http://www.ijwhr.net

doi 10.15296/ijwhr.2017.06

Open Access Systematic Review

IJWHR

International Journal of Women's Health and Reproduction Sciences
Vol. 5, No. 1, January 2017, 30–36
ISSN 2330-4456

Global Prevalence of *Helicobacter pylori* Infection in Pregnant Women: A Systematic Review and Meta-analysis Study

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Abstract

Objectives: Pregnant women are among the most vulnerable groups for *Helicobacter pylori* infection. The infection may cause nausea, vomiting, anemia, fetal growth restriction, fetal anomalies and low birth weight of infants. *H. pylori* prevalence during pregnancy is vary widely between different geographical regions and given the importance of this infection in pregnancy, systematic review and meta-analysis has been done.

Materials and Methods: The current study has been conducted based on PRISMA guideline. The time interval of the investigated studies was from the beginning of 2000 until March 2016. In order to achieve the related literature, databases sources such as Scopus, PubMed, Science Direct, Cochrane, Embase, Springer, Wiley online library, as well as Google Scholar search engine was used. The search was done using Mesh keywords. Furthermore, all the articles that met the inclusion criteria were evaluated. The data has been analyzed using the random-effects models for meta-analysis and the Stata 11.1.

Results: In 24 studies, a total of 19426 pregnant women had been investigated. The worldwide prevalence of *H. pylori* infection in pregnant women was calculated to be 46% (95% CI: 38-54). The lowest prevalence of *H. pylori* infection was seen in Europe, 25% (95% CI: 9-40) and the highest prevalence in South America 62% (95% CI: 53-71).

Conclusion: This meta-analysis shows that about half of the pregnant women worldwide are infected with *H. pylori* and the prevalence of this infection in South America and Africa is far more than other continents.

Keywords: Prevalence, *Helicobacter pylori*, Pregnant women, Systematic Review, Meta-Analysis

Introduction

Helicobacter pylori is a gram-negative bacillus known to be colonized in the stomach and play a role in the creation of multiple gastrointestinal disorders which is the most common chronic infection around the world (1). Pregnant women are among the most vulnerable groups to the mentioned infection;which has been shown with nausea, vomiting, anemia, fetal growth restriction, fetal anomalies and low birth weight (2,3).

In general, these bacteria have infected more than 50% of the population in the world (2). Various studies from different geographical regions has reported the prevalence of *H. pylori* during pregnancy in the range of 7.6 % to 94% that 7.5% to 42.9% has been seen in European countries, in Asian countries 24% to 61%, in the American countries 50% to 70% and in Africa more than 52% (4,5).

In general, countries with high rates of stomach cancer have a higher prevalence of infection with *H. pylori* and reduction in the prevalence of this bacteria reduced the incidence of gastric cancer in developed countries (6,7).

The prevalence of this infection is related to economic and social factors, including income level and living conditions during childhood, poor hygiene, and overcrowding (8,9). *H. pylori* prevalence during pregnancy is vary widely between different geographical regions (4,5). So, the increasing importance of the subject demands a systematic review and meta-analysis in order to put all the relevant documents together and presenting a complete picture of this problem in pregnant women around the world (10,11). Therefore, in the current study, which aimed to estimate the prevalence of *H. pylori* infection in pregnant women, systematic review and meta-analysis has been used.

Materials and Methods

The current study has been done based on PRISMA (Preferred reporting items for systematic reviews and meta-analyses) guideline (12). In order to avoid bias, factors

Received 10 July 2016, **Accepted** 22 December 2016, **Available online** 1 January 2017

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such as search, selection of studies, quality assessment and data extraction were done by two researchers independent of each other.

Data Sources

This study is a first systematic review and meta-analysis study. The results of this study are based on articles published in journals. The studies that have been reviewed were conducted from the beginning of 2000 until March 2016. In order to achieve the related literature, database such as Scopus, PubMed, Science Direct, Cochrane, Embase, Springer, Wiley online library, as well as Google Scholar was used. The search was done using Mesh keywords. These keywords included Prevalence, *Helicobacter pylor*i, Helicobacter infections, pregnant women, pregnancy, pregnancy complications, gestational which was also searched in combination by using AND and OR operators. A sample of PubMed search is shown in Appendix 1.

Inclusion and Exclusion Criteria

The main criterion for inclusion was investigated on the prevalence of *H. pylori* in the population of pregnant women. Exclusion criteria included (*a*) the non-random sample size, (*b*) not relating to the topic, (*c*) insufficient data, (*d*) date of the study, which was not between 2000 and 2016, and (*e*) Diagnosis was not based on laboratory findings.

Definitions

The diagnosis of *H. pylori* according to the laboratory findings contained serology, urea breath test, stool antigen or polymerase chain reaction (PCR) (8,9).

Qualitative Assessment

Two researchers independently used STROBE (The Strengthening the Reporting of Observational Studies in Epidemiology) (13) checklist which is an international and a standard checklist for qualitative assessment of studies and investigated the selected articles on various aspects of the methodology, including sampling techniques, variable measurements, statistical analysis and the aim of the study. The authors adopted a simple method for rating. Two points were given to each part of the checklist and at the end, the given points to the papers were compared by two researchers and in the case of differences a third researcher would do it all over again. The minimum point that would be given was 16 and those articles that meet the quorum qualitative assessment score were considered for the meta-analysis process.

Data Extraction

All final papers which were accepted for the study were extracted by a prepared checklist. The check-list included the author's name, year of study, place of study, study design, sample size, age, gestational age, a method of diagnosis of *H. pylori* infection and also the prevalence of *H. pylori* infection in pregnant women.

Statistical Analysis

In each study, the prevalence of *H. pylori* was considered as the probability of binomial distribution and its variance was calculated from the binomial distribution. To assess the heterogeneity of the studies, Cochrane test, and I2 index were utilized. Heterogeneity in the study was measured 99%, which puts the study among highest heterogeneity studies (I2 index less than 25% represents low heterogeneity, between 25%-75% average and more than 75% represents high heterogeneity). The DerSimonian and Laird method in the random-effect model were used to generate a 95% CI, which takes study heterogeneity into account to obtain the estimates. Regarding the heterogeneity of the studies and the significance of the I2 score, random effects size model in the meta-analysis was used (14). Data were analysis using Stata version 11.1 software and the significant level was set at 0.05.

Results

In the systematic review 610 articles were identified which, after examining the titles, 280 articles were excluded due to being a duplicated study. So the full text of 330 articles was examined and after checking the inclusion and exclusion criteria, finally 24 articles that have been done between the years 2000 to 2014 were decided to be qualified which entered into the final meta-analysis (Figure 1).

In total 19426 pregnant women had participated in the study. Details of the studies that were entered into the meta-analysis are shown in Table 1.

The global prevalence of *H. pylori* infection in pregnant women was calculated to be 46% (95% CI: 38 to 54). The lowest and the highest prevalence of the infection was in Finland in 2000 (7.6%) and Sudan in 2012 (94%), respectively (Figure 2).

The prevalence of *H. pylori* in pregnant women was analyzed separately for each continent which is displayed as GIS features in Figure 3. The lowest rate in pregnant women was reported to be among the Europeans 25% (95% CI: 9 to 40) and the highest prevalence in South America 62% (95% CI: 53 to 71).

In the investigation of the prevalence of *H. pylori* infection among pregnant women in the world in terms of diagnostic criteria (serology, urea breath test, stool antigen or PCR) the confidence intervals intersect each other which is not statistically significant (Figure 4).

Discussion

In the recent studies, it has proven that *H. pylori* not only causes digestive diseases but also may be associated with diseases related to insufficient absorption of nutrients such as cardiovascular disease, anemia, low birthweight, anemia and headache (3,33).

The current study is the first systematic review and meta-analysis study on the worldwide prevalence of *H. pylori* infection during pregnancy. In this study, the prevalence of *H. pylori* infection in pregnant women was estimated at 46%. The range of the prevalence of the infection

Table 1. The Details of the Studies Entered Into the Meta-analysis

Author Name	Country	Continent	Year	Sample Size	Mean Age (Mean ± SD)	Diagnostic Criteria	Prevalence of *Helicobacter pylori* (%)
Weyermann et al (4)	Germany	Europe	2001	898	30.7±5.2	UBT	22.9
Fukui et al (8)	Japan	Asia	2003	120		Serology	24.2
Poveda et al (9)	Chile	South America	2005	274		Serology	68.6
Farag et al (16)	Tanzania	Africa	2004	857	28.1±7.1	UBT	17.5
Baingana et al (17)	Uganda	Africa	2008	447		Stool-Ag	45.2
Shirin et al (18)	Israel	Asia	2004	185		Serology	45.9
Epstein et al (19)	USA	America	2012	82		Serology	43.9
Karaer et al (20)	Turkey	Asia	2007	296		Serology	56.8
Kenna et al (21)	United Kingdom	America	2003	404		Serology	41.8
Alvarado-Esquivel (22)	Mexico	South America	2008	343	24.2±5.9	Serology	52.2
Mulayim et al (23)	Turkey	Asia	2006	117		UBT	61.5
Laiho et al (24)	Finland	Europe	2000	772		Serology	7.6
Ugwuja and Akubugwo (25)	Nigeria	Africa	2008	349	27.04±4.8	Serology	24.1
Bromberg et al (26)	USA	America	2006	37	29.6±5	Serology	73
Baingana et al (27)	Uganda	Africa	2014	151		Serology	70
Santos et al (28)	Mexico	South America	2006	71		Serology	59.2
Mubarak et al (29)	Sudan	Africa	2012	179		Serology	94
Hollander et al (30)	Netherlands	Europe	2010	6837	29.7±5.3	Serology	46
Cardaropoli et al (31)	Italy	Europe	2010	2820	32.2±4.5	Serology	28.5
Kitagawa et al (6)	Japan	Asia	2001	1588		PCR	29.2
Seiskari et al (7)	Finland	Europe	2001	243		Serology	19
Karen (32)	Mexico	South America	2000	383		Serology	56
Karen (32)	Mexico	South America	2000	368		Serology	74
Abbasalizadeh (5)	Iran	Asia	2001-13	1605		Serology	45.9

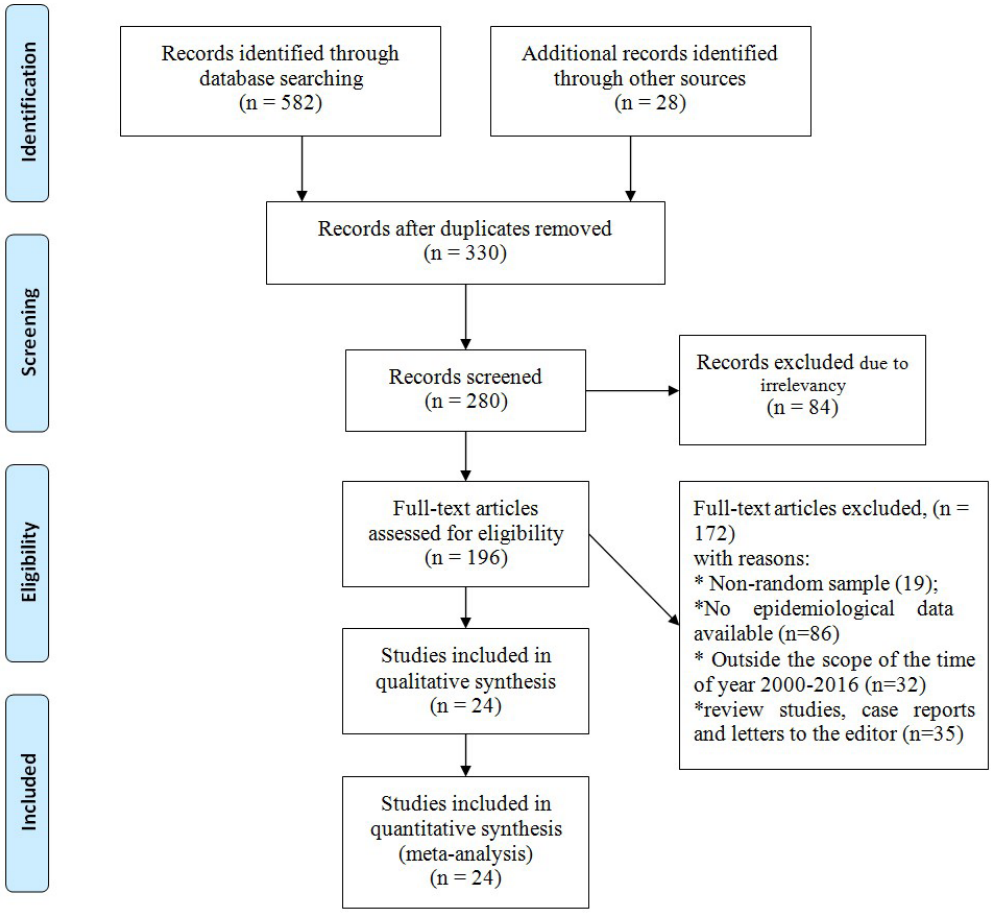

Figure 1. The Flowchart Stages of Entering the Articles Into Meta-analysis.

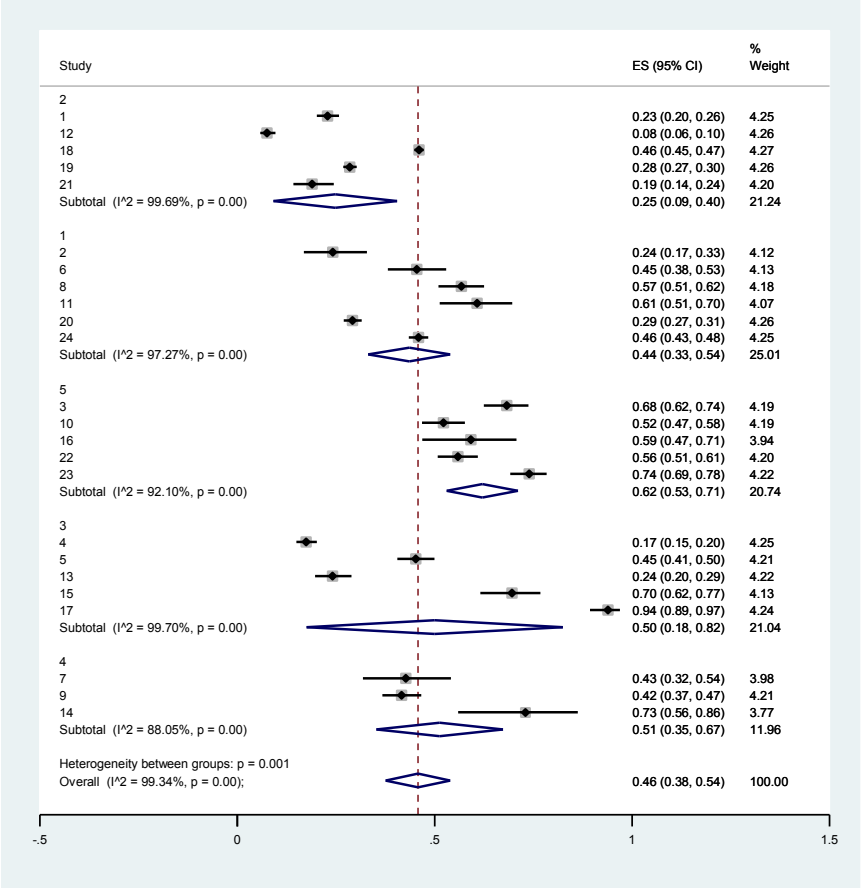

Figure 2. Forest Plots of the Global Prevalence of *Helicobacter pylori* Infection in Pregnant Women for Random Effects Meta-analyses (Squares represent effect estimates of individual studies with their 95% CI of the prevalence of *Helicobacter pylori* with the size of squares proportional to the weight assigned to the study in the meta-analysis. The diamond represents the overall result and 95% CI of the random-effects meta-analysis).

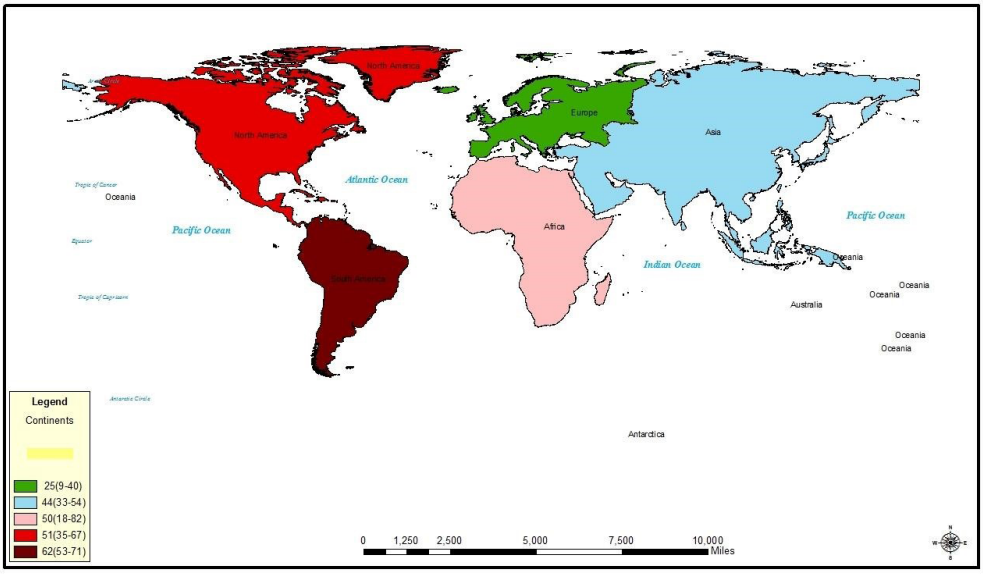

Figure 3. GIS of Global Prevalence of *Helicobacter pylori* Infection in Pregnant Women Based on Continent for Random Effects Meta-analysis.

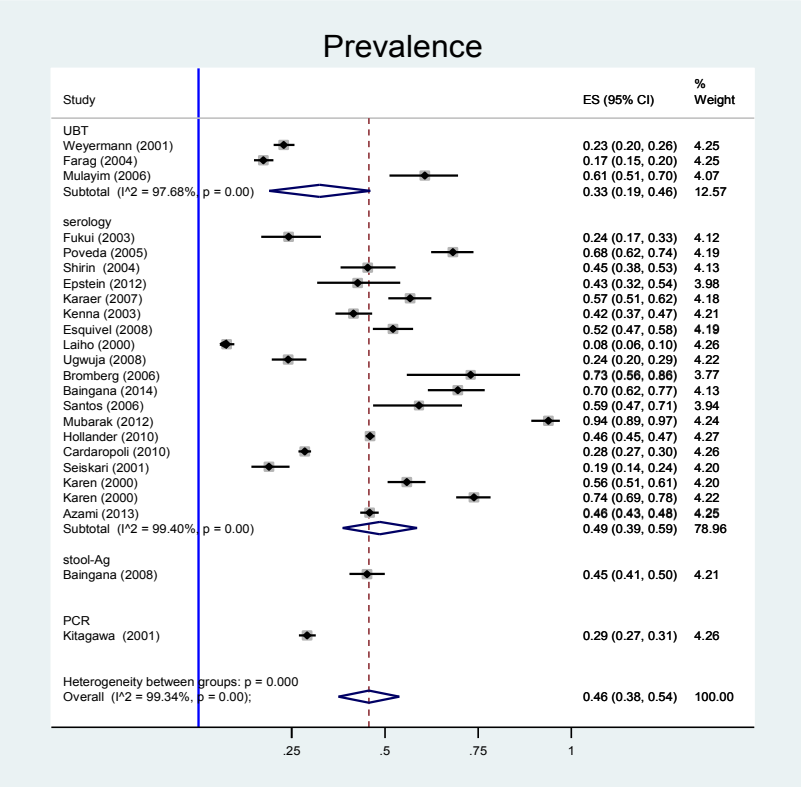

Figure 4. Forest Plots of the Global Prevalence of *Helicobacter pylori* Infection in Pregnant Women Based on a Diagnostic Method for Random Effects Meta-analyses.

in different studies was highly variable which have been reported between 8%-94%. The prevalence of this infection in pregnant women may reflect the prevalence among the general population so that the prevalence of *H. pylori* among pregnant women in the studies of Abbasalizadeh et al in Iran and Goodman et al in Mexico is estimated to be similar to the general population (5,32).

The prevalence of *H. pylori* infection among pregnant women varies based on their social and economic status and hygiene status. Even the diagnostic methods are different according to the mentioned differences, for example the prevalence of this infection in pregnant women in Europe and Japan is calculated to be 20 to 30%, in Turkey, Mexico, Texas and America 50% to 80%, in Egypt and Gambia is above 80% (15). In this study, the prevalence of infection in pregnant women was estimated separately for the 5 continents as follows Europe (25%), Asia (44%), Africa (50%), America (51%) and South America (62%). What is clear from the results, the prevalence of these infections is higher in developing countries such as South America countries compared to developed countries such as European countries, which is also shown in the study of Bures et al (33).

The prevalence of this infection has been reduced in a lot of countries, for instance, in previous studies the prevalence of the infection in Iran, France and Finland has been reported 85%, 21.5% and 31%, respectively (7,34) that can be consistent with better health and improvement of infrastructure in the countries which led to reduction of infection diseases while the prevalence of the mentioned diseases is still high in African and South American countries (15).

Diagnosis of *H. pylori* infection includes 1) invasive techniques (requiring endoscopy) such as rapid urease test, culture, and histology, and 2) non-invasive methods such as serology, urea breath test (UBT) and stool antigen test (33). Invasive methods due to ethical issues and UBT because of the use of radioactive materials, are prohibited in pregnancy (35). Invasive methods due to ethical issues and UBT due to the use of radioactive materials are prohibited in pregnancy (35). In most of the studies that investigated the prevalence of *H. pylori* among pregnant women (80%) based on diagnostic method, serology was the dominant method and this amount was measured to be 49% which had a slight difference with general estimation. While the mentioned prevalence has been obtained lesser through other diagnostic methods, for example, the prevalence based on UBT and stool antigen methods was measured 33% and 29%. The most obvious reason for a lower prevalence of *H. pylori*, in this rate, can be the low number of studies for UBT and stool antigen methods. On the other side this method rep-resents the rate of current infection while in serology method beside current infection, the previous infection will be also positive.

Conclusion

This meta-analysis shows that about half of pregnant women worldwide are infected with *H. pylori* and the

prevalence of this infection in the continent of South America and Africa is far more than other continents. It is suggested that, in order to control *H. pylori* in this high-risk group, a constant check of the *H. pylori* infection in pregnancy, appropriate hygienic facilities and improvement of education levels in women of gestational age take to an action.

Ethical Issues

The study was approved by the Women's Reproductive Health Research Center Ethical Review Committee as number IR.TBZMED.REC.1395.508.

Conflict of Interests

All authors declare that there is no conflict of interest.

Financial Support

Women's Reproductive Health Research Centre of the Tabriz University of Medical Science.

Acknowledgments

We would like to thank Women's Reproductive Health Research Centre of the Tabriz University of Medical Science for supporting this study.

Appendix 1: PubMed search strategy:

1– exp Helicobacter Pylori /
2– exp Helicobacter Infection/
3– exp Pregnant Women/
4– exp Pregnancy/
5– exp Pregnancy Complications/
6– exp Gestational/
7– exp Prevalence/
8– exp Epidemiology/
9– exp Iran
10– 7 or 8 or 9
11– 1/2/4/5/6 and 10
12– * Helicobacter pylori /exp [Prevalence]
13– 10 or 12

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