

Helicobacter pylori in children and adolescents (data from Slovenia)

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Helicobacter pylori (*H. pylori*) infection is acquired mainly in childhood and persist through life unless it is treated with specific eradication therapy (1). Transient infection is described but only in infants and in rare occasions. According to recent review more than half of the world population is still infected. This means that, based on regional prevalence estimates, there were approximately 4.4 billion individuals with *H. pylori* infection worldwide in 2015 with a wide variation in the prevalence of *H. pylori* between countries (2). In children, a comprehensive review and meta-analysis of original pediatric studies from 2011 to 2016 performed on healthy children estimated an overall seroprevalence rate of 33% (95% confidence interval (CI) 27–38) (3). The prevalence of *H. pylori* infection in children is decreasing in developed countries. The study from Iceland involved 205 children aged 7–17 years and found only 3.4% of infection (4). In a recently finished Slovenian study 240 children of similar age as in study from Iceland were included and 10.5% of infection were confirmed with monoclonal stool antigen test.

Children are not little adults, and this is especially true with respect to *H. pylori* infection. Infected children have a low rate of severe diseases such as peptic ulcer disease associated with *H. pylori* and almost an absence of gastric malignancies (5). Longstanding active chronic gastritis in adults may result in gastric mucosal atrophy with intestinal metaplasia. In the minority, these premalignant mucosal changes progress to dysplasia and cancer. However, the possible association between such kind of histological changes and gastric cancer is still controversial in the pediatric

population. In addition, the prevalence of premalignant changes is not consistent among published pediatric studies, for example in Slovenia the atrophy was observed in 32.5% of infected children, mostly of mild degree, and intestinal metaplasia was detected in 5.5% of children (6). Different factors can influence on the severity of clinical outcome of chronic infection including certain *H. pylori* genotypes. To date, *cagA* and certain allelic variants of *vacA* have been most consistently associated with severe gastroduodenal diseases in both children and adults. The prevalence of *cagA* gene and *vacA* alleles in children varies among different countries/regions. In Slovenia gene *cagA* have been found in 59,6% of cases, whereas pediatric *H. pylori* strains more commonly contain *vacA* s1 and m2 than *vacA* s2 and m1, with most strains harboring the *vacA* s1/m1 genotype (6, 7, 8).

Treatment failure is increasing worldwide because of a general increase in the antimicrobial resistance of *H. pylori*. The resistance rate of most used antibiotics in the eradication protocols is very high. Primary antimicrobial resistance rates of *H. pylori* in Slovenia were 23.4% to clarithromycin and 20.2% to metronidazole (9). With that keeping in mind the last published pediatric guidelines from 2017 suggested tailored eradication therapy according to the antibiotic susceptibility testing (10). A pediatric study from Slovenia provided strong evidence that in countries with a high prevalence of resistant *H. pylori* strains tailored therapy is essential. Eradication rate was achieved in 85,9% of pediatric patients (9). Although triple therapy tailored to antimicrobial susceptibility was highly successful in our study, an eradication rate greater than

90% was not achieved. Higher failure rates in single-resistant strains despite tailored treatment indicate missed resistance by sampling error. Therefore, two or more biopsies (antrum and corpus) for antibiotic susceptibility testing was suggested to detect resistant bacterial strains in case of mixed infection, having an uneven distribution of clarithromycin-susceptible and clarithromycin-resistant *H. pylori* strains in the stomach (11, 12). In addition, patient/parents' education is crucial for high adherence to therapy.

In adults it is accepted that *H. pylori* gastritis is an infectious disease, and that infection must be treated irrespective of symptoms due to possible serious consequences such as gastric carcinoma. Mass screening in areas with high gastric carcinoma burden have been implemented or considered. However, in childhood *H. pylori* infection rarely causes complications. Moreover, the growing evidence for a possible beneficial role of *H. pylori* infection against some chronic conditions like asthma and allergies. The advent of more sophisticated techniques for assessing the proteome as well as machine learning algorithms may lead to the identification of biomarkers that determine which infected children need eradication therapy because of higher risk of complications such as gastric cancer later in life.

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