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Review Article

A Systematic Review and Meta-Analysis Study to Investigate the Prevalence of Helicobacter pylori and the Sensitivity of its Diagnostic Methods in Iran

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Context: Helicobacter pylori is the most common infecting organism affecting humans, being almost half the population infected. The aim of this study was to find out the epidemiological features and the sensitivity of diagnostic methods of Helicobacter pylori infection in Iran, which can provide the logic of developing preventive approaches to control *Helicobacter pylori* infections and the associated diseases. Evidence Acquisition: By reviewing the databases of SID, MAGIRAN, SCOPUS, MEDLIB, Google, ISI and PUBMED, a total of 30 papers, published from 1994 to 2011, were extracted. Summary prevalence and 95% confidence intervals (95% CI) were calculated using randomeffects model. Statistical analyses were performed using STATA Ver.11.

Results: Among the 30 studies evaluated, the prevalence rate of Helicobacter pylori infections in Iran was estimated as 50.7% (95% CI: 44.4-56.9%). When the sensitivity of diagnostic methods was evaluated, ELISA, with an accuracy rate of 52.3% (95% CI: 43.8 to 60.8%) was found the most accurate diagnostic method available. The highest and the least Helicobacter pylori prevalence were 19.2% in Tehran and 74.27% in Mazandran respectively.

Conclusions: About half the population in Iran is infected with Helicobacter pylori, the pollution in different areas and preventive strategies should be carried out to control this infection. The prevalence rate of Helicobacter pylori infections in Iran showed only little changes during the years 1994 to 2011.

Keywords:Helicobacter pylori; Prevalence; Meta-analysis; Iran

1. Context

Almost half the population in the world is infected by H. pylori which is the most common infecting organism affecting humans (1, 2). Since the first experience of Helicobacter culture in 2004 by Marshall and Warren, a considerable amount of information has been acquired on clinical aspects of this infection (3). Helicobacter pylori is tightly associated with gastro-intestinal disorders, some important consequences of which can be chronic gastritis, peptic ulcer leading to gastric cancer, indigestion and non-ulcer dyspepsia (4-9).

In developing countries, the prevalence of H. pylori positive serology during childhood is higher than that in developed countries. This is vice versa during adulthood (10, 11). In a Meta-analysis study, the prevalence of H. pylori infection in China was reported as 58.07% (12). In another Meta-analysis study, the association between H. pylori infection and the risk of esophageal cancer (EAC) has been suggested (13). Also, the association between *H*. pylori infection in diabetic and non-diabetic individuals with dyspepsia was assessed. This study showed that the prevalence of H. pylori infection was considerably higher in diabetic patients compared to non-diabetic individuals (P = 0.001). According to these results, diabetes Mellitus is one of the risk factors that need attention in the evaluation of *H. pylori* infections among diabetic patients with dyspepsia (14).

The prevalence of H. pylori infection was 58% among residents of two villages in Northern Italy, considerably higher than the 34% observed in an earlier similar study of adults in northern Swedish communities (mean age = 52 years). A prevalence of 60% or more was reported for groups in Albania, Egypt, Iran, Turkey, and China (15). The prevalence of *H. pylori* infection was 3.0% among index children at age 4 and maternal infection was the only risk factor at multivariate analysis (16).

One of the main objectives of Meta-analysis studies,

Implication for health policy/practice/research/medical education:

This is the first systematic review and meta-analysis on prevalence of H. pylori in Iran that prepared in collaboration with Dr. Raffaele Zarrilli in Italy. In this review, we used nearly all of the papers published in Persian and English languages.

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which are a combination of different studies, is to reduce the difference between parameters as a result of an increase in the number of studies involved in the process of analysis and also to reduce the confidence level of these measures/figures.

The aim of this study was to investigate the studies carried out on the prevalence of *H. pylori* infection in Iran and to estimate the prevalence rate of this infection according to diagnostic methods, age group of individuals infected, gender, infection age and additional parameters.

2. Evidence Acquisition

This study was a systematic review and a Meta-analysis study on the prevalence of Helicobacter in Iran. The findings of this research were based on the papers published in internal and external journals. The papers were selected from the databases of SID, MAGIRAN, SCOPUS, MEDLIB, Google, ISI and PUBMED. Searching of the articles was carried out using the key words: Helicobacter, prevalence, and a combination of these words. To decrease bias two authors (Sayehmiri F, Darvishi Z) did search, selection of papers and extracting data of articles independently. First, all the articles related to Helicobacter pylori in Iran were collected. At this stage, the articles possessing the relevant key words in their title or abstract were entered into the list, excluding all the other articles not relevant to the prevalence of *H*. pylori. A check list of necessary information was prepared that included: title of the article, location of the study, location of sampling, sample volume, the methods of assessing infection, the mean age of individuals infected by H. pylori and the total prevalence of *H. pylori*.

According to the protocol, a total of 142 articles that were carried out from 1994 to 2011 were analyzed during the primary research. The abstracts of 94 articles, out of the 142, were then analyzed and a complete review of 45 of these papers, that included the basic information required, was then carried out. Due to unavailability of the prevalence rates, some articles were omitted and a total of 30 articles were finally entered into the process of analysis (17-46) (Figure 1 the study flowchart).

2.1. Statistical Analysis

The variance of each study was calculated according to the binomial distribution. The studies were combined together according to sample size and variance. Because of the study heterogeneity, random-effect model was used to combine the studies. To assess the heterogeneity of the studies, Cochrane Q test and the I² index were used. P-value of less than 5% was considered as significant in the heterogeneity test. To investigate the relationship between years of study and sample size meta-regression model was used.

Furthermore, considering the type of data analyzed, which were all prevalence rates, there was no need to determine the publication bias and to draw a funnel plot. The data were analyzed using STATA version 11.2.

3. Results

In the 30 papers assessed, the prevalence rate of Helicobacter pylori infection in Iran was estimated as 50.7% (95% CI: 44.4-56.9%) (Figure 2). The lowest prevalence rate (19.2%) was related to a study in Mazandaran province, the city of Sari and the highest prevalence rate (74.27%) were reported in a study in Tehran province, the city of Tehran. Details of the papers analyzed are found in Table 1.

In one classification, analysis was carried out based on the diagnostic methods. The sensitivity level of ELISA, according to this analysis, was estimated as 52.3% (95% CI: 43.8-60.8), the sensitivity of the urease method as 51.9% (95% CI: 36.9-66.9) and other diagnostic methods including touch cytology, histopathology as 45.8% (95% CI: 31.3-60.4). These results show that ELISA and urease are relatively more accurate methods to diagnose *H. pylori* infection (Table 2).

In another classification, the individuals under assay were divided into the two groups of symptomatic and nonsymptomatic individuals. The prevalence rate of infection among individuals with digestive disease symptoms, with a sample size of 1873 individuals, was estimated as 47.6% (95% CI: 56.1-39.2) and among healthy individuals, with a sample size of 7131 individuals, as 53.1% (95% CI: 45.4-60.8). Based on gender, the prevalence rate was estimated as 37.7% (95% CI: 95% CI: 27.5-48) in females and 35.7% (95% CI: 19.6-51.7) in males. In analysis based on the age groups, the prevalence rate among the age group below 20 years was estimated as 38.3% (95% CI: 28.1-48.5), among the age group between 20-40 years as 50.3 % (95% CI: 39.5-61) and among the age group above 40 as 60.1% (95% CI: 52.4-67.8). In this analysis, a significant difference was found among the three age groups which can be evidence to the conclusion that the rate of *H*. pylori infection increases as the age increases (Table 3).

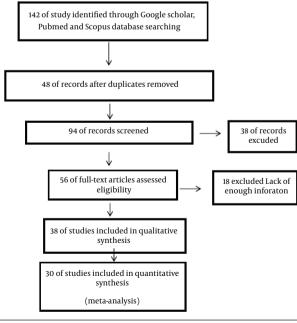
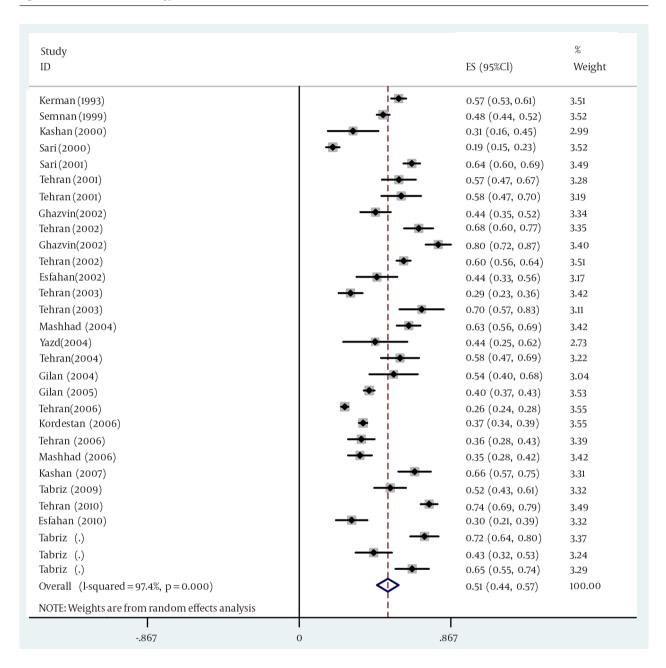


Figure 1. Study Flowchart

Figure 2. The Prevalence Rate of H. pylori Infection and its 95% Confidence Interval



According to the year and the location of studies assessed. The midpoint of each line illustrates the prevalence rate estimated in each study. The diamond sign shows the prevalence rate throughout the country for all the studies.

The Figure 3 shows the relationship between the prevalence of *H. pylori* infection and year of study, and sample size using meta regression models. In Figure 3 A the negative slope of the meta regression line showed that the prevalence of *H. pylori* infection in Iran has had a decreasing trend with a slow slop but it was not significant. In Figure 3 B the relation between sample size was compared to

the prevalence rate of H. pylori infection and according to this figure there isn't a significant relation between the sample size and prevalence (P = 0.06). At the following figure the circles show the weight of studies and it seems that studies with greater sample sizes are more prevalent and vice versa (Figure 3). In the Table 4, a summary of data related to meta-regression curves are shown.

City	year	Age,y	Sample Size	Diagnostic Method	Prevalence	95% CI		References	
Kashan	2000	4.1 ± 9.9	39	Urease	30.8	45.3	16.3	Taghavi et al. (30)	
Sari	2000	7-18	400	-	19.2	23.1	15.3	Tergar Fakheri et al. (39)	
Semnan	1999		700	Elisa	48	57.1	44.3	Moradi et al . (22)	
Ghazvin	2002	54.4	125	Urease	43.7	52.4	35	Hajagamohammadi et al. (17	
Sari	2001		394	Elisa	64.2	69.1	59.7	Baba mahmoodi et al. (38)	
Khorasan razavi	2004	12-75	195	Urease	62.56	69.4	55.8	Nakhaei Moghadam et al. (40	
Tehran	2002	30.65	120	Urease	68.3	76.6	60	Faghihi et al. (23)	
Yazd	2004	30-65	28	-	43.5	61.9	25.1	Benesh et al. (41)	
Ghazvin	2002	10-60	240	Elisa	2000.5	86.7	1993.3	Sheikholslami et al. (18)	
Tabriz	2009	3.21 ± 8.38	116	Serology	Children 60.3, Mothers 57.8, Fathers 37.9	61.1	42.9	Rafiei et al. (31)	
Kerman	1993	57.05	513	Urease	56.9	61.2	52.6	Zojajy (19)	
Tehran	2002	8.8 ± 48	576	Endoscopy	59.7	63.7	55.7	Yasseri (24)	
Tehran	2004	2.2 ± 24	137	Elisa	65.57	75.3	56.7	Sharifian et al. (32)	
Tehran	2004-2006	6-12	1665	Urease	26	28.1	23.9	Zamani et al. (25)	
Tehran	2003	-	170	Histopathology	29.4	36.2	22.6	Barati et al. (26)	
Tabriz	-	-	120	-	71.6	2000.7	63.5	Rahnama et al. (43)	
Tabriz	-	-	86	. 47	42.6	53.1	32.1	Rafeey et al. (44)	
Tabriz	2003	0.03 ± 8.3	96	-	64.6	74.2	55	Modaresi et al. (45)	
Kurdistan	2006	14.91± 15.32	1503	Elisa	36.5	38.9	34.1	Yazdanpanah et al. (33)	
Tehran	2006	39	152	-	35.52	43.1	27.9	Shokohizadeh et al. (46)	
Tehran	2010	43.9	311	-	74.27	2000.1	69.4	Neshandar et al. (34)	
Kashan	2007	17.13 ± 43.3	100	Elisa	66	75.3	56.7	Arj et al. (20)	
Tehran	2003	11.67 ± 39.68	50	Urease, IgG, Histology	70	2003.7	57.3	Baghaei et al. (42)	
Isfahan	2010	16-62	100	PCR	30	39	21	Salehi et al. (27)	
Guilan	2004	11.30 ± 32.38	50	Elisa	54	67.8	40.2	Ghanei et al. (28)	
Tehran	2001		100	Urease, Pathology	57	66.7	47.3	Gottaslou et al. (29)	
Guilan	2005	7-11	961	Elisa	40	43.1	36.9	Mansor et al. (35)	
Tehran	2001	48.3	1993	Citology	58.3	69.7	46.9	Vahidi et al. (36)	
Isfahan	2002		70	Elisa	44.44	56.1	32.8	Sanei et al. (21)	
Khorasan razavi	2006	4.77 ± 23.50	187	Elisa	34.7	41.5	27.9	Dolatian et al. (37)	
		-	-	-	50.7	56.9	44.4	-	

To assess publication bias we used funnel plot (Figure 4) that it showed there was a significant publication bias (P = 0.016). In another classification, the analysis was carried out based on the city of the study, according to which the highest prevalence rate (61.7%), with a sample size of 245 individuals, was related to Ghazvin province (95% CI: 26.6-96.8) and the lowest prevalence rate (36.5%), with a sample size of 73 individuals, was related to Kurdistan province (95% CI: 38.9-34.1) (Table 5).

4. Discussion

A data containing 9198 Helicobacter pylori-infected indi-

viduals were included in the current study. A total of 30 papers were entered into the final Meta-analysis. I^2 statistics showed a high variation among studies results (I^2 = 97.4, P = 0.000). In three studies, including those carried out in Gilan, Sari and Qazvin, sampling had been carried out in villages as well as in cities (17, 33, 38). The prevalence rate of H. Pylori was calculated for all the individuals in all the age groups, based on the status of the individuals, gender and age groups.

In our review, random effect models were used for metaanalysis, considering the possibility of significant heterogeneity between studies which was tested with the Q test.

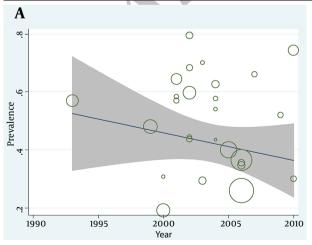
Table 2. Prevalence Rate of H.	nylori Infection in Iran According	to Different Diagnostic Methods

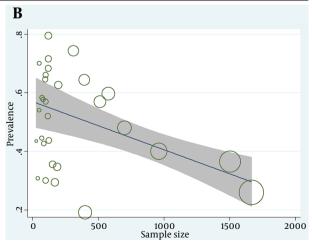
Diagnostic Methods	Study, No.	H. pylori, %, 95% CI
Total Recognize group	30	50.7 (44.4-56.9)
ELISA	10	52.3 (43.8-60.8)
Urease test	8	51.9 (36.9-66.9)
Other methods	5	45.8 (31.3-60.4)

Table 3. Prevalence Rate of H. pylori Infection in Iran According to Health Status, Age and Gender

	Study, No.	H. pylori, %, 95% CI
Total	30	50.7 (44.4-56.9)
Sex	•	-
Women	5	37.7 (27.5-48)
Men	5	35.7 (19.6-51.7)
Population		-
Patient	17	47.6 (39.2-56.1)
Healthy	13	53.1 (45.4-60.8)
Age, y		38.3 (28.1-48.5)
≤20	6	50.3 (39.5-61)
20-40	7	60.1(52.4-67.8)
>40	6	-

Figure 3. H. pylori Prevalence Rate According to the Year of Study and Sample Size





The fitted line show meta-regression line.

Table 4. The Unadjusted and Adjusted Regression Coefficients and Corresponding P Values for Correlation Between Potential Influential Factors and *H. pylori* Prevalence Using meta-Regression Models

Factors	Regression Coefficients	P	
Year of data collection	-	-	
Unadjusted	-0.00332003004	0.707	
Adjusted	0.0086586	0.21999	
Age group	-	-	
Unadjusted	0.1077322	0.017	
Adjusted	0.1222877	0.008	
Sample size	-	-	
Unadjusted	-0.0001338	0.060	
Adjusted	-0.000919	0.159	

Table 5. Prevalence Rate of *H. pylori* in Iran According to City

City	Random Effects OR, 95% CI	I ² ,%	Sample Size	Study, No.
Kashan	48.9 (14.4-2004.3)	93.8	139	2
Sari	41.8 (-0.025-0.86)	99.5	20004	2
Semnan	48 (44.3-51.7)	- /	700	1
Ghazvin	61.7 (26.6-96.8)	97.4	245	2
Khorasan Razavi	48.6 (21.3-75.9)	96.9	32003	2
Tehran	53.5 (39.1-67.8)	98.4	3295	10
Yazd	43.5 (25.1-61.9)	-	28	1
Tabriz	57.9 (45.3-70.5)	86.6	418	4
Kerman	56.9 (52.6-61.2)	-	513	1
Kurdistan	36.5 (34.1-38.9)	73	1503	1
Isfahan	36.7 (22.6-50.8)	73.4	170	2
Guilan	45.3 (32-58.6)	97.4	1011	2
-	50.7(44.4-56.9)	-	9198	30

In a study carried out in Sari in 132001, a significant correlation was reported between the prevalence rate of infection and home ownership and the family size (38). In the study by Azevedo et al. the major risk factors that have been emphasized were the socioeconomic indicators (15).

Among the limitations of the current study, the following can be mentioned: 1) There was not same method to measure variables and diagnostic tests among all studies as well as, 2) The majority of the studies were carried out in a preselected population (blood donors, individuals referring to health care centers and etc.). 3) In most studies, nutritional status and life style were not considered as influencing factors. 4) The range of age groups was considerably wide among different studies.

This study aimed to determine the prevalence rate of *H. pylori* infection in Iran. Almost half the population

in Iran is infected by *H. pylori*, the prevalence rate being different among different parts of the country. According to the findings of this study, it is suggested that, to prevent the spread of *H. pylori*, comprehensive health programs should be scheduled throughout the country. According to the results of this study, the risk of *H. pylori* infection significantly increases with age, and so, it is recommended that preventive procedures are more seriously followed for high risk age groups. It is also recommended that the ELISA and urease tests are used in diagnostic laboratories to increase the accuracy and perception of diagnostic methods.

Funnel plot (Figure 4) showed the effects of publication bias was significant in this study. Publication bias is very important in randomized clinical trials and case control studies, but it is not important in the meta-analysis that estimates prevalence publication bias.

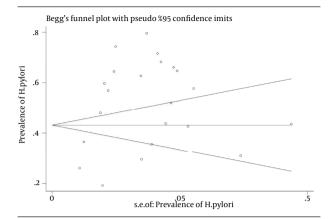


Figure 4. Funnel Plot to Assess Publication Bias

Authors' Contribution

Fatemeh Sayehmiri and Zahra Darvishi, setareh soroush: Data Collection; Kourosh Sayehmiri: Biostatistic analysis; Mohammad Emaneini and Morovat Taherikalani: study designs; Raffaele Zarrilli: final revision and grammer editing.

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