



A systematic review and meta-analysis of the correlation between *Helicobacter pylori* infection and chronic urticaria

Yu-Li Cui[^], Bo-Yang Zhou, Guang-Cheng Gao

Department of Dermatology, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Contributions: (I) Conception and design: GC Gao; (II) Administrative support: GC Gao; (III) Provision of study materials or patients: BY Zhou; (IV) Collection and assembly of data: YL Cui; (V) Data analysis and interpretation: YL Cui; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Guang-Cheng Gao. Department of Dermatology, Beijing Friendship Hospital, Capital Medical University, Beijing 100050, China. Email: bjgaoguangcheng@126.com.

Background: A meta-analysis was conducted to examine the correlation between *Helicobacter pylori* infection and chronic urticaria.

Methods: We searched Chinese and English databases, including CNKI, Wanfang, and Weipu, using search terms such as *Helicobacter pylori* infection, and chronic urticaria for articles published from the establishment of the databases to February 2021 examining the correlation between *Helicobacter pylori* infection and chronic urticaria. The retrieved articles contained data on *Helicobacter pylori* infection rates in chronic urticaria cases in different regions of the north and south in China. The retrieved articles underwent strict screenings according to inclusion and exclusion criteria. Revman5.3 software was used to perform a meta-analysis on the data of the included articles.

Results: A total of 39 documents were retrieved following the searches. According to the inclusion and exclusion criteria, a total of 6 articles on 6 studies, comprising a total of 1,320 patients, were finally included in the meta-analysis. The results showed that the heterogeneity was high ($I^2=58\%$). A random-effects model was performed. An analysis of the correlation between *Helicobacter pylori* infection and chronic urticaria revealed significant differences between the study group and the control group [odds ratio (OR) =3.00; 95% confidence interval (CI): 1.98–4.55; $P<0.00001$]. The infection rate of *Helicobacter pylori* among chronic urticaria cases in the northern population was 16.1% (95% CI: 15.6–16.6%); of these patients 12.2% were male and 21.4% were female. The infection rate of *Helicobacter pylori* among chronic urticaria cases in the southern population was 18.0% (95% CI: 17.5–18.5%); of these patients, 12.3% were male and 23.1% were female. There was no significant difference in the prevalence between the male population, the female population, and the general population in the north and the south ($P>0.05$).

Discussion: *Helicobacter pylori* infection is correlated with the occurrence of chronic urticaria. There is no significant difference in the infection rate of *Helicobacter pylori* in chronic urticaria cases in different regions of the north and south. This study had some limitations. First, the number of patients included in each study was low, which may affect the accuracy of the results. Second, the detection methods were not uniform; thus, further research is required to support the conclusions drawn.

Keywords: *Helicobacter pylori*; chronic urticaria; correlation; breath test

Submitted Jul 30, 2021. Accepted for publication Sep 15, 2021.

doi: 10.21037/apm-21-2324

View this article at: <https://dx.doi.org/10.21037/apm-21-2324>

[^] ORCID: 0000-0003-0277-2613.

Introduction

Helicobacter pylori infection has a certain correlation with chronic urticaria. As an infectious factor, *Helicobacter pylori* infection may be involved in the occurrence and development of chronic urticaria disease. Patients with chronic urticaria aged 41 to 55 years have the highest infection rate (1); thus, it is more necessary to screen for *Helicobacter pylori* infection in this population than other populations. Screening for *Helicobacter pylori* infection can provide clinicians with more optimized and personalized diagnosis and treatment strategies (2,3). Chronic urticaria is a common skin disease. Various factors cause temporary inflammatory congestion, and a large amount of fluid exudation in the blood vessels of the skin and mucous membranes cause local edema damage (4,5). In this study, a meta-analysis was conducted using relevant domestic published articles to explore whether *Helicobacter pylori* infection is related to chronic urticaria. The knowledge of the correlation between *Helicobacter pylori* infection and chronic urticaria may help clinician to find more effective methods to treat people with chronic urticaria. We present the following article in accordance with the PRISMA reporting checklist (available at <https://dx.doi.org/10.21037/apm-21-2324>).

Methods

Document sources and retrieval strategies

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) literature screening flowchart was used to select the included research articles (6-9), and formulate a search strategy in accordance with Cochrane international standards. The selected Chinese databases were WAN FANG DATA and Chinese National Knowledge Infrastructure (CNKI). The Chinese search terms included *Helicobacter pylori* infection, and chronic urticaria. The databases were searched from their establishment to February 2021 for relevant studies on the relationship between *Helicobacter pylori* infection and chronic urticaria. The languages were restricted to Chinese and English. The publications were limited to clinical trial studies, and the research selection was limited to observational studies on *Helicobacter pylori* infection and chronic urticaria. Under the search sequence, 3 documents of evidence-based medicine resources were first searched that had been evaluated and screened to understand whether there was any secondary

research evidence for this research topic. The original research evidence was then retrieved.

Literature inclusion and exclusion criteria

To be eligible to participate in this study, articles had to meet the following inclusion criteria: (I) the original article was published in Chinese or English; (II) the article was about a clinical observational study; and (III) the study group comprised patients with chronic urticaria, and the control group comprised healthy individuals. Articles were excluded from the study if they met any of the following exclusion criteria: (I) the article was about a non-observational study (e.g., a review, an animal experiment, a case study, or an academic theory); (II) the same content had been published repeatedly in multiple articles; and/or (III) the complete original data could not be obtained.

Data extraction

The following data were extracted from the articles: (I) basic information, such as the name of the first author, the number of cases, the age and gender of the patients, the region, and the year of publication; and (II) basic information about the research object(s), intervention measures, treatment course, and outcome indicators. In instances of incomplete documentation, the author was contacted and the information was obtained. If the researchers disagreed to provide the information, the decision was locally arbitrated.

Literature quality evaluation

According to the Cochrane bias risk assessment tool, the quality of the included articles was evaluated in relation to the random method, allocation plan hiding, blinding, result data completeness, selective reporting of research results, and other sources of bias.

Statistical methods

Revman5.3 software was used to conduct the meta-analysis on the data included in the analysis. The selected count data are expressed as odds ratios (ORs), and 95% confidence interval (CIs). The measurement data are expressed as odds ratios (OR), and 95% CIs. A forest map was drawn to show the differences in the research results. The heterogeneity

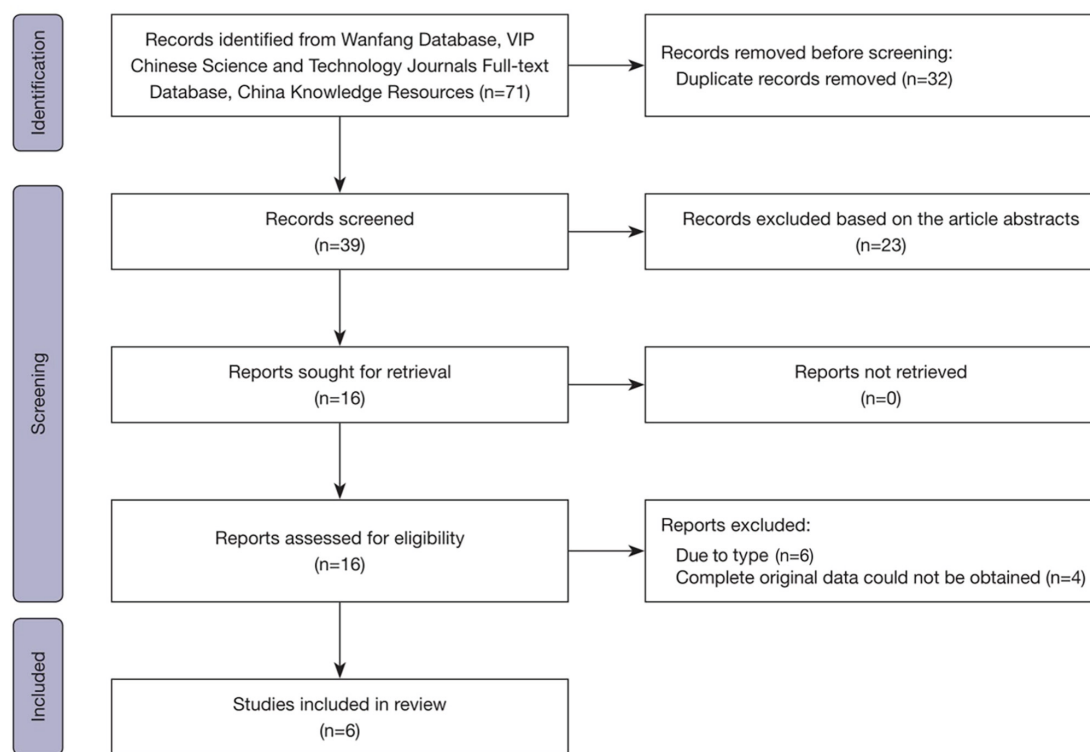


Figure 1 The flow chart of screening articles underwent meta-analysis.

of the various clinical trials was tested using a chi-square test; if $I^2 \geq 50\%$, a random-effects model was selected for the meta-analysis; if $I^2 < 50\%$, a fixed-effects model was selected for the meta-analysis. A funnel chart was produced and the symmetry of the funnel chart was compared and analyzed to determine whether there was any publication bias. Symmetry indicated no publication bias, while asymmetry indicated publication bias.

Results

Literature search results

The document retrieval work was independently completed by three people. The retrieval results and the process are shown in *Figure 1*. A total of 71 articles were screened in the search of the databases, and EndNote software was used for the analysis. Thirty-two duplicate articles were removed and 39 articles remained. After reading the title and abstracts, 23 articles were excluded based on the above exclusion and inclusion criteria, and 16 articles remained. After carefully reading the full text of the 16 articles, ten additional articles were excluded. The remaining six articles underwent meta-

analysis. All the articles were from Mainland China, and were published in the Chinese language (see *Figure 1*).

Basic characteristics of the included literature

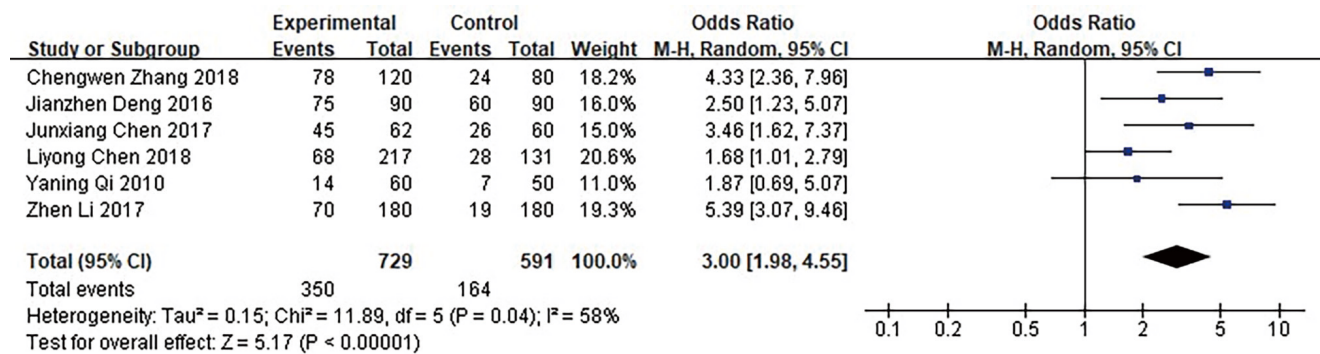
A total of 196 articles were retrieved. Based on the inclusion and exclusion criteria, a total of six (2-7) articles were finally included in the meta-analysis, comprising a total of 1,320 patients. The basic details of the included articles are set out in *Table 1*.

Meta-analysis of the correlation between *Helicobacter pylori* infection and chronic urticaria

Six studies were included (2-7) in the meta-analysis. The heterogeneity test results showed that the heterogeneity was high ($I^2 = 58\%$). A random-effects model was performed. The results revealed a correlation between *Helicobacter pylori* infection and chronic urticaria. There was a significant difference between the study group and the control group (OR = 3.00; 95% CI: 1.98–4.55; $P < 0.00001$). *Figure 2* shows the forest diagram.

Table 1 Basic details of the included articles

Author	Detection method	Total number of cases	Urticaria cases		Normal control	
			Number of people	HP (+)	Number of people	HP (+)
Liyong Chen (2)	¹³ C urea breath test	348	217	68	131	28
Junxiang Chen (3)	¹⁴ C urea breath test	122	62	45	60	26
Zhen Li (4)	¹⁴ C urea breath test	360	180	70	180	19
Jianzhen Deng (5)	¹⁴ C urea breath test	180	90	75	90	60
Chengwen Zhang (6)	¹⁴ C urea Breath Test	200	120	78	80	24
Yaning Qi (7)	¹³ C urea breath test	110	60	14	50	7

**Figure 2** Meta-analysis forest diagram of the correlation between *Helicobacter pylori* infection and chronic urticaria.

Infection rate of *Helicobacter pylori* in chronic urticaria cases in different regions of the north and south

The Huai River marks the boundary between north and south China. The infection rate of *Helicobacter pylori* among chronic urticaria cases in the northern population was 16.1% (95% CI: 15.6–16.6%); of these patients, 12.2% were male and 21.4% were female. The infection rate of *Helicobacter pylori* among chronic urticaria cases in the southern population was 18.0% (95% CI: 17.5–18.5%); of these patients, 12.3% were male and 23.1% were female. There was no significant difference in the prevalence between the male population, female population, and the overall population in the north and the south (P>0.05; see Table 2).

Publication bias

A funnel chart was drawn for the 6 included articles using the study on the correlation between *Helicobacter pylori* infection and chronic urticaria as the combined index. The

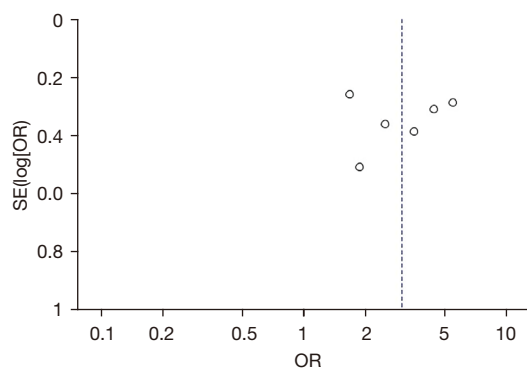
funnel chart was generally symmetrical, indicating that the included articles may not have certain publication bias (see Figure 3).

Discussion

The discovery of *Helicobacter pylori* infection is one of the most significant medical discoveries in the last century. *Helicobacter pylori* was discovered by 2 Australian scientists, Robin Warren and Professor Bobby Marshall, in 1982, after more than 30 years of in-depth research. The important role of *Helicobacter* in chronic gastritis, peptic ulcer, and gastric cancer has been fully demonstrated (10-13). The discovery of *Helicobacter pylori* explains the cause of chronic gastritis, peptic ulcers, and gastric cancer; however, many problems remain to be studied. For example, the relationship between *Helicobacter pylori* infection and other diseases is currently believed to be related to urticaria, which requires in-depth research. Chronic urticaria is an allergic skin disease, and has an incidence rate of 0.1–3.0% (1). The symptoms include

Table 2 Infection rate of *Helicobacter pylori* in chronic urticaria cases among populations in different regions of the north and south

Age group (years)	North			South		
	Male	Female	Overall	Male	Female	Overall
18–25	5.3	12.0	7.1	3.5	7.0	5.8
26–35	6.3	14.6	11.8	7.0	17.1	13.5
36–50	15.6	33.4	23.1	7.6	16.0	13.0
50–60	16.3	30.1	24.7	14.0	27.4	23.2
Above 60	23.2	41.9	35.7	28.0	42.8	36.5
Total	12.2	21.4	16.1	12.3	23.1	18.0

**Figure 3** Meta-analysis funnel chart of the correlation between *Helicobacter pylori* infection and chronic urticaria.

wheals and patches on the trunk, face, or limbs from time to time. Attacks range from several times a day to once every few days. The pathogenesis is complicated and not completely clear. A clear cause cannot be found for about 75% of patients. Most patients obtain satisfactory results after treatment with antihistamines. A few patients are difficult to treat, and the treatment process is long. It is prone to recur. Dermatologists can only rely on increased doses of antihistamines or a combined treatment for refractory urticaria. This disease has plagued many patients and first-line dermatologists. In recent years, studies have shown that *Helicobacter pylori* infection may be one of the causes of chronic urticaria. *Helicobacter pylori* infection can be eradicated. The related problems of *Helicobacter pylori* infection and chronic urticaria have attracted wide attention from doctors in the digestive and dermatological fields. The detection of *Helicobacter pylori* infection has gradually shown higher clinical applications in the diagnosis and treatment of chronic urticaria (14).

Cao *et al.* (15) showed that the positive rate of

Helicobacter pylori in an experimental group was 83.33%, which was significantly higher than that of 66.66% in the control group. The difference between the groups was statistically significant ($P < 0.05$). These results provide further evidence that chronic urticaria and *Helicobacter pylori* Bacillus infections are related. Wang *et al.* (16) studied the correlation between chronic urticaria and *Helicobacter pylori* infection, and found that the *Helicobacter pylori* infection rate in the urticaria group was significantly higher than that of the healthy group ($P < 0.05$). *Helicobacter pylori* infection may play a role in promoting the occurrence of chronic urticaria, which will increase the probability of chronic urticaria in healthy people. Thus, patients with chronic urticaria need to be tested for *Helicobacter pylori* infection first. It must be clear whether a patient has *Helicobacter pylori* infection before treatment to improve the therapeutic effect of chronic urticaria. *Helicobacter pylori* infection cannot be completely eliminated (17), and is the main cause of poor efficacy in patients with chronic urticaria (18). Previous studies have shown that *Helicobacter pylori* may be involved in the pathogenesis of chronic urticaria. Increasing the permeability of gastric mucosal blood vessels induces an increase in the probability of contact between the body and food allergens. Additionally, chronic infection produces significant stimulation of the immune system (19). Interleukin is a leading inflammatory mediator. It is thought that promoting the release process of interleukin results in increased sensitivity in the skin vessels (20), and ultimately induces chronic urticaria; however, these conclusions have not been confirmed, and further research is needed (21). This study only focused on the relationship between the *Helicobacter pylori* infection and the incidence of chronic urticaria. Just according these clinical evidence and results, it is difficult to say whether this relationship is

direct or indirect without pathology or etiology evidence. Further studies are needed. In this study, the meta-analysis of the data of 6 studies showed that compared to the control group, the proportion of chronic urticaria cases with scapular infection was high, which suggests that *Helicobacter pylori* infection is related to the occurrence of chronic urticaria.

In this study, the rate of *Helicobacter pylori* infection among chronic urticaria cases in the northern population was 16.1% (95% CI: 15.6–16.6%); of these patients, 12.2% were male and 21.4% were female. The infection rate of *Helicobacter pylori* among chronic urticaria cases in the southern populations 18.0% (95% CI: 17.5–18.5%); of these patients, 12.3% were male and 23.1% were female. There was no significant difference in the prevalence between the male population, the female population, and the overall population. The publication bias analysis results showed that the funnel chart data were symmetrical, and there was no publication bias. This study had some limitations. First, the number of patients included in each study was low, which may affect the accuracy of the results. Second, the detection methods were not uniform; thus, further research is required to support the conclusions drawn.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at <https://dx.doi.org/10.21037/apm-21-2324>

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://dx.doi.org/10.21037/apm-21-2324>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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References

1. Sánchez-Borges M, Ansotegui IJ, Baiardini I, et al. The challenges of chronic urticaria part 1: Epidemiology, immunopathogenesis, comorbidities, quality of life, and management. *World Allergy Organ J* 2021;14:100533.
2. Chen L, Zhang J, Chen Z, et al. Research on the correlation between chronic urticaria and *Helicobacter pylori* infection. *Journal of Modern Laboratory Medicine* 2018;33:146-8.
3. Chen J, Qin L. Study on the correlation between chronic urticaria and *Helicobacter pylori* infection. *Medical Information* 2017;30:75-6.
4. Li Z, Wu J, Wang Y, et al. The relationship between *Helicobacter pylori* infection and chronic urticaria. *Chinese General Practice* 2017;180-2.
5. Deng J. Study on the relationship between chronic urticaria and *Helicobacter pylori* infection. *Heilongjiang Medicine* 2016;20-2.
6. Zhang C. Correlation analysis between chronic urticaria (CU) and *Helicobacter pylori* infection (Hp). *Family Medicine* 2018;30.
7. Qi Y. The relationship between *Helicobacter pylori* infection and chronic urticaria. *Family Medicine* 2018;85.
8. Qi Z, Lin X, Xu R, et al. The effect of cetirizine combined with anti-*Helicobacter pylori* triple therapy on children's chronic urticaria and its effect on serum inflammatory factors and immunoglobulin levels. *Chinese Primary Medicine* 2015;05:731-4.
9. Lin L, Chen H, Zhang H. Correlation analysis between *Helicobacter pylori* and chronic urticaria. *China Practical Medicine* 2013;05:27-8.
10. He L, Chen J, Wang J. Discussion on the relationship between *Helicobacter pylori* and chronic urticaria and skin scratches. *Chinese Journal of Integrated Traditional Chinese and Western Medicine Dermatology and Venereology* 2013;02:101-2.
11. Sagrañes-Montalván A, Barreto-Suárez E, Nicolau-Pestana E, et al. Relación entre infección por *Helicobacter pylori* y urticaria crónica Relation between *Helicobacter pylori* infection and 2017 urticaria. *Rev*

- Alerg 2017;396-402.
12. Kim HJ, Kim YJ, Lee HJ, et al. Systematic review and meta-analysis: Effect of *Helicobacter pylori* eradication on chronic spontaneous urticaria. *Helicobacter* 2019;24:e12661.
 13. Dennis MF, Mavura DR, Kini L, et al. Association between Chronic Urticaria and *Helicobacter pylori* Infection among Patients Attending a Tertiary Hospital in Tanzania. *Dermatol Res Pract* 2020;2020:5932038.
 14. Liu D, Ye H. Discussion on the relationship between *Helicobacter pylori* infection and chronic urticaria in Meizhou City. *Chinese Journal of Integrated Traditional Chinese and Western Medicine Dermatology and Venereology* 2017;02:129-31.
 15. Cao Y, Li Z, Zhang H, et al. A clinical study on the treatment of *Helicobacter pylori*-positive chronic urticaria with Chinese and Western medicine sequential therapy. *Journal of Anhui University of Traditional Chinese Medicine* 2017;03:33-6.
 16. Wang L, Lu W, Mo R, et al. The regulatory mechanism of *Helicobacter pylori* infection on peripheral blood γ -interferon and interleukin-4 in patients with chronic urticaria. *Chinese Experimental and Clinical Infectious Diseases Magazine (electronic version)* 2017;05:504-7.
 17. Fischbach W, Malfertheiner P. *Helicobacter Pylori* Infection. *Dtsch Arztebl Int* 2018;115:429-36.
 18. Kutlubay Z, Zara T, Engin B, et al. *Helicobacter pylori* infection and skin disorders. *Hong Kong Med J* 2014;20:317-24.
 19. Usharauli D. Chronic infection and the origin of adaptive immune system. *Med Hypotheses* 2010;75:241-3.
 20. Brand CU, Yawalkar N, Hunziker T, et al. Human skin lymph derived from irritant and allergic contact dermatitis: interleukin 10 is increased selectively in elicitation reactions. *Dermatology* 1997;194:221-8.
 21. Wang L, Luo X, Cao Y, et al. Analysis of results of detection of *Helicobacter pylori* by C urea breath test in 462 patients with chronic urticaria. *Journal of Clinical Dermatology* 2017;10:695-6.
- (English Language Editor: L. Huleatt)

Cite this article as: Cui YL, Zhou BY, Gao GC. A systematic review and meta-analysis of the correlation between *Helicobacter pylori* infection and chronic urticaria. *Ann Palliat Med* 2021;10(10):10584-10590. doi: 10.21037/apm-21-2324