

# Association between Chronic Urticaria and Helicobacter Pylori Infection in Patients Visiting a Tertiary Hospital

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## ABSTRACT

**Objective:** This study aims to demonstrate the association between chronic urticaria and H.pylori infection for effective management of chronic urticaria.

**Methodology:** A case-control study was conducted in the Dermatology Department of Bakhtawar Amin Trust Hospital Multan from 30<sup>th</sup> Jan 2020 to 30<sup>th</sup> Jan 2021. The patients who recently visited the inpatient or outpatient ward of the hospital were a part of the study whereas the patients who were administered proton pump inhibitors or any antibiotics in the last 1 month were excluded from the study. The patients diagnosed with chronic urticaria were asked to collect one gram of stool and submit the sample. The sample was stored at -20 Celsius and tested for H.pylori infection. The strength of association between chronic urticaria and H.pylori infection was measured by conditional logistic regression. Two-tailed p values were noted and p<0.05 was regarded as statistically significant

**Results:** The study included 80 patients (40 controls and 40 cases). The median age was 32 years in controls while 35 years in cases. Both groups had a majority (n=56, 70%) of females. More than one half (n=23, 57%) of cases and controls (n=27, 67%) lived in urban region. There was a significant difference between the percentage of those who tested H.Pylori positive and had CU and those who were H.Pylori positive but did not have CU. In subjects infected with H.Pylori risk of CU is six times higher than those not infected

**Conclusion:** Relation between H.Pylori and Chronic urticaria is significant, which indicates H.Pylori tests for diagnosis of CU.

**Keywords:** Chronic Urticaria, H.Pylori, Stool antigen test

## INTRODUCTION

Urticaria also regarded as hives are itchy welts caused as a result of skin allergy. These welts appear on the skin as swelling or angioedema or both conditions simultaneously<sup>1</sup>. Urticaria rash is itchy and can affect the normal functioning of individual<sup>2</sup>. The rash may last for less than a day i.e acute urticaria or may last more than a month i.e chronic urticaria (CU)<sup>3</sup>. This condition is most common in females and adults more than in children<sup>4</sup>. About 0.3-5% of the world population is affected by urticaria. The prevalence of chronic urticaria in Pakistan is about 0.5-1%<sup>5</sup>. However, very scarce data is available regarding CU in Pakistan, the major causes of the condition have though been investigated but the etiology of the disease is still under investigation. A lot of research has been done for investigating the association between chronic urticaria and H.pylori infection and various hypothesis have been presented in this regard. A study predicted that H.pylori infection increases the permeability of the mucosa in the inner lining of the stomach which consequently exposes the digestive tract to allergens<sup>6</sup>. Another study observed that H-pylori infection may cause the immune system to release antibodies that trigger the release of histamine on skin<sup>7</sup>. Other researchers are still uncertain about this relationship.

In Pakistan, CU is difficult to manage as no special management is available for the patients. This condition is managed according to the signs and symptoms of the patient. This study aims to demonstrate the link between chronic urticaria and H.pylori infection for effective management of chronic urticaria.

## METHODOLOGY

A case-control study was conducted in the Dermatology Department of Bakhtawar Amin Trust Hospital Multan from 30<sup>th</sup> Jan 2020 to 30<sup>th</sup> Jan 2021. The first 40 consecutive patients were included in the case study group and the next 40 consecutive patients were included in the control group. The sampling of patients was done by using Epi Info 7. For every study patient, a control patient with the same demographic characteristics and age gap of not more than 10 years was selected. The patients who recently visited the inpatient or outpatient ward of the hospital were a part of the study whereas the patients who were administered

proton pump inhibitors or any antibiotics in the last 1 month were excluded from the study.

All the patients were examined by a medical examiner and the demographic features were noted through a questionnaire. The patients diagnosed with chronic urticaria were asked to collect one gram of stool and submit the sample. The sample was stored at -20 Celsius and tested for H.pylori infection. All the patients provided their written consent to become a part of the study.

All the data were analyzed by using Stata version 14.1. Wilcoxon signed-rank test was used to investigate the relationship between chronic urticaria and age. Mc Nemar test was used to demonstrate the association of chronic urticaria with other demographic factors including family history, sex, occupation, age, etc. The strength of association between chronic urticaria and H.pylori infection was measured by conditional logistic regression. Two-tailed p values were noted and p<0.05 was regarded as statistically significant.

## RESULTS

The study included 80 patients (40 controls and 40 cases). The median age was 32 years in controls while 35 years in cases. More than 1/3<sup>rd</sup> of controls (n=13, 32.5%) were aged between 20-and 29 years. The majority of cases (n=12, 30%) lay in a similar age group. Both groups had a majority (n=56, 70%) of females. More than one half (n=23, 57%) of cases and controls (n=27, 67%) lived in urban region. (Table 1)

The presence of infection in cases and controls is found through matched analysis. Every member of the case-control pair is either infected with H.Pylori or not and belongs to the control or case group. This has four possible results. Pairs in which both control and case have the same exposure are concordant pairs, while those exposed differently are discordant pairs. There was a significant difference between the percentage of those who tested H.Pylori positive and had CU and those who were H.Pylori positive but did not have CU. (Table 2)

H. Pylori was the only variable related to CU in crude analysis. In multivariate regression analysis, other than sex and age all other variables had to value less than 0.2. Predictors of CU were determined by forwarding and backward conditional logistic regression. Sex, age, presence of H.Pylori, and place of residence

influenced exposure. In subjects infected with H.Pylori risk of CU is six times higher than those not infected. (Table 3)

Table 1: Basic Characteristics of subjects in case and control group

Characteristics	Controls (n=40)	Cases (n=40)	P-value
Median age	32(28-46)	35(21-47)	.1231
Age groups			
<20	8(20%)	9(22.5%)	.3173
20-29	13(32.5%)	12(30%)	—
30-39	10(25%)	10(25%)	—
40-49	5(12.5%)	5(12.5%)	—
>50	4(10%)	4(10%)	—
Sex			1.0
Male	12(30%)	12(30%)	—
Female	28(70%)	28(70%)	—
Residence			.2008
Urban	27(67%)	23(57%)	—
Rural	13(32.5%)	17(42.5%)	—
Occupation			.4652
Self-employed	5(12.5%)	7(17.5%)	—
Formal employment	15(37.5%)	13(32.5%)	—
Non employed	20(50%)	20(50%)	—

Table 2: Occurrence of H.Pylori in case-control pair

H.Pylori Positive CU patients	H.Pylori positive non CU patients	
	Yes	No
Yes	3	9
No	1	28

Table 3: Chances of association between H.Pylori and CU

Variables	COR (95% CI)	P-value	AOR (95% CI)	P-value
Antigen test positive				
Yes	5.6(1.2-25.7)	.025	6.1(1.2-32.2)	.029
No		-		-
Sex				
Male		-		-
Female	0.6(0.3-2.4)	1	1.2(0.5-5)	.607
Mean age	0.8(0.7-1.2)	.239	0.8(0.7-1.2)	.233
Residence				
Urban	1.7(0.6-4.1)	.207	1.6(0.5-4.2)	.287
Rural		-		-
Treatment history				
Yes	4.4(0.8-20.7)	.054	4.7(0.8-24.1)	.061
No		-		-

## DISCUSSION

Chronic urticaria is a stressful condition as it has complicated triggering factors<sup>8</sup>. In various disorders including CU, H.Pylori is found to be a causative pathogen. A stool antigen test is used to detect this organism. This test has 98% specificity and 95% sensitivity because of which it is mostly used by dermatologists treating CU patients. Moreover, this test is also cheap, rapid, convenient, and noninvasive. The results of this study were similar to another which concluded that most adults are affected by CU<sup>9</sup>. The findings of our study are in line with the previous literature which shows that prolonged and frequent exposure to causative agents leads to CU<sup>10</sup>. However, another study conducted on children aged below eighteen years should different results<sup>11</sup>. This study showed that among the case and control groups, 30% were males while 70% were females. Another study showed similar findings that females are affected more as compared to males<sup>12</sup>. This may be based upon lower dehydroepiandrosterone (DHEA)-S explaining hormone imbalance during CU<sup>4</sup>. However, the literature does not carry strong evidence supporting this relation. A study showed that females are affected more by CU as they are more frequently exposed to household dust. During household chores, they touch raw food and are exposed to H.Pylori infection leading to CU<sup>3</sup>. The results of this study show that 10.2% of subjects in the control group and 26% of subjects with CU had H.Pylori infection. Another study showed the same results according to which CU

patients were infected more than the control group<sup>9</sup>. Another study showed that in countries where hygiene, sanitation, and diet are not up to the mark there is 90% more prevalence of H.Pylori infection as compared in the developed countries<sup>10</sup>.

In this study, it was found that in subjects infected with H.Pylori risk of CU is six times higher than those not infected. Various other studies had similar findings<sup>13</sup>. However, a study conducted by Federman et al. showed different results<sup>14</sup>. This can be due to difference in geographical locations that show increased prevalence due to the factors increasing the transmission of H.Pylori<sup>10</sup>. Moreover, different testing methods like the H. pylori antibody test are used in these studies unlike the antigen test used in the current study. This association has been explained by different theories. Studies show that H.Pylori makes the stomach lining more permeable thus exposing the GI tract to the allergens<sup>12</sup>. Moreover, antibodies produced in response to the infection cause histamine release in the skin. Nevertheless, some studies are skeptical about the association between CU and H.Pylori<sup>15</sup>. This association is very significant as eradicating bacteria leads to a cure. Studies conducted in Egypt, Pakistan, and the USA showed that eradicating bacteria led to cures in patients with CU.

## CONCLUSION

Link between H.Pylori and Chronic urticaria is significant, which indicates H.Pylori tests for diagnosis of CU. H.Pylori stool antigen test is a reliable method of detecting this organism.

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