Sana'a University Journal of Medical and Health Sciences https://journals.su.edu.ye/index.php/jchm
Vol. 17 | No. 1 | Page 21 – 27 | 2023 | ISSN: 2958-7476
Doi:10.59628/jchm.v17i1.210

The association of Helicobacter pylori infection with increased total IgE antibodies in Sana'a city, Yemen: a case-control study

Abdulsalam Mohammed Al-Mekhalfi[1], Eman Ali Hamzah[2], Arwa Mohammed Othman[2,*], Khaled Abdul Karim Al-Moyed[2], Walid M. S. Al-Murisi[1,] Ibtisam Al hajj Hassan[3]

[1] Department of Parasitology, Faculty of Medicine and Health Sciences, Sana'a University, Yemen.
[2] Department of Medical Microbiology, Faculty of Medicine and Health Sciences, Sana'a University, Yemen.
[3]Department of Dermatology, Faculty of Medicine and Health Sciences, Sana'a University, Yemen

***Corresponding author:** arwaothman@hotmail.com

ARTICLE INFO
Article history:
Received: April 20, 2023
Accepted: May 1 2023
Published: June, 2023

KEYWORDS
1. Helicobacter pylori
2. total IgE
3. food allergy
4. Yemen

ABSTRACT

Background: This study aimed to determine the association between *Helicobacter pylori* (*H. pylori*) infection and the total serum IgE antibodies.

Methods: This case-control study was conducted during a period from August 2018-July 2020. Two hundred individuals were enrolled in this study. They were divided into 100 individuals infected with *H. pylori* (case group) and 100 individuals were not infected with *H. pylori* (control group). Three ml peripheral blood was withdrawn from each individual. The blood sample was used for the detection of total IgE antibodies using an electrochemiluminescence immunoassay. A stool sample was collected from each individual for the determination of *H. pylori* antigen using a rapid immunochromatography assay.

Results: Total IgE antibodies were positive among 46% of *H. pylori*-infected cases versus 19% of controls. There was a statistically significant association between *H. pylori* infection and total IgE antibodies (p=0.001). Regarding the risk factors for *H. pylori* infection, there was a statistically significant association between smoking and *H. pylori* infection. In contrast, there was no statistically significant association between the type of water, washing vegetables, washing and chewing qat, and family history with *H. pylori* infection.

Conclusions: It could be concluded that total IgE antibody level increased in patients infected with *H. pylori* compared to the non-infected individuals.

1. Introduction:

Background

Helicobacter pylori (*H. pylori*) infection is a common, usually lifelong, infection that is found worldwide [1]. More than half of the world's population is infected with this pathogen and humans are considered the only reservoir of the pathogen [2, 3]. The stages of *H. pylori* infection are: crossing the gastric mucus layer, adhesion to the gastric epithelium, and then obtaining nutrients while avoiding to be defeated by the host immune response [4].

H. pylori infection generates a state of inflammation, which however is asymptomatic in the majority of patients. Gastric inflammation may evolve toward chronic gastritis, peptic ulcer, and gastric cancer in some cases. After entering the stomach, most *H. pylori* organisms are living free in the mucosal layer, some organisms attach to the epithelial surface of gastric epithelial cells, while small members

have been shown to invade epithelial cells [4, 5, 6].

Allergy (also called atopy) is defined as an immediate exaggerated immune response to common environmental harmless allergens which elicit an immunoglobulin E (IgE) antibodies response [7, 8]. IgE antibody class plays a key role in the pathogenesis of atopic diseases such as asthma, allergic rhinitis, and atopic dermatitis [9]. Hypersensitivity reaction may cause a wide range of symptoms from minor inconvenience to death. The reaction usually takes 15-30 minutes from the time of exposure to the allergen, although sometimes it may have a delayed onset (10-12 hours) [10, 11]. In the early phase of response, the primary cellular components are the mast cells and basophils. The reaction is amplified and/or modified in the late phase by eosinophils, neutrophils, and platelets [12].

Food allergens are defined as those specific components of food that are recognized by allergen-specific immune cells and elicit a specific immunologic reaction, resulting in characteristic symptoms. Current data proposes that food allergies are common, influencing about 10% of infants in some countries. The prevalence of food allergy cases has been growing in the last few years. This rising in allergy prevalence has especially affected developed countries, though there is now increased evidence in developing countries [13]. More than 90% of food allergies are due to the ingestion of peanuts, milk, eggs, wheat, soybean, fish, nuts such as walnuts and almonds [14].

The allergic process is described to be exacerbated by the presence of *H. pylori* which causes inflammation of the gastrointestinal mucosa resulting in a greater mucosal permeability which might allow more food allergens to cross epithelial to gastric submucosa. Allergic sensitization then occurs and the T-helper-2 (Th2) response leads to increase production of IgE antibodies, which then binds to the high-affinity receptor on the mast cell surfaces located in the skin and mucosa [15, 16]. We aimed to determine the association between *H. pylori* infection and the total serum IgE antibodies.

2. Methods

This study was a case-control study conducted on 200 subjects during a period from August 2018-July 2020. Two hundred individuals were enrolled in the study and were divided into two groups. The first group consisted of 100 patients who are infected with *H. pylori* (50 females and 50 males) whereas the second group consisted of 100 healthy controls (50 females and 50 males). They attended the main general hospitals in Sana'a city, namely: Al-Thawra Modern General Hospital, Al-Gumhouri Teaching Hospital, and Al-Kuwait University Hospital. The study was approved by Research Ethics Committee at the Faculty of Medicine and Health Sciences, Sana'a University. All procedures were performed according to the regulations and guidelines of the Research Ethics Committee.

Inclusion Criteria

Individuals of any age and gender.

Exclusion Criteria

Individuals who were malnourished and/or infected with parasites were excluded from the study. Pregnant women, patients with liver or kidney diseases as well as those who were treated with antibiotics or proton pump inhibitors were also excluded.

Data collection

Data such as demographic data, allergic symptoms, gastritis, and the relevant risk factors were collected from each participant using a predesigned questionnaire.

Specimen collection

A- Stool specimens

About one gram of fresh stool was collected in a clean, dry, waterproof container containing no detergents.

B- Blood specimens

Three ml of venous blood was withdrawn from each individual into a plain tube. The sample was allowed to clot at room temperature and was centrifuged at 3500 rpm for five minutes, and then serum was separated from each sample into Eppendorf tubes and stored at -20°C till being tested [17].

Stool analysis

The presence of *H. pylori* infection was detected by a monoclonal stool antigen test using a chromatographic immunoassay (Abon Biopharm, Hangzhou, Co., Ltd, China). The analysis was performed according to the manufacturer's instructions. A portion of the stool sample was mixed with the test diluent until the sample had been dissolved. The suspension was allowed to settle for 5 minutes at room temperature and then 100 µL of the liquid phase of the sample was placed on the *H. pylori* Ag test cassette. The test results were read after 15 minutes. One red line indicated a negative result while a double red line indicated a *H. pylori*-positive result.

In addition, all stool samples were examined microscopically using the modified formol-ether concentration method to exclude intestinal parasites infestation. Individuals with parasitic infections were subsequently excluded from the study [18].

Serum IgE test

Serum total IgE antibodies were measured using a quantitative electrochemiluminescence immunoassay "ECLIA" which works on a full automated immunoassay analyzer (Cobas e 411, Close system, Roche, Germany). Two monoclonal antibodies were used to detect IgE antibodies in the serum of the participants: Biotinylated monoclonal anti-IgE antibody and monoclonal anti-IgE antibody labeled with ruthenium. High IgE levels were determined based on the manufacturer's recommended threshold values by age range.

3. Statistical Analysis

All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) program version 20. Chi-square (χ^2) and Mann-Whitney U tests were used for the comparison of two variables. *p-value* ≤0.05 was considered statistically significant.

4. Results

The mean age of *H. pylori*-infected individuals was 35 ± 12.8 years while the mean age of controls was 35 ± 12.7 years. Serum IgE was found to be high in 46 (46%) of patients infected with *H. pylori* and in 19 (19%) of controls. Based on the age groups, the highest IgE levels were found in the age group 21 to 40 years old in both *H. pylori*-infected individuals and controls (69.6%, 63.1%, respectively). Twenty-four (52%) of males and 22 (48%) females in the patient group had high serum levels of IgE in comparison to 12 (63%) males and 7 (37%) females of the control group who had elevated IgE antibodies, table 1.

Table 1: Characteristics of the study population

Age groups/ years	*H. pylori*-infected patients				Controls			
	Total IgE antibodies results No.=100				Total IgE antibodies results No.=100			
	Positive		Negative		Positive		Negative	
	No.	%	No.	%	No.	%	No.	%
≤ 20	2	**4.3**	5	**9.3**	1	**5.3**	4	**4.9**
21–40	32	**69.6**	35	**64.8**	12	**63.1**	54	**66.7**
41–60	10	**21.7**	14	**25.9**	6	**31.6**	22	**27.2**
≥ 61	2	**4.3**	0	**00.0**	0	**00.0**	1	**1.2**
Total	**46**	**46**	**54**	**54**	**19**	**19**	**81**	**81**
Mean+SD	**35 ± 12.8**				**35 ± 12.7**			
Males	**24**	**52**	**26**	**48**	**12**	**63**	**38**	**47**
females	**22**	**48**	**28**	**52**	**7**	**37**	**43**	**53**
Total	**46**	**100**	**54**	**54**	**19**	**100**	**81**	**100**

The median of total IgE concentrations in patients infected with *H. pylori* was 113.8 with a range of 6-2500 IU/ml, while the median in the control group was 87.2 with a range of 6–509 IU/ml. The IgE antibodies median of the patients was statistically significant *versus* the median of the control group (Mann-Whitney U =3666.5, *p* = 0.001), table 2.

Table 2: The association of *H. pylori* infection with total IgE antibodies

Total IgE antibodies results	*H. pylori-positive* No.=100	*H. pylori-negative* No.=100	Mann-Whitney U (95% CI)	*P*
Median (range)	113.8 (6 – 2500 IU/ml)	87.2 (6 – 509 IU/ml)	3666.5	0.001

Table 3 shows the risk factors for *H. pylori* infection. Fifty-nine (49.2%) of *H. pylori*-infected patients and 61 (50.8%) controls drank treated water. Forty-eight (47.5%) of patients infected with *H. pylori* and 53 (52.5%) controls cleaned their water tanks regularly. Regarding chewing qat, 22 (46.8%) of patients washed qat before chewing, while 25 (53.2%) of the controls washed the plant before chewing. Seventy-five (53.2%) of the patients and 66 (46.8%) of the controls were chewing qat. Considering vegetables washing before ingestion, 88 (48.9%), patients and 92 (51.1%) controls washed vegetables before eating. Forty-five (56.2%) *H. pylori* patients had a family history of *H. pylori* infection, whereas 35 (43.8%) controls reported family history. There were no statistically significant results related to the type of water, cleaning water tank, washing and chewing qat, washing vegetables before consuming, and having a family history of *H. pylori* infection. Irrespective of type, smoking was found to be associated significantly with *H. pylori* infection among patients 45 (60%) compared to 30 (40%) controls (χ^2 =4.8, *p* =0.03).

Table 3: The risk factors for *H. pylori* infection in Sana'a city, 2019

Risk factors		*H. pylori*-infected patients No.= 100		Controls No.=100		Total No.= 200		OR	95%CI		χ^2	*P*
		No.	%	N	%	N	%		L	U		
Type of water	Piped	59	**49.2**	61	**50.8**	120	**100.0**	1.1	0.6	1.9	0.08	0.8
	Others	41	**51.2**	39	**48.8**	80	**100.0**					
Cleaning water tank	Yes	48	**47.5**	53	**52.5**	101	**100.0**	1.2	0.7	2.1	0.5	0.5
	No	52	**52.5**	47	**47.5**	99	**100.0**					
Washing qat	Yes	22	**46.8**	25	**53.2**	47	**100.0**	1.5	0.7	2.9	1.2	0.3
	No	53	**56.4**	41	**43.6**	94	**100.0**					
Chewing qat	Yes	75	**53.2**	66	**46.8**	141	**100.0**	1.5	0.8	2.9	1.9	0.2
	No	25	**42.4**	34	**57.6**	59	**100.0**					
Washing Vegetables	Yes	88	**48.9**	92	**51.1**	180	**100.0**	1.6	0.6	4.0	0.9	0.3
	No	12	**60.0**	8	**40.0**	20	**100.0**					
Smoking	Yes	45	**60.0**	30	**40.0**	75	**100.0**	1.9	1.1	3.4	4.8	0.03
	No	55	**44.0**	70	**56.0**	125	**100.0**					
Family history	Yes	45	**56.2**	35	**43.8**	80	**100.0**	1.5	0.9	2.7	2.1	0.2
	No	55	**45.8**	65	**54.2**	120	**100.0**					

OR: Odds ratio >1 (**at risk**), **CI:** Confidence interval, **L:** Lower, **U:** Upper, **χ 2:** Chi-square ≥3.84 (**significant**), ***p*:** Probability value ≤0.05 (**significant**)

5. Discussion

The result of this study showed a statistically significant association between *H. pylori* infection and total IgE antibodies (*p*=0.001). This result was in agreement with studies conducted in Iran by Rasmi and co-workers [19] who found *H. pylori* infection to be significantly associated with total plasma IgE levels; in Egypt by Shabrawy and Gharib [20] who reported H. pylori to be a predisposing risk factor for urticaria and food allergies. Our study is also in agreement with a study conducted in Italy by Figura and co-workers [21] who found CagA-positive *H. pylori* individuals with increased serum IgE levels than CagA negative *H. pylori* individuals. On other hand, our result disagreed with that reported by Kolho and co-workers [22] in Finland, who found *H. pylori* infection did not affect the manifestation of specific IgE to major food allergens in school-aged children. Moreover, this result disagreed with that

reported by Lee and co-workers [23] who stated that IgE hypersensitivity was not directly correlated with *H. pylori* infection among Korean individuals. In contrast, our findings were dissimilar to those reported by Konturek *et al* [24] who reported infection by *H. pylori* to be associated with a decreased risk for food allergy. Nevertheless, Melby *et al* [25] found that acquisition of *H. pylori* in school-age did not appear to influence the risk of asthma development in later childhood.

The association between *H. pylori* and allergy has not been fully explained and there are two propositions regarding *H. pylori* infection and allergy. The first one suggests that ulceration due to *H. pylori* infection causes damage to the gastric epithelial barrier. As a result of the damaged barrier, allergens and other intact macromolecules that enter into the stomach candiffuse into the sub-mucosa and be taken up by dendritic cells and macrophages. Dendritic cells and macrophages processed and presented these antigens to T helper in association with MHC class II molecules. Activated T helper cells are differentiated into Th2 subsets, which mount an IgE immune response that could result in allergic reactions [11, 21, 26, 27, 28, 29].

The second proposition suggests that *H. pylori* infection correlates with a reduced risk of atopy and allergic disorders. This suggestion is based on the hygiene hypothesis which links early environmental and microbial exposure to the decrease of atopic allergies and asthma. Early studies have shown that the hygiene hypothesis may be related to Th1/Th2 imbalance [30, 31].

This study reveals a statistically significant association between smoking and *H. pylori* infection (p=0.03). This finding may reflect less awareness of the mode of *H. pylori* transmission via the oral-oral route irrespective of smoking types. This result agreed with the findings reported by Cardenas and Graham [32] in the USA, who reported smoking to be associated with an increased prevalence of *H. pylori* infection. Moreover, the same result was reported by El-Barrawy and co-workers [33] in Egypt. Their study showed a significant association between *H. pylori* infection and smoking, especially among heavy cigarette smokers. Nevertheless, this study result disagreed with that found by Ferro and co-workers [34] in Portugal, who had reported no significant association between smoking and *H. pylori* seropositivity. They also reported that the strength of the association between smoking and *H. pylori* infection did not increase with the intensity or duration of smoking. Disagreement between this study result and Ferro and his co-worker's result may contribute to using different techniques, where this study detected *H. pylori* stool antigens, whereas Ferro and co-workers contribute detected *H. pylori* antibodies in patient serum.

6. Conclusions

The study concludes that total IgE antibody level increased in patients infected with *H. pylori* compared to the non-infected individuals, and a significant association between *H. pylori* infection and smoking.

Declarations

Ethics approval and consent to participate

The study was approved by the Faculty of Medicine and Health Sciences, Sana'a University, and heads of schools. Before samples collection, each participant gave a written informed consent.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article. The data of this study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

The authors didn't take any fund for this study

Authors' contributions

AMA, EAH, AMO and KAA contributed equally to the design, implementation, statistical analysis, and manuscript drafting. All authors read and approved the final manuscript.

Acknowledgments

The authors are grateful to all individuals who participated in this study.

7. References

[1] Crowe SE. *Helicobacter pylori* Infection. New England Journal of Medicine. 2019;380(12):1158-1165.

[2] Sachs G, Scott DR, Wen Y. Gastric Infection by *Helicobacter pylori*. Current Gastroenterology Reports. 2011;13(6):540-546.

[3] Zamani M, Vahedi A, Maghdouri Z, Shokri-Shirvani J. Role of Food in Environmental Transmission of *Helicobacter pylori*. Caspian Journal of Internal Medicine. 2017;8(3):146-152.

[4] Ruggiero P. *Helicobacter pylori* and Inflammation. Current Pharmaceutical Design. 2010;16(38):4225-4236.

[5] Ruggiero P. *Helicobacter pylori* Infection: What's New? Current Opinion in Infectious Diseases. 2012;25(3):337-344.

[6] Moyat M, Velin D. Immune responses to *Helicobacter pylori* infection. World J Gastroenterol. 2014;20(19):5583-5593.

[7] Douglass JA, O'Hehir RE. Diagnosis, Treatment and Prevention of Allergic Disease: The Basics. Medical Journal of Australia. 2006;185(4):228-233.

[8] Burton OT, Oettgen HC. Beyond Immediate Hypersensitivity: Evolving Roles for IgE Antibodies in Immune Homeostasis and Allergic Diseases. Immunological Reviews. 2011;242(1):128-143.

[9] Wu LC, Zarrin AA. The Production and Regulation of IgE by the Immune System. Nature Reviews Immunology. 2014;14(4):247-259.

[10] Li Z. Auto-immune Diseases Caused by Overactive Immune System. Topics in Health and Biomedical Engineering. 2018;1(1):6-8.

[11] Abbas AK, Lichtman AH, Pillai S. Cellular and molecular immunology. 10th edition. Philadelphia. ELSVIER. 2021.

[12] Fischer J, Biedermann T. Delayed immediate-type hypersensitivity to red meat and innards: current insights into a novel disease entity. J Dtsch Dermatol Ges. 2016;14(1):38-44.

[13] Loh W, Tang MLK. The Epidemiology of Food Allergy in the Global Context. Int J Environ Res Public Health. 2018;15(9):2043.

[14] Boye JI. Food allergies in developing and emerging economies: need for comprehensive data on prevalence rates. Clin Transl Allergy. 2012;2(1):25.

[15] Ma ZF, Majid NA, Yamaoka Y, Lee YY. Food Allergy and Helicobacter pylori Infection: A Systematic Review [published correction appears in Front Microbiol. 2016; 7:1232]. Front Microbiol. 2016; 7:368.

[16] Anvari S, Miller J, Yeh, CY, Davis CM. IgE-Mediated Food Allergy. Clinical Reviews in Allergy and Immunology. 2019; 57(2):244-260.

[17] Turgeon ML. Immunology and serology in laboratory medicine. Sixth edition. Florida, ELSEIVER,2014.

[18] Hoffman WA, Pons JA, Janer JL. The sedimentation-concentration method in Schistosomiasmansoni. Puerto Rican J Public Health Trop Med. 1934;2:283-298.

[19] Rasmi Y, Zafarshamspoor S, Sadreddini M, Sayyadi H, Hasani R, Gholizadeh S., et al. IgE Levels are Increased in Patients with *Helicobacter pylori* Infection. International Journal of Research in Applied and Basic Medical Sciences. 2015;1(1):51-55.

[20] Shabrawy RM, Gharib K. Helicobacter pylori Infection as a Risk Factor in Patients Suffering from Food Allergy and Urticaria. Egypt J Immunol. 2016; 23(1):67-75.

[21] Figura N, Perrone A, Gennari C, Orlandini G, Bianciardi L, Giannace R., et al. Food Allergy and *Helicobacter pylori* Infection. Italian Journal of Gastroenterology and Hepatology. 1999;31(3):186-191.

[22] Kolho KL, Haapaniemi A, Haahtela T, Rautelin H. *Helicobacter pylori* and Specific Immunoglobulin E Antibodies to Food Allergens in Children. Journal of Pediatric Gastroenterology and Nutrition. 2005;40(2):180-183.

[23] Lee SP, Lee SY, Kim JH, Sung IK, Park HS, Shim CS., et al. Correlation between *Helicobacter pylori* Infection, IgE Hypersensitivity, and Allergic Disease in K orean Adults. *Helicobacter*. 2014;20(1):49-55.

[24] Konturek PC, Rienecker H, Hahn EG, Raithel M. Helicobacter pylori as a protective factor against food allergy. Med Sci Monit. 2008;14(9):CR452-CR458.

[25] Melby KK, Carlsen KL, Håland G, Samdal HH, Carlsen KH. *Helicobacter pylori* in early childhood and asthma in adolescence. BMC Res Notes. 2020;13(1):79.

[26] Borch K, Sjostedt C, Hannestad U., et al. Asymptomatic Helicobacter pylori gastritis is associated with increased sucrose permeability. Dig Dis Sci. 1998; 43:749–53.

[27] Fukuda Y, Bamba H, Okui M., et al. Helicobacter pylori infection increases mucosal permeability of the stomach and intestine. Digestion 2001;63 Suppl 1:93–96.

[28] Matysiak-Budnik T, Coffin B, Lavergne-Slove A, Sabate JM, Mégraud F, Heyman M. Helicobacter pylori increases the epithelial permeability to a food antigen in human

gastric biopsies. Am J Gastroenterol. 2004;99(2):225-232.
[29] Gould HJ, Sutton BJ. IgE in allergy and asthma today. Nat Rev Immunol. 2008; 8(3):205-217.
[30] Leaker BR, Singh D, Lindgren S., et al. Effects of the Toll-like receptor 7 (TLR7) agonist, AZD8848, on allergen-induced responses in patients with mild asthma: a double-blind, randomised, parallel-group study. Respir Res. 2019;20(1):288.
[31] Zuo ZT, Ma Y, Sun Y, Bai CQ, Ling CH, Yuan FL. The Protective Effects of Helicobacter pylori Infection on Allergic Asthma. Int Arch Allergy Immunol. 2021;182(1):53-64.
[32] Cardenas VM, Graham DY. Smoking and *Helicobacter pylori* Infection in A sample of US Adults. Epidemiology. 2005;16(4): 586-590.
[33] El-Barrawy MA, Morad MI, Gaber M. Role of *Helicobacter pylori* in the Genesis of Gastric Ulcerations among Smokers and Nonsmokers. EMHJ-Eastern Mediterranean Health Journal. 1997;3 (2):316-321.
[34] Ferro A, Morais S, Pelucchi C., et al. Smoking and *Helicobacter pylori* Infection: An individual Participant Pooled Analysis (Stomach Cancer Pooling-StoP Project). European Journal of Cancer Prevention. 2018;28(5):390-396.