Evaluation of the Relationship Between Childhood Asthma and *Helicobacter pylori* Sero-Prevalence

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Abstract- In recent years, the prevalence of asthma and allergic rhinitis has increased in developed countries. Helicobacter pylori (*H. pylori*) infection can exacerbate asthma. The purpose of this study was to investigate the relationship between asthma and *H. pylori* seroprevalence in children. In this cross-sectional study, 100 children aged 5-15 years hospitalized in Besat hospital in Sanandaj were investigated from 2015 to 2016. Fifty children with asthma were considered as the case group and 50 non-asthmatic children as the control group. The questionnaires were completed, including demographic information, history of asthma, exposure to cigarette smoke, and family history of gastric and duodenal ulcers. Blood samples were collected from the children, and the serum level of specific antibodies (IgG) of *H. pylori* was measured. There were 42 and 31 boys in the case and control group, respectively. The mean age in the case group was 8.12±2.29 and in the control group was 8.9±2.52 years. In the case group, 48% were exposed to cigarette smoke and in the control group, 18%. There was a statistically significant difference between the groups in terms of gender and exposure to cigarette smoke (*P*=0.001 and *P*=0.013, respectively). There was no significant difference between the case and control groups in terms of H. pylori seroprevalence. (*P*=0.211). There was no significant association between asthma and *H. pylori* seroprevalence. (*P*=0.22). According to our study, there no correlation between childhood asthma and *H. pylori* seroprevalence.

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Keywords: Asthma; Children; Helicobacter pylori sero-prevalence; *H. pylori*-specific antibody (IgG)

Introduction

Along with the development of civilization and increased environmental pollution, the incidence of allergic diseases, including bronchial asthma has increased. According to WHO, 300 million people suffer from asthma around the world (1). The prevalence of this disease is 10-12% in adults and 15% in children. There are problems associated with childhood asthma such as frequent hospitalizations, referral to a doctor for health care, and absence from the school/kindergarten (2,3). In recent years, the prevalence of asthma and allergic rhinitis has increased in developed countries (4). This increase has been accompanied by many environmental factors including exposure to cigarette smoke, air pollution, allergens, obesity, and external infections (5,6). On the other hand, a new hypothesis proclaims that the incidence of allergic diseases increases due to changes in the natural microorganisms of the body. *Helicobacter pylori* (*H. pylori*), is a gram-negative bacteria, that colonizes the stomach before the age of 10 and usually after the first year of life. It is transmitted between families and widely distributed in the world population (7). *H. pylori* is recognized as a major cause of gastric ulcer disease and a known cause of gastric cancer. It is also implicated in dyspepsia with or without ulcer, iron deficiency anemia and Idiopathic thrombocytopenic

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purpura (ITP). *H. pylori* can be considered as a contributing factor in allergic diseases. In developed countries, it has been documented that with the widespread disappearance of *H. pylori* the severity of asthma increased (8,9). The infections, including *H. pylori*, can activate T helper 1 (Th-1) and lead to production of interferon γ (IFN- γ), IL-12, IL-18, IL-23 and tumor necrosis factor (TNF -α). On the other hand, it can inhibit T helper 2 (Th-2), which is involved in the allergic process. Based on this theory, the inverse relationship between *H. pylori* and asthma is justified (10,11). Some evidence suggests such an inverse relationship between *H. pylori* and asthma (5,7); however, other studies have reported different results (6). Therefore, the role of this organism in the development of asthma remains controversial (12,13). The importance of identifying the relation between *H. pylori* seroprevalence and reducing the prevalence of asthma is relevant when selecting an antibacterial therapy (14). In this context, there are limited systematic quantitative studies in children, (15) so we decided to evaluate the relationship between asthma and *H. pylori* seroprevalence in children.

Materials and Methods

This is a cross-sectional (case-control) study conducted from 2015 to 2016. One hundred children aged 5-15 years referring to Besat hospital in Sanandaj (Iran) were enrolled. They were divided into two groups: case and control. Each group consisted of 50 children. Patients with asthma were considered as case group. They had recurrent cough, wheezing, and dyspnea and their disease was confirmed by spirometry. The control group included non-asthmatic children. These children did not have any history of asthma, allergic rhinitis, eczema, or gastric disorders. Initially, written consent was obtained from parents, and a separate questionnaire was completed for each patient including age, sex, place of birth, place of living, history of asthma, exposure to cigarette smoke, and family history of gastric or duodenal ulcers. Two-milliliter blood samples were collected from both groups, and the serum level of specific antibodies (IgG) of *H. pylori* was measured by enzyme-linked immunosorbent assay sandwich method (ELISA Pishgaman Sanat Isattis Company, made in Iran). Finally, the results were recorded. The inclusion criteria were: children aged 5-15 years with confirmed asthma referring to Besat Hospital in Sanandaj. The exclusion criteria were: history or presence of peptic disorders, respiratory disease (except asthma), history of antibiotics use in the last month and history of blood (or blood products) transfusion. The study protocol was approved by the ethics' committee of Kurdistan University of Medical Sciences.

Statistical analysis

The data were statistically analyzed by SPSS (version 20) software. The quantitative descriptive data were analyzed by descriptive statistics,hhhh including absolute and relative frequency, mean and standard deviation. The qualitative data were calculated using the chi-square test and OR. The *P* of less than 0.05 was considered statistically significant.

Results

One hundred patients were enrolled. The case group with 50 asthmatic children and the control group with 50 non-asthmatic children. In the case group there were 42 boys (84%) and 8 girls (16%) and in the control group, 31 boys (62%) and 19 girls (38%). The mean age was different in the two groups. The mean age and standard deviation of children in the case group were 8.12±2.29 with the confidence interval of 7.47-7.77, and in the control group were 8.19±2.52 with the confidence interval of 7.23-8.92. In the case group, 24 (48%) were exposed to cigarette smoke and 9 in the control group (18%). There was a statistically significant difference between the groups in terms of gender (*P*=0.013) and exposure to cigarette smoke (*P*=0.001). There was no statistically significant difference in terms of place of living (*P*=0.181) and *H. pylori* seroprevalence (*P*=0.211). In the case group 8 (16%) and in the control group 4 (8%) children were *H. pylori* seropositive. Table 1 summarizes information about gender, place of living, *H. pylori* seroprevalence and exposure to cigarette smoke. According to the results, the odds ratio in patients with asthma and *H. pylori* seroprevalence was 0.45 with the confidence interval of 0.12-1.62. This study showed that there was no statistical correlation between asthma and *H. pylori* seroprevalence (*P*=0.22).

Table 1. Frequency of gender, living place, *H. pylori* seroprevalence and exposure to cigarette smoke in the case and control groups

Variable	Group	Case (%)	Control (%)	Total	X^2	*P*
Gender	Male	42 (57.5)	31 (42.5)	73	6.13	0.013
	Female	8 (29.6)	19 (70.4)	27		
Living place	Urban	33 (45)	39 (54)	72	1.78	0.181
	Rural	17 (60.7)	11 (39.3)	28		
H. pylori	Positive	8 (67)	4 (33)	12	1.51	0.211
	Negative	42 (47.7)	46 (52.3)	88		
Exposure to cigarette smoke	Yes	24 (72.7)	9 (27.3)	33	10.17	0.001
	No	26 (28.8)	41 (61.2)	67		

Discussion

Childhood asthma is a chronic disease with frequent exacerbation attacks which lead to many problems for children. These include frequent hospitalizations, referral to the doctor, and absence from school or kindergarten (2,3). Nowadays, in developed countries, the level of health has reached an acceptable level. Proper nutrition and smaller family sizes have led to reduced incidence of infections including *H. pylori*. This has been accompanied by an increase in the prevalence of childhood asthma. In childhood, the body should be exposed to microbial antigens until the immune system reaches normal maturation and consequently, it can prevent the onset of the allergic diseases. According to this theory, the colonization of some microorganisms like *H. pylori* can reduce the incidence of allergic diseases such as asthma (16). We could not prove any relationship between childhood asthma and *H. pylori* seroprevalence.

Some researchers found a negative correlation between asthma and *H. pylori*. Tsang (17) and Jaber *et al.*, (18) showed that asthma might not associate with *H. pylori*. Ribaldone and coworkers depicted that the prevalence of *H. pylori* infection among asthma and non-asthma groups was not statistically significant (14). The results of these studies are similar to our study.

Arram and colleagues depicted that *H. pylori* has an inverse relationship with asthma. (7) Zevit *et al.*, demonstrated that the prevalence of asthma in children with Helicobacter Pylori infection was 7.3% while in healthy children it was 9.1%. This means that the prevalence of asthma was reduced in patients with *H. pylori* infection (19). Another study (20) in the Netherlands reported that 8.7% of asthmatic children had *H. pylori* infection, and 29.2% of them were positive for cytotoxin-associated gene A (CagA). They showed that the strain of *H. pylori* with negative CagA was associated with an increased risk of developing asthma (20). The results of these studies were contrary to ours. The reason for this difference could be that the age of the children was low in our case group. The pathogenicity of Helicobacter pylori increases with age. Therefore, it may not be a pathogenic factor at a lower age. Also, the use of antibiotics in children with asthma is common, and these drugs also suppress the *H. pylori* infection (3). Another major difference was the method of *H. pylori* assessment as we used an *H. pylori*-specific antibody. The first study used a urea breath test (UBT) and the second study of anti *H. pylori* with CagA status for the evaluation of infection. Our sample size was small, and the results could change by increasing the sample size. Finally, it could be that the *H. pylori* species in our study were more of the CagA negative strains (5). Karimi and coworkers showed that *H. pylori* infection was not significantly different among children with or without asthma (P=0.380) (16). We used UBT to diagnose the infection. This is consistent with our study. Tsang *et al*., used a specific *H. pylori* IgG antibody to diagnose the infection as we did. Their results, like ours, did not show a significant difference in the prevalence of *H. pylori* in patients with asthma and control group (P>0.05) (17). We found that the prevalence of asthma was more common in males (57.5%). According to questionnaire data, these children were more exposed to cigarette smoke.

Our study limitations were small sample size, the patients' age and the parent's refusal for performing endoscopy on their children. The definitive diagnostic method for *H. pylori* infection in the children is endoscopy with biopsy from gastric mucosa and cultures, which is an invasive method. Therefore, we used the serology method (*H. pylori*-specific IgG) that was not very accurate and could be errors in the results (12,19,21).

In future studies, we suggest the use of more accurate diagnostic tests for assessment of the relationship between childhood asthma and *H. pylori* infection as well as a larger sample size.

Based on the results, there was no association between childhood asthma and *H. pylori* seroprevalence. On the other hand, there was a statistically significant difference between the groups in terms of gender and exposure to cigarette smoke.

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