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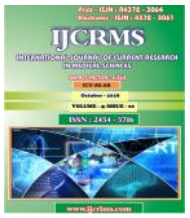

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Relationship between *Helicobacter pylori* infection and spontaneous abortion: A Systematic Review and meta-analysis

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Abstract

Introduction:
Abortion is one of the most common complications of pregnancy**.** Infection is one of the main causes of abortion, a cause which is more important in spontaneous abortion; infections account for only 5% of recurrent abortions**.** *Helicobacter pylori* is a gram-negative movable bacterium and urease enzymes. The aim of this study is to determine the Relationship between *Helicobacter pylori* infection and spontaneous abortion.

Method:
the methods used for this systematic review were based on the "Cochrane Systematic Study Booklet" and "Appropriate Items for Systematic and Meta-Analysis Study (PRISMA)" tool. To find references, the international Databases (MEDLINE PubMed interface), Google Scholar, and Web of Science) and domestic databases (SIDs and Magiran) and journals were searched; unlimited searching, in terms of both setting and language, was done until June 30, 2018.following keywords were used to provide a comprehensive context: helicobacter pylori; Abortion; spontaneous abortion; *H. pylori*; relationship; miscariage; Gastritis.

Result:
Based on the results of random effects model, the Relationship between *Helicobacter pylori* infection and spontaneous abortion in Pregnant women in 227 patients was 1.41 (95% confidence interval [CI]: 1.04, 1.93, I^2 = 83.5%) (p = 0.014) .

Discussion and conclusion:
Based on the results of the present systematic study, there is a significant relationship between *Helicobacter pylori* infection and abortion. Among the factors associated with HP inflammation during pregnancy, complications such as iron deficiency anemia and nausea in pregnancy are associated with a high prevalence of *Helicobacter pylori* especially in developing countries. More extensive research is needed in this domain, because this specific type of inflammation is preventable with timely treatment.

Keywords: *Helicobacter pylori*; Abortion;spontaneous abortion;*H. pylori*; relationship; miscariage; Gastritis.

Introduction

Abortion is one of the most common complications of pregnancy; it refers to cases where pregnancy ends before the 20th week of gestation for various reasons originating from both the mother and the fetus. If it occurs 3 consecutive times in the same patient, it is referred to as repeated abortion(1). Infection is one of the main causes of abortion, a cause which is more important in spontaneous abortion; infections account for only 5% of recurrent abortions(2). Many infectious agents are involved in abortion, most of which are only effective in spontaneous abortion and their role has not yet been proven in recurrent abortions and they have not attracted much attention in recent scientific sources(3). If abortion occurs without involving any specific medicine or device, it is called automatic abortion(4). *Helicobacter pylori* has infected more than half of the world's population; it is accompanied with severe inflammation in the stomach and is one of the causes of the development of various complications, including gastric cancer(5). *Helicobacter pylori* is a gram-negative movable bacterium and urease enzymes. This bacterium is transmitted through a variety of ways, such as oral-oral, fecal-oral and even contaminated equipment. The main route is to spread through fecal and it can be defecated through fecal-oral for a long period of time(6). *Helicobacter pylori* infection develops in the stomach mucus of 60% of the population. Histopathologic gastritis symptoms are observed in all of these cases; however, not all of them manifest clinical symptom and only 10 to 15% of them develop wound or adenocarcinoma of the stomach(7). *Helicobacter pylori* infection site is not only a gastrointestinal tract; it, also, can interfere with the gastrointestinal system and change the immune response to vaccination. In regard with helicopter pylori and ecology, vaginal environment is quite similar to that of the stomach, and the bacteria can be colonized in the microarray and phyllic conditions and people with asymptomatic infection(8).

The severity of infection with Helicobacter pylori: given the increasing the secretion of inflammatory cytokines and CD8 +, CD4 + in T cells and increasing IFN, studies have shown that infection with *Helicobacter pylori* activates immune cells in the uterus and endometrial surface cells, increases TH1 response to helicobacter, disturbs the ratio of TH2 / TH1 cytokines, causes abnormalities in the formation of natural vessels in the uterus and, ultimately, leads to abortion(9).the aim of this study is to determine the Relationship between *Helicobacter pylori* infection and spontaneous abortion.

Methods

Eligibility criteria

The methods used for this systematic review were based on the "Cochrane Systematic Study Booklet" and "Appropriate Items for Systematic and Meta-Analysis Study (PRISMA)" tool. Observational studies conducted on general population have been added and studies conducted on specific population have been removed. Results are summarized as reported in the research. The minimum sample size was 25 patients in each study. The target population covers the total population of pregnant women with *Helicobacter pylori* infection in Iran who entered the study. Relationship between *Helicobacter pylori* infection and spontaneous abortion was calculated in this study.

Searching strategies and databases

The review of references and resources was done using the Medical Subject Headings (MeSH) and keywords related to the source of information on Relationship between *Helicobacter pylori* infection and spontaneous abortion. To find references, the international Databases (MEDLINE PubMed interface), Google Scholar, and Web of Science) and domestic databases (SIDs and Magiran) and journals were searched; unlimited searching, in terms of both setting and language, was done until June 30, 2018. PRESS standard and the Health Sciences Librarian were used for designing the strategy.

MEDLINE application was used to search other databases. In addition, PROSPERO was used to provide a systematic search that was completed recently. To search for headlines and abstracts,

boolean (AND, OR, NOT), mesh, coordinate {truncation} * and related words were used; following keywords were used to provide a comprehensive context: *Helicobacter pylori;* Abortion; spontaneous abortion; *H. pylori;* relationship; miscariage; Gastritis.

Research selection and data extraction

According to the research protocol, two researchers observed the titles and abstracts separately according to the eligibility criteria; in the next step, after the removal of repeated studies, the full text of the paper was studied based on the eligibility criteria and the required information was extracted. Consensus method was used to solve the disagreements between two researchers. The extracted data included the general information (corresponding author, year and place), characteristics of the research (research design, sample size, location, study period, and risk of bias), and characteristics of participants.

Quality control

To assess the quality of the methodology and bias risk, each observation study was evaluated using a tool developed by Hoy et al; this 10-item scale evaluated the quality of the study in two dimensions, including external credentials (items 1 to 4 target populations, sampling frame, sampling method, and minimum indirect neglect) and internal validity (items 5 up to 9 covering methods for data collection, case definition, study tools, and data collection mode and item 10 covering assessing relevant assumptions or analyzes). The risk of abuse was assessed by two researchers separately and possible disparity of ideas was resolved by consensus.

Aggregation of data

All eligible studies were included within the systematic review. The data was combined using forest plot graph; random effects model was used to Relationship between *Helicobacter pylori* infection and spontaneous abortion. The heterogeneity of primary studies was assessed by performing I^2 tests.. Meta-analysis was performed using the STAT 14 statistical software.

Results

1. Selecting eligible papers and researches

In the initial search on various databases, a total of 261 articles were reviewed, 232 of which turned out to be repetitive during screening process of title and abstract. 19 articles were removed due to unrelated title; out of the remaining 10 articles, 2 articles met the inclusion criteria. Of the 8articles that were removed, 3 were reviews, 1were letters to editors, 2 had no complete text, and 2 had low quality and could not be considered in the research. (Figure 1).

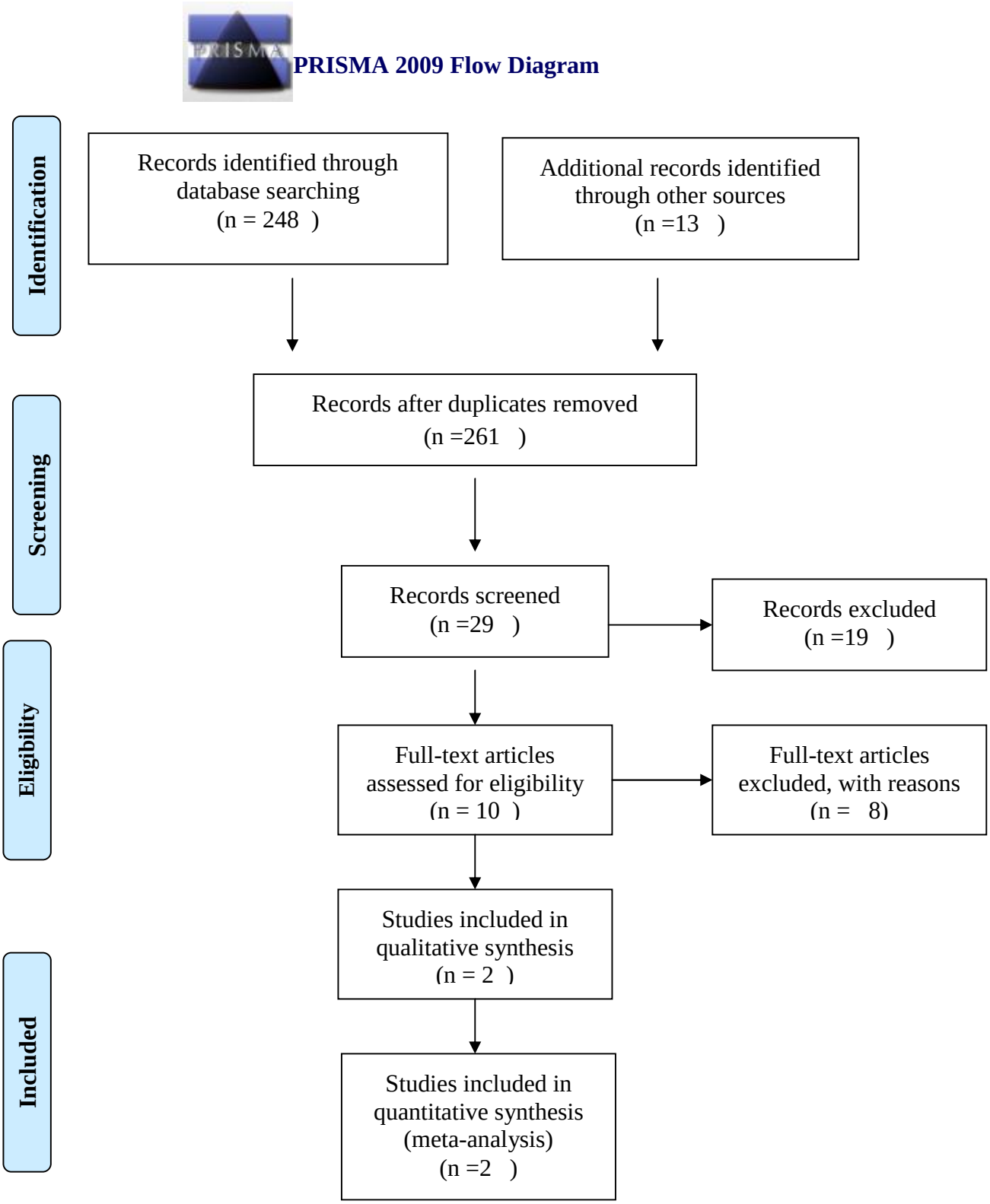

Fig. 1 Study selection process

2. Characteristics of the researches and papers

The final research was conducted on 227 participants; with an age range of 18 to 48years old; a cross-sectional design was used in all studies. Research was conducted in only 2 provinces out of 31 provinces of Iran. Of the 2 studies [10-11], one was from Semnan [10], one from Oroumiye [11]. Required data was collected through interview (n = 2) and had a low bias risk (n = 2) (Table 1).

Table 1: Characteristics of final included studies about Relationship between Helicobacter pylori infection and spontaneous abortion

ID	Author	Year	N	City	Case		control		Bias
					+	-	+	-	
1	Golmohammadlou	2015	100	Oroumiye	23(23%)	27 (27%)	24	26	Low
2	Malek	2007	117	Semnan	32(32%)	28 (28%)	17	50	low

Meta- analysis Relationship between *Helicobacter pylori* infection and spontaneous abortion

Based on the results of random effects model, the Relationship between *Helicobacter pylori* infection and spontaneous abortion in Pregnant women in 227 patients was 1.41 (95% confidence interval [CI]: 1.04, 1.93, I^2 = 83.5%) (table 2) (p = 0.014) .

Table 2:Relationship between *Helicobacter pylori* infection and spontaneous abortion in Iran

Study	Year	95% conf. Interval		RR	%weight	P
		Low	Up			
Golmohammadlou[10]	2015	0.632	1.453	0.958	59.91	0.014
Malek[11]	2007	1.309	3.377	2.102	40.09	
Pooled RR	----------	1.40	1.930	1.417	100	-------

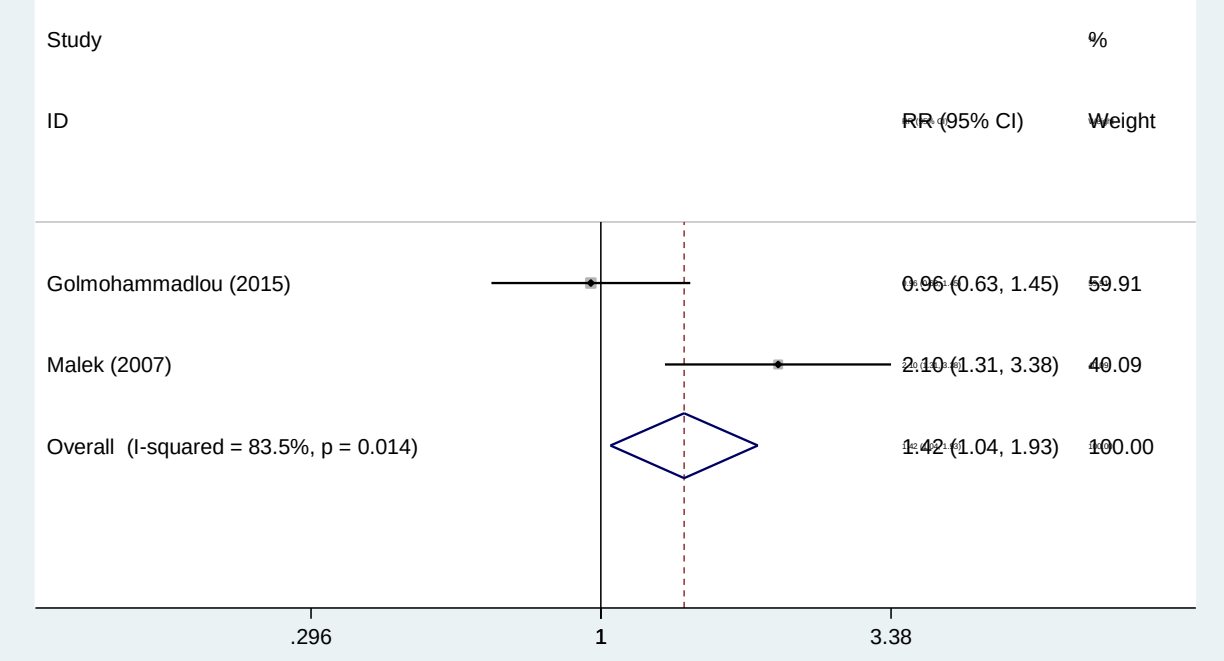

Fig. 2 : The Relationship between *Helicobacter pylori* infection and spontaneous abortion and its 95% interval for the studied cases according to the year and the city where the study was conducted based on the model of the random effects model. The midpoint of each section of the line estimates the% value and the length of the lines showing the 95% confidence interval in each study. The oval sign shows Relationship between *Helicobacter pylori* infection and spontaneous abortion for all studies.

Discussion

Helicobacter pylori is a gastro-intestinal bacterium. Studies show that this bacterium is the main causative agent of active and chronic gastric and is associated with gastric cancer(12). *Helicobacter pylori* is known as a specific pathogenic human germ bacterium; it has been shown to cause long inflammation including intra-gastric filtration in the gastric mucosa by neutrophils, lymphocytes and plasma cells(13). Since the majority of people have no signs of inflammation or show no specific symptoms, clinical diagnosis is difficult. The incidence of *Helicobacter pylori* infection is 50% in developed countries and 80% in developing countries Also, the occurrence of this bacterium has mounted up to a high percentage in different provinces of Iran(14).Recently, few studies have proven the relationship between *Helicobacter pylori* infection and abortion in women(15). The present study was conducted to assess the role of self-acting as a direct agent of gastritis and transient ischemia in spontaneous abortion. In the present study, 237 women turned out to have positive antibody titers of 96 (40.5%).The present research analyzed 2 studied related to HP and abortions in pregnant women. According to the results of these studies, there was a significant relationship between HP with spontaneous abortion, so that the inflammation of the HP increased the chance of abortion by 41%.

Limitations

One of the limitations of the present study is the small number of studies conducted on the Relationship between *Helicobacter pylori* infection and spontaneous abortion in Iran. However, as long as the present researchers can claim, the present principled revision and statistical analysis has been the first attempt to evaluate the Relationship between *Helicobacter pylori* infection and spontaneous abortion. Another limitation of this study is the inclusion of only 2 provinces out of 31 provinces of Iran, a fact which makes it difficult to generalize the results. Although investigators kept cautious of writers, institutes, journals and other related information, two independent reviewers supervised the selection of related papers and the third reviewer solved all the and possible disagreements.

Strengths

The researchers can claim that this study is the first systematic review conducted to determine the Relationship between *Helicobacter pylori* infection and spontaneous abortion. The present study was conducted on the basis of a systematic review plan and all databases were searched. Population-based studies were also applied to the final research.

Conclusion

Based on the results of the present systematic study, there is a significant relationship between *Helicobacter pylori* infection and abortion. Among the factors associated with HP inflammation during pregnancy, complications such as iron deficiency anemia and nausea in pregnancy are associated with a high prevalence of *Helicobacter pylori* especially in developing countries. More extensive research is needed in this domain, because this specific type of inflammation is preventable with timely treatment.

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