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Original Research Article

Relationship between *Helicobacter pylori* infection and pre-eclampsia among pregnant women in Ardabil

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ABSTRACT

Background: Studies have shown that certain infections can increase the risk of pre-eclampsia which one of the common infections among pregnant women was *H. pylori* with prevalence rate of 60-70% in developing countries. The aim of this study was to investigate the association between H. pylori infection and pre-eclampsia among pregnant women.
Methods: Blood and stool samples were taken from 108 women with pre-eclampsia and 108 healthy pregnant women. Blood samples analyzed by ELISA for specific antibodies against *H. pylori* cytotoxin associated gene A (Cag A) antigen and stool samples were studied in terms of the presence of *H. pylori* Cag A antigen. Collected data were analyzed using statistical methods in SPSS.20.
Results: 30 cases (27.8%) of pre-eclampsia women and 34 (31.5%) of healthy women were sero-positive for Cag A antibodies that was not statistically significant difference. Whereas, 67 cases (62.4%) in the case group and 48 cases (44.4%) in the control group had Cag A antigen in stool samples that was statistically significant difference.
Conclusions: Results showed that, based on detection of *H. pylori* antigen in stool samples, frequency of active *H. pylori* in women with pre-eclampsia was 1.8 times higher than the healthy women.

Keywords: Pre-eclampsia, *Helicobacter pylori*, Cag A

INTRODUCTION

Identifying health priorities is an essential step in providing health education programs and changes in planning any intervention in the provision of health services and health promotion in society. One of these priorities is reducing maternal mortality. One of the major causes of mortality among pregnant women is pre-eclampsia, that despite extensive research, the main cause of it is unknown. Pre-eclampsia is multifactorial and many factors such as high blood pressure, obesity (BMI >30), multiple pregnancies, race, ethnicity, socio-economic factors and genetic predisposition are effective in pre-eclampsia occurrence.[1-4] The prevalence of pre-eclampsia in pregnancy is 5-8% and its incidence is common in nulliparous pregnancy. Suffering from Pre-eclampsia deal to increase its risk in future pregnancies. Severe and earlier pre-eclampsia deal to higher risk of pre-eclampsia. In fact occur pre-eclampsia before 30th week of pregnancy, increase the risk of its relapse by 40%. Recent studies pointed to effective infections such as *cytomegalovirus, Chlamydia, pneumonia* and *H. pylori* in the pathogenesis of pre-eclampsia.[2] In terms of the relationship between *H.pylori* and pre-eclampsia, there are important points such as: the prevalence of both increases with age and is closely related with the economic and social conditions of individuals.[5] Therefore, by effective treatment of *H. pylori*, pre-eclampsia incidence rate can be reduced and also *H.pylori* can be prevented before pregnancy by screening.[6] According to the estimates, about 25-50% of people in developed countries and 70% in developing countries are infected with *H. pylori*.[7]

Low socioeconomic condition, population density and poor health indicators in childhood are risk factors for the pre-eclampsia occurence.[8] The evidences has shown that H. pylori with high virulence can cause inflammation and endothelial damage and also, increases platelet activity and thrombus formation in vessels.[9,10] There are several methods to diagnose this infection which some of them are invasive procedures that require to biopsy and endoscopy and some others are noninvasive such as stool tests and unease breath test (UBT).[11-14] Further serological tests are used for screening and these tests are not applicable for diagnosis because they have low specificity and are not necessarily indicatives of the infection.[15] Stool antigen analysis by ELISA method is convenient and cheap.[16] In stool samples, by PCR-ELISA method, there is more sensitivity due to the lack of need for live bacilli.[11]

The aim of this study was to investigate the Relationship between *H. pylori* infection and pre-eclampsia among pregnant women in Ardabil.

METHODS

In this case-control study, 108 pregnant women with pre-eclampsia, considering the history and primary evaluation of SBP higher than 140 mmHg or DBP higher than 90 mmHg and positive urine analysis of protein or 24-hour urine collection over 300 mg in 24 hours, and 108 healthy pregnant women were selected. After obtaining consent from all of the samples, they were studied in terms of maternal age, gestational age and body mass index before and after pregnancy, history of reumatismul disease and diabetes, respectively. 5 cc blood samples and stool samples obtained from the women. Stool samples were taken in plastic containers and sent to the laboratory as soon as possible. In case of delay in sending the samples, they could be kept at 2 to 8 °C in the refrigerator for up to two days and at -20 °C up to one month. The samples were measured for antigen rate by H. pylori antigen kit (Italy; DIA PR diagnostic) using ELISA method, in stool. Based on the kit instruction, values equal or higher than 1.1 were considered positive and less than 1.1 were considered negative. 5 cc venous blood sample was taken from each patient and was poured in tubes containing EDTA. The samples shouldn't heparinized or citrated. The samples could be kept in refrigerator for up to fourteen days at +2 to +4 °C and at -30 °C for a long time. When analyzing, the samples were located in a centrifuge for 5 minutes with 400 laps. The separated serum diluted with 1:101 dilutions, then the samples by ELISA method and DYNEX set were studied. The Cag A antigen, an indicator of a highly virulent strain of *H. pylori*. The set's calibration was performed by specifications in the kit brochure. Kit (anti *Helicobacter* Cag A ELISA IgG) was the product of Euro Immun U.K. company with serial number order NOE 12081-9601 G. The results were divided into three categories. The answers higher than or equal to 22 U/Ml was considered positive and less than 5 U/Ml negative. The rest of the answers were considered intermediate between these two periods. The information taken from the checklists along with information from blood and stool samples from the cases was analyzed in SPSS 21 using descriptive and inferential statistical methods.

RESULTS

Pregnant women with pre-eclampsia were similar with the control group in terms of age, incidence of diabetes, history of disease and smoking. 7% of women in the preeclampsia group and 12% in the control group were taking aspirin. Epigastric pain during pregnancy was seen in 22% of women in preeclampsia group and 37% of women in the control group. In women with pre-eclampsia, the rate of positivity for Cag A in laboratory testing with 27.8% was lower than the control group with 31.4% but the differences between two groups was not statistically significant as given in Table 1. Percentage of positivity of *H. pylori* stool antigen test in women with pre-eclampsia with 62% significantly was more than women in control group with 44% as shown in Table 2.

The chance of exposure to *H. pylori* in women with pre-eclampsia, based on stool serology tests, was 1.8 times more than the chance of exposure to H. pylori in healthy women (control group). The rate of infants with low birth weight (LBW) in women with pre-eclampsia with 38.5% was significantly more than the healthy women with 8% as shown in Table 3. In the case group in which the result of serology stool was positive, 33.6%, and in the control group 57.4% of infants have LBW and the difference was not statistically significant as in Table 4.

Table 1: Result of CAG A test between two groups.

Group Cag A	Women with pre-eclampsia		Control		P value
	n	%	n	%	
Postive	30	27.8	34	31.4	0.33
Negative	78	72.2	74	68.6	

Table 2: Result of stool antigen test between two groups.

Group Cag A	Women with pre-eclampsia		Control		P value
	n	%	n	%	
Postive	67	62	48	44.4	0.001
Negative	41	38	60	55.6	

Table 3: Low birth weight rate between two groups.

Group LBW	Women with pre-eclampsia		Control		p.value
	n	%	n	%	
Postive	40	37	7	6.5	0.001
Negative	68	63	100	93.5	

Table 4: Frequency of LBW by result of serology in two groups.

Group	Serology Test results	LBW		P value
		+	-	
Women with pre-eclampsia	Positive	33.6	66.4	0.82
	Negative	57.4	42.6	
Control	Positive	55.6	44.4	0.28
	Negative	44.4	55.6	

DISCUSSION

In this study, although Cag A positive antigen was in 30 (27.8%) women with pre-eclampsia and 34 (31.4%) women in the control group, but no significant relationship was observed between them. But in terms of the stool antigen test, 67 patients (62%) in the case group and 48 patients (44.4%) were positive in the control group that was statistically significant result.

In a study conducted by UstUn et al in which serum antigen Cag A was studied, there was a significant relationship between infection and pre-eclampsia.[5] In Ponzettoa et al study, Cag A positivity serology in 47 mothers with pre-eclampsia (51.1%) was compared with 47 pregnant women without complications (31.9%) that this relationship was not statistically significant.[1]

In a study conducted by Cardaropoli et al about the relationship between *H. pylori* infection and its association with pre-eclampsia and low fetal growth, results showed that *H. pylori* is associated with preeclampsia and low growth of fetal.[15]

In Bagheri et al study, the rate of the positive serum against *H. pylori* infection in women suffering from pre-eclampsia was higher than the control group but this was not statistically significant.[16] In this study, the number of samples that were higher than similar studies and according to the serologically in line studies in which the number of samples were more, It seems that the more number of samples, the less relationship between serology positivity Helicobacter pylori and pre-eclampsia. On the other hand, the relationship accuracy increases and this can be more closely linked to the high prevalence of infection in our study area. Generally, differences in study design, prevalence of *H. pylori* in different geographical areas, social and economic differences, diet, number of studied samples, comparison of the results and the most important issue, was the mechanism of different factors affect in suffering from pre-eclampsia.[6,17-19]

CONCLUSION

The results showed that the chance of exposure to *H. pylori* in women with pre-eclampsia based on stool serology tests is 1.8 times significantly more than the chance of exposure to *H. pylori* in healthy women. In comparing the pre-eclampsia fetal complications among the pre-eclampsia women with positive *H. pylori*, the frequency of low birth weight infants in the control group was higher than the other group but among women in the control group, with positive infection and healthy women individuals this relationship was not significant. Therefore, considering the relationship between positive stool test and preeclampsia occurrence we can use screening for high risk women and treatment for pre-eclampsia women.

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