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Original Article

Serological Detection of *Helicobacter pylori* Infection in Pregnant Women Related to ABO Blood Group

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Abstract

Helicobacter pylori was known as a pathogen related to peptic ulcers and gastric carcinoma. Some researches confirmed that the infected pregnant women with *H. pylori* have poor pregnancy outcomes so that its effects extended to other systems other than gastrointestinal tracts. This study aimed to evaluate *H. pylori* infection in pregnant women who had morning sickness (nausea and vomiting) related to the ABO blood group. In total, 202 pregnant women within the age range of 15-45 years with severe nausea and vomiting attended the outpatient and specialized clinic. The seroprevalence of *H. pylori* was 62% in pregnant women, especially at the age group of 20-24 years with 32.5% of the cases who had epigastric pain, nausea, vomiting, flatulence, and burning of the stomach, the majority of which related to O^+ (33.3%), followed by A^+ and B^+ (25.39%) blood groups. Most infected pregnant women with *H. pylori* were during the first (41.26%) and second trimesters (34.12%), especially in multigravida (68.25%) cases. This study found that hyperemesis (severe nausea and vomiting), dyspepsia, and other gastrointestinal symptoms during pregnancy were related to the infection with *H. pylori*; therefore, it is a risk factor for complications in pregnancy and its poor outcomes, especially in developing countries, such as Iraq. These results can be minimized by improving the socioeconomic and sanitation conditions. *H. pylori* infection in pregnancy is considered a health problem and should be treated before and during pregnancy. Further investigations are required in this regard and researchers are recommended to conduct studies on the RBC antigens to recognize the pathophysiology related to *H. pylori* infection.

Keywords: *Helicobacter pylori*, Hyperemesis gravidarum, Pregnancy

1. Introduction

Helicobacter pylori (*H. pylori*) infection was discovered at the beginning of 1982, which was more common in developing countries, compared to developed countries. *H. pylori* is a gram-negative bacillus known to be colonized in the stomach and plays a role in the multiple gastrointestinal diseases or disorders which is the most common acute and chronic infection in the world, such as peptic ulcers and gastric carcinoma usually during late adulthood (1). The World Health Organization and the International Agency for Research on Cancer accepted *H. pylori* as a definite carcinogen Class I in 1994 (2). Nausea and vomiting have been deemed routine signs and symptoms in pregnancy, especially in the first trimester, which represent very unpleasant stomach symptoms (morning sickness, increased temperature, burning sensation of stomach, epigastric pain, vomiting, headache, and pomposity) that could be due to hormonal changes in pregnant women. About 50%-90% of pregnant women have these symptoms in different degrees. In severe cases, it is called hyperemesis gravidarum occurring more than 3 times vomiting daily and decreasing about 5% of body weight. Ketonuria, drying, loss of food

elements, and disturbance of hydro-electrolyte all of these result in fetal growth retardation (3, 4). Severe morning sickness throughout the pregnancy has been associated with bad birth outcomes, including low birth weight, small for gestational age, and prematurity (5). Loss of weight or growth retardation during pregnancy has been proposed to perform a role in this regard (6).

Weight gain during pregnancy is recommended by the Institute of Medicine that produces a healthy newborn. The weight gain also provides sufficient postpartum maternal fat stores to support lactation without increasing obesity risk (7). Recent studies mentioned that colonized *H. pylori* in the stomach of pregnant women was associated with serious nausea and vomiting (8). *H. pylori* has cytotoxin related to gene A (CagA) positive serotypes more frequently presented among pregnant women with severe nausea and vomiting (9). Some studies mentioned that anemia related to iron deficiency is associated with the infection of *H. pylori* despite the attendance or the absence of the peptic ulcers.

H. pylori is the most common causative agent of gastrointestinal bleeding, diminishing the absorption of iron, and rise of iron absorption via the *H. pylori* (10).

The health of the pregnant woman is very important and needs different studies to determine the health problems that affect the pregnant woman and her fetus. There were limited data locally on the relationship of infection with *H. pylori* in pregnancy, especially in Iraq and developing countries. Therefore, the present study aimed to determine the *H. pylori* infection in severe hyperemesis pregnant women related to the ABO blood group and Rhesus (Rh).

2. Materials and Methods

This cross-sectional study was performed on women of childbearing age (15-45 years) in Tikrit, Iraq, from November 2019 to March 2020. A total of 202 pregnant women presented with the symptoms of morning sickness, including nausea and vomiting, burning sensation of the stomach, epigastric pain, flatulence, dyspepsia, or other symptoms, with no past record of *H. pylori* infection or receiving medication. The standard questionnaire and interviews were used to collect data. The patients who were selected from an outpatient clinic were then referred for the serologic detection of *H. pylori*.

Diverse techniques and methods were used in the diagnosis of *H. pylori* infection, including invasive and noninvasive methods. In the invasive methods (e.g., gastric biopsy) the specimens are sent for histopathological examination, culture, urase test, and polymerase chain reaction. Although they are specific and sensitive methods, they are unpreferable, especially in pregnant women. Noninvasive methods include fecal and blood sample evaluations to detect antigen (bacteria) and antibody, respectively. 3 mL of venous blood was collected from each pregnant woman and centrifuged; following that, the sera were separated for use. The screening for infection with *H. pylori* was conducted using the On-Site *H. Pylori* Ab Combo Rapid Test kit (CIK BIOTECH MT, Hannover, Germany). The blood groups ABO and Rh were used to identify the seropositive and seronegative pregnant women by the utilization of the normalized hemagglutination methods. The consequence of the current study (seropositive) was comparative with the seronegative pregnant women.

2.1. Statistical Analysis

The two-tailed Fisher's exact test and odds ratio with a 95% confidence interval were used to identify the associations.

3. Results

This cross-sectional study was carried out on 202 pregnant women presented with signs and symptoms of morning sickness at different gestational ages from urban and rural areas. They were then examined and investigated regarding *H. pylori* infection and ABO blood groups. The results showed 126 (62%) pregnant women with *H. pylori* infection, while 76 (38%) pregnant women were found seronegative in terms of *H. pylori* infection (Figure 1).

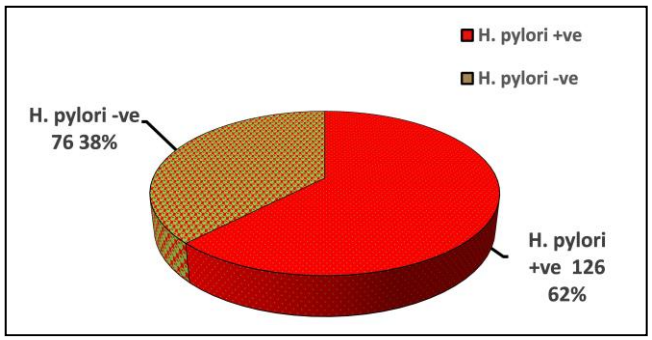

Figure 1. Prevalence of pregnant women with *H. pylori* positive

Table 1 shows the distribution of pregnant women with *H. pylori* infection based on age group in which the most affected pregnant women patients were at the 20-24-year age group (n=41, 32.53%), compared to the women with negative *H. pylori* infection (n=28, 36.84%) at the same age group. Most of the patients were from rural areas (n=86, 68.25%), while negative *H. pylori* was found in 51.31% (n=39) of those living in urban areas (Table 2). Epigastric pain was the most common sign and symptom of pregnant women with *H. pylori* infection (92/126), followed by nausea and vomiting (88/126), compared to non-infected cases (29/76) (Figure 2).

Table 1. Distribution of pregnant women with *H. pylori* infection based on age group

Age group (yr.)	*H. pylori +ve*		*H. pylori -ve*	
	NO.	%	NO.	%
15 – 19	28	22.2	13	17.10
20 – 24	41	32.53	28	36.84
25 – 29	29	23.01	16	21.05
30 – 34	14	11.11	8	10.52
35 – 39	11	8.73	8	10.52
40 – 45	3	2.38	3	3.94
Total	126		76	

Table 2. Distribution of pregnant women with *H. pylori* infection according to the place of residency

Place of residency	*H. pylori +ve*		*H. pylori -ve*	
	NO.	%	NO.	%
Urban	40	31.74	39	51.31
Rural	86	68.25	37	48.68
Total	126		76	

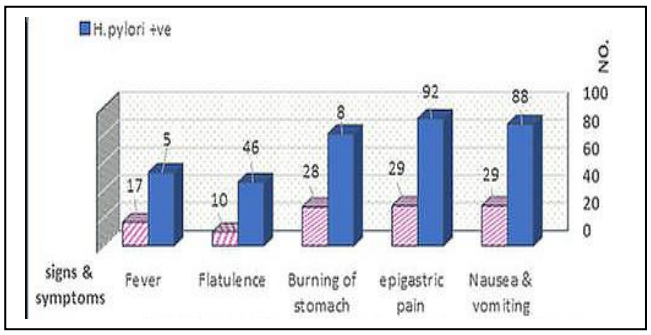

Figure 2. Frequency of the signs and symptoms of pregnant women with *H. pylori* +ve and *H. pylori* -ve

The most infected pregnant women with *H. pylori* were in the first trimester (n=52; 41.26%), followed by those in the second (n=43; 34.12%) and third (n=31; 24.60%) trimesters (Table 3). Regarding the parity of infected pregnant women with *H. pylori*, multigravida pregnant women were 68.25% more affected than primigravidae women (31.74%) (Table 4).

Considering the blood Rh factor, Rh +ve was the most common in pregnant women with *H. pylori* infection (n=116; 92%), compared to Rh -ve (n=10; 8%). The recorded data showed that among the pregnant women with *H. pylori* infection, 66 (87%) and 10 (13%) cases were Rh +ve and Rh -ve, respectively, as shown in figure 3. The recorded data showed that 42 (33.33%) pregnant women with O^+ blood group had positive *H. pylori* infection, compared to A^+ and B^+ that included 32 (25.39%) cases of *H. pylori* infection. The lowest prevalence of *H. pylori* was recorded in the pregnant women with AB^- blood group (n=1; 0.79%) (Table 5). Figure 4 illustrates the frequency of pregnant women with *H. pylori* infection that had a previous history of loss of fetus due to abortion (45/126) or congenital abnormality (5/126), while in the non-infected group, abortions and congenital abnormalities were observed in 30/76 and 1/76 women, respectively.

Table 3. Frequency of pregnant women with *H. pylori* infection related to gestational age

Gestational age	*H. pylori +ve*		*H. pylori -ve*	
	NO.	%	NO.	%
1st trimester	52	41.26	33	43.42
2nd trimester	43	34.12	19	25.0
3rd trimester	31	24.60	24	31.57
Total	126		76	

Table 4. Distribution of infected pregnant women with *H. pylori* based on parity

Parity	*H. pylori +ve*		*H. pylori -ve*	
	NO.	%	NO.	%
Primigravida	40	31.74	30	39.47
Multigravida	86	68.25	46	60.52
Total	126		76	

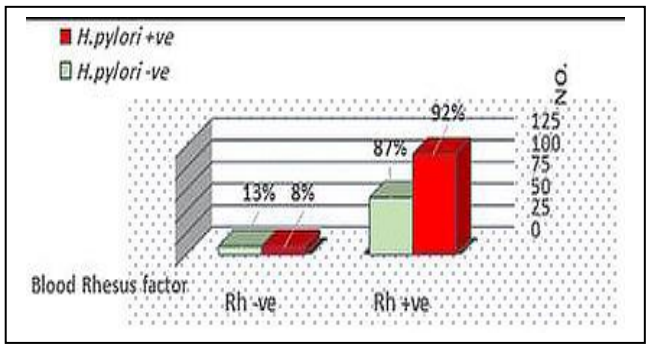

Figure 3. Pregnant women with *H. pylori* infection related to Rhesus blood factor

Table 5. Pregnant women with *H. pylori* infection related to blood group and Rh factor

Blood group and Rh factor	*H. pylori +ve*		*H. pylori -ve*	
	NO.	%	NO.	%
O +	42	33.33	27	35.52
A +	32	25.39	21	27.63
B +	32	25.39	16	21.05
AB +	9	7.14	5	6.57
O -	4	3.17	4	5.26
A -	4	3.17	1	1.31
B -	2	1.58	2	2.63
AB -	1	0.79	0	0
Total	126		76	

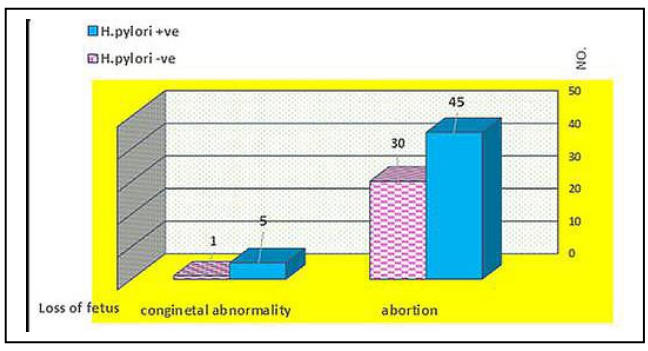

Figure 4. Pregnant women with *H. pylori* infection that had a previous abortion or fetal abnormality

4. Discussion

H. pylori infection may interfere with the absorption and metabolism of trace elements, especially during pregnancy increasing morbidities. The current study examined pregnant women with gastric upset and severe episodes of nausea and vomiting (morning sickness). It was found that 62% of the women had *H. pylori* infection, which was in agreement with the findings of studies previously performed in Turkey in which the prevalence rates of pregnant women with *H. pylori* infection were 56.8% and 61.5% in 2007 and 2006, respectively (11, 12). However, in Iran and Israel, the positive seroprevalence of *H. pylori* in pregnant women was estimated at 45.9%. The prevalence of *H. pylori* infection in pregnant women varies in different geographical regions ranging from 7.9% to 94%. In Asian, European, and American women, it ranged from 24% to 61%, 7.5% to 42.9%, and 50% to 70%, respectively; moreover, in African countries, it is more than 52% (13). In Chilean pregnant women, *H. pylori*-positive infection was estimated at 68.6% (14). A recent study by Baingana, Enyaru (15) estimated the prevalence of *H. pylori* infection at 60.5% in pregnant women in Kampala. However, other studies showed that about 24.1% of pregnant women had seropositive *H. pylori* associated with poor socioeconomic status (16). The differences in the seroprevalence of *H. pylori* in the present study with other studies may be due to study population, sample size variation, socioeconomic conditions, and level of education; moreover, they may depend on geographical area, poor sanitation, and crowded families, especially in developing countries, compared to developed countries, in addition to different methods in the diagnosis of *H. pylori* infections.

The most affected age group in the current study was 20-24-year-old (32.53%) pregnant women from rural areas (68.25%) rather than urban areas (31.74%). This result is in line with the findings of a study that determined the mean age group of pregnant women with *H. pylori* infection at 20.9±2.7 (18-35) years (17). Furthermore, a seroepidemiological study reported the

mean age group of pregnant women with *H. pylori* infection at 24.2 years (52.2%) (18). Other studies reported the mean ages of 29.6 and 32.2 years in 73% and 28.5% of the patients, respectively (19). These results may be attributed to the low educational level, poor sanitation, and crowded families in rural areas, especially in developing countries. All these will increase the acquisition of the bacteria and their spread. These socioeconomic factors may also have accounted for the higher prevalence of the bacteria in multiparous women and in women whose occupation was farming, compared to nulliparous or other occupational groups.

The epigastric pain is the most common sign and symptom of pregnant women with *H. pylori* infection (73%) (92/126), followed by nausea and vomiting (69.8%) (88/126) in the current study, compared to non-infected pregnant women during the first (first three months) (n=52; 41.26%) and second trimester (after first three months of gestational age) (n=43; 34.12%). These results are consistent with the findings of a study by Poveda, Carrillo (14) who indicated that 72.5% of the pregnant women had dyspepsia and *H. pylori* infection. Moreover, 79.4% of the women showed pregnancy hyperemesis (nausea and vomiting), and gastric discomfort was reported in 73.4% of the pregnant women who had *H. pylori* infection during the first three months, whereas 53.7% of them continued with gastric discomfort after the first three months.

Moreover, in line with the results of other studies, it was mentioned that infected pregnant women with *H. pylori* presented with vomiting (64.4%). Vomiting in early pregnancy compromised 62.4% of women, and persistent vomiting was observed in 66.4% of women in mid-pregnancy (20). The multigravida pregnant women had seropositive *H. pylori* in the present study (68.25%) which was more, compared to primigravida women (31.74%). This result is consistent with the findings of other studies that mentioned a 68.8% infection rate in the primigravida women, while 87.5% of the participants were married (17). In addition, a study conducted in Addis Ababa mentioned the infection rates of 30.8% and 34.1% in primigravida and multigravida women, respectively (21).

Regarding the ABO blood group and Rh factor, in this study, O^+, as well as A^+ and B^+ accounted for 33.33% and 25.39% of the infections in the cases, respectively; however, the less infected blood group was AB^- in one (0.79%) pregnant woman with positive *H. pylori* infection, which was in line with the results of a study conducted in the Kurdistan region of Iraq indicating O^+, A^+, and B^+ accounted for 41.8%, 32.0%, 19.5% of the infection in cases with seropositive of *H. pylori* (Rh^+ 92.5%), respectively (22).

This may explain more susceptibility of O blood group to *H. pylori* infection, and some studies concluded that the gastroduodenal mucosal cells expressed H antigen receptor to *H. pylori* that adhere to it, and these results are in line with the findings of other studies (23, 24). ABO blood group antigens on the RBC varies in human populations in the world, and they are considered the biomarkers of any individuals that stayed for lifelong.

The findings in the current study showed that the pregnant women with *H. pylori* infection had a previous history of loss of fetus due to abortion or congenital abnormality that occurred in 45/126 and 5/126 cases, respectively. These findings are in line with the results of other studies reporting that pregnancy with *H. pylori* infection is associated with many adverse pregnancy outcomes related to severe nausea and vomiting, including abortions, neonatal neural tube defects, anemia, intrauterine fetal growth retardation, pre-eclampsia, and thrombocytopenia (25, 26).

The relationship between *H. pylori* and hyperemesis gravidarum may be attributed to the hormonal changes during pregnancy, including elevated steroid and human chorionic gonadotropins. This results in fluid accumulation, followed by extracellular and intracellular volume displacement that leads to pH changes in the stomach and decreases the motility of

the gastrointestinal tract, which enhances the chance of *H. pylori* infection.

That causes gastritis leading to decreased gastric acid and increased colonization of *H. pylori* itself damaging the gastric cells that are producing gastric acid. Subsequently, *H. pylori* sequestrates the iron in lactoferrin, and then the availability of iron will be decreased by bacterial host competition for iron resulting in decreased iron absorption and anemia in pregnant women. In addition, decreased gastric acid will lead to difficulty in taking nutrients from animal protein, such as B12 (27).

Accordingly, severe anemia in pregnant women induces weight loss leading to insufficient weight gain, and it will be associated with bad pregnancy outcomes, such as preterm labor, small for gestational age, as well as prenatal and maternal mortality. These are the negative effects of *H. pylori* infection in pregnant women, which are either locally of gastrointestinal symptoms and systemically affects placenta resulting in preterm labor, small for gestational age, fetal malformations, and preeclampsia.

Furthermore, our findings which are in line with the results of a study by Moretti, Figura (28) indicate that the infected women with *H. pylori* have fertility problems, especially when they have CagA positive *H. pylori*. Moreover, the patients will have antibodies against it in the cervical mucus and follicular fluid which can decay the motility of sperm and cause immunological cross-reaction with spermatozoa, thereby preventing the fusion of sperm and oocyte, elevating the risk of preeclampsia, and increasing the risk of fetal mortality.

This study found that the hyperemesis (severe nausea and vomiting), dyspepsia, and other gastrointestinal symptoms during pregnancy are related to the infection with *H. pylori* so that it is a risk factor for complications in pregnancy, followed by poor outcomes, especially in developing countries, such as Iraq. These results can be minimized by improving the socioeconomic and sanitation conditions. *H. pylori* infection in pregnancy is considered a health problem and should be treated before and during pregnancy. Further investigations are required in this regard, and researchers are suggested to conduct studies on the RBC antigens to recognize the pathophysiology related to *H. pylori* infection.

Authors' Contribution

Study concept and design: A. Z. R.
Acquisition of data: A. Z. R.
Analysis and interpretation of data: A. Z. R.
Drafting of the manuscript: A. Z. R.
Critical revision of the manuscript for important intellectual content: A. Z. R.
Statistical analysis: N. I. S.
Administrative, technical, and material support: H. S.

Ethics

The medical ethical review committees of all participating study centers approved this study. Informed consent was obtained from all subjects.

Conflict of Interest

The authors declare that they have no conflict of interest.

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