***Helicobacter pylori* Seropositivity and its Relationship with Serum Malondialdehyde and Lipid Profile in Preeclampsia**

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Objective: To investigate *Helicobacter pylori* seropositivity rate in preeclamptic and healthy pregnant. Additionally, we compared serum malondialdehyde (MDA) levels and lipid profile between *H. pylori*-positive and negative cases. **Method:** This study included 53 preeclamptic and 30 healthy pregnant. Serum levels of total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL-C) and low-density lipoprotein (LDL-C), MDA, and *H. pylori* Ig G antibodies were measured. **Results:** Preeclampsia group had higher serum MDA levels compared with healthy pregnant ($P < 0.001$). While the rate of *H. pylori* seropositivity was 43/53 (81%) in the preeclampsia group, this was 18/30

(% 60) in normal pregnant (odds ratio (OR), 2.86; 95% confidence interval (CI), 1.05–7.82; $P = 0.036$). We further divided the preeclampsia group as *H. pylori*-positive and *H. pylori*-negative subgroups. In *H. pylori*-positive group, serum TC ($P < 0.01$) and LDL-C ($P < 0.01$) levels were significantly higher than those of *H. pylori*-negative group. Mean MDA concentration was higher in *H. pylori*-positive group than that of *H. pylori*-negative group ($P < 0.001$). **Conclusion:** *H. pylori*-positive pregnant may have a high risk for preeclampsia and *H. pylori* may be one of the causes for high MDA levels in preeclampsia. J. Clin. Lab. Anal. 23:219–222, 2009. © 2009 Wiley-Liss, Inc.

Key words: *H. pylori* seropositivity; preeclampsia; MDA; lipids

INTRODUCTION

Preeclampsia is a common disease of human pregnancy and a leading cause of both, maternal and neonatal morbidity and mortality, respectively (1). In preeclampsia pathogenesis, endothelial dysfunction and inflammation appear to play a major role. It was found that an increased level of pro-inflammatory cytokines in the circulation of preeclamptic women and maternal circulating activated leukocytes and monocytes may contribute to the process (2,3). *Helicobacter pylori* is a Gram-negative organism that causes chronic active gastric inflammation. This microorganism not only causes gastric ulcer or cancer but also increases the risk of coronary heart disease (4). There are also substantial reports demonstrating the presence of excess lipid peroxides in patients with *H. pylori* infection (5,6).

The purpose of this study is to investigate the possible association between *H. pylori* infection and preeclamptic women. Additionally, we compared lipid profile and

MDA concentrations between *H. pylori*-negative and positive subjects in both groups.

MATERIALS AND METHODS

Fifty-three preeclamptic subjects and 30 healthy pregnant were enrolled in this study. Preeclampsia was defined as the development of hypertension with proteinuria (7). Hypertension was defined as either measurements of systolic blood pressure of greater than 140 mmHg or diastolic blood pressure of greater than 90 mmHg on two consecutive measurements at least 6 hr apart. Proteinuria was defined as excretion of greater

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than 300 mg of protein in a 24-hr urine collection. Inclusion criteria were preeclampsia, gestational age corroborated by ultrasonography before 20 weeks' gestation, singleton fetus, no fetal structural anomaly, nonsmoker, normal response to glucose tolerance testing, no evidence of recent infections (e.g., rubella, toxoplasma, hepatitis B and C, cytomegalovirus, or syphilis), no any autoimmune disease, previous pregnancy with preeclampsia, and absence of uterine contractions.

Demographic data of both groups were recorded. Gestational age was determined using the first date of last menstrual period and confirmed by ultrasonography. The participants eligible for the study had been informed about the study before blood samples were collected.

Venous blood samples were collected into tubes without anticoagulant. Serum was separated by centrifugation after clotting and stored at -80°C until assayed. Serum MDA levels were determined spectrophotometrically according to the method described by Ohkawa et al. (8). Serum total cholesterol (TC), triglyceride (TG) and high-density lipoprotein (HDL-C), and low-density lipoprotein (LDL-C) were assayed in an autoanalyzer (Roche Hitachi P 1600 analyzer, Boehringer Mannheim, Germany).

TABLE 1. Clinical Characteristics of the Study Groups

	Preeclamptic patients (<i>n</i> = 53)	Normal pregnant (30)
Gestational age (weeks)	36.79 $\pm$ 1.67	36.73 $\pm$ 1.70
Maternal age (yr)	26.53 $\pm$ 4.77	26.33 $\pm$ 4.95
Nulliparity (no)	30 (56.6%)	19 (63.33%)
Systolic blood pressure (mmHg)	158.20 $\pm$ 17.39*	121.16 $\pm$ 6.11
Diastolic blood pressure (mmHg)	103.44 $\pm$ 9.55*	67.33 $\pm$ 10.15

Results were given mean $\pm$ SD. * $P < 0.0001$ compared with normal pregnancy group.

H. pylori infection was detected with a commercially available immunoglobulin G (IgG) enzyme-linked immunosorbent assay (Trinity kit, Biotech Co., New York). Serum samples with an ELISA unit of greater than 1.10 U/ml, between 0.90 and 1.10 and less than 0.90 were considered positive, borderline, and negative, respectively. Borderline results were omitted from further analysis.

Statistical Analysis

Results were expressed as mean $\pm$ SD. Comparisons between groups were evaluated using Student's *t*-test for continuous variables and a χ^2 test for *H. pylori* seropositivity, and the odds ratio (OR) and 95% confidence intervals (CIs) were calculated to assess the risk of preeclampsia associated with *H. pylori* infection. $P < 0.05$ was considered statistically significant.

RESULTS

The clinical characteristics of the three study groups are described in Table 1. Patients with preeclampsia and matched controls had similar age. The preeclampsia group had significantly higher systolic and diastolic blood pressure than the healthy control groups ($P < 0.0001$ for both).

Preeclampsia group had higher serum MDA levels compared with healthy pregnant ($P < 0.001$). There were no significant differences between normotensive pregnant and preeclamptic with regard to serum lipid profile. While the rate of *H. pylori* seropositivity was 43/53 (81%) in preeclampsia group, this was 18/30 (60%) in normal pregnant (OR, 2.86; 95% CI, 1.05–7.82; $P = 0.036$). We further divided the preeclampsia group as *H. pylori*-positive and *H. pylori*-negative subgroups. In *H. pylori*-positive group, serum TC ($P < 0.01$) and LDL-C ($P < 0.01$) levels were significantly higher than those of *H. pylori*-negative group (Table 2). Additionally, mean MDA concentration was higher in *H. pylori*-positive group than in *H. pylori*-negative group

TABLE 2. Serum MDA and Lipid Profile in Preeclampsia and Normal Pregnants, Divided According to *H. pylori* Seropositivity

	MDA ($\mu\text{mol/l}$)	TC (mg/dl)	TG (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)
Preeclampsia patients (<i>n</i> = 53)	3.90 $\pm$ 1.55	262.98 $\pm$ 66.03	315.32 $\pm$ 157.23	147.01 $\pm$ 49.71	50.98 $\pm$ 14.19
<i>H. pylori</i> (+)	4.18 $\pm$ 1.55*	277.05 $\pm$ 60.83**	329.30 $\pm$ 168.24	157.51 $\pm$ 46.18**	52.44 $\pm$ 14.41
<i>H. pylori</i> (–)	2.67 $\pm$ 0.77	202.50 $\pm$ 54.00	255.20 $\pm$ 76.03	101.90 $\pm$ 39.24	44.70 $\pm$ 11.75
Normal pregnant (<i>n</i> = 30)	2.55 $\pm$ 1.07***	241.97 $\pm$ 54.34	271.03 $\pm$ 114.68	135.73 $\pm$ 49.47	48.97 $\pm$ 7.61
<i>H. pylori</i> (+)	2.48 $\pm$ 1.01	246.78 $\pm$ 54.05	252.22 $\pm$ 101.56	144.61 $\pm$ 49.26	50.33 $\pm$ 7.10
<i>H. pylori</i> (–)	2.66 $\pm$ 1.19	234.75 $\pm$ 56.34	299.25 $\pm$ 131.46	122.41 $\pm$ 48.80	46.92 $\pm$ 8.21

MDA; malondialdehyde, TC; total cholesterol, TG; triglyceride, LDL-C; low-density lipoprotein-C, HDL-C; high-density lipoprotein-C. Results were given mean $\pm$ SD. * $P < 0.001$ compared with *H. pylori* (–) group; ** $P < 0.01$ compared with *H. pylori* (–) group; *** $P < 0.001$ compared with preeclampsia patients.

($P < 0.001$). In the healthy pregnant group, there was not any significant difference in terms of serum lipid profile and MDA concentration between *H. pylori*-positive and -negative subgroups (Table 2).

DISCUSSION

H. pylori represents one of the most common and medically prominent infections worldwide (9). Although preeclampsia is also one of the most significant health problems of human pregnancy, the exact cause of preeclampsia is still unknown. Several studies have reported that there is an imbalance between reactive oxygen species and antioxidants in preeclampsia (10,11). Indeed oxidative stress presents in normal pregnancy but in preeclampsia cases this is increased. In increased oxidative stress conditions, lipids are the major target of reactive oxygen species and lipid peroxides are formed by the reaction of reactive oxygen species with polyunsaturated fatty acids in the cellular membranes. The products of lipid peroxidation circulate in increased amounts and may mediate maternal endothelial cell damage. MDA is a breakdown product of oxidized lipids and a commonly used indicator of lipid peroxidation. In one study carried out on Indian women, serum MDA concentrations were significantly higher in preeclamptic patients as compared with normal pregnant and nonpregnant women (10). Kaur et al. (12) investigated the oxidant/antioxidant status in preeclamptic women and they found that while MDA levels were increased, antioxidant enzymes, superoxide dismutase, and catalase activities were decreased in preeclamptics compared with normotensive pregnant.

This situation results in increased superoxide anion and hydrogen peroxide and in turn greater lipid peroxidation. They also found a positive correlation between systolic and diastolic blood pressure with plasma malondialdehyde (MDA) levels. In other words, it may be speculated that lipid peroxidation may cause endothelial damage ultimately leading to elevated blood pressure. In also our study, in preeclampsia group, increased MDA levels were detected; this observation was in agreement with the previous studies (10–14).

The oxidative damage caused by the free radicals may be involved in the pathogenesis of *H. pylori* infection. Increased amounts of MDA have been found in patients infected with *H. pylori* (4,5). Additionally, Aslan et al. (15) observed an increased oxidative stress in *H. pylori* infection.

Recently, Ponzetto et al. (16) have shown that the prevalence of *H. pylori* infection in patients with preeclampsia is higher than that of normal pregnant. We also showed that *H. pylori* seropositivity rate was higher in the preeclampsia patients than in healthy

pregnants. Then, we divided the preeclampsia group and normal pregnant as *H. pylori*-positive and *H. pylori*-negative subgroups. In our study, we could not determine an increased MDA in *H. pylori*-positive normal pregnant. But in preeclampsia group, *H. pylori* seropositive patients showed higher serum MDA compared with seronegative ones.

H. pylori infection and serum lipid levels have often yielded contradictory results. Chimienti et al. (17) found significant differences in serum TC and LDL-C from the comparison of *H. pylori* (+) and *H. pylori* (–) subjects. They concluded that *H. pylori* infection per se significantly modified serum lipids in favor of atherogenicity. On the other hand, in another study, *H. pylori* IgG antibody when measured for infection determination, no significant differences were found in serum lipids and lipoproteins in healthy males. But, there were an endothelial dysfunction and vascular inflammation in subjects with seropositivity to *H. pylori* (18). In the study by Aslan et al. (15) serum TG, TC, and LDL-C levels were higher in *H. pylori*-infected subjects compared with *H. pylori*-negative ones. Also in males with *H. pylori*, it was found that serum TG and TC concentrations were significantly higher than in the males with no signs of infection (19).

Changes in the levels of lipids and lipoproteins in pregnancy is the physiological response to pregnancy. Also, in previous studies it was shown that preeclampsia is associated with abnormal lipid and lipoprotein metabolism (20–22). But, in our study, we did not find significant differences with regard to serum lipids and lipoproteins between normal and preeclamptic patients (*H. pylori* (+) plus (–) cases). Similar to our study, Punthumapol et al. (23) reported that there was not any significant difference in serum cholesterol, TG, HDL, and LDL between normal and preeclamptic women. Additionally, another study showed that the mean concentrations of LDL-C and triacylglycerols were not different between the two groups, but the mean HDL-C level was higher in the healthy pregnant women compared with the preeclamptic/eclamptic women (24). In our study, we did not investigate whether *H. pylori* infection is associated with endothelial dysfunction, but the higher mean TC and LDL-C levels in *H. pylori* seropositive patients than in seronegative ones in preeclamptic patients seems statistically interesting. Therefore, *H. pylori* infection may be a contributory factor in atherosclerosis in preeclampsia cases in their later life. This situation needs further detailed studies for clarification.

In our study, seropositivity is high in both study and control groups (81 and 60%, respectively). But, Ponzetto et al. (16) found lower *H. pylori* IgG seropositivity in preeclampsia cases and normal

pregnants in Italy (51.1 vs. 31.9%). One possible explanation for our result is the low socioeconomic level of our patient population. Numerous epidemiologic studies have shown that a major risk factor for *H. pylori* acquisition is low socioeconomic level in both undeveloped and developing countries. Our finding supports these associations.

As a conclusion, it is suggested that *H. pylori*-positive pregnant may have a high risk for preeclampsia, and *H. pylori* may be one of the causes for high MDA levels in preeclampsia.

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