Original Article

Serum homocysteine level in preeclampsia in a tertiary level hospital of Bangladesh

Sabrina Tymee[1] , Zahidur Rahman Khan[2], Syed Muhammad Baqui Billah[3]

[1]Assistant Professor (cc),Department of Biochemistry, Sher-e-Bangla Medical College,[2]Assistant Professor, Department of Biochemistry, Patuakhali Medical College, [3]Associate Professor, Department of Community Medicine, Sher-e-Bangla Medical College, Barisal

Abstract

Background: High concentrations of homocysteine (Hcy) are supposed to be a potential risk factor for endothelial dysfunction characterized by preeclampsia (PE).

Objectives: To determine the association of serum homocysteine (Hcy) with PE.

Methods: This cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College, from July 2018 to June 2019. Thirty diagnosed case of preeclampsia and thirty apparently healthy pregnant women were selected according to the selection criteria from indoor and outpatient Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital. Homocystine levels of all study subjects were estimated. The results were compared between these two groups.

Results: Mean serum homocystine (Hcy) level in pregnant women with PE was 13.74± 3.69 µmol/L and that of normal pregnancy was 5.89 ±1.70 µmol/L ($p < 0.001$). Serum Hcy level in severe PE (16.04 ±3.26µmol/L) was also significantly higher ($p < 0.001$) compared to mild PE (10.73 ±1.20 µmol/L). Serum Hcy level showed a significant positive relation (r=0.85, $p<0.001$) with PE.

Conclusion: Serum Hcy is increased in PE in comparison to healthy pregnancy. We suggest the assessment of serum Hcy in all pregnant women as a part of antenatal checkup.

Keywords: Preeclampsia, Pregnancy, Homocysteine.

Introduction

The biochemical changes in the blood during pregnancy are associated with various complications of pregnancy such as PE, a hypertensive disorder complicating 5-8% of all pregnancies and is an important cause of severe morbidity and mortality among mothers and infants.[1,2,3]

PE has been identified for developing hypertension, ischemic heart disease and cerebrovascular accident in later life.[4] Furthermore, it is associated with fetal growth restriction, low birth weight, preterm birth, respiratory distress syndrome, and admission to a neonatal intensive care unit.[5]

Homocysteine (Hcy) concentration has been studied as a risk factor for endothelial dysfunction and vascular disease.[6] Level of maternal serum Hcy normally decreases with gestation either due to physiological response to the pregnancy, increase estrogen, hemo-dilution from increase plasma volume or increased demand for methionine by both the mother and fetus.[7] Had the Hcy increased, it has the potential to be associated with PE.[8] PE is a public health threat in both developed and developing countries and is the 3rd leading cause for maternal mortality.[9,10] It is also a primary obstetrical cause for one of four perinatal deaths.[11] An estimated 50000 women worldwide die annually from PE. Though this incidence has been reduced in developed countries, it is still responsible for 20% of maternal mortality in developing countries like Bangladesh.[12] So, we aimed to determine the association of maternal serum homocysteine and PE, which could lead us to follow the etiopathogenesis and to initiate preventive measures of the adverse maternal and fetal outcome in later life.

Materials and Methods

This cross sectional comparative study was conducted from July 2018 to June 2019 in the Department of Biochemistry, Dhaka Medical College, Dhaka. Thirty diagnosed cases of preeclamptic patients and thirty apparently healthy pregnant women attending in the indoor and outpatient department of Obstetrics and Gynaecology, Dhaka Medical College Hospital, Dhaka , were enrolled in this study. We explained the purpose of

the study in details to each subject. After taking written informed consent from each mother when fulfilled the criteria we collected the data in a pre-designed data collection sheet including particulars of the patients, history and relevant investigations. Pregnant women with possible confounding variables like chronic hypertension, overt or gestational DM, kidney disease, liver disease, seizure, any chronic illness, receiving any anti folate drugs (antiepileptic, methotrexate) were excluded from the study.

After all aseptic precaution 5 ml of venous blood sample was collected from each study subject in a disposable plastic syringe and immediately transferred to a dry clean test tube which was allowed to clot at room temperature and clear serum was separated after centrifuging at 3000 rpm for 10 minutes into a sterile Eppendorf tube and the separated serum was used for biochemical assay or was stored at -20ºC if the analysis was delayed. All the biochemical tests were performed in the Department of Biochemistry, BSMMU, Dhaka. After collection of all samples, serum was used for the measurement of Hcy level, measured by Chemi-luminescent Microparticle Immune Assay (CMIA) technology.

We defined PE as a blood pressure (BP) of 140/90 mm Hg or above on two consecutive measures 4 hours apart. When the serum Hcy was above 15mmol/L, we considered it as hyperhomocysteinemia.[13]

All the data were entered in SPSS after meticulous checking. Continuous variables were expressed as mean ± SD and assessed between groups of patients by unpaired t-test. Categorical variables were compared using Fisher's exact test or Chi-square test and were presented as absolute frequencies with percentages. Correlation was done by Spearmans correlation coefficient test. All p values were two-tailed with significance level < 0.05 at 95% confidence interval (CI).

Results

The base line parameters (age, gestational age, BMI and blood pressure) were measured and outcome variable (serum homocysteine) was estimated.

Table I shows baseline demographic and para clinical characteristics of the study subjects. There was no significant difference between PE and normal pregnancy group in terms of age, gestational age and BMI reflecting homogeneity between groups. There were significant differences between groups in terms of systolic and.

diastolic blood pressure

Table I: Baseline demographic and para clinical characteristics of the study subjects. (n=60)

	Preeclampsia (n=30) Mean± SD	Normal (n-30) Mean± SD	p- value
Age (years)	25.20 ± 3.47	26.43 ± 4.07	0.212
Gestational age (weeks)	29.60 ± 2.14	29.60 ± 3.04	1.000
BMI (kg/m^2)	24.86 ± 0.94	25.06 ± 0.71	0.364
SBP (mm of Hg)	158.17 ± 15.00	118.67 ± 9.37	<0.001
DBP (mm of Hg)	108.17 ± 12.70	77.17 ± 6.78	<0.001

Figure-I shows simple Bar diagram where mean serum homocysteine level of PE and normal pregnancy was 13.74 µmol/L and 5.89 µmol/L respectively.

We checked the serum homocysteine level of both groups of patients. About 33.3% pre-eclampsia patients had hyperhomocysteinemia where apparently healthy pregnant women had no hyper-homocysteinemia.
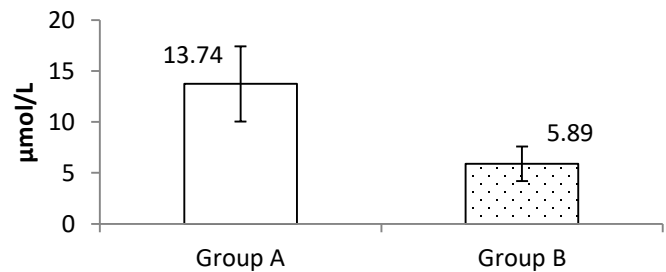

Figure I: Simple Bar diagram showing mean serum homocysteine level of group-A (Preeclampsia) and group-B (Normal pregnancy).

Discussion

In the present study, the mean age of PE and normal pregnancy was 25.20 ± 3.47and 26.43 ± 4.07 years respectively. The mean ± SD of gestational age was 29.60± 2.14 and 29.60± 3.04 weeks in PE and comparison group respectively. The mean ± SD of BMI was 24.86 ± 0.94 and 25.06 ± 0.71 in PE and normal pregnancy respectively. No statistical differences were found between two groups in terms of age, gestational age and BMI.

The age of healthy group with PE group was homogeneously distributed as was the distribution of gestational age and BMI. Similar result was also found in the other researcher's study.[14] The systolic BP and diastolic BP was higher

in PE patients compared to healthy pregnant. The mean ± SD of systolic BP was 158.17 ± 15 and 118.67 ± 9.37 mmHg in group-A and group-B respectively. In this study, the mean ± SD of systolic BP was significantly (p < 0.001) higher in PE group in comparison to that of normal pregnancy group. The mean ± SD of diastolic blood pressure was 108.17± 12.70 and 77.17± 6.78 mmHg in PE and normal group respectively. In this study, the mean ± SD of diastolic BP was significantly (p < 0.001) higher in PE in comparison to that of normal group.

Serum homocysteine was increased in PE patients (13.74 ±3.7 µmol/L) than that of healthy patients (5.89 ±1.70) µmol/L). Homocysteine increases due to increase of the oxidant activity and decrease the antioxidant concentrations in PE. Khosrowbeygi and Ahmadvand found higher homocysteine (14.05 ±1.43µmol/L) level in PE against lower value (6.38 ±0.3µmol/L) in normal pregnancy.[15] Other researchers also found significantly increased serum homocysteine level in PE than normal pregnant women.[16] But Bobic et al.[17] didn't find any difference in serum homocysteine level between PE and normal pregnancy. This dissimilarity might have occurred due to different methodology, variation in nutritional status in study subjects or excess trans placental transfer of homocysteine. However, many other studies done by other authors also found significantly increased serum homocysteine level in patients with PE.[18,6,8,14]

The positive relationship between serum Hcy and PE (r= 0.85, p<0.001) conforms to the hypothesis that homocysteine is related with PE in pregnancy. Shahbazian et al.[14] showed the similar positive correlation between serum Hcy and PE in their study.

Conclusion

This study established the relationship of higher level of homocysteine in PE compared with normal pregnancy. We suggest the measurement of serum homocysteine in all pregnant women as a part of antenatal checkup. Cohort study with large sample size could be carried out in all level of hospitals in Bangladesh for better understanding of the association of serum homocysteine in PE.

References

1. Lambe S, Mahajan B, Muddeshwar M. Comparative study of serum calcium, magnesium & zinc levels in preeclampsia & normal pregnancy. International Journal of Recent Trends in Science and Technology 2014; 9(3): 422-6.

2. Shenoy V, Kanasaki K, Kalluri R. Pre-eclampsia: connecting angiogenic and metabolic pathways. Trends Endocrinol Metab. 2010; 21(9): 529–36.

3 Salam RA, Das JK, Ali A, Bhaumik S, Lassi ZS. Diagnosis and management of preeclampsia in community setting in low and middle-income countries. J Family Med Prim Care. 2015; 4(4): 501–6.

4. Brown MC, Best KE, Pearce MS, Waugh J, Robson SC, Bell R. Cardiovascular disease risk in women with pre-eclampsia: systematic review and meta-analysis. Eur J Epidemiol. 2013; 28(1): 1–19.

5. Masoura,S., Kalogiannidis,I. and Margioula-Siarkou, C. et al .Minerva Ginecol, 2012: 64(2): 109-115

6. Maru L, Verma M, Jinsiwale N. Homocysteine as a predictive marker for pregnancy induced hypertension- A Comparative Study of Homocysteine Levels in Normal Versus Patients of PIH and Its Complication. J Obstet Gynaecol India. 2016; 66(1): 167–71.

7. Shilpa AV, Zubaida PA, Rajalekshmi G. Changes in homocysteine levels during normal pregnancy and preeclampsia and its relation with oxidative stress. Int J Res Med Sci. 2017; 5(1): 330-4.

8. Yelikar K, Deshpande S, Kulkarni M. Association of maternal serum homocysteine level with severity of preeclampsia: A case control study. International Journal of Reproduction, Contraception, Obstetrics and Gynecology 2016; 5: 2713–7.

9. Preeclampsia Foundation, FAQS:2013 (Available at:https://www.preeclampsia.org/health-information/faqs; accessed on 11 March 2019).

10. Tahmina HZ, Shahid AR, Hosna AU, Alam A. Study on outcome of eclampsia patients in district hospital in Bangladesh. J Dhaka Med Coll. 2014; 23(2): 223-6.

11. Hodgins S. Pre-eclampsia as underlying cause for perinatal deaths: time for action. Glob Health Sci Pract. 2015; 3(4): 525-7.

12. Warren CE, Hossain SMI, Nur RA, Sultana K, Kirk K. Landscape Analysis on Pre-eclampsia and Eclampsia in Bangladesh. Washington, DC: Population Council 2015; 1-48.

13. ACOG (American College of Obstetricians and Gynaecologists), Task Force on Hypertension in Pregnancy. Hypertension in Pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy, ObstetGynecol, 2013: 122(5): 1122-31

14. Shahbazian N, Jafari RM, Haghnia S. The evaluation of serum homocysteine, folic acid and vitamin B12 in patients complicated with preeclampsia. Electron Physician 2016; 8(10): 3057-61.

15. Khosrowbeygi A, Ahmadvand H. Circulating levels of homocysteine in preeclamptic women. Bangladesh Med Res Counc Bull. 2011; 37: 106-9.

16. Paul M, Dabla A. Estimation of Role of Serum Homocysteine and Serum Folate in Preeclamptic Women at Term Pregnancy. Global Journal for Research Analysis 2018; 7(6): 7-9.

17. Bobik MV, Habek CJ, Habek D. Maternal and Umbilical homocysteine in preeclampsia. Periodicum Biologorum 2016; 118(2): 117-22.

18. Sanlikan F, Tufan F, Gocmen A, Kabadayi C, Sengul E. The evaluation of homocysteine level in patients with preeclampsia. Ginekol Pol. 2015; 86(4): 287-91.