

The possible role of dental plaque as extra-gastric reservoir of *Helicobacter pylori* in gastric re-infection: A science-metric study

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Review Article

Abstract

BACKGROUND AND AIM: *Helicobacter pylori* (*H. pylori*) infection is one of the most common infections which still affects individuals worldwide. The main route for transmission of *H. pylori* infection is the oral route and this microorganism has been detected in dental plaque. In past decades, there have been a number of controversies about the station of dental plaque in the recurrence of gastric *H. pylori* Infection after eradication by triple therapy. In this study, attempts have been made to illustrate the current body of high quality evidence in this field.

METHODS: All relevant studies published between 2000 and 2017 were included in this review. The creditable databases were searched for relevant key words. The cross-sectional, experimental, and interventional investigations assessing the existence of *H. pylori* in the plaque, the state of plaque in gastric re-infection, the presence of co-infection between the oral cavity and stomach, the influence of triple therapy on the plaque, and the impression of periodontal treatments on prevention of recurrent gastric *H. pylori* infection were included.

RESULTS: Science metric review of literature demonstrated considerable disagreement with no definite conclusion. Due to the existing diversity in methodology and population groups, wide variation in results was reported.

CONCLUSION: Further homogenous studies are required to more clarify the “*H. pylori* in dental plaque” theory.

KEYWORDS: *Helicobacter Pylori*; Dental Plaque; Gastritis

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Helicobacter pylori (*H. pylori*) gastric infection is one of the most common infections worldwide in such a way that more than half of the world population are still infected with this microorganism. This incidence can reach 90%, even more, for populations living in the developing countries.¹⁻⁴ Anand et al.¹ and Al Sayed et al.² was the first investigator to report the existence of this microorganism in the oral cavity.^{1,2} Cheng et al.³ and Thomas et al.⁴ were the first ones to propose the hypothetical importance of existence of *H. pylori* in the dental plaque. Dental plaque provides a suitable environment for *H. pylori*, which is a gram negative and spiral

microorganism. The hypothesis for presence of *H. pylori* in oral cavity became interesting due to the discovery of an oral route transmission method for *H. pylori* contagion. Either the main extra-gastric reservoir for *H. pylori* is oral cavity or is just a transient sanctuary for *H. pylori* is not clear yet, but if the oral cavity plays a role as an extra-gastric reservoir, it has an important clinical implication.¹⁻⁵ Conventional treatment modality for *H. pylori* associated gastritis is comprised of a triple therapy within 14 days, so if the *H. pylori* is present in dental plaque it might not be eliminated through pharmacotherapy alone and recurrence is possible following successful gastric

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eradication of the microorganism.⁵⁻¹⁸ Interestingly, recurrence rate is considerable (approximately 13% annually) and this highlights the importance of eliminating H. pylori in other reservoirs as well. Thus, the question arises as is there any correlation between the risk of H. pylori reinfection and its existence in dental plaque? (For example, in periodontal pocket of subjects with periodontal disease).^{19,20}

The above mentioned hypothesis has been debated for several reasons. One of the most important claims is that in an immunocompetent subject, presence of H. pylori in dental plaque is not adequate for gastric reinfection and this is supported by the fact that dental plaque H. pylori is not a predictor of gastric reinfection in the future.²¹⁻²³ There is a pitfall for cross sectional studies assaying the simultaneous presence of H. pylori in the oral cavity and stomach of patients with dyspepsia and most of the studies debating the state of dental plaque H. pylori in gastric reinfection have used the cross sectional method.¹⁹⁻³⁴ The objective of these studies is the assessment of simultaneous existence of H. pylori in the oral cavity and stomach.⁵⁻³⁴ Navabi et al. reported 49.7% rate for the concurrent gastric and dental plaque H. pylori.²⁰ On the other hand, Gebara et al.⁵ and Ozdemir et al.¹⁰ evaluated the presence of H. pylori in dental plaque before and after triple therapy. The rationale for this method was to evaluate the effect of triple therapy as the treatment of choice for gastric infection on the dental plaque H. pylori, however some other investigators reported that elimination of dental plaque H. pylori by using the pharmacotherapy was difficult to achieve.³⁵⁻³⁷ The present study was carried out aiming to illustrate all high quality evidence about possible state of dental plaque (main extra-gastric reservoir of H. pylori) for gastric cancer recurrence.

Methods

In this science-metric study, all relevant

studies published in the English language between January 2000 and December 2017 were collected and included. In order to collect relevant studies, searching on creditable databases [Medline, Institute for Scientific Information (ISI) Web of Science, Scopus, and Google Scholar] was conducted by two investigators independently. The Medical Subject Headings (MeSH) system was used for performing the searches, so the key words were: "Helicobacter", "Helicobacter pylori", and "H. pylori" in combination with "dental plaque". The cross-sectional, experimental, and interventional investigations assessing the existence of H. pylori in the plaque, the state of plaque in gastric re-infection, the presence of co-infection between the oral cavity and stomach, the influence of triple therapy on the plaque, and the impression of periodontal treatments on prevention of recurrent gastric H. pylori infection were included. The abstracts of scientific congresses, grey literature, thesis, and non-English publications were not considered in the present study.

Results

Firstly, 125 studies were collected based on title/abstract search. In the next stage, the full text of each study was checked by two researchers separately and finally, 72 papers were included in the review. Regarding the laboratory assays for evaluation of H. pylori in dental plaque, at least four different methods were recruited as demonstrated in table 1.

Table 1. Helicobacter pylori (H. pylori) detection methods used in the studies assaying the presence of H. pylori in dental plaque and gastric mucosa (1-72)

Method	Studies [n (%)]
RUT	11 (34.3)
Culture	11 (34.3)
PCR	6 (18.9)
IP	4 (12.5)

RUT: Rapid urease test; PCR: Polymerase chain reaction; IP: Immunoperoxidase

Table 2. Development of research questions throughout time in the studies reviewed (1-72)

Research question	Studies [n (%)]
Concurrent presence of H. pylori in dental plaque and gastric mucosa of patients with dyspepsia	31 (42.5)
Evaluation of the presence of H. pylori in dental plaque following triple therapy	8 (11.0)
Comparison of H. pylori presence in dental plaque of periodontal and healthy subjects	20 (27.4)
Assessment of the effect of periodontal treatment on the elimination of dental plaque H. pylori	5 (6.8)
Assessment of different H. pylori strains with high virulence in dental plaque	9 (12.3)

H. pylori: Helicobacter pylori

Table 2 demonstrates the research question development throughout the time period. Table 3 presents the results of systematic reviews and meta-analysis performed on the subjects so far and as shown, most of the studies supported the role of dental plaque H. pylori in gastric H. pylori reinfection.

Table 3. Systematic review and meta-analysis studies regarding different aspects of the theory

Authors	Conclusion
Zou and Li ⁴⁰	Prevalence of H. pylori in oral cavity of patients with gastric H. pylori was higher and triple therapy had little effect on dental plaque H. pylori elimination.
Navabi et al. ²⁰	Concurrent presence of H. pylori in dental plaque and gastric mucosa of dyspeptic patients
Bouziane et al. ³⁸	Addition of periodontal treatment to triple therapy seemed to reduce the risk of gastric H. pylori recurrence.
Marbaix et al. ⁴¹	Association between oral H. pylori and gastric H. pylori infection
Adler et al. ⁴²	Dental plaque acted as a reservoir for H. pylori and maintenance of optimum oral hygiene was necessary to minimize the risk of gastritis recurrence.
Al Sayed et al. ²	
Ren et al. ³⁹	Periodontal treatment increased the chance of gastric H. pylori elimination.

H. pylori: Helicobacter pylori

Discussion

Despite the fact that the existence of H. pylori in dental plaque has been established for a long time, its clinical significance is not totally clear. This ambiguity seems to exist because of methodological diversities among numerous studies accomplished.

The most common methods are rapid urease test (RUT) and culture.^{5-37,43-46} In some studies, more than one laboratory test have

been used for evaluation of H. pylori to increase accuracy of diagnosis. Anand et al.⁸ recruited RUT and histology and Harido et al.⁴⁷ used polymerase chain reaction (PCR) and culture simultaneously. Oshowo et al. employed three diagnostic methods including PCR, histology, and RUT.⁴⁸ Immunoperoxidase (IP) assay was used in the study by Savoldi et al.⁴⁹ The rationale for using PCR and RUT as the diagnostic assays was their high accuracy for revealing the presence of H. pylori. Liu et al.⁵⁰ recruited nested PCR and Sahin et al.⁵¹ used PCR-RFLP (restriction fragment length polymorphism). Diouf et al.⁵² recruited reverse transcriptase (RT)-PCR. These examples demonstrate the variability of methods recruited in different studies. Furthermore, despite the fact that PCR is the most accurate method, it might lead to false positive results. Riggio and Lennon⁴⁴ and Patthy et al.⁴⁵ were the first to use PCR to assay the presence of H. pylori in subgingival plaque of subjects with periodontitis, moreover, Teoman et al.²⁶ claimed that PCR technique was superior to other methods for detection of H. pylori in dental plaque and samples obtained from gastric mucosa. On the other hand, some investigations have suggested the culture of microorganism as "gold standard" for proving its existence, however some strains of H. pylori might not be cultured readily. Culture is not as sensitive as PCR and since H. pylori is a microaerophilic microorganism, it might not be transferred to the laboratory easily. Thus, there is no consensus regarding the best method to unravel the presence of H. pylori in dental plaque so far.^{1,2,20,53}

In few studies, it was claimed that there is a higher chance of detecting H. pylori in supragingival and subgingival plaque among

subjects with periodontal disease.^{7,8,22,37} Survival of *H. pylori* in dental plaque depends on its ability to interact with other bacterial species and the number of these bacterial species is increased in chronic periodontitis.¹ Different clinical criteria are used for inclusion of case and control subjects including level of attachment, depth of probing, and bleeding on probing.

Interventional studies were the next to emerge following these reports. Czesnikiewicz-Guzik et al. stated that dental plaque control using mouth rinses was effective against dental plaque *H. pylori*.²¹ Tarullo et al. concluded that following triple therapy, local administration of metronidazole, calcium phosphate, and potassium sulphate in periodontal pocket was effective against dental plaque *H. pylori*, though it seemed that these interventions had an ephemeral effect on the existence of microorganism in the dental plaque.⁵⁴ Therefore, the next question was that whether mechanical debridement performed by a trained dentist would help avoid gastric *H. pylori* recurrent infection? Butt et al. were the first to address this question.⁵⁵ Sheu et al. claimed that dental disease was a risk factor in the recurrence of gastric *H. pylori* in a three-year follow-up study,⁵⁶ but to unravel the effect of dental disease elimination on the recurrence rate of gastric *H. pylori*, more well-designed clinical trials were demanded. Thus, Jia et al. stated that periodontal treatment was correlated with lower chance of *H. pylori* recurrence.^{57,58}

The second clinical trial was performed by Zaric et al. and they demonstrated that addition of periodontal treatment to triple therapy might lead to a reduction in gastric *H. pylori* recurrence rate.⁵⁹ Gao et al. concluded that elimination rate of *H. pylori* was higher in subjects receiving both periodontal treatment and triple therapy, but unfortunately, their study lacked a clinical trial design.⁶⁰ Bouziane et al.³⁸ performed a systematic review on the studies led by Jia

et al.^{57,58} and Zaric et al.⁵⁹ and it was revealed that periodontal treatment prior to or simultaneous with triple therapy reduces the risk of gastric *H. pylori* reinfection, but more studies were needed to support this claim.³⁸ More recent studies, including the one by Paladino et al. claimed that nonsurgical periodontal treatments reduced the risk of gastric *H. pylori* reinfection.⁶¹ Ren et al. confirmed this conclusion, though they stated that more powerful multicenter clinical trials were needed to establish a firm conclusion.³⁹ There is a heterogeneity in *H. pylori* detection methods in the interventional studies as well, so that Zaric et al.⁵⁹ used urea breath test (UBT) and Jia et al.^{57,58} recruited PCR. In the systematic review performed by Bouziane et al.,³⁸ UBT was not comparable to PCR in its detection accuracy.^{38,57-59}

Another aspect addressed in the more recent studies is the possible role of *H. pylori* strains' virulence on the gastritis. For instance, cytotoxin-associated gene A (CagA gene) has been associated with gastric carcinoma while vacuolating cytotoxin A (VacA) is mostly associated with inflammatory conditions. While in some studies, there is no difference between these two strains of *H. pylori* and it seems that geographical distribution of studies leads to such heterogeneity. In case of a higher incidence of potent *H. pylori* in plaque, the state of plaque *H. pylori* in gastric *H. pylori* reinfection might be more prominent.⁶²⁻⁷¹ Assumpcao et al. demonstrated that in 89% of the subjects, there was a similarity between genotype (CagA or VacA) of dental plaque and gastric *H. pylori*.⁶⁸ However, Wang et al. believed that there is the chance of detecting more than one strain of *H. pylori* in an individual at a single time.⁶⁹

In studies such as the one by Dye et al., it has been long stated that oral hygiene plays an important role in subjects with *H. pylori* infections undergoing triple therapy, and clinicians that undertake the care of patients with gastritis with positive gastric *H. pylori* might notice this in their patients and stress

the importance of oral hygiene.³⁷

One of the limitations of the present study was that dental plaque is not the only source of *H. pylori* and dorsum of the tongue and saliva should also be taken into consideration in such studies, although it was supposed in the present study that the majority of the studies accomplished have still focused on dental plaque as oral harbor of *H. pylori*.⁷²

Conclusion

It seems that there is enough evidence about the existence of *H. pylori* in the dental plaque which could lead to recurrence of gastric infection. If the role of this potential reservoir in the recurrence of gastric *H. pylori* infection was established, a significant revolution might occur in the treatment modality of

these patients and dentists might play a prominent role in management of these patients, organizing a multidisciplinary management protocol, and merging periodontal therapy with the triple therapy. Further randomized clinical trials (RCTs) seem necessary for assessing the power of this multidisciplinary clinical protocol in order to establish standard guidelines regarding the proper dental management of patients with gastritis.

Conflict of Interests

Authors have no conflict of interest.

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None.

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