



Letter

# What is the Relationship between *Helicobacter pylori* Infection and Gastroesophageal Reflux Disease (GERD)? A Comprehensive Analysis on Iranian Population

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Received: 11 Jan. 2021 Accepted: 13 Apr. 2021 ePublished: 29 June 2021

## Dear Editor,

*Helicobacter pylori* is a gram-negative, microaerophilic, and rod-shaped bacterium, which is colonized in human gastric-submucosa of approximately 4-4.5 billion people throughout the worldwide (1-2). The bacterium can cause chronic gastritis and increase the risk of developing gastric adenocarcinoma by 10 times, as well as peptic ulcer disease (3). According to the literature, *H. pylori* infection has clinical benefits in prevention of several diseases such as autoimmune diseases, asthma, celiac, and irritable bowel syndrome (4-7). There are several conflicting reports on the probable association between *H. pylori* infection and gastroesophageal reflux disease (GERD) (8-9).

GERD is a digestive complication in which acidic stomach juices revert up from the stomach into the esophagus and acidic pH causes tissue damages (10). The prevalence of GERD was lower in countries with high burden of *H. pylori* infection. *H. pylori* infection has a protective role in regression of GERD, though the main mechanism is still unclear (11,12). For the first time, we evaluated the impact of *H. pylori* infection in risk of GERD in an Iranian population with comprehensive statistical analysis.

We performed a systematic literature search using search terms including '*H. pylori*', '*Helicobacter pylori*', 'Gastroesophageal reflux diseases', 'Reflux oesophagitis', and 'Iran' in several international databases including Medline, Scopus, Embase, and Google Scholar and retrieved all the related articles. Then, the title, abstract, and full-text of relevant reports were screened, and all case-control studies on an Iranian population were included in the study. The required data such as first author, publication year, city, age, gender distribution, number of case and control in each individual studies, frequency of *H. pylori* infection in each groups, diagnostic methods, and reference numbers were extracted and summarized in the Table 1.

We pooled the data to investigate the probable

association between *H. pylori* infection and GERD by odds ratio (OR) corresponding to 95% confidence intervals (CIs). Furthermore, the association between *cagA* positive *H. pylori* strains and GERD risk was also measured in the current analysis. Heterogeneity was dignified by  $I^2$  index and Cochrane  $P$  value test; the random-effects models were applied for the case of significant heterogeneity. Otherwise, the fixed-effects models were used in lack of heterogeneity cases. Moreover, the publication bias was also determined by Begg's and Egger's  $P$  value test (23).

In the current quantitative analysis, we collected 107 relevant articles in the primary literature search. After reviewing the full-texts, 10 case-control studies were included. These studies were performed between 2003 and 2017 in various cities including Tehran (n=6), Tabriz (n=1), Babol (n=1), Urmia (n=1), and Rafsanjan (n=1). In the eligible studies, we pooled the data of 2,768 human subjects. There were 1,403 cases (mean age: 41.4 years, female: 37.2%, male: 62.8% ) and 1,365 controls (mean age: 40.1 years, female: 39.9%, male: 60.1%). The *H. pylori* infection rate was 38.6% in cases and 49% in healthy subjects. In these studies, the *H. pylori* infection was diagnosed based on the conventional microbiology methods, urease breath test, and ELISA. Our results indicated a significant inverse association between *H. pylori* infection and GERD in an Iranian case (OR: 0.6; 95% CI: 0.50-0.71;  $P=0.001$ ;  $I^2: 81.93$ ; Q-Value: 49.82;  $P=0.001$ ; Egger's  $P=0.69$ ; Begg's  $P=0.72$ ). Interestingly, infection with *cagA* expressing *H. pylori* strains can reduced the risk of susceptibility to GERD in the patients by 0.5 fold (OR: 0.54; 95% CI: 0.34-0.86;  $P=0.009$ ;  $I^2: 78.2$ ; Q-Value: 9.1;  $P=0.01$ ; Egger's  $P=0.53$ ; Begg's  $P=0.5$ ). Therefore, the summary OR showed that *H. pylori* infection can have an inverse association with developing GERD in an Iranian population (Figure 1).

The GERD is one of the common gastrointestinal disorders worldwide. It has been estimated that

**Table 1.** Characteristics of included studies

First author	Year of Publication	Area	Age (y)		Gender (F/M)		Case (n)	Control (n)	No. of <i>H. pylori</i> Infection		Diagnostic method	Ref.
			Case	Control	Case	Control			Case	Control		
Zali	2003	Tehran	49	49	NA	NA	51	51	23	22	UBT	13
Siadati	2014	Babol	49	43	244/330	191/155	574	346	189	110	Culture	14
Abdollahi	2011	Tehran	5.3	4.8	29/30	105/99	59	204	13	70	UBT	15
Somi	2008	Tabriz	43.1	42.7	45/47	47/46	92	93	75	81	UBT	16
Khoshbaten	2013	Tehran	45.7	47.2	40/70	40/70	55	55	25	32	Culture	17
Shavaliipour	2017	Tehran	45.7	41.2	29/21	27/23	50	50	27	31	Culture	18
Nobakht	2016	Tehran	58.3	58.3	NA	NA	367	367	102	216	Culture	19
Rasmi	2009	Urmia	26.4	25.9	38/47	45/24	85	69	60	56	ELISA	20
Mirzaei	2007	Rafsanjan	37.4	37.6	14/15	41/40	19	81	3	31	UBT	21
Masjedizadeh	2006	Tehran	54.1	52.2	20/31	29/20	51	49	45	38	UBT	22

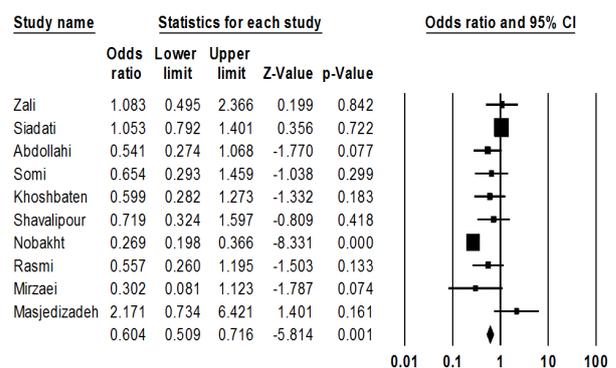
approximately more than 40% of people have experienced GERD in their lives (24). In recent years, the impact of the *H. pylori* infection in GERD has gain attention. However, there are conflicting results about the association between the bacterium and GERD (25,26). Therefore, it is necessary to conduct a larger experiment to determine the effect of *H. pylori* infection in GERD immune-pathogenesis. In the current report, we pooled all available data regarding the evaluation of *H. pylori* in GERD in an Iranian population. The results suggested that *H. pylori* infection particularly *cagA* positive strain can hamper the risk of developing GERD in an Iranian population. Our results confirmed the findings of a meta-analysis by Cremonini et al, indicating a significant association between the absence of *H. pylori* infection and GERD symptoms (27). Overall, it can be considered that *H. pylori* infection has an inverse association with developing GERD symptoms.

#### Conflict of Interests

None.

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**Figure 1.** The Odds Ratio at 95% Confidence Interval for the Assessment of Association between *H. Pylori* Infection and GERD in an Iranian Population .

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