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Evaluation of the relationship between Helicobacter Pylori infection and Hyperemesis Gravidarum

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Abstract

Background: Hyperemesis gravidarum (HEG) is one of the many problems during pregnancy; its etiology has not been clearly understood. Inflammatory factors like helicobacter pylori infection has been considered as a risk factor in some studies. The purpose of the present study is to find a relationship between Helicobacter Pylori (H.P) infection and hyperemesis gravidarum (HEG).

Methods: A case control study was performed on two groups of pregnant women who were in the first trimester of their pregnancies. Case group were pregnant women with hyperemesis gravidarum and control group were pregnant women with the same gestational age but without hyperemesis gravidarum. In both groups, IgG for H.P was measured and compared between the 2 groups.

Results: Totally, 175 pregnant women were evaluated; 78 women with HEG and 97 without. Both groups had no statistically significant difference according to age, gestational age, gravidity, and body mass index (BMI). 51 women out of 78 (65.4%) in HEG group and 43 women (44.3%) in the control group were IgG positive for HP, which showed a significant difference (p=0.005); OR= 2.37, CI 95%= 1.28-4.38.

Also, mean serum level of IgG was higher in the HEG group (42.1 ± 3.75 VS 32.6 ± 3.65, p= 0.05).

Between the different variables of age, gestational age, gravidity and HP infection, only HP infection was found as a risk factor for HEG using logistic regression model (p=0.011); OR= 2.522, CI 95%= 1.23-5.14.

Conclusion: HP infection is higher in HEG cases and may be considered as its risk factor.

Keywords: Pregnancy, Hyperemesis gravidarum, Helicobacter pylori.

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Introduction

Nausea and vomiting is a common and unpleasant problem during pregnancy with a frequency of 75% to 80% of pregnancies (1,2).

It usually starts between first and second missed menstrual period and can continue up to 14-16 weeks of pregnancy (1).

In some women nausea and vomiting is very severe and does not respond to simple diet manipulation and antiemetic agents. This culminates in dehydration, electrolytic imbalance and starvation ketosis and is called as hyper emesis gravid arum (HEG).

The frequency of HEG is about one in 200 to 1.5% of pregnancies (2,3) and although its definition has not yet been standardized, the accepted clinical pattern includes persistent vomiting, dehydration, ketosis, electrolyte imbalance and weight loss (more than 5% of body weight) (2).

A scoring system of Pregnancy- Unique Quantification of Emesis and Nausea (PUQE) has been used for its evaluation

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(4,5).

The exact etiology of HEG is not clearly defined, but it can be considered as a multi factorial problem (6), which is under investigation (7). A relationship between HP and HEG has recently been reported (1,2,8,9). Chronic infection with HP has been reported to have a role in producing HEG in a study (8). In this study 61.8% of pregnant women with HEG had positive HP genome, while 27.6% of pregnant women without HEG had this genome. The researchers concluded that chronic infection with HP should be considered as an important factor in the pathogenesis of HEG, even if it is not the sole factor (8).

Usual nausea and vomiting of pregnancy is normally accompanied with improvement in the pregnancy outcome including less abortion, preterm labor and still birth, and also, less instance of low birth weight, intrauterine growth restriction (IUGR) and fetal mortality (2). In contrast HEG is accompanied with more maternal complications including splenic avulsion, esophageal rupture, Mallory - Weiss tears, pneumo thorax, peripheral neuropathy, and preeclampsia, and also more IUGR and fetal mortality.

HP is a gram-negative bacterium, which is colonized in the gastric mucosa and causes an increased production of reactive oxygen species (ROS), and decreased plasma antioxidant like ascorbic acid (9). HEG may be considered as an oxidative stress state, which is determined, by high ROS activity and low antioxidant state.

Goldberg et al (10) performed a systematic review on 14 case- control studies about the relationship between HP and HEG in 2007. They concluded that the study does show a relationship, however, heterogeneity between studies has limited the results. In contrast in a study by Jacobson et al (11), a relationship between HP and HEG was not reported and therefore, there is no consensus on the role of HP on the genesis of HEG.

The purpose of the present study is to evaluate a relationship between HP and HEG. Regarding to the fact that in different studies, having employment, age, maternal BMI, psychogenic factors and race have been found as confounding factors (2,6,11), in the present study, the women were considered to be homogenous and confounding factors has been omitted using logistic regression model.

Methods

The study was conducted as a case control study on pregnant women who referred to the prenatal clinic of Akbarabadi Teaching Hospital in Tehran, Iran, between October 2009 - March 2010.

Women with HEG were the case group and the control group was women without. Sampling was performed as a convenient and non-random sequential sampling. Inclusion criteria were gestational age of 6-16 weeks of pregnancy (according to a reliable LMP and ultrasound confirmation), singleton, wanted pregnancy, being housewife, and BMI between18.5-24.9.

Exclusion criteria included molar pregnancy, history of any systemic disorder or drug use except ordinary supplementation (i.e. folic Acid), history of any gastro intestinal (GI) disorder or GI problems, smoking or drug abuse, hyperthyroidism, and known psychological problems.

All women had a low socioeconomic condition and the study was performed in a public hospital in downtown Teheran with mostly low income habitants.

A sample size of 90 in each group was considered sufficient in order to obtain a power of 90% (α= 0.05, 1-β= 0.085) with a significance level of 5%.

$$n = \frac{2 \times [z_{(1-\alpha/2)} + z_{(1-\beta)}]^2 \, s^2}{(\mu_1 - \mu_2)^2}$$

Written informed consent was obtained from all participants who were fully informed about the study and advised that the study had no extra expense for participants.

HEG was defined as vomiting of more than 3 times per 24 hours plus weight loss of more than 3 Kg and keton in the urine,

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and the score of PUQE of more than 13. PUQE is a scoring system for quantifying of the severity of nausea and vomiting which is based on 3 physical signs. These include nausea, vomiting and retching and its validity has been confirmed (6, 5,12,13). Duration of nausea (hour), the number of the episodes of retching and vomiting, during 24 hours, would be evaluated (5, 6,12,13). Total score is between 3-15, in which score of 3-6 is mild, 7-12 is moderate and 13-15 is considered as severe (6).

Two mili liter bloods was obtained from all eligible participants for measurement of HP antibody at the time of the entrance the study and thenIgG was determined by ELIZA (Radin, K5HPG, Italy).

Serum level of IgG of more than 20 Iu/ml was considered as positive and serum level of less than 15 Iu/ml was considered negative. The serum level between15-20 was considered suspicious and repeated 2-4 weeks later. If the second titer of IgG was less than 15 Iu/ml, it was considered as negative, and if it was higher than 20 Iu/ml, it was considered positive and the samples, which were between 15-20 Iu/ml, were removed from the study (excluded from the study).

The serum level of IgG, and also, positive or negative results of the tests were recorded in order to compare. The obtained data were analyzed using SPSS 17. Chi-square test, student t- test in the case with normal distribution and non-parametric tests for the cases without normal distribution were used for analysis. Odd ratio was calculated to determine the relationship between HP and HEG. In order to omit the effects of confounding factors, logistic regression model was used. P value of less than 0.05 was considered significant.

Results

175 pregnant women entered the study of whom, 78 were in the HEG group and 97 women were in the control group (without HEG).

The groups showed no significant difference according to age, gestational age, gravidity and BMI (Table 1).

In the HEG group, 51 cases (65.4%) were positive for HP IgG, against 43 cases (44.3%) in the control group which showed a significant difference (Table 1) (OR= 2.27, CI95%= 1.28-4.38). Also, serum IgG level was significantly higher in the HEG group (Table 1).

Using logistic regression stepwise model, age (OR= 0.982, CI95%= 0.917-1.0450, p=0.591), gestational age (p=0.951, OR= 1.005, CI 95%= 0.852-1.186), gravidity 1 (p=0.430, OR= 0.569, CI 95%=0.0141-2.306), gravidity 2 (p=0.359, OR= 0.527, CI 95%= 0.234- 2.069), gravidity 3 or more (p=0.220, OR= 0.298, CI 95%= 0.091-1.334), did not show any relationship with HEG and only HP had correlation with HEG (p=0.011, OR= 2.522, CI 95%= 1.236-5.143).

Discussion

In the present study, positive tests of HP IgG in the cases of HEG was higher and confounding factors like age, gestational age, BMI, number of previous pregnancies did not show correlation with HEG, and only HP showed a significant correlation.

In a study by Jacobson et al (11), correlation between sero positive cases of HP and

Table 1. The characteristics of women of both groups.

Characteristics		HEG group n=78	No HEG group n=97	p
Age (year) M± SD		28.02 ± 5.8	27.3 ± 5.4	0.423
Gravidity n (%)	1	30 (38.5%)	41 (42.3%)	0.852
	2	28 (35.9%)	34 (35.1%)	
	≥3	20 (25.6%)	22 (22.7%))	
Gestational age (weeks) M± SD		11.5 ±2.3	11.6 ±2.1	0.870
BMI (kg/m^2) M± SD		22.4 ±5.3	23.1± 4.7	0.606
Positive IgG n (%)		51 (65.4%)	43 (44.3%)	0.005
Serum level of IgG M± SD		42.1 ±3.75	32.6± 3.65	0.05

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HEG has not been shown, while, age, and race showed significant correlation with HEG.

The results of this study are not in agreement with the present study. At the same time, study (14) reported no correlation between less severe nausea and vomiting of pregnancy and HP, but, they found more cases of HP in the more severe cases of pregnancy vomiting.

The researchers concluded that HP probably potentiates the progression of mild nausea and vomiting to more severe one.

Also study (15), reported that although the cases of HEG were more sero- positive for HP than the cases without HEG, they couldn't show any correlation between HP sero- positivity and the duration of HEG or the time of its beginning. Therefore, the researchers concluded that HP probably increases the severity of HEG, but is not a sole factor.

The other study, which was performed on Hispanic pregnant women (16), could not show more HP sero-positive cases in the pregnant women with HEG than no HEG cases.

The result of the above mentioned studies are in agreement with the other studies (17-19).

In contrast, correlation between seropositivity for HP and HEG has been confirmed in studies (20-23). In a systematic review and met analysis which was performed on different case- control studies (24), the researchers showed that HP exposure has been accompanied with a greater risk of HEG. However, there was heterogeneity between studies, with variable reasons. This study stated that regarding the high prevalence of HP, public health consequence of HP with respect to HEG, should be considered significantly. Even the other study (25), suggested that screening of HP should be added to the HEG diagnostic tests.

HP infection was accompanied with more cases of HEG in a dose response manner and also stronger in Africans than non- Africans (26). Different etiologic factors have been suggested for HEG, of which the most recent is the correlation between HP infection and HEG and also cell free fetal DNA (27).

Pregnancy dependent hormones like HCG, progestin and estrogen have been studied a lot and other hormones like leptin, placental growth factor, prolactin, thyroid and adrenal hormones have been considered in the genesis of HEG. In addition, infections, immunologic, psycho logic, metabolic and anatomic factors have been reported, and it seems reasonable to performed more studies for finding the etiologic factors and pathogenesis of HEG (1,28).

Specific IgG tests and stool antigen for diagnosis of HP both have been suggested as good screening tests for HP in the cases of HEG (29) in early pregnancy. The other study (30), suggested the correlation between HP infection and HEG using stool antigen test, and reported that this test is better than serologic tests.

Endoscopic evaluation and biopsy for finding HP has been performed in one study in the case of HEG (31) and showed a significant difference with the cases without HEG. The study concluded that HP infection should be considered in the cases of refractory HEG (31). However, in study (32), stool antigen test for HP showed no significant difference in the cases with and without HEG.

Conclusion

HP infection was higher in HEG cases in this study, and may be considered as its risk factor, however, regarding the above - mentioned studies and controversies between the studies, the role of HP infection in the pathogenesis of HEG should be investigated more fully to consider the different confounding factors, and routine serologic analysis for HP infection is not suggested in all cases of HEG (17).

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