The relationship between the level of homocysteine in mother's serum and the intensity of preeclampsia

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Abstract: Determining the relationship between maternal serum homocysteine level and severity of preeclampsia. In a cross-sectional descriptive-analytical study, maternal homocysteine level was assessed in patients with mild and severe preeclampsia. The mean level was assessed by electro-immunoassay enzyme test. No significant difference was observed in age, parity and abortion history among pregnant mothers. The mean serum homocysteine level was 5.5±1.6 in control group, 6.3±1.9 in mild preeclampsia and 8.9±4.1 in severe preeclampsia. The mean serum homocysteine level was significantly higher in women with severe preeclampsia than in control group (P<0.001), but no significant difference between normal pregnant women and those with mild preeclampsia (P=0.12). This study revealed a direct relationship between concentration of serum homocysteine and severity of preeclampsia. However, in mild preeclampsia, the concentration of serum homocysteine slightly changes with no significant difference. It is deducted that low homocysteine concentration makes slight changes to vascular endothelium.
[Ezzatalsadat Haji Seid Javadi, Fatemeh Ghorbali, Mohammadreza Sarookhani, Amir Javadi, Sepehr Taghizadeh. **The relationship between the level of homocysteine in mother's serum and the intensity of preeclampsia.** *Life Sci J* 2012;9(4):1247-1249] (ISSN:1097-8135). http://www.lifesciencesite.com. 187

Keywords: Preeclampsia; Homocysteine; Intensity

1. Introduction

Preeclampsia is one of the most important factors for mortality during pregnancy. Etiology of preeclampsia is not yet clear, but what is certain is that a variety of disorders that lead to vascular spasm and endothelial dysfunction may play a crucial role in its occurrence (Cunningham, 2010). In its metabolism cycle, homocysteine is metabolized into cysteine or methionine, and these two need vitB2, vitB12, vitB6 and folic acid cofactors; hence, in cases of deficiency of the mentioned cofactors, hyperhomocysteinemia occurs (Cunningham, 2010).

Thickening the intima layer of arteries, Hyperhomocysteinaemia reduces the elasticity of the lamina and hypertrophies the Smooth muscle tissue. Also, Thiolactone, metabolite of homocysteine, attaches to LDL of macrophages and produces atherosclerotic plaque in vascular intima layer (Tug, 2003). Hyperhomocysteinemia causes oxidative stress, increased level of lipid peroxides, increased activity of antioxidants and reduced level of nitric oxide, which can lead to dysfunction of endothelial cells(Urmila, 2009).

Homocysteine level in normal non-pregnant people is about 5-15 *µmol/L*, while it decreases to 3.3 to 7.5 *µmol/L* during pregnancy (Cotter, 2001). This reduction may be the result of increased level of estrogen, Hemodilation, or due to increased consumption of methionine by the mother and fetus (Hoque, 2008).

Given the above, the level of homocysteine is expected to be higher in patients with preeclampsia than normal pregnant subjects. The aim of this study is to determine the relationship between maternal serum homocysteine level and severity of preeclampsia.

2. Material and Methods

In a descriptive-analytical case-control study on 168 pregnant mothers referred to the Kawthar Hospital of Qazvin University of Medical Sciences, the relationship between maternal serum homocysteine level and severity of preeclampsia was investigated.

All patients were divided into three groups: The first group (the control group) consisting of 60 pregnant women without hypertension and with gestational age of 37 who were nominated for termination of pregnancy. The second group included 55 pregnant women with mild preeclampsia, and the third group included 53 pregnant women with severe preeclampsia.

Exclusion criteria*:* Occurrence of Chronic HTN (blood pressure greater than or equal to 90/140

prior to the 20 th week of pregnancy or before pregnancy without symptoms of mild and severe preeclampsia), anemia (Hb < 11), chronic hepatic diseases, renal diseases, a history of repeated abortions (More than 2 abortions), placental abruption, smoking, diabetes, anti-folate drugs such as Methotrexate and anticonvulsants.

A 2*cc* blood sample was taken from all women under study after 8 hours of fasting and kept on EDTA anticoagulation. Immediately, the plasma was extracted and kept frozen till the test time. In this research, the homocysteine of blood was assessed using electroimmunoassay enzyme test (EIA) kit.

The obtained data was coded and then entered into a computer and statistically analyzed by SPSS software. ANOVA test was used for data analysis. Significance level for tests was determined as 95% ($P< 0.05$).

3. Results

The mean age was 26.5 ± 5.8 years in the control group, 28.8 ± 6.3 in mild preeclampsia group, and 27.7 ± 5.8 years in severe preeclampsia group that there was no significant difference in the mean age of the patients under study among the three groups (P=0.11).

The mean parity was 1.8 ± 0.9 in patients of the control group, 2.1 ± 1.5 in patients with mild preeclampsia, and 21.1 ± 1.4 in patients with severe preeclampsia that there was no significant difference in the mean parity of the patients under study among the three groups(P=0.4).

The mean serum homocysteine was 5.5 ± 1.6 *µmol/L* in the range of 3-10.3 *µmol/L* in control group patients, 6.3 ± 1.9 *µmol/L* in the range of 3-12.1 *µmol/L* in patients with mild preeclampsia, and 8.9 ± 4.1 *µmol/L* in the range of 5.3-27.8 *µmol/L* in patients with severe preeclampsia (Table 1).

Serum homocysteine level in patients with severe preeclampsia were significantly higher ($P<0.001$); but there was no significant difference in the mean serum homocysteine level between patients with mild preeclampsia and the control group patients (P=0.12) (Table 1).

Table 1. Age, parity and level of serum homocysteine between three groups of patients

	Groups			P_V
	Control Group (n=60)	Mild Preeclampsia (n=55)	Sever Preeclampsia (n=53)	
Age(year)	26.5 ± 5.8	28.8 ± 6.3	27.7 ± 5.8	0.11
Parity	1.8 ± 0.9	2.1 ± 1.5	2.1 ± 1.4	0.4
Homocysteine	5.5 ± 1.6	6.3 ± 1.9	8.9 ± 4.1	<0.001

4. Discussion

In this study, the mean maternal serum homocysteine in the third trimester of pregnancy in pregnant mothers in the control group was 5.5 ± 1.6 *µmol/L* that had decreased compared to non-pregnant people.

Total maternal serum homocysteine level was increased in preeclamptic women and hyperhomocysteinemia was associated with severity of preeclampsia (Khosrowbeygi, 2011).

Bergen, in the study "Department of Clinical Chemistry, Department of Public Health, Erasmus University Medical Centre, Rotterdam, Netherlands" showed that high homocysteine and low folate concentration in early pregnancy may adversely influence placentation and subsequently, affect the success of pregnancy and birth outcomes (Bergen, 2012).

Mislanova and et al. suggested that disordered placental folate-related metabolism may be one of the pathogenetic factors in preeclampsia (Mislanova, 2011).

Different studies have confirmed that elevated tHcy is a risk factor for sub-fertility, congenital developmental defects, preeclampsia, and intrauterine growth retardation(Murphy, 2011).

In the study by Walker at 1999, the mean serum homocysteine in pregnant women with normal pregnancies in the third trimester was 5.5 *µmol/L*(Walker, 1999) that the same was in our study.

In our study, the mean serum homocysteine was 5.5 ± 1.6 *µmol/L* in the control group patients, 6.3 ± 1.9 *µmol/L* in patients with mild preeclampsia, and 8.9 ± 4.1 *µmol/L* in patients with severe preeclampsia.

As is known, vascular spasm, endothelial destruction and dysfunction plays a vital role in occurrence of preeclampsia and hyperhomocysteinemia is one of the factors causing oxidative stress and endothelial cell dysfunction. In many studies, increased homocysteine level in preeclampsia has been proven, but fewer studies have proceeded to compare the homocysteine level in mild and severe preeclampsia.

In the study by Urmila and et al. in India(Urmila,2009), and the study by İngec and et al. in the Ataturk University School of Medicine, Izmir, Turkey(İngec, 2005), they showed that there was no significant difference in homocysteine level between pregnant women with normal blood pressure and those with mild preeclampsia, but there was a significant difference between pregnant women with severe preeclampsia and those with normal blood pressure.

In the study by Dudani and et al, there was a significant difference in homocysteine level between hypertensive pregnant women and those with mild preeclampsia (Dudani, 2006) which is inconsistent with our study.

Acilmis and et al. showed that maternal and fetal serum homocysteine levels were found to be significantly higher in severe preeclampsia group than in mild preeclampsia and control groups, suggesting that elevated level of serum homocysteine might be associated with severity of preeclampsia (Acilmis, 2011).

As can be observed, in all studies, there is a direct relationship between homocysteine level and severe preeclampsia.

In different studies, contradictory results have been obtained about the significant increase in homocysteine in mild preeclampsia. It may be concluded from the above discussions that low concentration of homocysteine slightly affects the endothelium and has a subtle role in occurrence of preeclampsia. More prospective studies are needed to clarify this issue. This important goal may be achieved by measuring serum homocysteine during the first trimester of pregnancy and follow up of patients in terms of affliction by preeclampsia.

Conclusion

This study revealed a direct relationship between serum homocysteine concentrations with severe preeclampsia. However, in mild preeclampsia the concentration of serum homocysteine changes trivially and there is no significant difference. It can be deducted that the low concentration of homocysteine makes trivial changes in vascular endothelium.

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References

1-Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Gilstrap LC, Wenstrom KD. Williams Obstetrics, 23rd ed. McGraw-Hill Professional, New York, 2010; 706-49.
2-Tug N, Celik H, Cikim G, Ozcelik O, Ayar A. The correlation between plasma homocysteine and malondialdehyde levels in preeclampsia. Neuro Endocrinol Lett 2003; 24(6):445-8.
3-Urmila S, HP Gupta, PK singh. Homocysteine: Association with preeclampsia and normotensive pregnancy. J obstet Gynecol India 2009; 59(3):235-8
4-Hoque MM, Bulbul T, Mahal M, Islam NA, Ferdausi M. Serum homocysteine in pre-eclampsia and eclampsia. Bangladesh Med Res Counc Bull 2008; 34(1):16-20.
5- Cotter AM, Molloy AM, Scott JM, Daly SF. Elevated plasma homocysteine in early pregnancy: a risk factor for the development of severe preeclampsia. Am J Obstet Gynecol 2001; 185(4):781-5.
6-Khosrowbeygi A, Ahmadvand H. Circulating levels of homocysteine in preeclamptic women. Bangladesh Med Res Counc Bull 2011; 37(3):106-9.
7-Bergen N, Jaddoe V, Timmermans S, Hofman A, Lindemans J, Russcher H, Raat H, Steegers-Theunissen R, Steegers E. Homocysteine and folate concentrations in early pregnancy and the risk of adverse pregnancy outcomes: the Generation R Study. BJOG 2012; 119(6):739-51.
8-Mislanova C, Martsenyuk O, Huppertz B, Obolenskaya M. Placental markers of folate-related metabolism in preeclampsia. Reproduction 2011; 142(3):467-76.
9-Murphy MM, Fernandez-Ballart JD. Homocysteine in pregnancy. Adv Clin Chem 2011; 53:105-37.
10-Walker MC, Smith GN, Perkins SL, Keely EJ, Garner PR. Changes in homocysteine levels during normal pregnancy. Am J Obstet Gynecol 1999; 180(3 Pt 1):660-4.
11-Ingec M, Borekci B, Kadanali S. Elevated plasma homocysteine concentrations in severe preeclampsia and eclampsia. Tohoku J Exp Med 2005; 206(3):225-31.
12-Dudani AL, Khoja A, Karira KA. Assessment of Homocysteine levels preeclampsia. Med Chanel 2006; 12(2):16-8.
13-Acilmis YG, Dikensoy E, Kutlar AI, Balat O, Cebesoy FB, Ozturk E, et al. Homocysteine, folic acid and vitamin B12 levels in maternal and umbilical cord plasma and homocysteine levels in placenta in pregnant women with pre-eclampsia. J Obstet Gynaecol Res 2011; 37(1):45-50.

9/25/2012