



## Original Research Article

## Correlation of serum IgG antibodies to helicobacter pylori in chronic skin disorders: A case-control study

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## ABSTRACT

**Background:** It is known that chronic idiopathic urticaria occasionally develops in association with Helicobacter pylori infection, but this relationship remains unproven. Also, many studies show.

**Materials and Methods:** We investigated the role of H. pylori infection in patients of chronic idiopathic urticaria, other chronic skin disorders as well as healthy controls using urease breath test and immunoturbidimetry for anti H. pylori IgG antibodies. Three groups of eighty-nine patients each were taken as cases, controls and placebo controls respectively. All patients having IgG titer of 10U/ml or above and Urease Breath Test Positivity were considered positive.

**Results:** The positive rate of anti H. Pylori IgG antibodies was 78.65% (70/89) in case group, 84.71% (22/89) in controls with other skin disorders and 32.58% (29/89) in placebo control group. While positive rate for Urease Breath Test were found to be 79.8% (71/89) in cases, 35.95% (32/89) in controls with other skin diseases and 32.58% (29/89) in placebo controls.

**Conclusion:** In chronic idiopathic urticaria a high titer of anti H. pylori IgG and Urease Breath Test positivity suggests that inclusion of anti H. pylori therapy in it's the management would be beneficial and would lead to lower rates of recurrence. Also, low positivity rates of Urease Breath Test and Anti H. pylori IgG in controls with other chronic skin diseases and placebo controls points towards no clear evidence to prove a causal relationship between these diseases and H. pylori infection.

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## 1. Introduction

Chronic Skin Disorders like Urticaria, Psoriasis, Rosacea and Alopecia Areata are postulated to have a possible relationship with H. pylori infection. A considerable number of reports link H. Pylori infection with the development of skin disorders, which can be manifestations of systemic vasculitides (Behçet's disease [BD]) or may be related to skin disorders with presumed autoimmune origin (urticaria, psoriasis, alopecia areata [AA], lichen planus, etc). Urticaria is defined as a transient, recurrent eruption of itchy wheals occurring daily or almost daily which persist for longer than

6 weeks. The clinical symptoms are caused by histamine and other vasoactive mediator release, which is induced by the binding of an allergen to the specific mast cell receptor.<sup>1</sup>

Its etiology often remains unestablished despite extensive investigative workup rendering cause specific management difficult. Foods, drugs, inhalants, systemic diseases, autoimmunity, and stress have frequently been implicated.<sup>2</sup> Focal bacterial and viral and parasitic infections have also been implicated at a rate as high as 43% of urticaria patients, and treating them empirically remains an unsubstantiated method in urticaria management.<sup>3,4</sup>

Recently a possible relation between CIU and H. pylori has been suggested. Various systematic reviews

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and meta-analyses proves that antibiotic therapy for *H. pylori* eradication increased the remission rate and induces improvement in CSU with few adverse events.<sup>5,6</sup> This seems to show that there is a positive correlation between a positive autologous serum skin test and *H. pylori* suggesting its role in autoimmune pathogenesis. Various studies have shown role of *H. pylori* in the pathogenesis of various extra gastric skin diseases like psoriasis, lichen planus, pruritus, prurigo, sweet's syndrome, rosacea, behcet's disease, alopecia areata<sup>7</sup> Also, different studies have described the relationship between the titre of anti *H. pylori* IgG antibody and urticaria.<sup>8,9</sup>

Off lately, there are many studies showing that immune response to *H. pylori* may have an indirect role in inducing urticaria and other chronic skin disorder. So, by conducting this case-control study, we want to find the role of *H. pylori* in etiopathogenesis of urticaria and its association with other chronic skin diseases.

## 2. Materials and Methods

A case control study was conducted on a total of 178 patients coming to the Out Patient Department of Dermatology, Venereology and Leprosy at Geetanjali Medical College and Hospital, Udaipur, from January 2020 to June 2020. Eighty-nine patients or more with chronic idiopathic urticaria in Case group (Group 1) and same number of patients visiting the Dermatology department having no complains of urticaria (Group 2-which served as a control group) and a Group 3- A placebo control group including healthy individuals were included in the study. Patients of any age group of both sexes, diagnosed with chronic idiopathic urticaria who provide valid informed consent were selected. Patients diagnosed with inducible urticarias, cholinergic urticaria, aquagenic urticaria, exercise induced urticaria, solar urticaria, cold urticaria, pressure urticaria, the presence of other concomitant serious medical and surgical disease were excluded from the study, patients who had taken proton pump inhibitors, antibiotics within the preceding 4 weeks were also excluded from the study. Written informed consent was taken for their participation in the study. Detailed history including name, age, sex, address, contact number, marital status, occupation, history of medication was noted. Selected patients will be thoroughly examined and any previous treatment was recorded. Anti *H. pylori* IgG antibodies in the serum were detected by Immunoturbidimetry. Techniques like Rapid Urease Test and Endoscopy are used for diagnosis but are difficult to counsel for and perform in a patient of chronic idiopathic urticarial.<sup>7</sup> A new anti-*H. pylori* IgG antibody Latex kit for *H. pylori* diagnosis (Denka kit), using Immunoturbidimetry with high sensitivity and specificity seems to overcome the problem with diagnosing techniques for OPD patient. This kit is a useful and reliable diagnostic method even for

patients with past *H. pylori* infection and hence was used in our study.<sup>10</sup>

The patients with idiopathic urticaria were divided into 3 groups as follows:

1. A high titer of anti *H. pylori* IgG antibody (40 U/ml),
2. A low titer of anti *H. pylori* IgG antibody (>10 U/ml, <40 u/ml) and
3. A negative titer (<10 u/ml).

Detailed clinical examination of the lesions and scoring were done by urticaria assessment score. General physical examination for the presence of lesions of any other associated skin disorder, examination of hair and oral cavity was also be done. Photographs were taken for documentation. All this information were recorded in a prescribed case record form. Baseline Investigation advised were CBC, TSH, RBS, LFT, RFT, HIV, HCV, and IgG. Ethical clearance was obtained.

### 2.1. Assessment score used

Urticaria assessment score-

Score	Wheal	Pruritus
0	None	None
1	Mild (<20 wheals/24hr)	Mild (present but not disturbing)
2	Moderate (20-50 wheals/24hr)	Moderate (disturbing but not interfering with daily activities/ Sleep)
3	Intense (>50 wheals/24 hrs. or large confluent areas of wheals)	Severe (severe itching, interferes with daily activities or sleep)

## 3. Results

In this study, 89 chronic urticaria patients were taken in the cases group, 89 controls with other dermatological diseases but no symptoms of urticaria constituted the control group and 89 healthy individuals were constituted as placebo control group. They were matched for age and sex. Patients included 35 men (39.32%) and 54 women (60.67%) in the age range of 35.2±15years. Controls included 37 men (41.57%) and 52 women (58.42%) with age range of 36±14.9 years. The Placebo control included 32 men (35.95%) and 57 women (64.04%) with age range of 35.6±14.3 years. No statistical difference was noted based on age and sex between three groups. All three groups were examined for *H. pylori* infection with Urease breath test (UBT) and levels of serum anti *H. pylori* IgG antibodies. Urease breath test and Immunoturbidimetry for serum anti *H. pylori* IgG levels were used due to them being non-invasive, safer, and cost-effective when compared to endoscopic evaluation for accurate detection of *H. pylori*.

**Table 1:** Characteristics of Cases (Patients of Chronic Idiopathic Urticaria), Controls (Patients of other Chronic Skin Disorders) and Placebo Controls (Healthy Individuals).

	Cases	Controls	Placebo control
A. Demographic data			
1. Age group:			
0-20years	21(23.59%)	15(16.85%)	19(21.34%)
21-40years	38(42.69%)	42(47.19%)	40(44.94%)
41-60years	17(19.10%)	24(26.96%)	26(29.21%)
>60years	13(14.60%)	08(8.98%)	4(4.49%)
2. Sex			
Men	35 (39.32%)	37(41.57%)	32(35.95%)
Women	54(60.67%)	52(58.42%)	57(64.04%)
B. Gastrointestinal Symptoms			
Present	27(30.33%)	12(13.48%)	8(8.98%)
Absent	62(69.66%)	77(86.51%)	81(91.01%)
C. Urticarial Assessment Score (UAS)			
Total	2.25 ±0.47	0	0
Total	89	89	89

**Table 2:** The Titers of Helicobacter Pylori specific IgG and Urease Breath Test Results in Cases (Patients of Chronic Idiopathic Urticaria), Controls (Patients of other Chronic Skin Disorders) and Placebo Controls (Healthy Individuals).

	Cases		Control		Placebo Control	
Anti H. Pylori >40U/ml	40	70	04	22	03	19
IgG Positive 10-40U/ml	30		18		16	
Anti H. Pylori IgG Negative (<10U/ml)	19		67		70	
Urease Breath Test Positive	71		32		29	
Urease Breath Test Negative	18		57		60	

**Table 3:** Results of Helicobacter Pylori specific IgG and Urease Breath Test in different Chronic Skin Disorders.

	Number of patients	Anti H. Pylori IgG Positive	Urease Breath Test Positive
Psoriasis Vulgaris	20	8	10
Lichen Planus	15	12	13
Rosacea	8	6	7
Alopecia Areata	16	10	12
Pruritis and Prurigo	26	12	14
Others (Behcet's Disease, Sweets Syndrome, HSP)	4	1	2

The sensitivity, specificity and accuracy of Denka kit were 92.2%, 93.3% and 92.8% respectively.

The positive rate of anti H. Pylori IgG antibodies was 78.65% (70/89) (high titer group (>40U/ml):40, low titer group (10-40U/ml): 30) and negative rate was 21.34% (19/89) (titer <10U/ml) in patients with idiopathic urticaria (cases). The positive rate of Urease Breath Test was 79.8% (71/89) (in high titer IgG group:40, in low titer IgG group:31) and negative rate was 20.22% (18/89) (in negative IgG group).

In controls who did not have Chronic Urticaria, the positive rate of Urease Breath Test was 35.95% (32/89) and negative rate was 64.04% (57/89) (in negative IgG group). The positive rate of anti H. pylori antibodies was 84.71% (22/89) (high titer group (>40U/ml):4, low titer group (10-40U/ml):18) and negative rate was 75.28% (67/89) (titer<10U/ml). The high titer group was mostly associated

with dermatological disorders like Psoriasis Vulgaris and Lichen Planus, while low titer group was associated with Rosacea, Alopecia Areata, Psoriasis Vulgaris.

In placebo control group the positive rate of Urease Breath Test was 32.58% (29/89) and negative rate was 67.41% (60/89) (in negative IgG group). The positive rate of anti H. pylori antibodies was 21.34% (19/89) (high titer group (>40U/ml):03, low titer group (10-40U/ml):16) and negative rate was 78.65% (70/89) (titer<10U/ml).

Gastrointestinal symptoms were noted in 30% of the patients and 13% of controls. Mean Urticaria Severity Score (UAS) was found to be 2.25 ±0.47.

#### 4. Discussion

Chronic Idiopathic Urticaria (CIU) remains one of the most difficult dermatological disorders to treat being till

date. While different infections have been implicated in the pathogenesis of Chronic Urticaria, recent studies show *H. Pylori* (HP) to be a possible causative factor. Chronic and asymptomatic nature of HP infection and its high endemicity makes this association worthy of further research.<sup>11</sup>

The role of HP in causing CIU is not entirely known with certainty, but some recent studies have reported a high titer of IgG antibodies against 19KDa *H. Pylori* associated lipoprotein in CIU patients.

In our case control study, majority of the patients were in third and fourth decade of life. Fifty four of our eighty-nine cases were females. Twenty-seven patients (30.33%) in our study population had a positive history of associated gastrointestinal symptoms. The presence of associated GI symptoms significantly increases the chances of HP infection being the causative factor in the pathogenesis of CIU, thereby increasing the chances of a positive response to HP eradication therapy.

In this study UBT positive patients (79.77%) underwent ELISA for Anti *H. pylori* IgG and infection was detected in 98.59% (70/71) patients, with 56.33% in high titer group (>40U/ml) and 42.25% in low titer group (10-40U/ml). These findings emphasize the role of these non-invasive tests in accurately diagnosing HP infection without needing invasive techniques like Rapid Urease Test and Endoscopy which most patients don't wish to undergo which leads to underdiagnosis and continued prevalence of HP infection in the Indian population. Hence it leads us to the conclusion that IgG antibodies to *H. Pylori* plays a role in pathogenesis of chronic idiopathic urticaria and inclusion of anti *H. pylori* therapy in the management of chronic idiopathic urticaria would be beneficial and would lead to lower rates of recurrence.

Another interesting finding in this study related to the possible association of HP infection in patients of Psoriasis Vulgaris, Lichen Planus, Rosacea, Alopecia Areata, Pruritus and prurigo and other diseases like Sweet's syndrome, Behcet's disease and Henoch-Schonlein purpura and who showed UBT positivity (35%). When these patients underwent ELISA for Anti *H. pylori* IgG, we found positive rate of 68.75% (22/32controls). These findings were supported by few previous studies. In a prospective study, Boixeda de Miquel et al, studied 44 patients diagnosed with rosacea; HP infection was determined, and infected patients were treated with eradication therapy. Complete improvement was observed in 10 (34.5%) patients, which makes it worthwhile to investigate every patient of Rosacea for HP infection.<sup>12</sup> In another study, Onsun et al enrolled 300 patients with plaque-type psoriasis and 150 non-psoriatic healthy controls to determine the prevalence of HP seropositivity in psoriasis using stool antigen test. The prevalence of HP infection was 61.3% in psoriatic patients (n=184) and 59.3% in controls (n=89/150; P>0.05). Also, Patients who received acitretin and who were also treated

for HP infection showed more rapid improvement than those who received acitretin alone.<sup>13</sup>

We also found a few studies that negated this association pointing towards no clear evidence to prove a causal relationship between these diseases and HP infection.<sup>8,14</sup> This is also supported by similar positivity rates in the placebo control group which shows no definitive association of *H. pylori* infection in other chronic skin disorders. These findings led us to the conclusion that larger scale studies are needed to find concrete evidence of investigational importance of HP in such diseases when no complains of urticaria were reported and importance of HP eradication therapy in management of respective diseases.

## 5. Conflict of Interest

The authors declare that there are no conflicts of interest in this paper.

## 6. Source of Funding

None.

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