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Helicobacter pylori: An integrated clinical and nutritional review

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Abstract

A spiral-shaped, Gram-negative bacterium called *Helicobacter pylori* chronically infects almost half of the world's population (Hooi *et al*., 2017). It greatly increases the risk of peptic ulcer disease and stomach cancer (Amieva & El-Omar, 2008; Suerbaum & Michetti, 2002), and it adds to chronic gastritis. Clinical and nutritional viewpoints on H. pylori are integrated in this review, starting with its microbiology and virulence characteristics, which allow it to survive in the acidic stomach environment and cause inflammation. These include urease activity and CagA/VacA toxins (Ansari & Yamaoka, 2019; Cover & Blaser, 2009). The difficulties presented by increasing antibiotic resistance (Savoldi *et al*., 2018; Yu *et al*., 2024) are discussed, as well as standard treatment plans and diagnostic techniques such as endoscopic biopsies (Chey *et al*., 2017; Moyer & Edelstein, 2019), stool antigen testing, and urea breath tests.

Probiotics, plant-based substances, and diets high in antioxidants (Yang *et al*., 2024; Liu *et al*., 2024) are among the nutritional elements that being investigated for their potential to improve eradication rates and modify infection outcomes. Additionally included are new treatment approaches like phage therapy and vaccinations (Liu *et al*., 2024; Wang *et al*., 2023). This study highlights a multidisciplinary strategy that integrates dietary, pharmaceutical, and new approaches to improve stomach health and H. pylori therapy.

Keywords: *Helicobacter pylori*, antibiotic resistance, chronic gastritis, peptic ulcer disease, probiotics, phytotherapy, micronutrients, gastric cancer

Introduction

Helicobacter pylori is a spiral-shaped, flagellated, microaerophilic (Marshall & Warren, 1984) [14], Gram-negative bacteria that is specially suited to invade the human stomach. An estimated 50% of people worldwide are infected with H. pylori, which was first identified in 1983 from gastric biopsy specimens of individuals suffering from chronic gastritis. Usually contracted as a child, the infection lasts a lifetime if left untreated. It is a known risk factor for gastric adenocarcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma, and it is the main cause of peptic ulcer disease and chronic gastritis. The World Health Organization has designated H. pylori as a Group I (definite) carcinogen (González & López-Carrillo, 2010) [7] due to its known carcinogenic potential.

In contrast to 30–50% in developed countries, the prevalence of H. pylori varies greatly (Hooi *et al*., 2017; Salahi-Niri *et al*., 2024) [10, 17] by region, reaching 85–95% in impoverished countries. Transmission is influenced by food practices, sanitation, and socioeconomic factors (Baryshnikova *et al*., 2023) [4]; crowded living arrangements and inadequate hygiene make people more vulnerable. The defenses of the stomach mucosa are further undermined by lifestyle choices like smoking, excessive salt consumption, and nutritional deficiencies (González & López-Carrillo, 2010; Haley & Gaddy, 2016) [7, 8]. On the other hand, diets high in fruits, vegetables, and antioxidants (Hwang *et al*., 1994; Haley & Gaddy, 2016) [9, 8] including beta-carotene, vitamin C, and vitamin E are linked to a decreased risk of stomach cancers and infection rates. Despite of improvements in diagnosis and therapy, H. pylori continues to pose a significant threat to global health, including severe gastrointestinal disorders and chronic gastritis.

Regional differences in H. pylori prevalence are significant, with rates in underdeveloped countries approaching 85–95% and in industrialized ones at about 30–50%. This discrepancy reflects food, sanitation, and socioeconomic factors: poor hygiene and cramped living circumstances encourage the spread of disease. Infection risk is also modulated by certain lifestyle factors. Smoking, excessive salt consumption, and micronutrient deficiencies (such as low vitamin levels) can all weaken the stomach mucosal

defenses and make people more vulnerable. On the other hand, diets high in fruits, vegetables, and antioxidants (Hwang *et al*., 1994; Haley & Gaddy, 2016) [9, 8] (beta-carotene, vitamin C, and vitamin E) are linked to lower risks of stomach cancer and H. pylori infection. All things considered, H. pylori continues to be a major worldwide health burden, resulting in chronic gastritis in almost all infected individuals and significantly increasing morbidity and mortality through stomach cancers and ulcer disease.

2. Microbiology

Morphology and Niche: The bacterium H. pylori is a helical, curved rod (Kusters *et al*., 2006) [11] that is between 2 and 4 µm length. It can penetrate stomach mucous because it is highly motile and flagellated, usually having four to six flagella. It can only develop in microaerophilic (lower oxygen) environments. It preferentially attaches to epithelial cells in the body mucosa and stomach antrum. Because it produces a lot of urease, H. pylori thrives in the acidic stomach, unlike many other infections. In order to thrive in an acidic stomach, H. pylori can locally elevate pH by hydrolyzing urea into ammonia and bicarbonate, which neutralizes the acidic pH and makes the microenvironment more hospitable.

2.1 Adhesion: Binding to the stomach epithelium is necessary for colonization. In order to engage host cell receptors (blood group antigens, sialyl-Lewis X) on epithelial surfaces, H. pylori produces outer membrane adhesins (e.g. BabA, SabA) (Ansari & Yamaoka, 2019) [3]. The bacteria prevent themselves from being flushed into the intestinal lumen by occupying attachment sites. Thus, colonization can be avoided by blocking adhesins or inhibiting urease. H. pylori usually remains in close touch with the epithelium after breaking through the mucus layer, frequently establishing microcolonies.

2.2 Virulence Factors: The cytotoxin-associated gene A (CagA) protein and the vacuolating cytotoxin (VacA) are two of the most significant H. pylori virulence factors. The majority of strains have vacA (with various allelic variations), and over 50% of strains have the pathogenicity island that codes for CagA. Through a type IV secretion pathway, CagA is delivered into stomach epithelial cells (Amieva & El-Omar, 2008; Cover & Blaser, 2009) [2, 6]. Once inside, CagA is phosphorylated and interferes with several signaling pathways, which causes an inflammatory cascade and an increase in IL-8 production. VacA is secreted and has the ability to cause epithelial cells to form huge intracellular vacuoles. Along with triggering apoptosis and autophagy pathways, VacA also creates anion-specific channels in host membranes.

CagA and VacA work together to cause chronic inflammation and damage to the epithelium. Other elements that support colonization and immune evasion include heat-shock proteins, flagella, urease itself (Sharndama & Mba, 2022) [24], and lipopolysaccharide. All things considered, these virulence factors and microbiological characteristics allow H. pylori to cause chronic inflammation and a protracted stomach infection.

3. Pathology

All infected individuals experience chronic active gastritis after H. pylori causes an acute inflammatory response during the initial infection. Bacterial adhesins and toxins boost host immunity, whereas the bacteria's urease-derived ammonia damages epithelial cells and breaks tight junctions. Reactive oxygen species are produced by the innate immune cells (macrophages, neutrophils), further damaging tissue. Chronic gastritis is the result of a persistent cytokine environment, especially IL-8 and TNF-α. This inflammation develops into clinical illness in certain cases. Due to a combination of bacterial causes and weakened mucosal defense, peptic ulcer disease, also known as stomach or duodenal ulcers, develops in about 10–15% of infected persons. In some instances, intestinal metaplasia, atrophic gastritis, and ultimately adenocarcinoma or MALT lymphoma can develop from chronic gastritis.

Bacterial, host, and environmental factors all affect how severe the outcome is. CagA-positive strains are strongly associated with an increased risk of ulcers and cancer and cause more severe inflammation. Epithelial damage is increased by VacA and other secreted proteases. It is possible for host genetic variables, such as IL-1 polymorphisms, to intensify inflammation. Diet and smoking are examples of environmental cofactors that affect development. In clinical terms, an H. pylori infection may manifest as asymptomatic or with epigastric discomfort. In addition to ulcers and gastric cancer, it is linked to extra-gastric disorders such as iron-deficiency anemia, idiopathic thrombocytopenic purpura (ITP), and potentially nutritional malabsorption. Regression of MALT lymphoma and ulcer repair are frequent outcomes of H. pylori eradication, highlighting its primary pathogenic involvement.

4. Clinical Implication

4.1 Diagnosis

Prior to starting treatment for H. pylori, a precise diagnosis is necessary. Invasive and noninvasive testing are examples of diagnostic techniques. For invasive diagnosis, endoscopy with stomach biopsy is necessary for fast urease tests, culture, or histology. Culture enables testing for antibiotic susceptibility but is technically difficult; histology (using certain stains) permits direct visualization of the organisms. In a matter of seconds, the quick urease test (biopsy on urea indicator) can identify urease activity. In the beginning, noninvasive tests are frequently favored. The urea breath test (UBT), which uses urea that has been tagged with ~13C or ^14C, is very sensitive and specific for current infections. According to the American College of Gastroenterology, UBT is the most accurate noninvasive test available. When validated immunoassays are employed, a stool antigen test is an additional dependable noninvasive choice that is likewise >90% sensitive/specific. Although serology (H. pylori IgG antibody) can show exposure, it is less specific (particularly in low-prevalence environments) and cannot differentiate between an active infection and one that has already occurred.

The most readily available tests in primary care are stool antigen and serology. UBT is perfect for eradication confirmation, however its availability and cost may be constrained. It's important to note that using an antibiotic or

proton pump inhibitor during the two to four weeks prior can result in false negatives because they suppress bacteria, therefore testing should ideally be done after therapy. All patients with active peptic ulcer disease, MALT lymphoma, or uninvestigated dyspepsia, as well as specific high-risk groups (e.g., commencing chronic NSAIDs, history of gastric cancer in family), should be tested (and treated), according to current standards. An invasive biopsy may be the last resort if clinical concern persists after a negative result typically rules out an active infection.

4.2 Treatment and Resistance

Eradication therapy is the mainstay of H. pylori management, with the goal of curing infection and repairing stomach ulcers. Triple therapy, which included a proton-pump inhibitor (PPI) plus clarithromycin, amoxicillin, or metronidazole for seven to fourteen days, was the standard first-line treatment. In the 1990s, this treatment was very successful, with cure rates exceeding 90% in certain areas. However, its global success has been undermined by antibiotic resistance. Metronidazole resistance surpasses 50–70% in certain populations, and clarithromycin resistance has surpassed tolerable thresholds, frequently above 15–30% in numerous regions. Since current eradication rates typically fall below 80%, empirical triple therapy now regularly fails.

According to global surveillance, metronidazole resistance has increased to around 60–80% and clarithromycin resistance to about 15–40% in recent years. Point mutations in the bacterial genome are mostly responsible for this resistance. As a result, when regional clarithromycin resistance surpasses around 15%, worldwide guidelines (Maastricht V/Florence Consensus, ACG) now recommend stopping routine clarithromycin triple therapy. As a first-line treatment in high-resistance conditions, bismuth quadruple therapy (PPI + bismuth salt + tetracycline + metronidazole) or concomitant/hybrid therapy (PPI + clarithromycin + amoxicillin + metronidazole) for 10–14 days is advised. In refractory patients, second-line "rescue" therapy may consist of regimens containing levofloxacin or rifabutin. Remarkably, rifabutin, a rifamycin, has demonstrated significant rates of eradication when used as a rescue treatment for H. pylori that is resistant to many drugs.

Treatment failure is also influenced by the intricacy of several medications and the adverse effects of antibiotics, such as nausea and diarrhea. Concerns regarding intestinal dysbiosis and additional resistance are raised by prolonged or repeated courses. Novel antibiotics and adjuncts are the focus of current research due to growing resistance and diminishing efficacy. For instance, vonoprazan-based regimens (a potassium-competitive acid blocker) and furazolidone, an earlier broad-spectrum medication, are being investigated in East Asia with varying degrees of effectiveness. Antimicrobial resistance is still the main issue, though. According to a recent meta-analysis, global eradication rates have been declining progressively as resistance has increased. Nowadays, while dealing with refractory cases, clinicians frequently obtain culture/susceptibility tests or modify medication based on local resistance data. In general, incorporating patient variables, evolving guidelines, and microbiological sensitivity is necessary for controlling H. pylori. Since infection clearance promotes ulcer healing, gastritis resolution, and the regression of early malignant alterations, it is imperative that the infection be eradicated as soon as possible. Resistance must be considered when selecting empirical regimens, though, as quadruple or sequential therapies are favored in many areas where ordinary triple therapy is no longer effective. In the age of growing resistance, maintaining high cure rates requires ongoing monitoring for resistance patterns and the creation of novel antibiotics or therapeutic approaches.

5. Nutritional Perspective

5.1 Diet

The risk of H. pylori infection and its clinical aftereffects are influenced by dietary variables. Increased consumption of foods that are smoked, pickled, or preserved in salt has been associated with severe gastric shrinkage in infected patients, potentially as a result of mucosal defenses being weakened. On the other hand, diets high in whole foods, fresh produce, and fruits seem to be protective. These foods contain antioxidant vitamins and phytochemicals, such as vitamin C, carotenoids, and flavonoids, which can counteract the oxidative stress brought on by infection and stop the growth of germs. For example, epidemiologic data indicate that high dietary amounts of beta-carotene, vitamin C, and vitamin E greatly lower the incidence of stomach cancer in people with H. pylori infection.

5.2 Probiotics

Live beneficial microorganisms, or probiotics, have been researched as supplements to treat H. pylori. There are several ways that Lactobacillus and Bifidobacterium species, as well as the yeast Saccharomyces boulardii, might inhibit H. pylori. Lactic acid, hydrogen peroxide, and bacteriocins, which are produced by these helpful bacteria, inhibit the growth of H. pylori. Additionally, they reduce inflammation by modulating host immunity and competing for adhesion sites on the stomach mucosa. Probiotics have been tested in clinical trials as an adjunct to conventional treatment. According to meta-analyses, taking probiotic supplements considerably lowers gastrointestinal adverse effects (such antibiotic-associated diarrhea) and somewhat raises eradication rates. One umbrella study, for instance, found that using probiotics reduced the risk of all side effects by half and enhanced eradication (pooled relative risk ≈1.10). When probiotics were included, the cure rate increased to 92.0% from 86.8% with antibiotic therapy alone, according to another study. The *strains* L. *reuteri*, L. *acidophilus*, L. casei, B. *bifidum*, and S. *boulardii* are frequently researched. In general, these are well accepted. Guidelines (such as Maastricht V) currently recommend that probiotics be taken into consideration to increase the effectiveness of eradication regimens and improve their tolerability in light of this research. Although probiotics by themselves cannot take the place of antibiotics, in practice, a multi-strain probiotic or Saccharomyces boulardii given with antibiotic therapy frequently decreases adverse effects and may modestly increase cure rates.

5.3 Phytotherapy

Many substances derived from plants have anti-H. pylori properties, and some of these have undergone clinical

testing. Allicin, which is found in garlic (*Allium sativum*), has potent antibacterial properties. Consuming fresh garlic cloves for three days dramatically decreased the H. pylori load in the stomach mucosa in one small study. *In vitro* and in mouse models, green tea catechins, particularly epigallocatechin gallate, or EGCG, also suppress H. pylori. Curcumin, an ingredient in turmeric, has antibacterial and anti-inflammatory properties; it has been demonstrated to eradicate H. pylori in culture. Proanthocyanidins found in cranberries prevent germs from adhering to surfaces; consuming cranberry extract or juice on a daily basis can inhibit colonization. Gingerols and licorice root (glycyrrhizin) also prevent H. pylori from growing. These botanicals appear to work by either preventing adherence to epithelial cells, inhibiting urease, or causing damage to the bacterial cell membrane. These extracts have been investigated as adjuncts in some therapeutic investigations. In Iran, for example, a randomized trial that supplemented normal antibiotic therapy with 500 mg of vitamin C per day (as a nutrition + moderate antioxidant) yielded a 78% eradication rate, compared to only 56% with antibiotics alone. In a similar vein, studies using broccoli sprout (sulforaphane-rich) preparations have demonstrated decreased H. pylori density in patients with the infection. Green tea extract significantly decreased colonization prevalence in animal studies. Antibiotics cannot be replaced by plant substances, but when used as adjuncts or in preventative measures, they may improve eradication or lower relapse.

Crucially, phytotherapy typically avoids encouraging antibiotic resistance and has minimal adverse effects. A summary of many anti-H. pylori plant extracts and their suggested mechanisms may be found (not illustrated). All things considered, adding specific functional foods-such as garlic, green tea, cruciferous vegetables, and herbs-can be a helpful adjunct to traditional therapy.

5.4 Micronutrients

Deficits in a number of micronutrients are linked to H. pylori infection, both as causes and effects of illness. Notably, H. pylori itself can consume ascorbic acid (vitamin C) and form reactive nitrogen species that degrade dietary vitamin C in the stomach, and chronic gastritis can hinder the absorption of vitamin B (by disrupting intrinsic factor–producing parietal cells). Serum levels of vitamin C, vitamin D, vitamin B, and folate are considerably lower in H. pylori-positive people than in uninfected controls, according to recent meta-analyses. H. pylori-infected patients, for instance, had significantly decreased vitamin B (SMD = –0.30) and vitamin D (SMD ≈ –0.34) levels, according to pooled data. It is encouraging to note that effective eradication frequently restores these deficiencies: patients who clear illness typically have greater vitamin D levels than those with prolonged infection, and serum B levels climb significantly after cure (SMD = +1.85). As a result, micronutrient supplementation has been investigated as a supplement. Vitamin C supplementation increased eradication success in one trial. Adding antioxidant vitamins (C, E, and D) to standard treatment results in a little but substantial improvement in cure rates (risk ratio ~1.22), according to another meta-analysis. It has been observed that successful eradication is associated with higher serum vitamin D levels, while treatment failure is associated with low vitamin D levels. Many specialists advise making sure that patients receive enough vitamin C and D while undergoing treatment because of this data. In conclusion, micronutrients are impacted by H. pylori and can have an impact on treatment; deficiencies worsen stomach damage, whereas their restoration (by diet or supplements) promotes the healing of the stomach mucosa and may enhance eradication results.

6. Emerging theerapies and future direction

New therapeutic strategies are being researched in light of the problems caused by antibiotic resistance. Although a safe and effective human vaccination is still a ways off, experimental vaccines against H. pylori (using CagA, VacA antigens, or whole-cell lysates with mucosal adjuvants) have demonstrated encouraging immune responses in animal models. In certain situations, new antibiotics are being used: salvage therapy can overcome multi-drug resistance with regimens based on rifabutin and furazolidone. Following eradication therapy, probiotics and even fecal microbiota transplantation (FMT) are being investigated as ways to reestablish a healthy microbiome.

Phage therapy is an innovative non-antibiotic strategy that targets H. pylori with bacteriophages, which are viruses that infect bacteria. Certain phages have been shown in recent preclinical research to dramatically lower H. pylori colonization in animal models. Although delivery to the stomach niche is technically challenging, phage treatment may completely circumvent antibiotic resistance. Peptide-based treatments and treatments that alter stomach acid in other ways (such as vonoprazan, which is now accessible in some areas as a strong acid blocker) are examples of additional advancements. Oral vaccinations using bioengineered probiotic strains that express H. pylori antigens are also being investigated. In the future, endoscopic image processing and artificial intelligence (AI) could enhance noninvasive diagnosis.

In conclusion, future research will focus on novel and individualized therapies, ranging from immunotherapy and gut microbiome modification to next-generation antibiotics. These strategies need a lot of clinical testing, despite their promise. For present, the most feasible approach to maximize recovery is to combine probiotic and nutritional supplements with optimal antibiotic regimes. The next generation of treatments and preventative measures will be guided by ongoing research into the pathophysiology, host interactions, and resistance mechanisms of H. pylori.

7. Conclusion

A common stomach pathogen with significant clinical and nutritional ramifications is *Helicobacter pylori*. Accurate diagnosis, adequate antibiotic therapy (including resistance), and consideration of dietary variables are all integrated into a holistic management strategy. Probiotics, micronutrients, and foods high in antioxidants are dietary and supplement therapies that can aid in stomach healing and eradication. Although they are not yet common, emerging therapies (new medications, vaccines, and phages) have promise. In the future, treating H. pylori as a disorder impacted by host food and micronutrition in addition to a bacterial illness may enhance patient results. Healthcare professionals can get

closer to the objective of completely controlling this infection and its aftereffects by combining the finest antibiotic treatment with focused nutritional assistance.

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