

A Study of Serum Homocysteine Levels in Pre-Eclampsia and Eclampsia in a Tertiary Care Hospital

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Abstract: Pre-eclampsia is a condition of high blood pressure during pregnancy and it is one of the important cause of maternal or fetal morbidity and mortality. Recently the pieces of evidence have found that increases in homocysteine levels are associated with adverse outcomes. In the present study, we tried to evaluate the serum Homocysteine, Serum Folate, and Vitamin B12 levels in pre-eclamptic pregnant women and eclamptic pregnant women compared with normal pregnant women. Methods: This cross-sectional prospective study was done in the Department of OBGY and Biochemistry, Prathima Institute of Medical Sciences, Naganoor, Karimnagar study period 9/8/2017 to 9/7/2018. Fifty females of normal pregnancy, thirty-five patients of pre-eclampsia and twenty-eight patients of eclampsia were included in the study. Pre-eclampsia was diagnosed when the BP was higher than 140/90mmHg observed on at least 2 occasions after the 20th week of pregnancy and protein urea of > 300 mg/24 hours. Eclampsia was defined as the onset of convulsions or coma in the patients who has signs and symptoms of pre-eclampsia. Results: In the normal pregnancy the mean values of homocysteine were 7.56 ± 2.3 $\mu\text{mol/L}$ in pre-eclampsia it was 15.55 ± 3.9 $\mu\text{mol/L}$ and in eclampsia it was 18.85 ± 4.56 $\mu\text{mol/L}$. The serum folic acid mean values were 12.9 ± 3.6 ng/ml in normal pregnancy, 10.24 ± 2.64 ng/ml in eclampsia and 8.54 ± 2.4 ng/ml in eclampsia. The vitamin B12 levels were measured in pictograms/ml the values recorded for the normal pregnancy, pre-eclampsia and eclampsia were 387 ± 48.9 , 315 ± 45.7 and 310 ± 52.6 respectively. The comparisons of homocysteine, Folic acid, and Vitamin B12 levels were measured between the three groups. The homocysteine levels between the controls and pre-eclampsia and eclampsia were found to be significant the P values were < 0.05 and < 0.01 but the valves were not found to be significant in between pre-eclampsia and eclampsia. Conclusion: Within the limitations of the present study it can be concluded that higher homocysteine levels were related with pre-eclampsia and eclampsia at the same time the folic acid and Vitamin B12 levels were also found to be reduced in women with pre-eclampsia and eclampsia.

Keywords: Homocysteine, Pre-Eclampsia, Eclampsia.

INTRODUCTION

Pre-eclampsia is a condition characterized by an onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive pregnant woman [1, 2]. Pre-eclampsia is a significant public health problem both in developing and developed countries and contributing to maternal and perinatal morbidity and mortality globally [3, 4]. According to the new ACOG (American College of Obstetricians and Gynecologists), diagnostic criteria for pre-eclampsia the presence of proteinuria has been eliminated. In absence of proteinuria new-onset hypertension with thrombocytopenia, elevated liver enzymes, renal insufficiency, pulmonary edema and cerebral or visual symptoms are defined as pre-eclampsia [5]. The exact etiopathogenesis remains unclear but definite risk factors for preeclampsia include primiparity, previous preeclamptic pregnancy, hypertension, renal diseases

thrombophilia, diabetes mellitus obesity and advanced maternal age [6]. Homocysteine is a sulfur-containing amino acid and it is an immediate product of methionine metabolism since methionine cannot be stored in the liver it is demethylated to homocysteine and stored until further used. The concentration of homocysteine depends on several factors including genetic influences and environmental factors. Homocysteine can be converted to methionine by folic acid and vitamin B12 which acts as essential co-factors. Also, homocysteine can be converted to cysteine through transsulphuration also required vitamin B12 enzyme [7] homocysteine damages the smooth muscle of the vessel walls and thus leading to accumulation of plaque. Hyperhomocysteinemia stimulates inflammation, activate the endothelium of blood vessels and initiates clotting cascade and inhibits fibrinolysis. It also results in loss of endothelial antithrombin function and

induction of a procoagulant [8, 9]. Homocysteine also reduces Nitric Oxide availability by interfering with its synthesis activation of transcription factors stimulating gene expression. Hyperhomocysteinemia promotes oxidation of LDL cholesterol molecules and alterations in the coagulation system and enhances platelet activation [10] we in the present study tried to evaluate the serum homocysteine, folic acid and vitamin B12 levels in normal pregnant women compare it with pre-eclampsia and eclampsia.

MATERIALS AND METHODS

This cross-sectional prospective study was done in the Department of OBGY and Biochemistry, Prathima Institute of Medical Sciences, Naganoor, Karimnagar study period 9/8/2017 to 9/7/2018. Institutional Ethical committee permission was obtained for the study. An informed consent was obtained from all the participants of the study after explaining the study in the local language. Fifty females of normal pregnancy, thirty-five patients of pre-eclampsia and twenty-eight patients of eclampsia were included in the study. Pre-eclampsia was diagnosed when the BP was higher than 140/90mmHg observed on at least 2 occasions after the 20th week of pregnancy and protein urea of > 300 mg/24 hours. Eclampsia was defined as the onset of convulsions or coma in the patients who has signs and symptoms of pre-eclampsia. Inclusion criteria were patients with signs and symptoms of pre-eclampsia, and eclampsia with normal renal and liver function tests was included. Exclusion

criteria were those with other significant illnesses and these not willing to participate in the study. Venous blood was collected in vacutainers under aseptic precautions. The samples were centrifuged at 2500rpm for 10 minutes. Serum was separated and collected. Estimation of serum homocysteine, folic acid, and vitamin B12 measurements was done by competitive chemiluminescent enzyme immunoassay method [11]. Serum folic acid concentration was investigated by chemiluminescent assay [12]. Serum Vitamin B12 concentration was evaluated by solid-phase competitive chemiluminescent assay methods [13] The data was collected and analyzed by SPSS version 17 software on windows format.

RESULTS

The Mean age of the patients in the control group was 23.5 ± 6.5 years, and in pre-eclampsia, it was 31.5 ± 4.5 years and 33.5 ± 2.5 years in cases of eclampsia. The Gestational age in normal pregnancy was 28.4 ± 3.54 weeks, pre-eclampsia 27.6 ± 4.2 and eclampsia was 29.78 ± 3.65 weeks. The BMI in normal pregnancy was 21.5 ± 2.6 Kg/m² in pre-eclampsia was 25.54 ± 1.74 kg/m² and in eclampsia, it was 26.67 ± 2.7 kg/m². The mean values of SBP in normal pregnancy was 109.5 ± 8.5 mmHg, 141.5 ± 14.5 mmHg in pre-eclampsia and 149.5 ± 10.6 mmHg in cases of Eclampsia. DBP was 75.5 ± 2.4 mmHg in normal pregnancies and 92.5 ± 5.2 mmHg in pre-eclampsia and 95.5 ± 6.6 mmHg in eclampsia (table 1).

Table-1: showing the variables recorded in the patients included in the study

Variable	Normal pregnancy (n=50)	Pre-eclampsia (n=35)	Eclampsia (n=28)
Age in years	23.5 ± 6.5	31.5 ± 4.5	33.5 ± 2.5
Gestational age in weeks	28.4 ± 3.54	27.6 ± 4.2	29.78 ± 3.65
BMI Kg/m ²	21.5 ± 2.6	25.54 ± 1.74	26.67 ± 2.7
SBP mmHg	109.5 ± 8.5	141.5 ± 14.5	149.5 ± 10.6
DBP mmHg	75.5 ± 2.4	92.5 ± 5.2	95.5 ± 6.6

In the study, the levels of Homocysteine, Folic acid, and Vitamin B12 were measured. In the normal pregnancy the mean values of homocysteine were 7.56 ± 2.3 µmol/L in pre-eclampsia it was 15.55 ± 3.9 µmol/L and in eclampsia, it was 18.85 ± 4.56 µmol/L. The serum folic acid mean values were 12.9 ± 3.6 ng/ml in normal

pregnancy, 10.24 ± 2.64 ng/ml in eclampsia and 8.54 ± 2.4 ng/ml in eclampsia. The vitamin B12 levels were measured in pictograms/ml the values recorded for the normal pregnancy, pre-eclampsia and eclampsia were 387 ± 48.9, 315 ± 45.7 and 310 ± 52.6 respectively (table 2).

Table-2: Serum Homocysteine, Folic Acid, and Vit B₁₂ Levels

parameter	Normal pregnancy	Pre-eclampsia	eclampsia
Homocysteine (µmol/L)	7.5 ± 2.3	15.55 ± 3.9	18.85 ± 4.56
Folic acid (ng/ml)	12.9 ± 3.6	10.24 ± 2.64	8.54 ± 2.4
Vitamin B12 (pg/ml)	387 ± 48.9	315 ± 45.7	310 ± 52.6

The comparisons of homocysteine, Folic acid, and Vitamin B12 levels were measured between the three groups. The homocysteine levels between the controls and pre-eclampsia and eclampsia were found to be significant the P values were < 0.05 and < 0.01 but the values were not found to be significant in between

pre-eclampsia and eclampsia. The folic acid levels were found to be significant between the control group and eclampsia however the values were not found to be significant between control versus pre-eclampsia and pre-eclampsia and eclampsia. The Vitamin B12 levels were found to be significant only between control and

Eclampsia and not significant in the other two groups table 3.

Table-3: Comparison of parameters between the groups

	Homocysteine	Folic acid	Vit B ₁₂
Control Vs Pre-eclampsia	< 0.05 *	> 0.35	> 0.45
Control Vs Eclampsia	< 0.01 *	< 0.05 *	< 0.05 *
Pre-eclampsia Vs Eclampsia	>0.125	> 0.17	> 0.23

* Significant p values

DISCUSSION

Homocysteine is critically important during pregnancy. High maternal homocysteine level causes endothelial damage and dysfunction, platelet dysfunction, thrombus formation and smooth muscle proliferation. Increased homocysteine levels also cause increased oxidative stress, thereby causing endothelial dysfunction and PET [7]. In our study, we found the mean serum homocysteine levels for preeclampsia and eclampsia was 15.55 ± 3.9 $\mu\text{mol/lit}$ and 18.85 ± 4.56 $\mu\text{mol/lit}$. In a similar study by Laskowaka M et al; and Ingec M *et al.* observed that mean serum homocysteine level for preeclampsia and eclampsia was 10.38 ± 3.5 and 16.7 ± 10.1 $\mu\text{mol/lit}$ respectively [14]. Ingec M *et al.* showed elevated homocysteine levels in severe pre-eclampsia and eclampsia but not in mild preeclampsia [15]. The minimally affected endothelial dysfunctions due to low levels of homocysteine may be a valid explanation for this finding. Cotter *et al.* [16] in their study have found that in early pregnancy increased homocysteine may be associated with a 4-fold increased risk for development of non-severe pre-eclampsia. While another study has suggested that mid-trimester plasma homocysteine concentrations in asymptomatic women are not predictive of the subsequent development of pre-eclampsia [17]. Homocysteine metabolism is influenced by multiple factors that include folate and Vitamin B₁₂. Elevated homocysteine concentrations can be treated by synthetic folic acid, food folate, and other B vitamins. It has been shown that folic acid use had the potential to improve endothelial dysfunction independently of homocysteine. Hence in the present study, we tried to study the levels of folate and Vitamin B₁₂. In the present study, the levels of folic acid 12.9 ± 3.6 ng/ml and in preeclampsia and eclampsia was 10.24 ± 2.64 ng/ml, 18.54 ± 2.4 ng/ml. The serum Vitamin B₁₂ levels in normal pregnancies were 387 ± 48.9 pg/ml and pre-eclampsia was 315 ± 45.7 pg/ml and 310 ± 52.6 pg/ml. D'Anna *et al.* [18] report suggests that deficiencies in B vitamins and folate are associated with an increased risk of preeclampsia agreeing with the results of our study. Some studies have shown that maternal circulating concentrations of Vitamin B₁₂ and folic acid are not significantly different in the hyperhomocysteinemic preeclamptic group compared with normal pregnant women [19-21]. Lopez *et al.* [22] found that the levels of homocysteine and folate are increased in preeclampsia, but values of vitamin B₁₂ are not changed compared with normal pregnancy. Therefore the current study suggests there is a clear increase in homocysteine levels

in preeclampsia and eclampsia and there is an inverse relation between homocysteine levels and folic acid and vitamin B₁₂ levels. Although some studies have found that there is no association with folic acid and vitamin B₁₂ levels and severity of eclampsia.

CONCLUSION

Within the limitations of the present study, it can be concluded that higher homocysteine levels were related with pre-eclampsia and eclampsia at the same time the folic acid and Vitamin B₁₂ levels were also found to be reduced in women with pre-eclampsia and eclampsia. Supplementation of folic acid and Vitamin B₁₂ may reduce the severity of preeclampsia and eclampsia.

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