

## IgE levels are increased in patients with *Helicobacter pylori* infection

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### Abstract

**Background and Aims:** Studies have not been able to prove an association between allergy and *Helicobacter pylori* (*H. pylori*) infection. The goal of this study is to evaluate the association of total immunoglobulin E (IgE) level, as a criterion for the presence of allergy, and *H. pylori* infection.

**Methods and Materials:** Seventy two patients with dyspepsia referring to endoscopy were included in this study. Anti-*H. pylori* IgG, anti-*H. pylori*-CagA IgG, and total plasma IgE levels were measured using enzyme linked immunosorbent assay and then statistically analyzed.

**Results:** Forty out of 72 patients had *H. pylori* infection, out of which 32 patients were CagA positive. Mean IgE level had a significant increase in the patients with *H. pylori* infection ( $p < 0.05$ ), but there was no significant difference between IgE levels of the CagA-positive and -negative groups ( $p = 0.175$ ).

**Conclusion:** Our study demonstrated a clear association between allergy and *H. pylori* infection.

**Keywords:** *Helicobacter pylori*, IgE, Allergy, Cag-A

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### Introduction

*Helicobacter pylori* (*H. pylori*) is the cause of chronic gastritis, peptic ulcer, and gastric cancer. Recent studies have also shown that it may be associated with non-gastric conditions such as asthma and allergy. About 50-60% of *H. pylori* strains produce a 128 kDa protein called CagA encoded by CagA gene. CagA positive strains are more pathogenic and associated with gastric and duodenal ulcers and gastric cancer. The mechanism of carcinogenesis by these strains includes the induction and expression of the oncogenes c-fos and c-jun, cell cycle dysregulation, and eventually cell damage(1, 2).

Primary immune response to *H. pylori* includes both humoral (local and systemic) and cellular responses. The dominant T cell response is of Th1 type which results in the activation of macrophages and increase in their

bactericidal activity by inducing the expression of cytokines such as interferon- $\gamma$  (IFN- $\gamma$ ), interleukin-18 (IL-18), IL-12, and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ). On the other hand, the number of IFN $\gamma$  secreting cells is associated with the severity of gastritis(3).

Cytokines secreted by Th2 cells like IL-4 increase immunoglobulin E (IgE) production and are involved in type I hypersensitivity reactions. A comparison between allergic and non-allergic people denotes an increased level of IL-4 in the former group. IL-4 and IgE levels are regulated by the suppressive effects of Th1-derived cytokine (e.g. IFN $\gamma$ ). Therefore, there is a balance among the Th2 cytokines, which augments the IgE response, and Th1 cytokines, which suppress the IgE response(4). Based on the animal models of intestinal worm infections, which have high IgE levels, it has been shown

that Th1 responses have been modified and gastric atrophy caused by *H. pylori* infection has been decreased. So, it has been postulated that, in allergic people with increased Th2 response, *H. pylori*-induced gastritis may be decreased. Furthermore, inflammation caused by *H. pylori* (especially, CagA+ strains) may damage the integrity of gastric barrier and, therefore, increase the transmission of food antigens and incidence of allergic reactions(5). We try to compare the total IgE level among the patients with and without *H. pylori* infection and also among the patients infected with CagA+ versus CagA- strains.

## Materials and Methods

Patients with a complaint of dyspepsia referring to the endoscopy unit for esophagogastrosopic studies were include in this study. The patients with a history of gastrointestinal surgery, malignancy, use of antibiotics, bismuth, H2 blockers, proton pump inhibitors, and non-steroidal anti-inflammatory drugs during the last 4 weeks were excluded from the study. The study was approved by Research Ethics Committee of Urmia University of Medical sciences and a written informed consent was taken from each patient before their participation.

The patients were evaluated for anti-*H. pylori* antibody (anti-*H. pylori* IgG and anti-*H. pylori* CagA IgG) if rapid urease tests were positive using commercial enzyme linked immunosorbent assay (ELISA) kits (DiaPro Co. Ltd., Milan, Italy). Total plasma IgE level was measured in all the patients and the patients with the IgE level of more than 160 IU/ml were considered positive.

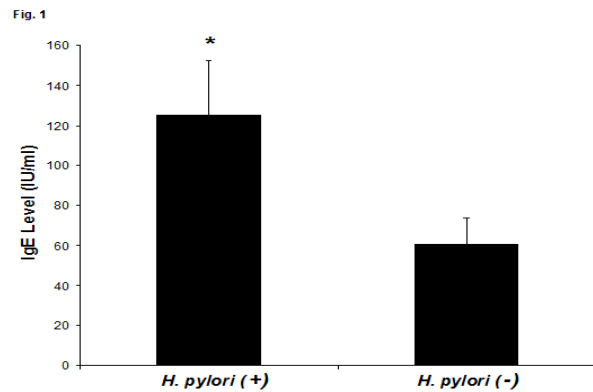
Statistical analysis was carried out using one-way ANOVA, Chi-square, and Mann-Whitney U tests. P-values <0.05 were considered statistically significant.

## Results

Seventy two patients with dyspepsia who underwent an esophagogastrosopy were entered into the study. Out of the 72 patients, 34 (47.2%) were male and 38 (52.8) were female with the mean age of  $41.4 \pm 14.85$  years

old. Forty patients (55.5%) had *H. pylori* infection and 23 (57.5%) of them were positive for anti-*H. pylori*-CagA antibody.

The IgE level in *H. pylori*+ and *H. pylori*- patients was  $124.9 \pm 27.2$  and  $60.5 \pm 13.1$  IU/ml, respectively (Figure 1).

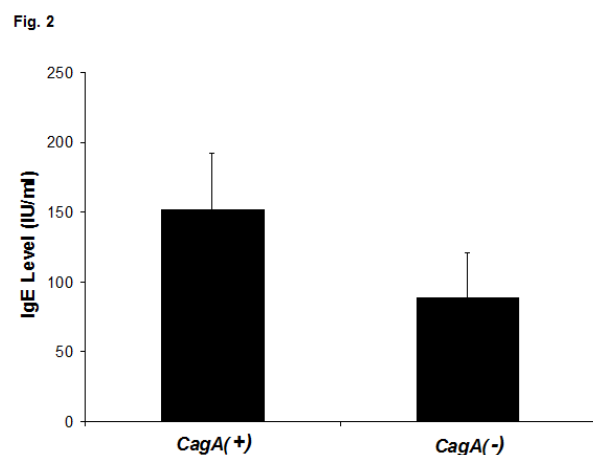


**Figure 1-** IgE level in *H. pylori* + and *H. pylori*- patients.

The IgE level in *H. pylori*+ patients was significantly more than that in *H. pylori*- patients.

\*  $p < 0.05$

The IgE level in *H. pylori*+ patients was significantly higher than *H. pylori*- patients ( $p < 0.05$ ). However, the IgE content of *H. pylori*-infected patients with anti-CagA antibody was more than that of *H. pylori*-infected patients without anti-CagA antibody ( $151.8 \pm 40.5$  and  $88.7 \pm 32.2$  IU/ml, respectively); the difference was not significant (Figure 2).

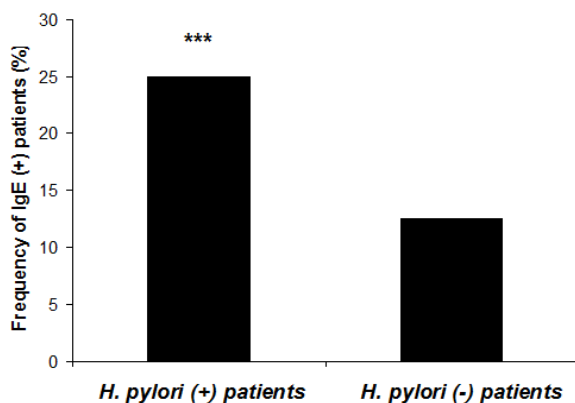


**Figure 2-** IgE content of *H. pylori*-infected patients with and without anti-CagA antibody.

The IgE content of *H. pylori*-infected patients with anti-CagA antibody was more than that of *H. pylori*-infected patients without anti-CagA antibody, but the difference was not significant.

As mentioned above, the patients with IgE level of more than 160 IU/ml were considered positive. IgE content of more than 160 IU/ml was present in 25.0% (10/40) *H. pylori*+ patients and 12.5% (4/32) of *H. pylori*- patients ( $p<0.001$ ) (Figure 3).

Fig. 3

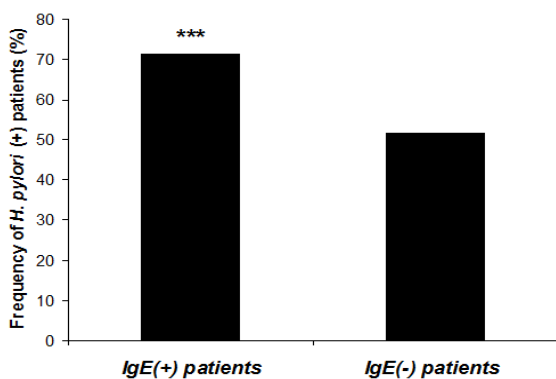


**Figure 3-** Frequency of IgE positive patients.

The frequency of IgE positive patients among *H. pylori*+ and *H. pylori*- patients was 25.0% and 12.5%, respectively.

\*\*\*  $p<0.001$

Fig. 4



**Figure 4-** Frequency of *H. pylori*+ cases among IgE+ and IgE- patients.

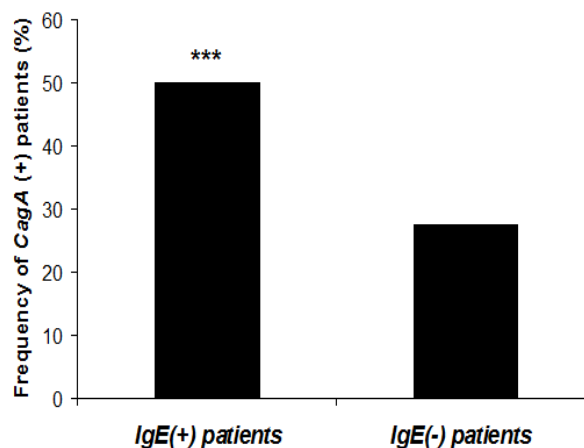
The frequency of *H. pylori* cases among IgE+ and IgE- patients was 71.4% and 51.7%, respectively.

\*\*\*  $p<0.001$

The overall frequency of *H. pylori* cases among IgE+ and IgE- patients was 71.4% (10/14) and 51.7% (30/58), respectively ( $p<0.001$ ) (Figure 4).

Anti-CagA antibody was present in 50.0% (7/14) of IgE+ patients and 27.6% (16/58) of IgE- patients ( $p<0.001$ ) (Figure 5).

Fig. 5



**Figure 5-** Frequency of CagA+ cases among IgE+ and IgE- patients.

Anti-CagA antibody was present in 50.0% of IgE+ patients and 27.6% of IgE- patients.

\*\*\*  $p<0.001$

## Discussion

The relationship between *H. pylori* and allergy has not been thoroughly clarified. There are two hypotheses regarding *H. pylori* infection and allergy. The first one states that allergic people are prone to be affected by *H. pylori* infection (6-8). In people with food allergy, the reaction of gastric mucosa to allergens would be manifested as paleness, edema, and exudation; these changes in the gastric mucosa of people infected with *H. pylori* can develop the infection via increasing the adhesiveness of bacteria to epithelial cells. Carrudo and et al. demonstrated that the rate of infection with *H. pylori* was higher among the children with food allergy than the control group(6).

De-lazzari et al. demonstrated that, after 6 months of treatment, ulcer relapse was observed in the patients with high IgE (35.9%) and normal IgE (11.9%). Therefore, considering its high percentage among people with high level of IgE, they concluded that immuno-allergic reaction intervenes in some forms of gastritis and peptic ulcer (7). In a study by Corrado et al., it was demonstrated that antibody against *H. Pylori* increases in the patients with atopic dermatitis (8).

However, the present study demonstrated positive correlation between high levels of IgE in patients with *H. pylori* infection. In addition, 25% of the people with infection and 12.5% of those without infection showed a high level of IgE in serum, which indicated a significant difference. The corresponding levels found in MerviLiutu's study were 64% and 39% as well as 36% and 26% in Kalho's study, respectively, which was not significant (9, 10). This significant relationship was also found for CagA. We should point out, however, that Corrado could not find any relationship between allergy and CagA in his study, because the level of IgG against CagA was not significantly high in the patients (6). The second hypothesis states that allergy might be secondary to *H. pylori* infection (9-12). Studenikin et al. observed a significant increase in IgE titer in the patients infected with *H. pylori* compared with the control group (12). Figuro et al. also demonstrated this positive relationship for *H. pylori*-CagA (5).

Gastric mucosa which acts as a barrier against antigens is destroyed by *H. pylori*. Thus, increase in the flow of food antigens passing through increases the possibility of allergic reaction. Because of the increased epithelial secretion of CagA+ strains, a special path is established for allergens which stimulate the IgE response in atopic people (5). Bacteria colonization in gastro defers its defecation and provides more bacterial penetration into the digestive system (13). Another mechanism relevant to the second theory is the stimulation of systemic sympathetic nervous system and increase in its tone due to *H. pylori* infection. The increased sympathetic tone may shift the immunological

responses toward Th2 that in turn increases the ability of the immune system to induce allergic reaction (14).

Despite considering the contradictory findings, our results demonstrated significantly positive correlation between *H. pylori* infection and the production of IgE antibody as an indicator for the susceptibility to allergy (5-8, 13, 15, 16), which can be used for optimizing the strategies for the treatment of allergic patients.

### Acknowledgments

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### Conflicts of interest:

The authors declare no conflict of interest.

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