Systematic Review and Meta-Analysis

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Association between *Helicobacter pylori* infection and irritable bowel syndrome

A systematic review and meta-analysis

Chenyu Li, BS[a,c], Yujun Shuai, BS[a,c], Xiaodong Zhou, PhD[a,*], Hongxia Chen, PhD[b]

Abstract

Background: In recent years, the incidence of IBS has gradually increased, and it is considered as one of the most common functional gastrointestinal diseases. However, the etiology of IBS is still unclear, and expectations are rising for more targeted treatments. Many clinical trials have explored the link between *Helicobacter pylori* (*H pylori*) and IBS, with different conclusions. Therefore, we conducted a meta-analysis to explore whether there is an association between *H pylori* and IBS, which is of great significance for targeted treatment of IBS.

Methods: We performed a systematic review and meta-analysis of the association between *H pylori* and IBS. We searched PubMed, EMBASE, Medline and the Cochrane Library to collect related studies. OR was used to describe the ratio of the probability of the *H pylori* infection occurring in IBS patients versus the controls. Heterogeneity was assessed by subgroup and meta-regression analysis.

Results: Eight studies, including 1861 patients, assessed the association between *H pylori* infection and IBS. The OR of *H pylori* in IBS patients compared to controls was 1.32 (95% CI: 0.94–1.87; P = 0.11). Subgroup analyses showed a difference between IBS patients diagnosed with Roman III criteria and those diagnosed with non-Roman III criteria.

Conclusions: Our study suggests that *H pylori* may have a positive effect on the development of IBS. Although the differences were not statistically significant, there were significant differences among subgroups of patients. Considering the limitations and heterogeneity, high quality studies are needed to further explore the effect of *H pylori* on the development of IBS.

Abbreviations: BDQ = bowel disorder questionnaire, CIs = confidence intervals, *H pylori* = helicobacter pylori, IBS = irritable bowel syndrome, OR = odds ratio.

Keywords: functional-disorders, helicobacter pylori, irritable bowel syndrome, meta-analysis

1. Introduction

Irritable bowel syndrome (IBS) is a common intestinal disorder, abdominal pain, stool pattern alteration, distention, bloating, straining, abdominal discomfort, and urgency are major symptoms observed in IBS.[1,2] Due to the differing symptoms experienced, patients diagnosed with IBS can be divided into three groups: diarrhea-predominant (IBS-D), constipation-predominant (IBS-C) and mixed-type (IBS-M). So far, the incidence of IBS has gradually increased to 20% in European and American countries, and to 10% in China,[3] which is considered as one of the most common functional gastrointestinal diseases.[4] In addition, it is twice as frequent in women[5] and is diagnosed more often in patients less than 50 years of age.[6] Although the pathogenesis of IBS may be related to visceral hypersensitivity,[7,8] disturbances in gastrointestinal (GI) flora,[9,10] and low-level mucosal inflammation[11–14] caused by chronic immune activation, the etiology of IBS is still unclear. The current therapeutic options for IBS treatment include low-dose antidepressants, spasmolytics, and 5-HT3 antagonists, however, the multiple side effects caused by drugs and the inadequacies of treatment when multiple symptoms coexist have led to increasing expectations for more targeted treatments.[15–18]

Helicobacter pylori (*H pylori*), a gram-negative bacterium, was classified as a grade 1 carcinogen by the world health organization in 1994. It is associated with chronic gastritis

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[a] Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, No. 17, Yongwaizheng Road, Donghu District, Nanchang, Jiangxi Province, [b] Department of Gynecology and Obstetrics, The First Affiliated Hospital of Nanchang University, [c] First Clinical Medical College, Nanchang University, Nanchang, China.

[*] Correspondence: Xiaodong Zhou, Department of Gastroenterology, First Affiliated Hospital of Nanchang University, Nanchang, Jiangxi 330006, PR China (e-mail: zhouxdncu@163.com)

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and is usually located on the epithelial surface of the stomach. Interestingly, it is also often detected in patients with IBS. In recent years, many clinical trials have explored the link between *H pylori* and IBS. Some articles have confirmed that the prevalence of *H pylori* is different between IBS and normal people,[19–23] while others have come to the opposite conclusion.[24–28] Therefore, we conducted a meta-analysis to summarize the data published so far to analyze whether there is an association between IBS and *H pylori*. This has important implications for the treatment of IBS and the eradication of *H pylori*.

2. Methods

2.1. Search strategy

We performed a search of PubMed, EMBASE, Medline and the Cochrane Library for studies published up until August 4, 2019. The databases were searched based on a combination of the following words: ("Helicobacter pylori" OR "Campylobacter pylori") and ("Irritable Bowel Syndrome" OR "Irritable Bowel Syndromes" OR "Syndrome, Irritable Bowel" OR "Syndromes, Irritable Bowel" OR "Colon, Irritable" OR "Irritable Colon" OR "Colitis, Mucous" OR "Colitides, Mucous" OR "Mucous Colitides" OR "Mucous Colitis"). There were no restrictions on the regional origin or language of the article. We also performed a manual search of the references from selected articles, reviews and conference abstracts which related to our research to identify additional relevant studies. The investigation was conducted independently by two investigators and differences were resolved through discussion.

2.2. Study selection

Studies were selected if they met the following criteria:

1. *H pylori* infection was detected by histology, fecal antigen test (FAT), rapid urease test (RUT), serology (IgG anti-body), or urea breath test (UBT);
2. investigated the relationship between *H pylori* infection and IBS;
3. including control group;
4. the IBS group and the control group were similar in age, sex and location;
5. the reported data were sufficient to calculate *H pylori* infection rates in the IBS group and the control group.

Two researchers (CYL, YJS) independently assessed the relevance of the resulting manuscripts, excluding manuscripts with the following criteria:

(1) duplicate studies;
(2) animal studies;
(3) letters, editorial, reviews, notes, case reports, and conference abstract;
(4) data from a previously published study were used.

2.3. Quality assessment

The quality of the included studies was assessed using the Newcastle-Ottawa scale (NOS), which judges the selection of the study groups according to three domains: selection, comparability and exposure.[29] NOS adopted the semi-quantization principle of star system for the evaluation of literature quality. The full score was 9 stars, and the higher the quality of the article, the more the number of stars.

2.4. Data extraction

The following data were extracted from each study by two researchers into a standard spreadsheet:

a) authors;
b) country of origin;
c) year of publication;
d) study design;
e) *H pylori* detection method;
f) IBS diagnosis criteria;
g) the total number of patients in the IBS and control groups;
h) number of patients with IBS and within this group, the number of patients who were H pylori-positive;
i) number of patients in the control group and within this group, the number of patients who were H pylori-positive;
j) the ratio of male to female in the IBS and control groups.

Any disagreements over the retrieved information were resolved by consensus.

2.5. Statistical analysis

All data analyses were conducted using statistical software (Review Manager version 1.4), including the heterogeneity test and outcomes combination. Two investigators independently analyzed the data and the primary outcome of this analysis was the odds ratio (OR) of *H pylori* infection in IBS versus controls. OR was used to describe the ratio of the probability of the *H pylori* infection occurring in IBS patients versus the controls. All data were calculated with 95% confidence intervals (CIs) and a random-effects model. We assessed the statistical heterogeneity among the summary data by the I^2 statistic and the chi square-based Q statistic that $I^2 < 40\%$ as heterogeneity might not be important and $> 75\%$ as considerable heterogeneity based on the suggestion in the Cochrane Handbook for Systemic Reviews of Interventions and heterogeneity was considered statistically significant if $P < .05$.[30–32] We did not generate funnel plots because there were fewer than 10 studies in each group.[32–34] In the next step, we conducted subgroup analysis on the following 3 cases to assess the sources of heterogeneity more accurately:

(1) race (Asian vs non-Asian),
(2) method of IBS diagnosis (Rome III vs non-Rome III).
(3) method of *H pylori* diagnosis (serology vs non-serologic methods).

2.6. Ethics and dissemination

This is a literature-based study that does not require ethical approval.

3. Results

3.1. Study selection

We searched 650 records in PubMed, EMBASE, Medline and the Cochrane Library. Of these, 36 duplicate studies were excluded. Two additional records were identified in the manual searches. After screening title and abstract, 482 studies were excluded, and the remaining 134 articles were retrieved for full-text review.

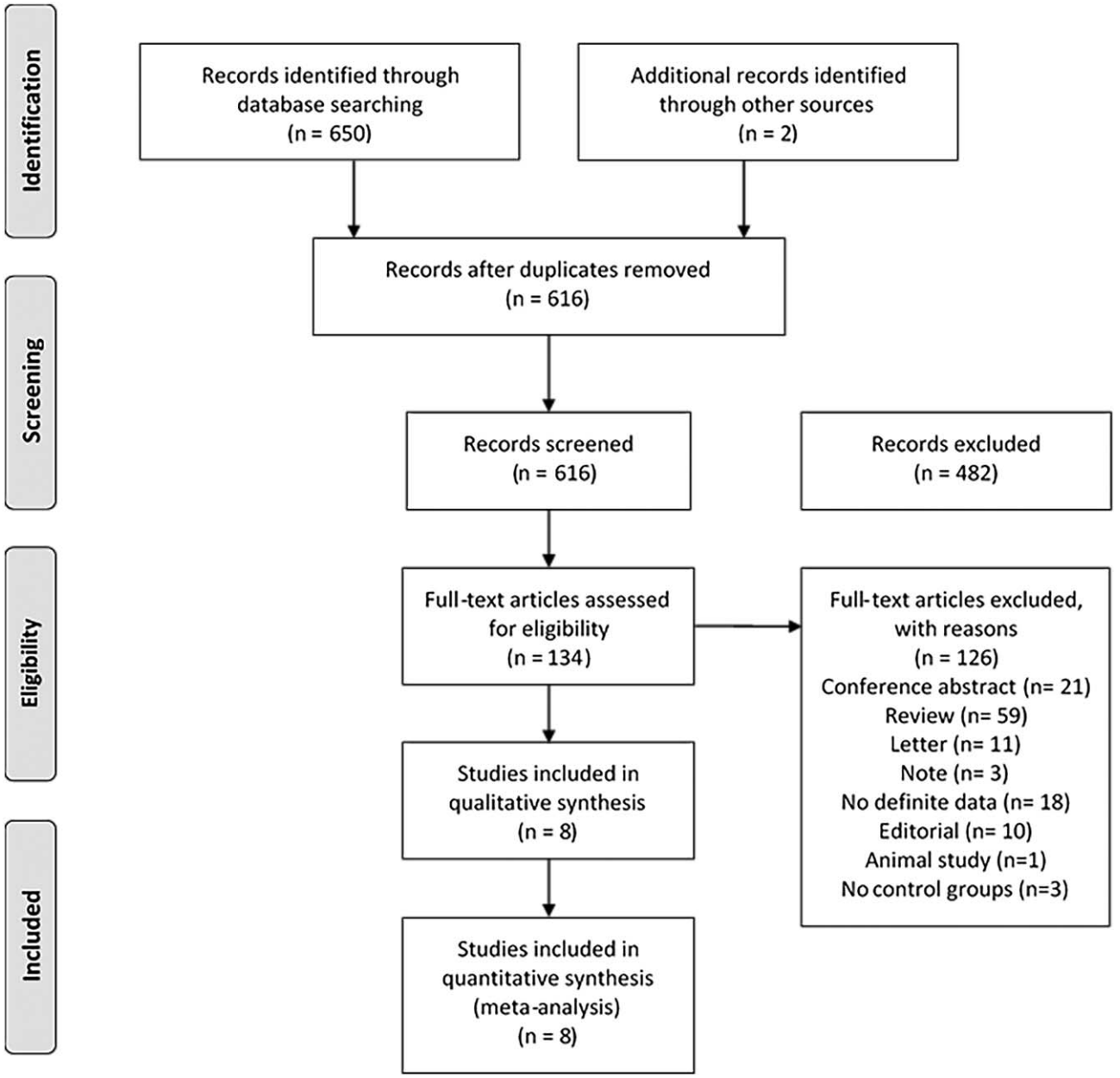

Figure 1. Flow diagram for identifying eligible studies to include in the meta-analysis.

Then, we excluded 126 articles because they did not meet the inclusion criteria. Finally, 8 articles were included in the present meta-analysis.[19,21–27] These studies included a total of 931 cases of IBS and 930 controls. A flowchart of the selection process for this study is presented in Figure 1.

3.2. Study characteristics

The characteristics of the included studies and patients are summarized in Table 1. The total population of the studies was 1861. Of the 8 studies, 5 studies were conducted in Asian populations, and the remaining 3 studies focused on European and American populations. There were 6 single center studies and 2 multicenter studies. All were case-control studies. The year of publication was ranged from 1995 to 2017. The mean age of IBS patients ranged from 31.0 to 59.7 years, and the mean age of patients in the control groups ranged from 39.0 to 59.7 years. The percentage of female patients ranged from 31.8% to 71.4% in the IBS groups, while in the control groups the percentage of female patients ranged from 33.8% to 55.4%.

IBS was diagnosed in five studies using the Rome III criteria.[19,21–23,26] One study used a validated and reliable questionnaire to determine the presence of IBS symptoms, which had been described in detail elsewhere previously.[25] One study used the Bowel Disorder Questionnaire (BDQ)[24] to determine the presence of IBS symptoms during the past year.[35,36] And in another study, IBS was diagnosed based on clinical and ultrasonography results.

Table 1

The characteristics of the included studies and patients.

Authors	Location	Method of IBS Detectio	Year	Method of Hp Detection	Study center	Mean age (IBS/control)	n, Total	n, IBS	F/M	H pylori-positive	n, Control	F/M	H pylori-positive	NOS*
Agréus et al	Sweden	Questionnaire	1995	IgG (serology)	Single	48.0	96	48	NR‡	16	48	NR	23	8
Han et al	China	Rome III	2010	RUT/^{14}C-UBT	Single	46.5	188	94	NR	58	94	NR	45	7
He et al	China	Rome III	2009	IgG (serology)	Single	59.7	220	110	40/70	67	110	40/70	50	8
Locke 3rd et al	America	BDQ†	2000	IgG (serology)	Multi	31.0/39.0	112	35	25/10	7	77	38/39	9	8
Sýkora et al	The Czech republic	Rome III	2016	IgG (serology)	Single	NR	61	5	NR	0	56	31/25	4	7
Yakoob et al	Pakistan	Rome III	2012	Histology	Single	41.0/42.0	330	170	54/116	116	160	54/106	88	6
Yang at al	China	Rome III	2017	RUT/^{14}C-UBT	Multi	41.5/42.0	670	335	158/177	180	335	183/152	140	7
Hasan et al	Iraq	Clinical and ultrasonography results	2017	IgG (serology)	Single	45.4/41.7	184	134	50/84	57	50	25/25	29	6

* Newcastle Ottawa scale (NOS) was used to assess the quality of bias control.
† BDQ: bowel disease questionnaire.
‡ NR: not reported.

Seven articles used apparently healthy individuals without abdominal pain or other frequent gastrointestinal symptoms as their patient controls, and the left one had patients who had abdominal pain or discomfort associated with intermittent diarrhoea but did not fulfill the Rome III criteria for IBS as controls. Five studies used serologic tests (IgG anti-body) and three studies used non-serologic tests (14C-urea breath test, biopsy specimen histology, or rapid urease test) to detect *H pylori*.

On the whole, the studies were observational and achieved relatively high scores in the quality assessment (NOS score). Three of them scored eight points in the quality assessment and five scored six or seven points.

3.3. Meta-analysis of OR

Eight studies, including 1861 patients, assessed the association between Helicobacter pylori infection and irritable bowel syndrome. Of these studies, which included 931 IBS patients and 930 controls (Fig. 2), 53.8% of patients in the IBS groups were found to have *H pylori* infection, while 41.7% of patients in the control groups had *H pylori* infection. The OR of *H pylori* in IBS patients compared to controls was 1.32 (95% CI: 0.94–1.87; $P=.11$). And this result had a moderate degree of heterogeneity ($I^2=59\%$, $P=.02$).

3.4. Subgroup analysis

We pre-estimated three subgroups that might contribute to heterogeneity. Stratified analyses by race, in which the studies were divided into two categories termed Asian (n = 5 studies, 843 patients with IBS and 749 healthy controls) and non-Asian (those including American and European, n = 3 studies, 88 patients with IBS and 181 non-IBS controls), showed a positive association in Asian (OR:1.45, 95% CI: 1.01–2.07, P = 0.04; $I^2=64\%$) and a little negative association in non-Asian (OR:0.95, 95% CI: 0.37–2.40, $P=.91$; $I^2=38\%$). The results of this analysis showed that there was no statistically significant difference between the two groups ($P=.41$, $I^2=0\%$) (Fig. 3).

We also analyzed serologic and non-serologic methods studies separately, and observed a difference prevalence of Helicobacter species among the patients diagnosed with *H pylori* by serologic methods (5 studies; OR = 1.00, 95% CI: 0.50–1.98) and the patients diagnosed with *H pylori* by non-serologic methods (3 studies; OR = 1.68, 95% CI: 1.33–2.11). There was moderate heterogeneity among the studies of patients diagnosed with *H pylori* by serologic methods ($I^2=67\%$), although no heterogeneity was observed for the studies of patients diagnosed with *H pylori* by non-serologic methods ($I^2=0\%$). (Fig. 4) Similar to the first subgroup, no statistically significant differences were observed ($P=.16$, $I^2=49\%$).

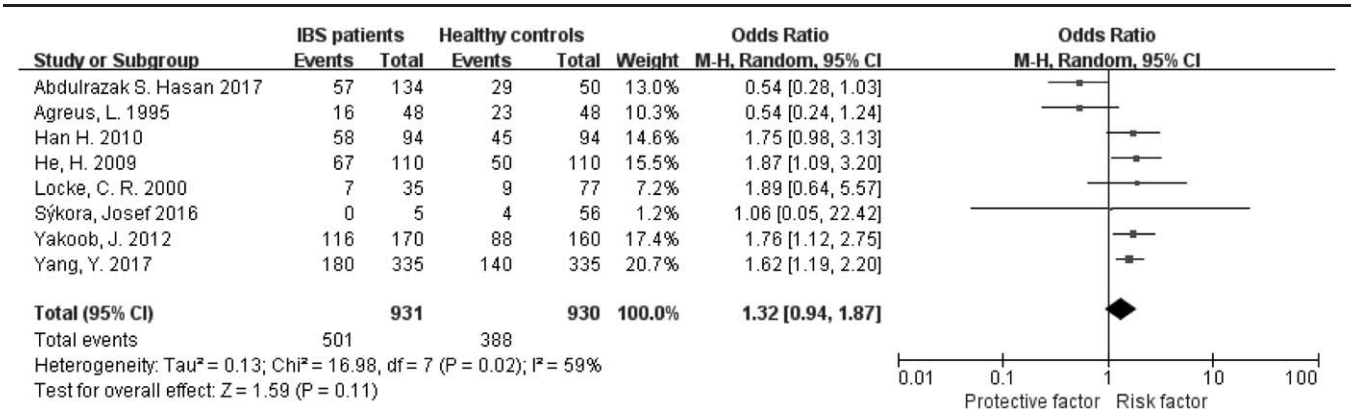

Figure 2. Forest plot of *H pylori* infection rate in IBS patients vs healthy controls.

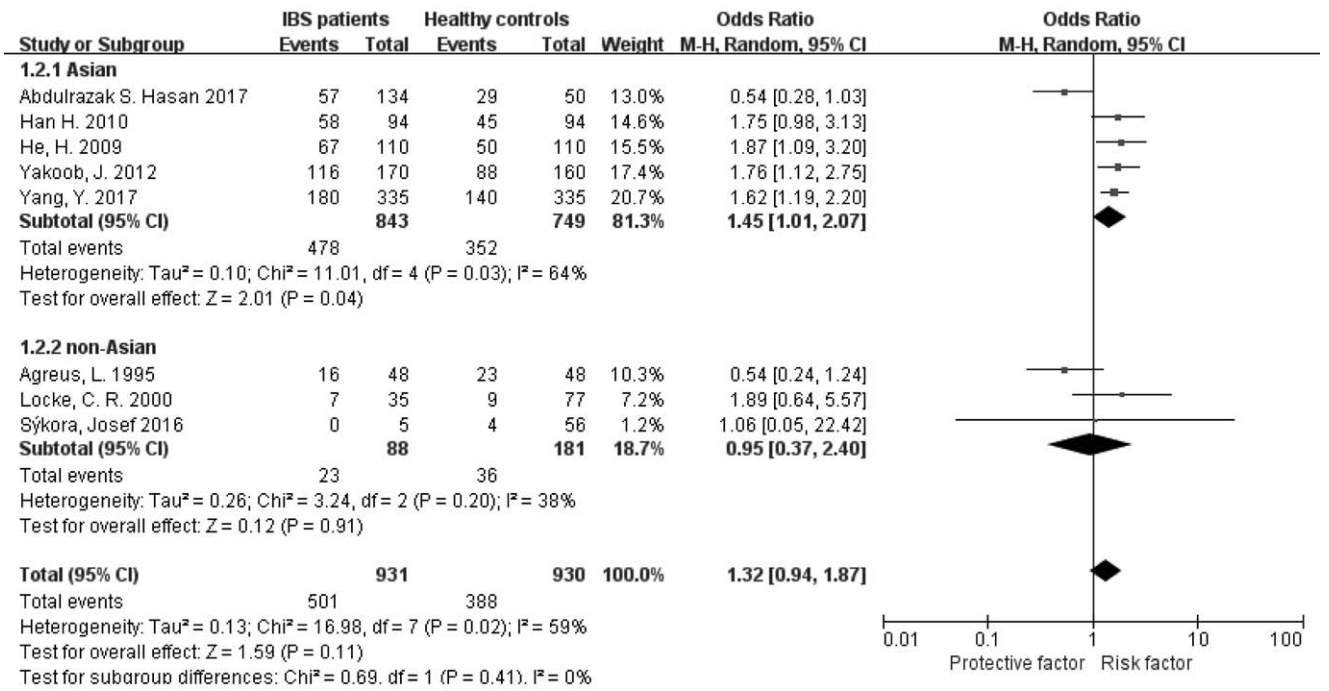

Figure 3. Forest plots of stratified analyses by race.

Finally, we separated the dataset into IBS patients diagnosed by Rome III and IBS patients diagnosed by other standards (Fig. 5). This analysis revealed a statistically significant increase in the OR of *H pylori* infection in IBS patients diagnosed by Rome III. (OR = 1.70, 95% CI: 1.38–2.10; $I^2 = 0\%$). It is worth noting that there were statistically significant differences and significant heterogeneity between the two categories ($P = .03$, $I^2 = 80\%$).

4. Discussion

This meta-analysis included 8 studies, a total of 1861 patients. Our meta-analysis observed a positive association between gastric *H pylori* infection and irritable bowel syndrome, but we did not observe statistically significant differences. Six of the eight studies showed a statistically significant OR greater than 1 for *H pylori* infection in IBS patients versus controls, while none of the

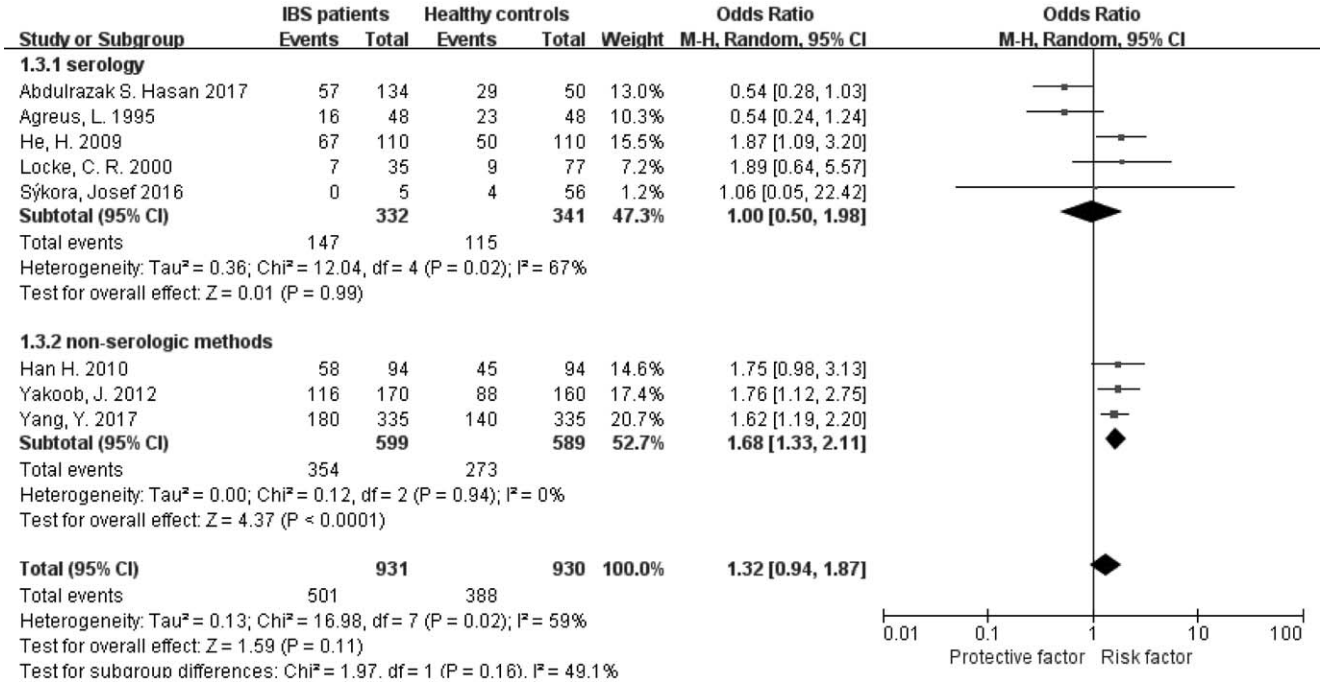

Figure 4. Forest plots of stratified analyses by method of *H pylori* diagnosis.

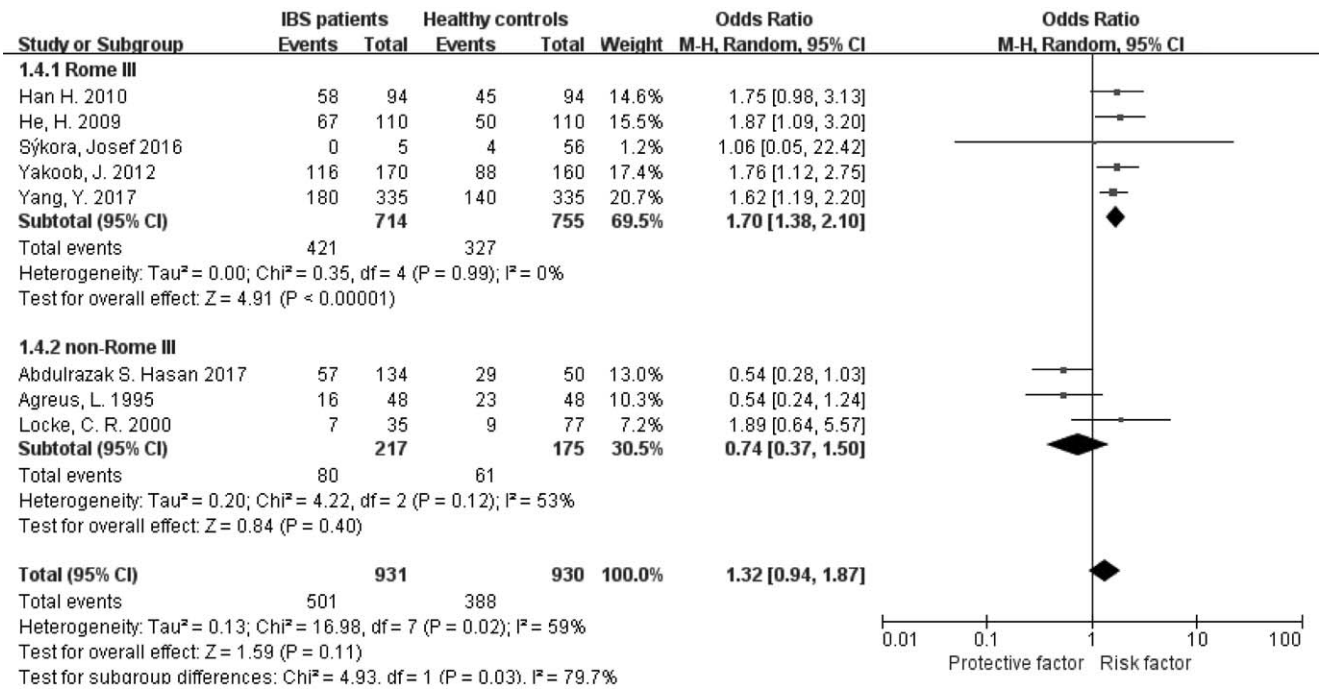

Figure 5. Forest plots of stratified analyses by method of IBS diagnosis.

included studies showed a statistically significant OR less than 1. It is worth noting that among the 8 studies we included, a study from Sýkora et al included 56 patients with abdominal pain and 56 healthy controls.[26] Since only 5 out of 56 patients have irritable bowel syndrome, it would have a significant impact on the experimental results. We looked forward to more researched in the future to provide more comprehensive data.

As a common infection of digestive tract, the relationship between *H pylori* infection and IBS has been controversial. One study from China showed no association between *H pylori* and IBS,[37] while another demonstrated that *H pylori* infection was a risk factor for functional dyspepsia in IBS patients in Taiwan[20] and to increase the likelihood for IBS patients with functional dyspepsia to consult their primary care physician.[38] In contrast, reports from the United States,[24] Japan[28] and Sweden[25] failed to show an association between *H pylori* and IBS. A case-control study by He et al[19] showed that, under the premise of similar population (n = 110), sex ratio and age composition, the infection rate of *H pylori* in IBS patients was significantly higher than that in healthy people, and the difference between the two groups was statistically significant. However, a study from Iraq[27] showed that the prevalence of *H pylori* infection in healthy controls was higher (58%) than that in IBS patients (43%). In addition, Malinen et al[39] studied the fecal flora of patients with IBS or without IBS and found that IBS was not associated with *H pylori* infection.

Our results (pooled OR 1.32, 95% CI: 0.94–1.87, $P = .11$) are very similar to those recently published by Ng et al[40] (pooled OR 1.47, 95%CI: 0.90–2.40, $P = .123$). Compared with their study, we conducted subgroup analysis, which showed a very positive correlation between IBS patients diagnosed in Rome III and *H pylori* infection and there was a negative correlation with *H pylori* infection in patients with IBS on the non-Roman III diagnostic criteria, the difference between the two groups was statistically significant ($P = .03$). We speculated that the differences in diagnostic criteria might result in unavoidable bias and the results of the questionnaire would cause a certain degree of error due to the different subjective consciousness of the respondents, so a unified and strict diagnostic criterion was very important. Moreover, a study reported that *H pylori* infection is prevalent worldwide, with higher rates in Asia and Africa than in Europe and North America[41] and our subgroup analysis supported this conclusion that there might be a more significant association between IBS patients and *H pylori* infection in Asian population than in European and American populations. According to the data mentioned, the infection rate of *H pylori* varies significantly among IBS patients in different regions and races, we looked forward to larger clinical trials in the future to verify the statistical significance of this difference, so that more targeted treatment regimens based on the differences could be developed.

Meanwhile, there are several limitations in this meta-analysis that should be acknowledged. First, our analysis includes studies that used IgG serological antibodies as the diagnostic method for *H pylori*. Given the high sensitivity and low specificity of serological tests, our results may include false positives. Moreover, several different methods of evaluating microbiology were used in the included studies, and differences in the specificity and sensitivity of these methods would have different degrees of influence on the experimental results. Second, some of the IBS patients in the studies may have been treated with *H pylori* eradication before testing for *H pylori,* which leads to a decline in the infection rate of *H pylori*. Third, we included the studies from 6 different countries, most of which were in Asia and changes in geography and population may affect the prevalence of *H pylori* detected. However, all eight included studies included control groups of healthy people corresponding to patients in terms of gender, age and region, which greatly reduce the effect of selection bias on the final results.

In conclusion, our study suggested that *H pylori* might have a positive effect on the development of IBS. Although the differences were not statistically significant, there were important differences among different patient subgroups. Therefore, further clinical studies are needed to study the effect of *H pylori* on the development of IBS. Since environmental hygiene and intestinal microbiome may be strong confounding factors, further studies on the mechanism of *H pylori* mouse model are also necessary to further determine the mechanism of this positive correlation. If *H pylori* is found to be a risk factor for IBS, it could have a profound impact on how *H pylori* is detected and treated, as well as how IBS is treated.

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Author contributions

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References

[1] JR M. A symptom-based approach to making a positive diagnosis of irritable bowel syndrome with constipation. Int J Clin Pract 2006;60:57–63.
[2] Surdea-Blaga T, Băban A, DL D. Psychosocial determinants of irritable bowel syndrome. World J Gastroenterol 2012;18:616–26.
[3] Chang FY, CL L. Irritable bowel syndrome in the 21st century: perspectives from Asia or South-east Asia. J Gastroenterol Hepatol 2007;22:4–12.
[4] Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. Gastroenterology 2006;130:1480–91.
[5] Müller-Lissner SA, Bollani S, Brummer RJ, et al. Epidemiological aspects of irritable bowel syndrome in Europe and North America. Digestion 2001;64:200–4.
[6] El-Salhy M, Gundersen D, Gilja OH, et al. Is irritable bowel syndrome an organic disorder? World J Gastroenterol 2014;20:384–400.
[7] Mertz H, Morgan V, Tanner G, et al. Regional cerebral activation in irritable bowel syndrome and control subjects with painful and nonpainful rectal distention. Gastroenterology 2000;118:842–8.
[8] Sloots CE, F-B RJ. Rectal sensorimotor characteristics in female patients with idiopathic constipation with or without paradoxical sphincter contraction. Neurogastroenterol Motil 2003;15:187–93.
[9] Kassinen A, Krogius-Kurikka L, Mäkivuokko H, et al. The fecal microbiota of irritable bowel syndrome patients differs significantly from that of healthy subjects. Gastroenterology 2007;133:24–33.
[10] Attaluri A, Jackson M, Valestin J, et al. Methanogenic flora is associated with altered colonic transit but not stool characteristics in constipation without IBS. Am J Gastroenterol 2010;105:1407–11.
[11] Ford AC, T NJ. Mucosal inflammation as a potential etiological factor in irritable bowel syndrome: a systematic review. J Gastroenterol 2011;46:421–31.
[12] Macsharry J, O'Mahony L, Fanning A, et al. Mucosal cytokine imbalance in irritable bowel syndrome. Scand J Gastroenterol 2008;43:1467–76.
[13] Piche T, Saint-Paul MC, Dainese R, et al. Mast cells and cellularity of the colonic mucosa correlated with fatigue and depression in irritable bowel syndrome. Gut 2008;57:468–73.
[14] Törnblom H, Lindberg G, Nyberg B, et al. Full-thickness biopsy of the jejunum reveals inflammation and enteric neuropathy in irritable bowel syndrome. Gastroenterology 2002;123:1972–9.
[15] Hussain Z, Q EM. Systematic review: Complementary and alternative medicine in the irritable bowel syndrome. Aliment Pharmacol Ther 2006;23:465–71.
[16] Jarcho JM, Chang L, Berman M, et al. Neural and psychological predictors of treatment response in irritable bowel syndrome patients with a 5-HT3 receptor antagonist: a pilot study. Aliment Pharmacol Ther 2008;28:344–52.
[17] J R. Treatment of irritable bowel syndrome in primary care. BMJ 2008;337:a2213.
[18] Ford AC, Talley NJ, Spiegel BM, et al. Effect of fibre, antispasmodics, and peppermint oil in the treatment of irritable bowel syndrome: systematic review and meta-analysis. BMJ 2008.
[19] He H, Li D. Helicobacter pylori infection and irritable bowel syndrome. Chin J Gastroenterol 2009;14:429–31.
[20] Su YC, Wang WM, Wang SY, et al. The association between Helicobacter pylori infection and functional dyspepsia in patients with irritable bowel syndrome. Am J Gastroenterol 2000;95:1900–5.
[21] Yakoob J, Abbas Z, Naz S, et al. Virulence markers of Helicobacter pylori in patients with diarrhoea-dominant irritable bowel syndrome. Br J Biomed Sci 2012;69:6–10.
[22] H H. Relationship between irritable bowel syndrome and helicobacter pylori infection. J Pract Med 2010;26:990–1.
[23] Yang Y, C LF. Role of helicobacter pylori eradication in diarrhea-type irritable bowel syndrome. Chin J Gastroenterol 2017;22:482–5.
[24] Locke CR3rd, Talley NJ, Nelson DK, et al. Helicobacter pylori and dyspepsia: a population-based study of the organism and host. Am J Gastroenterol 2000;95:1906–13.
[25] Agréus L, Engstrand L, Svärdsudd K, et al. Helicobacter pylori seropositivity among Swedish adults with and without abdominal symptoms. A population-based epidemiologic study. Scand J Gastroenterol 1995;30:752–7.
[26] Sýkora J, Huml M, Siala K, et al. Paediatric Rome III criteria-related abdominal pain is associated with helicobacter pylori and not with calprotectin. J Pediatr Gastroenterol Nutr 2016;63:417–22.
[27] Hasan AS, Jaafer AM, A AM. Rate of helicobater pylori infection among patients with irritable bowel syndrome. Gulf Med J 2017;6:16–21.
[28] Kawamura A, Adachi K, Takashima T, et al. Prevalence of irritable bowel syndrome and its relationship with Helicobacter pylori infection in a Japanese population. Am J Gastroenterol 2001;96:1946.
[29] Wells GA, Shea B, D OC (2014) The Newcastle-Ottawa Scale (NOS) for Assessing The Quality of Nonrandomised Studies in Meta-analyses.
[30] Higgins JP, T SG. Quantifying heterogeneity in meta-analysis. Stat Med 2002;21:1539–58.
[31] Deeks JJ, Altman DG, B MJ. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. Hoboken: Wiley-Blackwel; 2008. p.285–312.
[32] J. H (2011) Cochrane handbook for systematic reviews of interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration www.cochrane-handbook.org.
[33] Duval S, T R. Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56:455–63.
[34] Rothstein HR, Sutton AJ, B M. Publication bias in meta analysis: prevention, assessment and adjustments. Psychometrika 2007;72:269.
[35] Talley NJ, Phillips SF, Melton J3rd, et al. A patient questionnaire to identify bowel disease. Ann Intern Med 1989;111:671–4.
[36] Talley NJ1 PS, Wiltgen CM, Zinsmeister AR, et al. Assessment of functional gastrointestinal disease: the bowel disease questionnaire. Mayo Clin Proc 1990;65:1456–79.
[37] Zhao Y, Zou D, Wang R, et al. Dyspepsia and irritable bowel syndrome in China: a population-based endoscopy study of prevalence and impact. Aliment Pharmacol Ther 2010;32:562–72.
[38] Ford AC, Forman D, Bailey AG, et al. Irritable bowel syndrome: a 10-yr natural history of symptoms and factors that influence consultation behavior. Am J Gastroenterol 2008;103:1229–39.
[39] Malinen E, Rinttilä T, Kajander K, et al. Analysis of the fecal microbiota of irritable bowel syndrome patients and healthy controls with real-time PCR. Am J Gastroenterol 2005;100:373–82.
[40] Ng QX, Foo NX, Loke W, et al. Is there an association between Helicobacter pylori infection and irritable bowel syndrome? A meta-analysis. World J Gastroenterol 2019;25:5702–10.
[41] G MF. Review article: natural history and epidemiology of Helicobacter pylori infection. Aliment Pharmacol Ther 2002;16(Suppl 1):3–15.