World Applied Sciences Journal 28 (12): 1918-1922, 2013
ISSN 1818-4952
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DOI: 10.5829/idosi.wasj.2013.28.12.2226

# Comparison of Helicobacter Pylori Infection Between Pregnant Women with Hyperemesis Gravidarumand and Controls

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**Abstract:** *Background:* A small percentage of pregnant women experience a severe form of nausea and vomiting called Hyperemesis gravidarum. To compare the rate of H. pylori infection between an Iranian samples of pregnant women who were suffering from hyperemesis gravidarum (HG) in their first trimester and control pregnant women without HG. *Methods*: In this cross-sectional study 30 pregnant women who suffered from HG and 30 controls were enrolled. H. pylori specific serum IgG was measured using ELISA method. IgG titers of more than 10, less than 10 and between 5 and 10 U/mL were considered as seropositive, seronegative and suspicious for H. pylori infection, respectively. *Results:* No significant difference was seen between the two groups regarding age, gestational age and gravidity. Twenty-four patients (92.3%) in HG group had H. pylori infection, while this rate was only 7.7% (two patients) in control group ($P < 0.001$). No correlation was detected between IgG titers and either maternal age ($t=2.4$, $P = 0.12$) or parity ($x^2=0.2$, $P = 0.6$). *Conclusion:* There was significantly higher rate of H. pylori infection in HG pregnant women in their first trimester in comparison to controls.

**Key words:** Hyperemesis gravidarum · Helicobacter pylori · Pregnant women

## INTRODUCTION

Nausea and vomiting is a major complaint in 70-80% of pregnancies. The typical onset is between 4 and 8 weeks and continues until 14-16 week of pregnancy [1]. The condition is usually self limiting and peaks at around 9th gestational week. However, in up to 20% of cases, nausea and vomiting may continue until delivery. Nausea and vomiting occurs significantly more often in primigravidas and in women who were less educated, younger, non-smokers, obese, or those with a history of nausea and vomiting in a previous pregnancy [2].

A small percentage of pregnant women experience a severe form of nausea and vomiting called Hyperemesis gravidarum (HG). More than 59,000 pregnant women with HG are hospitalized in the US annually.

Asian populations tend to have higher incidence rates. For example, a Malaysian study identified 192 recorded cases (3.9%) out of 4,937 maternities [3].

HG is often associated with weight loss, ketonemia, ketonuria, dehydration and acidosis from starvation, alkalosis from loss of hydrochloric acid, electrolyte disturbances and even hepatic and renal damage [4].

Estimate of incidence of HG varies widely depending on diagnostic criteria sand different study populations. Some sources state a proportion of 0.5-2% of all pregnancies, whereas others provide an incidence of 0.3-1.5% of all live births [5, 6].

HG can be associated with serious maternal and fetal morbidity such as Wernicke's encephalopathy, fetal growth restriction and even maternal and fetal death [7].

Although the pathophysiology for HG is not clear, many hypotheses have been proposed to explain the etiology and pathophysiology of HG including psychological factors, gastrointestinal tract dysfunction, endocrinologic changes, infections, immunological and metabolic causes and anatomical factors. However, there is no single theory to provide an adequate explanation for all the manifestations of HG [5, 8-10].

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A number of risk factors associated with HG have been reported including nulliparity, [11] low maternal age [4, 12], multiple gestation [4, 13-14], metabolic disturbances, trophoblastic disorders,¡fetal anomalies [4, 14], previous pregnancy complicated by HG, [4] female sex of the fetus [13-14], psychiatric conditions [11, 15], both high and low maternal pregnancy weight and lower socio-economic status [4, 14, 16] Smoking, on the other hand, has been associated with a reduced risk of HG [12, 14].

Chronic infection with Helicobacter pylori (H. pylori) may also cause HG. H. pylori are a gram negative, spiral shaped, microaerofilic bacterium that colonizes the gastric mucosa of the human being and is associated with type B gastritis, peptic ulcer and cancers [17]. The prevalence rate is higher in developing countries especially among those with low socioeconomic status [18]. It is estimated that 50-65% of the world population is colonized with this bacterium [19], but despite this high prevalence, only a proportion of these people are clinically manifested, the reason may be related to host defense factors [20].

Recently several studies have implicated H. pylori infection as a possible cause for HG. However, there are also reports that did not show any relationship between H. pylori infection and occurrence of HG. Nevertheless, no conclusive evidence has been adduced to suggest a direct causal relationship between H. pylori infection and HG. So, the role of H. pylori infection in HG is controversial [8, 21-24].

The purpose of the present study was to investigate any possible association between infection with H. pylori and HG. In the case of this association, eradication of H. pylori may help to treat HG in a group of Iranian pregnant women which is a problem in the first trimester of pregnancy.

## MATERIALS AND METHODS

Sixty consecutive pregnant women in the first trimester of their pregnancy were entered into this cross-sectional study. Thirty women had HG (HG group) and 30 did not have HG (control group). The criteria for the presence of HG were pernicious vomiting (more than 3 times per day) without any obvious cause except of pregnancy, weight loss of more than 3 kg or 5% of body weight and the presence of at least +1 ketonuria. Inclusion criteria for experimental group included having HG, age of 15-45 years, gestational age < 20 weeks and exclusion of other causes of vomiting such as hyperthyroidism, molar pregnancy, infectious diseases, psychological disorders, multiple pregnancies and gastrointestinal disorders. Thirty pregnant women in their first trimester were entered as control group. Inclusion criteria for control group were the same as for HG group except for symptoms of HG. The control group was selected among asymptomatic pregnant women that were visited at the antenatal clinic of our hospital.

Venous blood was obtained at the first visit. H. pylori specific IgG antibody titer was measured using by enzyme-linked immune sorbent assay (ELISA) method. IgG titer less than 10 U/mL was considered negative and a titer more than 10 U/mL was interpreted as positive. IgG titer between 5 and 10 U/mL was considered as suspicious. Gestational age was determined using the date of the last menstrual period and was confirmed by ultrasonography. IgG measurement was done two times for all sera.

Statistical analysis was performed using SPSS software for Windows (ver. 10.0). Descriptive indices including mean, standard deviation (SD), frequency and percentage were used to express data. For comparison of categorical variables, the chi-squared test and for continuous variables, the student t test was applied. Significance level was set at $P < 0.05$.

Informed consent was obtained from all participants. The study protocol was in accordance with the Helsinki Declaration and approved in ethics committee of Urmia University of Medical Sciences.

## RESULTS

Table 1 presents demographic characteristics of both groups. The age of the women in both groups ranged was 15-45 years. Mean (SD) age of HG group was 26.1 (±2.5) years and in control group was 25.03 (±2.8) years ($P = 0.4$). There was no significant statistical difference between the two groups regarding demographic variables.

Table 2 presents h. pylori seropositivity in the studied groups. Twenty-four patients (92.3%) in HG group had H. pylori infection, while this rate was only 7.7% (two patients) in control group ($P < 0.001$; $x^2 = 32.8$).

Table 1: Demographic characteristics of patients and controls

| Parameters | HG group | Controls | P value |
|---|---|---|---|
| Age, year | 26.1 (±2.5) | 25.03 (±2.8) | 0.478 |
| Gravidity | 1.73 | 1.6 | 0.6 |
| Parity | 0.7 | 0.6 | 0.44 |
| Gestational week | 9.9 | 9.6 | 0.55 |
| H. Pylori seropositivity | 24 (92.3%) | 2 (7.7%) | 0.001 |

Table 2: H. pylori seropositivity in HG and control groups

| H. pylori serostatus | HG group | Controls | Total | P value |
|---|---|---|---|---|
| Positive | 24 (92.3%) | 2 (7.7%) | 26 | < 0.001 |
| Negative | 1 (5.9%) | 16 (94.1%) | 17 | |
| Suspicious | 5 (29.4%) | 12 (70.6%) | 17 | |

Table 3: Comparison of mean (standard deviation) H. pylori specific IgG titer between HG patients and controls

| H. pylori specific IgG titer | Maximum | Minimum | Mean (±SD) | P value |
|---|---|---|---|---|
| HG group | 62.6 | 4.7 | 23.4 (±13.9) | |
| Controls | 21.7 | 1.4 | 6.09 (±4.5) | < 0.001 |
| Total | 62.60 | 1.4 | 14.71 | |

In Table 3, mean (SD) values of H. pylori specific IgG antibody titer has been depicted. Mean (SD) IgG titer was 23.34 (±13.9) U/mL (range, 4.7-62.6) in HG groups and was 6.09 (±4.5) U/mL in control groups (range, 1.4-21.7).

One patient In HG group and 16 patients in control group had IgG titers of less than 5 U/mL. Borderline IgG titer (5-10 U/mL) was observed in 17 cases (5 patients (29.4%) in HG group vs. 12 cases (70.6%) in control group; $P < 0.001$).

We did not found any correlation between IgG titers and either maternal age ($t=2.4$, $P = 0.12$) or parity ($x^2=0.2$, $P = 0.6$).

There was no statistically significant difference in gestational age and gravidity between patients and controls ($chi^2=0.44$, $p=0.55$).

## DISCUSSION

It is estimated that H. pylori infection might be present in two-thirds of the world population. However, the pathogenic relationship between HG and H. pylori is not self evident because most of those infected with H. pylori do not complain of symptoms. In other words, the presence of H. pylori can be asymptomatic. Furthermore, the problems in diagnosis of H. pylori infection are more complicated during pregnancy since HG can mask an active H. pylori infection or HG may be worsened by superimposed H. pylori infection [21].

A possible explanation for an association between H. pylori infection and HG could be an increased accumulation of fluid and a displacement of intracellular and extracellular volumes which occur in the early phase of pregnancy as a result of increase in steroid hormones. These physiologic changes results in a change of gastric pH levels which could lead to the manifestation of a latent H. pylori infection in the gastrointestinal tract [25, 26].

The results of this study show that the seropositivity of H. pylori in the HG group was significantly higher than in control group. Recently, it was shown that H. pylori seropositivity was significantly high in pregnant women who suffer from HG. Our findings are in accordance with the previous studies [8, 25, 26]. However, some recent studies could not find such association. Thus this is one of the controversial issues in obstetric care [27, 28]. For example, Berker *et al*. reported insignificant difference between HG patients (70%) and controls (61.3%) regarding the presence of H. pylori infection using H. pylori specific IgG. Similar results were noted by Lee *et al*. [20] who demonstrated the prevalence of H. pylori infection in HG patients to be 65%, while this figure was 66.7% in controls.

Frigo *et al*. [25] reported statistically significant differences between HG patients and asymptomatic ones regarding H. pylori infection (90.5% vs. 46.5%). Kocak *et al*. [26] also found similar results (92% in HG patients vs. 45% in controls). Salimi-Khayati *et al*. [22] revealed significantly higher H.pylori seropositivity in HG patients (88.9%) than in control ones (40.7%).

In a total of 12 studies reviewed regarding H. pylori infection in HG patients, 11 relied on the serologic assay of H. pylori infection and the great majority of them showed significantly increased infection rate in HG patients. The authors of three studies were not able to demonstrate any meaningful difference in H. pylori infection rates between HG patients and controls [27, 28].

Several results were not able to demonstrate any significant differences between HG patients and asymptomatic ones as regards H. pylori IgG antibody seropositivity [27, 29].

Aytac *et al*. did not found any significant difference between HG patients and control ones (41.1% vs. 40%) suggesting no causal relationship between H. pylori infection and HG [5]. Karadeniz *et al*. reported the prevalence of H. pylori IgG antibody was 67.7% (21 of 31) in the patients with HG and 79.3% (23 of 29) in controls ($P = 0.31$). There was no statistically significant difference in study and control groups for H. pylori IgG Ab and H. pylori SA in that study.

Two recent studies found no association between HG and Hp seropositivity, one conducted in two US populations with disparate Hp seropositivity and the other by Berker *et al* from Turkey [27, 28].

## CONCLUSION

This study suggests an association between H. pylori infection and hyperemesis gravidarum. Serologic test, moreover, being a non-invasive, cheap and easy to use, we recommend its routine use in patients with hyperemesis gravidarum as well as in women who desire to become pregnant in the near future.

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