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Helicobacter pylori seropositivity and the incidence of hyperemesis gravidarum

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Summary

Background:

We studied the incidence of *Helicobacter pylori* infection in patients with hyperemesis gravidarum (HG) in comparison with non-HG pregnant women, and investigated whether there was a correlation between positive serology for *H. pylori* IgG, the time of onset, and the duration of HG symptoms.

Material/Methods:

54 pregnant women with HG were enrolled in a matched case-control study. For each case in the group, a pregnant woman without HG matched for age, parity and gestational age was selected as a control. The patients in the experimental group were asked the exact time of symptom onset, and both groups were monitored during pregnancy for symptoms and outcome. Serum *H. pylori* IgG antibody was measured by enzyme-linked immunosorbant assay (ELISA).

Results:

Positive serum *H. pylori* IgG antibody was detected in 88.9% of the patients in the experimental group vs. 40.7% of the controls ($P < 0.001$). Three of the four patients with abortions in each group were seropositive. Age, parity, level of education, symptom onset, and duration and outcome of pregnancy were comparable in both seropositive and seronegative patients with HG.

Conclusion:

Although more patients with HG were seropositive for *H. pylori* infection than controls, we were not able to demonstrate correlation between seropositivity for *H. pylori* and the time of onset or duration of HG symptoms. Although *H. pylori* infection may be an important factor in exacerbating HG, it may not represent the sole cause of the disease.

key words:

morning sickness • pregnancy complications • serologic detection

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BACKGROUND

Nausea and vomiting during pregnancy (morning sickness) occur in 50% to 90% of all pregnant women in the first trimester. The typical onset is between 4 to 8 weeks of gestation, with symptoms continuing until 14–16 weeks [1–4]. An association with pregnancy has been documented on papyrus texts dating as far back as 2000 BC [5].

Hyperemesis gravidarum (HG) is a severe form of nausea and vomiting in pregnancy, often associated with weight loss, ketonemia, ketonuria, dehydration, electrolyte imbalance, and possible hepatic and renal damage [6], necessitating hospitalization. The actual incidence of HG has not yet been established, but has been reported to be 0.3–2% [6].

Different biological and psychological factors may play a role in triggering HG. Elevated serum steroid hormone and HCG concentrations, as well as gastric motility disturbances in early pregnancy, are thought to play a role in this condition.

Several reports have recently been suggested that there is an association between HG and *Helicobacter pylori* infection [7–10]. The mechanism has been theoretically explained by a sub-clinical *H. pylori* infection as a result of changes in steroid hormone levels and gastric pH in pregnancy. Also, some case reports have suggested that eradication of *H. pylori* infection ameliorates clinical HG [9,10]. Nevertheless, no conclusive evidence has been adduced to suggest a direct causal relationship between *H. pylori* infection and HG [11,12]. Serologic detection of *H. pylori* is a noninvasive technique with higher sensitivity and specificity to predict *H. pylori* infection [13]. Due to this noninvasive diagnostic method, it is possible to detect *H. pylori* infection in pregnant women and newborns [14].

In this study, we examined the incidence of *H. pylori* infection in patients with HG in comparison with pregnant women without HG and attempted to determine whether there was a correlation between positive serology for *H. pylori* IgG and the time of onset and duration of HG symptoms.

MATERIAL AND METHODS

Fifty-four pregnant women with HG were enrolled in the HG/H. *Pylori* study. Criteria for the diagnosis of HG included severe vomiting (more than 3 times a day), weight loss (more than 3 kg or 5% of body weight), and ketonuria. Patients with HG secondary to trophoblastic disease and multiple pregnancies were excluded. All the patients in the experimental group were 15 to 38 years old. Their gestational age was between 6 and 16 weeks, and the course of pregnancy was otherwise unremarkable.

For each case in the experimental group, a pregnant woman without HG, matched for age, parity and gestational age, was selected as a control subject. Gestational

Table 1. Characteristics of experimental and control groups.

Variable	Hyperemesis gravidarum (n=54)	Controls (n=54)
Age (years)*	24.98±4.05	24.72±4.44
Primigravida**	46 (85.2%)	47 (87.1%)
Multigravida**	8 (14.8%)	7 (12.9%)
Gestational weeks at time of blood sample (wk)*	8.52±1.33	9.02±1.42

*Mean±standard deviation;

**Number (percent)

age was determined using the date of last menstrual period and confirmed by ultrasonography. The characteristics of the patients in both groups are presented in Table 1.

The patients in the experimental group were asked the exact time of symptom onset, and both groups were monitored during pregnancy for symptoms and outcome. Venous blood samples were obtained at the first visit. *Helicobacter pylori* IgG antibody was measured using enzyme-linked immunosorbent assay (ELISA) kits. (HELICOBACTER PYLORI IgG, RADIM, Italy). The results were tested for statistical significance by the McNemar test for assessing the relation between seropositivity and HG for matched groups, the chi-square test to compare seropositive and seronegative groups with regard to education and gravidity, the Mann-Whitney U test to compare symptom duration and symptom onset, the Student t-test to compare age, and the Fisher Exact test to compare abortion in the two groups. A p value less than 0.05 was considered significant.

RESULTS

Positive serum *Helicobacter* IgG antibody was detected in 48 of 54 patients in the experimental group (88.9%) vs. 22 of 54 (40.7%) in the control group (McNemar $p < 0.001$, O. R. =27; CI 95%=24.8–29.2).

In each group, abortion occurred in 4 (7.4%) persons, and 15 persons (27.8%) had less than 12 years of education. Three of the four patients with abortions in each group were seropositive. On average, the abortion occurred in the 15th week of gestation. All other pregnancies ran an uneventful course and all had a positive outcome. No fetal malformations were observed.

In the HG/H. *pylori* experimental group, age, parity, level of education, symptom onset, and duration and outcome of pregnancy were comparable in both seropositive and seronegative patients (cf. Table 2).

DISCUSSION

Our study revealed higher *H. pylori* seropositivity in pregnant women with HG than in controls. This result is similar to previous studies reporting a seropositive rate of more than 85% *H. pylori* infection in patients with HG [7,8,12,15]; (Table 3).

Table 2. Characteristics of experimental group with regard to *Helicobacter pylori* seropositivity.

	Seropositive (n=48)	Seronegative (n=6)	
Age (years)*	25.19±3.94	23.33±4.93	N.S.
Primigravida**	40 (83.3%)	6 (100%)	N.S.
Multigravida**	8 (16.7%)	0	N.S.
Education			
<12 years **	14 (29.2%)	1 (16.7%)	N.S.
≥12 years	34 (70.8%)	5 (83.3%)	N.S.
Symptom onset (gestational week)*	6.96±0.87	6.67±0.81	N.S.
Symptom duration (week)*	9.44±1.27	8.67±1.63	N.S.
Abortion	3 (6.3%)	1 (16.7%)	

*Mean±standard deviation;

**Number (percent)

Table 3. *Helicobacter pylori* seropositivity in hyperemesis gravidarum.

	Hyperemesis gravidarum	Controls	Significance of difference
Frigo et al [7]	95/105 (90.5)	60/129 (46.5)	P<0.001
Kocak et al [8]	87/95 (91.5)	52/116 (44.8)	P<0.001
Erdem et al [12]	40/47 (85.1)	25/39 (64.1)	P<0.05
Hayakawa et al [16]	18/34 (52.9)	6/29 (20.6)	P<0.0005
Our study*	48/54 (88.9)	22/54 (40.7)	P<0.001

Data presented as number (percent);

*McNemar test

One possible explanation is that, in the early phase of pregnancy, the increased accumulation of fluid and the displacement of intracellular and extracellular volume caused by the increase in steroid hormones results in a change of pH. In the gastrointestinal tract, this could lead to the manifestation of a latent *H. pylori* infection [7].

GI symptoms during pregnancy are more common in primigravida women, as well as in younger and less educated women [11]. Thus we matched the control subjects with cases for age, parity, and gestational age, and also matched the number of less educated women (<12 years of education) in both groups.

Although a significant rate of seropositivity for *H. pylori* in patients with HG was revealed, we could not demonstrate any correlation between the onset and duration of symptoms and seropositivity in the HG group. These results may reflect either the existence of underlying mechanisms other than *H. pylori* in the exacerbation of HG, or the complex nature of the *H. pylori* infection-related symptoms. This is consistent with findings by Erdem et al. [12] and Nakajima et al. [16], whose research failed to reveal a correlation between seropositivity for *Helicobacter pylori* in HG and the severity of clinical symptoms. Future studies may elucidate the association of HG and *H. pylori*.

Other case reports [9,10] have suggested that the etiological role of *H. pylori* in HG is due to a response to oral antibiotics. One of these was a report of two cases of severe HG who responded rapidly to oral erythromycin therapy [9]. Although there is controversy surrounding the use of antisecretory agents (as a part of classic therapy for *H. pylori* infection) during pregnancy, Jacoby et al. [10] administered these agents to three *H. pylori* seropositive patients and observed regression of symptoms. Their report failed to include histological examination following therapy, however.

CONCLUSION

According to the findings of our study, *H. pylori* infection would seem to be an important factor in the exacerbation of HG, but it does not seem to be the only cause of the disease. In regard to improved management of *H. pylori* infections, we recommend that women who are considering pregnancy in the near future should be tested for *H. pylori*, and the infection should be brought under control prior to pregnancy. Also, prospective, randomized trials are needed in pregnant women with HG to determine whether there is association between HG and *H. pylori* infection by showing the effectiveness of pharmacotherapy confirmed by direct gastric biopsy or urea breath test.

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