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Meta-analysis of the Prevalence of *Helicobacter Pylori* Infection among Children and Adults of Iran

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ABSTRACT

Helicobacter pylori infection is a common health problem related to many gastrointestinal disorders. This study aims to estimate the total and age specific prevalence of *Helicobacter Pylori* infection in Iran. We systematically reviewed all national and international databases and finally identified 21 studies were eligible for meta-analysis. Each of them were assigned a quality score using STROBE checklist. Due to significant heterogeneity of the results, random effects model was used to estimate the pooled prevalence and 95% confidence interval of *Helicobacter Pylori* infection. All statistical analyses were performed using STATA. V11 software. The pooled prevalence (95% confidence interval) of *Helicobacter Pylori* infection among all population, children and adults were estimated as 54% (53%- 55%), 42% (41%- 44%) and 62% (61%- 64%) respectively. *Helicobacter Pylori*, has infected more than half of Iranian people during the last decade. Preventive strategies as well as taking into account this infection during clinical visits should be emphasized to reduce its transmission and prevalence within the community.

Keywords: *Helicobacter*, Iran, meta-analysis, prevalence

INTRODUCTION

Helicobacter pylori infection is one of the most important bacterial infections involved about 50% of the population worldwide.[1] Infection with this bacterium has been proved to be associated with peptic ulcer disease, gastric adenocarcinoma, metabolic syndrome, chronic gastritis, and other gastrointestinal disorders.[1,2]

This infection is more common in developing countries compare to developed communities. Different studies have been conducted in many countries, reported the prevalence of *H. pylori* infection from <20% in European countries[3] to more than 80% in some Eastern Mediterranean countries.[1] Such variations in the estimated prevalence rates were also observed in the studies carried out in Iran.[1,2]

Different parts of Iran have different prevalence rates of *H. pylori* infection.[4-18] To implement national strategies for control or eradication of this infection, it is necessary to have a pooled estimate of *H. pylori* infection within the whole country. Meta-analysis is a complex of statistical methods used to combine the results of primary studies. This summarization of the results can increase the

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accuracy and power of the study because the estimation was performed in a larger sample size.[19-20]

Some systematic review/meta-analyses were carried out in Iran to estimate the overall prevalence of *H. pylori* infection. These meta-analyses used primary studies with different sampling methods such as random, symptomatic individuals and patients as well as health staffs. In the current study, we aimed to estimate the pooled prevalence of *H. pylori* infection combining only the results of the studies used representative samples of populations. We also entered more recent studies and adjusted the results according to their quality to decrease the potential biases.

METHODS

Search strategy

This study was a systematic review and meta-analysis of the *H. pylori* infection prevalence in Iran. All data was collected from the studies estimated this prevalence among general population selecting random sampling methods. We systematically searched all national (Magiran, SID, IranMedex, Medlib) and International (Google Scholar, PubMed, Scopus, Science Direct) databases. To prevent potential biases, searching databases as well as data extraction were carried out by two independent researchers (Afshari, Moosazadeh). Search strategy was performed using the following keywords or their Farsi equivalents:

"*H. pylori*," "*Helicobacter*," "*Helicobacter pylori*," "general population," "children," "adults," "prevalence," "seroprevalence," "seroepidemiology," "serology," "Iran".

In the first step, titles and abstracts of the primary selected articles were reviewed. Then, we reviewed the full texts of the papers identified during the first step and found more relevant articles. In order to increase the search sensitivity, we investigated references within the papers and found some relevant papers. Finally, we assessed the quality of the final selected papers using STROBE checklist.[21] During this step, all papers were dedicated a quality score from 0 to 22 and entered into the meta-analysis.

Inclusion criteria

All papers identified eligible during the multiple phases of the systematic search estimating the prevalence of *H. pylori* infection among Iranian population.

Excluding criteria

Studies conducted by case–control or experimental design or those conducted among nonrandomly selected populations such as patients, health workers, and endoscopic samples.

Data extraction

All required information such as author name, date of study conduction, total prevalence of *H. pylori* infection, age and gender-specific prevalences, method of diagnosis, study sample size, *P* value indicating the significance of the difference between genders and age groups, and mean age of the participants were extracted by complete review of the eligible articles.

Statistical analysis

The standard error of the prevalence rate in each study was calculated according to the binomial distribution. We used Cochrane Q-test as well as Tau square index to assess the heterogeneity of results. Because of the significant heterogeneity, a random-effect model was applied to combine the prevalence rates. To estimate the difference of prevalences between genders and age groups, *P* value meta-analysis method was used. $P < 0.05$ was considered significant. To investigate the effect of age, gender, diagnostic method, and date of the study, meta-regression models were used. All statistical analyses were performed using STATA version 11 software (Stata Corporation, College Station, TX, USA).

RESULTS

During the first part of the search in national and international databanks, 10,148 articles were found. Limiting the search strategy, 8677 were excluded. Reviewing titles and abstracts, 659 were removed in the next part of our search. During full-text review and having applied the exclusion/inclusion criteria, 13 irrelevant papers were omitted. In the final step, 21 articles including 15,680 participants were entered into the quality assessment and meta-analysis [Figure 1].

The prevalence of *H. pylori* infection varied between 13% (95% confidence interval [CI]: 9–17%) in Birjand[4] and 82% (95% CI: 79–85%) in Shiraz.[5] The least sample size belonged to the study carried out in Golestan[6] with 194 participants; whereas Nouraei[7] recruited 2561 individuals in the study conducted in Tehran in 2005 [Table 1].

As illustrated in Figure 2, the overall *H. pylori* infection rate was estimated as of 54% (95% CI: 53–55%; $Q = 3031$, $P < 0.0001$). Among 15 studies used ELIZA method for *H. pylori* infection diagnosis, the infection rate was estimated as 60% (95% CI: 59–61%; $Q = 2087$, $P < 0.0001$). These studies reported prevalences varied between 26% (95% CI: 24–28%) in Tehran[8] and 79% (95% CI: 74–85%) in Qazvin.[9] While, studies used stool antigen test reported *H. pylori* prevalence rate as 44% (95% CI: 42–46%; $Q = 959$, $P < 0.0001$). The minimum and maximum prevalences among these studies were 13% (95% CI: 9–17%) in the study conducted in Birjand[4] and 82% (95% CI: 79–85%) in Alborzi study.[5]

Among 11 studies investigating the association between *H. pylori* infection rate and age, eight papers found statistically significant associations.[6,7,9-14] Almost all of the studies compared prevalence rates of *H. pylori* between genders, five of which reported significant correlations.[4,8,10,15] Using *P* value meta-analysis method among the results of studies reported *P* values, the pooled *P* value for the association between age and *H. pylori* infection rate was 0.0001, whereas the pooled *P* value for

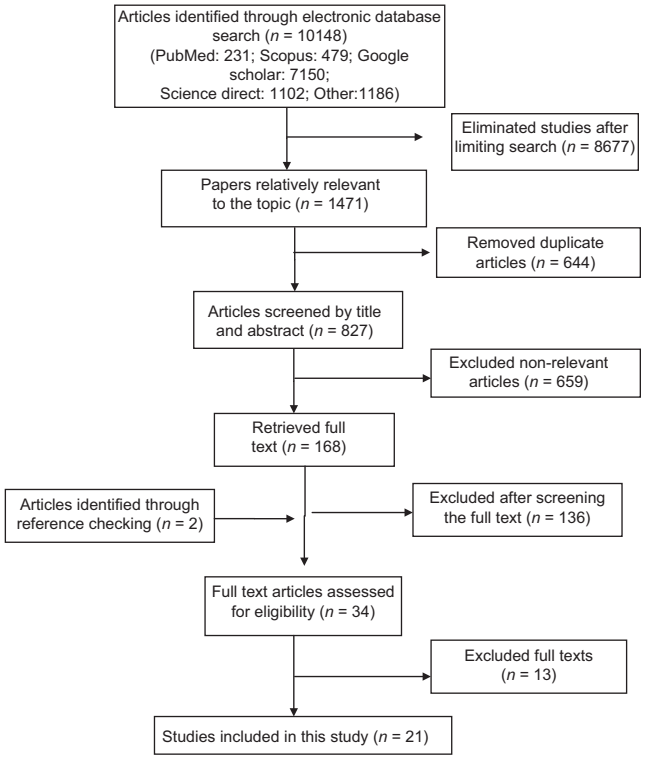

Figure 1: Literature search and review flowchart for selection of primary studies

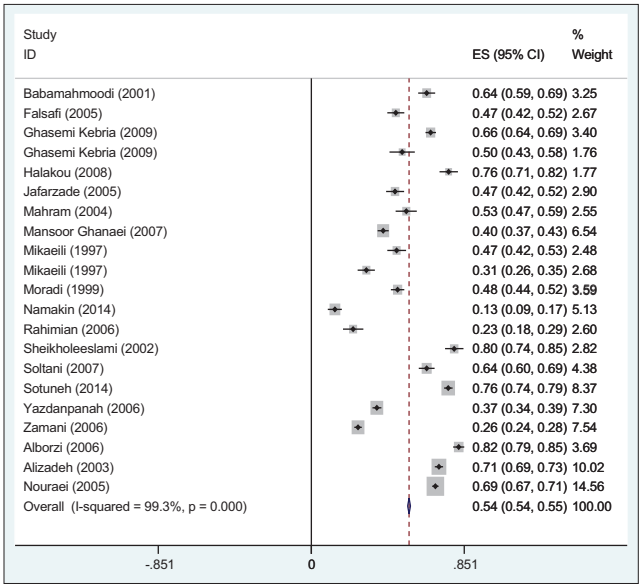

Figure 2: Forest plot for prevalence of *Helicobacter pylori* infection in Iran

Table 1: Characteristics of the studies entered into the final meta-analysis

Diagnostic method	Age groups	First author, Publication year	Prevalence	95% CI	Sample size	Age range	Mean age
Stool antigen test	Children	Mansoor Ghanaei (2009)	0.4	0.37-0.43	961	7-11	8.96
		Namakin (2014)	0.13	0.09-0.17	282	9-12	10.5
		Rahimian (2006)	0.23	0.18-0.29	215	6	6
		Soltani (2007)	0.64	0.60-0.69	458	4 months to 15 years	5.6
	-	Alborzi (2006)	0.82	0.79-0.85	593	9 months to 15 years	6.89
	Not reported	Falsafi (2005)	0.47	0.42-0.52	430	-	-
ELIZA	Children	Ghasemi Kebria (2009)	0.50	0.43-0.57	194	1-15	8.37
		Jafarzade (2005)	0.47	0.42-0.52	386	1-15	8.1
		Mahram (2004)	0.53	0.47-0.59	278	7-9	8
		Zamani (2006)	0.26	0.24-0.28	1665	6-12	9.18
		Alizadeh (2003)	0.71	0.69-0.73	1518	>6 years	36.4
	Adult	Sotuneh (2014)	0.76	0.74-0.78	1300	>60	69.23
		Nouraei (2005)	0.69	0.67-0.71	2561	18-65	35.5
	Mixed	Ghasemi Kebria (2009)	0.66	0.63-0.69	1028	1-83	-
		Halakou (2008)	0.76	0.71-0.81	263	1-80	31.75
		Mikaeili (1997)	0.47	0.42-0.53	358	6-20	-
		Mikaeili (1997)	0.31	0.26-0.35	353	6-20	-
		Moradi (1999)	0.48	0.44-0.52	700	0-70	35
		Sheikholeeslami (2000)	0.79	0.74-0.85	240	10-70	36.25
		Yazdanpanah (2006)	0.36	0.34-0.39	1503	10-100	32.15
	Not reported	Babamahmoodi (2001)	0.64	0.59-0.69	394	-	-
Pooled prevalence			0.54	0.54-0.55	15,680	-	-

CI=Confidence interval

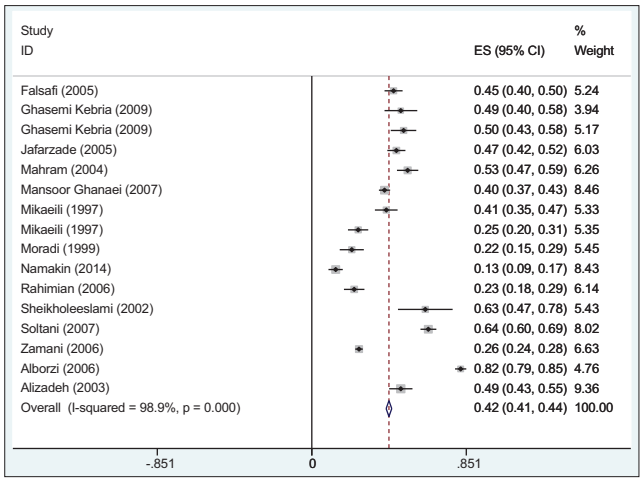

Figure 3: Forest plots indicating the prevalence rates of *Helicobacter pylori* infection among children

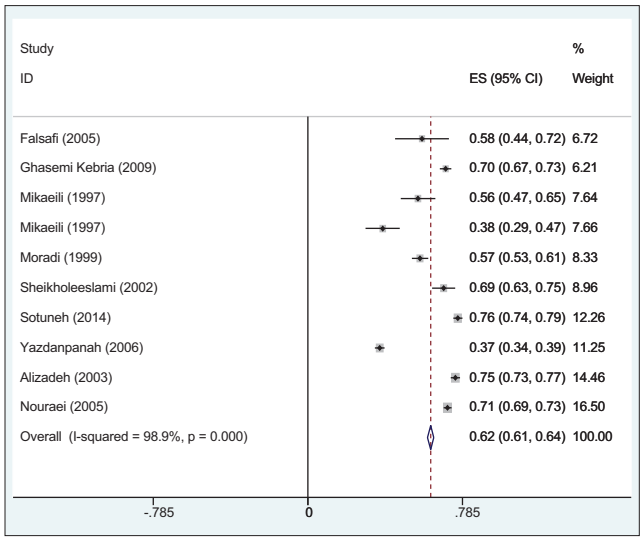

Figure 4: Forest plots indicating the prevalence rates of *Helicobacter pylori* infection among adults

the correlation between gender and *H. pylori* prevalence rate was 0.04.

As shown in Figure 3, among 16 studies assessed the *H. pylori* infection rate among children (under 15), the pooled prevalence of infection was estimated as 42% (95% CI: 41–44%; Q = 1322, $P < 0.0001$). These prevalences were differed from 13% (95% CI: 9–17%) in Namakin study[4] in Birjand (2014) to 64% (95% CI: 60–69%) in the study conducted by Jafar *et al.*[16] in Sanandaj (2007). *H. pylori* infection rate among adults was assessed among 10 studies. Furthermore, based on Figure 4, the overall prevalence of *H. pylori* infection among these groups was estimated as 62% (95% CI: 61–64%; Q = 820, $P < 0.0001$). Kordestan[17] and Amirkola[18] had minimum and maximum prevalences (36%; 95% CI: 34%–39% and 76%; 95% CI: 74–78%, respectively).

Using meta-regression models, the coefficients (*P* values) of the effects of study date, mean age, male percent, and diagnostic method on the heterogeneity were 0.0002 (0.9), 0.006 (0.055), 0.004 (0.6), and −0.1 (0.2), respectively. Adding these variables to the meta-regression model did not change the Tau square index.

DISCUSSION

We found in the current systematic review and meta-analysis that the prevalence of *H. pylori* infection among Iranian population is 54%. We also observed that this prevalence was significantly different according to age and *H. pylori* diagnostic method.

It should be noted that we entered studies randomly selected healthy individuals within the community. Eshraghian[1] in 2014 systematically reviewed the studies estimating the prevalence of *H. pylori* infection among healthy population of Eastern Mediterranean regional office countries. According to this study, the prevalence rate of *H. pylori* infection in eight investigated countries ranged from 22% to 87.6%. Kingdom Saudi Arabia[22,23] and Jordan[24] had similar prevalences to Iran while the infection rates in Libya, Tunisia, UAE, Egypt, and Oman were more than that reported among the Iranian population estimated in the current study.[1] Among the studies investigated the *H. pylori* infection rate outside the region, Japan,[25] England,[3] and Madagascar[26] had lower rates of the infection while *H. pylori* was more common in Taiwan[27] and China.[28] It should be noted that studies carried out in England and Madagascar and many other similar studies estimated the infection rate only among children, and such comparisons would be prone to some information biases. In addition, such differences may be due to the influence of factors such as nutritional habits and climates[4] as well as socioeconomic status and ethnic background[15] which are remarkably different in different parts of the world. Moreover, different methods of infection diagnosis applied in the above studies should be considered as a probable explanation for great variabilities in reported prevalences.

A great number of the studies entered in the current meta-analysis showed that *H. pylori* infection is associated with male gender. Similar findings were reported in surveys conducted among Asian South-Eastern countries.[25,28] Moreover, de Marte and Parsonnet in a meta-analysis[29] confirmed that *H. pylori* infection is more common in males than females only among adults. This study indicates that the mentioned predominance cannot be observed among children because different exposure to antibiotics as well as different immunity between males and females in these two age groups. It seems that the male predominance indicates more exposure of males to infection and also their long-term

clinical outcomes.[15] However, such association was not observed among Taiwanese.[27] Among studies carried out in Eastern Mediterranean countries, only Al-Balushi *et al*.[30] and Al Faleh *et al*.[22] assessed the relationship between gender and *H. pylori* infection. The latter study conducted among 16–18 years old individuals living in KSA, introduced female gender as a risk factor for *H. pylori* infection.

The association between age and *H. pylori* infection has been proven in the studies performed in Egypt,[31] KSA,[23,32] Oman,[30] Japan,[25] China,[28] Madagascar,[26] and the USA.[33] That was in keeping with those observed in our systematic review and meta-analysis. It should be explained by the long duration of exposure to *H. pylori* in the higher ages compared to children. It is also important to note that all of these studies have reported the infection prevalence diagnosed by two methods (ELIZA and stool antigen). The latter method had been applied only among children. However, we should consider the probable differences in the accuracy of these two diagnostic tests and report the different results between children and adults with cautious.

Many studies investigating the *H. pylori* prevalence estimated prevalence only in specific populations such as patients or candidates for endoscopy. While many similar studies assessed the *H. pylori* infection among patients or special subgroups or at last symptomatic individuals referring to health and medical centers, such participants were not a representative sample for the whole population, and the estimates could not be exactly generalized to the reference study area.

Initial reports of *H. pylori* infection from Iran indicated a high prevalence of more than 85%.[34] Our study indicates that the prevalence has decreased to near 50%. This is in concordance with better sanitation and improved infrastructures in the country and subsequent decrease in infectious diseases. This may have changed the pattern of gastrointestinal diseases in Iran as one can see a decrease in distal gastric cancers and acid peptic disease. This pattern was previously reported with immunoproliferative small intestinal disease which was once the most common cause of malabsorption in at least parts of Iran but now only is reported very rarely. This disease was also linked to gastrointestinal infections.[35,36]

According to the met regression models, each year increase in the study date increased the *H. pylori* infection rate more than 0.002% while this prevalence increased approximately 0.04% and 0.06% per one percent increase in the distribution of male gender as well as 1-year increase in the mean age of the participants, respectively. However, none of these coefficients were statistically significant. Moreover, the between studies variance was not changed after controlling the effects of these factors indicating that none of these factors are associated with heterogeneity among the studies.

One of the most important limitations in our systematic review and meta-analysis was different methods of infection diagnosis. Because of the different sensitivity and specificity of these diagnostic tests, combining the results should be performed with caution, even though this factor appeared to have negligible effect on the heterogeneity of the between-studies results. Larger multicenter studies are needed to provide exact information about *H. pylori* infection prevalence and its related factors within the country.

CONCLUSIONS

Our meta-analysis provided evidences that half of the Iranian population particularly adults and males are infected to *H. pylori*. Persistent monitoring of the situation of the infection, implementation of proper sanitary facilities, as well as improvement in the level of education, especially among adult population could be effective strategies to control this infection.

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Conflicts of interest
There are no conflicts of interest.

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