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HELICOBACTER PYLORI GASTRIC INFECTION IN PATIENTS OF CHRONIC URTICARIA – A HOSPITAL BASED CASE CONTROL STUDY FROM NORTH INDIA.

Dermatology

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ABSTRACT

Background: Aetiology of chronic urticaria(CU) remains obscure in many cases. Studies have indicated role of H. pylori gastric infection in CU. Aim of our study was to assess the association of H. pylori infection with CU and to compare it with controls. Clinico-epidemiological variables including gender, socioeconomic status and dyspepsia were studied in relation to H. pylori infection in CU patients. **Methods:** It was a case control study conducted in tertiary care hospital of North India in which 38 cases and controls each were enrolled. Stool was tested for presence of H. pylori antigen using rapid stool kit. **Results:** H. pylori positivity was more common 26(68.4%) in patients versus the 13(34.3%) controls ($p<0.01$). Females were more frequently infected with H. Pylori 21(80.8%) as compared to males 5(19.2%) ($p=0.017$). Urticaria persisted longer in H. pylori positive (2.1±0.8 years) as compared to those who tested negative (1.5±0.5 years) ($p=0.022$).Dyspepsia was more common 8(30.76%) in patients who tested positive for H pylori than those who tested negative 2(16.66%) ($p=0.013$). **Conclusions:** H. pylori stool antigen test is a non-invasive and accurate test to detect an active gastric infection and should be done in cases of CU with no obvious aetiology. H pylori may also play a role in persistence of the disease and thus detecting and treating the same might result in permanent remission in such cases. Female gender, patients belonging to low socioeconomic class and patients with dyspepsia should raise suspicion of an underlying H. pylori infection.

KEYWORDS

Chronic Urticaria, H Pylori, Gastric, Stool Antigen Test.

INTRODUCTION

Chronic Urticaria (CU) is a potentially debilitating disease characterised by transient pruritic skin lesions in the form of erythematous and oedematous wheals which occur daily or almost daily for a period six weeks or more. It affects around one percent of the general population and the disease may last for a variable period of months to decades.[1] Those cases of chronic urticaria where no obvious cause is evident are classified as chronic idiopathic urticaria and account for around 70 % of the total cases.[2] Various factors including drugs, autoimmune diseases, foods and food additives, dairy products etc. have been implicated. Besides this infections and infestations including bacterial, fungal and protozoal infections are believed to trigger the disease in chronic urticaria however the exact etiopathogenesis remains largely unknown.[3] Many studies have shown presence of antibodies against IgE immunoglobulin or against its receptor component (Fc€RIα) in around 30-50 percent cases suggesting an underlying autoimmune mechanism.[4] Helicobacter pylori (H. pylori) which is a spiral shaped gram-negative bacterium is often seen to colonise the gastric mucosa thus contributing to the production of various substances which induce inflammation and damage the host cells.[5] The prevalence of H. pylori in developed countries is found to be 20% to 40% while in developing countries it is 50% to 80%. H pylori infection is seen more in people of lower socioeconomic strata and the elderly.[6,7] Some studies have indicated an etiological link between H. pylori infection and chronic urticaria while many others have not been able to demonstrate any difference with respect to the healthy population.[8,9]

Various hypotheses have been postulated to explain the association of H. pylori infection with CU one of which includes the idea of immunologic stimulation by the bacterium through various cytokines causes a heightened cutaneous vessel sensitivity to agents increasing vascular permeability.[10] These may include role of mediators like interleukin 8 (IL-8), platelet-activating factor (PAF) and leukotrienes (LT) B4 and C4 which have been found to be elevated in gastric mucosa of patients having H. pylori infection which notably also have important cutaneous actions.[11] Another theory being put forth by some authors claims that patients of chronic urticaria may develop IgE antibodies against H. Pylori, in fact some studies have demonstrated higher total IgE in patients with chronic urticaria and coexistent H. Pylori infection as compared to those patients of CU without such infection.[12,13] Another proposed phenomenon states the role of increased gastric vascular permeability due to the H. pylori infection causing an increased penetration of food allergens through the host cells into the systemic circulation.[14]

We conducted this study to assess the association of H. pylori infection among patients of chronic urticaria and its comparison with the control population. Besides these important correlations were derived in relation to the factors like age, gender, socioeconomic status, disease duration and complaints of dyspepsia among cases with H Pylori antigen positivity in the stool sample.

MATERIAL AND METHODS

A hospital-based case control study was undertaken in OPD of dermatology department, at Government Medical College, Jammu. The study was completed within the period six months from October 2019 to March 2020. A total of 38 cases and an equal number of controls were selected for the study. Sample size was calculated using Epi Info program for windows version 10 using confidence interval of 95% and power of the study as 90%. Values of exposure for cases and controls were adopted from a study by Muhemmed et al.[15] A consecutive sampling method was used for selecting the cases. Patients with daily or almost daily occurrence of urticarial wheals for six weeks or more with no obvious cause on clinical and basic laboratory investigations were included in the study. Patients who were diagnosed with peptic ulcer, those who had received H. Pylori eradication therapy, proton pump inhibitors, H2 blockers, antibiotics or immunosuppressives in the last one month, pregnant and lactating mothers and those not willing to participate in the study were excluded. The controls were matched for age and gender with cases and were selected from healthy attendants willing to participate in the study and patients attending OPD for other minor skin ailments not having urticaria, gastrointestinal symptoms or any other condition known to be associated with H. Pylori. The data was obtained from the subjects after obtaining a verbal informed consent. A data was collected in the form of an anonymous proforma filled by the researcher which included relevant demographic data, history and clinical examination and results of laboratory investigations obtained from the subjects. Laboratory investigations which were advised in all cases and controls included: complete blood count, erythrocyte sedimentation rate, thyroid function test, urine examination, stool examination. Finally, H. pylori antigen detection in stool by immunochromatography method using rapid stool test Kit (Medtek, USA) having a sensitivity of around 95% and a specificity approaching 100 % was performed.

STATISTICAL ANALYSIS:

Data was entered and analysed using Microsoft Excel and Statistical Product and Service Solutions (SPSS 22.0). Numerical data was calculated in the form of mean, standard deviation and categorical data as frequencies and proportions. Chi square test was used to test association between categorical variables. Furthermore, t-tests for two independent samples were taken to compare groups at a particular point in time. Findings with p value of <0.05 was taken as significant.

RESULTS

The study included 38 cases and controls each. Mean age was 32.9±12.6 years for cases and33.1±13.8 years for controls. Females predominated both the groups contributing to 26 (68.4%) among cases and 24(63.1%) among controls. The population was relatively equally

distributed among upper, middle and lower socioeconomic class in both the groups. Both groups were comparable with respect to age, gender and socioeconomic status (p>0.05). Among cases the mean duration of urticaria was 1.8 years±0.8 and ranged from 6 months to 4 years [Table 1].

Table 1. Demographics and baseline characteristics of the study population.

Feature	Cases	Controls	p value
Age (yrs.), meanSD	32.9	33.113.8	0.947
Female	26 (68.4%)	24(63.1)	0.628
Male	12 (31.6%)	14(36.9)	
Socioeconomic status Upper Middle Lower	 10(26.3%) 15(39.5%) 13(34.2%)	 11(28.9%) 14(36.9%) 13(34.2%)	 0.564
Duration of urticaria (yrs) Mean and SD Min-Max	 1.8 ± 0.8 0.5-4yrs.		

SD: Standard Deviation, Min : Minimum, Max : Maximum.

H. pylori positivity in the stool sample was more common 26(68.4%) in patients suffering from chronic urticaria versus the 13(34.3%) control population. The difference showed a strong statistical significance (p<0.01) [Table 2].

Table 2: H. pylori positivity among cases and controls.

Stool for H. Pylori Antigen	Case No. (%)	Control No. (%)	OR	P value
Positive	26(68.4%)	13(34.3%)	4.16	p<0.01*
Negative	12(31.6%)	25(65.7%)		
Total	38(100%)	38(100%)		

OR: Odds Ratio.
**P value of <0.05 is taken as significant.*

While studying the relationship of H. pylori positivity in the stool sample of cases with various clinico-epidemiological factors, it was found that there was no statistical difference between cases which tested positive for H. pylori versus cases which tested negative as far as age distribution among both groups was concerned. However, in our study females were more commonly infected with H. Pylori 21(80.8%) as compared to males 5(19.2%) and the difference was statistically significant (p=0.017). Socioeconomic status although showed a trend indicating that a greater number of patients who tested positive belonged to lower socioeconomic class 12/26(46.1%) as compared to those who tested negative 3/12(25.0%). However, this difference was not statistically significant (p=0.222). On studying the mean duration of urticaria among H. pylori positive vs H. pylori negative cases it was seen that the duration of urticaria in those with stool sample positive for H. pylori was longer (2.1±0.8 years) as compared to those who tested negative for H. pylori (1.5±0.5 years) and the difference was statistically significant (p= 0.022) [Table 3].

Table 3: Relationship of H pylori positivity among cases with clinico-epidemiological factors.

Feature	Test positive	Test negative	Total	p value
Age (year) Mean ± SD	 32.5±12.5	 33.3±12.9	 32.9±12.6	 0.857
Gender Male Female	 5(19.2%) 21(80.8%)	 7(58.3%) 5(41.7%)	 12(31.6%) 26(68.4%)	 **0.017***
Socioeconomic status Upper Middle Lower	 6(23.1%) 8(30.8%) 12(46.1%)	 2(16.7%) 7(58.3%) 3(25.0%)	 8(21.0%) 15(39.5%) 15(39.5%)	 0.222
Duration (year) Mean ± SD	 2.1±0.8	 1.5±0.5	 1.8±0.8	 **0.022***
Total	**26(100%)**	**12(100%)**	**38(100%)**	

**P value of <0.05 is taken as significant.*

On studying whether the cases who tested positive for H. pylori in their stool sample also clinically had dyspepsia, it was found that the occurrence of dyspepsia was more common 8(30.76%) in those tested positive for H pylori than those who tested negative 2(16.66%) and this difference was statistically significant (p=0.013) [Table 4].

Table 4: Relationship of dyspepsia with H pylori positivity in stool sample of cases.

H pylori stool antigen	Dyspepsia			
	Yes (No. %)	No(No. %)	Total No.(%)	p value
Positive	8 (30.76)	18(69.24)	26(100)	**p=0.013***
Negative	2(16.66)	10(83.34)	12(100)	

**P value of <0.05 is taken as significant.*

DISCUSSION

Chronic Urticaria is a potentially distressful and difficult to manage disease for the dermatologists in their daily practice due to its diverse and incompletely understood etiopathogenesis.16 H. pylori besides its role in various gastroenterological diseases has been reported recently for its role in chronic urticaria.17 Testing for H. pylori antigen in the stool sample is considered as the most accurate non-invasive test for diagnosis of an active H. Pylori infection and has been validated by the American Gastroenterological Association and the American College of Gastroenterologists. [18,19]

Mean age in our study among cases was 32.9±12.6 years and 33.1±13.8 years for controls. Similar age group predominance in cases of chronic urticaria was found in many studies conducted in India & abroad.20,15 This indicates that chronic urticaria predominantly affects middle aged population and perhaps the disease requires multiple and repeated immunological and or infectious insults before it sets in. Females predominated both the groups in our study amounting to 26 (68.4%) among cases and 24(63.1%) among controls. Although both groups were comparable and there was no statistical difference between cases and controls, female predominance in urticaria has been frequently demonstrated in many previous studies.[15,21] This can perhaps be attributed to hormonal differences and fluctuations brought about by ovulation cycles and events like gestation. Some studies have depicted low levels of DHEAs hormone levels seen in females of reproductive age group which may contribute to occurrence of chronic urticaria in females of this age group.[23] The mean duration of chronic urticaria in our study was 1.8 years±0.8 and ranged from 6 months to 4 years. This was similar to some earlier studies conducted by Mogaddam et al. and Mallick et al. [1,23]

In our study, it was found that H. pylori positivity in the stool sample was much more common in patients of chronic urticaria 26(68.4%) as compared to 13(34.3%) controls and the difference showed a strong statistical significance (p<0.01). Also, the odds ratio was 4.16 suggesting that there is 4 times more chance of a H. pylori positive case to have chronic urticaria as compared to H. pylori negative people. This was in concordance with various studies in the past. Mogaddam et al. in a study conducted in Iran showed a stool antigen positivity of 36% in patients of chronic urticaria while it was 65% and 59.8% in two different studies by Mosbeh et al. and Tareen et al. [1,24,25]

We also conducted a group sub-analysis in our study with respect to various socioeconomic factors versus H. pylori antigen positivity among chronic urticaria patients. Patients of chronic urticaria who tested positive for H. pylori had similar age predominance as compared to those patients who tested negative. However, our study revealed that female patients of chronic urticaria had a higher prevalence of H. pylori colonisation in the gastric mucosa as compared to males. Around 80.8% females having chronic urticaria tested positive for H pylori as compared to only 19.2% males and the difference was statistically significant (p=0.017). Traditionally, H. pylori infection has been found to be associated more with male gender. [26,27] However, some studies especially those done in patients suffering from gastric malignancies showed a female predisposition.[28] This needs further evaluation by larger studies especially in patients of chronic urticaria. H. pylori positivity in our study showed an increasing trend although statistically insignificant, towards the patients belonging to lower socioeconomic status suggesting that people who are less privileged may be carrying a higher H. pylori load in the gastric mucosa. Similar findings have been observed in many previous studies.[6,29] We propose that increased H. Pylori prevalence in people belonging to lower socioeconomic strata may be attributed to unhygienic dietary practices and lack of access to clean drinking water. We also observed a higher mean duration of chronic urticaria

symptoms in patients who tested H. pylori positive as compared to those who tested negative. The difference was statistically significant. Similar finding was observed by Mallick et al.[23] It suggests that besides triggering Chronic urticaria H. pylori gastric colonisation may also play a role in persistence of Urticaria by perhaps providing a continuous antigenic cross-stimulation and in sustaining the cytokine cascade required for disease manifestation.

In our study we also tried to elicit if the symptoms of dyspepsia among urticaria patients had anything to do with H. pylori positivity and whether dyspepsia can serve as one of the clinical pointers to suspect H. pylori gastric infection possibly contributing to chronic urticaria. It was observed by us that dyspepsia as a complaint was much more frequent (30.76%) in those who tested positive for H. pylori than those who tested negative (16.66%) and this difference was statistically significant. This is in contraindication to some previous studies where dyspepsia showed no relation with H pylori positivity.[15,21] We wish to suggest that dyspepsia may serve as a potentially useful clinical indicator among patients of chronic urticaria to test and treat for an underlying H pylori gastric infection. However, before this can be brought into the standard clinical practice it needs to be further studied and validated by larger well-designed studies.

Limitations of our study included the smaller sample size, effect of H. pylori eradication therapy on chronic urticaria was not studied and other corroborative diagnostic tests (invasive and non-invasive) were not included.

We thus conclude that H pylori may play a role in persistence of urticarial symptoms besides initiating the disease process thus it should be included in the diagnostic armament of a clinician while investigating cases of chronic urticaria which don't reveal any obvious aetiology on history, examination or basic laboratory screening. For this purpose, stool examination for H. pylori antigen could serve as an excellent test due to its high sensitivity and specificity, its ability to differentiate between active infection and a recovered patient unlike H. pylori serology. Also, such patients should be specifically asked about complains of dyspepsia which may serve as a clinical indicator of an underlying H. pylori gastric infection.

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REFERENCES

1. Mogaddam MR, Yazdanbod A, Ardabili NS, Maleki N, Isazadeh S. Relationship between Helicobacter pylori and idiopathic chronic urticaria: effectiveness of Helicobacter pylori eradication. Advances in Dermatology and Allergology 2015;32:15.
2. Buss YA, Garrelfs UC, Sticherling M. Chronic urticaria-which clinical parameters are pathogenetically relevant? A retrospective investigation of 339 patients. J Dtsch Dermatol Ges 2007; 5:22–29.
3. Grattan CEH, Marsland AM. Urticaria. In:Griffiths CEM, Barker J, Bleiker T,Chalmers R, Creamer D, editors. Rook's textbook of dermatology. Vol 2. 9th ed Oxford: Wiley-Blackwell; 2016 p. 42.1-18.
4. M. Hide, D. M. Francis, C. E. H. Grattan, J. Hakimi, J. P. Kochan, and M. W. Greaves, "Autoantibodies against the high-affinity IgE receptor as a cause of histamine release in chronic urticaria," The New England Journal of Medicine, vol. 328, no. 22, pp. 1599–1604, 1993.
5. Y. Tuzun, S. Keskin, and E. Kote, "The role of Helicobacter pylori infection in skin diseases: facts and controversies," Clinics in Dermatology, vol. 28, no. 5, pp. 478–482, 2010.
6. 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(4): 362-9.
7. Pawłowicz R, Wytrychowski K, Panaszek B. Eradication of Helicobacter pylori, as add-on therapy, has a significant, but temporary influence on recovery in chronic idiopathic urticaria: a placebo-controlled, double blind trial in the Polish population. Postepy Dermatol Alergol 2018; 35(2): 151-5.
8. B. Wedi, S. Wagner, T. Werfel, M. P. Manns, and A. Kapp, "Prevalence of Helicobacter pylori-associated gastritis in chronic urticaria," International Archives of Allergy and Immunology, vol. 116, no. 4, pp. 288–294, 1998.
9. A. G. Abdou, E. I. Elshayeb, A. G. A. Farag, and N. F. Elnaidany, "Helicobacter pylori infection in patients with chronic urticaria: correlation with pathologic findings in gastric biopsies," International Journal of Dermatology, vol. 48, no. 5, pp. 464–469, 2009.
10. Rebora A, Drago F, Parodi A. May Helicobacter pylori be important for dermatologists?. Dermatology 1995; 191:6-8
11. Pasechnikov V, Mashentseva E, Sohier M. Mucosal interleukin-8, platelet-activating factor, endothelin-1, leucotrine B4 and leucotriene C4 production in patients with Helicobacter pylori infection. Gut 1996; 39:40.
12. Realdi G, Dore MP, Fastame L. Extradigestive manifestations of Helicobacter pylori infection: fact and fiction. Dig Dis Sci 1999; 44:229-36.
13. Liutu M, Kalimo K, Uksila J, Kalimo H. Etiologic aspects of chronic urticaria. Int J Dermatol 1998; 37:515-519.996; 39:40.
14. Buhner S, Reese I, Kuehl F et al. Pseudoallergic reactions in chronic urticaria are associated with altered gastroduodenal permeability. Allergy 2004; 59(10):1118–23.
15. Muhemmed, F., & Mohammed, K. (2018). Association of chronic urticaria with Helicobacter Pylori infection in Erbil: A case-control study. Zanco Journal of Medical Sciences (Zanco J Med Sci), 20(2), 1376 – 1384.
16. M. S. Hasan, M. S. I. Khan, and J. Nayeem, "Study on association between chronic idiopathic urticaria and Helicobacter pylori infection in armed forces personnel," Journal of Armed Forces Medical College, Bangladesh, vol. 12, no. 2, pp. 122–126, 2016.
17. K. I. AL-Hamdi and L. S. Khashan, "Role of Helicobacter pylori in chronic ordinary urticaria: A case-control and therapeutic study," The Medical Journal of Basrah University, vol. 35, no. 1, pp. 39–47, 2017.
18. Talley NJ. American Gastroenterological Association. American Gastroenterological Association medical position statement: evaluation of dyspepsia. Gastroenterology 2005;129:1753-5.
19. 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.
20. Yadav M K, Rishi J P, Nijawan S. Chronic urticaria and helicobacter pylori. Indian J Med Sci 2008; 62(4):157-62.
21. Sianturi GN, Soebaryo RW, Zubier F, Syam AF. Helicobacter pylori Infection: prevalence in chronic urticaria patients and incidence of autoimmune urticaria. Acta Med Indones 2007; 39(4): 157-62.
22. James WD, Berger TG, Elston DM. Andrews' Diseases of the skin clinical dermatology. London British Library Cataloguing in Publication Data;2011.
23. Mallick, Y. and S. A. Hussain. "Frequency of Helicobacter pylori infection in patients of chronic spontaneous urticaria." Journal of Pakistan Association of Dermatology *29 (2019): 145-150.*
24. Mosbeh AS, Aladl A, Tealeb AS, Ali MS.Role of helicobacter pylori in chronic urticaria among egyptian patients with dyspepsia: a case–control study. Int J Dermatol Clin Res 2017; 3(1): 26-31.
25. Tareen A, Butt T, Ali B. Helicobacter pylori infection in patients with chronic urticaria and dyspepsia, experience from a developing country. J Pak Assoc Derma 2016; 26(3): 206-13.
26. Bohmer CJ, Klinkenberg-Knol EC, Kuipers EJ, et al. The prevalence of Helicobacter pylori infection among inhabitants and healthy employees of institutes for the intellectually disabled. Am J Gastroenterol. 1997;92:1000–4.
27. Martel, Catherine, Parsonnet, Julie, et al. Helicobacter pylori Infection and Gender: A Meta-Analysis of Population-Based Prevalence Surveys. Digestive diseases and sciences 2007;51:2292-301.
28. Agah S, Khedmat H, Ghamar-Chehred ME, Hadi R, Aghaei A. Female gender and Helicobacter pylori infection, the most important predisposition factors in a cohort of gastric cancer: A longitudinal study. Caspian J Intern Med. 2016;7(2):136-141.
29. 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.