

Chronic urticaria and dyspepsia: Association and treatment, an experimental study

Hamad Ayed Alfahaad

Department of Dermatology, College of Medicine, Najran University, KSA

Abstract

Objective To determine the prevalence of *Helicobacter pylori* infection among chronic idiopathic urticaria patients and to assess their urticarial response after the eradication of *H. pylori*.

Methods This study was a non-controlled, interventional study that was carried during the period from January 2016 to November 2016 at Dermatology Clinic, King Khalid Hospital, Najran, KSA. A total of 104 patients were included in our study. The patients who were positive for *H. pylori* were started on the eradication therapy. The effectiveness of the eradication therapy was assessed by repeating the *H. pylori* Urea Breath Test (UBT) after 4 weeks. Urticarial response was assessed 12 weeks after the eradication.

Results The prevalence of chronic idiopathic urticaria (CIU) at our dermatology clinic was 0.6%. The patients were predominantly females (76.4%), and the highest number (69.4%) belonged to the age group '20-50 years'. Of the study subjects (62.5%) had positive *H. pylori*, (91%) achieved eradication of *H. Pylori* while (9%) not. Of the cases (75.6%) showed significant improvement in their urticarial symptoms after eradication of *H. pylori*, while (24.4%) showed no significant improvement of their urticarial symptoms.

Conclusion *H. pylori* should be specifically investigated for all chronic urticaria patients and the eradication therapy advised for those who have are positive for *H. pylori*.

Key words

Chronic urticaria, *Helicobacter pylori*.

Introduction

Urticaria is marked by itchy wheals that vary in flare-type dermal reactions, distribution, number and size.¹ Urticaria can be an acute (less than 6 weeks) or a chronic urticaria (more than 6 weeks).² Chronic urticaria (CU) is either idiopathic chronic (55%) and autoimmune chronic (45%) without urticarial vasculitis and physical urticaria.

CU is a case marked by almost daily

spontaneous appearance of hives and/or angioedema.³ The causes of CU may be unknown or known causes.⁴ However, a patient may have more than one subtype of urticaria at the same time. Detailed history, a ruling out of severe systemic disease and physical workup are all necessary for accurate diagnosis of chronic urticaria.⁵

The term chronic idiopathic urticaria (CIU) refers to the condition in which the underlying etiology remains unidentified in approximately 75% of cases. It also refers to the case where wheals develop without any external stimuli that can be identified. The cause of CIU is functionally active and circulating immunoglobulin G (IgG) autoantibodies that are

Address for correspondence

Dr. Hamad Ayed Alfahaad,
Department of Dermatology,
College of Medicine, Najran University,
KSA
Email: hamadyam@gmail.com

specific for the Immunoglobulin E (IgE) receptor (FcRI) that is present on basophils and mast cells or for IgE itself.³

The etiological and pathogenic causes of CIU remain unknown. In the 1980s, *Helicobacter pylori* was found in patients with CIU. Some researchers have found out a relationship between CU and the infection of *H. pylori*. However, it is still controversial whether *H. pylori* is an etiological agent for CU or not.⁶

H. pylori is a gram-negative bacterium. It is among the most frequently detected bacterium in the human intestinal flora and still among the most common chronic bacterial infections that affect humans.⁷ It induces acute gastritis, which becomes chronic active gastritis later on.⁸

There is no standard test for diagnosing *H. pylori* infection. There are two categories of them: invasive and non-invasive tests. The sensitivity of histopathology tests and rapid urease test (RUT), which are two direct diagnostic tests, is decreasing. However, the sensitivity of serology (an antibody-based test) is quite high, despite its low specificity. Even though serological test is an effective screening tool for determining the infection of *H. pylori*, it does not differentiate between past exposure to *H. pylori* and the active infection. That is why other tests are needed before *H. pylori* eradication therapy for further confirmation.⁹

Stool antigen test (SAT) and urea breath test (UBT), among the indirect tests, are non-invasive, rapid, highly sensitive and specific¹⁰ and considered the best and more effective methods than serological or urinary antibody-based tests to detect the active infection and monitor the treatment response.¹¹

Proton pump inhibitors (PPI) administration may give false-negative results, so, it should be

discontinued at least 2 weeks before repeating the test.¹²

H. pylori infection can be treated with triple therapy, each taken twice a day for 14 days: clarithromycin 500 mg, amoxicillin 1000 mg and PPI (e.g. omeprazole 20 mg).¹³

After the treatment, many patients were recovered from both the infection and the urticaria. So, the eradicating therapy of *H. pylori* is considered very effective in CU patients. Therefore, detecting *H. pylori* is considered an essential test for all CU patients.⁷

Although *H. pylori* is frequently seen in patients who suffer from CIU, the correlation between *H. pylori* eradication and urticarial improvement is not confirmed.¹⁴ This study was aimed to assess the prevalence of *H. Pylori* infection among CIU in our population and to assess the response of the urticaria after the eradication of *H. pylori*.

Methods

The study was a non-controlled interventional prospective study that was conducted at the Dermatology Department at King Khalid Hospital, Najran, KSA, over the period from January 2016 till November 2016. By consecutive sampling, 104 patients with history of urticarial lesions of > 6 weeks were included in this study. Exclusion criteria were patients less than 12 or greater than 60 years old, patients being treated with PPIs or other antibiotics within previous four weeks, pregnant females, patients of physical urticaria and patients suffering from other concomitant serious surgical and medical diseases. Seventy two patients who met the study criteria were enrolled in the study (**Table 1**).

Formal consent was obtained from all participants and local authorities. Each patient's

Table 1 Classification of cases according to age group and gender (n=104).

Age (years)	CIU		CU		Total
	Male	Female	Male	Female	
12-20	3	9	3	4	19
21-35	5	16	3	5	29
36-50	6	23	4	8	41
51-60	3	7	2	3	15
Total	17	55	12	20	104
	72		32		

CIU: chronic idiopathic urticaria, CU: chronic urticaria.

preliminary screening panel comprised complete history and physical examination, complete laboratory tests (complete blood count, routine urine and stool examination, renal and liver function, fasting blood glucose, erythrocyte sedimentation rate, antinuclear antibody, complement assays, and thyroid function test) as baseline and to exclude other causes except *H. pylori*. The *H. pylori* urea breath test (UBT) was performed in all study subjects. Patients with a known cause received treatment accordingly, whereas patients with CIU got enrolled in the study and each patient with chronic urticaria was provided with an evaluation sheet for follow-up.

Immediately after taking all investigations from the participant, the positive *H. pylori* patients were started on the first course therapy which was consisted of clarithromycin 500 mg BID, omeprazole 20 mg, amoxicillin 1000 mg BID for a period of 14 days. Urea breath test (UBT) was used to assess *H. pylori* eradication 4 weeks after the treatment. If the infection of *H. pylori* persisted, patients received the second course of same treatment for an extra week. All infected patients were given prescription of antihistamines to use as 'rescue medicine'. Patients who became non-infected were given antihistamines when necessary. After completing the treatment, all patients were observed in follow-up visits for a period of six months. Moreover, judging the each patient's objective response after 12 weeks from the

eradication treatment of *H. pylori* on the basis of improvement of urticarial symptoms (frequency, severity and duration) and the need for rescue medication as follows: *significant response*: improvement of urticarial symptoms and no need or infrequent need for antihistamines, while *no significant response*: little improvement of urticarial symptoms or frequent need for antihistamines).

Pearson χ^2 test and Fisher's exact test were used to explore the significant association of selected characteristics among the study patients.

Results

104 out of 1759 patients who were seen in the clinic during the study period were suffering from chronic urticaria. The patients were predominantly females 75 (72 %), Saudis (87.1%) and non-smokers (95%). The female participants were 75 patients; 55 cases were CIU and 20 cases were CU while male participants were only 29 patients, 17 of them suffered from CIU and the other 12 suffered from CU. Only 72 (69.2%) patients were diagnosed with chronic idiopathic urticaria, (55 females, 17 males, male to female ratio was 1:3). The mean age was 38.5 \pm 15.8 years, and the highest number (69.4%) belonged to the age group '20-50 years'.

45 (62.5%) patients of CIU showed positive *H. pylori* infection i.e. 11 (24.4%) males and 34 (75.6%) females, while 27 (37.5%) patients showed negative *H. pylori*; 6 (22.2%) males and 21 (77.8%) females. 36 of 45 *H. pylori*-positive patients i.e. (80%) presented with G.I.T symptoms like dyspepsia and heartburn. Male and female percentages were approximately the same in *H. pylori*-positive patients (64% and 62%, respectively) but the female had more frequent GIT symptoms than males (88% vs. 54.5%), (Table 2).

Table 2 Prevalence of *H. pylori*-positive patients and G.I.T symptoms among different age group.

Age (years)	GIT symptoms		No GIT symptoms	
	Male	Female	Male	Female
12-20	1	3	2	0
21-35	2	9	1	2
36-50	2	14	1	0
51-60	1	4	1	2
Total	6	30	5	4

Table 3 Objective response to treatment

<i>H. pylori</i> eradication treatment	<i>H. pylori</i> response to treatment		Urticarial improvement of cured subjects	
	No. of subjects	Cured	Significant	Not significant
1st course	45	32	28	4
2nd course	13	9	6	3
Persistent <i>H. pylori</i>	4	0	0	4
		41	34	11
Total		45		45

The patients' response to the eradication therapy of *H. pylori* was as the following: 32 (71%) patients cured with the first course, 9 (20%) patients cured with the second course of eradication therapy, and 4 (9%) patients had persistent *H. pylori* even after two courses of eradication therapy.

The urticarial symptoms response after the eradication therapy was significant in 34 (75.6%) patients in whom *H. pylori* was eradicated whereas not significant in 11 (24.4%) patients; 7 (15.4%) patients with eradicated *H. pylori* and 4 (9%) patients with persistent *H. pylori* infection as illustrated in **Table 3**.

Discussion

The current study aimed to investigate the association of *H. pylori* and chronic urticaria and to assess the impact of eradication therapy of *H. pylori* on chronic idiopathic urticaria. The study came to the conclusion that *H. pylori* needs to be included in investigation of chronic idiopathic urticaria patients for proper management. In this study, we used the experimental approach to assess the efficacy of *H. pylori* treatment in CIU patients. There are conflicting reports of the relationship between the infection of *H. pylori* and CIU based on several Western studies. The

present study is medically valuable as it proves that there is a high level of prevalence of infection of *H. pylori* among the target population. There is high prevalence of the infection of *H. pylori* (62.5%) among CIU patients. Studies from African countries, reported a prevalence of *H. pylori* infection of 65.7% and 75.5% in Ethiopia and Morocco, respectively. The prevalence of the *H. pylori* infection was 93.6%, when tested with serology and 80% when histology tests were applied. In Brazil, a high prevalence of 41.1% was reported in patients from 2 to 19 years of age.¹⁵

The present study proves that there is high prevalence of *H. pylori* in CIU patients, in accordance with previous studies¹⁵⁻¹⁷ and stresses the effectiveness of eradication therapy in treating *H. pylori* infection.^{19,20} In CIU patients infected with *H. pylori*, urticarial symptoms were resolved after *H. pylori* eradication therapy was applied. This result agrees with recent studies, such as the study of Tareen *et al.*⁷ carried out in 2016, which affirms that the eradicating therapy of *H. pylori* is effective in CU patients and that detecting *H. pylori* is essential for the diagnosis of all CU patients. Another recent study conducted in 2015, by Gu *et al.*⁶ found out a relationship between CU and the infection of *H. pylori*.

Some researchers showed no relationship between allergic diseases and infection of *H. pylori* in men in particular, like the Japanese study carried out in 2007.²¹ However, other researchers, like Bruscky *et al.*²² suggested that *H. pylori* and the occurrence of CU are correlated as *H. pylori* is considered an etiological agent of CU. Researchers have confirmed the correlation between CU and the infection of *H. pylori*. However, it is still controversial whether *H. pylori* is an etiological agent for CU or not.¹¹ The therapy of eradicating *H. pylori* is effective in CU patients. Therefore, detecting *H. pylori* is essential for the diagnosis of all CU patients.⁷

In a recent study conducted in 2015, the researchers recommended the inclusion of the infection of *H. pylori* in the diagnosis of patients showing no response to treatment.²³ Another 2007 study proved that eradicating the infection of *H. pylori*, using triple therapy, effectively minimizes the score of urticarial activity in patients suffering from CU and showing negative and positive autologous serum test.²⁴

The difference in the results of the above studies is probably because of the various methods that were used for detecting and establishing infection of *H. pylori* or the recurrences shortly after successful therapy or *H. pylori* resistance to therapy. The pathogenic mechanism between CIU and the infection of *H. pylori*, remains unknown. *H. pylori* is likely to reveal the existing antigens or facilitate the absorption of antigens, by inducing inflammation in the gastrointestinal tract. If this happens, IgE antibodies responsible for the symptoms of urticaria may continue to be produced even after *H. pylori* eradication. Hence, the infection of *H. pylori* is likely to perpetuate the tendency of an infected person for contracting urticaria. The infection of *H. pylori* is frequent. However, it just provokes urticaria in some patients infected

with *H. pylori*. Therefore, long-duration studies are required to establish natural history of the infection of *H. pylori*, taking into consideration the symptoms of urticaria, reinfection, as well as, retreatment. Only then, studies would be able to implement the Koch's postulate and *H. pylori* can be labeled a cause of CU.²⁵

Conclusion

The study concludes that *H. pylori* needs to be investigated in all patients with chronic urticaria, and the infected patient should receive *H. pylori* eradication therapy. Moreover, the current study proved that eradication therapy of *H. pylori* is effective in the management of chronic urticaria. The author recommends that *H. pylori* should be among the diagnostic work-up of all chronic urticaria patients and consider the costs and accessibility for the diagnosis and monitoring of *H. pylori* infection.

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