Helicobacter pylori in the population of the developmental age

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ABSTRACT

Helicobacter pylori – Gram-negative rod, discovered more than 30 years ago, has a proven influence on inflammation of gastric and duodenal mucosa. The worldwide prevalence of H. pylori infection in the human population is estimated at 50% and is considered to be one of the most frequent bacterial infections in people. Many studies suggest that infection takes place in the early childhood within the family. The gastric mucosa is its natural habitat. In last time more and more findings about existence of this bacteria in another places of gastrointestinal tract and correlation with many diseases, especially an inflammation of oral cavity. The percentage of H. pylori detectability in the oral cavity ranges from 0 to 100%. Thus, more studies aimed at final determination of the bacterium reservoir in the oral cavity seem to be necessary.

Keywords: Helicobacter pylori, oral cavity, children, dental plaque, saliva

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INTRODUCTION

The first findings about *Helicobacter pylori* (*H. pylori*) dated back to the beginnings of 80-ties in the 19th century when Polish scientist, Walery Jaworski, described a spiral bacterium living in the gastric juice. In 1982 year, Australian researchers, Marshall and Warren, proved a correlation between *H. pylori* infection and inflammation of gastric and duodenal mucosa. The scientists were awarded with the Nobel Prize for their discovery in 2005 year. In 1994 year, International Agency of Research on Cancer recognized *H. pylori* as a cancerogen of class I in pathogenesis of gastric cancer [1]. More and more findings about a correlation between *H. pylori* infection and blood and skin diseases or cardiovascular and respiratory disorders have been reported recently [2,3].

Much attention has been paid to *H. pylori* presence in the oral cavity and its role in inflammation of the oral cavity. The bacterium is most frequently isolated from periodontal pockets[4]. It has been proven *H. pylori* is always present in the pockets deeper than 4mm [5]. Apart from gingivitis and periodontal diseases, *H. pylori* accompanies such pathologies of the oral cavity as thrush, coated tongue or halitosis. A correlation has also been found between *H. pylori* infection and subjective symptoms of burning, numbness and dry mouth [6].

H. pylori bacterium discovered more than 30 years ago has not been completely described and still is an object of the scientific research which contributes to presenting new aspects of pathogenesis of many diseases.

Characteristics of a microorganism

H. pylori is a Gram-negative rod occurring in morphological forms: spiral (a vegetative form) and coloidal (a mould spore). In favorable conditions, a coloidal form can transform to a vegetative form [7]. In his study Cai et al. proved that *H. pylori* strains were able to form a biofilm too [8].

According to updated knowledge, a human being is a main carrier of this bacterium, and mucus covering the gastric mucosa is its natural habitat (Fig. 1, Fig. 2). Its survival is possible due to the production of urease and local alkalization of the environment. According to Lewis, besides urease, pathogencity of *H. pylori* depends on the vacuolizing cytotoxin VacA, protein CagA, adhesion ability, flagelle and antygens [7].

Epidemiology of *H. pylori* infection

The worldwide prevalence of *H. pylori* infection in the human population is estimated at 50% and is considered to be one of the most frequent bacterial infections in people. Polish epidemiological data on its prevalence in 2004 year carried out within the target project ordered by the Ministry of Health and the Committee of Scientific Research (CZ No. 08-19, No. contract: C007/P05/2000) entitled: *Helicobacter pylori* infection in Poland – Epidemiological studies in children and adults with regard to risk of stomach and duodenal ulcers and stomach cancer' proved infection in 84% of adults and 32% of children up to 18 years old [9].

H. pylori infection is spread via person-to-person transmission by either the oral-oral, gastro-oral and fecal-oral route. The oral-oral route depends mainly on environmental factors. *H. pylori* present in the dental plaque can be transmitted due to inadequate hygiene of the oral cavity or use of the same soiled crockery and cutlery [10,11].

In people, one of gastric and/or duodenal mucosa reactions to *H. pylori* infection is inflammation of these organs. Intensity of inflammation and its clinical symptoms depend on virulence of strains, density of bacterium colonization in the stomach as well as the host's immune response.

Virulence of *H. pylori* bacterium is conditioned by its gen structure and specific gene-encoded proteins taking part in the process of on-going gastric mucosa inflammation. The study of bacterium genome performed by Maciorkowska et al. in the families *H. pylori* infected proved a correlation between the vacA genotype of Helicobacter pylori and intensification and activity of gastritis. The grade of inflammatory lesions found in antral mucosa was differentiated and depended on the alleles reported. The greatest differentiation of lesions was reported in patients with allele s1 (antral gastritis of severe and medium grade was found in 61.0% of the examined and low grade gastritis in 10.2%), while in case of allele s2, lesions were less differentiated, but of high and moderate intensity. In 60% of cases, alleles m1 and m2 were associated with antral inflammation of high activity.

In the patients examined, s1m2 genotype of *H. pylori* vacA was most frequently reported in both children and parents. The presence of s1m2 genotype was associated with the high grade and high activity of inflammation. Additionally, the study proved a high percentage of familial infections with the same strain (68%). The genotype vacA of bacterium strains identical to that in mothers was found in most of the children (68.2%) [12].

Huddles of small children in families with many children, sharing a bed and a bedroom with infected siblings, toys and objects soiled with gastric contents affect the route of transmission. Professional exposure of nurses and physicians performing endoscopy has also been included in

this group. The fecal-oral route is caused by contamination of the water sources with feces and the presence of *H. pylori* on the surface of the sewage pipes, forming a biofilm [13].

Low socioeconomic status, bad sanitary conditions, improper hygiene habits with regard to age still remain risk factors of this bacterium infection [7,14]. This thesis is confirmed by the higher prevalence of this infection in the developing countries (about 70%) and lower in the developed countries (about 30%) [14]. Incidence of the infection increases with age, intensifies in the second ten years of life and is comparable in men and women. In children, the highest percentage of the infected is reported in the first year of age and in the 13-18-year-olds [9]. The high percentage of the one-year-olds suggests that infection takes place in the early childhood within the family. A close contact between parents and children plays a key role in this infection. Many authors highlight the transmission of the infection via the parents-children route. They indicate that the risk increases when a mother is infected with *H. pylori* [12]. It has been assumed that there is no transmission of the infection neither in a fetus's life nor in the first six months of life, because a mother's antibodies passed onto a child protect it for about 6-7 months [15,16].

Diagnosis methods of *H. pylori*

Shortly after the discovery of the bacterium in the stomach by Marshall and Warren, the studies proved that *H. pylori* occurred in other sites of the gastrointestinal tract. In 1989 year, the bacterium was cultured from the material obtained from the oral cavity [17]. In 1997 year, the first complete sequence of *H. pylori* genome was established, which facilitated the isolation of the bacterium DNA. Since then the numerous studies have been performed showing that the bacterium rod exists in the saliva, supragingival and subgingival dental plaque, gingival and periodental pockets, pulp, oral mucosa and dorsal surface of the tongue as well as in various other lesions of the oral cavity and neoplastic lesions [18,19]. Another diagnostic test was determination of *H. pylori* antibodies in the saliva, though the opinions about this method are contradictory. Some researchers found this method comparable to complete blood analysis, while other scientists entirely inadequate. Currently, this method is neither applied nor recommended in clinical practice due to its low sensitivity and specificity.

H. pylori infection is diagnosed by means of invasive investigations including gastroscopy with a biopsy. Mucosa bioptates obtained can be used in an urease test, histopathological examination and bacterium culture. Non-invasive methods include the assessment of specific IgG antibodies with a serological test or an urea breath test - unavailable in many health centers due to its cost as well as the examination of *H. pylori* antigens in the feces [20]. Widely available evaluation of serum IgG antibodies may only be used in epidemiological studies and does not reflect factual infection with the bacterium in a patient during this examination.

In *H. pylori* infection diagnostics, biomolecular methods can be used where samples of saliva, gastric juice or feces are taken. DNA fragments encoding CagA and VacA toxins can be multiplied by the method of polimerase chain reaction (PCR) due to determination of specific primers for individual areas in the bacterium genome. This method is characterized by high sensitivity and specificity, though its high cost limits its availability and usage [20,21].

Since saliva is the material easy to obtain and store [21], present examinations concentrate on working out other methods using the material from the oral cavity. The latest publications have provided information about tests detecting urease (HPS) or flagellin (HPF) in the saliva [22]. Regarding the fact that *H. pylori* infection may be contracted in early childhood, younger and younger children with dyspeptic symptoms in the medical history have to be examined with a fast, non-invasive and painless test. Saliva tests seem to meet these criteria as well as other methods being currently worked out may find their application in pediatric diagnostics. This is important because of changes in the oral cavity due to the bacterium present in the oral cavity. It has been suggested that *H. pylori* presence influences the condition of oral mucosa, dentition or even correlates with chronic tonsilitis [23].

DISCUSSION

Determination of *H. pylori* presence in the oral cavity suggests further examinations should be performed to answer the question whether its presence influences pathological processes in the oral cavity or reversely – inflammation of the oral mucosa facilitates the bacterium colonization and whether infection of the oral cavity coexists simultaneously with gastritis. To date conclusions have been divergent despite numerous studies conducted. The percentage of *H. pylori* detectability in the oral cavity ranges from 0 to 100% [18]. This may be due to various diagnostic methods and techniques and sites of sample collection for examination.

The studies performed by Ding et al. in adults proved that *H. pylori* infection found in the oral cavity was reported in 60% of the examined regardless the sex, age or the higher incidence of the infection in people with periodontal diseases and caries [24].

In other studies conducted in the group of 101 people, this bacterium presence in the dental plaque was determined in 65% of the examined while in the stomach, only in 50%. In people with periodontal diseases, the incidence of *H. pylori* was significantly higher in both the stomach and oral cavity. The simultaneous presence of Helicobacter in the dental plaque and the stomach was reported in 78% of people with periodontitis and 30% of healthy people [25].

To date studies carried out in children have referred mainly to a correlation between rods of *H. pylori* present in the oral cavity and caries. The studies performed among Chinese children have shown that inappropriate hygiene of the oral cavity is a significant factor of H. pylori infection, because this bacterium may contribute to the development of caries [26].

In children, the situation is slightly different, since children rarely develop parodentosis and the material collection from the gingival pocket is more superficial than in adults. Thus, some authors speculate that *H. pylori* occurs in the oral cavity in childhood but it should be sought in other sites than gingival pockets. Interestingly, Ogay et al. isolated the DNA material of rods in the inflamed dental pulp and suggested that canals of dental roots could be a reservoir of *H. pylori* in childhood [18]. Reversal migration of the bacterium from the stomach caused by reflux or vomits has been suggested. However, Parzęcka's et al. study performed among 146 children aged from 3 to 18 years old proved that the oral cavity was not always a reservoir of bacteria in case of reflux disease of the esophagus and *H. pylori* infection of gastric muscosa [27].

The study carried out by Namiot et al. in adults proved the presence of H pylori antigens in the dental plaque without coexisting gastritis in 23.5% of patients. [28]. This explains at least one of the research questions indicating a correlation between *H. pylori* infection in the oral cavity and gastritis.

It is worth pointing out that eradication of the bacterium from the stomach by means of the systemic therapy does not eradicate simultaneously the bacterium from the dental plaque [19].

Additionally, the study of Namiot et al. [29] concluded that despite removing the dental plaque, *H. pylori* antigens were still reported in the saliva. Dental treatment, check-up of periodontal health and maintaining adequate oral hygiene combine with systemic eradication of *H. pylori* can be effective prophilactic and therapeutical procedure in gastritis and *H. pylori*-related oral cavity infections as well as prevent from reinfections in both environments. Thus, more studies aimed at final determination of the bacterium reservoir in the oral cavity seem to be necessary.

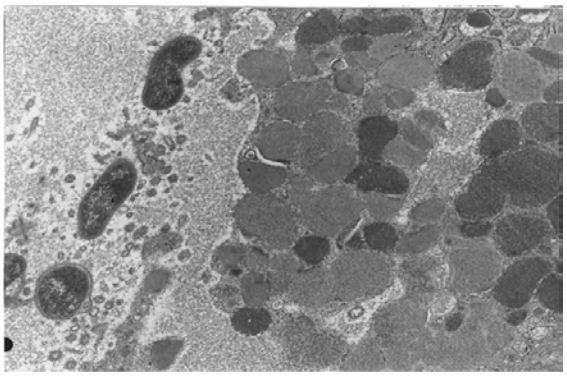

Figure 1. Gastric mucosa with H. pylori. Electron microscope. Magnification 7000 x *(E. Maciorkowska)*

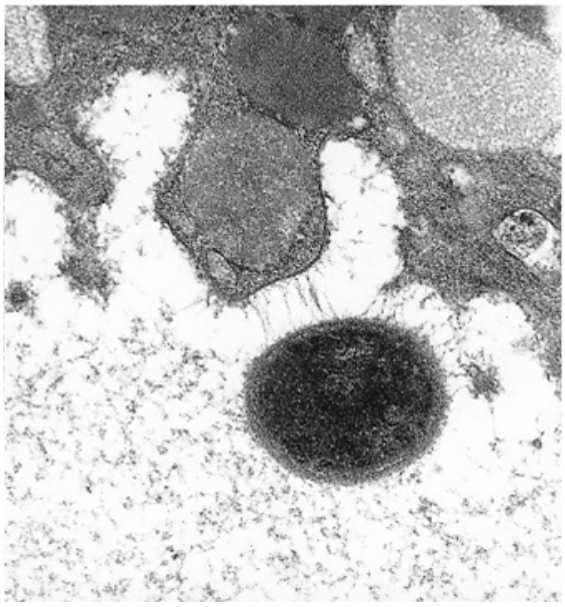

Figure 2. H. pylori bacterium combining with mucosa by means of thin 'fibers'. Magnification 2000x *(E. Maciorkowska)*

Current studies also concentrate on the forms of bacteria inhabiting the oral cavity and their influence on on-going pathological processes. The question whether cocoidal forms can be potentially dangerous should also be answered. To date various studies have given no equivocal answer. Duś et al. [13] presented transformation of a spiral form into a coloidal form observed in electron microscopy. The authors suggest that the detailed knowledge of transformation abilities will facilitate understanding of the mechanisms responsible for *H. pylori* infection and reinfection. Thus, further studies are required to determine processes regulating the phenomenon of the bacterium transformation.

CONCLUSIONS

Helicobacter pylori is an object of many studies, because prevalence of *H. pylori* infection in

the human population is very high and it is confirmed that this bacterium induces growing of gastric cancer. Last years, more and more findings about reservoir of H. pylori in the oral cavity are published. It creates possibility to answer the questions about the mechanisms responsible for *H. pylori* infection, but it requires more studies, especially in children.

Conflicts of interest

We declare that we have no conflicts of interest.

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