Original Paper

Study on Association between Chronic Idiopathic Urticaria and Helicobacter Pylori Infection in Armed Forces Personnel

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Abstract

Introduction: Chronic Idiopathic Urticaria (CIU) has an estimated prevalence of 35-65% and impacts 15 to 25% of the population at some point in their lives. Studies have shown the possible involvement of Helicobacter pylori (H. pylori) infection in chronic idiopathic urticaria (CIU), but the relationship remains controversial.

Objective: To quantitatively assess the association between H. pylori infection and chronic idiopathic urticaria.

Materials and Methods: This was a case-control type of analytical study and 100 patients were enrolled fifty patients of CIU fulfilling inclusion criteria with no identifiable cause were taken as case and patients without urticaria were taken as control, attending in the department of Dermatology & Venereology, CMH Dhaka for treatment from May 2015 to Aug 2016. Helicobacter pylori infection was confirmed by serum IgG for H. pylori test.

Results: The result showed that H. pylori infection significantly affected a high percentage of patients 30 (60%) with chronic idiopathic urticaria. Male respondents were more positive 16(53.3%) than female 14(46.7%), in the middle aged 31-50 year about 18(60%) and triple drug therapy was successful in 16(53.33%) patients in whom H. pylori was detected.

Conclusion: Urticaria is a common clinical disorder with complex triggering factors. Chronic urticaria has provided evidence that enteric infection with H. pylori may induce the disease. In this case control study, it was evident that chronic idiopathic urticaria was associated with positive serum IgG for H. Pylori. A trial of H. pylori eradication therapy may be offered to patients with CIU and evidence of H. pylori infection.

Key-words: Chronic idiopathic urticaria, Helicobacter pylori, Armed Forces.

Introduction

Chronic idiopathic urticaria (CIU) is defined as the occurrence of daily or almost daily, wheals and itching for at least 6 weeks, with no obvious cause. The term chronic idiopathic urticaria makes no assumption about number of patients. It is associated with various aggravating factors including drugs, food and food additives, infections and infestations (hidden or overt bacterial, viral, fungal, and protozoal agents), systemic diseases etc have been reported as possible initiating factors. But the etiology for most cases remains unknown and therapy is largely directed at symptomatic care. Up to 50% of the population show evidence of past or present H. pylori infection and at least 30% of patients with CIU have infection with this organism[1]. It is definitely suspected in the etiopathogenesis of gastro-intestinal disorders, such as gastritis, peptic ulcer, gastric carcinoma and lymphoma[2]. Recent epidemio-logical and experimental data have pointed to a strong relation of H. pylori infection with the development of many extra gastric diseases, such as cardiovascular, immunologic, and some skin diseases[3].

Despite numerous studies, the role of H. pylori in chronic urticaria is still a challenge for researchers. The pathogenesis by which H. pylori can induce or maintain urticaria are not fully understood. There are several hypotheses about the role of H. pylori in chronic urticaria.

According to some hypotheses, an autoimmune mechanism in which molecular mimicry between H. pylori lipopoly-saccharide (LPS) and Lewis group antigen, can occur in autoimmune type-B gastritis[4,5]. Thus, positive autologous serum skin tests in patients with chronic urticaria, have

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been associated with H. pylori infection[6]. In some patients with chronic urticaria, but not all, autologous serum skin tests became negative after eradication of H. pylori infection. In some cases, specific IgE antibodies have been described for H. pylori antigens, both in patients with chronic urticaria and in patients with complete remission after eradication of H. pylori infection[7].

In addition, it was demonstrated that H. pylori can increase serum and tissue levels of nitrous oxide (NO), a free radical which plays an important role in various physiological processes in the skin, including vasodilatation, inflammation and immunomodulation[8].

H. pylori induces a strong inflammatory response in the gastric mucosa and results in the expression of a wide spectrum of cytokines, chemokines and eicosanoids such as interleukin-8 (IL-8), prostaglandin E2(PGE2) and leukotriene B4(LTB4). Released from the epithelial cells, these potent pro-inflammatory mediators promote inflammation and tissue damage locally as well as induce migration and activation of neutrophils, macrophages, lymphocytes and plasma cells to the site of infection[9].

In H. Pylori infected patients with chronic urticaria, significant increases in gastric eosinophil infiltration and in production of gastric juice eosinophil cationic protein production (ECP) were described and H. pylori eradication resulted in a significant decrease in both[10].

Another proposed mechanism is the increased gastric vascular permeability during H. pylori infection, resulting in increased exposure of the host to food allergens[11]. In support of this hypothesis, duodenal ulcer patients have a higher incidence of allergic manifestations compared with control groups[12].

On the other hand, the severity of urticarial symptoms can be related to H. pylori density and the intensity of inflammatory infiltration observed in the gastric biopsy[13].

H. pylori modulates also the endocrine and physiological functions of the stomach. Studies have shown that serum pepsinogen (PG)I, sPGII and gastrin (G-17) levels are high in the presence of H. pylori infection related to non-atrophic chronic gastritis, knowing the relationship between gastrin, mast cells and skin. In addition, it was demonstrated that their serum levels significantly decreased after eradication of H. pylori infection[9]. Thus present study is conducted to find out the correlation of chronic idiopathic urticaria with H.pylori infection.

Materials and Methods

Case-control type of analytical study and 100 patients were enrolled in this study. 50 patients of CIU fulfilling inclusion criteria with no identifiable cause were taken as case (Group-A) and patients without urticaria were taken as control (Group-B), attending in the department of Dermatology and Venereology, CMH Dhaka for treatment from May 2015 to Aug 2016. Purposive type of non-probability sampling method was followed in this study. Total sample Size: 50 patients and 50 controls.

The preliminary screening panel for each patient included the complete history, physical examination and laboratory tests i.e Complete blood count including differential count, total IgE, total eosinophil count, sedimentation rate, serum IgG for H. pylori, urine routine examination, liver function test, serum test for hepatitis B and C, stool examination for parasites and ova. Inclusion criterias were (1) Clinically diagnosed case of CIU, (2) Both male and female patients; (3) Age of the patients between 15-60 years, (4) Patient who gave informed consent. Exclusion criterias were (1) Patients suffering from other than CIU, (2) Patient suffering from hematological, renal or liver disorder, (3) Patients of CIU with pregnancy, (4)Patients with urticarial vasculitis, (5) Patients who had taken proton pump inhibitors and antibiotics within the preceding 4 weeks, (5) Chronic urticaria with known etiology: physical urticaria, cholinergic urticaria, hives caused by food allergy, medications, connective tissue and thyroid diseases, malignancies, patients who were receiving corticosteroids, immunosuppressive therapy, patients with ASST (+).

Statistical analysis of the results was obtained by computer based software SPSS-20 and the data was analyzed using Chi square test and paired t test in appropriate situations. P value <0.05 was considered as minimum level of statistical significance.

Results

Table-I: Distribution of patients according to sex (n=100)

Sex	Group		P value
	Case (A)	Control (B)	
Male	20 (40%)	30 (60%)	0.157
Female	30 (60%)	20 (40%)	
Total	**50 (100%)**	**50 (100%)**	

*Chi-square test was done to measure the level of significance.

Table-I shows the distribution of patients according to sex. In Group-A female 30(60.0%) is predominant than

JAFMC Bangladesh. Vol 12, No 2 (December) 2016

123

male 20(40.0%) at the ratio of 3:2. In Group-B, male 30(60%) is predominant than female 20(40%). The difference between these two groups are not statistically significant (P=0.157).

Table-II: Distribution of patients according to age group (n=100)

Age group	Group		P value
	Case (A)	Control (B)	
<=20	2 (4%)	6 (12%)	
21-30	10 (20%)	14 (28%)	
31-40	20 (40%)	24 (48%)	0.053
41-50	10 (20%)	2 (4%)	
>=50	8 (16%)	4 (8%)	
Total	**50 (100%)**	**50 (100%)**	
Mean±SD	38.96 ± 10.632	33.00 ± 10.607	

*t test was done to measure the level of significance

Table-II shows the distribution of patient according to age group. In Group-A, majority of patient, 20(40%) cases was found in 31-40 years of age group. In Group-B, majority of patient 24(48%) cases was found in 31-40 years of age group. The Mean±SD of Group-A and Group-B are in 38.96±10.632 and 33.00±10.607 years respectively. The different between Group-A and Group-B is not statistically significant (P=0.053).

Table-III: Distribution of patients according to occupation (n=100)

Occupation	Group		P value
	Case (A)	Control (B)	
Military personnel	12 (24%)	22 (44%)	
Housewife	28 (56%)	16 (32%)	
Student	2 (4%)	6 (12%)	0.236
Civil employee	8 (16%)	6 (12%)	
Total	**50 (100%)**	**50 (100%)**	

Table-III shows the distribution of patient according to occupation. In Group-A majority are housewives 28(56%) cases followed by military personnel 12(24%) cases. In Group-B majority are military personnel 22(44%) cases followed by housewife 16(32%) cases. The difference between Group-A and Group-B are not statistically significant (P=0.236).

Table-IV: Distribution of patients according to Serum IgG for H.pylori (n=100)

Serum IgG for H.pylori	Group		P value
	Case (A)	Control (B)	
Positive	30 (60%)	16 (32%)	
Negative	20 (40%)	34 (68%)	0.047
Total	**50 (100%)**	**50 (100%)**	

*Chi-square test was done to measure the level of significance

Table-IV shows the distribution of patients (Group-A) according to serum IgG for H. pylori were about 60% cases (30 respondents) positive for IgG and 20(40%)

patients were negative. On the contrary, among the controls (Group-B) 32% (16 respondents) was positive and 68% (34 respondents) were negative for IgG.

Table-V: Distribution of cases according to sex (n=50)

Sex	Serum IgG for H.pylori		P value
	Positive	Negative	
Male	16 (53.3%)	4 (20%)	
Female	14 (46.7%)	16 (80%)	0.096
Total	**30 (100%)**	**20 (100%)**	

*Chi-square test was done to measure the level of significance

Table-V shows the distribution of sex for positivity of IgG for H. pylori, male respondents were more positive 16(53.3%) than female respondents 14(46.7%). Among the 20 negative results, 16 respondents (80%) were female and 4 respondents (20%) were males.

Table-VI: Distribution of Improvement after triple therapy according to sex (n=30)

Occupation	Serum IgG for H.pylori		P value
	Positive	Negative	
Military personnel	12 (40%)	0 (0%)	
Housewife	12 (40%)	16 (80%)	
Student	2 (6.7%)	0 (0%)	0.239
Civil employee	4 (13.3%)	4 (20%)	
Total	**30 (100%)**	**20 (100%)**	

Table-VI shows eradication therapy was successful in 16(53.33%) patients, 8(26.66%) patients did not respond to therapy and 6(20%) patients did not complete the study.

Table-VII: Distribution of cases according to age group (n=50)

Age group	Serum IgG for H.pylori		P value
	Positive	Negative	
<=20	2 (6.7%)	0 (0%)	
21-30	6 (20%)	4 (20%)	
31-40	10 (33.3%)	10 (50%)	
41-50	8(26.7%)	2 (10%)	0.815
>=50	4 (13.3%)	4 (20%)	
Total	**30 (100%)**	**20 (100%)**	
Mean±SD	38.53 ± 10.521	39.60 ± 11.335	

*t test was done to measure the level of significance

Table-VII shows among the cases highest number of H. pylori infection were found in middle aged 31-50 year about 18(60%) followed by young aged 21-30 year and below about 8(26.7%).

Table-VIII: Distribution of cases according to occupation (n=50)

Occupation	Serum IgG for H.pylori		P value
	Positive	Negative	
Military personnel	12 (40%)	0 (0%)	
Housewife	12 (40%)	16 (80%)	
Student	2 (6.7%)	0 (0%)	0.239
Civil employee	4 (13.3%)	4 (20%)	
Total	**30 (100%)**	**20 (100%)**	

Table-VIII shows the incidence of serum IgG for H.Pylori amongst different occupation of the respondents, housewives and military personnel have the highest percentage (40%).

Discussion

In this study it was found that from Table-I, in group A (patient) female was predominant than male which was 30(60.0%) and 20(40.0%) cases respectively at the ratio of 3:2 whereas Kulthanan K et al 2007 describes the male and female association were 21% and 79% respectively[14]. In another study of Lee N et al CU was significantly higher in females than in males (2,466.8 vs 1,819.2 per 100,000 person-years, P<0.001)[15]. In Group-B male was predominant than female which was 30 (60.0%) and 20(40.0%) cases respectively. The difference between these two group is statistically significant (P=0.157).

Table-II in this study showed that in group A less than 21 years of age group was found in only 2(4%) cases, 10(20%) cases in 21-30 years, 20(40%) cases in 31-40 years, 10(20%) cases in 41-50 years and 8(16%) cases in 50 years to above group. In group B less than 21 years of age group was found in 6(12%) cases, 14 (28%) cases in 21-30 years, 24(48%) cases in 31-40 years, 2(4%) cases in 41-50 years and 4(8%) cases in 50 years to above group. The Mean±SD of group A and group B were in 38.96±10.632 and 33.00±10.607 years respectively. The different between group A and group B is not statistically significant (P=0.053). In Mogaddam MR et at study both groups (patient and control), 58% were male and 42% were female. The mean age in the patients group was 37.64±16.04 years and in the control group it was 37.55±16.26 years[16].

In this study when searched the positivity for IgG levels to detect H. pylori, it was found that, in case of serum IgG positive respondents, male respondents were greater than the female counterparts. But the result was not significant (P=0.096). In group A majority were housewives 28(56%) cases followed by military personnel, civil employee and student which are 12(24%) cases, 8(16%) cases, and 2(4%) case respectively. In group B majority are military personnel 22(44%) cases followed by housewife, student and civil employee which are 16(32%) cases, 6(12%) cases and 6(12%) cases respectively (Table-III). The difference between group A and group B are not statistically significant (P=0.236).

One of the important diagnostic tools was to see the IgG level in serum to detect H. pylori infestation among the patients. Study showed the distribution of patients (Group-A) according to serum IgG for H. pylori were about 60% cases (30 respondents) positive for IgG and 10 patients (40%) were negative. On the contrary, among the controls (Group B) 32% (16 respondents) was positive and 68% (34 respondents) were negative for IgG. Chi-square test was done to measure the level of significance. The P value was 0.047. So the result was significant (Table-IV). Gaiga, P et al. 2002 found 80% CIU cases who were positive with H. pylori infestation[17].

From Table-V of this study it was found that distribution of sex for positivity of IgG for H. pylori, male respondents were more positive 16(53.3%) than female respondents 14(46.7%). Among the 20 negative results, 16 respondents (80%) were female and 4 respondents (20%) were males. In a study of Lee N et al H. pylori positivity was significantly higher in females than in males (26333 vs 18845 per 100000) among adolescent and adults older than 15 years[15].

Thirty patients with positive H. pylori antibodies received triple therapy. Patients were evaluated for the relief of symptoms. Eradication therapy was successful in 16(53.33%) patients, 8(26.66%) patients did not respond to therapy and 6(20%) patients did not complete the study (Table-VI). This finding suggests that anti H. pylori triple drug therapy is significantly effective in the treatment of CIU. Mogaddam MR et al found response to eradication of H. pylori was evident in 91.67% patients in whom H. pylori was eradicated while 8.33% patients showed no response[16]. A study of Qazi N et al also have shown there is a possible role of H. pylori infection in the pathogenesis of CIU which is consistent with this study[18].

Table-VII of this study delineated that among the cases highest number of H. pylori infection were found in middle aged 31-50 year about 18(60%) followed by young aged 21-30 year and below about 8 (26.7%). Bonamigo RR et al had a research that showed young aged (20-30 years) females had higher affection of H. pylori (43.4%)[19].

The incidence of serum IgG for H. pylori amongst different occupation of the respondents, it was seen that the housewives and military personnel have the highest percentage (40%) of positive serum IgG (Table-VIII). In Tachihara R et al it was the housewives who had incidence of 20% only[20].

Conclusion

Urticaria is a common clinical disorder with complex triggering factors. Chronic urticaria has provided evidence that enteric infection with H. pylori may induce the disease. In this small case control study, it was evident that chronic idiopathic urticaria is associated with positive serum IgG for H. Pylori. Response to eradication therapy was evident in whom H. pylori infection was eradicated while few patients showed no response despite eradication of H. pylori. It is suggested that H. pylori infection should be included in the diagnostic work up of patients with no response to habitual treatment for CIU. This study support further investigation into the involvement of H. pylori infection in CIU and offer the possibility of an effective treatment without adverse effect for such a chronic, symptomatic, quality-of-life-affecting disease.

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JAFMC Bangladesh. Vol 12, No 2 (December) 2016

126