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Review Article

The Effect of *Helicobacter pylori* Infection on Overweight: A Systematic Review and Meta-Analysis

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Abstract

Background: The association between *Helicobacter pylori* infection and overweight, as one of the most common health issues, remains controversial. In this study, we systematically reviewed the effect of *H. pylori* infection and overweight to get a reliable answer.

Methods: We used the Preferred Reporting Items for the Systematic Review and Meta-Analysis statement. We searched the association between *H. pylori* and overweight infection in international databases including Medline, Web of knowledge and Scopus, without any limitations of language, publication type, and publication status in search step of this systematic review from 2000 to 2020. We surveyed the title, abstract and full text of each research studies, and we used Newcastle-Ottawa quality for assessing the quality of each paper. A random effects model was used to calculate the pooled odd ratio with 95% confidence intervals.

Results: Fifteen papers were eligible for this review. The selected studies reported different Odd Ratio between overweight and *H. pylori* infection but Odds Ratio (95% confidence interval) in our systematic and meta-analysis study was estimated at 1.42 (95%CI; 1.12, 1.81) and it was statistically significant (*P*: 0.003).

Conclusion: *H. pylori* infection is significantly associated with overweight, therefore, the eradication of *H. pylori* infection is suggested because this infectious might be resulted in overweight.

Keywords: *Helicobacter* pylori; Overweight; Meta-analysis

Introduction

Overweight is one of the major health concerns. About two billion adults have overweight and 609 million adults are obese, approximately 39% of the world's adult population. The prevalence of obesity increased from 1975 to 2016 worldwide (1). Excessive caloric intake and decreased physical activity and totally industrialized life are the main reasons for the increasing prevalence of obesity (2).

Raised Body Mass Index (BMI) is a major risk factor for a number of diseases, including diabetes, cardiovascular diseases, musculoskeletal disorders and some cancers, such as endometrial, breast, ovarian, prostate, liver, gallbladder, kidney, and colon cancer (3) and also childhood asthma (4). Overall, obesity is responsible for significant morbidity and health care expenditure (5). Moreover, obesity is related to diabetes melli-

tus and hypertension (6). Recently researchers suggested a likely association between *Helicobacter pylori* and overweight. Because the results of the studies are inconsistent, therefore, the association remains still unclear.

Besides, *H. pylori* infection is one of the most important bacterial infections that could infect about half of the world population (7). Infection with this bacterium has been found to be associated with gastrointestinal disorders such as gastritis, non-ulcer disease, peptic ulcer disease, duodenal ulcer and gastric adenocarcinoma (8). A significant association was observed in *H. pylori* infection and other non-gastric diseases such as type 2 diabetes mellitus and insulin resistance (9, 10).

Specifically, high prevalence of *H. pylori* infection (88%) was reported among morbidly obese patients who underwent upper endoscopy prior to bariatric surgery (11). The prevalence of *H. pylori* infection was 57.2% among obese adults and 27.0% among non-obese adults (12). In spite of the information mentioned, in Taiwan, *H. pylori* prevalence among 414 morbidly obese and 683 control patients were 43.7% and 60.0%, respectively. There is an inverse relationship between *H. pylori* infection and overweight. *H. pylori* infection could down-regulate the obesity (13).

The association between *H. pylori* infection and overweight remains unclear and controversial. An ecological study reported an inverse correlation between *H. pylori* prevalence and the rate of overweight/obesity in developed countries of the world (14). In contrast, eradication of *H. pylori* was associated with significant weight gain as compared to untreated *H. pylori* patients (15). Another study has reported a linear relationship between *H. pylori* prevalence and obesity in developing countries (16). In another study, significantly successful eradication of *H. pylori* infection was observed in 55.0% of the overweight/obese patients and 85.4% in normal adult (17). While in a study, overweight/obese non-diabetic patients found a significantly lower rate of *H. pylori* eradication than control group (18). Therefore, overweight may be independent risk factors for *H. pylori* eradication failure (17).

Due to the conflicting results of the literature about the *H. pylori* infection and overweight, we performed this systematic and meta-analysis study to find out the effect of *H. pylori* infection on overweight.

Methods

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (19) statement in this study.

The present study was approved by the Ethics Committee of Hamadan University of Medical Sciences, Hamadan, Iran. The protocol of this study has been registered for Hamadan University of Medical Science (No. 9712077464).

Search method

For this purpose, we searched the international databases such as Medline, Web of knowledge, Scopus, and Science Direct from 2000 to 2020. We used the MeSH keywords such as *H. pylori,* Overweight, Obesity, and Body Mass Index.

There are several overweight definitions according to the WHO Expert Consultation for Asians, European and American countries. Therefore, overweight patients were defined based on BMI≥25 and the comparison group with BMI<24.9 as control group to cover the most countries that included in this study (20). The outcome of interest was the relationship between *H. pylori* and overweight. Therefore, we used the related references of the papers to do a perfect search.

There were no limitations of language, date, publication type, and publication status in search step of this systematic review. Of course, some of the studies were excluded: any research had not enough information or were not consistent with our definitions or repetitive or have not a control group. The articles were searched until three months before meta-analysis.

Paper selection

First, we reviewed the title, abstract of the papers. Based on definitions explained in previous section, we selected studies investigated the associa-

tion of *H. pylori* infection with overweight in all populations, regardless of age, sex, and race. After that, we used the Newcastle-Ottawa statement (NOS) (21) for assessing the quality of each study.

Data collection

The required data including the name of the first author, publication year, country, subjects source, sample size, mean age (year), *H. pylori* detected methods and Odds Ratio (OR) entered into a pre-designed excel file. The data of relevant papers were extracted.

Statistical analysis

Weighting averaging was used to combine odds ratio reported by different studies. Each study was given a weight equal to its inverse variance. Q and I^2 tests were used for the evaluation of heterogeneity and the analysis was performed with a random-effects model.

Results

The article selection process in this study demonstrated in Fig. 1. Overall, 1987 papers were retrieved by related keywords. Out of these, 449 articles were published in Medline, 850 articles were published in Scopus, and 688 articles were published in Web of knowledge and finally among these articles, 15 studies were eligible for the review. The forest plot of the selected articles demonstrated in Fig. 2 and the funnels plot was given for the Meta-analyses in Fig. 3.

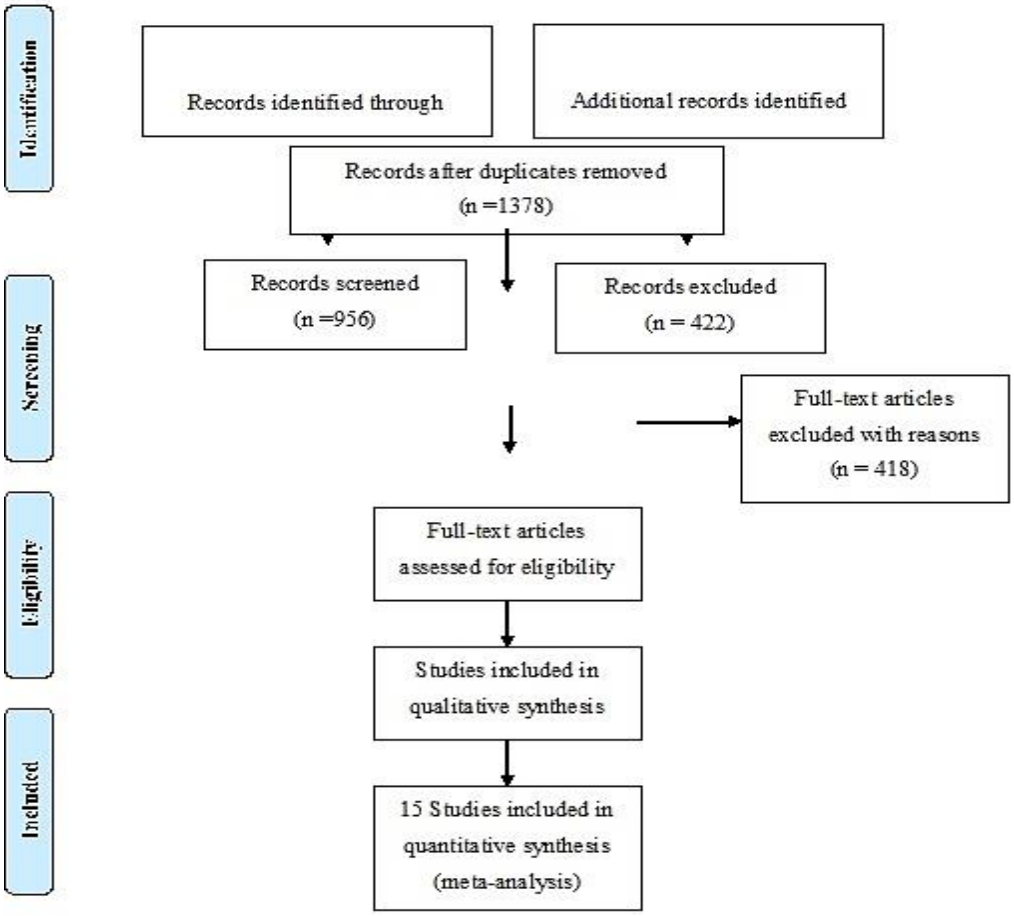

Fig. 1: Flow diagram of the articles selection process

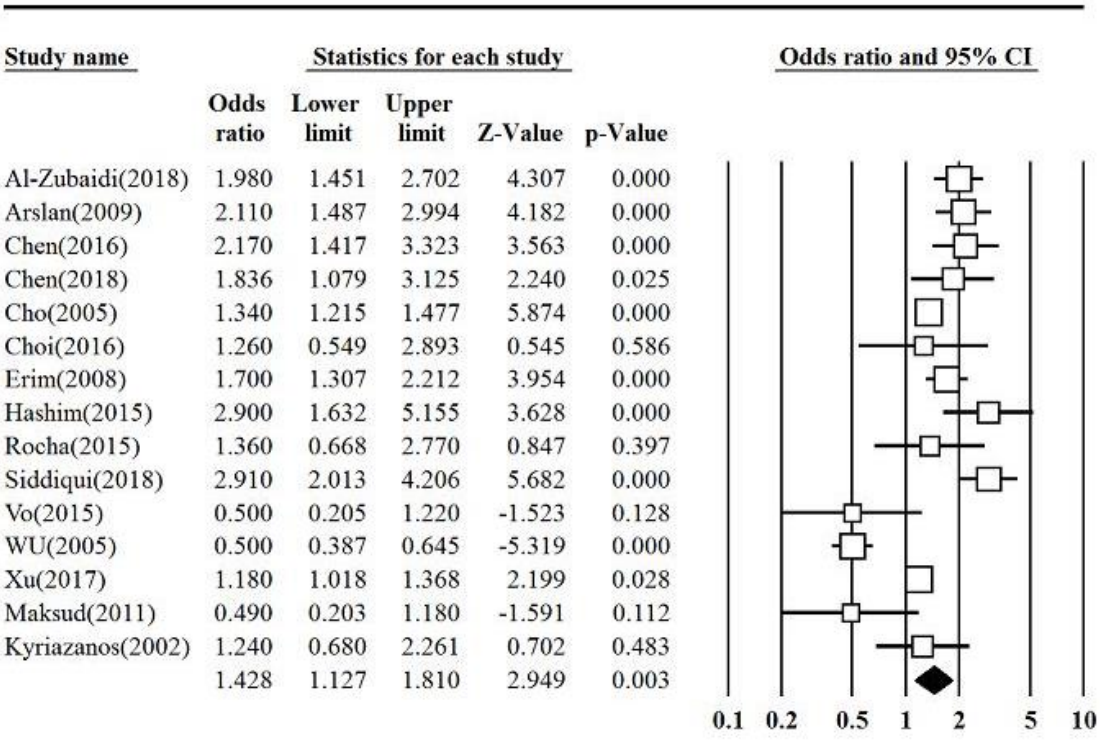

Fig. 2: Forest plot of the selected articles

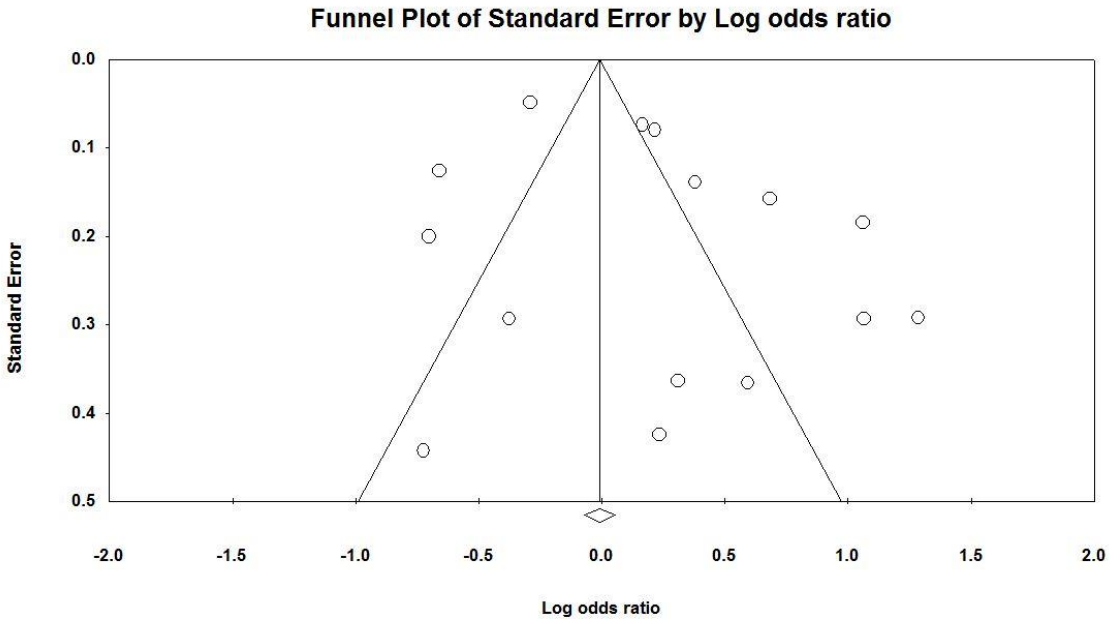

Fig. 3: Funnel plot of the selected articles

All of the studies were carried out on both sexes and adults were the most dominant population of the studies. The serological methods that detect antibodies in serum or antigens in stool samples were the most common *H. pylori* diagnostic method among the selected articles (Table 1).

In addition, the selected articles were conducted in different geographical regions, in European, Asian and American countries and also among the developed and developing communities (Table 1).

Seven of the selected articles reported that the obesity can be a risk factor for *H. pylori* infection, because obese patients significantly had more *H. pylori* infection than non-obese patients. Whereas, eight of the selected articles had a lower risk in different ethnic population and reported that overweight is a protective factor for *H. pylori* infection (Table 1).

However, the selected studies reported different Odd Ratio ranged from 0.5 (22) to 2.91 (23), the pooled odds Ratio retrieved of these studies was 1.42 (95% CI; 1.12 to 1.81), that it is statistically significant (*P*=0.003).

Table 1: Characteristics and the quality score of the included studies

Publication year	***Nation***	***Subjects source***	***Sample size***	***Mean age (yaer)***	*H. pylori* ***test***	***BMI (kg/m²)***	***Association (OR)***	***NOS****	***Reference***
2018	Saudi Arabia	General	680	31.22 ± 8.10	Histology	≥30	Yes (1.98)	10	[23]
2018	Pakistan	General	662	44 ± 16	Histology	>23	Yes (2.91)	9	[28]
2018	Taiwan	General	2604	58.7± 13.2	UBT*1	≥24	Yes (1.836)	10	[24]
2017	China	General	2977	49 ± 19	Serology	≥24	No (1.18)	9	[31]
2016	Taiwan	BE*2	736	53.8±13.7	RUT*3	≥27	No (2.17)	9	[35]
2016	Korea	Child	164	9.89±3.28	Serology	*4	Yes (1.26)	8	[25]
2015	Bahrain	General	200	38.6±11.06	RUT*3	>25	Yes (2.9)	9	[27]
2015	Brazil	General	137	39.7 ± 12.0	Histology	≥25	No (1.36)	9	[33]
2015	USA	Child	319	10.5 ± 4.7	SAT*5	*6	No (2.0)	8	[32]
2011	Brazil	BP*7	100	35.4	Histology	≥25	No (0.49)	8	[30]
2009	Turkey	General	214	24.3±5.4	Serology	≥30	Yes (2.11)	8	[12]
2008	Ohio	BP*7	2684	44 ± 13	Serology	>30	Yes (1.7)	9	[26]
2005	USA	General	7003	45.2±0.45	Serology	≥25	No (1.34)	9	[34]
2005	Taiwan	General	1097	31.9 ± 9.2	Serology	≥25	No (0.5)	8	[13]
2002	Salamis	General	122	22.4 ± 2.4	Serology	≥25	No (1.24)	8	[29]

***** Newcastle-Ottawa quality assessment scale
*****1 Urea Breath Test
*2 Barrett's esophagus
*****3 Rapid Urea Test
*****4 Body weight ≥90th percentile
*5 Stool Antigen Test
*6 Body weight ≥85th percentile
*7 Bariatric patient

Discussion

The association between *H. pylori* infection and overweight was mentioned from a decade ago (24). We retrieved the inconsistent studies (23, 31), both with and without adjustment for confounding factors (such as age and gender), we concluded that Odd Ratio (95% CI) is 1.42 that it

is statistically significant (*P*: 0.003) and *H. pylori* infection might be resulted in overweight.

However, the epidemiological studies (23, 24, 28) showed an association between *H. pylori* infection and overweight, but the mechanisms of *H. pylori* infection and overweight were not invariably defined. *H. pylori* infection affects the gastric cells that lead to gastric secretion.

H. pylori infection induces an inflammatory response in many types of gastric cells, especially those responsible for leptin and ghrelin production, that it could affect the regulation of leptin and ghrelin expression. Leptin decreases appetite and food intake, in other words; it is a hormone for regulating energy balance by inhibiting hunger. In obesity, a decreased sensitivity to leptin occurs (similar to insulin resistance in type 2 diabetes), resulting in an inability to detect satiety despite high energy stores and high levels of leptin. Therefore, *H. pylori* infection could lead to overweight by decreasing the sensitivity to the leptin (25).

H. pylori eradication increases the gastric secretion of ghrelin, which leads to increased appetite and weight gain, means that ghrelin stimulates food intake and promotes weight gain. However, the eradication of *H. pylori* decreases gastric leptin expression, and this decrease was accompanied by overweight, but the precise effect of gastric secretion of ghrelin on circulating ghrelin levels is not straightforward (26-28). Meanwhile, eradication of *H. pylori,* resulted in a short-term weight gain that it is related to the eradication and their ulcer healing, so that, thereafter the effect did not last. That way, the decreasing incidence of this infection may be contributing to an increase in appetite and food intake (15).

In total, *H. pylori* infection causes gastritis or peptic ulcer in a likely mechanism that make an influence on immunological cytokines, leptin, and ghrelin production. Since, Gastric *H. pylori* colonization could reduce serum levels of leptin and ghrelin, by inhibiting their gastric production because ghrelin and leptin are present in gastric secretions. Moreover, *H. pylori* colonization may affect their levels in gastric juice. Therefore, *H. pylori* status affects leptin and ghrelin homeostasis, presumably via intra-gastric interactions (29).

Unfortunately, *H. pylori* was associated with metabolic disturbances. *H. pylori* infection also ameliorates glucose homeostasis that leads to overweight. Eradication of *H. pylori* could improve carbohydrate metabolism possibly in relation to an increase in GLP-1 (Glucagon-like peptide-1) secretion. GLP-1 secretion may be related to alterations in intestinal microbiota, specifically *Lachnobacterium* genus, *Bifidobacterium adolescentis* and *Coriobacteriaceae* family (30).

Knowledge more about *H. pylori* infection could help us to inhibit infection (31-37). Obesity, by itself, is a cause of several diseases. The data in our study may be influencing the *H. pylori* infection eradication and obesity control and lifestyle strategy.

The results of the selected papers were different, because they were performed in various geographical areas and have different diagnosis methods and also different sample sizes. Due to the importance of dietary habits, especially in developing countries, the conclusion reported in this paper could be affected. However, we performed this retrospective study to explore the effect of *H. pylori* infection on overweight, but, we could not distinguished that the infection influences the overweight or vice versa and the exact mechanism that influence this process. They are the limitations of our study researched in the future.

Conclusion

The purpose of our research was to provide a plan to permit accurate assessment of the effect of *H. pylori* infection on overweight. *H. pylori* infection is associated with overweight and these data could be considered in the development of *H. pylori* eradication and overweight control strategies.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or

falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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