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Evaluation of the relationship between preeclampsia and positive rectovaginal culture of group B *Streptococcus* and *Helicobacter pylori* positive serology

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Abstract

Introduction: Identifying the incidence of pathogen colonizations in pregnant women with preeclampsia can be effective in providing proper treatment and reducing complications.
Objectives: We evaluated the frequency and association between positive rectovaginal culture of group B *Streptococcus* (GBS) and positive *Helicobacter pylori* serology with preeclampsia in two groups of pregnant women (with and without preeclampsia).
Patients and Methods: The present case-control study included pregnant women with preeclampsia and healthy pregnant controls during 2019-2020. Blood and rectovaginal samples were obtained and the data were statistically analyzed using SPSS software.
Results: Fifty-four people were included in the study. The mean gestational age was 36 ± 3.4 months in the preeclampsia group and 37 ± 2.9 months in the control group. There was no significant relationship between preeclampsia and *H. pylori*-positive serology ($P=0.84$). Additionally, the association between positive *H. pylori* serology and the severity of preeclampsia was not significant ($P=0.15$). However, there was a significant relationship between positive *H. pylori* tests with early- and late-onset preeclampsia ($P=0.04$). However, there was no statistically significant relationship between the positive rectovaginal culture of GBS and preeclampsia, the severity of preeclampsia, the onset time, or the weight of newborns.
Conclusion: There was a significant relationship between *H. pylori* infection and late-onset preeclampsia in preeclamptic mothers. *H. pylori* screening and eradication therapy before pregnancy can prevent preeclampsia and its serious consequences in both the mother and the fetus.

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Introduction

Preeclampsia is a pregnancy-related disorder that is characterized by increased blood pressure (BP) and the excessive presence of urine protein. This disease can affect almost all organs and lead to the morbidity and mortality of the mother and fetus (1). The pathophysiology of preeclampsia is not clearly understood; however, a defect in chromosome 13, increased oxidants and inflammation, decreased function of the immune system, and hyperlipidemia have been reported to be involved (2,3). A study on 635 000 pregnant women with preeclampsia demonstrated that obesity and primiparous pregnancy are also influential in increasing the risk of developing the disease (4). Additionally, a family history of BP, alcohol consumption, anxiety, and diabetes also increase the risk of developing preeclampsia (4,5).

Key point

In a study on 54 pregnant women with or without preeclampsia, we found no significant relationship between preeclampsia and helicobacter pylori-positive serology. However, we found a significant association between positive helicobacter pylori test with early- and late-onset of preeclampsia. Helicobacter pylori screening and eradication therapy before pregnancy can prevent preeclampsia and its serious consequences for both mother and fetus.

Hypertensive disorders occur in a high percentage of pregnant women and preeclampsia is the most serious hypertensive condition as well as the second

leading cause of maternal death in developing countries (6,7). Although the incidence of hypertension increases in the elderly, preeclampsia often affects young pregnant women (8). Individuals with severe preeclampsia are at a risk for placental abruption, pulmonary edema, renal failure, coagulation disorders, and death. Patients with mild to moderate preeclampsia usually have a lower risk of developing complications; however, several complications have been reported (9).

Furthermore, microbial colonization can increase the levels of antioxidants in pregnant women and, in the long term, weaken the immune system by inducing an immune response (10,11). *Helicobacter pylori* is the only observed bacterium that causes gastric infections in pregnant women. Recent studies have focused more on the extra-gastrointestinal manifestations of *H. pylori* including cardiovascular, hematological, and respiratory complications, as well as pregnancy-related complications including preeclampsia, low-birth weight, and preterm birth. Although the number of studies conducted on *H. pylori* infection and preeclampsia are limited (12,13), it is important to further investigate this association since any infection is associated with a nonspecific immune response. *Streptococcus* B is another microorganism that causes various complications in pregnant women. In addition, it may cause serious complications in infants and individuals with immunodeficiency disorders (14). It has been reported that streptococcal infection increases the response of cytokines which is associated with and may even be a cause of preeclampsia (15).

Any bacterial or viral infection in pregnant women may increase the risk of preeclampsia. There are limited studies that evaluated the association between *H. pylori* infection and preeclampsia. In addition, although the role of *Streptococcus* B colonization in preeclampsia seems important, few studies have investigated this association as well. Therefore, in this study, we evaluate the frequency of positive rectovaginal culture of group B *Streptococcus* (GBS) and positive serology of *H. pylori* in pregnant women with or without preeclampsia.

Patients and Methods

Study design

This case-control study included healthy pregnant women or with preeclampsia during 2019 and 2020 that visited the Firouzabadi educational and medical center in Tehran. Around 57 eligible cases met the inclusion criteria and were selected at the time of admission using the available sampling method.

Inclusion and exclusion criteria

The inclusion criteria included the age range of 15-45 years, singleton pregnancy, normal hemoglobin level, no history of chronic hypertension, no history of thrombophilia, and no history of lupus or other underlying diseases. Exclusion criteria included the patient's reluctance to participate in the research, smoking or drug use, history of chronic illnesses such as diabetes, chronic hypertension, chronic gastrointestinal disease, renal disease, history of heart attack or stroke, body mass index (BMI) above 40 kg/m^2, asthma, or malignancies.

Methods of data collection

After obtaining informed consent, a questionnaire was prepared for the patients of both the control and case groups, and the demographic information was documented. At the time of admission, 5 cc blood samples were taken from the two eligible groups for laboratory evaluation. In addition, the cases were asked precisely about the history of supplements they were taking.

The patients' demographic information and laboratory results were recorded in the pre-designed information form and demographic checklist and finally, the data were statistically analyzed with SPPS software.

The studied variables included maternal age at delivery, gestational age at delivery, birth weight, number of pregnancies, maternal race, BP, and the level of urinary protein.

Microbiological and biochemical analysis

Using two separate sterile swabs, samples were taken from the vaginal entrance (approximately 2 cm) and then from the rectum entrance (1 cm). The samples were placed in a sterile non-nutrient transfer medium and were sent to the laboratory for investigation. The positivity of the samples was evaluated through microbiological diagnostic tests. Blood samples were also examined for *H. pylori* serology and other biochemical tests.

Data analysis

Data were analyzed by descriptive statistics (mean), independent t-test, and the chi-square test using the SPSS 25-software. A *P* value less than 0.05 was considered significant.

Results

In this study, 54 participants were included for data analysis since three of the 57 participants had a history of chronic hypertension which resulted in their exclusion from the study.

Pregnancy frequency was equal in both groups ($P=0.52$). The mean gestational age of the participants in the preeclampsia and control groups was 36 ± 3.4 and 37 ± 2.9 months, respectively ($P=0.15$).

There was a significant difference in the systolic and diastolic BPs of the two study groups. The mean systolic BP of the preeclampsia and healthy groups was 146.32 and 93.33 mm Hg, and the mean diastolic BP of the preeclampsia and healthy groups was 11.47 and 78.25 mm Hg, respectively (Table 1). These results indicated an increase in BP levels in pregnant women with preeclampsia.

In addition, the mean age of the preeclampsia and

Table 1. Evaluation of the demographic variables

Parameters	Preeclampsia group (n=39)	Controls (n=43)	*P* value
Age (y)	29.13 ± 6.22	30.16 ± 5.52	0.22
Weight (kg)	74.20 ± 11.92	70.03 ± 17.25	0.43
Gestational age (wk)	36.16 ± 3.4	37 ± 2.9	0.15
Gravida	3.4 ± 1.9	3.5 ± 1.8	0.52
Systolic blood pressure (mm Hg)	146.32 ± 11.21	118.47 ± 9.85	0.01
Diastolic blood pressure (mm Hg)	93.33 ± 5.69	78.25 ± 5.07	0.02

control groups was 29.13 ± 6.42 and 30.16 ± 5.61 years, and the mean weight of the preeclampsia and control groups was 70.03 ± 20.25 and 74.2 ± 11.92 kg, respectively. However, there was no significant difference between the mean age and weight of pregnant women in both study groups ($P>0.05$).

A shown in Table 2, no statistically significant difference was detected between the case and control groups in terms of serum levels of white blood cells count (WBC), aspartate aminotransferase (AST) and alanine aminotransferase (ALT), bilirubin, and blood urea nitrogen (BUN) ($P>0.05$). However, the two groups were significantly different in terms of the levels of serum lactate dehydrogenase (LDH), creatinine, hemoglobin, and platelets ($P<0.05$).

The frequency of positive rectovaginal culture of GBS and positive *H. pylori* serology in the two groups is illustrated in Table 3. Five and two patients in the preeclampsia group had *H. pylori* and streptococcus, respectively. The results showed that there was no significant relationship between H. pylori serology and positive rectovaginal culture of streptococcus with preeclampsia ($P>0.05$).

Moreover, a significant relationship between the positive serology of *P* with early- and late-onset preeclampsia was observed ($P=0.04$). Additionally, in 66.6% of pregnant women, *H. pylori*-positive serology was associated with late-onset of preeclampsia.

On the other hand, there was no statistically significant association between positive rectovaginal cultures of streptococcus and preeclampsia, the severity of preeclampsia, the onset time, and the weight of newborns ($P>0.05$; Table 4).

Discussion

Given that preeclampsia is still one of the most important causes of maternal and fetal morbidity and mortality, it is important to identify the inflectional factors of this disease. The maternal mortality ratio is used as a global indicator to assess the level of health and treatment of each country. Therefore, further research leading to increased maternal health is particularly important (11).

In this study, we found no significant correlation between positive serology of *H. pylori* with preeclampsia or preeclampsia severity; however, the findings demonstrated a significant relationship between *H. pylori*-positive serology and early- and late-onset preeclampsia (Table 3). In a similar study, Di Simone et al reported that more cytotoxin-associated gene A (CagA) antibodies were found in women with preeclampsia compared to

Table 2. Frequency of the biochemical factors in the two groups

Parameters	Preeclampsia group (n=21)	Controls (n=33)	*P* value
WBC (10^3/μL)	13000±1000.62	11806.06±2100.52	0.22
AST (IU/L)	52.4±7.7	29.39 ±17.25	0.43
ALT (IU/L)	56.71±3.6	35.12±3.6	0.21
Bilirubin (mg/dL)	0.93±4.9	1.16 ±2.7	0.15
Blood urea nitrogen (mg/dL)	8.88±3.6	6.87±2.1	0.26
Lactate dehydrogenase (U/L)	755.85±3.6	363.6364	0.017
Hemoglobin (g/dL)	12.90±3.6	11.93±3.6	0.011
Creatinine (mg/dL)	0.90±3.6	0.64±3.6	<0.001
PLT (10^3/μL)	153.00±3.6	224.45±3.6	0.001

Table 3. The frequency of positive rectovaginal culture of *Streptococcus* group B and positive serology of helicobacter pylori in the two groups

Parameters		Preeclampsia group (n=21) No. (%)	Controls (n=33) No. (%)	*P* value
Helicobacter pylori	Positive	5 (23.8)	7 (21.2)	0.82
	Negative	16 (76.2)	26 (78.8)	
Group B *Streptococcus*	Positive	2 (9.2)	3 (9.9)	0.12
	Negative	19 (90.8)	30 (90.1%)	

Table 4. The relationship between preeclampsia, helicobacter pylori, streptococcus group B, and related factors

	Parameters		Serology test (%)		*P* value
			Negative	Positive	
Helicobacter pylori	Preeclampsia	With	61.9%	58.3%	0.82
		Without	38.1%	41.7%	
	Preeclampsia	Mild	80.0%	43.8%	0.15
		Severe	20.0%	56.3%	
	Preeclampsia	Early	4.8%	33.3%	0.04
		Late	95.2%	66.6%	
	Baby weight (kg)	2.4-3.2	29.7%	49.6%	0.11
		3.3-4.0	34.7%	35.7%	
		>4.0	32.5%	17.5%	
Streptococcus group B	Preeclampsia	With	49.0%	40. %	0.72
		Without	51.0 %	60. 0%	
	Preeclampsia	Mild	48.8%	40.0%	0.13
		Severe	52.2%	60.0%	
	Preeclampsia	Early	57.7%	60.0 %	0.78
		Late	40.0%	40.0%	
	Newborn weight (kg)	2.4-3.2	33.5%	40.6%	0.32
		3.3-4.0	24.6%	20.0%	
		>4.0	41.9%	40.0%	

healthy women. They also reported that higher rates of *H. pylori*-positive serology and antibodies against *H. pylori* were associated with umbilical arterial impairment with Doppler evaluation (16). Another similar study showed that pregnancy-related diseases were more common in cases that had *H. pylori* than in cases without *H. pylori*. Additionally, the frequency of preeclampsia in the *H. pylori*-positive subgroup was significantly higher than in other subgroups. Furthermore, at the end of pregnancy, *H. pylori*-negative groups showed better fetal growth than the *H. pylori*-positive group (17). A study by Nabiel et al showed that the frequency of antibodies against helicobacter was significantly associated with preeclampsia. They stated that *H. pylori* and *Chlamydia trachomatis* were involved in the development of preeclampsia (18).

In the present study, only 5 patients (9.8%) showed a positive rectovaginal culture of streptococcus, and no statistically significant relationship was observed between the positive rectovaginal culture of *Streptococcus* and preeclampsia, severity of preeclampsia, the onset time, and the weight of newborns. However, studies have shown contradictory findings in the United States. Some findings have pointed to the effective and significant role of the streptococcus serotype in patients with preeclampsia (14), while other studies have statistically rejected this relationship (14,19). In the United States, GBS is the most common infectious disease and the most common cause of mortality in neonates. In addition, GBS causes both early and late infections in infants. Early-onset GBS infection occurs in the first week of life, while late-onset disease occurs after the first week of life in newborns (20). Although this relationship remained unclear in our study, probably due to the GBS effects in pregnant women, further research may help reduce fetal complications (20).

In our study, the levels of various factors, such as systolic and diastolic BPs, LDH, hemoglobin, creatinine, and platelets were significantly different in the healthy and preeclampsia groups, which was consistent with other studies (21,22). Various variables have been identified as blood markers in patients with preeclampsia which may be important in the treatment of patients with preeclampsia (21,23).

The main purpose of our study was to identify the association between *H. pylori* and *Streptococcus* B with the occurrence of preeclampsia in pregnant women. The only significant association was found between streptococcus colonization in mothers and neonatal birth weight. No other association with microbial colonization was observed.

Conclusion

The findings of the present study demonstrated a significant relationship between *H. pylori* infection with early- and late-onset of preeclampsia in affected mothers. Therefore, the *H. pylori* test in the last weeks of pregnancy can play an important role as an adjunct test in the early diagnosis and treatment of high-risk individuals. Furthermore, screening for *H pylori* and eradication therapy before pregnancy can prevent preeclampsia and its serious consequences for both the mother and the fetus.

Limitations of the study

Our study was conducted on a limited number of patients. We suggest further investigations on this subject.

Authors' contribution

SS collected the data, wrote the paper, and planned the experiments. HS, MN conceived and designed the analysis and collected the data. MBA conducted the analysis. All authors read and signed the

final manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research followed the Declaration of Helsinki. The Ethics Committee of Firouzabadi Educational and Medical Center approved this study. The Institutional Ethical Committee of Medical Center in Tehran approved all the study protocols (IR.IUMS.FMD.REC.1397.344). Accordingly, written informed consent was taken from all participants before any intervention. Besides ethical issues (including plagiarism, data fabrication and double publication) were completely observed by the authors.

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