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The Contracting Helicobacter pylori Infections

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Abstract

One of the most common bacterial infections in the world is Helicobacter pylori (H. pylori). Infection raises the chance of stomach adenocarcinoma, mucosa-associated lymphoid tissue lymphoma, and peptic ulcer disease in addition to causing chronic gastritis. Approximately 50% of people worldwide are infected by the disease, and as of right now, no cure guarantees complete eradication. This review emphasizes current diagnostic options, the difficulties in eliminating H. pylori and the need for alternative therapeutic approaches based on deepening our understanding of host H. pylori infections. It attempts to give a broad overview of our knowledge regarding H. pylori infection and its management.

Introduction

There has been intense research into the pathogen since Marshall and Warren's groundbreaking discovery of *H. pylori* in the early 1980s [1]. An ongoing *Helicobacter pylori* (*H. pylori*) infection results in persistent inflammation, gastric mucosal atrophy, and an increased risk of gastric cancer [2]. Patients with *Helicobacter pylori* (Hp)-naïve disease typically have gastric phenotypes, which indicate gastric mucosa without intestinal metaplasia (IM), in addition to gastric dysplasia and stomach cancer. The latter is among the most common cancers and the fourth leading cause of cancer-related deaths worldwide at the moment. The primary cause of peptic ulcer disease (PUD) and chronic gastritis has been identified as *H. pylori* [3]. The stomach lining is colonized by the spiral-shaped gram-negative bacterium *Helicobacter pylori*.

Although coiled bacteria have been reported multiple times in medical literature, the medical community disregarded any proof of the bacteria in the stomach because they believed it to be a pollutant. When *H. pylori* was discovered, the mechanisms behind the development of several diseases were fundamentally rethought [4]. It was established that bacteria play a part in the development of MALT lymphoma, stomach cancer, peptic ulcer disease, and chronic gastritis. The fundamentals of how to prevent and treat them have evolved. Barry Marshal and Robin Warren won the 2005 Nobel Prize in Medicine and Physiology for this discovery [5]. It has been noted that intestinal microbes play a major role in the development of stomach and duodenal diseases. This leads to the hypothesis that *Helicobacter pylori* may not be the only pathogen in the stomach [6]. Because of the overall decrease in treatment success brought about by rising antimicrobial resistance, treatment guidelines have had to be rethought, and the concepts of antibiotic use and antimicrobial stewardship have to be adopted. Eliminating the empirical use of the triple treatments of clarithromycin, metronidazole, and levofloxacin is one of the necessary adjustments [7]. The purpose of this review is to elucidate the pathways and trends of *H. pylori* transmission and to pinpoint effective preventative strategies.

Pathways and Trends of *Helicobacter pylori* Transmission

The five main modes of transmission of *Helicobacter pylori* are fecal-oral, oral-oral, gastric-oral, anal-oral, and genital-oral. Suggest that there are several ways for *H. pylori* to spread [8]. the main routes of *H. pylori* transmission, such as occupational and foodborne exposure, as well as human-to-human and animal-to-human transmission [9]. The most frequent routes of *H. pylori* transmission seem to be fecal-oral. Usually, children and patients who are prone to vomiting choose the gastric–oral route. whereas occupational exposure and animal-to-human contact are linked to significant environmental and occupational restrictions. The genital–oral and anal–oral pathways, however, are still speculative [10].

Epidemiology of *Helicobacter pylori*

To address the possible oral transmission rates, two meta-analyses examined the possible association between *H. pylori* and periodontal disorders. It was discovered that individuals with *H. pylori* infection had a higher prevalence of periodontal disease. Additional research examined the possible contribution of dietary items and drinking water, as well as socioeconomic variables, to the spread of the illnesses [11]. Inflammatory bowel disease (IBD) incidence and prevalence are generally lower in areas or nations with high *H. pylori* infection rates. Some hints regarding the processes behind the negative (inverse) connections between *H. pylori* and IBD may be found in the impact of chronic *H. pylori* infection on the gastric mucosa's acid barrier function [12]. Age, sex, eating patterns, living arrangements, yearly income, drinking water sources, hand-washing practices, smoking, and

periodontitis are risk factors for *H. pylori* infection. *H. pylori* transmission, which is classified as habit-based, zoonotic, and family-based transmission, may be impacted by these risk factors [13]. Figure (1).

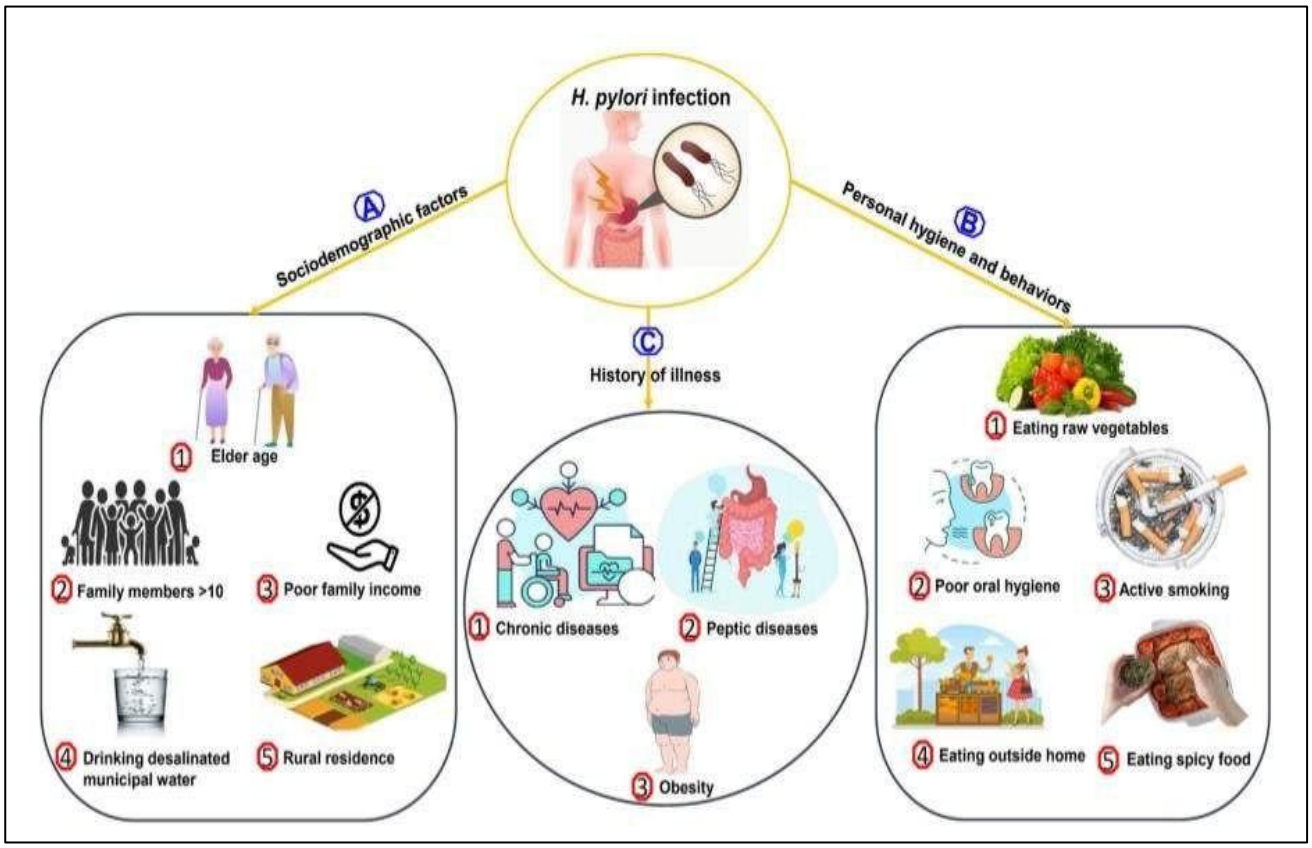

Figure 1: The most common risk factors associated with Helicobacter pylori infection. Source [14].

Pathophysiology of *H. pylori*

Recent data on the pathophysiology of *Helicobacter pylori* infection has shown that the bacteria can adapt to the harsh acidic environment of the stomach, colonize the gastric mucosa by interacting with mucin 5 (MUS5AC) and other host cell receptors, form biofilm, interfere with host metabolic pathways, induce neuroimmune cross-talk, and downregulate gastric barrier homeostasis, all of which have an impact on the development of the disease [15]. Different gastritis phenotypes that indicate potential progression to other gastroduodenal diseases result from the pathophysiology of *H. pylori* infection, which is dependent on intricate bacterial virulence mechanisms and their interaction with the host immune system and environmental factors. Additionally, there is proof that the spiral-to-coccoid transition is a special strategy employed by *H. pylori* to endure in the hosts gastrointestinal tract (GIT) [16]. Figure (2).

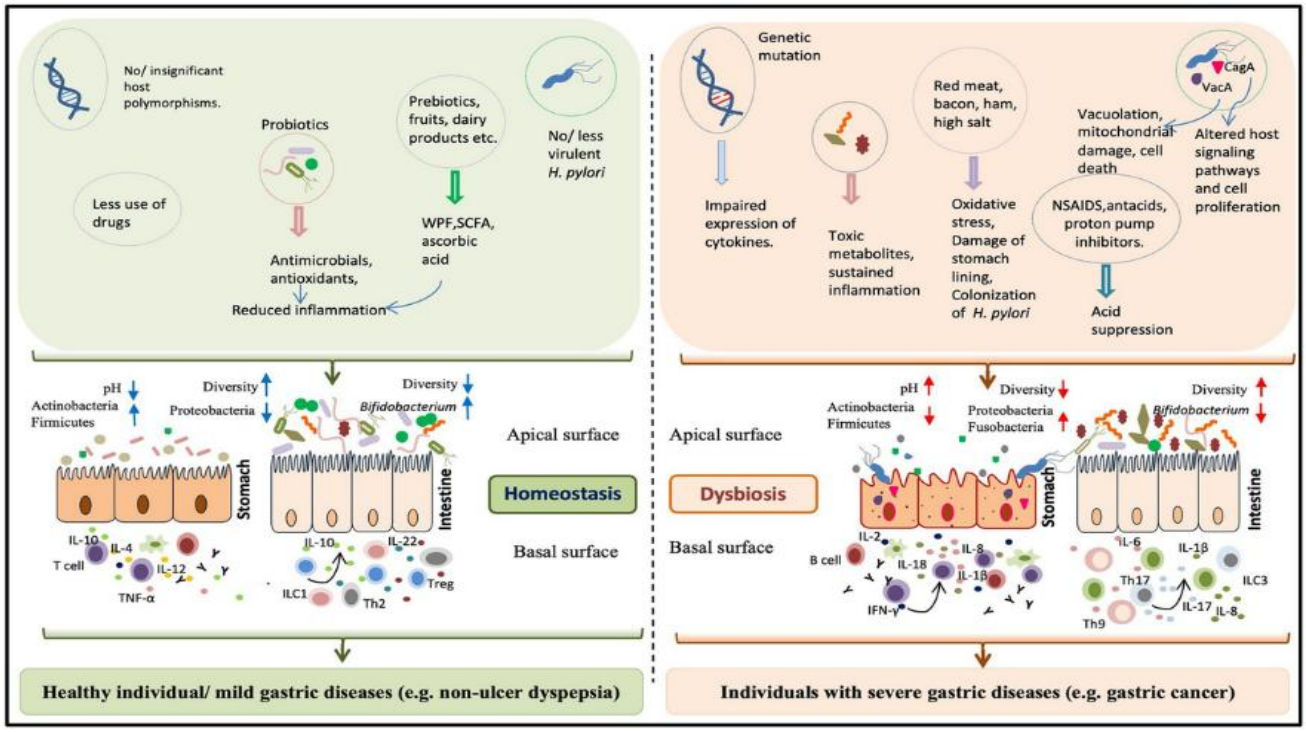

Figure 2 The effect of Helicobacter pylori and other factors on gastric health and diseases. Source [17].

The high degree of genetic variability displayed by *H. pylori* may play a significant role in both the infection's clinical outcome and its adaptability to the host stomach. Massive inter-strain genetic variation, greater than that of any other bacterial human disease, is caused by the high mutation rate and inherent competence characteristic of this species [18]. Rapid exploration of the fitness landscape and quick adaptability to the shifting conditions of the stomach environment are assumed to be the sources of such a malleable genome's adaptive utility. The lifestyle of *H. pylori* is therefore a never-ending race to preserve a suitable pool of standing genetic variation capable of withstanding selection events, even though diversity is also lost due to frequent bottlenecks. Methylome evolution may produce enough transcriptome diversity to offer an additional complex layer of adaptive potential, albeit this is not yet fully understood [19]. *H. pylori* has evolved the capacity to employ the host's cellular components to elude the immune system and proliferate in intracellular niches as a result of their co-evolution with hosts. Bacteria must avoid the host immunological reaction in order to thrive [20]. In addition to a number of other strategies, such as DNA mutation and recombination, bacteria, such as *H. pylori*, achieve this goal epigenetically via changing the host cells' chromatin [21]. This demonstrates how *H. pylori* frequently uses DNA methylation to mute the genes of the human stomach mucosa. Several mechanisms are included in epigenetics [22]. However, DNA methylation is often linked to the inheritance of repressed genes because it endures after DNA replication. Changes in gene

expression that are heritable can result from chromatin alteration that is passed on to daughter cells [23]. Chronic stomach inflammation and oxidative stress are brought on by *H. pylori* and are linked to mitochondrial dysfunction. By interacting with the inner membrane of the mitochondria, its pro-apoptotic cytotoxin VacA causes increased permeability and reduced ATP synthesis. Additionally, as seen in infected mice, *H. pylori* causes mutations and damage to mitochondrial DNA concurrently with the development of gastric intraepithelial neoplasia [24]. It has been demonstrated that some H. pylori virulence factors, such as cholesterol-α-glucosyltransferase (CGT), vacuolating, and cytotoxin A (VacA) and cytotoxin-associated gene A (CagA), take advantage of host cholesterol during pathogenesis. As a result, statins that inhibit cholesterol synthesis may be the best way to lower the incidence of GC linked to *H. pylori* [25]. Although *H. pylori* virulence factors may act synergistically, some are critical for bacterial colonization and thus chronic infection, while others may act only as additional stimuli that stimulate further responses. These include several bacterial antigens such as BabA, SabA, or OipA , AlpA, DupA, GGT, NAP, catalase, or Hsp60 [26].

H. pylori uses its adhesions to colonize the host successfully. The pathogen damages the host tissues by producing several of effector proteins and toxins [27]. *H. pylori* layers of the stomach epithelium connect with the host. It's interesting to note that this bacterium can move between two forms based on the physiological activities needed [28]. Researchers exploited the relationship between DNA structure and physiological function to discover a universally functioning small RNA (sRNA) regular of virulence in the infectious pathogen *Helicobacter pylori* and suggested that sRNA expression is influenced by a variable thymine (T) stretch in its promoter. They showed that sRNA post-transcriptionally represses several major pathogenic factors of *H. pylori*, including CagA and VacA, by base pairing with their mRNAs. They also showed that sRNA transcription is regulated by the nickel-responsive transcriptional regulator NikR hence called NikS, for nickel-regulated (sRNA), thus linking virulence factor regulation to nickel concentration [29].

Methods for Diagnosing *H. pylori*

Preventive screen-and-treat methods are made possible by the role that *H. pylori* infection plays in the development of stomach cancer. *H. pylori* infection is diagnosed using invasive endoscopy-based and non-invasive techniques, such as breath, stool, and serological testing.Their application is contingent upon local availability and the unique medical history of each patient [30]. Figure (3).

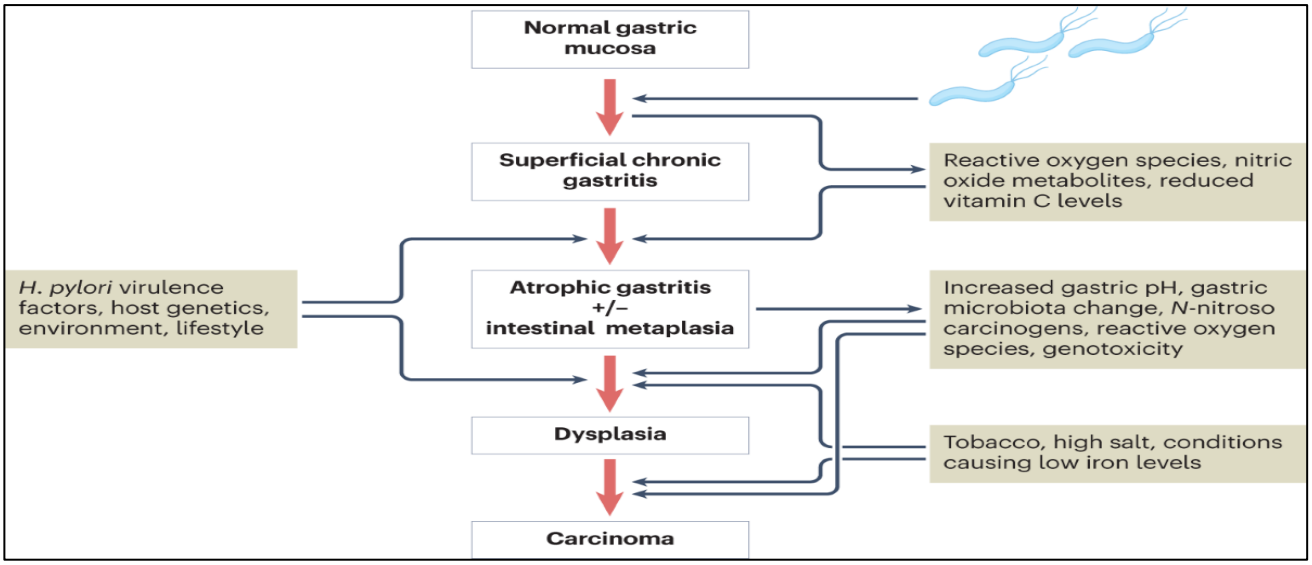

Figure 3: Helicobacter pylori infection. Source [30].

Blue laser imaging (BLI), linked color imaging (LCI), white-light endoscopy (WLI), and narrow-band imaging with magnification endoscopy (NBIME) are usually used to view every lesion that appears in the patient demographics, as well as their endoscopic and microscopic characteristics, and magnifying endoscopy is an example of an invasive procedure. [31]. For the main diagnosis of an *H. pylori* infection, non-invasive diagnostic procedures, including the stool antigen test and the urea breathing test, are advised. Epidemiological research and early screening can both benefit from serology [32]. In addition to providing additional details regarding the extent of inflammation and precancerous lesions in the stomach mucosa, the histology demonstrated its usefulness in identifying *H. pylori*. The primary application of molecular techniques is the identification of *H. pylori* antibiotic resistance. The gold standard and suggested method for testing for antibiotic susceptibility is to use cultures from stomach biopsies [33].

Mechanism of *H. pylori* Bacteria to Resist Treatment

There appear to be three different types of resistance: single-drug resistance, multidrug resistance, and heteroresistance. These profiles most likely share basic processes and clinical consequences. The most researched strategies involve chromosomally encoded mutations that interfere with antibiotics cellular function through target-mediated mechanisms [34]. Less research has been done on other biological characteristics that contribute to drug resistance in *H. pylori*, which may indicate more intricate physiological alterations (such as poor control of drug absorption and/or efflux, or the development of biofilm and coccoid) that are still mostly unknown [35]. In light of the concerning rise in antibiotic resistance, particularly to metronidazole and clarithromycin, complementary and alternative approaches are being considered. Antibacterial therapy effectiveness is contingent on a number of

factors, including medication susceptibility, dosage, formulation, adjuvant use, length of treatment, and rates of reinfection [36]. One of the main risk factors for *H. pylori* resistance is the mutations in the genes that encode the antibiotic target protein [37].

Treatment options for Helicobacter bacteria

Today, the rate at which *H. pylori* is eradicated is declining due to antibiotic resistance. The decreasing incidence of *H. pylori* eradication brought on by metronidazole-only resistance may be overcome by quadruple concurrent therapy [38]. The chronic condition known as functional dyspepsia (FD) is challenging to cure. Its pathogenesis may be influenced by *Helicobacter pylori*. Although the benefit is minimal, there is strong evidence that *H. pylori* eradication therapy cures and improves FD symptoms [39]. Treatment of *H. pylori* involves using a potent acid suppressant in different combinations with antibiotics and/or bismuth. It should be chosen because furazolidone-based bismuth-containing quadruple treatment is cost-effective and reasonably safe [40]. The use of probiotics as adjuvants in therapy is a compelling observation since the organism's immune-mediated responses against the bacterium can change the microbiota [41].

Conclusion

Therefore, even if the condition is now more curable, research into treatment resistance and pharmaceutical compliance is still underway. As an alternate method of using natural remedies to treat *H. pylori* infections, taking into account the importance of nanotechnology in creating fresh approaches to treating *H. pylori* infections.

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