

Elevated Circulating Homocysteine Level in Patients with Mild Pre-eclampsia

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Background: Pre-eclampsia is a disease unique to pregnancy that complicates 5-7% of low risk pregnancies and as many as 25% of high risk pregnancies. Hyperhomocysteinemia is one of the chronic risk factors for pre-eclampsia. This study was designed to evaluate the plasma homocysteine level in patients with mild pre-eclampsia, because hyperhomocysteinemia can be corrected with a combination of folic acid and vitamin B₆.

Materials and Methods: A cross-sectional comparative study was carried out on 60 primigravida attending the "antenatal clinic" of Services Hospital, Lahore. Out of these 60 primigravida, 30 pre-eclamptic primigravida (30-38 weeks of pregnancy) were patients of mild PET and 30 primigravida (30-38 weeks of pregnancy) were having uncomplicated pregnancy. Blood samples were taken in EDTA containing tubes and tested for homocysteine level by a Bio-Rad enzyme-linked immunoassay (EIA) microtitre method.

Results: In mild pre-eclamptic patients the fasting plasma homocysteine level was significantly raised than controls.

Conclusion: Hyperhomocysteinemia is one of the important risk factor in the causation of pre-eclampsia which can be corrected by folic acid vitamin B₆ supplementation.

Key Words: Hyperhomocysteinemia: Mild PET, Primigravida.

Introduction

Pre-eclampsia (PET) is pregnancy induced hypertension which classically includes a triad of clinical signs and symptoms - hypertension, proteinuria and pathologic oedema.¹

It is a disease unique to pregnancy that complicates 5.7% of low risk pregnancies² and as many as 25% of high risk pregnancies.³ It is of two types mild pre-eclampsia and severe pre-eclampsia. In mild pre-eclampsia there is a diastolic blood pressure of 90-100 mm Hg with 24 hour urinary protein excretion of more than 300 mg with no signs and symptoms of impending eclampsia.⁴ Clinical studies documented a familial tendency toward development of pre-eclampsia, although the pattern of inheritance is unclear.⁵ Exact etiology is uncertain. There are many risk factors which play an important role. One of the important chronic risk factor is hyperhomocysteinemia.⁶

Hyperhomocysteinemia can result from genetic or nutrient-related disturbances in the trans-sulfuration or remethylation pathway for homocysteine metabolism. A common mutation in the methylenetetrahydrofolate reductase gene, (677T), and a heterozygous state of cystathionine β-synthase gene can cause hyperhomocysteinemia. Inadequate intake of vitamin B₁₂, B₆ or folate may underlie some cases of elevated homocysteine levels.⁷

Plasma homocysteine concentration is generally lower in pregnant women than in non-pregnant individuals, probably as a result of hormonal changes associated with pregnancy. It is 3.3-7.5 μmol/l at 36-42 weeks gestation.⁹ It is found that elevated maternal plasma homocysteine plays a role in the pathogenesis of vascular disease in the uteroplacental circulation in placental insufficiency.¹⁰ Endothelial cell dysfunction is important in the pathogenesis of pre-eclampsia. Homocysteine is thought to damage endothelial cells by several mechanisms. Potential mechanisms are generation of hydrogen peroxides. Depletion of nitric oxide-mediated detoxification of homocysteine, enhanced endothelial cell factor V activity, impaired endothelial thrombomodulin expression and activation of the contact pathway for intrinsic coagulation by homocysteine crystals in endothelial cells.¹¹ Plasma homocysteine of more than 10.2 μmol/l has been reported to be associated with a doubling of risk of vascular disease.¹² The aim of this study was to evaluate the plasma homocysteine level in patients of mild PET.

Materials and Methods

The study includes 30 primigravida with mild pre-eclampsia (30-38 weeks of gestation) and 30 primigravida with normal pregnancy (30-38 weeks of gestation) taken as control group. The objective

was to have an assessment of the levels of plasma homocysteine in “normal healthy pregnant females” and to compare their levels with those obtained from mild PET patients. The patients were diagnosed and documented as mild pre-eclampsia on the basis of:

1. A systolic blood pressure 90-100 mm Hg on at least 2 occasions 6 hours apart.
2. A significant proteinuria more than 300 mg/24 hour.

Both patients and controls with 10-12 hours fast were called. After taking informed consent a 5 ml venous blood was obtained from antecubical vein of pre-eclamptic patients and normal healthy pregnant female subjects into vacutainer tubes containing tripotassium EDTA (for preparation of plasma). The sample were centrifuged, the plasma was removed within an hour and stored at -20°C until analyzed for homocysteine. Plasma total homocysteine level was estimated by a Bio-Rad enzyme-linked immunoassay (EIA) microtitre method.

Statistical Analysis

All values were expressed as mean ± standard deviation (SD). Student “t” test was used to compare means with two categories of study variable. Statistical analysis was carried out using the SPSS® (Statistical Package for Social Sciences), Software Version 10 for Windows®. A P value less than 0.05 was considered significant.

Results

The mean plasma homocysteine level in mild PET patients was significantly raised ($p < 0.001$) when compared with their control group (Table 1).

Table 2 shows the demographic and clinical features of mild PET group and control group.

Discussion

The results of this study show that the plasma homocysteine level was significantly raised in patients

of mild PET group.

Table 1: Mean ± SD of plasma homocysteine level in control and mild PET group.

Study Group	Plasma Homocysteine Level $\mu\text{mol/l}$ Mean \pm SD	*p value
Control group n = 30	5.66 \pm 0.51	< 0.01
Mild pre- Eclampsia group n = 30	9.67 \pm 2.83	

Malinow (1998) found that maternal vein plasma homocysteine level was $5.43 \pm 1.40 \mu\text{mol/l}$ in the third trimester of pregnancy.¹⁴ In another study by walker et al (1991) the plasma homocysteine level was $5.6 \mu\text{mol/l}$ in third trimester of pregnancy. All these studies show that the plasma homocysteine level in normally low between $5-6 \mu\text{mol/l}$ in the third trimester of pregnancy. In the present study the mean plasma homocysteine level in control subjects was $5.66 \pm 0.515 \mu\text{mol/l}$.

In a study by Wang and his workers (2000), circulating homocysteine level in placental vascular disease and pre-eclampsia were found to be higher. In the same study, the plasma homocysteine level in the control group was $5.9 \mu\text{mol/l}$ but in the pre-eclamptic patients it was upto $9.4 \mu\text{mol/l}$ which showed a significant increase over the control group. Similar high levels of about $9.8 \pm 3.3 \mu\text{mol/l}$ were found in a study done by Cotter et al (2001).

Conclusion

Hyperhomocysteinemia may be diagnosed by

Table 2: Demographic and Clinical Features of Mild Pre-eclampsia and Control Group.

Patients Characteristics	Control Mean \pm SD n = 30	Mild Pre-eclampsia Group Mean \pm SD n = 30	*P value
1. Age (years)	26.07 \pm 4.03	25.63 \pm 3.43	0.66 (NS)
2. Duration of Gestation (weeks)	35.27 \pm 2.19	35.77 \pm 2.29	0.39 (NS)
3. Systolic BP (mmHg)	114.33 \pm 6.26	143.67 \pm 6.15	< 0.01 (HS)
4. Diastolic BP (mmHg)	73.67 \pm 5.56	96 \pm 4.09	< 0.01 (HS)

measuring fasting homocysteine level. Hyperhomocysteinemia is found in patients of eclampsia. These pregnant women are likely to benefit from the therapies that lower the circulating homocysteine levels in the form of folic acid, B₆ and B₁₂ supplementation.

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