Association between Hyperemesis Gravidarum in Iraqi Women with Helicobacter pylori Infection
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ABSTRACT
Background: Helicobacter pylori are gram-negative microaerophilic bacteria, and it is considered prevalent bacteria that affect people when transmitted fecally or orally. The infection in the acute stage manifests as stomach pain and acute gastritis, but the chronic infection causes peptic ulcers and gastritis, 2% of which may progress to stomach cancer. Nausea and vomiting during pregnancy, which may occur in 75% of pregnant women in the first three months and hyperemesis gravidarum, which is extreme, persistent nausea and vomiting during pregnancy that occurs in about 2% only.
Objective: Finding out how H. pylori infection relates to hyperemesis gravidarum was the main objective of this work.
Subjects and Methods: One hundred blood samples were taken from people aged (16-35) years for the period from 10/1/2021 to 1/3/2022. Subjects were divided into four groups. The first group included twenty-five patients with severe H.G, the second group had twenty-three patients with mild H.G, the third group had twenty–two patients with a few H.G, and the fourth group included thirty pregnant without H.G. Measurements were made for all study groups to anti-IgA Ab, anti-IgG Ab, and anti-Cag A Ab level by enzyme-linked immunosorbent assay (ELISA) technique.
Results: The statistical analysis showed a highly significant increase in the concentration of IgA in H.G compared to the control group (p > 0.01), a highly significant elevation in the concentration of IgG in H.G compared to the control group (p > 0.01), and a significant increase in concentration of anti-CagA Ab in H.G compared to control group (p>0.05).
Conclusion: The present study shows that infection with Helicobacter pylori plays a role in hyperemesis gravidarum.
Keywords: Pregnant women, H.pylori, ELISA.

INTRODUCTION
Helicobacter pylori (H. pylori) infects more than half of the world’s humans. A gram-negative bacterium called H. pylori colonizes the stomach epithelium. It is a flagellated, helical bacillus, microaerophilic, fastidious bacterium, and slow-growing. This bacteria is known to be associated with gastric epithelial cells, which contributes to the success of its infection and is one of the major causes of gastric cancer.

H. pylori has microbiological features that allow it to live in extremely adverse conditions, such as the gastric acidic climate. Infection can be transmitted primarily via the oral-fecal route, in particular via polluted water and food. As shown by the isolation of the bacterium in saliva and dental plaque, oral-oral transmission is also possible.

The bacteria are a peptic ulcer and chronic gastritis pathogenic cause. Its infection can also be associated with several elderly cardiovascular disorders, such as arteriosclerosis, coronary heart disease, and cerebral infarction, with deleterious effects on their health. To survive in the stomach, it creates an exceptionally potent urease that can neutralize gastric acid, pierce, and colonize the gastric epithelium. Acute H. pylori infection also affects the mechanism of the parietal cell proton pump, increases cytokine production, and stimulates neural pathways that stimulate somatostatin and inhibit the production of both histamine and acid secretion. These mechanisms combat the stomach's acidic condition (the first line of defense) and are crucial to H. pylori's survival and colonization. In addition to its role in acid neutralization, urease contributes to the pathogenicity of H. pylori by developing ammonia (disrupting cell junctions and destroying epithelium) and reactive oxygen species, triggering lipoygenase, inducing angiogenesis, factor-induced hypoxia, and apoptosis. H. pylori induce activation of most components of innate immunity (epithelial, neutrophil, macrophage, and dendritic cells) and adaptive immunity (B and T cells).

Following bacterial adhesion, the cag type IV secretion system translocates the terminal gene product of the cag island, CagA, into host cells. Gastric epithelial cell hyperproliferation and gastric cancer develop in transgenic mice that overexpress CagA, this molecule has been identified as a bacterial oncoprotein. CagA is a 120–140 kD protein with a carboxyl-terminal variable region containing tyrosine phosphorylation motifs (glutamate-proline-isoleucine-tyrosine-alanine, EPIYA). H. pylori infection is a leading cause of the peptic ulcer, gastric cancer, gastric lymphoma, and pregnancy-related clinical events, including HG and preterm birth (PTB). It has also been shown that pregnant women with H. pylori infection experience
substantially higher pregnancy-related diseases than those without H. pylori \(^{(10)}\).

The connection between maternal \(H. \text{ pylori}\) infection and nausea and vomiting while pregnant has been the subject of numerous obstetric investigations. In addition to maternal serum, the fetal umbilical cord and maternal fecal material were examined for signs of \(H. \text{ pylori}\) infection \(^{(11)}\).

Prevalence of hyperemesis gravidarum varies from 0.3 to 1.5% of all live births. The exact cause is not well known and is probably multifactorial. It is the most common cause of hospitalization in the first half of pregnancy and second only to preterm labor for pregnancy overall. The etiology of H.G remains unknown, but a number of possible causes have been studied as endocrinal, immunological, psychological, metabolic, genetic, and even infectious such as \(H. \text{ pylori}\) infection \(^{(12)}\).

The aim of the study to find the association between Helicobacter pylori infection and Hyperemesis gravidarum.

SUBJECTS AND METHODS

Studied subject samples

The study included one hundred women during the first trimester of pregnancy from ALAlawia Teaching Hospital for Maternity in Iraq during the period from October 2021 until March 2022. Ages of total pregnancy ranged from (16-35) years. Total patients were divided into four groups as follows: Group one: Included 25 pregnant with severe vomiting. Group two: Included 23 pregnant with mild vomiting, and Group three: included 22 patients with few vomiting. Group four: Included 30 pregnant without vomiting.

Ethical considerations

The study concept for human studies was approved from Baghdad University's College of Science and Al Alawia Teaching Hospital for Maternity by The Institutional Ethics Committee. Additionally, before taking part in the study, each individual gave written, informed consent. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Blood samples collection:

Five milliliters of blood were drawn, put in a vacuum gel plain tube, and left to stand at room temperature until the coagulant formed, centrifuged at 3000 rpm for 10 minutes. The serum samples were divided into Eppendorf tubes. Until immunological tests were conducted, the serum samples were kept at (-20°C).

Detection of anti-\(Helicobacter \text{ pylori}\) IgA, IgG, and anti-Cag Ab levels by enzyme-linked immunosorbent assay (ELISA).

All the studied pregnant with H.G group, and pregnant without H.G (control group) individuals were supplied to determine the antibacterial \(H. \text{ pylori}\) Ab IgA (Demeditec / Germany), and estimate the level of anti-\(H. \text{ pylori}\) Ab IgG (Demeditec / Germany) and anti-Cag A (Shanghai YL Biotec / China) by using the ELISA technique according to the protocol of the kit as per method \(^{(13)}\).

Statistical analysis

Quantitative data were presented as mean±standard deviation (SD) and were compared by one-way ANOVA test \(^{(14)}\) followed by LSD test as post-hoc test. P<0.05 was considered significant.

The mean level of anti-\(H. \text{ pylori}\) IgA antibody in sera of pregnant women with H.G and control group

In the current investigation, there was a significant increase in the concentration of \(H. \text{ pylori}\) IgA Ab in the sera of pregnant women with various levels of H.G (\(p \leq 0.01\)) compared to the command group (Figure 1), and there is also an obvious difference between severe group and each of mild and few groups.LSD (9.358)
The mean of anti-\textit{H. pylori} IgA Ab (U/ml) in a different group of the study:

The mean level of anti-\textit{H. pylori} IgG antibody in sera of pregnant women with HG compared to the control group.

The study's findings showed a highly substantial elevation ($P \leq 0.01$) in the concentration of \textit{H. pylori} IgG Ab in pregnant women with severe vomiting, pregnant women with mild vomiting, and pregnant women with few vomiting compared to the control group (Figure 2), and there is also an obvious difference between severe group and each of mild and few groups. LSD (29.07).
The mean level of anti-

*Helicobacter pylori* Cag A antibody in sera of pregnant women with H.G and control group

The concentration of Cag A antibodies in sera of pregnant with H.G of severe, mild, and few vomiting were significantly higher compared to the control group (Figure 3), and there is also an obvious difference between severe group and each of mild and few groups. LSD (1.389).
DISCUSSION

The result of the present study coincided with the study\(^{(15)}\) that also revealed that IgA-based serologic tests were much less useful and accurate than IgG-based tests, which demonstrated sensitivities of up to (100%) and specificities of (58–97%), indicating that IgG tests are more accurate and reliable. One possible explanation for these findings is that *H. pylori* infection is essentially an ongoing situation, so the systemic response starts with an increase in IgM and then progresses to an increase in IgA and IgG antibodies. IgG levels are elevated in nearly all *H. pylori* infections, but IgA levels exceed cut-off values in just about two-thirds of cases. While another study\(^{(16)}\) found a significant increase (p˂0.05) in the level of *H. pylori* IgA Abs when contrasted between study groups.

IgA directed against *H. pylori* has been shown to be inefficient at detecting *H. pylori* infection. In other words, the method's sensitivity is only marginally improved by IgA detection. Additionally, techniques based on antibody detection are unable to differentiate between an infection that is currently present and a contact that occurred in the past (the presence of live *H. pylori* in the stomach tissue). Blood contains quantities of long-lasting antibodies. The selection of antigens utilized to cover the ELISA wells is yet another crucial element of these procedures. In terms of specificity, these tests are effective at identifying local *H. pylori* strains in each nation\(^{(17)}\).

One study\(^{(12)}\) agrees with the present study, two groups were created from them: part 1, which consisted of 100 patients with vomiting, and part 2 (controlling group) that included 100 pregnant women without vomiting. In the first part, the authors found the mean of IgG (47.02 ± 36.51) while in the second part the mean (24.97 ± 19.58), and p-value ≤ 0.01.

Another study\(^{(18)}\) showed a serum anti-*H. pylori* IgG antibody by ELISA > 1.1 was associated with hyperemesis gravidarum at a sensitivity of 86.67%, and a specificity of 65.91%.

The result of this study was coinciding with one study\(^{(19)}\), which revealed that serum *H. pylori* IgG antibodies seropositivity was significantly different between the patient group (88%) and the control group (30%). Positive serum IgG concentrations were found in 44 / 50 of hyperemesis patients (88%) compared with 15 / 50 controls (30%). The statistical difference between the hyperemesis group and the control group was evident.

This result is in agreement with the result done by some researchers\(^{(20)}\) who claimed that the study groups had higher anti-*H. pylori* IgG Ab titers and the difference was very significant between the groups (P≤0.01). In primigravida women, the *H. pylori* group had a higher *H. pylori* IgG antibody titer than the control group, and this difference was statistically significant (P ≤0.05). The research groups, according to authors, had higher anti-*H. pylori* IgG Ab titers and the difference was determined to be extremely significant (P≤0.01). In primigravida women, there was a statistically significant difference in the *H. pylori* IgG antibody titer between the studied group (P ≤ 0.05). When comparing the
multigravida women in the vomiting group to the control group, the IgG antibody titer was likewise greater in the vomiting group, and the difference was also statistically significant (P ≤ 0.05). Despite the fact that 86.67% of study participants and control patients were found to be H. pylori IgG seropositive, the difference between the two groups was not statistically significant (P ≤ 0.05). They also proposed that the association between H. pylori infection and H.G could be brought on by the increased fluid accumulation and displacement of intracellular and extracellular volumes during the early stages of pregnancy as a result of increased steroid hormone, which in turn results in a change in the pH in the gastrointestinal tract. A latent H. pylori infection may become active as a result of this shift in acidity (21). Reduced immunity to the bacteria is another reason for this association since pregnancy is associated with changes in both humoral and cell-mediated immunity (22). Abnormal gastric emptying, decreased gastrointestinal motility, and hypersensitivity to gastric or duodenal distention in pregnancy all contribute to the predisposition of H. pylori to produce nausea and vomiting (23). Chronic infection has been found in cases of recurrent vomiting during pregnancy that is not responsive to supportive care (24).

The findings of the current study corroborate those of the different studies by (25) subanalysis of H. pylori-positive women revealed that patients who were CagA-positive were more likely than CagA-negative patients to experience daily vomiting. This study adds to the growing body of research showing that infection with the bacteria is linked to decreased total maternal weight gain and validates the link the elimination of H. pylori throughout patients with severe vomiting makes it an appealing target for future intervention research, but more crucially, which discovered evidence that H. pylori contribute to pregnancy with vomiting, and, reduced birth weight. H. pylori infection is linked to NVP, according to prior research, however, the degree and extent of these correlations differed amongst people and nations (26). Another study found that H. pylori continued to be a risk factor for daily vomiting even after correcting for ethnicity and socioeconomic level which provides more support for the hypothesis that H. pylori are causally engaged in the pathophysiologic state of H.G., many studies conducted by (27). Between the cases and controls in this sample, there were 170 women total, and the observed proportion of IgG-positive women was the same. IgG seropositivity, as well as CagA seropositivity, were not significantly linked to HG. The results remained unchanged after controlling for confounding variables such as the age of pregnant, and prior vomiting. Additional fecal antigen correction did not affect the findings regarding these correlations. Confounders and IgG seropositivity adjustments had no impact on the outcome. In this investigation, H. pylori exposure was not substantially linked to severe nausea and vomiting in Norwegian immigrant women. This was true regardless of how the exposure to the bacterium was identified—lgG seropositivity, CagA seropositivity, or the presence of H. pylori antigens in feces. These data may point to a lower association between H. pylori and HG than previously believed, particularly in populations where H. pylori infection is fairly common.

CONCLUSION:

The current study clearly demonstrated a substantial correlation between infection by H. pylori and nausea and vomiting, enabling us to conclude that H. pylori should be eliminated and taken into account as one of the risk factors for H.G, pointing to H. pylori as one contributing component of this pregnancy problem.

REFERENCES


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