



Research Article

Public Health Perspectives of Zoonotic Potential of *H. pylori*

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Abstract | *Helicobacter pylori* is a gram-negative, microaerophilic bacterium that colonizes the human gastric mucosa, leading to various gastrointestinal diseases, including chronic gastritis, peptic ulcer disease, and gastric cancer. *H. pylori* infect over 50% of the population worldwide, with particularly high prevalence rates in developing countries due to poor sanitation and limited access to healthcare. Hence, it is considered a major global health concern, while many individuals remain asymptomatic, persistent infection can lead to severe pathologies. The bacterium's ability to survive the harsh acidic environment of the stomach is facilitated by its urease activity, which neutralizes gastric acid, and its motility, which allows it to penetrate the mucus layer. Virulence factors, such as the cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA), play a critical role in the pathogenicity of *H. pylori*, promoting cellular damage and immune evasion. Transmission occurs predominantly through fecal-oral and oral-oral routes, but growing evidence suggests a potential animal source of transmission, complicating the epidemiology of the infection and its control. Clinically, *H. pylori* infection presents with a range of symptoms, from asymptomatic colonization to severe conditions like peptic ulcers and gastric cancer. Diagnostic methods include non-invasive techniques, such as urea breath tests and stool antigen tests, while endoscopy is typically reserved for more severe cases. Prevention primarily revolves around improved sanitation and hygiene practices, while treatment typically involves a combination of antibiotics and proton pump inhibitors. However, the increasing incidence of antibiotic resistance poses significant challenges to eradication efforts, highlighting the need for novel therapeutic strategies and the development of a vaccine.

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Introduction

Helicobacter pylori (*H. pylori*) is a gram-negative, spiral-shaped bacterium that colonizes the

human stomach, often persisting throughout life if left untreated. It was first identified in 1983 by Marshall and Warren, it remains one of the most prevalent bacterial pathogens globally, contributing

to various gastrointestinal diseases, including chronic gastritis, peptic ulcer disease (PUD), gastric cancer, and mucosa-associated lymphoid tissue (MALT) lymphoma (Marshall and Warren, 1984; Powers-Fletcher and Couturier, 2015). It is classified as a Group I carcinogen by the International Agency for Research on Cancer (IARC), which underscores its significant public health importance (IARC, 2014).

H. pylori infections are predominantly acquired in childhood and show significant geographic variation in prevalence (Smith *et al.*, 2022). Infections are found in over 50% of the global population, with rates exceeding 80% in some developing regions due to poor sanitation, inadequate healthcare, and limited access to clean water (Hooi *et al.*, 2017).

Risk factors to *H. pylori* infection, includes socioeconomic status, overcrowding, consumption of contaminated food or water, and close contact with infected individuals or animals (Hooi *et al.*, 2017). The primary modes of transmission include fecal-oral, oral-oral, and gastro-oral routes, with studies suggesting that environmental sources like contaminated water and unwashed vegetables also play a role (Stefano *et al.*, 2018; Zamani *et al.*, 2017).

Recent studies highlight the zoonotic potential of *H. pylori*, with domestic animals such as dogs, cats, and livestock implicated as reservoirs. Close human-animal interactions, particularly in rural and agricultural settings, may facilitate transmission (Shaaban *et al.*, 2023; Momtaz *et al.*, 2014). Also, *H. pylori* strains have been detected in milk, meat, and other animal-derived products, further supporting its zoonotic risk (Elhelw *et al.*, 2020).

Although many individuals with *H. pylori* remain asymptomatic, its infection can lead to severe complications, including chronic gastritis, PUD, and gastric cancer, one of the leading causes of cancer-related deaths worldwide (Kusters *et al.*, 2006). Beyond the gastrointestinal tract, *H. pylori* has been linked to extra-gastric conditions such as iron deficiency anemia and idiopathic thrombocytopenic purpura (Kusters *et al.*, 2006).

Effective management of *H. pylori* requires early detection and treatment. Standard therapy involves a combination of antibiotics and proton pump inhibitors (PPIs), though rising antibiotic resistance

complicates eradication efforts. Public health interventions focused on improving sanitation, surveillance of animal reservoirs, and vaccine development are essential to mitigate the burden of *H. pylori* infection globally (Chey *et al.*, 2017; Shaaban *et al.*, 2023).

This review examines the prevalence, risk factors, zoonotic potential, transmission modes, and public health implications of *H. pylori* infection, with an emphasis on strategies for prevention and management. By highlighting the interconnected nature of human, animal, and environmental health, it underscores the importance of a comprehensive approach to controlling this pathogen.

Epidemiology

Global prevalence of H. pylori

Helicobacter pylori is among the most prevalent bacterial pathogens worldwide, infecting over 50% of the global population. Its prevalence varies significantly across regions due to differences in socioeconomic conditions, healthcare infrastructure, and public health initiatives. A systematic review and meta-analysis by Hooi *et al.* (2017) estimated the global prevalence at 44.3%, with considerable variation across continents. For example, Africa reported the highest prevalence (70.1%), while Oceania had the lowest (24.4%). These disparities highlight the influence of environmental and lifestyle factors on *H. pylori* infection rates (Hooi *et al.*, 2017).

The global prevalence of *Helicobacter pylori* infection is highly variable across different regions and countries. A systematic review and meta-analysis from 2017 found that approximately 4.4 billion individuals worldwide were infected with *H. pylori* in 2015. The prevalence rates are particularly high in regions like Africa and low in Oceania, with substantial variation within continents based on socioeconomic factors, sanitation, and healthcare access.

In Africa, the prevalence of *H. pylori* infection is notably high, reporting an overall pooled prevalence of 70.1%. Several African countries exhibit alarming infection rates, such as Nigeria, where the prevalence reaches 87.7%. This high prevalence is attributed to lower socioeconomic conditions, poor sanitation, and limited access to healthcare. In many parts of Africa, overcrowded living conditions and contaminated

water sources facilitate the transmission of *H. pylori*, facilitating its spread. Additionally, the limited availability of effective treatments contributes to the persistence of the infection in the population (Hooi *et al.*, 2017).

Conversely, in developed continents like Europe, the prevalence of *H. pylori* varies considerably between countries. In countries such as Switzerland, the infection rate is relatively low at 18.9%, and moderately high in Germany, with prevalence of 20–40% owing to better sanitation systems, advanced healthcare infrastructure, and effective public health measures. However, prevalence rate in North America 23.1% (Naja *et al.*, 2007) and Australia 24.6% (Hooi *et al.*, 2017) are low. While Asia with prevalence (48.8%) approaching those seen in parts of Africa (Nguyen *et al.*, 2017; Venneman *et al.*, 2018). The possible causes of discrepancies in the prevalence rate across continents have been reported to be due to urbanization with better access to health facilities and portable water (Smith *et al.*, 2019), host genetic makeup, age and gender, immune response of the host, pathogenicity of the *H. pylori* strains, and environmental factors (Ofori *et al.*, 2019). Additionally, Oceania had the lowest *H. pylori* prevalence, rate of 24.4%. Countries like Australia and New Zealand have low infection rates, primarily due to high standards of living, comprehensive sanitation systems, and widespread access to healthcare. These factors reduce the transmission of *H. pylori*, contributing to the lower infection rates in the region. The disparities between Oceania and other regions highlight the significant role that public health infrastructure and sanitation play in controlling the infection (Hooi *et al.*, 2017).

Several factors contribute to these spread of geographic differences in *H. pylori* prevalence. Socioeconomic status plays a major role, as regions with lower income levels often struggle with overcrowded living conditions, limited access to clean water, and inadequate sanitation, all of which promote the spread of the infection. Additionally, access to healthcare is a crucial factor, countries with better healthcare systems can more effectively diagnose and treat *H. pylori*, leading to lower prevalence rates. In contrast, regions with limited healthcare access face challenges in providing necessary treatments, contributing to the persistence of the infection. Hygiene and sanitation also play a vital role, with poor sanitation being a

key factor in higher infection rates, particularly in developing countries (Smith *et al.*, 2019, 2022; Hooi *et al.*, 2017).

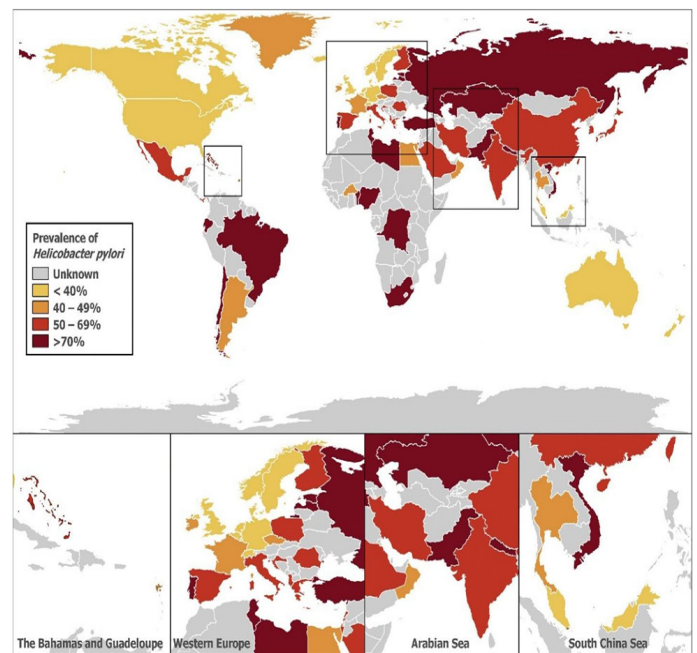


Figure 1: Global prevalence of HP choropleth map (Hooi *et al.*, 2017).

Regional prevalence

Helicobacter pylori infection is endemic across Africa, with prevalence rates far exceeding the global average of 44.3% (Smith *et al.*, 2022). The high prevalence is largely attributed to socioeconomic disparities, poor sanitation, and limited access to healthcare services, which exacerbate transmission risks. This regional burden is due to inadequate public health infrastructure and a lack of awareness about the pathogen and its complications.

In West Africa, the prevalence of *Helicobacter pylori* (*H. pylori*) infection varies significantly across regions. In Nigeria, rates range from 52% to as high as 87.7%, with notable regional and demographic differences. For instance, in Keffi, Northern Nigeria, 56.3% of the population tested positive, with variations linked to gender and the type of infection (symptomatic vs. asymptomatic) (Ishaleku and Ihiabe, 2010; Oti *et al.*, 2017). In Delta State, located in the South-South region, the prevalence is 52%, and risk factors such as alcohol consumption and smoking are highlighted as contributing factors (Omosor *et al.*, 2017). The South-West region of Nigeria exhibits one of the highest rates, with 80% prevalence among patients diagnosed with duodenal ulcers, underscoring the strong link between infection and gastrointestinal

pathology (Ajayi *et al.*, 2021). Similarly, in Ghana, infection rates reported was 14.2% among children in rural areas. This was attributed to lack of pipe and borehole drinking water. All of the positive *H. pylori* children practiced open-air defecation in rural areas (Awuku *et al.*, 2017). Togo (70.41%), The Republic of Benin reported a prevalence of 71.5%, with no significant associations between infection rates and variables such as age, sex, marital status, or education (Lawson-Ananissah *et al.*, 2015; Smith *et al.*, 2022).

In Central Africa, *H. pylori* prevalence is also alarmingly high from reported the acquisition of *H. pylori* by Baka pygmies of Cameroon through secondary contact with their non-Baka agriculturist neighbours (Nell *et al.*, 2013). The prevalence rate of *H. pylori* infection amongst asymptomatic patients from Harare, Zimbabwe was 67.7% (Mungazi *et al.*, 2018).

East Africa also experiences significant rates of *H. pylori* infection. In Rwanda, the prevalence is 75%, with a clear association to peptic ulcer disease and gastric malignancies. Studies from Ethiopia show infection rates reaching 88.9% in males and 82.8% in females, indicating slight gender variation (Asfaw, 2018). The primary risk factors in this region include overcrowding, unsanitary living conditions, and the widespread use of untreated water for domestic purposes (Smith *et al.*, 2022).

North Africa presents high prevalence rates as well, with Egypt reporting 66.12% among children. The contributing factors include a high population density, poor hygiene practices, and a reliance on street food vendors. Morocco (63.8%) is high due to low socioeconomic status, inadequate health care access and access to potable water (Sokpon *et al.*, 2016).

In Rwanda, Southern Africa, reported 75% positivity rate to *H. pylori* in patients attending the University Hospital Butare over a period of 12 months, which was found to be similar to the prevalence of other sub-Saharan African countries (Walker *et al.*, 2014). A study on genomic evolution *H. pylori* in two South African families revealed that transmission episodes were significantly more frequent between individuals living in the same house and close relatives, however transmission did not always occur within families (Didelot *et al.*, 2013).

Nigeria stands out as a hotspot for *H. pylori* infection, with prevalence rates exceeding 80% in some regions, such as the South-West among duodenal ulcer patients (Ajayi *et al.*, 2021). Variability exists across the country due to differences in environmental factors and healthcare access. For instance, in the South-South region, Delta State records a prevalence of 52%, with smoking and alcohol consumption identified as major risk factors (Omosor *et al.*, 2017).

In Northern Nigeria, studies in Keffi show a prevalence of 56.3%, with infections linked to demographic variables like gender and symptomatic status (Ishaleku and Ihiabe, 2010). Similarly, research in the South-East reports high prevalence rates, emphasizing the need for improved healthcare and diagnostic infrastructure (Smith *et al.*, 2022).

Despite these high prevalence rates, the clinical manifestations of *H. pylori* infection in Nigeria are often less severe than in other regions. Gastric erosion remains the most common pathology observed in dyspeptic patients (Smith *et al.*, 2022). Addressing the burden of *H. pylori* in Nigeria requires improved public health strategies, including better sanitation, access to healthcare, and education on prevention and treatment.

Helicobacter pylori: Microbiology and growth conditions

Helicobacter pylori is a microaerophilic, spiral-shaped, non-sporulating, gram-negative bacterium that predominantly resides in the human stomach, specifically the antrum. Its dimensions are approximately 0.5 µm in width and 2.5 µm in length. *H. pylori* is motile, possessing two to six flagella that enable it to navigate the gastric mucosa and withstand the mechanical contractions of the stomach (Nwachukwu *et al.*, 2020). These flagella contribute significantly to the bacterium's ability to penetrate the gastric lining. Additionally, *H. pylori* produce the enzyme urease, which plays a crucial role in neutralizing the acidic environment of the stomach (Figure 1), thus ensuring its survival in such a hostile environment (Praszkier *et al.*, 2016).

Cultivation of *H. pylori* requires specific media supplemented with horse or sheep blood and antibiotics. The bacterium thrives under conditions of 5–15% oxygen and 5% CO₂ at temperatures ranging from 30°C to 37°C, which are typical for the gastrointestinal tract of warm-blooded animals. On

solid media, growth is typically observed after two to five days, and colonies are described as small, round, and translucent (Shaaban *et al.*, 2023; Ríos-Sandoval *et al.*, 2024).

The bacterium exhibits significant genomic variability, with a genome size of approximately 1.6 to 1.7 megabase pairs. Notably, it contains “plasticity zones” harboring strain-specific genes that are linked to antibiotic resistance (e.g., clarithromycin, metronidazole) and virulence. These genetic features enable *H. pylori* to evade immune responses and resist antibiotic treatments, complicating eradication efforts (Alm and Trust, 1999; Wroblewski *et al.*, 2010).

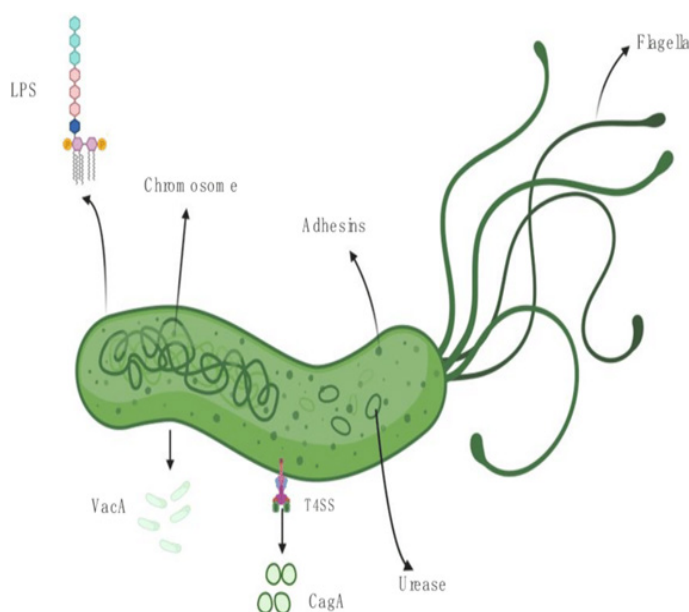


Figure 2: Insights of *H. pylori* structure and virulence factors (Sășăran *et al.*, 2021).

Pathogenesis of *Helicobacter pylori*

Virulence factors of *Helicobacter pylori*: The pathogenesis of *H. pylori* involves several mechanisms by which the bacterium interacts with host cells and induces disease. Upon attachment to gastric epithelial cells, *H. pylori* inject CagA, a protein encoded within the cag pathogenicity island (PAI), into the host cells through a type IV secretion system. Once inside, CagA undergoes phosphorylation and disrupts signaling pathways, leading to increased cell proliferation, inflammation, and disruption of tight junctions, which are all implicated in the development of gastric adenocarcinoma (Hatakeyama, 2014). Additionally, the VacA toxin, secreted by *H. pylori*, induces vacuolation in epithelial cells, impairs T-cell activation, and promotes tissue damage and ulcer formation (Ghazanfar *et al.*, 2024).

Furthermore, *H. pylori* is capable of forming biofilms, which are structured bacterial communities embedded in an extracellular matrix. Biofilms protect the bacteria from host immune responses and antibiotics, contributing to its resistance and complicating treatment strategies (Yonezawa *et al.*, 2015; Elshenawi *et al.*, 2023).

Survival in the gastric environment

H. pylori has evolved several mechanisms that allow it to survive in the highly acidic environment of the stomach. The bacterium's spiral shape and flagella are essential for motility through the mucus layer to reach a less acidic environment near the gastric epithelium. The flagella allow the bacterium to move through the mucus, while its spiral shape facilitates penetration and adherence to the gastric epithelial cells (Cover and Blaser, 2009). Moreover, *H. pylori* produce urease, an enzyme that hydrolyzes urea into ammonia and carbon dioxide. This process neutralizes the gastric acid locally, raising the pH around the bacterium, which is critical for its survival. However, this process also contributes to epithelial damage and inflammation, fostering a conducive environment for the infection (Fagoonee and Pellicano, 2019).

Adherence to gastric epithelial cells

Adherence to the gastric epithelium is a key step in *H. pylori* pathogenesis, and the bacterium employs several mechanisms to facilitate this process. Among these, lipopolysaccharides (LPS), vacuolating cytotoxin (VacA), cytotoxin-associated gene A (CagA), outer membrane proteins (OMPs), and adhesins such as blood group antigen-binding adhesion (BabA2) and sialic acid-binding adhesin (SabA) play pivotal roles in its attachment to gastric epithelial cells. These components enable *H. pylori* to induce a chronic inflammatory response and establish a long-term infection (Yonezawa *et al.*, 2015). BabA binds to Lewis b antigens on epithelial cells, while SabA interacts with sialylated structures expressed during inflammation, ensuring the bacterium's close contact with the host cells and facilitating the delivery of virulence factors (Hage *et al.*, 2015). CagA and VacA are particularly critical in the pathogenicity of *H. pylori*, with CagA being instrumental in cellular disruption and VacA in promoting tissue damage (Mohamed and El-Gohari, 2012; Ríos-Sandoval *et al.*, 2024).

Virulence factor-mediated pathogenesis

H. pylori harbor several virulence factors that mediate its pathogenicity. The *cag* pathogenicity island (CagPAI) encodes a type IV secretion system that facilitates the injection of CagA into host cells. Once inside, CagA interacts with cellular signaling proteins like SHP-2, leading to cytoskeletal rearrangements, loss of cell polarity, and increased epithelial permeability, all of which contribute to inflammation and oncogenesis (Mustapha *et al.*, 2014; Hanada *et al.*, 2014). The VacA toxin also plays a critical role in pathogenesis by forming pores in host cell membranes, inducing vacuole formation, disrupting mitochondrial function, and promoting apoptosis in both epithelial and immune cells. Furthermore, VacA impairs antigen presentation and T-cell activation, which helps *H. pylori* evade the host immune response (Sgouras *et al.*, 2015).

The outer membrane proteins (OMPs) and lipopolysaccharides (LPS) of *H. pylori* contribute to immune evasion. OMPs such as HopQ facilitate bacterial adherence to host cells, while LPS molecules mimic host antigens, reducing immune recognition and aiding in immune tolerance (Sgouras *et al.*, 2015).

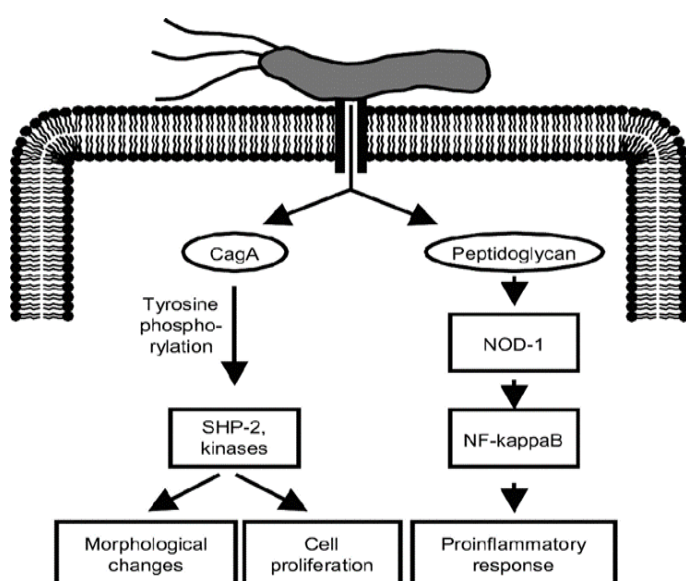


Figure 3: Schematic representation of the different roles of the *Cag* type IV secretion system in immune modulation, cell proliferation, and morphological changes (Kusters *et al.*, 2006).

Immunological aspects of *H. pylori* infection

H. pylori infection triggers both innate and adaptive immune responses, which play crucial roles in the host's defense and the bacterium's persistence. In the innate immune response, *H. pylori* is recognized

by Toll-like receptors (TLRs) such as TLR2 and TLR4, leading to the activation of NF- κ B and the production of pro-inflammatory cytokines like IL-8. These cytokines recruit neutrophils and macrophages, which release reactive oxygen species (ROS) and proteases, causing tissue damage. However, *H. pylori* has evolved mechanisms to modulate these immune responses to avoid clearance. For example, VacA inhibits phagosome maturation, reducing the bactericidal capacity of macrophages, while modified LPS reduces TLR4-mediated immune activation.

In adaptive immunity, a Th1 response characterized by the production of IFN- γ drives macrophage activation and further inflammation, but it is insufficient to clear the infection due to *H. pylori*'s immune evasion strategies. The Th17 response, marked by IL-17 production, recruit neutrophils and contributes to mucosal damage. Regulatory T cells (Tregs) help suppress excessive inflammation, but they may also facilitate bacterial persistence by dampening effective immune responses. These complex immunological interactions contribute to the chronic nature of *H. pylori* infection and complicate efforts to eradicate it.

Mechanisms of transmission

The main route of transmission of *Helicobacter pylori* (*H. pylori*) remains unproven, though several possible pathways have been suggested. These include direct transmission (human-to-human) and indirect transmission through environmental sources such as water and food. The routes of direct transmission may include the gastro-oral, oral-oral, and fecal-oral pathways, but a predominant transmission mechanism has not been conclusively identified (Stefano *et al.*, 2018).

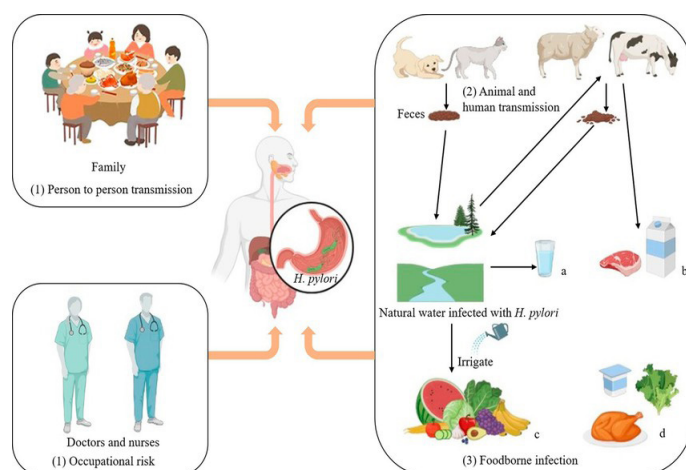


Figure 4: Transmission routes of *H. pylori* (Liu *et al.*, 2024).

Gastro-oral transmission

H. pylori is often acquired in early life, and vomiting of achlorhydric mucus could serve as a vehicle for transmission. The transmission might occur via gastric juice, especially during vomiting in childhood, and could be associated with poor hygienic conditions (Stefano *et al.*, 2018).

Oral-oral transmission

The gastric microbiome can colonize the mouth through regurgitation or vomiting. *H. pylori* has been cultured directly from saliva, and its DNA has frequently been detected in saliva, subgingival biofilm, and dental plaque (Anand *et al.*, 2014; Gebara *et al.*, 2006). As such, the mouth might act as a reservoir for *H. pylori*.

Fecal-oral transmission

H. pylori DNA has been detected in human feces (Smith *et al.*, 2022), but attempts to culture *H. pylori* from feces have been limited due to the bacterium's persistence in a non-culturable, coccoid form (Stefano *et al.*, 2018).

Transmission by water

H. pylori can also spread indirectly via environmental contamination. Hygienic conditions often contribute to household contamination of treated water. People, particularly children, living in poor housing conditions or consuming raw vegetables, are at higher risk of contracting *H. pylori* infections (Mohammed and El-Gohary, 2012). Studies have also shown that raw vegetables can be contaminated by irrigation water, untreated sewage, or unpurified water sources (Zamani *et al.*, 2017). Proper washing of vegetables can help reduce the risk of contamination (Atapoor *et al.*, 2014).

Transmission by food

Food products can become contaminated under poor hygiene conditions during handling. Additionally, infections may be transmitted through food consumed from street vendors (Hasosah *et al.*, 2015), either directly via vendor-to-consumer contact or indirectly via contaminated food sources such as meat, raw milk, and vegetables, which are considered primary sources of infection (Zamani *et al.*, 2017). Food products like milk, meat, and vegetables are particularly studied because the infection is often acquired during childhood, when milk consumption is more prevalent (Anand *et al.*, 2014).

Zoonotic potential of helicobacter pylori

While *H. pylori* is typically considered a human pathogen, recent studies suggest that it or similar organisms could be isolated from several animals, including primates, pigs, and cats. These animals may serve as reservoirs, and human contact with them could explain the widespread prevalence of *H. pylori* infection (El-Gohari *et al.*, 2015).

A study in Egypt found that dogs might be carriers of *H. pylori*, with a prevalence rate of 41.7%. This suggests that dogs could be a source of transmission, particularly in environments with close human-animal contact (Elhelw *et al.*, 2020). Similarly, a study in Nigeria found ulcers in various animal species, with a reported prevalence of 42.2% among companion and exotic animal patients. This indicates that gastrointestinal conditions, including *H. pylori*-related ulcers, may be more widespread in animals than previously recognized (Oyetayo *et al.*, 2021).

In addition, *H. pylori* has been detected in both gastric biopsies and milk samples from cattle, suggesting that cattle may serve as reservoirs. This raises concerns about the risks associated with consuming unpasteurized milk or undercooked beef (El-Gohary *et al.*, 2015). A study in Egypt also revealed that 50% of dogs, cats, cows, and sheep tested positive for *H. pylori*, with dogs and cats showing higher prevalence rates compared to cows and sheep (Shaaban *et al.*, 2023). Dairy products made from unpasteurized milk, such as cheese, cream, and butter, could therefore serve as potential sources of *H. pylori* (Mousavi *et al.*, 2014), highlighting the zoonotic nature of this infection.

Further research on the genetic strains of *H. pylori* has shown that they are present in cows, sheep, goats, and humans. For instance, 21.6% of cows, 13.3% of sheep, and 26.6% of goats tested positive for *H. pylori* (Momtaz *et al.*, 2014). This suggests the possibility of cross-species transmission, with close interactions between humans and these animals increasing the risk. Although *H. pylori* was found in a higher percentage of human samples, the presence of the bacterium in animals further supports the need for awareness regarding potential animal sources of transmission (Shaaban *et al.*, 2023).

The potential zoonotic transmission of *H. pylori* from other animals, such as macaque monkeys, has been

considered, but due to the rarity of human contact with such primates, they are not likely to play a significant role in human infection transmission (Mohammed and El-Gohary, 2012).

Disease manifestations of H. pylori

Colonization by *Helicobacter pylori* (*H. pylori*) is not a disease in itself, but rather a condition that affects the risk of developing various clinical disorders of the upper gastrointestinal tract, and potentially the hepatobiliary tract (Kusters *et al.*, 2006). Testing for *H. pylori* is necessary to identify the cause of an underlying condition, such as peptic ulcer disease, or for disease prevention purposes in individuals with a family history of gastric cancer. In these cases, a positive test result warrants treatment, while a negative result might suggest further investigation for other causes or preventive measures (Kusters *et al.*, 2006).

Acute gastritis

Acute gastritis associated with *H. pylori* infection typically occurs during the early phase of colonization. This can result from direct ingestion of contaminated material or procedures involving such material. During this stage, individuals may experience nonspecific symptoms, including fullness, nausea, and vomiting, alongside inflammation of the stomach lining, also known as pangastritis. In some cases, the infection can cause a reduction in stomach acid production (hypochlorhydria), which may persist for months (Kusters *et al.*, 2006). In children, particularly in developing countries with high exposure to *H. pylori*, the infection may resolve on its own. However, adults are less likely to naturally clear the infection unless conditions like atrophic gastritis develop. Research suggests that certain individuals are more prone to *H. pylori* colonization, while others can prevent or clear the infection (Malaty *et al.*, 1994).

Chronic gastritis

When *H. pylori* infection becomes chronic, the type of gastritis that develops largely depends on the level of acid production in the stomach. In individuals with normal acid production, *H. pylori* primarily colonize the lower part of the stomach (antrum), leading to mild inflammation in that area, while the upper part (corpus) is less affected (Figure 5). If acid production is reduced due to conditions such as stomach cell damage, the use of acid-blocking medications (PPIs), or surgery, the bacteria spread throughout the stomach, causing more widespread inflammation (pangastritis)

(Kuipers *et al.*, 1995). Chronic inflammation can further diminish acid production, but eradicating the bacteria often helps restore normal acid levels. People with genetic predispositions that enhance inflammation are at a higher risk of developing severe gastritis, which can lead to complications like stomach lining damage, intestinal changes, or even cancer. Although *H. pylori* is the most common cause of gastritis, other factors include infections such as cytomegalovirus, autoimmune conditions like Crohn's disease or pernicious anemia, and irritants such as alcohol and nonsteroidal anti-inflammatory drugs (NSAIDs) (Kusters *et al.*, 2006). The persistent inflammation caused by *H. pylori* induces the production of pro-inflammatory cytokines, leading to the infiltration of neutrophils and mononuclear cells, which can cause damage and atrophy of the gastric mucosa (Kusters *et al.*, 2006).

Peptic ulcer disease (PUD)

Peptic ulcer disease occurs due to a combination of bacterial and host factors, leading to defects in the stomach or duodenal lining that penetrate the muscularis mucosa, with a minimum diameter of 0.5 cm (Kusters *et al.*, 2006). Gastric ulcers often form along the lesser curvature of the stomach at the junction between the corpus and antrum, while duodenal ulcers are more commonly found in the duodenal bulb, a region highly exposed to gastric acid. In Western countries, duodenal ulcers are more prevalent than gastric ulcers, but this pattern is reversed in other regions. Gastric ulcers typically develop in individuals over 40 years of age, while duodenal ulcers are more common in those aged 20 to 50 (Kusters *et al.*, 2006).

H. pylori is strongly associated with both gastric and duodenal ulcers. The infection is the primary cause of peptic ulcers, responsible for 95% of duodenal ulcers and 85% of gastric ulcers (Figure 5). Infected individuals face a 3 to 10 times greater lifetime risk of developing ulcers compared to uninfected individuals (Nomura *et al.*, 1994). Eradication therapy has significantly reduced ulcer recurrence, transforming the disease from a chronic condition requiring ongoing maintenance or surgery into one that can largely be cured. However, ulcers may recur due to reinfection, NSAID use, or other unknown factors (Hentschell *et al.*, 1993). Ulcer formation depends on the severity and location of the mucosal inflammation. Decreased acid production often leads

to gastric ulcers at the corpus-antrum junction, while normal or high acid production is linked to duodenal ulcers in the distal stomach or proximal duodenum (Kusters *et al.*, 2006).

The incidence of peptic ulcers has fluctuated over the past 150 years. It rose in the late 19th century and then steadily declined in later generations, likely due to improved hygiene, better living conditions, and a reduced prevalence of *H. pylori*. In Western countries, the introduction of *H. pylori* eradication therapy has further decreased ulcer incidence (Kuipers *et al.*, 1995). However, diagnosing *H. pylori* remains crucial to ensure appropriate treatment, especially in regions with a high prevalence.

Complications of peptic ulcers include bleeding, perforation, and strictures. Bleeding is the most common complication, occurring in 15 to 20% of cases, and accounts for 40% of upper gastrointestinal bleeding episodes. Endoscopic therapy is the primary treatment for bleeding ulcers, followed by acid suppression and *H. pylori* eradication to prevent recurrence. Perforations typically require surgical intervention, while strictures, often caused by recurrent ulcers, may resolve with eradication therapy or require endoscopic dilation or surgery (Gisbert *et al.*, 2004).

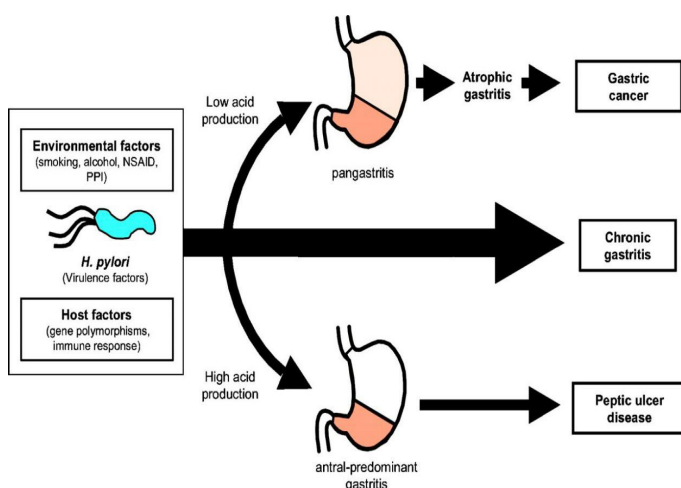


Figure 5: Schematic representation of the factors contributing to gastric pathology and disease outcome in *H. pylori* infection (Kusters *et al.*, 2006).

H. pylori, NSAIDs, and ulcer risk

H. pylori and NSAIDs are the two main causes of gastroduodenal ulcers, and their combined effects increase the risk of ulcer formation. Eradicating *H. pylori* in NSAID users reduces the incidence of ulcers, but does not completely eliminate the risk.

For high-risk patients, additional protective measures, such as proton pump inhibitor (PPI) therapy, are often necessary (Hawkey *et al.*, 1998).

Non-ulcer dyspepsia

Non-ulcer dyspepsia, or functional dyspepsia, refers to upper gastrointestinal symptoms without structural abnormalities. *H. pylori* is present in 30 to 60% of patients with non-ulcer dyspepsia, but its prevalence is similar in individuals without the condition. Eradicating *H. pylori* provides modest symptom relief in some patients and can be cost-effective in certain cases. In populations with low *H. pylori* prevalence, empirical acid-suppressive therapy is typically preferred, while a test-and-treat approach is more suitable in regions with higher *H. pylori* prevalence (Kusters *et al.*, 2006).

Gastric cancer

H. pylori is classified as a carcinogen, strongly associated with the development of gastric adenocarcinoma. Chronic gastritis can progress to atrophic gastritis, intestinal metaplasia, and dysplasia (Figure 6). The presence of CagA-positive strains promotes epithelial-mesenchymal transition (EMT), angiogenesis, and cell proliferation, creating a pro-oncogenic environment. Individuals infected with CagA-positive strains have an elevated risk of developing gastric cancer (Kusters *et al.*, 2006).

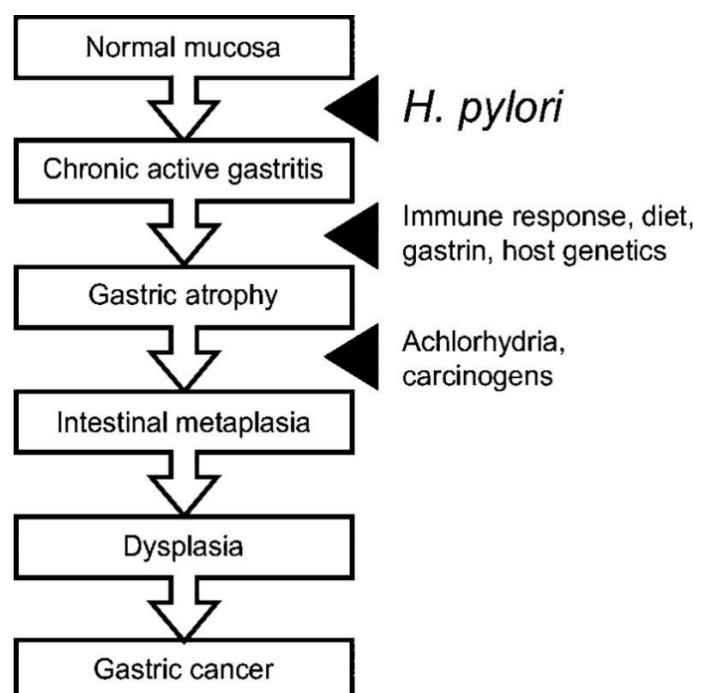


Figure 6: Model representing the role of *H. pylori* and other factors in gastric carcinogenesis (Correa *et al.*, 1975).

Mucosa-associated lymphoid tissue lymphoma

H. pylori infection is also implicated in the development of mucosa-associated lymphoid tissue (MALT) lymphoma. Chronic antigenic stimulation by *H. pylori* triggers B-cell proliferation, and over time, genetic mutations or chromosomal translocations can lead to malignant transformation (Kusters *et al.*, 2006).

Extra-gastric manifestations

H. pylori infection has been linked to several extra-gastric manifestations. For example, idiopathic thrombocytopenic purpura (ITP), where antibodies to *H. pylori* cross-react with platelet antigens, leading to immune-mediated destruction (Kusters *et al.*, 2006). Another manifestation is iron deficiency anemia, which occurs because reduced gastric acid secretion impairs iron absorption, exacerbating the anemia (Kusters *et al.*, 2006).

Diagnosis of H. pylori

The diagnosis of *Helicobacter pylori* (*H. pylori*) infection is broadly categorized into invasive and non-invasive methods. Invasive tests include endoscopic imaging, histology, rapid urease test (RUT), and culture, while non-invasive options involve the urea breath test (UBT), serology, and stool antigen test (SAT). Molecular methods, such as conventional and quantitative polymerase chain reaction (PCR) targeting *H. pylori* DNA in stool or biopsy samples, are also utilized due to their high sensitivity and specificity (Makristathis *et al.*, 2019; Smith *et al.*, 2022). It is crucial that patients do not take antibiotics or medications for *H. pylori* treatment at least one month or 24 hours prior to testing (Mohamed and El-Gohary, 2012).

Non-invasive tests

Non-invasive methods are preferred due to their ease of use, accuracy, and ability to avoid procedures like endoscopy. Among the most commonly used non-invasive tests are:

- The urea breath test (UBT), which detects *H. pylori* by measuring the breakdown of urea into carbon dioxide and ammonia, is considered highly accurate, sensitive, and specific (Smith *et al.*, 2022). It uses carbon-13 or carbon-14-labeled urea to identify the presence of the bacteria.
- The stool antigen test (SAT) detects *H. pylori* antigens in stool samples. It is particularly useful for monitoring treatment success and detecting *H. pylori* in symptomatic patients (Calik *et al.*, 2016).

Serological testing detects antibodies to *H. pylori* but cannot distinguish between active or past infections. As a result, it is not typically used for ongoing studies such as antimicrobial susceptibility testing (Abadi, 2018). However, it is useful in epidemiological studies to understand the prevalence of the infection (Makristathis *et al.*, 2019). While these methods are effective for diagnosing human infections, they are less practical for detecting zoonotic strains in animals.

Invasive tests

Invasive tests are typically used when non-invasive methods are insufficient or when direct evidence of *H. pylori* infection is needed, such as in cases of severe gastrointestinal symptoms or to confirm eradication post-treatment. These tests primarily involve tissue biopsies obtained during endoscopy and offer highly specific results, including the identification of bacterial strains and the assessment of histopathological changes in the gastric mucosa.

Endoscopy with biopsy is considered the gold standard for diagnosing *H. pylori* infection. During the procedure, a flexible tube with a camera is inserted into the stomach to visually examine the gastric lining. Biopsies are taken from the stomach and duodenum for histological examination, bacterial culture, or molecular testing. Although endoscopy can be uncomfortable and presents challenges such as cost, availability, and expertise, it remains a crucial diagnostic tool. It allows for the collection of biopsies, particularly from the antrum and corpus of the stomach, necessary for RUT and culture testing, and provides important insights into gastric mucosal features associated with *H. pylori* infection (Abadi, 2018; Dore and Pes, 2021).

Histology involves staining biopsy samples with special dyes, such as Giemsa or Warthin-Starry, to identify *H. pylori* under a microscope. This method also allows for the evaluation of gastric tissue for signs of chronic inflammation, intestinal metaplasia, or gastric cancer, which are often linked to *H. pylori* infection (Smith *et al.*, 2022). Histology is important as it provides information on the presence of *H. pylori* and the degree of active or chronic inflammation, making it essential for diagnosing the infection and assessing related conditions like gastric cancer (Lee and Kim, 2015).

The rapid urease test (RUT) is commonly used with

biopsy samples to detect *H. pylori* urease activity. In this test, the biopsy is placed in a urea-rich medium. If *H. pylori* is present, its urease enzyme hydrolyzes the urea, changing the pH of the medium and causing a color change. The test provides quick results and is highly sensitive and specific (Bordin *et al.*, 2021).

Bacterial culture and antibiotic susceptibility testing (AST) can be performed using tissue biopsies. Culturing *H. pylori* is technically challenging due to its fastidious growth requirements, including microaerophilic conditions and specialized media. However, culturing the bacteria enables testing for antibiotic resistance, providing valuable information for guiding treatment decisions (Seriki *et al.*, 2018). While culture has the advantage of assessing bacterial susceptibility and virulence factors, it is less sensitive than molecular methods and can be expensive and time-consuming (Palamides *et al.*, 2020; Dore and Pes, 2021). Moreover, mishandling biopsy samples can lead to bacterial death and false negatives (Harrison *et al.*, 2017).

Molecular techniques, particularly polymerase chain reaction (PCR), are increasingly used to detect *H. pylori* DNA and identify virulence factors, such as the *cagA* and *vacA* genes. PCR amplifies specific gene sequences unique to *H. pylori*, enabling the detection of the bacteria even in low abundance. PCR is also valuable for detecting genetic mutations related to antibiotic resistance, aiding in treatment decisions (Chey *et al.*, 2017). Additionally, advanced molecular methods, including multiplex PCR, next-generation sequencing (NGS), and whole genome sequencing (WGS), can identify zoonotic strains and genetic mutations associated with cross-species transmission. These techniques are particularly useful in cases where *H. pylori* is suspected to have originated from animal sources, providing insights into strain-specific mutations and evolutionary relationships between human and animal strains (Chey *et al.*, 2017).

Prevention and control of Helicobacter pylori infection

Preventing and controlling *Helicobacter pylori* infections necessitate a comprehensive, multifaceted approach that combines public health initiatives, improvements in sanitation, educational campaigns, and effective medical interventions. Key strategies include:

Improved sanitation and hygiene: Enhancing

sanitation, particularly in underdeveloped regions, is crucial for limiting *H. pylori* transmission. This involves ensuring access to clean water, improving waste management systems, and promoting hand hygiene. Health programs aimed at educating communities, particularly children, on proper hygiene practices can substantially reduce the transmission of the bacterium.

Health education and public awareness: Educating the public on the transmission routes of *H. pylori*, the importance of hygiene, and recognizing symptoms of infection is essential for prevention. Public health campaigns should focus on promoting safe food handling, maintaining sanitary living environments, and encouraging individuals to seek medical advice when gastrointestinal symptoms arise.

Early diagnosis and treatment: Timely detection of *H. pylori* through non-invasive diagnostic tools like breath tests and stool antigen assays is essential for preventing complications such as peptic ulcers and gastric cancer. Early treatment with a combination of antibiotics and proton pump inhibitors (PPI) is the standard, though increasing antibiotic resistance underscores the necessity of rational antibiotic use and the development of alternative treatment strategies.

Antimicrobial stewardship: The rise of antibiotic resistance among *H. pylori* strains, particularly to clarithromycin and metronidazole, emphasizes the need for prudent use of antibiotics. Tailoring treatment based on antibiotic susceptibility testing, limiting unnecessary prescriptions, and exploring novel therapies are pivotal in controlling resistance and ensuring effective treatment.

Zoonotic transmission control: Emerging evidence suggesting that domestic animals, including pets and livestock, may harbor *H. pylori* and act as reservoirs for human infections necessitates further investigation into potential zoonotic transmission. In areas where animal-to-human transmission is a concern, controlling human exposure to animals may help reduce the risk of infection.

Vaccine development: Despite the absence of a currently available vaccine, research into the development of a *H. pylori* vaccine holds great promise. A successful vaccine would significantly

reduce infection rates, especially in high-prevalence regions, and contribute to the global reduction of diseases linked to *H. pylori*, such as ulcers and gastric cancer.

Conclusions and Recommendations

Helicobacter pylori remain a significant global health challenge, with its high prevalence and associated morbidity underscoring the importance of effective diagnostic, preventive, and treatment strategies. The bacterium's unique ability to persist in the acidic environment of the stomach, along with its virulence factors, enables it to cause a wide range of gastrointestinal disorders, including gastritis, peptic ulcers, and gastric cancer. Although human-to-human transmission is well-documented, emerging evidence of animal reservoirs suggests a more complex transmission dynamic that warrants further investigation.

Despite advances in diagnostic techniques and treatment regimens, including antibiotic therapy and proton pump inhibitors, the increasing issue of antimicrobial resistance complicates eradication efforts. Preventive measures focusing on improved sanitation, hygiene, and public health interventions remain key to controlling the spread of *H. pylori*. The development of a vaccine and novel therapeutic options are critical to addressing the limitations of current treatment strategies, offering hope for more effective management in the future. Continued research into the bacterium's biology, transmission pathways, and resistance mechanisms will be essential in overcoming the challenges posed by *H. pylori* and reducing its impact on global health.

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Novelty Statement

This review explores the zoonotic potential of *Helicobacter pylori*, an often-overlooked aspect in public health. It highlights emerging transmission pathways, animal reservoirs, and antimicrobial resistance trends. Emphasizing a One Health

approach, the study underscores the need for integrated control strategies

Author's Contribution

OSJ collected and analyzed the data. EFA collected the data online and did further comparative analysis. ORA designed the review and wrote the manuscript. OAO edited the manuscript and supervised activities. All authors read and approved the final version of the manuscript.

Conflict of interest

The authors have declared no conflict of interest.

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