World of Science: Journal on Modern Research Methodologies

Volume 2 Issue 7, Year 2023
ISSN: 2835-3072
https://univerpubl.com/index.php/woscience

Helicobacter Pylori

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Article Information

Received: May 29, 2023

Accepted: June 30, 2023

Published: July 31, 2023

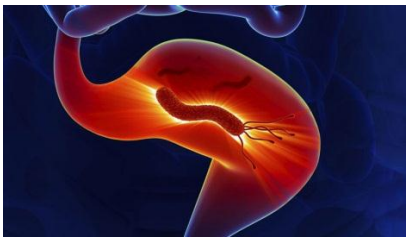
Keywords: *Helicobacter Pylori.*

ABSTRACT

Helicobacter pylori (H.pylori) are a short, helical, S-shaped, Gram negative microorganism. It is mostly found in the pyloric region of the stomach and causes chronic gastric infection. It is estimated that these bacteria infect more than half of the world's population. The mode of transmission and infection of H.pylori is still not known exactly, but the fecal–oral and oral–oral routes via water or food consumption are thought to be a very common cause.

In the last three decades, research interest has increased regarding the pathogenicity, microbial activity, genetic predisposition, and clinical treatments to understand the severity of gastric atrophy and gastric cancer caused by H.pylori.

Studies have suggested a relationship between H.pylori infection and mal absorption of essential micronutrients, and noted that H.pylori infection may affect the prevalence of malnutrition in some risk groups. On the other hand, dietary factors may play a considerably important role in H.pylori infection, and it has been reported that an adequate and balanced diet, especially high fruit and vegetable consumption and low processed salty food consumption, has a protective effect against the outcomes of H.pylori infection. The present review provides an overview of all aspects of H.pylori infection, such as clinical features, treatment, and nutrition. (Fig. 1).



(Fig. 1) WWW.Gmcdhcc.com

1- Introduction

H. pylori was first identified in the stomach of dogs as a spiral microorganism by Giulio Bizzozero in 1892 [1]. As they are Campylobacter-like spiral microorganisms, they were named Campylobacter pyloridis by Barry Marshall and Robin Warren in 1983 [2]. Goodwin et al. named it "*Helicobacter pylori*" in 1989, as it has a helical structure and is mostly found in the pyloric region of the stomach [3].

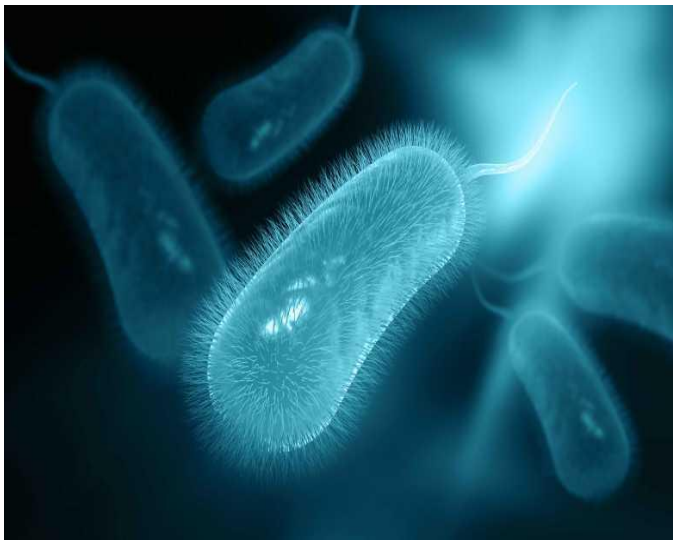
H. pylori is a 0.5–1 µm wide, 2–4 µm long, short helical, S-shaped Gram-negative microorganism and infects more than half of the world's population [4]. The relationship between *H.pylori* and gastric cancer was investigated in 1991 and

1994, and the International Agency for Research on Cancer, a branch of the World Health Organization, reported that *H.pylori* is carcinogenic in humans, which was reconfirmed in 2009 on the basis of epidemiological data [5,6].

In the United States, the National Institute of Health reported in 1994 that *H.pylori* may be the primary cause of peptic ulcer disease and should be treated. Marshall and Warren were awarded the Nobel Prize in 2005 for their work on *H.pylori* in the field of physiology "for discovering the role of *H.pylori* bacteria in gastritis and peptic ulcer disease" [7]. *H.pylori* plays a role in the development of diseases such as gastritis and mucosa-associated lymphoid tissue lymphoma, as well as peptic ulcer and gastric cancer [8].

The mode of transmission of *H.pylori* is not known exactly, but the fecal oral or oral–oral routes via water or food consumption are thought to be a very common cause [9]. The frequency of *H.pylori* infection increases with age. The rate of development is higher in societies with low socioeconomic status [10]. The fact that *H.pylori* survives in the stomach and creates chronic inflammation shows that it can be resistant to both the immune response and acid [11].

Many antibiotic treatments are used for the treatment of *H.pylori*, and studies show that the number of strains resistant to antibiotics used for treatment is increasing rapidly [12,13], which has led to the search for alternative agents to create safer and more effective results in addition to antibiotic treatments [14]. It is thought that dietary factors may play a considerably important role in *H.pylori* infection, and it has been reported that an adequate and balanced diet, especially high and abundant fruit and vegetable consumption, has a protective effect against the outcomes of *H.pylori* infection [15]. However, some studies have suggested a relationship between *H.pylori* infection and mal absorption of essential micronutrients(Fig. 2), and it may cause malnutrition in some groups in the long term [16].



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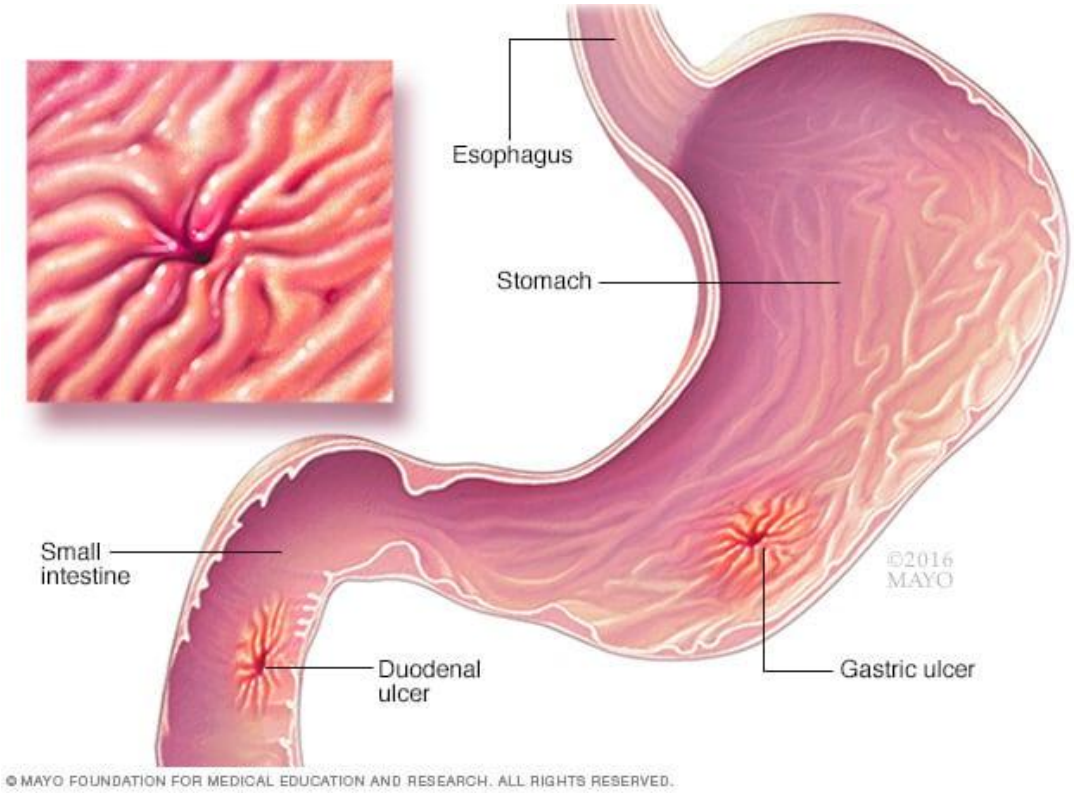
1-2. Pathogenesis

These bacteria is easily killed in hydrochloric acid solutions with a pH below 4. It is quite paradoxical for a microorganism whose primary site is the stomach. *H.pylori* continues to live in the lower part of the stomach by penetrating the mucus layer of the stomach through the contribution of its spiral shape and flagella [17].

To neutralize the acidic pH-related bactericidal activity against *H.pylori*, which can colonize the gastric epithelial surface, *H.pylori* hydrolyses urea to ammonia and carbon dioxide with the urease enzyme it produces [6]. In addition to its toxic effects on gastric mucosal epithelial cells, the ammonia formed increases the mucosal pH [18]. By damaging the protective mucus layer, which is rich in phospholipid and lipase, with the bacterial protease enzyme, it also delays the diffusion ability of H ions and increases its damaging effect [19].

It is known that *H.pylori* secretes a vacuole-forming cytotoxin (VacA) that adheres to the surface epithelium with adhesion proteins and causes vacuolization. The vacuole forming cytotoxin induces host cell death through pore formation and apoptosis in mitochondrial membranes [20]. In addition to VacA, cytotoxin-associated antigen (CagA), known as an oncoprotein, is delivered into gastric epithelial cells and disrupts vesicular trafficking and autophagy pathways. Various studies have shown that cytotoxin-associated antigens affect the cell shape of bacterial proteins, disrupt cell assembly activity, increase cell motility, and are responsible for gastric ulcers and cancers [21–22].

Lipopolysaccharide (LPS), found in the outer membrane of *H.pylori*, is an effective immunomodulator in the human body and causes chronic inflammation by triggering the immune system. LPSs of *H.pylori* can mimic Lewis blood group antigens and, during infection, LPS can produce pathogenic anti-Lewis antibodies [23]. Lewis blood group antigens in the glycoprotein structure found on gastric epithelial surfaces mediate the binding of BabA, known as an adhesion, which binds to blood group antigens on the outer membrane of *H.pylori*, to surface mucosal cells and the gastric pit, (Fig. 3) and causes tissue destruction [24].



(Fig. 3) WWW. Mayo Clinic. Com

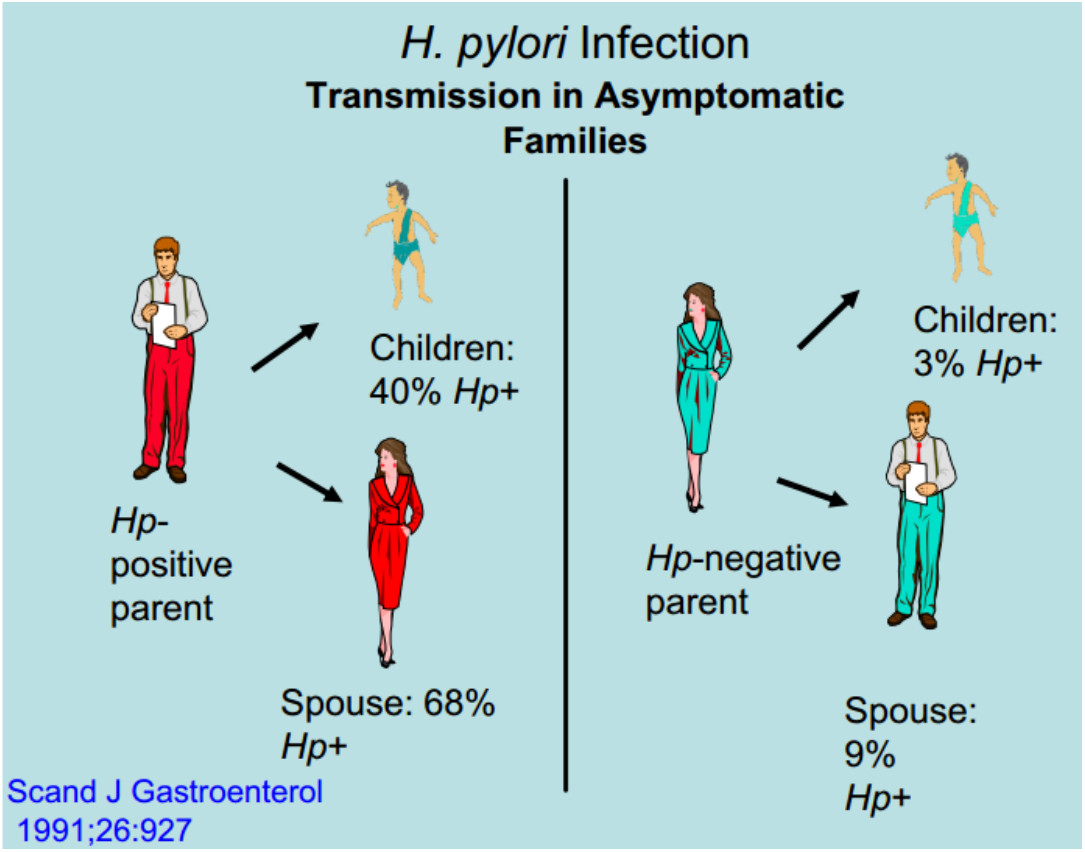
1-3. Transmission

The mode of transmission of *H.pylori* is not known exactly, but it is thought that it can be transmitted directly from one person to another or indirectly from the environment to people [25]. Person-to-person transmission is thought to be the primary mode of transmission, especially in developed countries.

Food- and waterborne transmission are more likely in developing countries and the bacteria spreads more rapidly in areas with poor hygienic conditions [26,27]. In a study evaluating the prevalence of *H.pylori* infection in the rural community, Goodman et al. reported that people who are consumers of raw vegetables are more likely to be infected. Moreover, swimming in streams and rivers and using streams as drinking water may increase infection because of contamination by irrigation water or unpurified water [28].

Although some studies suggested that the transmission of *H.pylori* is from environmental contamination to food products, there is insufficient evidence to confirm this information [26,29]. It is accepted that interpersonal transmission routes are more frequent than environmental exposures. However, special attention should be paid to the sources of contamination (unhygienic water) that may lead to contamination through food [25].

Person-to-person transmission is thought to occur through the oral–oral, faecal–oral, gastric–oral, (Fig. 4) or sexual routes [25]. The literature indicates that H. pylori is present in the dental plaque and saliva of infected individuals [30,31], which shows that H. pylori infection spreads at a much higher rate than expected and, especially, transmission between family members is very frequent [32].



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1-4. Diagnosis

Histological diagnostic tests which is using gastric biopsy specimens include rapid urease testing, culture, and polymerase chain reaction (PCR) [33]. Where invasive methods are time-

consuming and not cost-effective, non-invasive diagnostic methods are used. Non-invasive tests include serological evaluation, stool antigen analyses, and the commonly used urea breath tests [34].

Each of the diagnostic tests used to detect the presence of H. pylori has advantages, disadvantages, and limitations, and the necessity of endoscopy is taken into account when classifying the methods. Also neither is the gold standard due to poor sensitivity or specificity. Combinations of more than one test give more reliable results [35].

1-5. Treatment

The treatment is carried out with a combination of antimicrobial agents and anti-secretory agents, and gastric pH must be increased with anti-secretory agents to achieve the bactericidal effect of antimicrobial agents. Alternatively, herbal medicines and probiotics are used as complementary therapy to help eradicate *H.pylori*, although their mechanism of action is not yet clear [36]. The increasing prevalence of antimicrobial resistance in *H.pylori* from person to person has led to the failure of eradication therapy with decreased compliance with clinical nutrition therapies [37].

In the treatment of H. pylori, drug resistance can easily develop against antibiotics used alone, so the recommended treatment is a combination of several antibiotics [34].

According to several international guidelines, first-line therapy for the treatment of *H.pylori* infection is a triple therapy consisting of a clarithromycin antibiotic given for 7–14 days, using any antibiotic from amoxicillin or metronidazole, and a PPI or ranitidine bismuth citrate [38,39]. Many antimicrobial agents, anti-secretory agents, and proton pump inhibitors are used in the *H.pylori* treatment protocol, including clarithromycin, amoxicillin, levofloxacin, metronidazole, tetracycline, rifabutin, and bismuth-containing compounds [36,40].

If the treatment is not successful, second-line treatment is started. This treatment is carried out according to individual antibiotic resistance and sensitivities, or experimentally [39]. Second-line therapy is usually designated as tetracycline, metronidazole, a bismuth salt, or PPI.

After failure of the second-line treatment, antimicrobial susceptibility test should be performed on the *H.pylori* culture from which the gastric biopsy was taken, and local resistance to

antibiotics should be taken into account and treatment should be continued [41].

It has also been stated that PPIs, which have been used for a long time in the treatment of *H.pylori* infection, may prevent the absorption of micronutrients as well as their benefits [42]. The United States Food and Drug Administration has suggested that long-term use of PPIs may cause an increased risk of hypomagnesemia and fractures [43].

Table 2. Currently recommended eradication regimens

Eradication therapy	Components	Notes
PPI-based triple therapy	• Esomeprazole 20 mg twice daily, OR omeprazole 20 mg twice daily • Amoxicillin 1 g twice daily • Clarithromycin 500 mg twice daily[9]	• First-line recommendation in Australian guidelines[9] • Drugs prescribed in a 7-day course • Combination prescriptions include Nexium Hp7 and Probitor Hp7
Quadruple therapy	• Omeprazole 20 mg once daily • Bismuth subsalicylate 120 mg four times daily • Metronidazole 400 mg three times daily • Tetracycline 500 mg four times daily[9]	• Uncommonly used • Prescribed as a 7- or 14-day course • First-line choice under ACG guidelines for areas with known clarithromycin resistance

ACG, American College of Gastroenterology

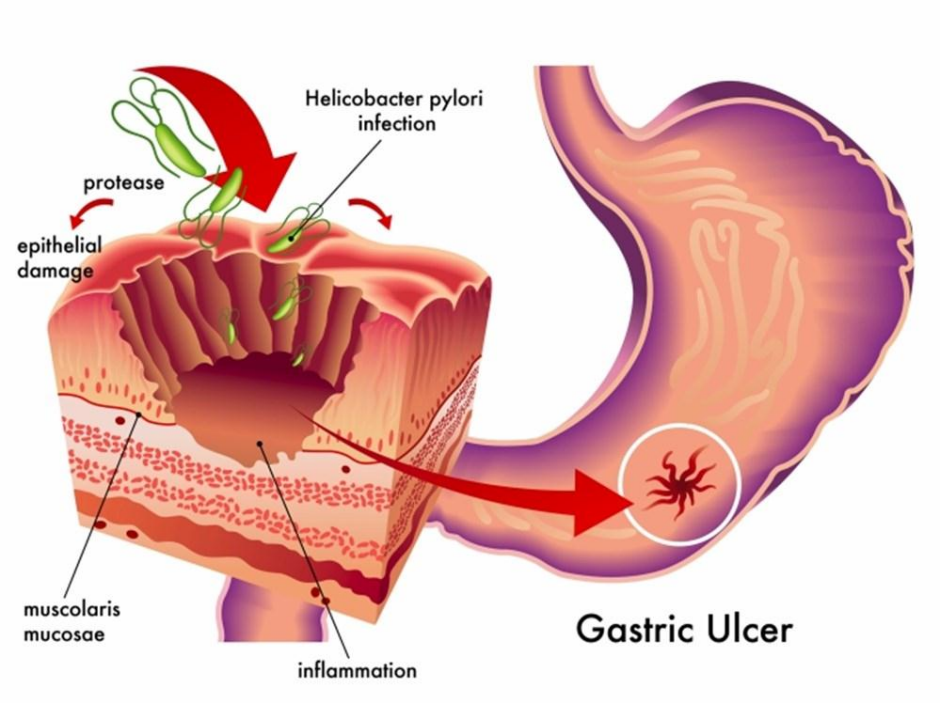
1-6. Epidemiology

Many studies on the prevalence of *H.pylori*, and its risk factors and pathways are found. It is claimed that half of the world's population is infected with *H.pylori*, but it is clear that more evidence-based research is still needed.

The incidence of this infection is higher in low socioeconomic status groups and developing countries [44]. Vilaichone *et al*. found that the prevalence of *H.pylori* varies not only from country to country but also in different regions of the same country [45]. Its prevalence is significantly difficult to determine, as no health system compiles registry-based results of the prevalence of *H.pylori* in developing countries [46].

According to the regional prevalence estimates, there are approximately 4.4 billion *H.pylori*-infected people worldwide [47]. In the study of Mezmale et al. (2020), a high prevalence of *H.pylori* infection was determined in Russia, Jordan, Iran, China, Canada, and Latin American countries [48]. Studies conducted in Turkey show that the rate of *H.pylori* infection is high. (Fig.5)

The prevalence of H. pylori infection is similar in males and females, and the incidence of H. pylori infection is 73.2% between the ages of 14 and 30, 71.5% between the ages of 31 and 45, 68.6% between the ages of 46 and 60, and 70.4% between the ages of 61 and 88 [49].



(Fig.5) **(Fig. 4) WWW. Sogati. Com**

1-7. Complications

The infection with *H.pylori* sometimes leads to many complications that may includes:

- ✓ **Chronic Gastritis**
- ✓ **Stomach Cancer**
- ✓ **Peptic Ulcers**
- ✓ **Anemia**
- ✓ **Insulin Resistance**

Fig. WWW.Alto nivel.Com

1-8. Conclusions

1. *H.pylori* is estimated to infect half of the world's population and causes permanent infections as well as many health issues such as gastritis and MALT lymphoma, as well as peptic ulcer and gastric cancer.
2. In *H.pylori* infection, there are some treatment limitations due to its ability to create resistance to antibiotic treatments in treatment strategies. Therefore, it has become necessary to seek alternatives to fight against *H.pylori* infection.
3. Combination treatments, including with phytochemicals and probiotics found in natural products, seem to have beneficial effects in the eradication of *H.pylori*.
4. Information should be provided during and after treatment. It is important to provide optimal nutrition through the determination of strategies and the application of a suitable diet for the person by authorised dietitians.
5. Besides, there have been some promising effects for probiotics added to treatment strategies; however, detailed research is needed.
6. Most importantly, a diet rich in fruits and vegetables and reduced in salt and processed meat products has good prophylactic potential, especially against cancer in the eradication of *H.pylori*.

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