

Frequency of *Helicobacter pylori* antigen in stool of patients with chronic urticaria

Humaira Maryum Agha, Krishan Lal, Sadaf Ahmed Asim,
Yasmin Channa, Farah Saleem

Hamdard Collge of Medicine and Dentistry, Altamash Institute of Dental Medicine, Dow
International Medical College, Al Tibr Medical College and Hospital, Karachi, Pakistan

Objective: To determine the frequency of *Helicobacter pylori* antigen in stool of patients with chronic urticaria who presented at our tertiary care hospital.

Methodology: This descriptive cross-section study was carried out at department of dermatology in collaboration with department of pediatrics, Al-Tibri Medical College & Hospital and Isra University Karachi Campus, during a period of one year. Patients with chronic urticaria of both genders and all ages were selected by non-probability convenience sampling. Patients with known co-morbidities and other causes of urticaria as well as those with acute urticaria were excluded.

Results: Out of 116 patients, 73 had positive *H. pylori* antigen in their stool. Females patients (67.2%, n=43) and those who had angioedema (66.7%, n=16) were more likely to have *H. pylori* antigen positive. Serum level of immunoglobulin E was found quite elevated in patients who were positive for *H. pylori* antigen.

Conclusion: Considerable number of patients with chronic urticaria had *H. pylori* antigen in their stool. This antigen is internationally recognized to be the cause of chronic urticaria in many countries. (Rawal Med J 202;45:523-526).

Keywords: Urticaria, urea-breath test, *helicobacter pylori*.

INTRODUCTION

Chronic urticaria is a very distressing disease for patients as well as for physicians. Chronic urticaria by definition is appearance of wheals with or without angioedema for more than six weeks duration. Individual lesion lasts for less than twenty-four hours and new lesions continue to appear at different sites.^{1,2} According to different studies, about 1% of the general population is affected by chronic urticaria.³ Almost 45% chronic urticarias are autoimmune in etiology, while 55% are idiopathic.^{4,7} Underlying infections, food, food additives, preservatives, metabolic disorders, hormonal disturbances, malignancies and emotional states are considered to be the causes of chronic idiopathic urticaria (CIU). *Helicobacter pylori* infection (*H. pylori*) has recently emerging a key causative factor for chronic urticaria.⁷

H. pylori, a gram negative bacterium harbored in stomach, is a cause of inflammatory response in upper gastro-intestinal tract and results in chronic gastritis and gastric and peptic ulcers.⁸⁻¹⁰ Worldwide incidence of *H. pylori* infection is 60% according to

various studies.¹¹ Most patients, especially children, are asymptomatic carriers.^{12,13} Different methods for detection of *H. pylori* are available, like upper Gastrointestinal (GI) endoscopic biopsy and histology with rapid urea test and culture, urea breath test and detection of *H. pylori* antigen in stool by EIA (Enzyme Immuno Assay).¹³ Endoscopic biopsy is the gold standard for detection of infection.¹⁴ However, it is an invasive and expensive procedure. Detection of *H. pylori* antigen in stool is reliable and non-invasive procedure.¹⁵ Treatment of CIU is purely symptomatic unless the cause is known. Histamine (H1/H2) receptor blocking agents with or without Montelukast and/or synthetic immunosuppressant are the treatment options.¹⁶ 50% patients with CIU undergo spontaneous remission within one year and 85% within five years.³ If positive, *H. pylori* should be eradicated by recommended triple drug regimen (amoxicillin 1000mg, clarithromycin 500mg and omeprazole 20 mg twice daily) for two weeks.¹⁵ A newer treatment option available is Omelizumab.¹⁷ It is humanized, monoclonal, anti-

IgE antibody ($^{rhuMab-E25}$), which binds with free IgE in serum and makes it inactive.¹⁸ Multiple studies regarding association of H. pylori and chronic urticaria are available, few local studies of frequency of H. pylori antigen in stool patients with chronic urticarial are available. Therefore, this study was undertaken to reveal the situation of such association.

METHODOLOGY

This descriptive cross-sectional study was carried out at the department of Dermatology in collaboration with department of Pediatrics, Al-Tibri Medical College and Hospital and Isra University, Karachi Campus. Patients were enrolled by non-probably convenience sampling. Patients of all ages and both genders were included in the study after taking informed consent. Patients with acute urticaria, also those with known cause were excluded from the study. Patients with known co-morbidity like diabetes mellitus, thyroid disease, chronic infections, and those on drug therapies for any disease were also not included. More than one underlying cause was also an exclusion criterion.

Detailed history and clinical examination was done by consultant dermatologist before concluding the final diagnosis of chronic urticarial. All patients had Complete Blood Counts (CBC), ESR, Serum IgE level, urine detail report, stool for H. pylori antigen and worms, HBsAg and anti-HCV antibody. Other relevant investigations were done, where required.

Statistical Analysis: SPSS version 22 was used to analyze data. Percentages and frequencies are reported for categorical variables, and means \pm SD were reported for non-normal continuous data. $p < 0.05$ was considered significant.

RESULTS

Out of 116 patients, 52(44.8%) were male and 64(55.2%) female. Mean age was 28.3 ± 15.78 years (range 5 months to 60 years). Overall, 73(62.9%) patients were those whose stool was positive for H. pylori antigen. Out of which, 52 were adults and 21 children. Patients who were affected by angioedema were 24(20.7%) (Table 1).

Table 1. Study patients characteristics.

Patient Characteristics	Frequency (%)
Male : Female	14 : 91 \rightarrow 1 : 6.5
Mean age in years	47 \pm 12.9
Medical comorbidities	
Diabetes mellitus	19 (18.1%)
Hypothyroidism	7 (6.7%)
Obesity	7 (6.7%)
Trauma	2 (1.9%)
No associated condition (idiopathic)	70 (66.7%)
CTS	
Right	79 (75.2%)
Left	21 (20.0%)
Bilateral	5 (4.7%)
Positive Tinnel Sign	98 (93.3%)
Positive Phalen Sign	103 (98.1%)
Signs and symptoms	
Night pain	95 (90.5%)
Daytime pain	54 (51.4%)
Hand stiffness	32 (30.5%)
Wrist pain	88 (83.8%)
Numbness	5 (4.7%)
Tingling	12 (11.4%)
Muscle weakness	7 (6.7%)

Table 2. Age and gender distribution (n=116).

	Male	Female	Total	% Age
Less than 1 year	2	3	5	4.27
1-10 Years	6	7	13	11.11
11-20 Years	10	8	18	15.38
21-30 Years	8	15	23	19.65
31-40 Years	15	20	35	29.91
41-50 years	7	8	15	12.93
51-60 years	4	3	7	5.98
Total	52	64	116	100

Different strata of ages, gender distribution are shown in Table 2. Majority patients belonged to age group 21 to 40 years. Majority of the patients (68%, $n=79$) had urticaria of less than six months of duration, 20% ($n=23$) patients had disease between six months and one year duration. Only a small number of the patients (12%, $n=14$) suffered for more than a year. This is because majority patients get treatment before one year. Serum level of IgE was found quite elevated in patients who were positive for H. pylori antigen.

DISCUSSION

Chronic urticaria affects patient's quality of life very badly. It not only disturbs routine activities but also creates problems in sleep, job, mental and physical well-being as well as social interactions.¹⁹ Most of time, it is a manifestation of some systemic diseases, drug reaction, food, infections and infestations. Infection as underlying cause is treatable but ignored in majority cases. *H. pylori* is a cause of gastritis and other GI symptoms in many patients and its prevalence is estimated to be 60% worldwide with 25% incidence in developed countries and more than 80% in developing countries.¹¹ Stool antigen detection is a non-invasive and reliable method for detecting *H. pylori* infection as well as silent carrier state.

This study showed that there were 73(62.9%) patients with chronic urticaria who have positive *H. pylori* antigen in their stool. Current study, local and regional studies show more or less comparable results, i-e 59.8%, 70% and 70%, respectively.^{15,20,21}

However, a study conducted in Shandong province of China by Sun et al showed totally different results.²² Only 29% patients with chronic urticaria had positive *H. pylori* by serology. This difference may be due to a different lifestyle, eating habits or a difference in method of detection.

Apart from the studies mentioned above, another study done by Fuduka, Japan showed this association in 52% patients.²³ There is vast difference in the results of two studies and conducted in the same region of East Asia.^{22,23} Hook-Nikanne et al studied some 231 patients of chronic urticaria in Finland and found only 24% association with *H. pylori* serology.²⁴ This again is very contrast to our study as well as other studies of our region.

Detection and treatment of underlying cause will give a permanent relief to patients rather than giving temporary and symptomatic treatment. If further studies are encouraged in different areas of our country, we can have multiple small studies, which, when compiled will give a big picture of such an association in our country. The limitations of this study is that we did not have follow-up after eradication of *H. pylori* antigen; therefore an association between the two variables cannot be established.

CONCLUSION

This study concludes that, substantial number of patients with chronic urticaria had positive results of *Helicobacter Pylori* antigen in stool.

Author Contributions:

Conception and design: Humaira Maryum Agha
Collection and assembly of data: Humaira Maryum Agha, Yasmeen Channa, Farah Saleem
Analysis and interpretation of the data: Humaira Maryum Agha, Krishan Lal
Drafting of the article: Humaira Maryum Agha, Krishan Lal
Critical revision of the article for important intellectual content: Sadaf Ahmed
Statistical expertise: Sadaf Ahmed
Final approval and guarantor of the article: Humaira Maryum Agha
Corresponding author email: Humaira Maryum Agha: humairamaryum@yahoo.com
Conflict of Interest: None declared
Rec. Date: Jun 28, 2020 Revision Rec. Date: Jul 7, 2020 Accept Date: Jul 28, 2020

REFERENCES

- Grattan CEH, Black AK. Urticaria and Mastocytosis In: Rook A, DA Burns, SM Breathnach, NH Cox and CEM Griffiths, editors. Textbook of dermatology. London: Blackwell Science. 2010;14:949-4.
- Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, et al. The EAACI/GALEN/EDF/WAO Guideline for the definition, classification, diagnosis and management of Urticaria. The 2013 revision and updated. Allergy 2014;69:868-7.
- Maurer M, Weller K, Bindslev-Jensen C, Giménez-Arnau A, Bousquet PJ, Bousquet J, et al. Unmet clinical needs in chronic spontaneous urticaria. A GALEN task force report. Allergy. 2011;66:317-3.
- Kaplan AP. Urticaria and angioedema In: Allergy and allergic diseases. Vol 2, 2nd edition. Kay AB, Kaplan AP, Bousquet J, Holt PG. Blackwell Publishing, London 2008;81:1853-7.
- Graves MW. Pathophysiology of chronic urticaria. Int Arch Allergy Immunol. 2002;127:3-9.
- Graves MW. Chronic idiopathic urticaria. Curr Opin Allergy Clin Immunol 2003;3:363-8.
- Gaig P, Olona M, Muñoz Lejarazu D, Caballero MT, Domínguez FJ, Echechipia S, et al. Epidemiology of urticaria in Spain. J Investig Allergol Clin Immunol. 2004;14:214-2.
- Tuzunx Y, Keskin S, Kote E. The role of Helicobacter pylori infection in skin diseases: facts and controversies. Clin Dermatol. 2010;28:478-2.
- Suerbaum S, Michetti P. Helicobacter pylori infection. N Eng J Med. 2002;247:1175-8.
- Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patient with gastritis and peptic ulceration. Lancet. 1984;323:1311-5.
- Pounder RE, Ng D. The prevalence of H.Pylori infection

- in different countries. *Aliment Pharmacol Ther.* 1995;9:33-9.
12. Suzuki H, Marshall BJ, Hibi T. Overview: *Helicobacter Pylori* and extra gastric disease. *Int J Hematol.* 2006;2:91-3.
13. Shakouri A, Compalati E, Lang DM, Khan DA. Effectiveness of *Helicobacter pylori* eradication in chronic urticaria: evidence based analysis using the grading of recommendations, assessment, development and evaluation system. *Curr Opin Allergy Clin Immunol.* 2010;10:362-9.
14. Kotacinska-Flont M, Antczack-Marczack M, Pawtowski M, Kuna P. Anti-*Helicobacter pylori* IGE titre in patients with chronic idiopathic urticaria and the effect of *Helicobacter pylori* eradication on urticaria. *Post Dermatol Allergol.* 2012;2:80-5.
15. Tareen A, Butt T, Ali B. *Helicobacter pylori* infection in patients with chronic urticaria and dyspepsia, experience from a developing country. *J Pak Assoc Dermatol.* 2016;26:206-3.
16. Sussman G, Goncalo M, Sanchez-Borges M. Treatment Dilemmas in chronic urticaria. *J Eu Acad Dermatol Venerol.* 2015;29:16-3.
17. Maurer M, Church MK, Goncalo M, Sussman G, Sanchez-Borges M. Management and treatment of chronic urticaria. *J Eu Acad Dermatol Venerol.* 2015;29:33-7.
18. Chang TW, Chen C, Lin CJ, Metz M, Church MK, Maurer M. The potential pharmacological mechanisms of Qualizumab in patients with chronic spontaneous urticaria. *J Allergy Clin Immunol.* 2014;135:337-4.
19. Kang MJ, Kim HS, Kim HO, Park YM. The impact of chronic idiopathic urticaria on quality of life in Korean patients. *Ann Dermatol.* 2009;21:226-9.
20. Qazi N, Samdani AJ, Jamali S, Begum S, Shah M. Chronic idiopathic urticaria and *Helicobacter pylori* infection: Effect of eradication therapy on relief of symptoms. *JLUMHS* 2013;12:172-6.
21. Yadav Mk, Rishi JP, Nijwam S. Chronic urticaria and *Helicobacter Pylori*. *Ind J Med Sci.* 2008;62:157-2.
22. Sun L, Erxun K, Li J, Yang J, Han C. Correlations between anti-mast cell autoantibodies and chronic idiopathic urticaria. *Ann Dermatol.* 2014;26:145-9.
23. Fuduka S, Shimoya T, Umegaki N, Mikami T, Nakano H, Munakata A. Effect of *Helicobacter pylori* eradication in the treatment of Japanese patients with chronic idiopathic urticarial. *J Gastroentrol.* 2004;39:827-3.
24. Hook-Nikanne J, Varjonen E, Harvima RJ, Kosunen TU. Is *Helicobacter pylori* infection associated with chronic urticaria. *Acta Dermatol Venerol.* 2000;80:425-6.