

ROLE OF EXTENDED FAMILY FOR INTRAFAMILIAL  
TRANSMISSION OF *HELICOBACTER PYLORI* INFECTION  
IN BULGARIAN CHILDREN

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**Abstract**

*Helicobacter pylori* infection is one of the most common chronic bacterial infections worldwide. The infection is usually acquired during the first years of childhood and transmission from infected mother is considered an important epidemiological factor. The aim of this study was to assess the *H. pylori* positivity in Bulgarian symptomatic children in association with the presence or absence of family anamnesis of gastroduodenal diseases among their parents, siblings and grandparents. *H. pylori* infection was evaluated in 362 children in two groups: 181 children with family anamnesis of gastroduodenal diseases and 181 children without family anamnesis. All patients underwent esophagogastroduodenoscopy and gastric biopsy samples for microbiological examination for *H. pylori* were taken. *H. pylori* infection among children with family history of gastroduodenal diseases was significantly more frequent (69.1%) compared with the group of patients without a family anamnesis (21.0%,  $p < 0.0001$ ). In addition to the significance of the infected parents (69.4%) and siblings (52.0%), infected grandparents were also associated with high prevalence of the infection (77.8%, 21/27 cases) in the children. In conclusion, *H. pylori* infection among children with family history of gastroduodenal disease was 3.3-fold higher than that in the group without family anamnesis. The significance of the grandparents in the extended family households should be considered.

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**Key words:** *Helicobacter pylori*, family, children, diseases, infection, siblings, parents, grandparents

**Introduction.** *Helicobacter pylori* infection is one of the most frequent infections in humans and is linked to chronic gastritis, peptic ulcers, gastric cancer and mucosa-associated lymphoid tissue (MALT) lymphoma [1]. Eradication of the infection is curative, reducing peptic ulcer recurrences to only 5–10% [2].

The global prevalence of the infection in children has been lower (32.6%) compared with that in adults (48.6%) and the infection has been more common in the developing countries (50.8%) compared with the developed countries (34.7%) [1]. The overall frequency of *H. pylori* infection among Bulgarian children was 24.2%, about two-fold lower than that (48.4%) in children and adolescents in Latin America and the Caribbean and more than two-fold higher than that (3–10%) in Japanese children and adolescents [3–5].

Transmission of the infection is mostly by oral-oral route (through saliva while kissing the child, food pre-mastication or contaminated utensils), fecal-oral route (through contaminated water, objects or food) and gastro-oral route (by vomiting or regurgitation) [6–8]. The infection is an anthroponosis and close family contact has a crucial role in the transmission [9].

Mother-to-child transmission is the most likely cause for intrafamilial spread of the infection. In Bulgaria, the model of extended family [10] or family with more than one generation of parents and children is more common than in the western European countries. However, the role of grandparents for the transmission of the infection is not well understood. The aim of this study was to assess the *H. pylori* positivity in Bulgarian symptomatic children in association with the presence or absence of family anamnesis of gastroduodenal diseases among their parents, siblings and grandparents.

**Materials and methods.** Totally, 362 children aged from 0 to 18 years were evaluated (Table 1). The patients were divided into two groups. Totally, the first group involved 181 children with a family history of gastroduodenal diseases such as gastroesophageal reflux disease (GERD), chronic gastritis, peptic ulcer or gastric cancer. Data were collected through anamneses and according to results of *H. pylori* tests.

In the first group 40.3% (73) of the children were girls and 59.7% (108) were boys. The control group encompassed 181 children without a family anamnesis (Table 1). In the control group, 39% (71) of the children were girls and 61% (110) were boys. All patients underwent esophagogastroduodenoscopy and two gastric biopsy specimens per patient were taken to detect *H. pylori*. Samples were placed into Stuart transport medium (Oxoid, UK), were homogenized and were used for direct staining with carbolfuchsin, as well as for a rapid urease test with 10% urea and for culture and strain isolation. The culture was used with two types media: a non-selective medium with Columbia agar base (Oxoid) and 5% defibrinated

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Frequency of *H. pylori* positivity in children with and without family anamnesis

| Groups of children                                       | No. of children | Girls     | Boys       | Aged 0-7 years | Aged 8-18 years | <i>H. pylori</i> positive | % of <i>H. pylori</i> positive | P value        |
|----------------------------------------------------------|-----------------|-----------|------------|----------------|-----------------|---------------------------|--------------------------------|----------------|
| Family anamnesis of gastroduodenal diseases              |                 |           |            |                |                 |                           |                                |                |
| Mother                                                   | 59              | 21        | 38         | 5              | 54              | 39                        | 66.1                           | 0.0001         |
| Father                                                   | 49              | 17        | 32         | 4              | 45              | 37                        | 75.5                           | 0.0001         |
| Both parents                                             | 13              | 9         | 4          | 1              | 12              | 8                         | 61.5                           | 0.0029         |
| Parents                                                  | 121             | 47        | 74         | 10             | 111             | 84                        | 69.4                           | 0.0001         |
| Sister/s                                                 | 17              | 10        | 7          | 5              | 12              | 11                        | 64.7                           | 0.0003         |
| Brother/s                                                | 8               | 6         | 2          | 0              | 8               | 2                         | 25.0                           | 0.68           |
| Siblings                                                 | 25              | 7         | 18         | 7              | 18              | 13                        | 52.0                           | 0.002          |
| Grandmother/s                                            | 15              | 10        | 5          | 1              | 14              | 12                        | 80.0                           | 0.0001         |
| Grandfather/s                                            | 12              | 8         | 4          | 0              | 12              | 9                         | 75.0                           | 0.0002         |
| Grandparents                                             | 27              | 13        | 14         | 3              | 24              | 21                        | 77.8                           | 0.0001         |
| Several family members                                   | 21              | 9         | 12         | 2              | 19              | 15                        | 71.4                           | 0.0001         |
| <b>Total number of children with family anamnesis</b>    | <b>181</b>      | <b>73</b> | <b>108</b> | <b>29</b>      | <b>152</b>      | <b>125</b>                | <b>69.1</b>                    | <b>0.0001</b>  |
| <b>Total number of children without family anamnesis</b> | <b>181</b>      | <b>71</b> | <b>110</b> | <b>28</b>      | <b>153</b>      | <b>38</b>                 | <b>21.0</b>                    | <b>control</b> |

sheep blood (NCIPD, Bulgaria), and a selective medium with the addition of the selective supplement of Dent for *H. pylori*: vancomycin 10 mg/l, trimethoprim 5 mg/L, cefsulodine 5 mg/L and amphotericin B 5 mg/L. The incubation of the plates was performed microaerobically with CampyGen envelopes (Oxoid, UK). The research is approved by The Ethics Commission of the Medical University – Sofia.

**Statistical analysis.** Chi-square test and Fisher's exact test of independence were made to compare the variables of interest.

**Results.** In our study, we found a very high *H. pylori* prevalence (69.1%, 125/181 children) in children with family history of gastroduodenal diseases, which was 3.3-fold higher than in the group without family history (21.0%, 38/181,  $p < 0.0001$ ).

The positivity rate among the children with infected mothers, fathers, sisters, brothers, grandmothers and grandfathers was 66.1% (39/59 patients), 75.5% (37/49), 64.7% (11/17), 25.0% (2/8), 80.0% (12/15) and 75% (9/12), respectively.

Overall, the children with infected parent/s were *H. pylori* positive in 69.4% (84/121), and those with infected grandparent/s were positive in 77.8% (21/27).

Of the children from extended families with several infected members, 71.4 (15/21) were *H. pylori* infected.

**Discussion.** *H. pylori* infection is often acquired during the first five years of children's life [11]. The infection transmission can often be by oral-oral route and the presence of *H. pylori* in the oral cavity supports the importance of this mechanism [12]. The oral cavity has been considered the second most frequently *H. pylori* colonized site in the human body following the gastric mucosa [12].

The characteristics of the family is of high importance for the increase or decrease in risks for the child to get infected by *H. pylori*.

Infected mothers are considered the main source of the infection in developed countries or regions, while other family members such as siblings as well as other mechanisms are deemed more frequent in developing countries with high infection prevalence [7]. The risk of infection has been considered  $\geq 4$ -fold higher if one of the parents is infected [6]. In an Italian study [6], in most ( $> 91\%$ ) of the families with *H. pylori* positive children, the mother was positive as well.

Low socioeconomic and living conditions, overcrowding, water source, poor sanitation, and presence of parents or siblings with history of peptic ulcers or gastritis have been reported to be among risk factors of the infection [2, 13, 14].

GARG et al. [10] evaluated prevalence of *H. pylori* infection among US Hispanic households with extended family model (with two or more nuclear families) and observed odds of the infection to be 3.2 for children with one infected sibling and 9.4 for those living with one or more infected sibling or non-sibling compared to the rest. In the present study, nonetheless, only the presence of positive sister was a risk factor of the infection, unlike that of the positive brother.

The extended family model involves the cohabitation or rising children by both parent and grandparent generations. Although the role of the infected parents, especially that of the infected mother as a risk factor of infection transmission has been established [10], the route of transmission of the infection in extended family model is not well elucidated yet.

Impressively, we found that both the infected grandmother and the infected grandfather were risk factors for the infection transmission to the children. This is most likely due to the close family contact in the so-called "extended family", a model typical of the Bulgarian patriarchal family, in which grandparents help in raising their grandchildren. In a Japanese study [15], *H. pylori* seropositivity rate in children was higher when mothers and grandmothers were seropositive, while infected fathers and grandfathers were not associated with higher positivity rate in children. Notably, in the present study, both parents and both grandfathers were associated with significantly higher rates of the infection in the children compared to the control group.

**Conclusion.** In conclusion, positivity of the mother or the father, the sister/s as the grandmother/s or the grandfather/s were risk factors of *H. pylori* infection in Bulgarian pediatric patients. The infected brother/s were not associated with

increased prevalence of the infection in the children. The intrafamilial transmission pattern of the infection in the countries with extended family models differs from that in most western countries and in families without more than two generations living together or in close contact between each other. In addition, in the countries with extended families, there are peculiar characteristics. In Bulgaria, the brothers were not associated with higher risks of the infections, while both parents, both grandparents and the sisters were important risk factors of *H. pylori* infection.

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