Comparison of Helicobacter Pylori Infection in Normal Pregnancy and Preeclampsia

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ARTICLE INFO	ABSTRACT
Article type: Short Communications *Article History:* Received: 16-Jan-2022 Accepted: 28-Dec-2022 *Key words:* Helicobacter Pylori Preeclampsia Pregnancy	Preeclampsia is a hypertensive disorder that affects 2–7% of pregnancies, remaining a major contributor to maternal and fetal mortality and morbidity with uncertain pathogenesis. Some evidence suggests the role of infectious agents in development of preeclampsia. This study assessed the potential relationship between H. Pylori infection and development of preeclampsia. This case-control study was conducted in one educational hospital in Mashhad, Iran, in 2021. Study participants were selected through convenience sampling. A total number of 34 normotensive and 34 women with preeclampsia in their third trimester enrolled in the study. We assessed serum levels of hemoglobin, hematocrit, platelets, creatinine, and serum levels of H. pylori (IgG and IgA) in all participants, comparing the infection rates between the study groups. There were no significant difference in age, BMI, number of previous pregnancies, hemoglobin, hematocrit, platelet count and creatinine levels among different study groups (P>0.05). The H. Pylori test was positive in 30 (88.2%) pregnant women in preeclampsia group and 23 (67.6%) in the control group (P=0.041). H. Pylori infection was significantly more prevalent in women with preeclampsia compered to healthy pregnant women in third trimester. This suggests a potential association between H. Pylori infection and the development of preeclampsia.

Introduction

Hypertensive disorders of pregnancy are considered as common and potential life-threatening complications affecting up to 10% of pregnancies (1). Preeclampsia is a well-known form of hypertensive disorders of pregnancy characterized by a new onset increase in blood pressure and proteinuria after 20 weeks of gestation (1-2). The prevalence of preeclampsia varies among different countries (1). While developing countries have reported a decreasing rate of the disorder, developing countries are still challenging with this complication of pregnancy (3). The prevalence of preeclampsia has increased from 0.04 to 0.07 over a 9 years period in Iran indicating the growing concern regarding the possible maternal and neonatal complications of the disorder (3). Preeclampsia may progress to multi organ dysfunction leading to significant maternal and fetal complications (2). While Approximately 16% of maternal deaths are attributed to preeclampsia , the stillbirth rate varies from 9 per 1000 in severe preeclampsia to 30 per 1000 in severe preeclampsia (4). Although the exact pathogenesis of preeclampsia is not clearly understood, however

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some possible mechanisms including alterations in prostaglandin activity, endothelial cell damage, changes in nitric oxide levels, increased endothelin levels, and increased immune responses has been suggested (5). Recently some studies suggested a possible relationship between increased inflammatory responses and C-reactive protein (CRP) level and development of preeclampsia (6-7). Bacterial and viral infections are among the well-known causes for inducing inflammatory responses and increasing CRP level (6-7). Periodontal disease as well as urinary tract diseases are among the well-known risk factors of preeclampsia (8). It has been hypothesized that chronic subclinical infections increase cytokine levels affecting vascular endothelial function and increases the risk of preeclampsia (9). H. pylori infection is one of the most common chronic infections which is mostly asymptomatic (10). The incidence of h. pylori infection varies in different part of the world mostly depending on lifestyle and general health (10). Although the exact prevalence of h. pylori infection is not clearly understood; however, in developing countries, the estimated prevalence of h. pylori has been reported to be up to 95% and up to 50% in developed countries (11).

While h. pylori infection is a common chronic infection affecting both genders of any age; however, there are conflicting results regarding the effect of the infection on development of preeclampsia. Given the increasing rate of preeclampsia in Iran and its adverse maternal and fetal complications, we decided to evaluate the role of h. pylori in preeclampsia patients

Materials and Methods

The present case-control study was approved by the Local Research Ethics Committee, Mashhad University of Medical Sciences, Mashhad, Iran and conducted at one educational Hospital in Mashhad, Iran. The sample size was calculated based on error type 1 equal to 0.05, type 2 equal to 0.2 and the estimated prevalence of H. Pylori in two groups of 40% and 10% (12). In each group 34 pregnant women were selectes using convenient sampling. Every participant filled an informed consent form before participating the study. The case group was chosen from patients with preeclampsia admitted to the hospital. All the included women were aged between 19 and 35 years, and had body mass index between 25 and 19 cm/kg^2. Pregnant women with any underlying disease including autoimmune disorders, diabetes, and kidney disease were excluded.

Diagnosis of preeclampsia was made by a gynecologist according to the clinical and laboratory criteria including: hypertension (systolic blood pressure ≥140 mmHg and diastolic blood pressure ≥90 mmHg), abnormal renal function (24-hour urine protein ≥300 mg, or urinary protein/creatinine ratio of 0.3 and/or 30 mg/dl (one plus protein on dipstick, fixed protein in random urine samples) and central nervous system impairment from week 20 of gestation until day 7 of postpartum. one milliliter of venous blood sample was obtained from every woman and the level of h. pylori antibodies (IgG and IgA) evaluated by ELISA method using ELISA kit (Germany).

Demographic, clinical and laboratory data were analyzed by SPSS software and was presented as central indices, distribution and frequency in appropriate tables and graphs. In order to compare the quantitative data between groups, Student T test or Mann-Whitney test was used after assessing the condition of normality by Kolmogorov Smirnoff test. Chi-square test was used to assess H. pylori frequency between to study groups. In all analyses P-value <0.05 was considered as statistically significances.

Results

The mean ± standard deviation age of the patients in preeclampsia group was 27.1 ± 3.75 years and in the control group was 26.3 ± 4.99 years. The Mean ± standard deviation o except for the gestational age which was higher in control group (P<0.001), other variables including age, BMI, and number of previous pregnancies were not significantly different among the study groups (P=0.478, P=0.902 and P=0.849 respectively) (Table 1). None of the serum biochemical markers including hemoglobin, hematocrit, platelet count and creatinine levels were not significantly different among study groups (P=0.791, P=0.733, P=0.113 and P=0.582 respectively) (Table 2). H. pylori test was positive in 30 (88.2%) pregnant women of preeclampsia group and 23 (67.6%) in control group. Chi-square test showed a significant difference between the two groups (p = 0.041).

Table 1. The mean and standard deviation of demographic and obstetric variables among study groups

Variable	Case group (Mean+SD)	Control group (Mean+SD)	t	P-Value
Age (years)	27.14 ± 3.75	26.38 ± 4.99	0.713	0.478*
Body mass index (kg/m^2)	22.53 ± 2.12	$22.59+1.78$	0.124	0.902*
Gestational age (weeks)	34.47 ± 2.73	37.76 ± 2.58	5.108	<0.001*
Variable	**(mean$\pm$SD)**	**(mean$\pm$SD)**		
Number of previous pregnancies	1.91 ± 1.08	$1.76+0.78$	-	0.849**
Inter quartile range (25-75)	(1-3)	(1-2)		

** Mann-Whitney test * Independent sample T-test

Table 2. The mean and standard deviation of laboratory findings among study groups

Variable	Case group (Mean±SD)	Control group (Mean±SD)	t	P value*
Hemoglobin (mg/dl)	12.32 ± 1.73	12.21 ± 1.81	0.26	0.791
Hematocrit (%)	37.09 ± 4.83	37.50 ± 5.06	-0.34	0.733
Platelet count (*10^3)	182.41 ± 66.88	207.29 ± 60.79	-1.60	0.113
Creatinine (mg/dl)	0.74 ± 0.08	0.73 ± 0.08	0.55	0.582

*Independent sample T-test

Discussion

The present study revealed that in contrast to healthy pregnant women in their third trimester of pregnancy, pregnant women developing preeclampsia are more likely to have h. pylori infection.

Preeclampsia is a hypertensive disorder with coagulopathy, significantly impacting pregnancies and posing a substantial risk to both mother and fetus (4). Nowadays, maternal mortality due to preeclampsia declined in developed countries, but While maternal mortality due to preeclampsia has decreased in developed countries, near-term mortality, long-term morbidity, and neurologic complications affecting fetal or preterm delivery continue to be unresolved issues (4). The disease provides considerable burden for both mother and fetus. Those born from mothers with a history of preeclampsia are at increased risk of developing adverse cardiovascular complications and metabolic syndrome in future (13). Recent lines of evidence suggested chronic subclinical infections as a possible causes of preeclampsia and h. pylori as a preventable and curable infection is a potential target for further decreasing the rate of preeclampsia (9). The impact of h. pylori infection on some pregnancy outcomes has been studied in the literature. Among them, intrauterine growth retardation (IUGR) has been reported to be a common complication of pregnancy associated with h.

pylori infection (12). Moreover, the helicobacter pylori infection has been linked to development of gestational hypertension (14). The adverse effect of chronic h. Pylori infection on the vascular system, as atherosclerotic changes in placenta and spiral arteries, have been reported in IUGR cases (12). In addition, studies have shown that h. pylori infection may accelerate platelet aggregation and fibrinogen formation by affecting lipid peroxidase (13). Even more, cytotoxin associated gene-A positive strand of h. pylori induce secretion of anti-cytotoxin associated gene-A antibodies cross reacting with trophoblasts and inducing functional impairment to human placenta (15).

Although the exact mechanism of how h. pylori affecting the pregnancy is not clearly understood but some clinical studies provided controversial results regarding the relationship between h. pylori infection and development of preeclampsia. Similar to our results, a recent study from our country evaluated the relationship of the h. pylori and preeclampsia. They demonstrated that women developing preeclampsia are 1.8 times more likely to have positive h. pylori antigen in their stool samples (16). Ponzetto et al. (2006) demonstrated that women with preeclampsia have higher h. pylori positive serologic results in contrast to women with normal pregnancy (51.1% versus 31.9%). Similarly, another study by Malik et al. (2019) reported that h. pylori positive serologic results

are higher in pregnant women with preeclampsia (13,17). However, a previous study by Conde-Agudelo et al. (2008) demonstrated that presence of antibodies to h. pylori was not associated with increased risk of preeclampsia (8). Moreover, some studies evaluated the relationship between the h. pylori stool antigen and development of preeclampsia. The study by Shabana et al. (2016) which evaluated 100 pregnant women, demonstrated that women who had positive h. pylori stool antigen tests were more likely to develop preeclampsia complicated with IUGR (18). Moreover, Hasan et al. (2020) evaluated the presence of h. pylori infection in pregnant women undergoing Oesophago gastro duodenoscopy and demonstrated that women with preeclampsia were more likely to be seropositive for the infection and will develop more severe preeclampsia (19). It is noteworthy to mention that some studies evaluated infection with multiple pathogens including h. pylori. Among them, Ahmad et al. (2020) demonstrated that h. pylori infection and not the C. trachomatis infection evaluated with enzyme-linked immunosorbent assays were related to development of preeclampsia (20). Also, the complex relationship between h. pylori infection and preeclampsia has been addressed in study by Shedid et al. (2018) (21). They demonstrated a triangle of danger for pregnant women consisted of h. pylori infection, preeclampsia, and obesity. According to their results, women with high BMI are more likely to develop severe preeclampsia which is associated with h. pylori infection (20). Although we demonstrated the possible link between the infection and development of preeclampsia but we could not establish such relationship for obesity as the BMI was not significantly different among our case and control group (21).

However, in this study, we could not demonstrate a causality relationship. Also it was better to assess other influencing factors such as nutritional habits, other digestive symptoms, BMI and biochemical factor in two groups.

Conclusion

The present study demonstrated the relationship between preeclampsia and h. pylori infection. So it seems that taking a detailed medical history of digestive symptoms and assessing h. pylori at the beginning of pregnancy will be helpful, especially in especially in women who are at risk and have past medical history of preeclampsia.

Acknowledgements

Conflicts of interest

The authors declared no conflicts of interest.

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