The role of Helicobacter Pylori in Hyperemesis Gravidarum

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OBJECTIVE: The aim of this study was to investigate the role of Helicobacter Pylori in the etiology of hyperemesis gravidarum.
STUDY DESIGN: 50 pregnant women who consulted our clinic for nausea, vomiting and weight loss and diagnosed with hyperemesis gravidarum as a result of the examinations and inspections, constituted the study group and 88 pregnant women who didn't have such complaints constituted the control group. In both groups, serum Helicobacter Pylori IgG was investigated. The results were evaluated using the Fisher's Exact Test.
RESULTS: Helicobacter Pylori IgG was detected to be positive in 48 of 50 patients (96%) who were diagnosed with hyperemesis gravidarum, whereas Helicobacter Pylori IgG was detected to be seropositive in 73 of 88 patients in the control group (82.9%). The intergroup difference was found to be statistically significant.
CONCLUSIONS: Helicobacter Pylori infection plays a role in the etiology of hyperemesis gravidarum.
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Key Words: Hyperemesis gravidarum, Helicobacter Pylori

Nausea and vomiting which are the first subjective findings of pregnancy may either remain within limits that may be accepted as physiologic or may be a component of a disease resulting in serious outcomes in pregnant women. Hyperemesis gravidarum is a clinical condition which may lead to fluid-electrolyte imbalance characterized by ketonuria, and weight loss as well as severe nausea and vomiting in pregnancy. It usually starts following the 4th week of pregnancy and ends before the 20th week. The etiology of Hyperemesis gravidarum is not well-known and the increasing HCG and steroid levels observed in pregnancy are the factors, mostly considered.[1,2]

Helicobacter Pylori is a slow-growing, relatively motile, gram-negative, microaerophilic, spiral microorganism, presumed to be colonized in the gastric mucosa. It is observed in approximately 40% of the population in well-developed countries and in up to 95% of the population in other countries.[3]

In certain trials, the fact that the H. pylori IgG frequency, an indirect marker of H. pylori infection in the stomach, was detected to be higher in the group consisting of pregnant women with Hyperemesis gravidarum, compared to the asymptomatic pregnant group, suggested that H. pylori infection could trigger hyperemesis.[1,2]

In our study, we aimed at investigating the role of Helicobacter Pylori in the etiology of Hyperemesis gravidarum by comparing the serum Helicobacter Pylori IgG levels of pregnant women with Hyperemesis gravidarum and the control group consisting of pregnant women with no complaints.

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Material and Methods

fifty pregnant women who consulted the Haydarpaşa Numune Training and Research Hospital, Obstetrics and Gynecology Clinic for nausea, vomiting and weight loss and diagnosed with hyperemesis gravidarum as a result of the examinations and inspections performed and 88 pregnant women who didn't have such complaints were included in the study as the study and control group, respectively. Both groups consisted of women who were between 6th and 15th weeks of pregnancy.

The diagnosis of hyperemesis gravidarum was established by the positive ketone results obtained in the qualitative measurement of ketones in urine performed in pregnant women in the first trimester (between 6^{th} and 15^{th} weeks of pregnancy), who had vomiting 3 times a day or more and experienced a weight loss of 3 kg and more within the last one month. The urinary analyses were performed using Urisys 2400, Hitachi Ltd., Tokyo, Japan. [0 (-), 5 mg/dl (+), 15 mg/dl (++), 50 mg/dl (+++), 150 mg/dl (++++)].

Healthy pregnant women in the first trimester with no complaints of nausea and vomiting, in whom no ketones were detected in urine were included as the control group.

In all pregnant women, transvaginal USG was performed using a 6.5 Mhz probe, following the gynecologic examination (Hitachi EUB-515A, Japan). Ultrasonography evaluated whether the pregnancy was intrauterine or not, the discrimination of single or multiple pregnancy, fetal cardiac activity, yolk sac and the crown-rump length. The pregnant women whose last date of menstruation and crown-rump length were inappropriate, ectopic pregnancies, abortuses, mole pregnancies and multiple pregnancies were excluded from the study.

Table 1. The anthropometric and laboratory data of the pregnant women in the hyperemesis gravidarum and control groups.

	The group with hyperemesis gravidarum (n=50)	The control group (n=88)	P-value
Age (years)	25.6 ±5.1 (17-43)	26.8 ±5.2 (16-39)	0.18*
Week of pregnancy (according to SAT)	9.7 ±2.2 (6-15)	10.5 ±2.3 (6-15)	0.052*
Mean USG Measurements (BPD,CRL)	9.4 ±2.2	10.3 ±2.2	0.018**
Gravida	1.96 ±1.03(1-5)	2.38 ±1.7 (1-12)	0.07*
Parity	0.9 ±0.9 (0-4)	1.1 ±1.55 (0-11)	0.19*
Number of vomiting/day	4.4 ±1.7 (3-10)	0	
Weight loss (within the last month)	3.5 ±1.6 (0-10)	0	
Ketone (urinary)	1.7 ±0.8 (1-3)	0	
H.Pylori IgG titer	1.284±0.393 (0.117-2.028)	1.054±0.463 (0.137-1.851)	0.0025**

*P> 0.05 non-significant

**P< 0.05 significant

5 cc of venous blood were obtained from the antecubital area from all the women in the study and control group, irrespective of the fasting or fed state. Serum was separated via 6-minutes centrifuge at 4000 cycle/min and stored at -20°C. Sera collected were diluted at a ratio of 1/101. The patients' sera, positive control, negative control and the cut-off standard were studied together on the same micoelisa plate in the micoelisa device (Biomaster-Biokit, Italy), as directed by the manufacturer, using quantitative Helicobacter pylori IgG ELISA kit (IBL, Hamburg, Germany). At the end of the test, the results were automatically read by the device at 450 nm, and the absorbance values of the obtained results were recorded as positive or negative, by comparing to the cut-off value (cut-off standard = 0.538).

The results obtained were recorded using the Microsoft Office 2000 Excel program. The Instat program was used for the statistical calculations.

After the serum H. Pylori IgG titers of the women in the study and the control group were identified, an evaluation was made using the Fisher's Exact Test. P< 0.05 was accepted as the limit of statistical significance.

Results

No significant difference was observed between the age, gravida, parity and the mean week of pregnancy of the patients in both groups. The anthropometric and hormonal data are provided in Table 1 for the cases constituting the hyperemesis gravidarum group and the control group.

The mean H. Pylori IgG titers of the women in the study and the control group were detected as 1.284±0.393 (0.117-2.028) and 1.054±0.463 (0.137-1.851), respectively. When H. Pylori IgG titers of the two groups were compared, P was detected to be 0.0025 and found to be statistically significant (Table 1).

Helicobacter Pylori IgG was detected to be positive in 48 of 50 patients (96%) who were diagnosed with hyperemesis gravidarum, compared to 73 of 88 patients in the control group (82.9%). By the Fisher's Exact Test, the P value, odds ratio and the 95% confidence interval were detected as 0.03, 4.93 and 1.078-22.55, respectively.

The difference between the H. Pylori IgG positivity ratios of the patients with hyperemesis gravidarum and the patients in the control group was found to be statistically significant.

Discussion

Helicobacter Pylori is a slow-growing, relatively motile, gram-negative, microaerophilic, spiral microorganism, presumed to be colonized in the gastric mucosa. It is observed in approximately 40% of the population in well-developed countries and in up to 95% of the population in other countries.[3] It has been considered to be associated with peptic ulcer and recently, with functional dyspepsia.[4]

It's been suggested that pH changes may occur in the stomach due to the intracellular and extracellular fluid exchange and fluid retention with the effect of the increased levels of steroid hormones in hyperemesis gravidarum and that the H. pylori infection manifestation which may develop as a result of this, may trigger hyperemesis gravidarum.[1,2]

The hypothesis that H. Pylori infection may trigger hyperemesis gravidarum in pregnant women has originated from the detection of a higher H. Pylori IgG frequency (an indirect marker of H. Pylori infection in the stomach) in the pregnant women with hyperemesis gravidarum, compared to the asymptomatic group in certain trials.[1,2] In some of the tri-

als supporting this hypothesis, a rapid improvement was reported following erythromycin treatment administered for other reasons in patients with serious hyperemesis who required intravenous fluid treatment,[5] Similarly, various trials were published, which reported a clinical improvement following administration of antibiotics and proton-pump inhibitors or H2-receptor blockers for 2 weeks in patients followed with a diagnosis of persistent hyperemesis gravidarum.[6]

Karaca C et al.[7] reported that H. Pylori IgG was high in pregnant women with hyperemesis and that a low socioeconomic level was a major risk factor for H. Pylori infection in pregnant women with hyperemesis gravidarum. While another study by Kazerooni T et.al.[8] again reported a high H. Pylori IgG in pregnant women with hyperemesis, Berker et.al.[9] reported no statistical significance between pregnant women with or without hyperemesis, with respect to H. Pylori IgG.

In our study, Helicobacter Pylori IgG was detected to be positive in 48 of 50 patients (96%) who were diagnosed with hyperemesis gravidarum, whereas Helicobacter Pylori IgG was detected to be seropositive in 73 of 88 patients in the control group (82.9%). The intergroup difference was found to be statistically significant.

As the use of clarithromycin is not safe in pregnancy, agents such as amoxicillin and metronidasole may be administered for the H. Pylori eradication, however these are not as effective as clarithromycin.[10] The American Disease Control and Prevention Center has stated that metranidasole can be used in each trimester of pregnancy. An alternative treatment is co-administration of amoxicillin and omperazole; however, none of these treatments are as effective as the triplet therapy for the eradication of H. pylori (amoxicillin, clarithromycin, omeprazole). Consequently, although H. Pylori plays a major role in the etiology of hyperemesis, we still don't have adequate safe and effective therapeutical choices.

In our study, we administered a fluid-electrolyte therapy and an antiemetic treatment instead of an antibiotic treatment protocol for Helicobacter pylori both in the group with hyperemesis gravidarum and the control group.

Performing H. Pylori eradication in pregnant women with risk factors prior to pregnancy in order to provide protection against the disease is not a practical approach because the H. Pylori incidence reaches a level of 90% in countries of low socioeconomic status, as our country. In addition, besides H. pylori eradication, performing endoscopy or IgG examination for H. Pylori screening in people with no peptic complaints in the society is quite costly. However, Helicobacter pylori screening and eradication may be recommended prior to pregnancy for women with a history of severe with hyperemesis gravidarum in their previous pregnancy. Helicobacter pylori IgG measurement should be considered as a suitable alternative, with its higher sensitivity and specificity, compared to other antibody measurements.

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