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
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

<table>
<thead>
<tr>
<th>Author Name</th>
<th>Country</th>
<th>Continent</th>
<th>Year</th>
<th>Sample Size</th>
<th>Mean Age (Mean ± SD)</th>
<th>Diagnostic Criteria</th>
<th>Prevalence of Helicobacter pylori (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weyermann et al (4)</td>
<td>Germany</td>
<td>Europe</td>
<td>2001</td>
<td>898</td>
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<td>Fukui et al (8)</td>
<td>Japan</td>
<td>Asia</td>
<td>2003</td>
<td>120</td>
<td></td>
<td>Serology</td>
<td>24.2</td>
</tr>
<tr>
<td>Poveda et al (9)</td>
<td>Chile</td>
<td>South America</td>
<td>2005</td>
<td>274</td>
<td></td>
<td>Serology</td>
<td>68.6</td>
</tr>
<tr>
<td>Farag et al (16)</td>
<td>Tanzania</td>
<td>Africa</td>
<td>2004</td>
<td>857</td>
<td>28.1±7.1</td>
<td>UBT</td>
<td>17.5</td>
</tr>
<tr>
<td>Baingana et al (17)</td>
<td>Uganda</td>
<td>Africa</td>
<td>2008</td>
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<tr>
<td>Shirin et al (18)</td>
<td>Israel</td>
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<td>2004</td>
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<td>Serology</td>
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<tr>
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<td>USA</td>
<td>America</td>
<td>2012</td>
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<tr>
<td>Kenna et al (21)</td>
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<td>41.8</td>
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<tr>
<td>Alvarado-Esquivel (22)</td>
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<td>2008</td>
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<td>24.2±5.9</td>
<td>Serology</td>
<td>52.2</td>
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<td>Turkey</td>
<td>Asia</td>
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<td></td>
<td>UBT</td>
<td>61.5</td>
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<tr>
<td>Laiho et al (24)</td>
<td>Finland</td>
<td>Europe</td>
<td>2000</td>
<td>772</td>
<td></td>
<td>Serology</td>
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<td>Ugwuja and Akubugwo (25)</td>
<td>Nigeria</td>
<td>Africa</td>
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<td>349</td>
<td>27.0±4.8</td>
<td>Serology</td>
<td>24.1</td>
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<td>Bromberg et al (26)</td>
<td>USA</td>
<td>America</td>
<td>2006</td>
<td>37</td>
<td>29.6±5</td>
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<td>73</td>
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<tr>
<td>Baingana et al (27)</td>
<td>Uganda</td>
<td>Africa</td>
<td>2014</td>
<td>151</td>
<td></td>
<td>Serology</td>
<td>70</td>
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<tr>
<td>Santos et al (28)</td>
<td>Mexico</td>
<td>South America</td>
<td>2006</td>
<td>71</td>
<td></td>
<td>Serology</td>
<td>59.2</td>
</tr>
<tr>
<td>Mubarak et al (29)</td>
<td>Sudan</td>
<td>Africa</td>
<td>2012</td>
<td>179</td>
<td></td>
<td>Serology</td>
<td>94</td>
</tr>
<tr>
<td>Hollander et al (30)</td>
<td>Netherlands</td>
<td>Europe</td>
<td>2010</td>
<td>6837</td>
<td>29.7±5.3</td>
<td>Serology</td>
<td>46</td>
</tr>
<tr>
<td>Cardaropoli et al (31)</td>
<td>Italy</td>
<td>Europe</td>
<td>2010</td>
<td>2820</td>
<td>32.2±4.5</td>
<td>Serology</td>
<td>28.5</td>
</tr>
<tr>
<td>Kitagawa et al (6)</td>
<td>Japan</td>
<td>Asia</td>
<td>2001</td>
<td>1588</td>
<td></td>
<td>PCR</td>
<td>29.2</td>
</tr>
<tr>
<td>Seiskari et al (7)</td>
<td>Finland</td>
<td>Europe</td>
<td>2001</td>
<td>243</td>
<td></td>
<td>Serology</td>
<td>19</td>
</tr>
<tr>
<td>Karen (32)</td>
<td>Mexico</td>
<td>South America</td>
<td>2000</td>
<td>383</td>
<td></td>
<td>Serology</td>
<td>56</td>
</tr>
<tr>
<td>Karen (32)</td>
<td>Mexico</td>
<td>South America</td>
<td>2000</td>
<td>368</td>
<td></td>
<td>Serology</td>
<td>74</td>
</tr>
<tr>
<td>Abbasalizadeh (5)</td>
<td>Iran</td>
<td>Asia</td>
<td>2001-13</td>
<td>1605</td>
<td></td>
<td>Serology</td>
<td>45.9</td>
</tr>
</tbody>
</table>

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.
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 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

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**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.**

<table>
<thead>
<tr>
<th>Study</th>
<th>UBT</th>
<th>Serology</th>
<th>Stool-Ag</th>
<th>PCR</th>
<th>Heterogeneity between groups: p = 0.000</th>
</tr>
</thead>
<tbody>
<tr>
<td>ES (95% CI)</td>
<td>% Weight</td>
<td>ES (95% CI)</td>
<td>% Weight</td>
<td>ES (95% CI)</td>
<td>% Weight</td>
</tr>
<tr>
<td>0.23 (0.20, 0.26)</td>
<td>4.25</td>
<td>(0.29, 0.33)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
</tr>
<tr>
<td>0.17 (0.15, 0.20)</td>
<td>4.25</td>
<td>(0.29, 0.33)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
</tr>
<tr>
<td>0.41 (0.31, 0.50)</td>
<td>4.07</td>
<td>(0.29, 0.33)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
</tr>
<tr>
<td>0.33 (0.19, 0.46)</td>
<td>12.57</td>
<td>(0.29, 0.33)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
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<tr>
<td>0.24 (0.17, 0.33)</td>
<td>4.25</td>
<td>(0.37, 0.47)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
</tr>
<tr>
<td>0.45 (0.38, 0.53)</td>
<td>4.13</td>
<td>(0.37, 0.47)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
</tr>
<tr>
<td>0.43 (0.32, 0.54)</td>
<td>3.86</td>
<td>(0.37, 0.47)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
</tr>
<tr>
<td>0.97 (0.61, 1.49)</td>
<td>4.18</td>
<td>(0.37, 0.47)</td>
<td>4.12</td>
<td>(0.37, 0.47)</td>
<td>0.29 (0.27, 0.30)</td>
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<td>...</td>
</tr>
</tbody>
</table>

**Prevalence**
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.

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Acknowledgments
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References

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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