Oral Signs of *Helicobacter Pylori*- Review of Clinical Outcomes

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**Abstract**

*Helicobacter pylori* (*H. pylori*) infection is the most common chronic bacterial infection worldwide and it plays a very important role in the pathogenesis of peptic ulcer, gastric carcinoma, and lymphoid tissue lymphoma. High reinfection rates after successful eradication treatments make the oral cavity a possible reservoir area for the survival of the bacterium. Therefore, the relationship between *H. pylori* and oral/gastric diseases is being investigated and has become a remarkable issue in recent years. In the oral cavity, *H. pylori* was first isolated from a dental plaque sample in 1989. Investigation into the relationship of *H. pylori* with oral diseases has shown that oral *H. pylori* may cause halitosis, glossitis, recurrent aphthous stomatitis and dental caries. Hence, the aim of this review is to demonstrate the relationship between *H. pylori* and oral diseases in the context of the previous/latest research.

**Keywords**: *Helicobacter Pylori*; Dental Plaque; Saliva; Halitosis; Oral Diseases

**Abbreviations**: PCR: Polymerase Chain Reaction; VSC: Volatile Sulfur Compounds; *P. gingivalis*: Porphyromonas Gingivalis; *T. denticola*: Treponema Denticola; *T. forsythia*: Tannerella Forsythia; *P. intermedia*: Prevotella Intermedia; RAU: Recurrent Aphthous Ulcers; RAS: Recurrent Aphthous Stomatitis; *H. pylori*: *Helicobacter Pylori*

**Introduction**

*Helicobacter pylori* (*H. pylori*) is a spiral-shaped, gram-negative, urease-producing and highly pathogenic microaerophilic bacteria which causes development of highly serious gastrointestinal disorders and is mainly acquired in childhood [1-4]. Almost 50% of the global population is affected by the gastric *H. pylori* infection. The infection is more prevalent in developing countries in comparison to developed nations [5]. The prevalence of *H. pylori* infection mainly depends on age, geographic area and ethnicity [6]. Low levels of education and low socioeconomic status lead to an increase in the prevalence of *H. pylori* [7]. Although the pathway of transmission of *H. pylori* is not completely known, it is thought that the transmission could occur by faecal-oral, oral-oral or iatrogenic routes. Diarrhea is often seen in childhood and the transmission of *H. pylori* from the feces to the mouth can be accomplished by sharing infected toys or foods. Additionally, the detection of *H. pylori* in the breast milk suggests that the organism can move through the fingers or nipples to the breast and contaminate the milk. The fecal-oral route of transmission seems to be possible only when there is close contact with infected individuals.

Gastro-oral transmission can occur through vomiting and gastrointestinal reflux. Infection can occur through ingestion of food or exposure to vomit-infected objects colonized by *H. pylori*. Oral-oral transmission can occur either permanently or temporarly through the dental plaque and saliva. The findings on identical strains of *H. pylori* in the mouth and stomach strengthen the hypothesis that the oral cavity may be a reservoir for the bacteria. Close person-to-person contact between members of the same family can promote oral-oral transmission. Another mechanism for the oral-oral mode of transmission is through kissing. However, this appears to be an unlikely route of transmission. The increased prevalence of *H. pylori* in the presence of crowded living conditions and poor self-care has also been reported. The higher prevalence of the infection among children whose mothers chew or taste their food before feeding them demonstrates that saliva could be a transmitter medium of the infection [8]. Also, *H. pylori*-like organisms can be seen in other animals, where infections with Helicobacter species have been reported in dogs and cats [9].

**Oral Cavity as an Extra Gastric Reservoir Area for *H. Pylori* Survival**

The oral cavity is the entrance of the gastrointestinal system, has a complex flora including 350 different species. The oral temperature varies between 35-37 °C, which provides an ideal environment for the growth of *H. pylori*. Also, dental plaque has a low oxidation-reduction potential and this environment enhances the...
reproduction of facultative anaerobic bacteria, suggesting that the acidic pH resulting from the fermentation of carbohydrates creates a very favorable environment for the reproduction of H. pylori as a microaerophilic bacterium [10]. H. pylori was also detected in periodontal pockets of patients with periodontal diseases, on the dorsum of the tongue and in saliva samples [1,11].

**Detection of Oral H. Pylori**

Cytology, urease test, culture, and polymerase chain reaction (PCR) are the methods used for the detection of H. pylori from dental plaque and saliva samples [5]. The use of the urease test for the detection of the H. pylori infection in the oral cavity shows low sensitivity due to the presence of a wide variety of bacteria with urease activity in the oral cavity. Streptococcus, actinomyces and Hemophilus species are some of the urease active bacteria in the oral cavity. For this reason, the urease test is not a suitable method for H. pylori detection in the oral cavity [3]. While histological methods using classical hematoxylin and eosin staining methods can be used to visualize H. pylori, the use of Warthin-Starry and Giemsa staining can enhance the histological identification of microorganisms. Antimicrobial susceptibility tests can be performed using culture methods. Serological tests detect levels of antibodies such as IgG and IgA in serum raised in response to an infection of H. pylori.

A number of different PCR methods have been developed for the diagnosis of H. pylori infection, which can help to differentiate H. pylori strains [9]. Currently, there is no gold standard method for isolating H. pylori from the oral cavity. However, it is stated that the best method for the detection of H. pylori from dental plaque is the PCR method. The use of molecular methods for the detection of bacteria is becoming increasingly widespread because of the difficulties in cultivating bacteria other than gastric mucosa and the necessity of using non-invasive methods [5]. The results of the PCR method need to be examined very carefully as differences in the primers and the genes used in the amplification can affect the results [12].

**Helicobacter Pylori in the Dental Plaque and Saliva**

The presence of H. pylori in the dental plaque and saliva has been investigated in many studies [2,12-25]. The studies conducted thus far with the aim finding an association between oral and gastric H. pylori infection have demonstrated conflicting results. Burgers et al. [13] and Song et al. [24,25] conducted a study to determine the association between oral H. pylori and gastric H. pylori. Both of the researchers detected oral H. pylori in the dental plaque and saliva samples of gastric H. pylori negative patients. Therefore, they stated that H. pylori may be present in the oral cavity independently from the gastric colonization and may belong to the normal oral flora. Valtez-Gonzales et al. [17] received dental plaque samples from 40 healthy children with no dyspepsia between the ages of 2-11 and examined the presence of H. pylori. In total, 35% of these children showed the presence of H. pylori in dental plaque samples. In this study, it was demonstrated that the oral cavity of children, particularly dental plaque, may be a reservoir area for H. pylori. Rasmussen et al. [18] attempted to demonstrate the presence of H. pylori in the oral cavity and the association between oral and gastric presence of the bacterium. A total of 78 adult patients with continuous abdominal pain were included in their study. At the same time, dental plaque and saliva samples were received from patients before each endoscopic procedure and examined with PCR. The investigators found an H. pylori prevalence rate of 70% among saliva and dental plaque samples. Finally, the researchers reported a high association between gastric and oral H. pylori. Liu et al. [19] conducted a study to examine the prevalence of oral H. pylori in the Chinese population and the incidence of gastric infection among patients with oral H. pylori. Out of the total of 443 adult patients with dyspeptic complaints, 263 (59.4%) had H. pylori in their dental plaque samples and 273 (61.6%) had gastric H. pylori. Gastric infection was found to be significantly higher in patients with oral H. pylori. Investigators found a strong association between the presence of oral / gastric H. pylori, indicating that the oral cavity is an important reservoir for this pathogenic microorganism.

Tiwari et al. [20] received saliva samples from 80 patients suffering from dyspepsia and 20 healthy adult control groups. Seventy-two of the 80 dyspeptic patients (90%) had gastric H. pylori. In saliva samples, H. pylori was detected in 70 (87.5%) of the 80 dyspeptic patients and in 12 (60%) of the 20 healthy individuals that constituted the control group. Since the investigators detected high levels of H. pylori in saliva samples, they noted that saliva has an important role in bacterial infection and may cause re-infections. Assumpção et al. [21] included 99 dyspeptic adult patients in their study. A total of 95 patients (96%) were found to be gastric H. pylori positive. Furthermore, H. pylori was not detected in the dental plaque specimens of any patient without gastric H. pylori. The researchers found a correlation between gastric colonization and oral colonization of H. pylori. Beasley et al. [21] received dental plaque and saliva samples from 14 patients before endoscopy and investigated the presence of urease C gene of H. pylori. The investigators were unable to detect H. pylori in any dental plaque and saliva samples.

Hardo et al. [22] examined dental plaque specimens from 62 adult patients with dyspepsia. They reported an H. pylori detection rate of 1.6% in dental plaque samples. No H. pylori was detected in any of the dental plaque samples of 61 patients. Hence, the researchers were unable to show a relationship between the presence of gastric H. pylori and oral H. pylori. Li et al. [23] received saliva samples from 56 patients with dyspeptic complaints and 40 patients were found to be gastric H. pylori positive. Among these patients, 30 (75%) of them had H. pylori in their saliva samples. H. pylori was detected in the saliva samples of 3 gastric H. pylori negative patients. The researchers did not find a clear relationship between the gastric colonization of H. pylori and the presence of H. pylori in saliva. Bharath et al. [16] investigated the genetic presence of the bacterial urease gene using the real-time PCR method among both adult and pediatric patients aged between 10 and 80 years who had dyspeptic complaints. Six of the 56 patients had H. pylori in the supragingival dental plaque, while none of the patients had H. pylori in gastric biopsy specimens. The researchers suggested that patients may have previously received eradication therapy which was the cause of these outcomes and that this treatment was able to eradicate H. pylori in the gastric mucosa but was not effective on the dental plaque.

H. Pylori and Halitosis

*H. pylori* has an important role in the gastrointestinal diseases that cause halitosis. With the oral colonization of *H. pylori*, the prevalence of volatile sulfur compounds (VSCs) producing periodontopathic microorganisms, such as *Porphyromonas gingivalis* (P. gingivalis), *Treponema denticola* (T. denticola), *Tannerella forsythia* (T. forsythia), *Prevotella intermedia* (P. intermedia) are increased [26-28]. On the other hand, Suzuki et al. [26] indicated that the presence of *H. pylori* in the oral cavity may be associated with halitosis caused by periodontal pocketing and inflammation, rather than the bacteria’s VSCs producing ability. The researchers found that the prevalence of *P. intermedia* was higher among the *H. pylori*-positive patients, while the prevalence of *P. gingivalis* and *T. denticola* was independent from the presence of *H. pylori* in the patients with periodontal symptoms. *P. intermedia* was detected in various parts of the oral cavity, including supragingival plaque, periodontal pockets, and the dorsum of the tongue. Katsinelos et al. [29] found a positive relationship between the presence of gastric *H. pylori* and halitosis according to the results of organoleptic measuring. The researchers reported that halitosis decreased after the eradication therapy. Chen et al. [30] conducted a subjective halitosis assessment with the organoleptical method and found that patients with gastric *H. pylori* were more likely to have halitosis than those without halitosis. Schubert et al. and other researchers [31-34], performed subjective halitosis assessment using the organoleptical method and could not demonstrate a relationship between the presence of gastric *H. pylori* and halitosis.

**H. Pylori and Oral Diseases**

Recurrent aphthous ulcers (RAU) are a common disease characterized by the periodic development of painful, single or multiple ulcerations in the oral mucosa. The symptoms of immunocompromised individuals are even more severe. Several possible etiologic factors have been proposed, including focal stimulation of mucosal T-cell functions by endogenous (autoimmune) or exogenous (hyperimmune) antigens. However, evidence of important causal factors is still lacking; for this reason, treatment of RAU with current methods is insufficient and is usually palliative [35]. Previous studies [35-38] have shown an increase in the formation of aphthous ulcers in the oral cavity with the presence of oral *H. pylori*. Also, there have been studies investigating the relationship between oral *H. pylori* presence and other mucosal lesions [39-42]. Lamaroone et al. [43] studied the effects of *H. pylori* in the etiology of RAU formation. They examined the surface of ulcerations and the dorsum of the tongue of 22 patients with RAU, and the dorsum of the tongue of 15 healthy subjects as a control group. The researchers stated that *H. pylori* is not involved in the pathogenesis of RAU. However, they indicated that the tongue dorsum may be a reservoir area for *H. pylori*.

Adler et al., [44] reported that glossitis was seen more frequently in patients who had gastric *H. pylori* Gall-Troselj et al. [45] found that glossitis and burning mouth syndrome were more common in the presence of *H. pylori*. Tomnny et al. and other researches [27,46,47], reported that the incidence of recurrent aphthous stomatitis (RAS) increases in the presence of *H. pylori*. Lamaroone et al. [43,48] demonstrated that RAS was not associated with *H. pylori* Mansour-Ghanai et al. [48] were only able to isolate *H. pylori* from one oral aphthous lesion thus, they were unable to demonstrate a relationship between a positive *H. pylori* ELISA test and the presence of *H. pylori* in RAS lesions. Lamaroone et al. [43] investigated the association of *H. pylori* and RAS by using a highly sensitive technique, nested PCR, in 22 patients with RAS with ages ranging from 12-36 years. Samples were taken from the lesions and the dorsum of the tongue of each patient. Additionally, samples from the dorsum of the tongue of 15 healthy individuals with ages ranging from 13-40 years who were taken as controls. The results showed that only one sample from a lesion (4.5%) and one sample from the tongue (4.5%) of two different patients with RAS were positive for *H. pylori*. In the control group, only 3 samples (20%) were positive for *H. pylori*. These findings suggest that *H. pylori* does not play a role in the pathogenesis of RAS and the dorsum of the tongue may be a reservoir of *H. pylori* in some individuals.

**H. Pylori & Caries, Oral Hygiene Habits, and Periodontal Health**

The relationship between periodontal health and oral/gastric *H. pylori* has been studied in many studies [3,19,49-61]. The association between periodontal disease and *H. pylori* infection was tested in a case-control study among 134 dyspeptic patients presenting for upper gastrointestinal endoscopy [50]. The periodontal status of the patients was evaluated as diseased or healthy. Among the cases, 30 subjects out of 65 (46.2%) had periodontal disease compared to only 20 out of 69 (29%) in comparison to the controls. Although the univariate analysis suggested that the relationship was significant, when analyzed by logistic regression, the difference was found to be insignificant. Silva et al. [54] reported that periodontal health was worse in the presence of oral *H. pylori*. However, the researchers did not find a significant association between the presence of gastric *H. pylori* and periodontal health. Al-Asqah et al. [49] examined 62 patients with a gingivoperiodontal disease and 39 patients with dyspeptic complaints without a gingivoperiodontal disease. They reported that 60% (37/62) of the periodontitis patients had gastric *H. pylori* compared to only 33% (13/39) of the patients without periodontitis. Furthermore, they reported that the prevalence of *H. pylori* in the dental plaque was higher among periodontitis patients (79%, 49/62) than in patients without periodontitis (43%, 17/39). They also reported that the presence of the bacteria in both locations was higher among periodontitis patients (46.8%, 29/62) than in patients without periodontitis (10.3%, 4/39). The researchers demonstrated a positive relationship between oral and gastric *H. pylori* presence and periodontal disease.

Souto et al. [55] evaluated the presence of oral *H. pylori* among 56 periodontally healthy and 169 chronic periodontitis patients and found a statistically significant relationship between the presence of chronic periodontitis and bacterial oral colonization. Sambashivaiah et al. [52] found no relationship between periodontal disease and oral *H. pylori*.

Additionally, Butt et al. [56] also failed to demonstrate an association between the oral presence of *H. pylori* and gingival and periodontal health in 78 patients with dyspeptic complaints. Namiot et al. [57] investigated the relationship between oral...
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