

## THE ROLE OF HELICOBACTER PYLORI INFECTION IN THE PATHOGENESIS OF CHRONIC URTICARIA

Ghazzawi IM<sup>1</sup> & Obidat NA<sup>2</sup>

### ABSTRACT:

**Objective:** To determine the prevalence of *H. pylori* infection in patients with idiopathic chronic urticaria (ICU) and to see if eradication of the bacterium affects the course of the urticaria.

**Patients and Methods:** One hundred patients with idiopathic chronic urticaria and 43 healthy subjects (matched for age and sex) underwent serological testing for *H. pylori* infection. All patients with idiopathic chronic urticaria were examined for *Helicobacter pylori* infection with the <sup>13</sup>C-urea test as well as the serological testing. Gastric biopsy was obtained from 36 patients. Patients with proven *Helicobacter pylori* infection were given treatment for 2 weeks. Six weeks afterwards they were tested again for *Helicobacter pylori* infection, and their urticaria was clinically assessed.

**Results:** There was no significant difference in the seroprevalence of *H. pylori* infection between idiopathic chronic urticaria patients and healthy subjects. *Helicobacter pylori* was detected in 76% of patients and 69.8% of controls. Out of the 76 patients treated, only 24 showed complete remission of their urticaria after successfully eradicating *Helicobacter pylori* infection, the others only having some improvement in their symptoms.

**Conclusion:** Patients with idiopathic chronic urticaria have similar high rates of *H. pylori* infection as healthy subjects. Bacterium eradication is associated with improvement of urticaria symptoms, suggesting a possible role of *Helicobacter pylori* in the pathogenesis of this skin disorder.

**KEY WORDS:** Idiopathic chronic urticaria, H.Pylori, Pathogenesis.

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### BACKGROUND

Chronic urticaria is a common disease that is always a challenge to the dermatologist due to its evasive etiology. It is a cause of serious

1. Dr. Imad M. Ghazzawi MD, FRCP(EDIN)  
Department of Gastroenterology
  2. Dr. Nidal A.Obidat MD  
Department of Dermatology
- 1-2. King Hussein Medical Center,  
Amman, Jordan.

#### Correspondence:

Dr. Imad Ghazzawi  
P. O. Box 3345,  
11821 Amman, Jordan  
E-mail: ghazjo@yahoo.co.uk

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personal, social, economic, and occupational disability comparable with that associated with severe coronary heart disease<sup>1</sup>.

Chronic urticaria is one of the most frequent skin diseases, with an incidence ranging from 1.2% to 23%<sup>2</sup>. In most cases of chronic urticaria the cause is not detected even after intensive clinical investigations<sup>3</sup>. A number of factors have been implicated in the pathogenesis of chronic urticaria, including focal/systemic infections, atopy, food/drug allergy, physical urticarias, autoimmune diseases, and others<sup>4,5</sup>.

Recent investigations pointed to a potential role of *Helicobacter pylori* (*H. pylori*) infection of the upper gastrointestinal tract as a possible causative agent in idiopathic chronic urticaria (ICU). This study was set up to determine the prevalence of *H. pylori* infection in patients

with ICU, and measure the effectiveness of eradication of H pylori on the skin disease.

**PATIENTS AND METHODS**

This study was conducted between January 2000 and February 2002 at King Hussein Medical center. One hundred patients with ICU (62 women and 38 men) were enrolled into the study. Their age range was 14 to 63 years (mean, 42.7 years), and the disease duration was between 6 months and 15 years (mean, 36.2 months). As controls we used 43 age- and sex-matched unrelated healthy blood donor volunteers (28 women and 15 men), their age was between 20 and 66 years of age (mean, 44.2 years). ICU was diagnosed by history and clinical findings. Patients with chronic urticaria of other origin were excluded from the study, including those with focal/systemic infections, atopy, food/drug allergy, physical urticarias (except dermatographism), autoimmune diseases, and malignancies. All patients were examined for H. pylori infection with <sup>13</sup>C-urea breath test<sup>6,7</sup>, and for an enzyme-linked immunosorbent assay (ELISA) for specific IgG antibodies against H. pylori<sup>8,9</sup>.

If both tests were positive, gastroscopy and mucosal biopsy were proposed to the patients. All patients were well informed about the study, and proper consent was obtained. Controls only had serological testing for H pylori infection at the start of the study to assess the prevalence of H pylori in the general population.

A 2-weeks treatment schedule of amoxicillin (1000 mg b.d.), clarithromycin (500 mg b.d.), and pantoprazole (40 mg b.d.) was administered to patients with proven H pylori infection (both tests positive) in the study group.

Six weeks after completing the therapy, <sup>13</sup>C urea breath test performed, and the severity of ICU was assessed. Chi-square test was performed for statistical analyses.

Complete remission was defined as the complete disappearance of the urticaria within 2 weeks of completing treatment. Spontaneous remission was defined as the disappearance of the urticaria after 4 weeks of completing treatment. Those cases with persisting urticaria, but with fewer symptoms than at the start of the study, were defined as partial remission.

**RESULTS**

The study group and the control group were comparable in terms of age (42.7 vs 44.2 years) and sex (62% vs 65% women). The urease breath test and IgG antibodies against H pylori were positive in 87 patients (87%) and 76 patients (76%) respectively in the ICU group. Of the 76 patients with proven H pylori infection 36 patients accepted endoscopy, and H pylori was demonstrated in all of them by histologic examination. Of the 43 control subjects, 30 (69.8%) had positive serology for IgG (Table-I).

Therapy to eradicate H. pylori infection was given to the 76 patients with positive tests. Patients were observed for 6 weeks after completion of the 2-week treatment schedule. Successful eradication of H pylori infection (negative <sup>13</sup>C urea breath test) was achieved in all 68 patients treated. Of those, only 22 patients (32.4%) had complete remission (11 patients within one week only); 29 patients (42.6%) had partial remissions, and 17 patients (25%) showed no change in their skin disease. In the 24 patients who did not receive treatment as they were H pylori negative, 5 patients

Table-I: Helicobacter pylori testing in patients with idiopathic chronic urticaria and in control subjects. (All data are presented as number (percentage) of cases)

Category	Urease test		IgG		Total
	(+)	(-)	(+)	(-)	
Patients	87 (87%)	13 (13%)	76 (76%)	24 (24%)	100
Controls	-	-	30 (69.8%)	13 (30.2%)	43

Table-II: Idiopathic chronic urticaria after treatment for Helicobacter pylori infection.  
(All data are presented as number (percentage) of cases)

Category	Complete remission	Partial remission	No change	Total
Treated group	22 (32.4%)	29 (42.6%)	17 (25%)	68
Untreated group	2 (8.3%)	3 (12.5%)	19 (79.2%)	24
Treated not eradicated	2 (25%)	3 (37.5%)	3 (37.5%)	8
Total	26	35	39	100

showed some improvement (2 complete remission and 3 partial remission) and 19 patients showed no change in their disease (Table-II). Of the 8 patients treated but not eradicated, 2 patients showed complete remission, 3 partial remission and 3 were not improved.

### DISCUSSION

Conventionally, chronic urticaria is defined as the daily, or almost daily, occurrence of urticarial wheals for at least 6 weeks<sup>10</sup>. The etiology of chronic urticaria is unknown, and an exogenous allergen cannot be identified as the cause in the vast majority of subjects. Several factors have been identified that appear to be important in the pathogenesis of individual cases, some drugs, food additives, physical factors and internal diseases<sup>3-5</sup>.

The term idiopathic chronic urticaria (ICU) is used in situations in which urticarial vasculitis and predominant physical urticarias have been excluded<sup>11</sup>. ICU is thought to affect at least 0.1% of the population<sup>11,12</sup> and has a chronic relapsing course, with approximately 20% of patients still having the disease after 10 years<sup>3</sup>.

Recent evidence suggests that most instances of chronic urticaria are autoimmune, and 27% to 50% of patients with ICU have been found to have functional autoantibodies directed against the alpha-chain of the high-affinity IgE receptor or less commonly against IgG<sup>10,13,14</sup>. Some recent studies point to infections due to Helicobacter pylori as being of major importance in the pathogenesis of ICU<sup>15-18</sup>. However, other reports have failed to confirm this association<sup>19-21</sup>.

A number of hypotheses have been suggested about why H pylori infection could induce

chronic urticaria, including the induction of inflammatory cytokines and the possible association of H pylori infection with autoimmune disease<sup>17</sup>.

H pylori, a gram-negative microaerophilic bacterium, which is of pathogenic importance in gastric diseases, such as peptic ulcer<sup>22</sup> and gastric carcinoma<sup>23</sup>, has recently been associated with several extradigestive diseases<sup>24</sup>. Recently, H pylori has been reported as a possible cause of Henoch-Schonlein purpura<sup>25</sup>, Sweet's syndrome<sup>26</sup>, rosacea<sup>27,28</sup> and Sjogren's syndrome<sup>29</sup>.

As there are no published studies about the prevalence of H pylori infection in the Jordanian population, a control group was used in our study and from this we found a high prevalence rate of H pylori infection in the normal Jordanian population (69.8%). According to seropositivity for IgG, there was no statistical difference ( $P > 0.05$ ) between controls and ICU patients (76%).

Fiftyone patients (75% of infected patients in whom the bacterium was eradicated after therapy) showed a total or partial remission of urticaria symptoms. Conversely, symptoms improved only in a minority (20.8%) of uninfected patients. Although many of our patients improved after successful eradication of H pylori infection, only 32.4% showed complete remission of their urticaria after. Reduction in frequency of urticaria symptoms and reduction of antihistamine requirement could partly be due to the natural course of the disease.

Although similar results were reached in some studies<sup>18,19</sup>, most literature from the West gives remission rates in 95% to 100% of

patients infected with *H pylori*<sup>15-17</sup>. The discrepancy between these results and ours may be explained by the fact that all these studies were done in countries with a relatively low prevalence of *H pylori* infection (30% to 40%)<sup>30</sup> compared with ours (69.8%).

### CONCLUSION

Although the prevalence of *Helicobacter pylori* infection is high in patients with idiopathic chronic urticaria, complete remission was only achieved in a small number of patients after the eradication of the bacterium, suggesting a possible role of *Helicobacter pylori* in the pathogenesis of some cases of this skin disorder. A controlled, randomized clinical trial to investigate this association further is recommended.

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