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The Prevalence of Helicobacter pylori in the Stools of Pregnant Women with Hyperemesis Gravidarum

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ABSTRACT

Objectives: This study aimed to investigate the role of Helicobacter pylori (HP) in hyperemesis gravidarum (HG) by detecting HP immunoglobulin G (IgG) antibody in serum and HP antigen in stool.

Methods: Pregnant women between the ages of 18 and 35 and between 6 and 18 weeks of gestation who applied to the obstetrics clinic between January and December 2022 were included in the study. While pregnant women with HG were considered in the HG group, those without HG were considered in the control group. The sociodemographic and obstetrics characteristics and laboratory results of the participants were evaluated and compared between the groups. Anti-HP IgG screening was performed in serum, and the fecal HP antigen test was applied to stool samples.

Results: A total of 60 pregnant women, 30 (50.0%) in the HG group and 30 (50.0%) in the control group, were included in the study. While stool HP antigen positivity was found in 20 (66.7%) pregnant in the HG group, it was detected in 10 (33.3%) pregnant in the control group (p=0.010). However, serum HP IgG antibody positivity was in 22 (73.3%) pregnant in the HG group and 17 (56.7%) pregnant in the control group (p=0.176).

Conclusion: The HP stool antigen test may be employed at diagnosis because it is non-invasive, exhibits high specificity and sensitivity, and is economical and also an active infection marker. Further studies with larger studies are now essential to elucidate this subject.

Keywords: Antigens, Helicobacter pylori, hyperemesis gravidarum

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INTRODUCTION

Nausea and vomiting, which can be observed at a frequency of 50–60% in the first trimester of pregnancy and which generally disappear in the second trimester, can become resistant in 0.5–2% of cases and may lead to a clinical condition that causes weight loss and hypovolemia, known as hyperemesis gravidarum (HG).[1] HG is a severe complication of pregnancy (at least 5%) and can lead to electrolyte and acid-base imbalance as well as weight loss and ketonuria.[2] In addition to genetic and socioeconomic factors for HG, which is more common in developed Western countries, other risk factors include multiple pregnancies, molar pregnancy, hyperthyroidism, asthma, and gastrointestinal diseases like peptic ulcer. Endocrine factors (beta-human chorionic gonadotropin [HCG], estrogen, progesterone, thyroid hormones, and adrenal hormones), immunological factors, nutritional disorders, and psychological causes are responsible for the etiopathogenesis of HG.[3,4]

In addition to nausea and vomiting, HG can cause hypovolemia and hematocrit elevation due to hemoconcentration, as well as laboratory results such as an increase in urine density, keto-

nuria, hyponatremia, metabolic alkalosis, urea, and creatinine elevation, deterioration in liver function tests, and an increase in total bilirubin.[5] Gastrointestinal disorders such as gastroenteritis, hepatitis, and pancreatitis; genitourinary disorders such as pyelonephritis, and nephrolithiasis; metabolic disorders such as hyperthyroidism, porphyria, Addison's disease; and neurological disorders such as migraine and vertigo should be excluded in the differential diagnosis of patients with HG.[3] In addition to benign complications such as weight loss, alkalosis, and hypokalemia, severe life-threatening complications such as Wernicke's encephalopathy, central pontine myelinolysis, Mallory–Weiss tears, and liver and kidney failure can also be observed in HG.[4]

Antiemetics such as pyridoxine, doxylamine, prochlorperazine, and chlorpromazine therapy, antihistamines such as dimenhydrinate and diphenhydramine, motility regulators such as metoclopramide, and centrally-acting antiemetics such as corticosteroids can be used in HG, as well as supportive treatments such as diet, psychological support, acupuncture, and ginger.[2] Intravenous fluid and electrolyte replacement should be performed in cases requiring hospitalization, with total parenteral nutrition in severe cases.[5]

Helicobacter pylori (HP), a gram-negative spirochete, is a bacterium that lives under the gastric mucosa layer, can cause acute or chronic peptic ulcer as a result of suppression of the immune system, and can be transmitted by the fecal-oral or oral-oral routes.[6] Gastric pH generally rises due to increased steroidal hormones, immune system diseases, and the physiological effects of pregnancy, and HP infection can easily develop as a result. It is difficult for the antibiotics used in the treatment of HP infection to reach the bacteria through the bloodstream since these are located under the mucus layer. The most commonly employed therapeutic regimen in HP infection is macrolide group antibiotics together with a proton pump inhibitor.[7]

The objective of this study is to evaluate the relationship between HG with HP immunoglobulin G (IgG) antibodies and HP antigen positivity.

METHOD

Pregnant women between the ages of 18 and 35 and between 6 and 18 weeks of gestation who applied to the obstetrics clinic of our hospital between January and December 2022 were included in the study. The study group consisted of participants who could not be fed orally, who experienced severe nausea and vomiting more than 3 times a day, with at least +1 ketone positivity in the urine, and with at least 5% weight loss since the beginning of pregnancy. When the vomiting started and how many times it occurred a day were recorded during history-taking. Pregnant women without HG were included in the control group. Women with multiple pregnancies, thyroid disease, gastrointestinal disease, hepatitis, severe infection, trophoblastic disease, and psychosocial disorders were excluded. The flowchart of the study is shown in Figure 1.

DSS research sample size calculation software was used to calculate the sample size. At least 30 participants were required for each group to reveal differences at α=0.05 and β=0.20.[8]

The patients' sociodemographic characteristics, examination and ultrasound findings at the time of admission, and laboratory results were recorded. The age, gravida, parity, number of living children, complaints, ultrasonographic measurements, occupations, and education levels of all participants included in the study were also evaluated. Body mass index was calculated as body weight (kg)/ body length (m^2). Gestational weeks were determined based on the most recent menstrual period and ultrasonographically. Venous blood was obtained from all participants at their first outpatient clinic visits. The sera were then separated. Stool samples were also collected. Both

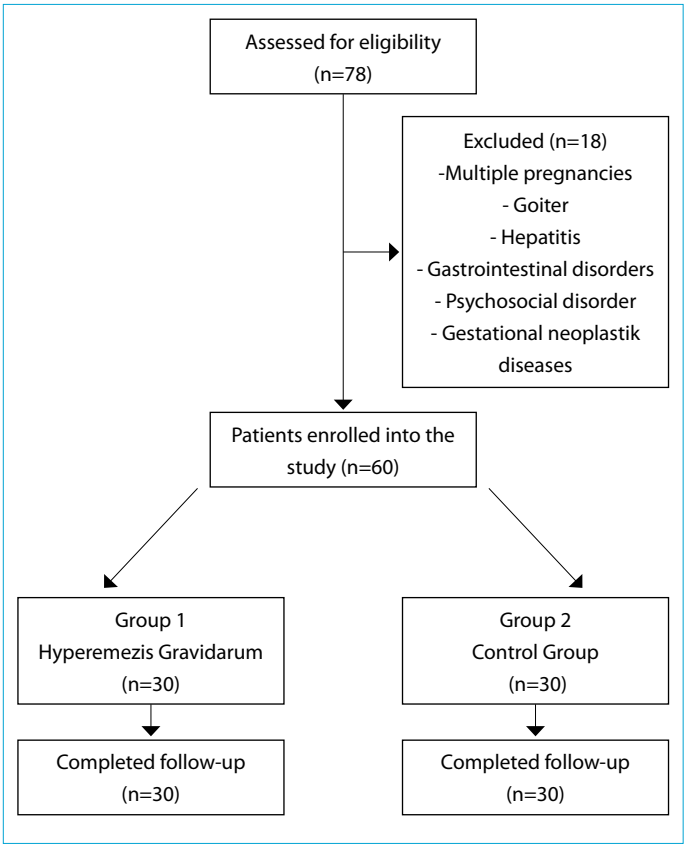

Figure 1. Flowchart of the study.

serum and stool samples were evaluated within 1 h. Anti-HP IgG screening was performed in serum samples with the rapid chromatographic qualitative membrane-based immunoassay method using a rapid cassette (Acon) kit. When four drops are placed into the well of the serum kit cassette, these react with the particles coated with HP antigen in the test kit. This mixture proceeds chromatographically through the test and reacts with immobilized anti-Helicobacter IgG. If the specimen contains an HP antibody, the colored line becomes prominent in the test area, and the development of this line indicates a positive result. If the specimen does not contain HP antibodies, no colored lines are formed, and the test is considered negative. Stool samples were studied using the qualitative lateral flow immunoassay method with the help of an immunochromatographic card test (Linear). The fecal HP antigen test includes a membrane coated with monoclonal antibodies against HP antigens in the test area. During the test, stool material reacts with anti-HP antibodies that have been previously dried on the strip, and the mixture moves across the membrane. In the presence of a positive result, the antigens reacting with the antibodies form a colored line. If there are no HP antigens in the stool, indicating the presence of active infection, no colored line is formed, and the test is considered negative. In addition, complete blood count, routine biochemistry, thyroid stimulating hormone, free T3, and free T4 were evaluated from blood samples taken on the first visit of the patients participating in this study. In addition, ketones and leukocytes were checked and recorded at complete urinalysis.

Data were analyzed on SPSS version 15.0 for Windows software (SPSS, Chicago, IL, USA). The Shapiro–Wilk test was used to determine the normality of the distribution of all continuous variables. Continuous variables were expressed as mean, standard deviation, and nominal data as frequency and percentages. Student's t-test was used to compare normally distributed variables between the groups, and the Mann–Whitney U-test for non-normally distributed variables. Categorical data were analyzed using Pearson's Chi-square or Fisher's exact test as appropriate. $P<0.05$ was considered statistically significant.

RESULTS

A total of 60 pregnant women, 30 (50.0%) in the HG group and 30 (50.0%) in the control group, were included in the study. The sociodemographic and obstetric characteristics of the participants are summarized in Table 1.

Table 1. Sociodemographic and obstetric characteristics of the participants

	Hyperemesis gravidarum (n=30)	Control (n=30)	p
Age (years)	26.6±4.7	28.0±6.0	0.309*
BMI (kg/m2)	29.2±4.4	25.3±5.6	0.118*
Gravity	2.0 (1.0-2.0)	2.0 (1.0–2.0)	0.412†
Parity	1.0 (0–1.0)	1.0 (0–1.0)	0.571†
Number of miscarriages	0.0 (0–0.0)	0.0 (0–0.0)	0.621†
Gestational age at admission (weeks)	10.0±2.7	10.5±2.0	0.461*
Professional status			
Working	8 (26.7)	10 (33.3)	0.573‡
Housewife	22 (73.3)	20 (66.7)	
Educational level			
Illiterate	5 (16.7)	3 (10.0)	0.407§
Primary education	10 (33.3)	12 (40.0)	
High school	11 (36.7)	7 (23.3)	
University	4 (13.3)	8 (26.7)	
Economic status			
Lower level	14 (46.7)	16 (53.3)	0.278§
Intermediate level	14 (46.7)	9 (30.0)	
High level	2 (6.6)	5 (16.7)	
Smokers	3 (10.0)	6 (23.3)	0.299§

Data are presented as mean±standard deviation, median (minimum-maximum) and n (%).

*Student t-test, †Mann–Whitney U test, ‡Pearson's Chi-square test, §Fisher's exact test.

No significant difference was found between the HG group and the control group in terms of all laboratory parameters (p>0.05). Laboratory test results of the participants are summarized in Table 2.

Serum HP IgG antibody positivity was in 22 (73.3%) pregnant in the HG group and 17 (56.7%) pregnant in the control group (p=0.176). On the other hand, while stool HP antigen positivity was found in 20 (66.7%) pregnant in the HG group, it was detected in 10 (33.3%) pregnant in the control group (p=0.010). The presence of HP antigen and IgG antibody according to groups are summarized in Table 3.

Table 3. Presence of Helicobacter pylori antigen and IgG antibody according to groups

	Hyperemesis gravidarum (n=30)	Control (n=30)	p
Serum HP IgG antibody			
Positive	22 (73.3)	17 (56.7)	0.176
Negative	8 (26.7)	13 (43.3)	
Stool HP antigen			
Positive	20 (66.7)	10 (33.3)	0.010
Negative	10 (33.3)	20 (66.7)	

HP: Helicobacter pylori, Ig: Immunoglobulin.
Data are presented as n (%).
Pearson's Chi-square test.

DISCUSSION

Ninety percent of nausea and vomiting in the first trimester of pregnancy can be controlled with mild and conservative methods.[9] However, the severity of nausea and vomiting may sometimes worsen, become continuous, and cause weight loss, dehydration, ketonuria, and acid-base imbalance. The etiopathogenesis of HG has not been fully elucidated, although the hormonal, immunological, psychological, gastrointestinal system, and nutritional disorders have all been implicated. High B-HCG hormone levels reduce gastric acidity, and HG is observed more frequently in these patients. In recent years, a relationship between dyspeptic symptoms and HP has been observed in peptic ulcers, and it is thought that HP may play a role in HG.[10]

Other tests used to detect HP are the urea breath test, rapid urease test, HP antigen stool test, and culture and histological evaluation. The non-invasive urea breath test exhibits a teratogenic effect since it involves radioactive carbon atoms, and its use is not recommended during pregnancy. Endoscopic biopsy, the gold standard, is less commonly employed today because of its high cost. Studies comparing pregnant women with HG and healthy pregnant women in Turkey have reported figures of HP IgG positivity of 60–80% in HG and 40–50% in the controls.[11-13] Reported rates in the USA are approximately 50% and 30%, respectively.[14,15] Alataş compared 100 participants at

Table 2. Laboratory test results of the participants

	Hyperemesis gravidarum (n=30)	Control (n=30)	p
Hb (g/dL)	11.4±1.7	11.5±1.4	0.569
Htc (%)	34.3±2.1	34.5±1.4	0.413
Leukocyte count (mcl)	11875.6±975.7	12336.6±1251.8	0.117
Platelet count (103) (mcl)	208.0±55.6	199.3±49.3	0.526
BUN (mg/dL)	14.4±6.0	13.2±5.4	0.413
Creatinine (mg/dL)	0.3±0.1	0.3±0.1	0.412
Alanine aminotransferase (U/L)	21.7±7.9	20.0±5.0	0.330
Aspartate aminotransferase (U/L)	22.2±8.6	22.8±8.3	0.785
Na (mEq/L)	133.1±3.0	133.8±3.5	0.418
K (mEq/L)	3.5±0.2	3.5±0.2	0.108
Cl (mmol/L)	102.6±6.6	101.8±6.4	0.367
TSH (µIU/mL)	2.1±1.2	1.8±1.0	0.203
fT4 (ng/dL)	1.3±0.4	1.2±0.4	0.327
fT3 (pg/dL)	3.1±0.6	3.2±0.3	0.330

Hb: Hemoglobin, Htc: Hematocrit, BUN: Blood urea nitrogen, Na: Sodium, K: Potassium, Cl: Chlorine, TSH: Thyroid stimulating hormone.
Data are presented as mean±standard deviation.
Student t-test.

gestational weeks 35–40 with 30 healthy nurses in terms of HP seropositivity. HP positivity was observed in 22% of the pregnant group and 40% of the health-care workers, the difference between the two groups being insignificant.[16] However, the result was not significant since the health workers were in the at-risk group.

Conflicting results have been reported in studies investigating HP seropositivity in pregnancies with and without HG, and the relationship between them has not been established. The rate of HP seropositivity varies from country to country in studies involving the prevalence of HP, having been reported as 19% in England, 25% in France, 81% in India, and 85% in Algeria, with higher values being determined in developing countries. The reported prevalence of HP in Turkey is approximately 30–40%.[12,13] In one multicenter study, the prevalence of HP was reported as 52.4% in patients with active dyspeptic complaints in the second trimester, and as 46.6% in those without dyspeptic complaints.[17] The first investigation of whether a relationship exists between HG and HP was conducted in 1998. A comparison of 105 pregnant women with HG and 129 controls revealed HP IgG antibody positivity values of 90.5% in the HG group and 46.5% in the control group.[18] The equivalent rates in another study were 91.5% and 44.8%, respectively.[19] Two separate studies from Iran reported rates of 81.5% and 88.9% in women with HG.[20,21] A study from Israel reported HP IgG positivity in 45.9% of term pregnant women.[22]

Ozdil et al. evaluated 41 women with HG and 40 asymptomatic pregnant women and reported HP IgG positivity rates of 46.3% and 67.5%, respectively, with positivity rates in stool antigen tests of 52.5% and 36.5%, respectively. The results of both tests were insignificant, but they highlighted the fact that the HP IgG antibody was more positive in the control group and the HP stool antigen in the study group. The authors concluded that stool antigen tests were superior to serological tests.[23] Cevrioglu et al. investigated the presence of HP in 27 women with HG and 97 asymptomatic pregnant women using serological and stool antigen tests. HP was detected in 85.2% of the women with HG and 72.5% of the asymptomatic pregnant women, the difference being insignificant. Examination of the stool antigen test revealed HpSA positivity in 40.7% of women with HG and 12.4% in asymptomatic pregnant women, and this difference was also significant.[24] HP was thus determined to play a role in HG. Aytac et al. performed stool antigen tests on 52 women with HG and 55 asymptomatic pregnant women and reported HP positivity frequency in stool antigen tests of 42.3% and 40%, respectively, although the difference was insignificant.[25] Karadeniz et al. investigated 31 women with HG and 29 control pregnant women and reported HP IgG positivity in 67.7% of the HG group and 79.3% of the control group. In the stool antigen test, the frequency of HP positivity was 22.6% and 6.9%, respectively, and the results of both tests were insignificant.[19] Those authors observed a high prevalence of HP due to the low socioeconomic levels of the participants in both groups but were unable to establish any relationship between HP and HG. In a study evaluating the relationship between socioeconomic level and HP in pregnancies, HP seropositivity was significantly higher, at a frequency of 89.9%, in pregnant women with HG and low economic levels, compared to 68.1% in the group with low economic status without HG.[26] In the present study, serum IgG antibody positivity was determined in 73.3% of the HG group (control group 56.7%), the difference between the groups being insignificant, while HP antigen positivity in stool was 66.7% (control 33.3%), which was significant.

The limitations of this study include the fact that it was conducted in a tertiary care institution and a single center.

CONCLUSION

The frequency of HP positivity in pregnant women with HG was 4 times higher than that in asymptomatic patients in this study, and HP was determined to play a role in HG. Active HP infection should be investigated, especially in pregnant women with resistant HG, and it should be eradicated in pregnant women with positivity. The HP stool antigen test may be employed in the diagnosis because it is non-invasive, exhibits high specificity and sensitivity, is economical, and is also an active infection marker. Further research on the subject is needed to gain a deeper understanding.

Disclosures

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Conflict of Interest: None declared.

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Ethics Committee Approval: Approval was obtained from the ethics committee of Pamukkale University Medical Faculty Hospital (Approval date: October 27, 2009, and Approval number: 33), and written and verbal consent were obtained from the participants.

Authorship Contributions: Concept – S.T., M.E.S.; Design – S.T.; Supervision – S.T., H.A.I.; Materials – S.T.; Data collection and/or processing – S.T., H.A.I.; Analysis and/or interpretation – S.T., H.A.I.; Literature search – S.T.; Writing – S.T., H.A.I.; Critical review – S.T., H.A.I.

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