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Original Article

A survey on *Helicobacter pylori* seropositivity status in Iranian children with atopic dermatitis

Saeedeh Farajzadeh*, Iraj Esfandiarpour, Sedigheh Amini Ranjbar***, Farshid Darvish Damavandi¶, Zahra Kamyabi¶, Behrooz Vares**, Sodaif Darvish Moghaddam¶¶, Armita Shahesmaeili†, Nasrin Bazargan‡, Gholam Reza Hoseinpoor**, Saman Mohammadi****

Departments of Pediatric Dermatology*, Dermatology**, Pediatric Gastroenterology***, Gastroenterology¶¶, Pediatric Immunology and Allergy,‡,
¶Dermatologist in Private Practice
†General Practitioner

Abstract

Objective To evaluate the presence of anti-*Helicobacter pylori* antibody in the sera of children with and without atopic dermatitis (AD) in Kerman province, Iran.

Patients and methods In the current study the cases consisted of 128 patients with AD, aged from 6 month to 16 years. One hundred and twenty eight healthy children matched for sex and age were chosen as control subjects. The enrolled patients were selected consequentially from the cases referred to the dermatology and pediatric clinics of Afzalipour hospital, an academic medical referral center in the capital of Kerman province. The diagnosis of AD was made based on the UK working party's diagnostic criteria for atopic dermatitis. The control subjects were chosen randomly among children who were referred to the center for periodic vaccination program and before receiving the vaccines. The subjects in control group who had a personal or family history of allergies (including asthma, atopic dermatitis or allergic rhinitis) were excluded as well. A sample consisting of 3 milliliters of blood was obtained from each subject in the study (including the cases and the controls) for *H. pylori* serology. In children under 1 year of age, the amount of collected blood samples we reduced to the minimum in the acceptable range. The status of infection with *Helicobacter pylori* was determined in all subjects quantitatively by measurement of specific IgG antibody via enzyme-linked immunosorbent assay (ELISA) method (Trinity Biotech Monbind Captia™, USA).

Results The mean age of the cases with AD and the controls were 5.74 ± 4.05 and 6.05±3.36 years, respectively. Of all the children in both cases and controls 45.5 % and 55.8 % were females, respectively and the remaining were males. Anti-*H. pylori* IgG antibody was positive in the cases with AD and the control group 25.2 % and 24%, respectively that was not statistically significant.

Conclusion The results of this study showed no association between *H. pylori* infection and AD.

Key words
Atopic dermatitis, *Helicobacter pylori*, children.

Address for correspondence
Dr. Saeedeh Farajzadeh,
Dermatology and Leishmania Research Center,
Afzalipour Hospital,
Kerman University of Medical Sciences,
Kerman, Iran 7616913911
Phone: +98 341 3222250-60
Email: safaderm@yahoo.com
s_farajzadeh@kmu.ac.ir

Introduction

Atopic dermatitis (AD) is a complex and multi-factorial disease.[1] The pathogenic mechanisms of atopic dermatitis are not completely verified, but food allergies, infections and environmental factors have been considered by some researchers.[2-5] The association between AD and

infection with *Helicobacter pylori* has been proposed in some studies.[6,7] In a study conducted in Japan, Sakurane *et al*. studied the association between skin diseases and *H. pylori* infection. Among 198 subjects with refractory skin diseases (including AD), 102 patients were positive for *H. pylori* infection. After eradication of *H. pylori,* symptoms of skin diseases improved in more than 50% of the patients.[8] In another study conducted in Germany, the role of *H. pylori* in chronic hives has been proved. The authors proposed that some mechanisms such as an increase in gastrointestinal mucosal permeability for antigens, immunomodulation, autoimmunity or vascular wall dysfunction might be involved in this association.[9]

On the contrary several studies have shown a reverse association between *H. pylori* and atopic diseases including AD.[10,11] Linnenberg *et al*. in Denmark demonstrated that the presence of low health-markers would result in a lower incidence of atopy.[12] In another study conducted in UK a 30% decline in incidence of the three atopic disorders was seen in patients with active *H. pylori* infection. It was proposed that childhood infections may have an essential role in the proper development of immune system.[10]

Approximately 50% of worlds' population is infected with *H. pylori*.[13] *H. pylori* infection in children has been associated with a variety of gastrointestinal diseases including gastritis and duodenal ulcer.[14] Detection *of H. pylori* infection is confirmed by several methods such as gastric biopsy, histology, culture, polymerase chain reaction (PCR), rapid urease test (RUT) and urea breath testing (UBT).[15] Most of these procedures are invasive and could be affected by factors that may lead to false negative results. Serologic diagnosis of *H. pylori* infection by measuring specific immunoglobulin G (IgG) is a safe method with high sensitivity and specificity.[16,17,18] Clarifying the pathogenic mechanisms leading to AD may help in better control and treatment of this chronic and recurrent disorder. Although there are a few reports from different countries on *H. pylori* infection in children with AD, reports from Iran are lacking. So we conducted this study in Kerman, the largest province of Iran to investigate the status of *H. pylori* infection in Iranian children with AD.

Patients and methods

In the current study the cases consisted of 128 patients with AD aged from 6 month to16 years. One hundred and twenty eight healthy children matched for sex and age were chosen as controls. The enrolled subjects were selected consequentially from the cases referred to the dermatology and pediatric clinics of Afzalipour hospital, an academic medical referral center in the capital of Kerman province. The diagnosis of AD was made based on the UK working party's diagnostic criteria for atopic dermatitis.[19] The control subjects were chosen randomly among children who were referred to the center for periodic vaccination program and before receiving the vaccines. All of the subjects who received antihistaminic, antibiotics and/or acid reducing medications since last four weeks before the enrollment were excluded from the study. The subjects in control group who had a personal or family history of allergies (including asthma, atopic dermatitis or allergic rhinitis) were excluded, as well.

Informed consents obtained from parents of all children and for those above 12 years of age from both children and their parents. All the required data such as medical history and physical examination results gathered and recorded in a pre-planned special data sheet. A sample consisting of 3 milliliters of blood was

Table 1 The frequency of *Helicobacter pylori* IgG level in the atopic diseases and food allergy.

Disease	*IgG level*		*P value*
	Positive, N (%)	*Negative, N (%)*	
Atopic dermatitis			
Yes	34 (25.2)	101 (74.8)	0.82
No	31 (24)	98 (76)	
Allergic rhinitis			
Yes	8 (27.6)	21 (72.4)	0.71
No	59 (24.5)	182 (75.5)	
Asthma			
Yes	3 (20)	12 (80)	0.65
No	64 (25.1)	191 (74.9)	
Food allergy			
Yes	6 (24)	19 (76)	0.92
No	61 (24.9)	184 (75.1)	

obtained from each subject in the study (including the cases and the controls) for *H. pylori* serology. In children under 1 year of age we reduced the amount of the collected blood samples to the minimum in the acceptable range. The status of infection with *H. pylori* was determined in all subjects quantitatively by measurement of specific IgG antibody via enzyme-linked immunosorbent assay (ELISA) method (Trinity Biotech Monbind Captia^{TM}, USA).

The collected data were analyzed by SPSS16 software. Central tendency and dispersion measures were calculated. Chi square and Mann-Whitney tests were used to compare studied variables in the two groups. *P* value less than 0.05 was considered as significant level.

Results

In this survey, 128 children with AD and 128 healthy children were entered as cases and controls, respectively. The mean age of the cases and the controls were 5.74±4.05 and 6.05±3.36 year, respectively. Of all the children in both case group and control group, 45.5% and 55.8% were females, respectively and the remaining were males. As a result no significant difference was seen based on gender and sex. Anti-*H. pylori* antibody was positive in 25.2% and 24% of the case group and the control group respectively. No significant association between positive results for IgG antibody and AD was found. There was no significant association between IgG level and other variables including rhinitis, asthma and food allergy as well (**Table 1**).

Discussion

Atopic dermatitis (AD) is a complex and multifactorial disease. The prevalence of AD has increased in the recent years.[1] The pathogenic mechanisms of AD are not completely understood. There are increasing evidences supporting idea that changing patterns of microbial exposure in early life may be a basic underlying factor that may lead to allergic conditions such as AD.[13] Corrado *et al*. in a study in Italy reported an increase in anti-*H. pylori* IgG antibody in children with AD, as the sole manifestation of food allergy, so they concluded that such an increase in *H. pylori* antibodies may occur prior to clinically obvious AD. The gastric mucosal damage caused by *H. pylori* may trigger an allergic reaction to food. Accordingly an increase in the serum level of IgE leads to the synthesis and release of cytokines that sustain chronic allergic

inflammations such as AD.[6] However, there is another theory suggesting that food allergy may begin prior to infection with *H. pylori*. In patients with food allergy, the gastric mucosa may become inflamed and as a result promote *H. pylori* adhesion.[21] In a study conducted in Turkey Murakami *et al*. reported a 14-year-old girl with AD and *H. pylori* infection in which after eradication of *H. pylori* infection, the clinical signs of AD almost fully disappeared.[22] In a study conducted in Japan Sakurane *et al*. investigated 198 patients with refractory skin diseases (including AD) for *H. pylori* infection. Positive anti *H. pylori* antibodies were detected in 102 out of 198 of these patients. Eradicative therapies were effective and led to improvement of the symptoms of chronic urticaria, nummular dermatitis and prurigo chronica multiforme in 60%, 54% and 50% of the patients, respectively. They concluded that persistent infection with *H. pylori* in such chronic skin diseases, may act as a triggering factor that deteriorates the state of the disease into an intractable and chronic form.[8] In another study conducted in Germany, Wedi *et al*. reviewed the role of *H. pylori* in skin diseases. They pointed out increased mucosal permeability to alimentary antigens, immunomodulation, an autoimmune mechanism or impairment of vascular integrity as possible mechanisms in which *H. pylori* may trigger skin diseases.[9] In a study accomplished in Mexico, Lopez *et al*. expressed that there is no evidence to support a direct causal effect for *H. pylori* infection in allergic diseases, but *H. pylori* may somehow has an indirect role in such diseases.[7]

On the other hand Mccune *et al*. in a study in UK demonstrated a 30% decline in the incidence of the 3 atopic disorders (including asthma, AD and allergic rhinitis) in patients who had active *H. pylori* infection. It was proposed that childhood infections may have an essential role in the appropriate development of immune system.[10] Linnenberg *et al*. and Cremonini *et al*. in a study in Denmark have indicated that early childhood infections may downregulate immune system, leading to a decline in both allergic reactions and autoimmune disorders, as well.[12]

There might be some plausible factors in explaining why some studies disagree on a possible role for *H. pylori* in AD. The possible factors are as follow:

The definition of groups varies in some studies: different studies have used various criteria to make a diagnosis of AD, and methods to assess the *H. pylori* infection were different as well. Some studies used invasive methods (such as urea breath test) to assess *H. pylori* infection, whereas others (as ours) measured the positivity of anti-*H. pylori* antibody as a marker for the infection.

1. Age: as the rate of *H. pylori* infection varies among different age groups, the mean age of the participants may have a possible effect on the positivity of *H. pylori* in different studies.
2. There may be a possible role for genetic and HLA factors on this association.
3. Study design: different study designs may lead to different results, e.g. cohort, cross-sectional or case-control study.
4. Information and selection biases and confounding.
5. Different sample size.

Conclusion

Our study showed no association between AD and infection with *H. pylori* in Iranian children. Still this association is a controversial issue. So a large sample size clinical trial may provide a reasonable answer to this question. On the other

hand studies from countries with different ethnic and racial origins may help to find out the effect of possible genetic factors on this association if any.

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