

## **Helicobacter pylori (H.p.) Infection: A possible cause of Chronic Idiopathic Urticaria (Prevalence and Effectiveness of Eradication)**

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### **Abstract:**

Chronic idiopathic urticaria (CIU) is one of the most frequent skin diseases with an incidence ranging from 1.2% to 23% , however its causes remains unknown in the vast majority of cases. A possible relationship between chronic urticaria and *Helicobacter pylori* (H.p.) has been recently suggested.

The aim of this study was to determine the prevalence of *Helicobacter pylori*(H.P.) infection in patients with C.I.U. and to investigate the effectiveness of eradication therapy of (H.p.) infection on this skin disease.

100 patients (40 males and 60 females) with C.I.U as well as 45 apparently healthy (age, sex, matched controls) were enrolled in this study underwent serological testing for H.pylori infection with the 13C –urea test as well as by specific IgG antibodies against the H. pylori (ELISA technique). Positive patients were treated with, Omeprazole – Clarithromycin + Amoxicillin for 10 days. Eradication and clinical course were followed up two months after the treatment in comparison to the negative cases as a control group. The clinical evaluation and follow up were demonstrated as worse, same, less and disappearance of flares.

In our results there was significant difference in the sero prevalence of H.pylori infection between idiopathic chronic urticaria patients and healthy subjects. H.pylori was detected in 75% of patients and 20% of controls. Out of 75 patients treated , only 24 showed complete remission of their urticaria after successfully eradicating H.pylori infection ,the others only having some improvement in their symptoms.

The mean IgG titer was 86.8 + 42.4 among patients group, where it was 16.+ 42.8 among the control group (p< 0.05) .

After treating the positive patients with appropriate antibiotics for 10 days there are a significant decrease of H.P. specific IgG as compared to the negative cases and also bacterium eradication is associated with a remission of urticarial symptoms. as compared to the negative cases. In conclusion, *Helicobacter pylori* affects a high percentage of patients with idiopathic chronic urticaria and bacterium eradication was associated with a remission of urticarial symptoms suggesting a possible role of H. pylori in the pathogenesis of this skin disorder.

### **Introduction**

Urticaria is a common disease affecting up to 15-20% of the population at least once during their life time (Carsten *et al.*, 2000). Chronic urticaria presents with almost daily occurrence of wide spread itchy, recurrent, urticarial wheals with individual lesions lasting less than 24 hours for at least six weeks. Chronic idiopathic

urticaria (CIU) is a term used for chronic urticarial patients in which food and drug allergy, urticarial vacuities and physical urticaria have been excluded (Liutu *et al.*, 1998). The etiology of urticaria often remains unknown, it is recognized only in minority of cases, it may be provoked by single or severs simultaneous

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pathogenic factors (Liutu *et al.*, 1998). Allergic to a wide variety of agents have been suspected, as well as hypersensitivity to food additives or drugs. Infection have been also regarded as possible etiologic factor in urticaria (Gravcs, 2002). Several infectious agents have been implicated as an etiologic or an exacerbating factor of chronic urticaria, and the treatment of the underlying infections leads to its resolutions.

### Patients and methods

One hundred patients with CIU (40 males and 60 females) were enrolled into this study. Their age range was 20 to 60 years (mean, 44 years), and the disease duration was between six months and fifteen years (mean, 36 months). We used 45 age and sex matched unrelated healthy blood donor volunteers (30 females and 15 male) as controls, their age was between 20 and 65 years of age (mean, 45.4 years). CIU was diagnosed by history and clinical findings. Patients with CIU of other origin were excluded from the study, including those with focal/systemic infections, atopy food/drug allergy, physical urticaria, autoimmune diseases, and malignancies. All patients were examined for H.pylori infection with 13-C urea breath test(6,7), and for an enzyme-linked immunosorbent assay (ELISA) for specific IgG antibodies against H.pylori (8,9). All patients were well informed about the study. 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.

Patients with positive (H.p.) specific IgG titer (**n =75 out of 100**) were treated for 10 days by triple therapy Omeprazole, 20mg twice daily + clarithromycin, 500 twice daily + amoxicillin 1 gm twice daily for 10 days, then another clinical re-evaluation of patients was also done after

therapy of (H.P.) infection and the severity of CIU was assessed as worse same less or disappearance of flares. Statistical analysis: Data obtained were collected, tabulated and statistical analyzed. *P values* of < 0.001 or less were considered significant.

Scoring was carried out according to the following criteria : (table1)

1. Three or more + ve findings at a mild degree is considered a mild case.
2. Three or more + ve findings at a moderate degree in considered a moderate case.
3. Three or more + ve findings at a sever degree is considered a sever case.
4. Any other variation is considered a moderate case.

### Results

In this study, a significant increase in H.P. specific IgG level was detected in patients with (CIU) in comparison with the control group 75/ 100 (75%) versus 20/45 (44.4%),  $p < 0.001$  (table 2).

The mean H.P. specific IgG titer in patients was 86.8 (+-) 42.4, while in the control group it was 48.0(+-) 38.87 ( $p < 0.05$ ).

1. As regards the clinical features of (CIU), it was found that H.P0 specific IgG + ve patients were older (42 + 8.4 versus 36 + 8.2 }years,  $p < 0.05$  and urticaria lasted for longer duration 30.28% verses 36.56%)  $p < 0.05$  than H.p. IgG - ve patients
2. Also the majority of our chronic urticarial patients were females in the 3<sup>rd</sup> and 4<sup>th</sup> decades of life (chart 2).
3. Gastro intestinal symptoms were present in 58 (77%) of our chronic urticaria patients who had an elevated IgG titer and the effect of anti- helicobacter pylori triple therapy on CIU symptoms, shows that 40% of patients had the same condition while 60% was less than before the treatment.

**Table (1): Scoring of chronic idiopathic urticaria patients**

Degree	No. of wheals	% of body area involved	Associated itching	Duration	Angioedema	Score
Mild	1-5	25%	Mild doesn't bother the patient	6 weeks	No	+ ve
Moderate	5-10	25 – 50%	Moderate, bothers the patient	6 weeks - 1 year	Slight degree	++ ve
Severe	> 10	> 50%	Sever, interfering with daily activity	> 1 year	Eyelids, lips, face	+++ve

Statistical analysis :Data obtained were collected , tabulated and statistical analyzed .*P values of < 0.05 or less were considered significant.*

**Table 2 : Helicobacter pylori testing in patients with idiopathic chronic urticaria and in control subjects .**

Category	Urase test		IgG		Total
	(+)	(-)	(+)	(-)	
Patients	87(87%)	13(13%)	75(75%)	25(25%)	100
Controls	—	—	20(44.4%)	23(55.6%)	45

**Table 3: Comparison between patients with CIU and healthy controls as regards detection of H. pylori specific IgG.**

Group	Total No.	+ve H.p. specific IgG.	
		No	%
Group I	100	75	75
Group II	45	20	44.4
$X^2$	4.64		
<i>P.value</i>	<0.001 (S)		

**Table 4: Clinical features of CIU in positive versus negative H.p. specific IgG.**

Feature	Patients No=100		<i>T. Test</i>	<i>P. value</i>
	+ ve H.p. specific IgG. (No.75)	- ve H.p. specific IgG. (No.25)		
Age (mean years)	42+ 8.2	34-9.1	3.32	<0.05 (S)
Wheals > 2.4hs	60 (80%)	15 (60%)	4.12	<0.05 (S)
Gastrointestinal symptoms	58 (77%)	6 (24%)	4.2	<0:05 (S)

(S) = significant =  $p < 0.05$ .

**Outcome of to urticaria after treatment.**

CIU symptoms	No. of cases	%
Same	40	40
Less	60	60

### Discussion

Chronic urticaria is one of the most frequent skin disease and still its etiology is recognized only in a minority of cases (Greaves, 2000).

Recent evidence suggest that most instances of chronic urticaria are autoimmune , and 27% to 50% of patients with ICU have been found to have functional auto antibodies directed against the alpha – chain of the high-affinity IgE receptor or less commonly against IgG. ( Greaves , 2000 ; Valsccchi & Pigatto, 1998 and Wcdi *et al.* , 1998) Infection especially hidden or overt have been regarded as possible etiologic factor ( Juhlin ., 1981).

Some recent studies point to infections due to helicobacter pylori as being of major importance in the pathogenesis of ICU (Esteban Daiulin, 2000 ; Kolibasova *et al.*, 1994 ; Kolibasova Von *et al.*, 1996) and (Bonomigo *et al.* , 1999). 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 (Kolibasova Von *et al.*, 1996) .

Rebera, *et al.* (1995) first described the role of Helicobacter pylori in chronic idiopathic urticaria (Rebora *et al.* ,1995). As in our study they detected higher prevalence of H.pylori infection in the patients than in the control group, these results are coincident with what was reported by other authors (Kolibasova *et al.* , 1994 and Kolibasova Von *et al.*, 1996). But in contrast to these results, Bong, do not found any statistically significant difference between patients and controls (Bong., 1999) . This may explained by the fact that this studies were done in countries with a relatively low prevalence of H.pylori infection (30%to40%) compared with ours (60 %). We further investigate the connection between CIU and H. pylori, we treated the 75 patients with positive H. pylori IgG in our study suffering from CIU. In 60 out of 75 patients(80%), clinical improvement of the urticaria was found after eradication of H. pylori and decrease

in frequency of CIU in most cases in a follow up period of 2 months from the start of treatment. This was in agreement with that of (Wustlich *et al.*, 1999 and Di compli *et al.*, 1998).

A recent study in this particular showed a significant decrease in the typical symptoms of urticaria, such as wheals, erythema, and purities after eradication of H.pylori (Wustlich *et al.*, 1999 and Di compli *et al.*, 1998). The reason behind this phenomenon, however, are unknown, probably an increase in mast cell de - granulation, which could be induced by peculiar H.pylori cytotoxic strains, may act as a trigger in subjects with an individual susceptibility to develop urticaria.

These results may suggest that H. pylori has a role in initiating/ or aggravating urticarial lesions and its eradication mostly leads to improvement of the attacks.

Sixty patients (80%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 %) of uninfected patients . Although many of our patients improved after successful eradication of H.Pylori infection , only35% showed complete remission of their urticaria. 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 18,19 most literature from the west gives remission rates in 95% to 100% of patients infected with H.pylori 15-17. 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 (30-40%) compared with ours (60%).

The significant association between H. pylori infection and chronic urticaria leading to the suggesting that investigating H.P. infection must be included in the diagnosing management of chronic idiopathic urticaria especially if they not respond well to conventional therapy.

## Références

1. **Greaves M (2000)** : Chronic urticaria. *J Allergy Clin. Immunol* 105: 664-72.
2. **Gasbarrini A, Ponzetto A, Francheschi F, et al. (1998)** : Helicobacter pylori infection and extra digestive diseases. Current opinion in Gastroenterology, 14 (suppl): S 65.
3. **Rebora A, Drago F, Parodi A. (1995)** : May Helicobacter pylori be important for Dermatologists? *Dermatology*, 191(1): 6.
4. **Carsten BJ, Aldo Finzi and Malcom Greaves (2000)** : Chronic urticaria: diagnostic recommendations. *J of Eur Academy of Dermatology and Venereology*, 14: 175-180.
5. **Greaves MW (1995)** : Chronic urticaria. *New England J Med*, 332: 1767-1772.
6. **Liutu M, Kalimo K, Uksila J, et al (1998)** : Etiologic aspects of chronic urticaria. *Int. J. Dermatol*, 1998; 37 (7) : 515.
7. **Greaves MW (2002)** : Pathophysiology of chronic urticaria. *Int Arch. Allergy Immunol*. 127: 3-9.
8. **Shiotani A, Okada K, Yanaoka S, Sakuranc M and Matsunaka M (2001)** : Beneficial effects of Helicobacter pylori eradication in dermatologic diseases. *Helicobacter*, 6: 60-65.
9. **Rebora A, Drago F and Parodi A (1995)** : May Helicobacter pylori be important for Dermatologists? *Dermatology*, 191:6-8.
10. **Greaves MW (2000)** : Urticaria. *International Journal of Dermatol*. 39 : 446 – 452.
11. **Juhlin L (1981)** : Recurrent urticaria: A clinical investigation of 330 patients. *Br J Dermatol*, 104: 369-381.
12. **Valscchi R and Pigatto P (1998)** : Chronic urticaria and Helicobacter pylori. *Acta Derm Venereol*, 78: 440-442.
13. **Wedi B, Wagner S, Werfel T, Manns MP and Kapp A (1998)** : Prevalence of Helicobacter pylori-associated gastritis in chronic urticaria. *Int Arch.*, 14: 175-180.
14. **Esteban Daiulin, Isabel Jimeno/ Alonso and Aman» Gareia-Diez (2000)** : Helicobacter pylori and idiopathic chronic urticaria. *International Journal of Dermatology.*, 39: 446-452.
15. **Kolibasova K, Cervenkova D, Hegyi E et al. (1994)** : Helicobacter pylori: etiological factor in chronic urticaria. *Dermatol.*, 42: 235-236.
16. **Kolibasova Von K, Cervenkova D, Hegyi E et al. (1996)** : Helicobacter pylori infection and chronic urticaria. *J Am Acad. Dermatol*, 34: 685-686.
17. **Bonomigo RR, Leite CS, Bakis L, et al (1999)** : Association of Helicobacter pylori and chronic idiopathic urticaria. *Rev. Assoc. Med. Bras.*, 45: 9.
18. **Daiiden K, Jiniene/-Alonso I and Garda Die/ A (2000)** : Helicobacter pylori and idiopathic chronic urticaria. *Int J Dermatol.*, 39: 446-452
19. **Huok-Nikanne J, Varjonen K, Ilarvina RJ and Kosunen TU (2000)** : Is Helicobacter pylori infection associated with chronic urticaria? *Acta Dermatol. Venereol.*, 80: 425-426.
20. **Bong RH. (1999)** : Helicobacter pylori infection and chronic urticaria British association of Dermatologists annual meeting. Edinburgh, Uni Ted KING DOM, 29 June-3 July, *Br. J. Dermatol.*, 141 55 : 16.
21. **Wustlich S, Brehler R, Luger TA, et al. (1999)** : Helicobacter pylori as a possible bacterial focus of chronic urticaria – *Dermatology.*, 198:130.
22. **Di campli C, Gasbarrini A, Nucera, E. et al (1998)** : Beneficial effects of Helicobacter Pylori eradication on chronic idiopathic urticaria. *Dig. Dis Sci.*, 43: 1226.

## هليوباكتري بايلوري والارتكاري المزمنة

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أبو العطا

أقسام الأمراض الجلدية و الأمراض المتوطنة و الباثولوجية الإكلينيكية و الميكروبيولوجي  
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هليوباكتري بايلوري هو السبب الشائع لالتهابات المعدة والقرحة وهي حاليا  
تعتبر من العوامل الأساسية لكثير من أمراض الجهاز الهضمي. وهناك دراسات كثيرة  
لهذا الميكروب وعلاقته بالارتكاري المزمنة. ولمعرفة احتمالية هذه البكتريا كسبب  
لمرض الارتكاري المزمدة في المرضى المصريين، تم الحصول على عينات من السيرم  
من المرضى (100) ومن غير المرضى المتطوعين (45) وتم اختيار هذه العينات  
باختبار اليوريز و باستخدام طريقة الاليزا لقياس نسبة الأجسام المضادة (ج) ضد  
الهليوباكتري بايلوري.

**كانت النتائج إيجابية في:**

- 75% من المرضى.

- 20% لغير المرضى.

**وهو إحصائيا يعتبر معدلا كبيرا (P < 0.001).**

وبعد العلاج وجدنا أن 60% من المرضى اختفت منهم الأعراض وعليه فإن  
هذه الدراسة تدعم العلاقة بين الارتكاري المزمنة الغير معروفة السبب والهليوباكتري  
يلوري كسبب من الأسباب المحتملة.

وأیضا نستخلص من هذه الدراسة أن نسبة انتشار الهليوباكتري بايلوري عالية في  
مرضى الارتكاري المزمنة للمشتركين في الدراسة، ولذلك نوصى بضرورة تحري  
وجود الميكروب في مرضى الارتكاري المزمنة حيث أن علاج هذا الميكروب قد  
يساعد في شفاء هؤلاء المرضى.