



Association of Chronic Urticaria with *Helicobacter pylori* Infection in Duhok City, Kurdistan Region of Iraq

Sarah R Al-Naemi¹, Barzan K Al-Mirani² and Nawfal R Hussein^{3,*}

¹Department of Dermatology, College of Medicine, University of Duhok, Duhok, Iraq

²Department of Dermatology, Azadi Teaching Hospital, Duhok, Iraq

³College of Medicine, University of Zakho, Zakho, Iraq

*Corresponding author: College of Medicine, University of Zakho, Zakho, Iraq. Email: nawfal.hussein@yahoo.com

Received 2019 May 01; Revised 2019 October 08; Accepted 2019 October 09.

Abstract

Background: *Helicobacter pylori* (*H. pylori*) infection is associated with gastric and extra-gastric manifestations such as idiopathic urticaria.

Objectives: The aim of this report was to investigate the relationship between *H. pylori* positivity and chronic urticaria.

Methods: This case control study was carried out between June 2018 and March 2019. The study was conducted at the Dermatology Consultation Unit, Azadi Teaching Hospital, Duhok, Iraq. A total of 49 patients with chronic urticaria were recruited in the study. During the study period, 95 subjects were recruited as a control.

Results: The overall *H. pylori* positivity was 106/144 (73.6%). A significant association was found between family members number and *H. pylori* positivity ($P = 0.04$; OR = 1.15; CI = 1 - 1.3). The positivity was 38/49 (77.6%) positive for the patients' group versus 70/95 (73.7%) for the control group ($P = 0.7$; OR = 1.16; CI = 0.53 - 2.57).

Conclusions: The prevalence of *H. pylori* infections was high in the region. No association was found between *H. pylori* positivity and chronic urticaria. Further study is needed to explore the effect of *H. pylori* eradication on urticaria treatment outcome.

Keywords: Chronic Urticaria, *H. pylori*, Duhok, Iraq

1. Background

Helicobacter pylori (*H. pylori*) is a Gram-negative bacillus that causes gastritis and ulceration (1). *H. pylori* predisposes to gastric cancer, which is the second most common cause of death due to cancers (1). The pathogenesis of this microorganism thought to have multifactorial etiology (2). Bacterial virulence factors, host genotypes, immune response, and environmental factors are thought to play a role in the pathogenesis of this microorganism (2). Several reports have linked *H. pylori* to a variety of extra-gastric diseases (3). These include ischemic heart disease, skin diseases such as idiopathic urticaria, autoimmune thyroiditis, thrombocytopenic purpura, iron deficiency anemia in pediatrics, Raynaud's phenomenon, scleroderma, migraine, and Guillain-Barre' syndrome (3). The exact mechanism behind this is not fully understood. However, activation of the cascade of coagulation, stimulation of atherosclerosis formation, and antigenic mimicry between the microorganism and host epitopes have been proposed as hypothetical mechanisms explaining the relationship between *H. pylori* and extra-gastric disorders (3).

Chronic urticaria is a dermatological disorder that is characterized by widespread, temporary wheals that occur on a daily basis for at least six weeks (4). Several causes have been proposed to explain chronic urticarial; this includes infections including bacteria, viral, fungal, or protozoan infection. Additionally, auto-immune antibodies are detected in about 50% of the cases suggesting inflammatory mechanisms as an etiology of this disorder (4). Several studies showed a possible relationship between *H. pylori* infection and chronic urticarial; however, such a relationship remains controversial. *H. pylori* infection was studied thoroughly in our locality (5-7).

2. Objectives

No study has been conducted investigating the association of *H. pylori* with chronic urticaria in Duhok city. Therefore, this study was designed to investigate the association between infection with this microorganism and chronic urticaria.

3. Methods

3.1. Study Design

This case control study was carried out between June 2018 and March 2019. The study was conducted at the Dermatology Consultation Unit, Azadi Teaching Hospital, Duhok, Iraq. During the survey, enrolled subjects were interviewed using a standardized questionnaire information that included age, gender, and address. The questionnaire composed of questions regarding demographical data about patients including age, gender, place of residency, and family members number (Appendix 1 in Supplementary File).

3.2. Studied Population

During the study period, all subjects who were presented to the dermatology unit with chronic urticaria were enrolled in the study. The inclusion criteria included patients with chronic urticaria, as defined as temporary wheals that occur on a daily base for at least six weeks, and agreed to be involved in the study by signing informed consent. Patients with acute urticaria, inducible (physical) urticaria, who received antibiotics in the prior two weeks, and who did not agree to sign the consent were excluded.

3.3. ELISA

A 5cc syringe and needle were used to obtain 5 mL of blood from each subject. Then, the blood samples were centrifuged at 1500 rpm for 3 min to obtain the serum. The HCV AB (fourth generation) with 100% sensitivity and specificity and the hepatitis B-specific HBsAg with a 100% sensitivity and 97.5% specificity were studied by commercial DIA.PRO diagnostic Bioprobes ELISA kit (Italy), following the manufacturer's instruction. Anti-*H. pylori* IgG ELISA (EUROIMMUN Germany) was utilized for the detection of the presence of *H. pylori*-specific IgG, according to the manufacturer's instructions. The recommended cut-off values were used.

3.4. Statistics

Linear regression was used to explore such a relationship between variables and outcomes when the variables were continuous while chi-square test was used for categorical data. P value of < 0.05 value was considered as significant.

3.5. Ethics

This project and the consent were approved by the Ethics Committee of the College of Medicine, University of Duhok. Informed consent was obtained from all recruited subjects.

4. Results

4.1. Characteristics of Patients

During the study period, 49 patients with chronic urticaria were recruited in the study. Among the recruited samples, 10/49 (20.4%) were male. The average age of participants was 36.5 ± 11 years. All patients were examined for HBsAg and HCV-AB. All patients were negative for these two viral infections. Complete blood count was normal in 47/49 (95.9%) of the recruited samples. Thyroid function was normal in all patients. Additionally, during the study period, 95 subjects were recruited as a control. Among them, 30/95 (31.6%) were male and the average age of the control group was 32.6 ± 11.4 years.

4.2. *H. pylori* Positivity

The overall *H. pylori* positivity was 106/144 (73.6%). Then, *H. pylori* positivity was compared between the patients' group and control group. The positivity was 38/49 (77.6%) positive for the patients' group versus 70/95 (73.7%) for the control group ($P = 0.7$; OR = 1.16; CI = 0.53 - 2.57). Then, we studied the association between *H. pylori* positivity and risk factors. No associations were found between *H. pylori* positivity and age, gender, and residency. A significant association was found between family members number and *H. pylori* positivity ($P = 0.04$; OR = 1.15; CI = 1-1.3) (Table 1). In addition, the prevalence of *H. pylori* positivity was higher in subjects residing in the city compared to rural areas (76.3% for city vs. 50.9% for rural areas, $P = 0.013$).

Then, the associations between *H. pylori* and risk factors were studied within the patients' group. No association was found between *H. pylori* and age, gender, family member number, or the duration of urticaria (Table 2).

5. Discussion

Infection with *H. pylori* is common and the colonization of gastric mucosa with *H. pylori* is not a disease in itself (1). However, such an infection carries risk of developing various conditions ranging from gastritis to gastric adenocarcinoma (8). In addition, infection with *H. pylori* has been linked to extra-gastric disease such as parkinsonism, asthma, heart diseases, and urticaria (9).

H. pylori infects around 50% of the world's population (1). The prevalence of infection is ranging from 20% in developed countries to up to 80% in developing countries (1). In a study conducted in Duhok, the prevalence of *H. pylori* was studied in different age groups (5). The prevalence of infection was 36% in children younger than 18 years old. In the same study, the prevalence of *H. pylori* was 78% in the adult population (5). In agreement with this, the overall

Table 1. The Association Between *H. pylori* Positivity and Different Variables

Factors	<i>H. pylori</i> Positive	<i>H. pylori</i> Negative	P Value	Odds Ratio	Confidence Interval
Family number	7.3 ± 3	7.2 ± 3	0.04	1.15	1.01 - 1.32
Age	33.8 ± 11.3	34 ± 11.4	0.65	1	0.97 - 1.04
Gender			0.15	0.56	0.25 - 1.23
Female	24/38 (63.2%)	80/106 (75.4%)			
Male	14/38 (36.8%)	26/106 (24.5%)			
Residency			0.013	0.36	0.16 - 0.81
City	29/38 (76.3%)	54/106 (50.9%)			
Rural	9/38 (23.7%)	52/106 (49.1%)			

Table 2. The Association Between *H. pylori* Positivity and Different Variables in Patients with Urticaria

Factors	<i>H. pylori</i> Positive	<i>H. pylori</i> Negative	P Value	Odds Ratio	Confidence Interval
Family number	7.7 ± 3	7.8 ± 3	0.8	1.02	0.82 - 1.23
Age	36.5 ± 11	23.8 ± 10	0.93	1	0.94 - 1.07
Duration of disease in months	37.2 ± 39	37.2 ± 40.1	0.9	0.99	0.98 - 1.02
Gender			0.71	1.38	0.25 - 7.61
Female	29/37 (78.4%)	10/12 (83.3%)			
Male	8/37 (21.6%)	2/12 (16.7%)			
Residency			0.67	0.76	0.20 - 2.81
City	16/37 (43.2%)	6/12 (50%)			
Rural	21/37 (56.8%)	6/12 (50%)			

H. pylori prevalence was 73.6% in our study. In a study conducted in Iran, the prevalence of *H. pylori* was nearly 90% of the adult population and estimated to be > 50% of children (10). Then, we investigated *H. pylori* associated with various risk factor and we found that *H. pylori* positivity was associated with a higher family number. The same result was found when *H. pylori* was studied in the pediatric age group in Duhok (11). Additionally, we found a higher *H. pylori* positivity in subjects residing in the city. This is difficult to explain and further studies are needed to investigate this. No association was found between *H. pylori* infection and age, gender, or residency. In a study conducted in Turkey, the prevalence of *H. pylori* infection was less in females, elderly, and unmarried subjects (12). In studies conducted in Iran, low socioeconomic status and education level, higher family member number, and poor oral hygiene were found to be risk factors for *H. pylori* infection (13). In another study conducted in Nigeria, around 82% of the recruited samples were positive for *H. pylori*. Low socioeconomic status, unclean water source, overcrowding, and smoking were significant risk factors for *H. pylori* infection (14). In another study conducted in China, *H. pylori* prevalence rate was 63.4%, and women had higher infection rate (15). In the same study, no significant association

between *H. pylori* prevalence and smoking was found (15).

The association between *H. pylori* infection in chronic urticaria has been studied with controversial results. Several studies showed that *H. pylori* eradication led to a better treatment outcome with a better remission of urticaria symptoms (16, 17), suggesting a possible role for *H. pylori* in the pathogenesis of urticaria. On the other hand, the prevalence of *H. pylori* positivity in subjects with chronic urticaria was not significantly higher than that in the control group (17). However, the severity of urticarial was higher in patients with the *H. pylori* infection. Additionally, after the eradication of *H. pylori* therapy, more than eighty percent of the *H. pylori*-positive urticaria group experienced complete remission after receiving eradication therapy for *H. pylori* (17). One project from Germany showed a better outcome and remission of symptoms after *H. pylori* eradication (18). On the other hand, another study showed that the symptoms of urticaria was triggered by *H. pylori* eradication (19). Large, randomized, double-blinded, controlled studies are required to study the therapeutic effect of *H. pylori* eradication in subjects with chronic urticaria. In our study, no significant difference in *H. pylori* positivity was found between the patients' group and control group. In a study conducted in Basrah, Southern Iraq, the preva-

lence of *H. pylori* was significantly higher in patients with urticaria than the control group (20). The discrepancy between the two studies could not be explained precisely. However, the discrepancy might be due to a small sample size used in our study, patient's genetic makeup, and the virulence of the microorganism.

To conclude, the prevalence of *H. pylori* positivity was high in our city. No association was found between *H. pylori* and chronic urticaria. Further studies are needed to investigate the effect of *H. pylori* eradication on the treatment outcome of chronic urticaria.

Supplementary Material

Supplementary material(s) is available [here](#) [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Footnotes

Conflict of Interests: Nothing to declare.

Ethical Approval: Research proposal and consent was reviewed and approved by the Ethics Committee in the Duhok Department of Health.

Funding/Support: This project was funded by the College of Medicine, University of Duhok, Kurdistan region of Iraq.

Informed Consent: Written informed consent was obtained from all subjects.

References

- Atherton JC. The pathogenesis of Helicobacter pylori-induced gastro-duodenal diseases. *Annu Rev Pathol.* 2006;**1**:63–96. doi: [10.1146/annurev.pathol.1.110304.100125](#). [PubMed: [18039108](#)].
- Hussein NR. The association of dupA and Helicobacter pylori-related gastro-duodenal diseases. *Eur J Clin Microbiol Infect Dis.* 2010;**29**(7):817–21. doi: [10.1007/s10096-010-0933-z](#). [PubMed: [20419465](#)].
- Gravina AG, Zagari RM, De Musis C, Romano L, Loguercio C, Romano M. Helicobacter pylori and extragastric diseases: A review. *World J Gastroenterol.* 2018;**24**(29):3204–21. doi: [10.3748/wjg.v24.i29.3204](#). [PubMed: [30090002](#)]. [PubMed Central: [PMC6079286](#)].
- Kilic G, Guler N, Suleyman A, Tamay Z. Chronic urticaria and autoimmunity in children. *Pediatr Allergy Immunol.* 2010;**21**(5):837–42. doi: [10.1111/j.1399-3038.2010.00986.x](#). [PubMed: [20609133](#)].
- Hussein NR, Robinson K, Atherton JC. A study of age-specific Helicobacter pylori seropositivity rates in Iraq. *Helicobacter.* 2008;**13**(4):306–7. doi: [10.1111/j.1523-5378.2008.00618.x](#). [PubMed: [18665942](#)].
- Hussein NR, Mohammadi M, Talebkhan Y, Doraghi M, Letley DP, Muhammad MK, et al. Differences in virulence markers between Helicobacter pylori strains from Iraq and those from Iran: potential importance of regional differences in H. pylori-associated disease. *J Clin Microbiol.* 2008;**46**(5):1774–9. doi: [10.1128/JCM.01737-07](#). [PubMed: [18353934](#)]. [PubMed Central: [PMC2395113](#)].
- Hussein NR, Saleem ZS, Balatay AA, Abd KH, Daniel S, Taha AA, et al. Seroprevalence of Helicobacter pylori infection in renal transplant recipient attending Duhok Kidney Disease Center. *Transplant Proc.* 2016;**48**(1):92–5. doi: [10.1016/j.transproceed.2016.01.006](#). [PubMed: [26915849](#)].
- Hussein NR. Helicobacter pylori and gastric cancer in the Middle East: A new enigma? *World J Gastroenterol.* 2010;**16**(26):3226–34. doi: [10.3748/wjg.v16.i26.3226](#). [PubMed: [20614477](#)]. [PubMed Central: [PMC2900713](#)].
- Figura N, Franceschi F, Santucci A, Bernardini G, Gasbarrini G, Gasbarrini A. Extragastric manifestations of Helicobacter pylori infection. *Helicobacter.* 2010;**15** Suppl 1:60–8. doi: [10.1111/j.1523-5378.2010.00778.x](#). [PubMed: [21054655](#)].
- Hosseini E, Poursina F, de Wiele TV, Safaei HG, Adibi P. Helicobacter pylori in Iran: A systematic review on the association of genotypes and gastro-duodenal diseases. *J Res Med Sci.* 2012;**17**(3):280–92. [PubMed: [23267382](#)]. [PubMed Central: [PMC3527048](#)].
- Yahya NB. Helicobacter pylori seropositivity in children in Duhok city, Iraq. *Sci J Univ Zakho.* 2018;**6**(3):82–7. doi: [10.25271/sjuoz.2018.6.3.508](#).
- Ozaydin N, Turkyilmaz SA, Cali S. Prevalence and risk factors of Helicobacter pylori in Turkey: A nationally-representative, cross-sectional, screening with the (1)(3)C-Urea breath test. *BMC Public Health.* 2013;**13**:1215. doi: [10.1186/1471-2458-13-1215](#). [PubMed: [24359515](#)]. [PubMed Central: [PMC3880349](#)].
- Malekzadeh R, Sotoudeh M, Derakhshan MH, Mikaeli J, Yazdanbod A, Merat S, et al. Prevalence of gastric precancerous lesions in Ardabil, a high incidence province for gastric adenocarcinoma in the northwest of Iran. *J Clin Pathol.* 2004;**57**(1):37–42. doi: [10.1136/jcp.57.1.37](#). [PubMed: [14693833](#)]. [PubMed Central: [PMCI770167](#)].
- Bello AK, Umar AB, Borodo MM. Prevalence and risk factors for Helicobacter pylori infection in gastro-duodenal diseases in Kano, Nigeria. *Afr J Med Health Sci.* 2018;**17**(1):41. doi: [10.4103/ajmhs.ajmhs_36_17](#).
- Zhu Y, Zhou X, Wu J, Su J, Zhang G. Risk factors and prevalence of Helicobacter pylori infection in persistent high incidence area of gastric carcinoma in Yangzhong City. *Gastroenterol Res Pract.* 2014;**2014**:481365. doi: [10.1155/2014/481365](#). [PubMed: [24550981](#)]. [PubMed Central: [PMC3914443](#)].
- Magen E, Mishal J, Schlesinger M, Scharf S. Eradication of Helicobacter pylori infection equally improves chronic urticaria with positive and negative autologous serum skin test. *Helicobacter.* 2007;**12**(5):567–71. doi: [10.1111/j.1523-5378.2007.00522.x](#). [PubMed: [17760727](#)].
- Abdou AG, Elshayeb EI, Farag AG, Elnaidany NF. Helicobacter pylori infection in patients with chronic urticaria: Correlation with pathologic findings in gastric biopsies. *Int J Dermatol.* 2009;**48**(5):464–9. doi: [10.1111/j.1365-4632.2009.04042.x](#). [PubMed: [19416374](#)].
- Hellmig S, Troch K, Ott SJ, Schwarz T, Folsch UR. Role of Helicobacter pylori infection in the treatment and outcome of chronic urticaria. *Helicobacter.* 2008;**13**(5):341–5. doi: [10.1111/j.1523-5378.2008.00620.x](#). [PubMed: [19250508](#)].
- Magen E, Schlesinger M, Hadari I. Chronic urticaria can be triggered by eradication of Helicobacter pylori. *Helicobacter.* 2013;**18**(1):83–7. doi: [10.1111/hel.12010](#). [PubMed: [23067254](#)].
- I. Al-Hamdi K, S. Khashan L. Role of Helicobacter pylori in chronic ordinary urticaria: A case-control and therapeutic study. *Med J Basrah Univ.* 2017;**35**(1):39–47. doi: [10.33762/mjbu.2017.126395](#).