Review

Review of Research on Routes of *Helicobacter pylori* Infection

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Abstract

In recent years, many scholars conducted in-depth research on *Helicobacter pylori* and identified it as an important pathogen of chronic gastritis and peptic ulcer. *H. pylori* also causes also and contributes to precancerous lesions (atrophic gastritis and intestinal metaplasia) and is closely related to occurrence and development of gastric adenocarcinoma and gastric mucosa-associated lymphoma. This study summarizes biological characteristics, epidemic status, and infection route of *H. pylori* and reviews research on roles of natural environments, especially drinking water, during infection.

In 1982, Marshall *et al.* [1] observed *Helicobacter pylori* from gastric mucosal slices and discovered a potential etiological relationship between *H. pylori* and gastric cancer. In recent years, many scholars performed in-depth research on *H. pylori* and identified this bacterium as important pathogen of chronic gastritis and peptic ulcer; *H. pylori* also causes and is a contributing factor to precancerous lesions (atrophic gastritis and intestinal metaplasia) and is closely related to occurrence and development of gastric adenocarcinoma and gastric mucosa-associated lymphoma [2]. In 1994, *H. pylori* was listed a class I carcinogen by the International Agency for Research on Cancer [3]. This study summarizes biological characteristics, epidemic status, and infection route of *H. pylori* and reviews research on roles of natural environments, especially drinking water, during infection.

Biological characteristics

H. pylori is a Gram-negative bacterium with a length of 2–4 μm and width of 0.5–1 μm . This organism is also microaerophilic, suitably living at 34–40 °C, 5%–8% O₂, 5%–10% CO₂, and high-humidity environments. Although it can survive at pH<4 acidic conditions, *H. pylori* can only reproduce at pH=5.5 to 8.0 [4]. *H. pylori* can adapt to acidic environments to a certain extent. In other words, in acidic environments, intracellular cytoplasmic pH value of *H. pylori* approaches neutral state. Thus, *H. pylori* remains capable of growth and reproduction [5] in acidic environment of gastric

juices.

H. pylori is generally present in suitable environments and is spherical in shape in in vitro culture, water and milk, and make contact with antibodies This spherical type may be a self-protecting state, posing difficulty in cultivating viable bacteria [4,6].

Epidemic status

Human *H. pylori* infection is prevalent worldwide. However, infection rate varies widely across the world. In some developing countries, infection rate of *H. pylori* can reach up to 80%, whereas in developed countries, such as the United States, infection rate totals 7.5% [7–9].

Pandeya *et al.* [10] surveyed 1355 adults in Australian communities using serological methods to detect *H. pylori* and calculated an infection rate of 15.5%. People born in Australia and New Zealand are less infected by this bacterium. Aje *et al.* [11] conducted a study on 46 pairs of control group with indigestion in Nigeria. Results showed higher infection rate of *H. pylori* (67.4%) in digestive population than that of the control group (78.3%). However, causes of such results remain unclear. Dattoli *et al.* [12] performed serological tests among 1104 children aged 4 to 11 years old in Salvador, Brazil and measured an infection rate of *H. pylori* of 28.7%. Kesanos *et al.* [13] researched on *H. pylori* infection among 101 Albanians and 101 Greeks in the Western Balkans and determined an infection rate of 54%

among Albanians; infection rate in Greeks reached 34%. Epplein *et al.* [14] performed a case–control study on 689 low-yield class African-Americans and observed an infection rate of as high as 79%. Sonnenberg *et al.* [15] used laboratory databases to analyze biopsy information of 78,985 Americans and measured 7.5% infection rate. Li *et al.* [16] conducted a large-scale systematic research on gastrointestinal diseases in Shanghai and investigated 3153 people aged 18 to 80 years old and detected an infection rate of 73.3%.

Childhood is a critical period of infection, and most *H. pylori* infections occur initially among children below 10 years old. Upon infection, *H. pylori* survives in the body for a long time and is rarely eradicated. Children of developed countries exhibit significantly lower infection rate than those in developing countries. In the United States, infection rate of children under 12 totals 10% to 15%. In France, infection rate of children under 10 is 3.5%, whereas in northern Nigeria and Zambia, children under five years present an infection rate of 50%. In each province in mainland China, average infection rate of children measures 63.9% [17]. Previous studies also showed relatively low infection rate among populations with good economic condition, good health condition, and good health habit [10–16, 18], implying possible patterns and routes of *H. pylori* infection.

Infection routes of *H. pylori*

Infection routes of *H. pylori* remain unclarified. These routes may be human–human spread and environmental infection.

Human–human spread

Human–human spread results from direct contact with people and mainly occurs among families or acquaintances, such as parents and children, husband and wife, and brothers and sisters. Areas with good health conditions and low infection rate feature low probability of maternal–neonatal spread, whereas spread among siblings serves as the main route [19]. Cervantes *et al.* [20] observed that *H. pylori* infection among siblings can be used as means of precaution for younger brothers and sisters, especially when age difference is less than three years old. Human–human spread can be divided into two specific forms, namely, oral–oral spread and fecal–oral spread.

Oral–oral spread Studies on oral–oral spread showed that *H. pylori* can survive in vomit for specific periods, even reaching up to 10% survival after 24 h. As a result of vomiting or reflux, *H. pylori* can also subsist in saliva, gingiva, and

plaque [21], providing convenient conditions for oral–oral spread. Hongying *et al.* [22] conducted a questionnaire survey and serological tests among 478 children in Kunming and performed logistic regression analysis [odds ratio (OR) = 2.260] and noted that shared tableware and shared toothbrush (OR = 2.094) are independent risk factors for *H. pylori* infection. Kivi *et al.* [23] investigated, sampled, and identified 104 subjects among 39 families to explore specific routes of spread among family members. Results showed that in addition to mother and child, siblings and spouse can also spread bacteria through shared use of daily necessities and kisses. Zou *et al.* [24] performed meta-analysis on a previous study summary and discovered significantly higher infection rate of *H. pylori* (45.0%) in mouths of people with *H. pylori* in the stomach than those without (23.9%). With drug treatment, removal rate of *H. pylori* in the stomach can reach up to 85.8%, whereas that of *H. pylori* in mouth reaches 5.7%, indicating that infection and retention of *H. pylori* in the mouth possibly serve as important route of recurrent infection in the stomach.

Some studies do not support the above view. De Sousa *et al.* [25] did not find *H. pylori* population in saliva and plaque compared with *H. pylori* population in the stomach. Vale *et al.* [26] also found no evidence of spread among spouses.

Fecal–oral spread *H. pylori* can be cultured in secretions of final interception and rectum [27]; the bacterium is generally spherical in human feces and difficult to culture. However, polymerase chain reaction (PCR) can detect its DNA [28], proving biological conditions for fecal–oral spread. Results of animal experiments support this route of spread. Cellini *et al.* [29] fed 24 mice (12 infected and 12 uninfected mice) in a cage with separate compartments and fed another 24 mice (12 infected and 12 uninfected mice) in a cage without separate compartments. Results showed that mice in the cage without compartment were infected by fecal–oral spread. Oshio *et al.* [30] conducted an animal experiment with gerbils and also witnessed such results. Laporte *et al.* [31] conducted a cohort study in France and observed that teenagers with diarrhea in welfare houses can spread *H. pylori*, demonstrating fecal–oral spread in populations.

Drinking water and food are the main intermediate media during fecal–oral spread. Although *H. pylori* is sensitive to chlorination disinfection, tap water with chlorination disinfection does not carry live bacteria. However, local water treatment and pipe networks present significant differences. Residual chlorine concentrations of terminal

water differ, and secondary contamination may occur. The biofilm formed by microorganisms on tap water pipe wall may also protect *H. pylori*, allowing its survival in tap water. Thus, *H. pylori* are often detected in tap water. Tap water containing residual chlorine can still be used for culture of viable bacteria after 5 min chlorination disinfection, surviving organisms presenting spherical form even after 24 h [32]. In some areas with poor water treatment and poor sanitary condition, *H. pylori* is detected in tap water [33] and is commonly found in some areas [34,35]. By contrast, *H. pylori* can survive for shorter periods in milk [36].

Environmental infection

Water, food, and other media containing *H. pylori* may cause *H. pylori* infection.

Water-borne infection *H. pylori* can survive in many water bodies. Cellini *et al.* [37] and Queralt *et al.* [38] detected *H. pylori* in marine waters, rivers, surface waters, and sewage. Viable bacteria are not easily cultured in the environment because of their spherical shape, but they can be detected by PCR. Cellini *et al.* [39] reported that live bacteria can be cultured in seawater samples, probably because spiral rod-shapes *H. pylori* can parasitize some microorganisms in seawater, allowing detection of this bacterium. Moreno *et al.* [40] used improved membrane separation and enrichment techniques and fluorescence in situ hybridization to successfully culture viable bacteria, providing new evidence for environmental infection. Many studies on population epidemiology confirmed infection routes of *H. pylori*. Xiaoqin *et al.* [41] investigated and detected 1127 subjects in Guizhou Province and used logistic regression and respectively observed significantly higher positive rates (64.2% and 36.6%) of anti-Hp-IgG and IgM of people drinking river water than those drinking tap water (50.6% and 27.3%) and well water (57.3% and 28.1%). Lihua *et al.* [42] conducted investigations, sampling, and detection among 938 children and teenagers aged 3 to 18 years old in Gan Su and noted significantly higher infection rate of those drinking river water (78.1%) and well water (75.9%) than that those consuming tap water (68.1%). Tianzhe *et al.* [43] conducted a meta-analysis on previous research literature and discovered that drinking water habits are mostly correlated with *H. pylori* infection. Drinking unboiled water (OR = 3.08, 95% confidence interval (CI) = 1.02–9.26) and unclean water (OR = 2.01, 95% CI=1.35–3.00) is also an independent risk factor for infection.

Infection from food Few studies reported food infections. Papiez *et al.* [44] observed that infection rate of *H. pylori* in shepherds reaches as high as 97.6% among Polish people. This value is much higher than that of the general population (65.1%). Quaglia *et al.* [36] indicated that *H. pylori* can survive in goat's milk for some time, and shepherds may be infected by drinking goat's milk. Some researchers reported that raw vegetables and meat can also increase risk of infection.

Conclusion

Various epidemiological studies showed that environmental mediators are important sources of *H. pylori* infection and feature significance to economic development and public health. However, no direct evidence shows that *H. pylori* can infect populations through environmental mediators. As a result of its biological characteristics, difficulty arises from culturing viable *H. pylori* in environmental samples. Results of PCR detection provide insufficient direct evidence. Thus, infection routes remain controversial. Recently, Moreno *et al.* [40] cultured viable bacteria obtained in sewage. When this method is successfully used in other environmental samples, it will serve as an important culturing method for *H. pylori*; although curative rate of *H. pylori* with drug treatment approximates 80% (slightly different according to strain virulence and drug resistance), recurrence rate is also high, and developing countries exhibit significantly higher yearly recurrence rate (13%) than developed countries (2.67%) [45–47]. In-depth studies covered the use of epidemiology, genomics, animal models, and other means to explore direct evidence of environmental infection routes of *H. pylori* and to conduct risk assessment of environmental infection and pathogenicity; these research will provide scientific basis for development of public health policies that guide clinical treatment and intervening risk factors and solid foundation for effective prevention and treatment of *H. pylori* infection and diseases.

Declarations

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No.

Competing interests

The author declare that he has no competing interest.

Authors' contributions

H Li made the literature analysis and wrote, discussed and revised the manuscript of this review.

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