

## Association of chronic urticaria with Helicobacter Pylori infection in Erbil: A case-control study

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### Abstract

**Background and objective:** Chronic urticaria is one of the most frequent skin diseases and still its etiology is recognized only in a minority of cases. Some recent studies point out to infections due to Helicobacter Pylori as being of major importance in the pathogenesis of chronic urticaria. This study aimed to find out the association of chronic urticaria with H. pylori.

**Methods:** A case-control study was conducted in Erbil city within the period of April 1<sup>st</sup>, 2013 to January 1<sup>st</sup>, 2014. The study included 55 cases with chronic urticaria and 55 controls that were free from features of chronic urticaria. Data was collected through direct interview and the results of laboratory investigations were recorded in a specially designed questionnaire. Enzyme-linked immunosorbent assay test was used for detection of Helicobacter pylori antigen in the stool sample.

**Results:** The age of the 55 cases and 55 controls enrolled ranged from 13 to 65 years. Stool for Helicobacter pylori antigen test was positive in 69.1% of cases and 29.1% of controls (OR = 5.44,  $P < 0.001$ ). The mean age  $\pm$  SD of positive Helicobacter pylori patients were  $35.75 \pm 12.64$  years, with male to female ratio 1:2.8. No statistically significant association was found between Helicobacter Pylori infection with dyspepsia and duration of urticaria.

**Conclusions:** There was a strong association of chronic urticaria with Helicobacter pylori infection. Investigating for Helicobacter pylori in all cases of chronic urticaria and conducting further trials on Helicobacter pylori eradication is recommended.

**Keywords:** Chronic urticaria; Helicobacter Pylori; Erbil.

### Introduction

Urticaria is a group of disorders that share a distinct skin reaction pattern, namely the occurrence of itchy wheals anywhere on the skin. Wheals are short-lived elevated erythematous lesions ranging from a few millimeters to several centimeters in diameter and can become confluent.<sup>1</sup> Angioedema is an acute, evanescent, circumscribed edema that usually affects the eyelids, lips, lobes of the ears, and external genitalia, mucous membrane of gastrointestinal and respiratory tracts, resulting in abdominal pain, coryza and asthma. The swelling occurs in the deeper parts of the skin or the subcutaneous tissues.<sup>2</sup> Acute urticaria evolves over days

to weeks, producing evanescent wheals that individually rarely last more than 12 h, with complete resolution of the urticaria within six weeks of onset. Daily or most daily episodes of urticaria and/or angioedema lasting more than six weeks are designated chronic urticaria. Chronic urticaria predominantly affects adults and is twice as common in women as in men.<sup>2</sup> Chronic urticaria is a frustrating problem for both physicians and patients.<sup>3</sup> Possible eliciting factors of Chronic urticaria revealed focal infection as the cause of urticaria in 43% of the patients, out of which Helicobacter Pylori (H. Pylori) was responsible for 60%.<sup>4</sup> Recent observations had suggested a possible

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etiopathogenic role of *H. Pylori* in some cases of Chronic urticaria.<sup>5</sup> Chronic infections and parasitic infestations have long been suggested to be an important causal factor for chronic urticaria, but this has never been consistently proven. It has been approximately 15 years since *H. Pylori* was first isolated from the human stomach.<sup>6</sup> *H. Pylori*, a microaerophilic gram-negative bacteria, is associated with the duodenal and gastric ulcer, gastric cancer, and atrophic gastritis and is a ubiquitous infection in the population.<sup>7</sup> Its prevalence is directly proportional to age and inversely correlated with socio-economic status in developing countries.<sup>8</sup> There is increasing evidence for systemic effects of gastric *H. Pylori* infection, which may be involved in extra gastrointestinal disorders such as vascular, autoimmune and skin diseases. A possible relationship between chronic idiopathic urticaria and *H. Pylori* infection has been suggested in preliminary studies, in which antibiotic eradication of *H. Pylori* lead to regression of urticaria in up to 100% of cases.<sup>9-11</sup> Regarding the possible mechanisms involved in the relationship between *H. Pylori* infection and chronic urticaria, a number of speculations and theories have been put forward. One possible explanation might be that the immunologic stimulation induced by infection might, through mediator release, causes a non-specific increase of the skin vessel sensitivity to agents increasing vascular permeability.<sup>12</sup> A number of agents might act through this mechanism. As a matter of fact, increased production of interleukin 8 (IL-8), platelet-activating factor (PAF) and leukotrienes (LT) B4 and C4 has been observed in the gastric mucosa of *H. Pylori* infected patients and these mediators exert evident actions on the skin.<sup>13,14</sup> Another possibility would be that urticaria patients might develop specific IgE antibodies to *H. Pylori*, an attractive explanation that still requires confirmation.<sup>15</sup> In this context, Liutu et al.<sup>16</sup> have reported greater rates of total IgE increase in patients with chronic urticaria

and *H. Pylori* infection than in those with chronic urticaria but without such infection. There have also been observations reported of increased serum *H. Pylori* IgE and basophil-bound IgE in subjects with infection<sup>17</sup> and increased basophil counts in peripheral blood in patients with dyspepsia and *H. Pylori* positivity have also been reported.<sup>18</sup> Since no study have been conducted concerning the role of *H. Pylori* in patients with chronic urticaria in Erbil city, we carried out this study to overcome this gap and to provide a baseline data for future studies on this subject. This study aimed to find out the association of chronic urticaria with *H. Pylori*, and to estimate disease risk associated with *H. Pylori*. It also aimed to identify the association of cases and controls with socioeconomic factors including age, sex, occupation, educational level and the residence.

## Methods

This case-control study was conducted at the Dermatology and Venereology Consultation Department from where the cases were selected and the controls were taken in the medical ward in Rizgary Teaching Hospital in Erbil city. The study was conducted within the period of April 1<sup>st</sup>, 2013 to January 1<sup>st</sup>, 2014. A convenience sampling method was used for selecting the cases. Any patient with urticaria for more than six weeks was included in the study. Full clinical and laboratory tests were conducted to exclude those patients with any finding which may be a cause of the urticaria. For the controls, an equal number of persons was chosen and matched by age and gender with cases and free from features of urticaria, gastrointestinal symptoms and any other condition in which *H. Pylori* may exist. The Epi Info computer program version 6 was used for sample size determination. For this purpose, 95% CI and 90% power of the study was used and a proportion of 72% among cases and 40% among control group as found in

a study conducted by Rostamy in Iran.<sup>19</sup> As a result, 55 persons were identified for the cases and 55 for the controls as a sample size for the current study. The followings patients were excluded from the study; patients suffered from physical urticaria, patients consuming proton pump inhibitor within two weeks, antibiotic and Bismuth within four weeks preceded enrolling in the study. The data was collected through direct interview and clinical examination of the patients and controls, in addition to the results of the laboratory findings. The purpose of the study was explained for each participant and verbal consent was obtained from them before inclusion in the study, and anyone wasn't interested to be involved in the study was excluded. An anonymous questionnaire form was prepared to collect data, and filled by the researcher through direct interview. The questionnaire was composed of two parts; the first part was composed of data about socio-demographic characteristics of the study sample e.g. age, sex, residency, marital status, educational level and occupation, while the second part was composed of data about history, clinical and laboratory findings from the study sample. The following laboratory investigations were applied to all the participants in the study: complete blood count (hemoglobin, white blood cells, differential count), erythrocyte sedimentation rate, thyroid function test, hepatitis B virus, hepatitis C virus, general urine examination, general stool examination and *H. pylori* antigen detection in stool by enzyme linking immunosorbent assay (ELISA) test. *H. Pylori* antigen Enzyme Immunoassay test (EIA) KIT was used for detection of *H. Pylori* antigen in the stool sample with specificity 98% and sensitivity 95% of the test.<sup>20</sup> The *H. Pylori* Antigen EIA test Kit is a solid phase EIA based on sandwich principle for the qualitative and quantitative detection of *H. Pylori* antigen in stool.<sup>20</sup> Data were analyzed using the statistical package for the social sciences

(version 19). Chi square test of association was used to compare between proportions of the two study groups. When the expected count of more than 20% of the cells of the table was less than 5, Fisher's exact test was used. A *P* value of  $\leq 0.05$  was considered statistically significant.

## Results

This study involved 110 persons (55 cases and 55 controls) with their ages ranged from 13-65 years with a mean  $\pm$  SD of  $35.15 \pm 13.60$  years for cases and  $36.58 \pm 12.25$  years for controls. The highest proportion of the cases (34.5%) were from 20-29 years age group, and the lowest proportion was from <20 years age group (5.5%). The highest proportion (32.7%) of the controls were from the age group 20-29 years, followed by the age group 30-39 years (27.3%), and the lowest proportion (3.6%) were among the age group <20 years. There was no statistically significant association between age groups of the study sample ( $P = 0.316$ ). The study sample composed of 30.9% male and 69.1% female in both cases and controls. Around 73% of the cases were from urban and 27.3% from rural areas, while 90.9% of controls were from urban and 9.1% were from rural areas. Twenty-two (40.0%) patients were housewives and 4 (7.3%) were students. Nearly two-thirds 35 (63.6%) of the controls were housewives and 3 (5.5%) were students and one was unemployed (1.8%), and this finding was statistically significant ( $P = 0.027$ ). Details of socio-demographic characteristics of cases and controls are shown in Table 1. The stool for *H. Pylori* antigen test was positive in 69.1% of cases and in 29.1% of controls. The odds ratio (OR) of cases to controls was 5.44 and this finding was statistically significant ( $P < 0.001$ ) as shown in Table 2.

**Table 1:** Socio-demographic characteristics of cases and controls.

Variables	Study sample		Total No. (%)	P value
	Cases No. (%)	Controls No. (%)		
<b>Age (years)</b>				
< 20	3(5.5)	2(3.6)	5(4.5)	0.316
20-29	19(34.5)	18(32.7)	37(33.6)	
30-39	15(27.3)	15(27.3)	30(27.3)	
40-49	8(14.5)	9(16.3)	17(15.5)	
50-59	7(12.7)	7(12.7)	14(12.7)	
≥60	4(7.3)	3(5.5)	7(6.4)	
<b>Sex</b>				
Male	17(30.9)	17(30.9)	34(30.9)	0.58
Female	38(69.1)	38(69.1)	76(69.1)	
<b>Residency</b>				
Urban	40(72.7)	50(90.9)	90(81.8)	0.013
Rural	15(27.3)	5(9.1)	20(18.2)	
<b>Occupation</b>				
Unemployed	14(25.4)	11(20)	25(22.8)	0.027
Employed	15(27.3)	6(10.9)	21(19.1)	
Student	4(7.3)	3(5.5)	7(6.4)	
House wife	22(40.0)	35(63.6)	57(51.8)	
Total	55(100.0)	55(100.0)	110(100.0)	

**Table 2:** Stool for H. Pylori results among cases and controls.

Stool for H. Pylori Antigen	Study sample		Total No. (%)	OR	P value
	Case No. (%)	Control No. (%)			
Positive	38(69.1)	16(29.1)	54(49.1)	5.44	<0.001
Negative	17(30.9)	39(70.9)	56(50.9)		
Total	55(100.0)	55(100.0)	110(100.0)		

The highest rate of the positive +H. Pylori among cases was among 20-29 years age group with 36.8%, with mean  $\pm$  SD  $35.75 \pm 12.64$ . While the highest rate of positive +H. Pylori among controls was among 20-29 years and 30-39 years age groups with 31.3%, with mean  $\pm$  SD  $35.96 \pm 13.25$ . These findings were not statistically significant ( $P = 0.94$ ). The highest rate of the positive +H. Pylori cases and controls were among female 28 (73.7%) and 10 (62.5%), respectively. This

finding was not statistically significant ( $P = 0.517$ ) as shown in Table 3. In this study 19 (50%) of positive +H. Pylori cases had dyspepsia, at the same time 19 (50.0%) of them weren't complaining from peptic ulcer disease (**PUD**) symptoms, while 4(23.5 %) of negative --H. Pylori cases had dyspepsia symptoms and 13 (76.5%) were free from dyspepsia symptoms and this finding was not statically significant ( $P = 0.66$ ) as shown in Table 4.

**Table 3:** Age and sex distribution of the positive + H. Pylori cases and controls.

Variables	Study sample		Total No. (%)	P value
	Case No. (%)	Control No. (%)		
<b>Age (years)</b>				
< 20	2(5.3)	0(0.0)	2(3.7)	0.94
20-29	14(36.8)	5(31.3)	19(35.1)	
30-39	10(26.3)	5(31.3)	15(27.7)	
40-49	5(13.2)	3(18.8)	8(14.8)	
50-59	5(13.2)	2(12.5)	7(13)	
$\geq 60$	2(5.3)	1(6.3)	3(5.5)	
<b>Sex</b>				
Male	10(26.3)	6(37.5)	16(29.6)	0.517
Female	28(73.7)	10(62.5)	38(70.4)	
Total	38(100.0)	16(100.0)	54(100.0)	

**Table 4:** Relation of stool positive +H. Pylori and dyspepsia.

Stool for H. Pylori antigen	Dyspepsia		Total No. (%)	P value
	Yes No. (%)	No No. (%)		
Positive	19(50.0)	19(50.0)	38(69.1)	0.66
Negative	4 (23.5)	13(76.5)	17(30.9)	
Total	23(41.8)	32(58.2)	55(100)	

## Discussion

Chronic urticaria is one of the most frequent diseases in dermatology and till now its etiology is recognized only in a minority of cases.<sup>21</sup> Some recent studies point to infections due to *H. Pylori* as being of major importance in the pathogenesis of chronic idiopathic urticaria.<sup>22-24</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>24</sup> In this study *H. Pylori* antigen Enzyme Immunoassay test KIT (ACON, Germany) was used for detection of *H. Pylori* which directly detect the antigen in the stool specimens for active infection with 98% specificity and 95% sensitivity.<sup>20</sup> Stool antigen test have been recommended by both the American Gastroenterological Association and the American College of Gastroenterologist as the most accurate noninvasive test for diagnosis and for confirmation of eradication of *H. Pylori*.<sup>25,26</sup> while the serology tests detects IgG antibody in patient serum with current or prior infection and cannot distinguish current and past infection with sensitivity and specificity of  $\leq 90\%$ .<sup>27,28</sup> Thus, serology tests are not recommended by the AGA for initial diagnosis of *H. Pylori* infection.<sup>27</sup> Furthermore, they are not recommended by either AGA or the ACG for monitoring infection or confirming eradication of the organism.<sup>27,28</sup> In the current study 110 persons were participated (55 cases and 55 controls) with age and sex matching, their ages ranged from 13-65 years with mean $\pm$ SD 35.145 $\pm$ 13.593 years for cases, and 36.582 $\pm$ 12.252 years for controls. This was near to that found in India,<sup>29</sup> Portugal<sup>30</sup> and Indonesia,<sup>31</sup> while far from that found by Rostamy MM in Iran<sup>19</sup> when their age ranged from 18-84 years and Taiwan<sup>32</sup> ages ranged from 27-68 years with a mean of 45.5 years. This indicate that chronic urticaria doesn't occur in early childhood and even adolescent years, because

generally chronic urticaria predominantly affects adults<sup>2</sup> and chronic urticaria is in need to microbiological and immunological changes of long duration, response, reaction of the body and finally development of pathogenesis of urticaria and then liberation of cytokines, histamines that lead to development of wheal and angiodema. In this study 69% of cases were female and 31% of them were male, with the male to female ratio of 1:2.2. This finding agrees with that found by Sadighha A et al. in Iran,<sup>33</sup> in which male to female ratio was 1:2, and in Indonesia study<sup>31</sup> where male to female ratio 1:4.3. This may be due to low levels of dehydroepiandrosterone (DHEA)-S in females, suggesting a possible role for hormone imbalance.<sup>2</sup> In this study the highest proportion of cases and controls (72.7%, 90.9% respectively) were from urban area & this may be due to the fact that majority of patients attending the Rizgary Teaching Hospital for different specialties were from inside city, while those in rural areas usually attend to health service facilities in their locality. In the present study, we found that majority of cases with chronic urticaria were housewives and this was statistically significant; this may be due to the housewife environment which plays a role in developing chronic urticaria such as dust which contains house dust mites, consumption of raw contaminated foods during the preparation of foods in comparison to other occupations. In the present study, stool for *H. Pylori* antigen test in 69.1% of cases while 29.1% of controls were positive and odds ratio was 5.44. This indicates that those people with positive +*H. Pylori* have 5.44 times more likelihood to get chronic urticaria, in comparison to those who are free from *H. Pylori*. This finding was consistent with that done by Rostamy MM in Iran,<sup>19</sup> Qazi et al. in Pakistan,<sup>34</sup> Abu El-Emin et al. in Egypt,<sup>35</sup> Garza et al.,<sup>36</sup> in Turkey<sup>37</sup> while it was inconsistent with that found by Ghazzawi et al.<sup>38</sup> in Jordan and Sianturi

et al. in Indonesia.<sup>31</sup> Rostamy in Iran<sup>19</sup> found that in 53 chronic urticaria cases the frequency of positive IgG antibodies against H. Pylori antigens was about 69.8% and 40% for controls. He concluded that infection with H. pylori has a significant relationship with chronic urticaria. Qazi et al. in Pakistan<sup>34</sup> found that 95% of chronic urticaria cases were positive for H. Pylori antibodies, by detecting antibodies in serum by ELISA technique. All patients with positive +H. Pylori antibodies of the study received the eradication therapy for H. Pylori, and statistically significant improvement was obtained. Abu El-Emin et al. in Egypt<sup>35</sup> found that a significant H. Pylori specific IgG level was detected in patients with chronic idiopathic urticaria in comparison with the control group 75/100 (75%) versus 20/45 (44.4%), clinical improvement of the urticaria was found after receiving triple therapy for eradication of H. Pylori, and decrease in frequency of chronic idiopathic urticaria in most cases in a follow-up period of 2 months from the start of therapy. Garza et al.<sup>36</sup> in Mexico found that in 30 patients with chronic urticaria, the frequency of positive IgG antibodies against H. Pylori antigens was 60%, and that of IgA, fecal H. Pylori antigens and rapid urea and histology was 33.31%, 60% and 83%, respectively. In general, the difference between study results was probably due to socioeconomic, race, method used for H. Pylori infection. The study found positive +H. Pylori were most commonly among female cases (73.7% females vs. 26.3% males) and controls (62.7% females vs. 37.5% males). This may be explained by the fact that chronic urticaria already more common in female which may be due to low levels of dehydroepiandrosterone (DHEA)-S in females, suggesting a possible role for hormone imbalance.<sup>2</sup> Moreover, the majority of our study sample females were housewives who are exposed to raw foods due to preparing and handling foods more than the males. This was consistent with that found by Jaff

in Kurdistan region of Iraq.<sup>39</sup> In the current study, there was no statistical difference between those with PUD symptoms and H. Pylori infection, which agrees with that found in Indonesia<sup>31</sup> and Egypt.<sup>35</sup> In the current study, the highest rate of chronic urticaria was found in those with duration of 2-12 months duration, and the highest rate of positive +H. Pylori cases (68.9%) was among this duration. This may be that the average duration of chronic urticaria is within this period or those people within this duration of symptoms, they weren't using any medicine for the elimination of H. Pylori, because usually and routinely neither antibiotics nor protein pump inhibitor is used as the treatment of urticaria.

### Conclusions

The study concluded that there is a significant association of chronic urticaria with infection by H. Pylori, indicating to include the H. Pylori tests in diagnostic workup for chronic cases of urticaria and conducting further randomized controlled studies including using H. Pylori eradicating drugs.

### Conflicts of interest

The authors report no conflicts of interest.

### References

1. Yosipovitch G, Ansari N, Goon A, Chan YH, Goh CL. Clinical characteristics of pruritus in chronic idiopathic urticaria. *Br J Dermatol* 2002; 147:32-6.
2. James WD, Berger TG, Elston DM. *Andrews' Diseases of the skin clinical dermatology*. London: British Library Cataloguing in Publication Data; 2011.
3. Champion RH. A practical approach to urticarial syndromes: A dermatologist's view. *Clin Exp Allergy* 1990; 2:221-4.
4. Wedi B, Wagner S, Werfel T, Manns MP, Kapp A. Prevalence of *Helicobacter pylori* gastritis in chronic urticaria. *Int Arch Allergy Immunol* 1998; 116:288-94.
5. Federman DG, Krisner RS, Moriarty JP, Concato J. The effect of antibiotic therapy for patients infected with H. pylori who have chronic urticaria. *J Am Acad Dermatol* 2003; 49:861-4.
6. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* 1984; 1:1311-5.

7. Graham DY. *Helicobacter pylori* infection in the pathogenesis of duodenal ulcer and gastric cancer: a model. *Gastroenterology* 1997; 113:1983-91.
8. Graham DY, Malaty HM, Evans DG, Evans DJ, Klein PD, Adam E. Epidemiology of *Helicobacter pylori* in an asymptomatic population in the United States. Effect of age, race, and socioeconomic status. *Gastroenterology* 1991; 100:1495-501.
9. Tebbe B, Geilen CC, Schulzke JD, Bojarski C, Radenhausen M, Orfanos CE. *Helicobacter pylori* infection and chronic urticaria. *J Am Acad Dermatol* 1996; 34:685-6.
10. Bonamigo RR, Leite CS, Bakos L. Association of *Helicobacter pylori* and chronic idiopathic urticaria. *Rev Assoc Med Bras* 1999; 45:9-14.
11. Di Campi C, Gasbarrini A, Nucera E, Franceschi F, Ojetti V, Sanz-Torre E. Beneficial effects of *Helicobacter pylori* eradication on idiopathic chronic urticaria. *Dig Dis Sci* 1998; 43:1226-9.
12. Rebora A, Drago F, Parodi A. May *Helicobacter pylori* be important for dermatologists?. *Dermatology* 1995; 191:6-8.
13. Ahmed A, Holton J, Vaira D, Smith SK, Houtl JR. Eicosanoid synthesis and *Helicobacter pylori* associated gastritis: increase in leukotriene C4 generation associated with *H. pylori* colonization. *Prostaglandins* 1992; 44:75-86.
14. Pasechnikov V, Mashentseva E, Sohler M. Mucosal interleukin-8, platelet-activating factor, endothelin-1, leucotriene B4 and leucotriene C4 production in patients with *Helicobacter pylori* infection. *Gut* 1996; 39:A40.
15. Realdi G, Dore MP, Fastame L. Extradigestive manifestations of *Helicobacter pylori* infection: fact and fiction. *Dig Dis Sci* 1999; 44:229-36.
16. Liutu M, Kalimo K, Uksila J, Kalimo H. Etiologic aspects of chronic urticaria. *Int J Dermatol* 1998; 37:515-519.996; 39:A40.
17. Andersen LP, Norgaard A, Bennedsen M. Immune Response cellular and humoral against *Helicobacter pylori*. In: López-Brea M, ed. *Helicobacter pylori: Challenges for the XXI century. Microbiology, clinical and treatment*. Barcelona: Prous Science SA; 1999. PP.157-76.
18. Karttunen TJ, Niemela S, Kerola T. Blood leukocyte differential in *Helicobacter pylori* infection. *Dig Dis Sci* 1996; 41:1332-6.
19. Rostamy MM. Prevalence of *H pylori* infection in chronic urticaria. *J Paki As Derm* 2010; 20: 142-5.
20. Pronovost AP, Rose SL, Pawlak J, Robin H, Schneider R. Evaluation a new immunological and microbiological results. *J Clin Micro* 1994; 32:46-50.
21. Greaves M. Chronic urticaria. *J Allergy Clin Immunol* 2000; 105(4):664-72.
22. Daiulin E, Jimeno I. *Helicobacter pylori* and idiopathic chronic urticaria. *Inter J Dermatol* 2000; 39:446-52.
23. Kolibasova K, Cervcnkova D, Hegyi E. *Helicobacter pylori*: etiological factor in chronic urticaria. *Dermatosen* 1994; 42:235-6.
24. Kolibasova K, Cervcnkova D, Hegyi E. *Helicobacter pylori* infection and chronic urticaria. *J Am Acad Dermatol* 1996; 34:685-6.
25. Talley NJ. American Gastroenterological Association. American Gastroenterological Association medical position statement: evaluation of dyspepsia. *Gastroenterology* 2005;129:1753-5.
26. Talley NJ, Vaki NB. Practice parameters Committee of the American College of Gastroenterology. Guidelines for the management of dyspepsia. *Am J Gastroenterol* 2005; 100: 2324-37.
27. Chey WD, Wong BC. Practice parameters Committee of the American College of Gastroenterology. American College of Gastroenterology guidelines on the management of *Helicobacter pylori* infection. *Am J Gastroenterol* 2007; 102:1808-25.
28. Talley NJ, Vaki NB, Moay Yedi P. American Gastroenterological Association technical review on the evaluation of dyspepsia. *Gastroenterology* 2005; 129:1756-80.
29. Yadav M K, Rishi J P, Nijawan S. Chronic urticaria and *Helicobacter pylori*. *Indian J Med Sci* 2008; 62(4):157-62.
30. Moreira A, Rodrigues J, Delgado L, Fonseca J, Vaza M. Is *Helicobacter pylori* infection associated with chronic idiopathic urticaria?. *Allergol et Immunopathol* 2003; 31(4):209-14.
31. Sianturi G N, Soebaryo, Zubier F, Syam AF. *Helicobacter pylori* Infection: Prevalence in Chronic Urticaria Patients and Incidence of Autoimmune Urticaria. *Indones J Intern Med* 2007; 39(4):157-62.
32. Chiu Y, Tai W, Chuah S, Hsu P, Wu D, Wu K. The Clinical Correlations of *Helicobacter pylori* Virulence Factors and Chronic Spontaneous Urticaria. *Gastroenterol Res Pract* 2013; 43: 672-7.
33. Sadighha A, Shirali R, Zahed G M. Relationship between *Helicobacter pylori* and chronic urticaria. *JEADV* 2009; 23:169-76.
34. Qazi N, Samadani A J, Jamali S, Begum S, Shah M. Chronic Idiopathic Urticaria and *Helicobacter Pylori* Infection: Effect of Eradication Therapy on the Relief of Symptoms. *JLUMHS* 2013; 12 (3):172-6.
35. Abu El - Emin A, Fathe A, Khedr M, Abu El-Ata A. *Helicobacter pylori* Infection: A possible cause of Chronic Idiopathic Urticaria (Prevalence and Effectiveness of Eradication). *The Egyptian Journal of Hospital Medicine* 2008; 30:145-50.
36. Garza YL, López GI, Paz MD. Prevalence of seropositividad to antibodies IgG and IgM against *Helicobacter pylori* in the medical residents of the University Hospital of Puebla. *Rev Alerg Mex* 2006; 53:69-72.



37. Baskan EB, Turker T, Gulden M, Tunali S. Lack of correlation between Helicobacter Pylori infection and autologous serum skin test in chronic idiopathic urticaria. *Int J Dermatol.* 2004; 12: 110-3.
38. Ghazzawi IM, Obidat NA. The role of Helicobacter pylori infection in the pathogenesis of chronic urticaria. *Pak J Med Sci* 2004; 20(2): 101-4.
39. Jaff MS. Relation between ABO blood groups and Helicobacter pylori infection in symptomatic patients. *Clin Exp Gastroenterol* 2011; 4: 221-6.