

*Helicobacter pylori* has been of interest to scientists and clinicians for many years, often causing diagnostic difficulties, especially in the youngest age group, in children. The presence of this bacterium in the population depends on the geographic region, however, it is assumed that even half of the world's population may be infected with *Helicobacter pylori*. In developing countries, the percentage is as high as 80%, compared to developed countries, where the incidence ranges between 20-50%. The following factors contribute to the spread of infection: lack of hygiene, low socioeconomic status, or insufficient financial outlays for prophylaxis and health protection.

*Helicobacter pylori* was recognized in 1994. as a type I carcinogen for gastric cancer. In addition, the bacterium causes a number of gastrointestinal ailments called dyspeptic symptoms, however, not all patients develop gastric symptoms. In some cases, the existence of bacteria is mute, or manifests itself with a decrease in immunity, or it becomes a trigger factor for other disease states located outside the stomach, e.g. asthma, ischemic heart disease, non-alcoholic fatty liver, type 2 diabetes, celiac disease, caries, diseases inflammatory bowel disease, as well as multiple sclerosis, and many skin diseases, e.g. vitiligo, urticaria, psoriasis, alopecia, rosacea, or primary immune thrombocytopenia, anemia, Henoch-Schönlein purpura and many others.

Invasive diagnosis for *Helicobacter pylori* involves gastroscopy, in which biopsy samples are taken from the gastric mucosa, and then assessed in a pathomorphological examination, also the urease test is being made during gastroscopy procedure. Non-invasive diagnostics is constantly developing, and the most important tests include the breath test and the detection of *Helicobacter pylori* antigens in the blood and feces. Saliva becomes a valuable material for non-invasive diagnostics, in which inflammatory markers that increase during *Helicobacter pylori* infection in the digestive system are determined.

The oral cavity is the first segment of the digestive tract in which this bacterium can become colonized. Molecular studies have shown the presence of *Helicobacter pylori* in the oral cavity of people with dyspeptic ailments, and the confirmed presence of *Helicobacter pylori* in biopsy samples collected during gastroscopy.

Among patients diagnosed with *Helicobacter pylori* in the oral cavity, increased inflammation of the oral cavity which leads to periodontal diseases and caries. The relationship between oral diseases such as periodontitis, recurrent aphthous stomatitis, glossitis, burning mouth syndrome, and the presence of *Helicobacter pylori* in supra- and subgingival plaque is clearly known to exist.

The aim of the study was to evaluate cytokines (TNF- $\alpha$ , IL-8) and other markers of inflammation (ND-1, sICAM, calprotectin, metalloproteinase-9, metalloproteinase-2, lactotransferrin, TLR-2) in the saliva of children with existing, confirmed *Helicobacter pylori* infection gastric mucosa.

The study included 117 children with dyspeptic symptoms hospitalized in the Department of Paediatrics, Gastroenterology, Hepatology, Nutrition and Allergology, University Children's Clinical Hospital in Białystok. The mean age for the examined group of children was  $13.3 \pm 3.4$  years. The mean age of boys was  $11.8 \pm 3.5$  years (minimum 4.6 years, maximum 17.6 years). The mean age of the girls was  $14.1 \pm 3.1$  years (minimum 6.3 years, maximum 17.8 years). The control group consisted of children with dyspeptic symptoms in whom the presence of *Helicobacter pylori* in the gastric mucosa was not confirmed by gastroscopy.

Children infected with *Helicobacter pylori* - the study group (Hp+) constituted 38.5% (N=45), and children from the control group (Hp-) 61.5% (N=72). In both groups, the clinical symptoms were analyzed, which occurred chronically and were an indication for gastroscopy i.e. abdominal pain, loss of appetite, weight loss, as well as symptoms of anemia and recurrent urticaria.

In the study group (Hp+) in 27 children and in 25 children from the control group, the concentrations of selected inflammatory markers in saliva (TNF- $\alpha$ , IL-8) and other inflammatory markers (ND-1, sICAM, calprotectin, metalloproteinase-9, metalloproteinase-2, lactotransferrin, TLR-2) were measured. The concentration of selected inflammatory markers in saliva in the studied samples were tested using a standardized enzyme immunoassay ELISA, and the obtained results were statistically analyzed using Statistica version 12.

The concentration of IL-8 in saliva was statistically significantly higher in the group of children infected with *Helicobacter pylori* (mean 378.8 pg/ml ( $\pm 149.8$ )) compared to the control group (mean 282.4 pg/ml ( $\pm 163.2$ )). Moreover, the levels of IL-8 were significantly increased in the group of children infected with *Helicobacter pylori* with clinical symptoms such as abdominal pain ( $p=0.036$ ), loss of appetite ( $p=0.014$ ) and weight loss ( $p=0.005$ ).

The concentration of neutrophilic defensin-1 was significantly increased in children infected with *Helicobacter pylori* (mean 50.6 pg/ml ( $\pm 47.1$ )) compared to the control group (mean 38.3 pg/ml ( $\pm 62.7$ )), moreover, there was also a positive, significant correlation between concentration of neutrophilic defensin-1 and metalloproteinase-2 in the group of infected children ( $r=0.41$ ;  $p=0.034$ ).

The concentrations of TNF- $\alpha$  and ICAM-1 adhesion molecules were comparable in both groups. Nevertheless, a positive, significant correlation was found between sICAM-1 and calprotectin in the group of infected children ( $r=0.43$ ;  $p=0.027$ ).

The assessed concentrations of metalloproteinases-2 and -9 turned out to be statistically insignificant in the study group compared to the control group. There was a statistically significant positive correlation ( $r=0.46$ ;  $p=0.017$ ) between metalloproteinase-9 and metalloproteinase-2 in the group of infected children.

It turned out that the concentrations of TLR-2 in saliva were statistically significantly higher in children infected with *Helicobacter pylori* (on average 4.1 pg/ml ( $\pm 6.0$ )), compared to the control group (average 0.7 pg/ml ( $\pm 0.4$ )) ( $p<0.001$ ), especially in children with clinical symptoms such as abdominal pain ( $p=0.001$ ), loss of appetite ( $p=0.001$ ) and weight loss ( $p=0.030$ ).

The study of the concentration of markers of inflammation in saliva in children infected with *Helicobacter pylori* created new possibilities of insight into the pathogenetic mechanisms of developing inflammation in the mouth. This type of comprehensive research is also used to monitor the current disease process and create new opportunities for better in-depth diagnostics of children infected with *H. pylori*.