

REVIEW PAPER

## Saliva testing for *Helicobacter pylori* infection in children and adolescents – a literature review

Magdalena Zakrzewska<sup>1</sup>, Mateusz Zakrzewski<sup>1</sup>, Anna Gladka<sup>1</sup>,  
Katarzyna Czarniecka-Bargłowska<sup>2</sup>, Elżbieta Maciorkowska<sup>3</sup>

<sup>1</sup>Department of Developmental Age Medicine and Paediatric Nursing, Medical University of Białystok, Białystok, Poland

<sup>2</sup>Department of Maxillofacial Surgery, University Clinical Hospital in Białystok, Białystok, Poland

<sup>3</sup>Department of Pediatrics and Pulmonary Diseases, University Clinical Hospital in Białystok, Białystok, Poland

### ABSTRACT

*Helicobacter pylori* is known as one of the most common Gram-negative bacteria in the world. Infection takes place via oral-oral, gastro-oral, and faecal-oral routes. The oral-oral route is considered to be the most common route of transmission. The presence of *H. pylori* in the saliva is considered as a factor inducing periodontal disease and tooth decay, as well as changes such as aphthous ulcers, leucoplakia, and lichen planus. Furthermore, existing bacteria in dental plaques such as *Streptococcus mutans* and *Prevotella intermedia* may produce bacteriocins that promote the growth of *H. pylori*. Recent studies have focused on infection of *H. pylori* mainly in adults, although infection often occurs in early childhood. As such, more studies concerning the developmental population are needed. Saliva, as an easily available biological material, may soon become an important source in the diagnosis of *H. pylori* infections, especially in children and adolescents.

### KEY WORDS:

children, *Helicobacter pylori*, saliva.

### INTRODUCTION

*Helicobacter pylori* is a Gram-negative rod of which humans are the main carriers. Its natural habitat of development is chiefly the mucus covering the stomach epithelium. The bacterium was discovered by Valery Jaworski. However, 30 years ago Barry Marshall and Robin Warren showed the relationship of *H. pylori* infection with inflammation of the stomach and duodenum. In 1994, the bacterium was recognised by the International Agency for Research on Cancer as a class 1 carcinogen involved in the pathogenesis of gastric cancer [1].

The prevalence of *H. pylori* infection in the human population around the world is estimated to be, on average, 50% and seems to be on the decline. According to epidemiological data 84% of adults and 32% of children were infected in Poland in 2004 [2], while a study carried out in 2010 in children in urban areas of Upper Silesia showed *H. pylori* infection in only 15.7% of the examined group. This lower incidence of infection seems to be related to the improvement of socio-economic conditions, greater attention to individual hygiene, the use of probiotics, and frequent antibiotic therapy commonly applied in children due to respiratory tract infections [3–5].

### ADDRESS FOR CORRESPONDENCE:

Magdalena Zakrzewska, Department of Developmental Age Medicine and Paediatric Nursing, Medical University of Białystok, 37 Szpitalna St., 15-001 Białystok, ORCID: 0000-0002-2756-6659,  
e-mail: [magdalena.maciorkowska@gmail.com](mailto:magdalena.maciorkowska@gmail.com)

## REVIEW

### EPIDEMIOLOGY AND ROUTES OF *HELICOBACTER* INFECTION ACQUISITION

Infection takes place via the oral-oral, gastro-oral, and faecal-oral routes [1]. In each of these three routes of transmission, infection occurs through the oral cavity, hence detailed investigations regarding the presence of *H. pylori* in the oral cavity have been of interest for some time. Current research shows that the bacterium resides in supragingival and subgingival plaques, in gingival and periodontal pockets, in dental pulp, on the dorsal surface of the tongue, in the mucous membranes, and in oncological lesions located in the oral cavity. Its relationship with the occurrence of pathological conditions such as caries, oral mucosa changes, periodontal diseases, plaque deposition, and other oral mucosal lesions is of continuous interest [6, 7].

The oral-oral route is considered to be the most common route of transmission of *H. pylori* infection, usually occurring in early childhood within the family. This is due to the close contact between parents and children and between siblings. Studies show that the main reason is a lack of adequate oral hygiene, the use of shared dishes and cutlery, and sharing a bed or bedroom with an infected person [8, 9]. Some studies have stated that the risk of infection increases significantly when the mother is infected. Urita *et al.* performed a study of children from multigenerational families, in which they showed that not only infection in the mother but also in the grandmother is a significant risk factor for infection in children, while a larger number of family members and the presence of infection in the father or grandfather did not affect the transmission of infection [10]. A study conducted by Maciorkowska *et al.* showed that the *H. pylori* bacterial genome was evaluated in the same family in saliva in children and adults infected with *H. pylori*. These patients underwent gastroscopy examinations, and the presence of bacterial DNA was assessed by means of specific primers in collected specimens from the stomach. Genomic testing showed a high percentage of familial infections with the same strain, and in most children (68.2%) the mother's vacuolating cytotoxin A (*vacA*) bacteria were found. Moreover, it was shown that siblings in the examined families were infected with a strain of the same *vacA* genotype in 58.8% of cases [11].

Another way by which *H. pylori* may be found in the saliva is through the oral-gastrointestinal route. Infection may occur through contaminated items such as toys shared by large groups of children. Contaminated endoscopic equipment may also be a source of infection for patients and medical personnel [12]. The gastro-oral route of *H. pylori* infection is also considered in the context of retrograde movement of stomach contents to the mouth during episodes of reflux or vomiting. Parzęcka *et*

*al.* evaluated the prevalence of bacteria in the oral cavity in patients with gastroesophageal reflux disease. The authors concluded that the oral cavity is not always a reservoir of bacteria in the case of gastroesophageal reflux disease and concomitant *H. pylori* infection [13].

Infection can also occur through close contact with domestic animals. There is literature indicating the presence of *Helicobacter* in the saliva of dogs or cats. Jankowski *et al.* conducted a study among 30 dogs diagnosed with gastritis. The presence of the *H. pylori* genome in saliva was demonstrated in 76.6% of the studied animals. A number of species of bacteria were found with *Helicobacter heilmannii* being the most common, but *H. salomonis*, *H. bizzozeronii*, and *H. pylori* were also detected. The study suggests that *Helicobacter* is relatively common in dogs with gastritis, and their saliva may be a source of infection for humans and other animals [14]. Abdel-Raouf *et al.* came to similar conclusions, finding *H. pylori* in saliva in 45.3% of domestic dogs and 44.4% of domestic cats. The authors also found the presence of bacteria in salivary samples of 35.3% of stray dogs and 38.9% of stray cats [15].

### SALIVA AS A MATERIAL FOR TESTING FOR *HELICOBACTER PYLORI* – METHODS, UTILITY, PITFALLS

Currently, the gold standard in the diagnosis of *H. pylori* infection in children and adolescents is an invasive method – gastroscopy with mucosal biopsies with a subsequent urease test and histopathological exam or bacterial culture of the biopsied tissue. Recently, some biomolecular studies have presented saliva as a biological material to indicate *H. pylori* infection. Currently this method is used only in clinical tests [16]. The described method can probably be used in the future because saliva is easy to collect and store and it can be used to diagnose many diseases, including infectious, autoimmune, endocrine, cardiological, and neoplastic conditions and may also be used in assessing drug concentrations or in toxicological tests [17]. There are several ways to collect saliva: drainage (the patient swallows the saliva and allows its free flow to the sialometer), spitting out/expectoration (the subject actively spits saliva into the sialometer every 15–30 seconds), suction (collection of saliva accumulating on the bottom of the mouth using a vacuum aspirator), and absorption (using cotton swabs or gauze located near large salivary glands) [18]. Moreover, in an analysis carried out by Román-Román *et al.*, *vacA* genotypes found in saliva and biopsies in the same patients were consistent in 51.1% of cases. The authors suggested that *H. pylori* may find its way to the oral cavity by different routes, and saliva may be involved in transmission of infection as well as being a source of re-infection [19]. Interesting results are presented by Yamada *et al.*, who performed an examination of saliva, urine, and gastric juices.

In 39 patients with confirmed of *H. pylori* DNA in gastric juices, they detected the bacterial genome in 71.8% of saliva samples. Urine samples from 26 of these patients were also collected, and a positive DNA result was obtained in 50% of the samples. The amount of DNA material of bacteria in gastric juices correlated with the presenting genome of *H. pylori* in saliva but did not correlate with the presence of *H. pylori* DNA in the urine [20].

#### PREVALENCE AND CLINICAL CONSEQUENCES OF *HELICOBACTER PYLORI* PRESENCE IN THE MOUTH

The presence of bacteria in the saliva raises questions and poses new challenges for scholars. The question remains whether there is a connection between gastritis and the presence of *H. pylori* in the oral cavity and saliva. The presence of *H. pylori* in the saliva is considered as a factor inducing periodontal disease: tooth decay and changes such as aphthous ulcers, leucoplakia, lichen planus, and even inflammatory processes in the palatine tonsils [21–23]. Therefore, attention should be paid to the hygiene of the oral cavity, which is the first section of the gastrointestinal tract, and early symptoms of many systemic diseases are often first noticed here [24, 25]. Since *H. pylori*'s isolation from the mouth, it is believed that this location may be a reservoir for further infection. Adler *et al.* showed that *H. pylori* found in saliva, and supra and subgingival plaques, may be considered as a reservoir of bacteria and one of the possible sources of infection and reinfection [26]. On the other hand, some authors suggest that the mouth is a natural living environment of *H. pylori*, which is located in small quantities, and only an imbalance in the bacterial flora can cause reinfection. With a proper microenvironment and normal immune response, this bacterium should not be a source of *H. pylori* infection in the stomach mucosa. Czesniekiewicz *et al.* also question the influence of this bacterium on the formation of periodontal diseases, recurrent aphthous stomatitis, inflammation of the tongue, and other inflammatory changes in the oral mucosa [27]. Quing-Hua Zou and Ren-Qing Li presented that re-infection of the gastric mucosa is quite frequent [28]. Interestingly, Lukes *et al.* analysed the genome of *H. pylori* detected in the throat and the stomach in the same individuals. The study confirmed the presence of bacteria in the throat [29]. On the other hand, Portuguese researchers, Veiga *et al.*, negated the influence of *H. pylori* in the stomach and oral cavity on the frequency of caries. Studies in teenagers showed that in only 35.9% of the whole studied group, was *H. pylori* found in the gastric mucosa and only 1.9% of the bacteria was in the oral cavity. No correlation was found between the presence of this organism and dental caries. They confirmed the relationship between infection and sociodemographic factors such as age, place of residence, and socio-economic status [30].

## CONCLUSIONS

There are still many questions about the mechanisms of *H. pylori* transmission, correlation with gastric mucosal infection, and the removal of dental plaques on the bacteria residing in saliva. It is not known whether its presence affects the pathological processes in the oral cavity or conversely the existing inflammation facilitates bacterial colonisation.

The presented data from the literature indicate a lack of conclusive findings, which in turn greatly motivate further research into the universality of *H. pylori* and its incompletely understood pathogenicity in clinical and social aspects.

In addition, a large number of available studies have focused on the infection of *H. pylori* in adults, although the infection often occurs in early childhood.

According to the latest recommendations, the examination of the presence of *H. pylori* in saliva remains only in scientific investigations. However, further studies are needed to evaluate the diagnostic profit from detecting the bacteria in saliva probes.

## DISCLOSURE

The authors declare no conflict of interest.

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