50% in developed and 85–95% in developing countries [9–12]. More specifically, the infection rate is 30% in Western countries and 20–30% in North America, in which it is 23% in the province of Ontario and 13% in Quebec. Infection rates are higher in Africans (25%), Asians (30%), and South Americans (34%) and significantly lower in Caucasians (8%) who reside in Canada [13–15]. The pathogen is more prevalent in North Americans, Aboriginals, and recent immigrants [16].

In 2006, the Canadian North *Helicobacter pylori* Working Group (CAN*Help*) was established to identify specifically the impact of *H. pylori* infection in the Canadian Arctic communities [15–17]. The rate of documented infection in these communities was 55% in the 2008 survey. In one study, 95% seropositivity was revealed in the native community in northwestern Manitoba and a 67% infection rate in children two years of age. The pathogen is also prevalent in Aboriginals of Russia, Alaska, and Greenland, and the infection ratio ranged from 47% to 88% [18–20]. Furthermore, the infection rate is relatively higher in immigrants from countries such as India or China than in those born in Canada from the same ethnic groups [14].

H. pylori infection prevalence increases with age within the first ten years of life [21–23]. The incidence of *H. pylori* infection in childhood varies greatly [24]. The childhood infection rate in some underdeveloped countries is reported

to be 90% [25, 26], while in developed countries, it ranges from as low as 1.8% to as high as 65% [27, 28]. Details about the global prevalence are elaborated in Table 1.

1.1. Factors Contributing to H. pylori Infection. The exact mechanism of *H. pylori* infection is currently unknown; however, socioeconomic and environmental factors are known to play an important role [1, 31]. *H. pylori* infection occurs in early childhood and remains silent for years; only 30% of individuals develop observable signs and symptoms of gastritis. Transmission occurs through oral-oral, fecal-oral, and gastro-oral routes [32, 33]. As an example, mother-to-child transmission occurs if the mother's saliva is contaminated or due to poor hand hygiene. The pathogen is transmitted by direct means, e.g., kissing or sharing utensils [34], or by indirect means, such as drinking water, air, animals, flies, and food [33]. The occurrence of *H. pylori* infection supports the transmission of fecal contaminants in the institutionalized young population during the epidemic of gastroenteritis [35]. Similarly, in refrigerated food, the pathogen may survive for a short period and is the source of infection [36]. Additionally, it is associated with dietary habits, particularly milk, meat, and vegetables [1, 37–39]. One Indian study revealed that the prevalence is more common in the lower socioeconomic group [40]. Drinking unfiltered water, tobacco, and meat consumption are risk factors for developing *H. pylori* infection. Moreover, drinking unboiled water in restaurants in urban areas increases the spread of the pathogen [41, 42]. The acquisition and transmission of the pathogen increase in dense living conditions, when using nonsteroidal anti-inflammatory drugs, in the blood group O, with obesity, and with a family history of gastric disease [43–46]. Eating fried food has a positive correlation with infection [47].

Antibiotic resistance is another contributing factor for *H. pylori* infection as antibiotic resistance is primarily responsible for failing to completely eradicate *H. pylori*. In certain cases, a patient will undergo 14 days of quadruple therapy and, subsequently, either develop the infection again or develop complications of *H. pylori* infection. The main cause of antibiotic resistance is the overuse of antibiotics; metronidazole shows the highest resistance rate and is widely used in most countries for various gastrointestinal illnesses [48–53].

A major contributor to the increased prevalence of bacterial infections, including *H. pylori* infection, is the global emergence of antibiotic-resistant bacteria, threatening the efficacy of antibiotics which have transformed medicine and saved countless lives [54–56]. The leading cause of antibiotic resistance is the overuse or misuse of antibiotics due to a misguided perception in many people that antibiotics can cure any kind of illness. This has caused people to view antibiotics as a cure-all and routinely request them from their physicians, even for viral illnesses. This, compounded with the improper use of antibiotics, leads to resistance. Additionally, incorrectly prescribed antibiotics also promote antibiotic resistance. Research reveals that in 30–50% of cases, the indication for treatment, antibiotic choice, and duration of antibiotic therapy is incorrect [57, 58]. In many countries, antibiotics are available over the counter without prescription; this ease of obtaining antibiotics also contributes to the problem [59, 60]. Lack of regulation and easy availability of a variety of cheap antibiotics in the market as well as online lead to the misuse and overuse of antibiotics [59].

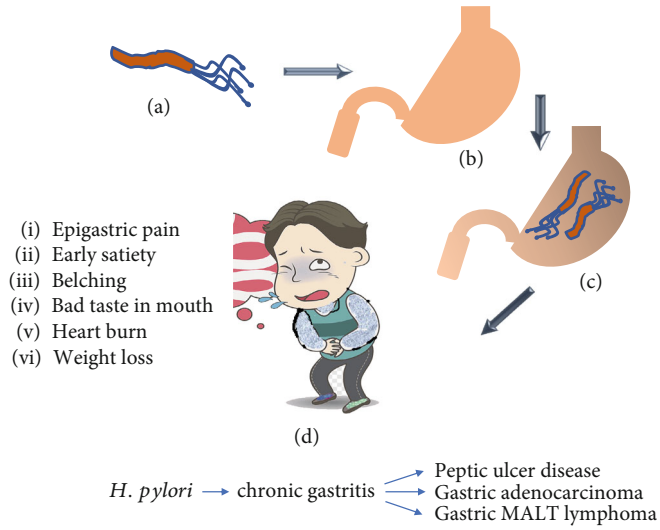
Table 1: Global data on *H. pylori* infection.

Category	Prevalence	Reference
Infected people	4.4 billion (by 2015)	[29]
Developing countries	50.8%	[30]
Developed countries	34.7%	[30]
H. pylori rate in females	42.7%	[30]
H. pylori rate in males	46.3%	[30]
H. pylori rate in children	32.6%	[30]
Africa	70.1%	[11]
South Asia (Pakistan)	81.0%	[11]
South Asia (India)	63.5%	[11]
Western Asia	77.2%	[11]
North America	20%–30%	[13]
United States of America	30%–40%	[13]

Finally, the lack of new drug development by the pharmaceutical industry due to the decreased financial incentives and challenging regulatory requirements is contributing to the antibiotic resistance crisis [59, 61, 62]. New research policies and coordinated efforts to control antibiotic resistance are greatly needed [63]. This will help in the eradication of bacterial pathogens.

1.2. The Clinical Course of H. pylori Infection. *H. pylori* infection is not a disease in itself, but it presents with a spectrum of clinical disorders of the upper gastrointestinal tract and hepatobiliary tract [1]. Dyspepsia is the predominant symptom, and a patient may present with epigastric pain, early satiety, nausea, vomiting, and heartburn [64] (Figure 1). *H. pylori* infection positivity is two times more common in dyspeptic patients than in asymptomatic individuals [65], and the first warning sign for peptic ulcer disease and gastric cancer is dyspepsia [66]. The association between gastroesophageal reflux disease (GERD) and *H. pylori* infection is still in debate. However, esophageal inflammation is increased by *H. pylori*, and it increases the incidence of Barrett's esophagitis (BE) and GERD [67, 68]. A casual causative factor for chronic gastritis is *H. pylori* infection, which leads to the persistent inflammation of the gastric mucosa that may progress to gastric atrophy and intestinal metaplasia [69].

The lifetime risk of developing ulcer disease is 10–20%, distal gastric cancer risk is 1–2% [70–72], and mucosa-associated lymphoid tissue (MALT) lymphoma risk is <0.1% [73] in *H. pylori*-positive patients (Figure 1). Both gastric and duodenal ulcers are strongly associated with this pathogen. In the initial decade after the *H. pylori* discovery, it was found that 95% of duodenal ulcers and 85% of gastric cancer occurred with *H. pylori* [72]. The development of peptic ulcer disease (PUD) is commonly caused by *H. pylori* and nonsteroidal anti-inflammatory (NSAID) use; nevertheless, every individual using NSAID and infected with *H.*



(a) *H. pylori* entry, adherence to gastric mucosa (b) exploitation of human immune system (c) multiplication, tissue damage and transmission to susceptible host (d) sign, symptoms and complication of *H. pylori* infection.

Figure 1: Schematic representation of *H. pylori* mechanism, symptoms, and complications.

pylori does not develop PUD [74, 75]. Patients with duodenal ulcers usually complain of abdominal pain two to three hours after taking meals on an empty stomach or abdominal pain at night, whereas patients with gastric ulcers complain of nausea, vomiting, weight loss, and postprandial abdominal pain. The complication of PUD is bleeding, perforation, penetration, gastric outlet obstruction, and gastric malignancy (adenocarcinoma and MALT) [76]. Bleeding is the most common complication of PUD, and almost 40–60% of upper gastrointestinal bleeding is caused by PUD [77]. With regard to gastric cancer, which is the fifth most common cancer and the third leading cause of death globally, *H. pylori* is the major risk factor for its development. The precancerous lesion is usually started by the *H. pylori* infection with the transformation of the normal mucosa to nonatrophic gastritis that may lead to atrophic gastritis and intestinal metaplasia [78].

All these complications of *H. pylori* are attributed to the severity of gastric inflammation, which is determined by multiple hosts and bacterial factors. The cytotoxin-associated gene-A pathogenic island (*cag* PAI) is a well-characterized *H. pylori* virulence determinant. It is a 42 kb insertion element that consists of 32 genes that encode the bacterial type 4 secretion system. The *cag* A pathogenic island is 60–70% present in the western strain of *H. pylori* and almost 100% of the East Asian *H. pylori* strain. The *cag* PAI presence is associated with more severe gastritis, peptic ulceration, atrophic gastritis, and gastric cancer [79, 80]. Among host factors, the evidence emphasizes *H. pylori*-induced acid production. Increased production of acid limits *H. pylori* gastritis to the antrum, which increases the risk of duodenal ulceration, while reducing acid secretion promotes more proximal inflammation that favors the risk of atrophic gastritis, gastric ulcer disease, and gastric cancer [81].

1.3. Diagnosis and Management. Accurate diagnosis of *H. pylori* infection is essential for the effective treatment of various gastroduodenal diseases. Multiple tests have been developed over time for the detection of *H. pylori* infection. Each test has its benefits and limitations. In a clinical setting, the use of a single test is generally adequate for the diagnosis. Generally, the tests are divided into two categories, i.e., invasive and noninvasive tests (Table 2) [1, 82].

Invasive tests are based on the endoscopic biopsy taken from the gastroduodenal part for histology, culture, rapid urease test, and molecular methods. Noninvasive tests are based on peripheral samples, such as the blood, breath samples, and stool specimens, for the detection of antibodies, bacterial antigen, and urease activity. Fecal antigen tests and urea breath tests are the most widely used noninvasive tests in clinical settings for the detection of *H. pylori* infection and during follow-up after eradication antibiotic treatment, while blood samples are used for screening and epidemiological studies [83]. However, the complications of *H. pylori* infection are not diagnosed by noninvasive tests. *H. pylori*-infected individuals usually develop certain antibodies in their circulation, such as IgA, IgG, and IgM. These antibodies are determined by specific serological tests which are noninvasive, rapid, cheap, and helpful in diagnosing the *H. pylori* infection or when there are equivocal test results by other methods due to complications, e.g., bleeding ulcers, or when the patient is on antibiotics or antisecretory treatment [84]. The detection of serological responses to cytotoxin-associated gene A (*cag* A) gives useful information about serious gastroduodenal infections, such as gastric malignancy and MALT.

cag A is common in Western and East Asian strains of *H. pylori*. However, this is not useful in other countries as the bacterial virulence strains are different in other countries [86]. Serum antibodies were detected via the enzyme-linked

Table 2: Diagnosis of *H. pylori*.

Methods	Sensitivity, specificity, pros	Cons	References
Invasive tests			[1, 85]
Endoscopy	>95% definitive diagnosis	Time-consuming, needs special skill	
Histology	>95% gold standard	Observer dependency, high cost	
Culture biopsy	>95% alternative gold standard	Expensive, complicated	
Rapid urease test	>90% cost-effective and rapid test	Sensitivity specificity is low in gastric bleeding and intestinal metaplasia	
Noninvasive tests			[1, 85]
Urea breath test	>95% simple, safe detection of eradication of infection	False-negative findings in case of bleeding and antibiotic use; less accurate in intestinal metaplasia, atrophic gastritis, and gastric cancer	
Fecal antigen test	>90% simple, fast, inexpensive	False-negative results with the use of PPI, bismuth, antibiotics, and low bacterial load; the problem of keeping and carrying sample	
Serology	80–90% cost-effective, applicable for patients treated with antibiotics and PPI, used for epidemiological studies	Insufficient reliability for routine screening, cannot distinguish between ongoing infection and previous contact, not applicable for confirming cure after therapy	

immunosorbent assay (ELISA), latex agglutination, or immunochromatography [84, 87].

Different antibiotic regimens have been used for the eradication of *H. pylori* infection. Generally, a single drug does not cure the infection. Usual treatment regimens consist of multiple antibiotics that are taken for two weeks (14 days). The standard triple therapy (STT) was established in the past for the eradication of this pathogen. STT consists of amoxicillin, clarithromycin, and proton pump inhibitor; however, the efficacy of the STT regimens has changed over time in many countries mainly because of antibiotic resistance, and other factors contributing to reduced eradication are patient compliance, genetic polymorphism, obesity, smoking, and reinfection. Most of the treatment regimens involve taking proton pump inhibitors, which reduce gastric acid production and allow the bacterial-damaged tissues to heal [88, 89].

Initial regimens to eradicate *H. pylori* in patients suffering from peptic ulcer disease relied on proton pump inhibitors (PPIs) to inhibit the final step in the acid secretion pathway (gastric H^+ and K^+-ATPase) [90] (Figure 2). However, PPIs and antibiotics were subsequently found to work synergistically with each other to eradicate *H. pylori*. Since then, antibiotics have been included in eradication regimens. Current treatments rely on acid suppression combined with at least two antibiotics. The role of acid suppression has been attributed to the antibacterial activity of PPIs, either directly through the inhibition of urease activity or through increased stability and activity of antibiotics [91–93].

One of the widely used first-line antibiotic regimens is the quadruple therapy for 14 days, which involves taking bismuth, tetracycline, PPI, and metronidazole [88, 89, 94]. The quadruple therapy is superior to the triple therapy (STT) [95]. Concomitant therapy consists of three antibiotics, i.e., metronidazole or nitroimidazole, amoxicillin, tetracycline, and PPI, for 14 days [88, 89, 94]. Concomitant therapy is better than STT [96]. Sequential therapy, which involves taking a PPI and amoxicillin for five days followed by clarithromycin, tinidazole, and PPI for another five days is less effective than the concomitant therapy; however, there is still debate about which one is superior [97, 98]. Some studies recommend a treatment of levofloxacin once daily along with PPI, cefuroxime, and bismuth for 7 to 14 days [99], while some suggest rifabutin-based therapy for rescue [100]. As PPI has a shorter duration of action, now, the longer-acting potassium competitive acid blocker (P-CAB), which has a rapid onset of action and is effective for a longer duration, is also used in some countries, such as Japan, and is considered a more potent first-line treatment in reducing gastric secretion [101]. In case primary therapy fails, the second line should be selected based on the previous therapy used and local antibiotic resistance data [88]. Different antibiotic regimens are shown in Figure 3 [88, 102].

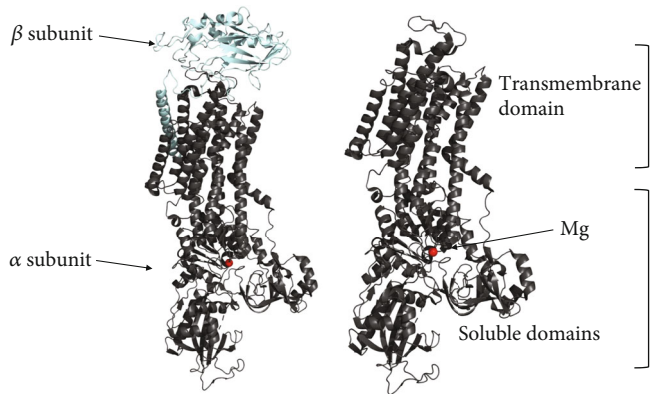


Figure 2: Three-dimensional atomic structure of the gastric proton pump. The gastric proton pump consists of two subunits (α and β); the α subunit is shown in black, and the β subunit is shown in cyan. The overall structure is shown to the left, and a zoomed-in representation omitting the β subunit is shown to the right (PDB ID 5YLU).

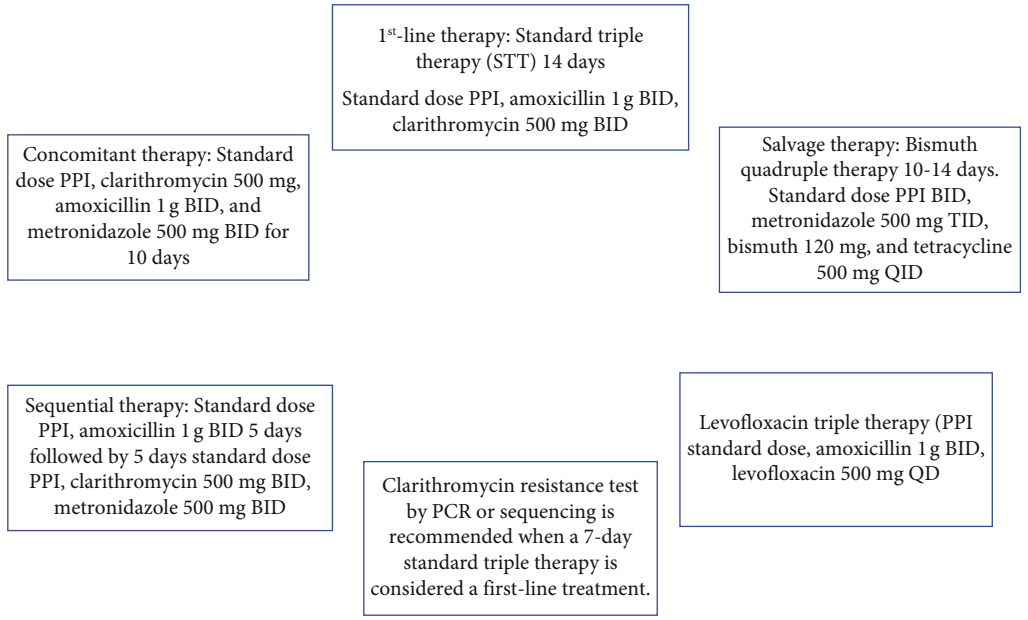


Figure 3: Treatment recommendation for *H. pylori*.

1.4. Modern Approach. A novel approach utilizes the susceptibility-guided strategy that is published in the 2017 Maastricht VI guidelines to create a tailored therapy against *H. pylori* infection. The new approach depends on choosing the antibiotics according to local antibiotic resistance data. Maastricht guidelines propose different regimens of quadruple therapy, primarily concomitant therapy, and bismuth-based therapy [94]. Modifications in usual antibiotic regimens (metronidazole, amoxicillin, and clarithromycin) used in the treatment of *H. pylori* infection have also been proposed, such as sequential, hybrid, and reverse hybrid therapies [103, 104]. However, eradication efficacy is rarely above 90%, which has been the main goal of modified antimicrobial therapy, and this is due to complex multiple antibiotic use at one time and possible side effects of antibiotics limiting the compliance and effectiveness of therapy [105].

New proposals support the use of 14 days of triple therapy, usage of four drug regimens, higher doses of PPI, or the use of a novel PPI, i.e., vonoprazan (P-CAB) and probiotic supplementation with antibiotics [106]. Probiotics, such as *Lactobacillus* spp, *Bifidobacterium* spp, and *Saccharomyces boulardii*, are not directly involved in the eradication of *H. pylori* infection; rather, they reduce the side effects of antibiotics [103, 107, 108].

The 2022 Maastricht VI guidelines support susceptibility testing before prescribing antibiotics for *H. pylori* infection [104] by obtaining a culture from gastric mucosa following endoscopic biopsy and using agar dilution, disc diffusion, or an E test for the detection of antibiotic sensitivity [109]. The gold standard is the agar dilution method, but it is expensive, time-consuming, and labor-intensive [110]. The other method to test antibiotic sensitivity is by genotype molecular testing from the stool and stomach biopsy specimens using real-time polymerase chain reaction (PCR) and fluorescence in situ hybridization (FISH), while commercially available kits are used to detect point mutations related to specific antibiotic resistance [111]. Moreover, whole-genome sequencing techniques have been used to identify drug-resistant mutations [112]. These practices will need to be established in clinical settings as it is debatable whether each dyspeptic patient should be subjected to endoscopy. However, noninvasive techniques, i.e., PCR testing on stool samples or DNA extraction from stool samples, make it possible to avoid invasive testing, such as endoscopy, for the detection of antibiotic sensitivity [113, 114]. The prospects in *H. pylori* management [103, 115] are shown in Table 3.

Table 3: Prospects in the management of *H. pylori* infection.

(i)	Susceptibility-guided therapy/antibiotic sensitivity testing
(ii)	PPI-high dose
(iii)	Novel antibiotics
(iv)	Clarithromycin avoidance, if used previously
(v)	Antibiotic course for 14 days
(vi)	Probiotics with antibiotics
(vii)	Vonoprazan (P-CAB) instead of PPI
(viii)	PCR/DNA extraction (from stool sample) for making a diagnosis
(ix)	Nanotechnology use

2. Conclusion

H. pylori infection prevalence has been reduced overall, but the pathogen is still present in different communities globally. Poor socioeconomic factors, hygiene, eating processed food, restaurant meals, meat, and unfiltered water have been the major contributing factors to *H. pylori* infection and its complications. Antibiotic resistance creates major problems in curing the infection and controlling the prevalence of *H.*

pylori. However, antibiotic susceptibility testing is a novel way to provide a tailored therapy to achieve a complete cure.

Lifestyle modifications are necessary to minimize the risk of *H. pylori* infection. These include proper hand washing, reducing the consumption of frozen/processed food, washing packed salads/vegetables properly before eating, and drinking boiled water. Overuse and misuse of antibiotics need to be discouraged, and completion of the antibiotic course along with probiotics should be promoted.

Hence, providing awareness through various ethnic media channels to various communities and demographic groups is the most important tool available to achieve these measures. Furthermore, routine screening for *H. pylori* infection in both immigrant and nonimmigrant populations will help in curing the infection. Ongoing research into new drugs and vaccines is greatly needed with a global collaborative effort to eradicate this pathogen, as *H. pylori* is a serious global health issue and a major cause of gastric cancer.

Data Availability

Previously reported (statistics) data were used to support this study. These prior studies (and datasets) are cited at relevant places within the text as references [1–98].

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] J. G. Kusters, A. H. van Vliet, and E. J. Kuipers, "Pathogenesis of Helicobacter pylori infection," *Clinical Microbiology Reviews*, vol. 19, no. 3, pp. 449–490, 2006.

[2] A. Morris and G. Nicholson, "Ingestion of Campylobacter pyloridis causes gastritis and raised fasting gastric pH," *The American Journal of Gastroenterology*, vol. 82, no. 3, pp. 192–199, 1987.

[3] K. M. Fock, D. Y. Graham, and P. Malfertheiner, "*Helicobacter pylori* research: historical insights and future directions," *Nature Reviews Gastroenterology & Hepatology*, vol. 10, no. 8, pp. 495–500, 2013.

[4] M. D. Burkitt, C. A. Duckworth, J. M. Williams, and D. M. Pritchard, "*Helicobacter pylori*-induced gastric pathology: insights from in vivo and ex vivo models," *Disease Models & Mechanisms*, vol. 10, no. 2, pp. 89–104, 2017.

[5] B. Bauer and T. F. Meyer, "The Human Gastric Pathogen *Helicobacter pylori* and Its Association with Gastric Cancer and Ulcer Disease," *Ulcers*, vol. 2011, Article ID 340157, 23 pages, 2011.

[6] L. E. Wroblewski, R. M. Peek, and K. T. Wilson, "*Helicobacter pylori* and gastric cancer: factors that modulate disease risk," *Clinical Microbiology Reviews*, vol. 23, no. 4, pp. 713–739, 2010.

[7] D. Bravo, A. Hoare, C. Soto, M. A. Valenzuela, and A. F. Quest, "*Helicobacter pylori* in human health and disease: mechanisms for local gastric and systemic effects," *World Journal of Gastroenterology*, vol. 24, no. 28, pp. 3071–3089, 2018.

[8] S. M. Alexander, R. J. Retnakumar, D. Chouhan et al., "*Helicobacter pylori* in human stomach: the inconsistencies in clinical outcomes and the probable causes," *Frontiers in Microbiology*, vol. 12, article 713955, 2021.

[9] C. Burucoa and A. Axon, "Epidemiology ofHelicobacter pyloriinfection," *Helicobacter*, vol. 22, Supplement 1, 2017.

[10] World Gastroenterology Organisation, "World Gastroenterology Organisation global guideline: *Helicobacter pylori* in developing countries," *Journal of Clinical Gastroenterology*, vol. 45, no. 5, pp. 383–388, 2011.

[11] G. Khoder, J. S. Muhammad, I. Mahmoud, S. S. M. Soliman, and C. Burucoa, "Prevalence of *Helicobacter pylori* and its associated factors among healthy asymptomatic residents in the United Arab Emirates," *Pathogens*, vol. 8, no. 2, 2019.

[12] R. H. Hunt, S. D. Xiao, F. Megraud et al., "Helicobacter pylori in developing countries. World Gastroenterology Organisation global guideline," *Journal of Gastrointestinal and Liver Diseases*, vol. 20, no. 3, pp. 299–304, 2011.

[13] P. Willems, J. de Repentigny, G. M. Hassan, S. Sidani, G. Soucy, and M. Bouin, "The prevalence of *Helicobacter pylori* infection in a quaternary hospital in Canada," *Journal of Clinical Medical Research*, vol. 12, no. 11, pp. 687–692, 2020.

[14] F. Naja, N. Kreiger, and T. Sullivan, "*Helicobacter pylori* infection in Ontario: prevalence and risk factors," *Canadian Journal of Gastroenterology*, vol. 21, no. 8, pp. 501–506, 2007.

[15] K. J. Goodman, K. Jacobson, and S. Veldhuyzen van Zanten, "*Helicobacter pylori* infection in Canadian and related Arctic Aboriginal populations," *Canadian Journal of Gastroenterology*, vol. 22, no. 3, pp. 289–295, 2008.

[16] N. Jones, N. Chiba, C. Fallone et al., "*Helicobacter pylori* in First Nations and recent immigrant populations in Canada," *Canadian Journal of Gastroenterology*, vol. 26, no. 2, pp. 97–103, 2012.

[17] J. Cheung, K. Goodman, R. Munday et al., "*Helicobacter Pylori* infection in Canada's Arctic: searching for the solutions," *Canadian Journal of Gastroenterology*, vol. 22, no. 11, pp. 912–916, 2008.

[18] J. K. Johansen, A. Sehested, T. Myrhøj, K. Ladefoged, and K. A. Krogfelt, "*Helicobacter pylori* infection in Greenlandic patients with dyspepsia," *International Journal of Circumpolar Health*, vol. 63, no. sup2, pp. 219-220, 2004.

[19] O. V. Reshetnikov, Y. P. Nikitin, M. V. Kholmogortsev, S. A. Kurilovich, and O. A. Pycllik, "Helicobacter pylori in a Chukotka Native male population," *International Journal of Circumpolar Health*, vol. 57, Supplement 1, pp. 293–295, 1998.

[20] J. Zhu, M. Davidson, M. Leinonen et al., "Prevalence and persistence of antibodies to herpes viruses, *Chlamydia pneumoniae* and *Helicobacter pylori* in Alaskan Eskimos: the GOCADAN study," *Clinical Microbiology and Infection*, vol. 12, no. 2, pp. 118–122, 2006.

[21] J. Younger and A. Duggan, "*Helicobacter pylori* infection in elderly patients," *The Lancet*, vol. 360, no. 9337, p. 947, 2002.

[22] M. C. Bateson, "*Helicobacter pylori* infection with age," *The Lancet*, vol. 339, no. 8801, p. 1121, 1992.

[23] S. K. Tiwari, G. Manoj, G. V. Kumar et al., "Prognostic significance of genotyping *Helicobacter pylori* infection in patients in younger age groups with gastric cancer," *Postgraduate Medical Journal*, vol. 84, no. 990, pp. 193–197, 2008.

[24] D. Mahalanabis, M. M. Rahman, S. A. Sarker et al., "*Helicobacter pylori* infection in the young in Bangladesh: prevalence, socioeconomic and nutritional aspects," *International Journal of Epidemiology*, vol. 25, no. 4, pp. 894–898, 1996.

[25] B. A. Salih, "*Helicobacter pylori* infection in developing countries: the burden for how long?," *Saudi Journal of Gastroenterology*, vol. 15, no. 3, pp. 201–207, 2009.

[26] E. Hestvik, T. Tylleskar, D. H. Kaddu-Mulindwa et al., "*Helicobacter pylori* in apparently healthy children aged 0-12 years in urban Kampala, Uganda: a community-based cross sectional survey," *BMC Gastroenterology*, vol. 10, p. 62, 2010.

[27] E. Roma and E. Miele, "*Helicobacter pylori* infection in pediatrics," *Helicobacter*, vol. 20, Supplement 1, pp. 47–53, 2015.

[28] H. M. Malaty, V. Paykov, O. Bykova et al., "*Helicobacter pylori* and socioeconomic factors in Russia," *Helicobacter*, vol. 1, no. 2, pp. 82–87, 1996.

[29] J. K. Y. Hooi, W. Y. Lai, W. K. Ng et al., "Global prevalence of *Helicobacter pylori* infection: systematic review and meta-analysis," *Gastroenterology*, vol. 153, no. 2, pp. 420–429, 2017.

[30] M. Zamani, F. Ebrahimtabar, V. Zamani et al., "Systematic review with meta-analysis: the worldwide prevalence of *Helicobacter pylori* infection," *Alimentary Pharmacology & Therapeutics*, vol. 47, no. 7, pp. 868–876, 2018.

[31] S. Kayali, M. Manfredi, F. Gaiani et al., "*Helicobacter pylori*, transmission routes and recurrence of infection: state of the art," *Acta Bio Medica: Atenei Parmensis*, vol. 89, no. 8-S, pp. 72–76, 2018.

[32] T. Yılmaz, M. D. Bajin, R. Günaydın, S. Ozer, and T. Sözen, "Laryngopharyngeal reflux and *Helicobacter pylori*," *World Journal of Gastroenterology*, vol. 20, no. 27, pp. 8964–8970, 2014.

[33] R. P. Allaker, K. A. Young, J. M. Hardie, P. Domizio, and N. J. Meadows, "Prevalence of *Helicobacter pylori* at oral and gastrointestinal sites in children: evidence for possible oral-to-oral transmission," *Journal of Medical Microbiology*, vol. 51, no. 4, pp. 312–317, 2002.

[34] H. Brenner, D. Rothenbacher, G. Bode, P. Dieudonné, and G. Adler, "Active infection with *Helicobacter pylori* in healthy couples," *Epidemiology and Infection*, vol. 122, no. 1, pp. 91–95, 1999.

[35] R. Laporte, P. Pernes, P. Pronnier, F. Gottrand, and P. Vincent, "Acquisition of *Helicobacter pylori* infection after outbreaks of gastroenteritis: prospective cohort survey in institutionalised young people," *BMJ*, vol. 329, no. 7459, pp. 204-205, 2004.

[36] R. E. Poms and S. R. Tatini, "Survival of *Helicobacter pylori* in ready-to-eat foods at 4°C," *International Journal of Food Microbiology*, vol. 63, no. 3, pp. 281–286, 2001.

[37] S. Kabir, "Detection of *Helicobacter pylori* DNA in feces and saliva by polymerase chain reaction: a review," *Helicobacter*, vol. 9, no. 2, pp. 115–123, 2004.

[38] D. A. Ferguson, C. Jiang, D. S. Chi, J. J. Laffan, C. Li, and E. Thomas, "Evaluation of two string tests for obtaining gastric juice for culture, nested-PCR detection, and combined single- and double-stranded conformational polymorphism discrimination of *Helicobacter pylori*," *Digestive Diseases and Sciences*, vol. 44, no. 10, pp. 2056–2062, 1999.

[39] D. A. Ferguson, C. Li, N. R. Patel, W. R. Mayberry, D. S. Chi, and E. Thomas, "Isolation of *Helicobacter pylori* from saliva," *Journal of Clinical Microbiology*, vol. 31, no. 10, pp. 2802–2804, 1993.

[40] R. S. Mhaskar, I. Ricardo, A. Azliyati et al., "Assessment of risk factors of *Helicobacter pylori* infection and peptic ulcer disease," *Journal of Global Infectious Diseases*, vol. 5, no. 2, pp. 60–67, 2013.

[41] D. Palli, N. E. Caporaso, Y. H. Shiao et al., "*Helicobacter pylori*, and p53 mutations in gastric cancer: a molecular epidemiology study in Italy," *Cancer Epidemiology, Biomarkers & Prevention*, vol. 6, no. 12, pp. 1065–1069, 1997.

[42] R. K. Phukan, K. Narain, E. Zomawia, N. C. Hazarika, and J. Mahanta, "Dietary habits and stomach cancer in Mizoram, India," *Journal of Gastroenterology*, vol. 41, no. 5, pp. 418–424, 2006.

[43] I. Segal, R. Ally, and H. Mitchell, "*Helicobacter pylori*–an African perspective," *QJM*, vol. 94, no. 10, pp. 561–565, 2001.

[44] V. H. Chong, K. C. Lim, and N. Rajendran, "Prevalence of active Helicobacter pylori infection among patients referred for endoscopy in Brunei Darussalam," *Singapore Medical Journal*, vol. 49, no. 1, pp. 42–46, 2008.

[45] C. Dube, T. C. Nkosi, A. M. Clarke, N. Mkwetshana, E. Green, and R. N. Ndip, "*Helicobacter pylori* antigenemia in an asymptomatic population of Eastern Cape Province, South Africa: public health implications," *Reviews on Environmental Health*, vol. 24, no. 3, pp. 249–255, 2009.

[46] A. Ogihara, S. Kikuchi, A. Hasegawa et al., "Relationship between *Helicobacter pylori* infection and smoking and drinking habits," *Journal of Gastroenterology and Hepatology*, vol. 15, no. 3, pp. 271–276, 2000.

[47] Y. Zhu, X. Zhou, J. Wu, J. Su, and G. Zhang, "Risk factors and prevalence of *Helicobacter pylori* infection in persistent high incidence area of gastric carcinoma in Yangzhong city," *Gastroenterology Research and Practice*, vol. 2014, Article ID 481365, 10 pages, 2014.

[48] F. Mégraud, "H pylori antibiotic resistance: prevalence, importance, and advances in testing," *Gut*, vol. 53, no. 9, pp. 1374–1384, 2004.

[49] F. Mégraud, "The challenge of *Helicobacter pylori* resistance to antibiotics: the comeback of bismuth-based quadruple therapy," *Therapeutic Advances in Gastroenterology*, vol. 5, no. 2, pp. 103–109, 2012.

[50] J. Chen, P. Li, Y. Huang, Y. Guo, Z. Ding, and H. Lu, "Primary antibiotic resistance of *Helicobacter pylori* in different regions of China: a systematic review and meta-analysis," *Pathogens*, vol. 11, no. 7, 2022.

[51] A. Shiotani, H. Lu, M. P. Dore, and D. Y. Graham, "Treating *Helicobacter pylori* effectively while minimizing misuse of antibiotics," *Cleveland Clinic Journal of Medicine*, vol. 84, no. 4, pp. 310–318, 2017.

[52] J. Yaxley and B. Chakravarty, "*Helicobacter pylori* eradication - an update on the latest therapies," *Australian Family Physician*, vol. 43, no. 5, pp. 301–305, 2014.

[53] W. Wu, Y. Yang, and G. Sun, "Recent insights into antibiotic resistance in *Helicobacter pylori* eradication," *Gastroenterology Research and Practice*, vol. 2012, Article ID 723183, 8 pages, 2012.

[54] Z. Golkar, O. Bagasra, and D. G. Pace, "Bacteriophage therapy: a potential solution for the antibiotic resistance crisis," *The Journal of Infection in Developing Countries*, vol. 8, no. 2, pp. 129–136, 2014.

[55] C. L. Ventola, "The antibiotic resistance crisis: part 1: causes and threats," *Pharmacy and Therapeutics*, vol. 40, no. 4, pp. 277–283, 2015.

[56] S. Sengupta, M. K. Chattopadhyay, and H. P. Grossart, "The multifaceted roles of antibiotics and antibiotic resistance in nature," *Frontiers in Microbiology*, vol. 4, p. 47, 2013.

[57] C. E. Luyt, N. Bréchot, J. L. Trouillet, and J. Chastre, "Antibiotic stewardship in the intensive care unit," *Critical Care*, vol. 18, no. 5, p. 480, 2014.

[58] "Antibiotic resistance threats in the United States, 2013," 2013, https://stacks.cdc.gov/view/cdc/20705.

[59] C. A. Michael, D. Dominey-Howes, and M. Labbate, "The antimicrobial resistance crisis: causes, consequences, and management," *Frontiers in Public Health*, vol. 2, p. 145, 2014.

[60] E. Nature, "The antibiotic alarm," *Nature*, vol. 495, no. 7440, p. 141, 2013.

[61] J. G. Bartlett, D. N. Gilbert, and B. Spellberg, "Seven ways to preserve the miracle of antibiotics," *Clinical Infectious Diseases*, vol. 56, no. 10, pp. 1445–1450, 2013.

[62] I. M. Gould and A. M. Bal, "New antibiotic agents in the pipeline and how they can help overcome microbial resistance," *Virulence*, vol. 4, no. 2, pp. 185–191, 2013.

[63] B. Spellberg and D. N. Gilbert, "The future of antibiotics and resistance: a tribute to a career of leadership by John Bartlett," *Clinical Infectious Diseases*, vol. 59, Supplement 2, pp. S71–S75, 2014.

[64] P. Moayyedi, B. E. Lacy, C. N. Andrews, R. A. Enns, C. W. Howden, and N. Vakil, "ACG and CAG clinical guideline: management of dyspepsia," *The American Journal of Gastroenterology*, vol. 112, no. 7, pp. 988–1013, 2017.

[65] B. Suvak, A. C. Dulger, O. Suvak, E. Aytemiz, and O. Kemik, "The prevalence of *Helicobacter pylori* among dyspeptic patients in an earthquake-stricken area," *Clinics*, vol. 70, no. 1, pp. 69–72, 2015.

[66] A. B. Olokoba, O. A. Obateru, M. O. Bojuwoye, O. K. Ibrahim, and L. B. Olokoba, "That dyspepsia in the young could be cancer," *Nigerian Medical Journal*, vol. 54, no. 2, pp. 143–145, 2013.

[67] F. X. Liu, W. H. Wang, J. Wang, J. Li, and P. P. Gao, "Effect of *Helicobacter pylori* infection on Barrett's esophagus and esophageal adenocarcinoma formation in a rat model of chronic gastroesophageal reflux," *Helicobacter*, vol. 16, no. 1, pp. 66–77, 2011.

[68] F. R. Polat and S. Polat, "The effect of *Helicobacter pylori* on gastroesophageal reflux disease," *Journal of the Society of Laparoendoscopic Surgeons*, vol. 16, no. 2, pp. 260–263, 2012.

[69] P. Sipponen and H. Hyvärinen, "Role of Helicobacter pylori in the pathogenesis of gastritis, peptic ulcer and gastric cancer," *Scandinavian Journal of Gastroenterology. Supplement*, vol. 28, no. sup196, pp. 3–6, 1993.

[70] P. B. Ernst and B. D. Gold, "The disease spectrum of Helicobacter pylori: the immunopathogenesis of gastroduodenal ulcer and gastric cancer," *Annual Review of Microbiology*, vol. 54, no. 1, pp. 615–640, 2000.

[71] E. J. Kuipers, "Review article: exploring the link between *Helicobacter pylori* and gastric cancer," *Alimentary Pharmacology & Therapeutics*, vol. 13, Supplement 1, pp. 3–11, 1999.

[72] E. J. Kuipers, J. C. Thijs, and H. P. Festen, "The prevalence of *Helicobacter pylori* in peptic ulcer disease," *Alimentary Pharmacology & Therapeutics*, vol. 9, Supplement 2, pp. 59–69, 1995.

[73] R. M. Peek and J. E. Crabtree, "*Helicobacter* infection and gastric neoplasia," *The Journal of Pathology*, vol. 208, no. 2, pp. 233–248, 2006.

[74] B. B. Zhang, Y. Li, X. Q. Liu, P. J. Wang, B. Yang, and D. L. Bian, "Association between vacA genotypes and the risk of duodenal ulcer: a meta-analysis," *Molecular Biology Reports*, vol. 41, no. 11, pp. 7241–7254, 2014.

[75] M. Feldman, L. S. Friedman, and L. J. Brandt, *Sleisenger and Fordtran's Gastrointestinal and Liver Disease E-book: Pathophysiology, Diagnosis, Management*, Elsevier Health Sciences, 2020.

[76] M. Narayanan, K. M. Reddy, and E. Marsicano, "Peptic ulcer disease and Helicobacter pylori infection," *Missouri Medicine*, vol. 115, no. 3, pp. 219–224, 2018.

[77] A. Lanas, L. A. García-Rodríguez, M. Polo-Tomás et al., "The changing face of hospitalisation due to gastrointestinal bleeding and perforation," *Alimentary Pharmacology & Therapeutics*, vol. 33, no. 5, pp. 585–591, 2011.

[78] P. Díaz, M. Valenzuela Valderrama, J. Bravo, and A. F. G. Quest, "*Helicobacter pylori* and gastric cancer: adaptive cellular mechanisms involved in disease progression," *Frontiers in Microbiology*, vol. 9, p. 5, 2018.

[79] J. F. Tomb, O. White, A. R. Kerlavage et al., "The complete genome sequence of the gastric pathogen *Helicobacter pylori*," *Nature*, vol. 388, no. 6642, pp. 539–547, 1997.

[80] N. S. Akopyants, S. W. Clifton, D. Kersulyte et al., "Analyses of the cag pathogenicity island of *Helicobacter pylori*," *Molecular Microbiology*, vol. 28, no. 1, pp. 37–53, 1998.

[81] E. J. Kuipers, "*Helicobacter pylori* and the risk and management of associated diseases: gastritis, ulcer disease, atrophic gastritis and gastric cancer," *Alimentary Pharmacology & Therapeutics*, vol. 11, Supplement 1, pp. 71–88, 1997.

[82] Y. K. Wang, F. C. Kuo, C. J. Liu et al., "Diagnosis of *Helicobacter pylori* infection: current options and developments," *World Journal of Gastroenterology*, vol. 21, no. 40, pp. 11221–11235, 2015.

[83] S. Kayali, R. Aloe, C. Bonaguri et al., "Non-invasive tests for the diagnosis of *Helicobacter pylori*: state of the art," *Acta Bio Medica: Atenei Parmensis*, vol. 89, no. 8-S, pp. 58–64, 2018.

[84] H. Suzuki, T. Masaoka, S. Nomura et al., "Current consensus on the diagnosis and treatment of H. pylori-associated gastroduodenal disease," *The Keio Journal of Medicine*, vol. 52, no. 3, pp. 163–173, 2003.

[85] P. Sabbagh, M. Mohammadnia-Afrouzi, M. Javanian et al., "Diagnostic methods for *Helicobacter pylori* infection: ideals, options, and limitations," *European Journal of Clinical Microbiology & Infectious Diseases*, vol. 38, no. 1, pp. 55–66, 2019.

[86] D. Vaira, J. Holton, M. Menegatti et al., "New immunological assays for the diagnosis of *Helicobacter pylori* infection," *Gut*, vol. 45, Supplement 1, pp. I23–I27, 1999.

[87] W. D. Chey, B. C. Wong, and Practice Parameters Committee of the American College of Gastroenterology, "American College of Gastroenterology guideline on the management of *Helicobacter pylori* infection," *The American Journal of Gastroenterology*, vol. 102, no. 8, pp. 1808–1825, 2007.

[88] W. D. Chey, G. I. Leontiadis, C. W. Howden, and S. F. Moss, "ACG clinical guideline: treatment of *Helicobacter pylori* infection," *The American Journal of Gastroenterology*, vol. 112, no. 2, pp. 212–239, 2017.

[89] C. A. Fallone, N. Chiba, S. V. van Zanten et al., "The Toronto consensus for the treatment of *Helicobacter pylori* infection in adults," *Gastroenterology*, vol. 151, no. 1, pp. 51–69.e14, 2016.

[90] K. Abe, K. Irie, H. Nakanishi, H. Suzuki, and Y. Fujiyoshi, "Crystal structures of the gastric proton pump," *Nature*, vol. 556, no. 7700, pp. 214–218, 2018.

[91] J. P. Gisbert, "Potent gastric acid inhibition in *Helicobacter pylori* eradication," *Drugs*, vol. 65, no. 1, pp. 83–96, 2005.

[92] D. R. Scott, G. Sachs, and E. A. Marcus, "The role of acid inhibition in *Helicobacter pylori* eradication," *F1000Research*, vol. 5, 2016.

[93] P. Malfertheiner, S. F. Moss, P. Daniele et al., "Potassium-competitive acid blocker and proton pump inhibitor-based regimens for first-line *Helicobacter pylori* eradication: a network meta-analysis," *Gastro Hep Advances*, vol. 1, no. 5, pp. 824–834, 2022.

[94] P. Malfertheiner, F. Megraud, C. A. O'Morain et al., "Management of *Helicobacter pylori* infection—the Maastricht V/Florence consensus report," *Gut*, vol. 66, no. 1, pp. 6–30, 2017.

[95] B. Z. Li, D. E. Threapleton, J. Y. Wang et al., "Comparative effectiveness and tolerance of treatments for *Helicobacter pylori*: systematic review and network meta-analysis," *BMJ*, vol. 351, article h4052, 2015.

[96] J. P. Gisbert and X. Calvet, "Review article: non-bismuth quadruple (concomitant) therapy for eradication of *Helicobacter pylori*," *Alimentary Pharmacology & Therapeutics*, vol. 34, no. 6, pp. 604–617, 2011.

[97] J. W. Chung, J. P. Han, K. O. Kim et al., "Ten-day empirical sequential or concomitant therapy is more effective than triple therapy for *Helicobacter pylori* eradication: a multicenter, prospective study," *Digestive and Liver Disease*, vol. 48, no. 8, pp. 888–892, 2016.

[98] A. G. McNicholl, A. C. Marin, J. Molina-Infante et al., "Randomised clinical trial comparing sequential and concomitant therapies for *Helicobacter pylori* eradication in routine clinical practice," *Gut*, vol. 63, no. 2, pp. 244–249, 2014.

[99] Z. Song, W. Fu, and L. Zhou, "Cefuroxime, levofloxacin, esomeprazole, and bismuth as first-line therapy for eradicating *Helicobacter pylori* in patients allergic to penicillin," *BMC Gastroenterology*, vol. 19, no. 1, p. 132, 2019.

[100] M. Heep, D. Beck, E. Bayerdörffer, and N. Lehn, "Rifampin and rifabutin resistance mechanism in *Helicobacter pylori*," *Antimicrobial Agents and Chemotherapy*, vol. 43, no. 6, pp. 1497–1499, 1999.

[101] D. Y. Graham and M. P. Dore, "Update on the use of vonoprazan: a competitive acid blocker," *Gastroenterology*, vol. 154, no. 3, pp. 462–466, 2018.

[102] H. K. Jung, S. J. Kang, Y. C. Lee et al., "Evidence-based guidelines for the treatment of *Helicobacter pylori* infection in Korea 2020," *Liver*, vol. 15, no. 2, pp. 168–195, 2021.

[103] P. Malfertheiner, F. Megraud, T. Rokkas et al., "Management of *Helicobacter pylori* infection: the Maastricht VI/Florence consensus report," *Gut*, vol. 71, no. 9, pp. 1724–1762, 2022.

[104] A. Mestrovic, N. Perkovic, J. Bozic et al., "Randomised clinical trial comparing concomitant and hybrid therapy for eradication of Helicobacter pylori infection," *PLoS One*, vol. 15, no. 12, article e0244500, 2020.

[105] H. Taguchi, S. Kanmura, T. Maeda et al., "*Helicobacter pylori* eradication improves the quality of life regardless of the treatment outcome: a multicenter prospective cohort study," *Medicine*, vol. 96, no. 52, article e9507, 2017.

[106] P. Roszczenko-Jasinska, M. I. Wojtys, and E. K. Jagusztyn-Krynicka, "*Helicobacter pylori* treatment in the post-antibiotics era-searching for new drug targets," *Applied Microbiology and Biotechnology*, vol. 104, no. 23, pp. 9891–9905, 2020.

[107] B. G. Zhou, L. X. Chen, B. Li, L. Y. Wan, and Y. W. Ai, "Saccharomyces boulardii as an adjuvant therapy for *Helicobacter pylori* eradication: a systematic review and meta-analysis with trial sequential analysis," *Helicobacter*, vol. 24, no. 5, article e12651, 2019.

[108] Z. Lv, B. Wang, X. Zhou et al., "Efficacy and safety of probiotics as adjuvant agents for *Helicobacter pylori* infection: a meta-analysis," *Experimental and Therapeutic Medicine*, vol. 9, no. 3, pp. 707–716, 2015.

[109] Q. Ma, H. Li, J. Liao, Z. Cai, and B. Zhang, "Tailored therapy for *Helicobacter pylori* eradication: a systematic review and meta-analysis," *Frontiers in Pharmacology*, vol. 13, article 908202, 2022.

[110] S. K. Ogata, A. C. Gales, and E. Kawakami, "Antimicrobial susceptibility testing for *Helicobacter pylori* isolates from Brazilian children and adolescents: comparing agar dilution, E-test, and disk diffusion," *Brazilian Journal of Microbiology*, vol. 45, no. 4, pp. 1439–1448, 2014.

[111] R. Gingold-Belfer, Y. Niv, H. Schmilovitz-Weiss, Z. Levi, and D. Boltin, "Susceptibility-guided versus empirical treatment for *Helicobacter pylori* infection: a systematic review and meta-analysis," *Journal of Gastroenterology and Hepatology*, vol. 36, no. 10, pp. 2649–2658, 2021.

[112] B. G. Nezami, M. Jani, D. Alouani, D. D. Rhoads, and N. Sadri, "*Helicobacter pylori* mutations detected by next-generation sequencing in formalin-fixed, paraffin-embedded gastric biopsy specimens are associated with treatment failure," *Journal of Clinical Microbiology*, vol. 57, no. 7, 2019.

[113] R. J. Gong, C. X. Xu, H. Li, and X. M. Liu, "Polymerase chain reaction-based tests for detecting *Helicobacter pylori* clarithromycin resistance in stool samples: a meta-analysis," *World Journal of Clinical Cases*, vol. 9, no. 1, pp. 133–147, 2021.

[114] D. Y. Graham and S. F. Moss, "Antimicrobial susceptibility testing for Helicobacter pylori is now widely available: when, how, why," *The American Journal of Gastroenterology*, vol. 117, no. 4, pp. 524–528, 2022.

[115] S. Suzuki, M. Esaki, C. Kusano, H. Ikehara, and T. Gotoda, "Development of *Helicobacter pylori* treatment: how do we manage antimicrobial resistance?," *World Journal of Gastroenterology*, vol. 25, no. 16, pp. 1907–1912, 2019.