Original Article

Serum Folate Level in Preeclampsia in a Tertiary Level Hospital

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ABSTRACT

Background: Despite a fairly higher incidence, the underlying etiology of preeclampsia is still in dark. Maternal folate deficiency remains a frequent and mostly unrecognized disorder. In addition, folic acid supplementation improves the endothelial function, dysfunction of which is one of the pathogenic agents of preeclampsia. **Objectives:** To determine the relation of serum folate level with preeclampsia.

Methods: This cross-sectional study was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka from July 2018 to June 2019. After receiving approval of Ethical Review Committee, 30 diagnosed case of preeclampsia and 30 apparently healthy pregnant women were selected according to the selection criteria from indoor and outpatient department of Obstetrics and Gynecology, Dhaka Medical College Hospital, Dhaka. Blood samples were collected and serum folate level of all study subjects were estimated by automated analyzer (Architect plus ci 4100) and were recorded in the preformed data collection sheets. Correlation of serum folate with systolic and diastolic blood pressure was done followed by linear regression.

Results: Serum folate was significantly lower (5.50 ± 2.11 & 14.15 ± 3.13) ng/ml, p<0.001) in preeclamptic & healthy pregnant group respectively. Serum folate has negative correlation with systolic (SBP) (r=-0.732, p <0.001)) & diastolic blood pressure (DBP) (r=0.74). Serum folate was significantly associated with SBP and DBP on linear regression (p<0.001)

Conclusion: Serum folate level is low in preeclampsia in comparison to healthy pregnant. This study suggests the measurement of serum folate in all pregnant women as a part of antenatal checkup and regular supplementation of folate in antenatal period.

Keywords: Folate, Preeclampsia, Normal Pregnancy, Systolic BP, Diastolic BP

Introduction

Preeclampsia is the most common form of pregnancy specific hypertensive disorder with multisystem involvement that usually occurs after 20 weeks of gestation. It is primarily defined by the occurrence of new onset hypertension plus new onset proteinuria with a blood pressure (BP) of ≥140/90 mm Hg on two consequent measures 4 hours apart. Proteinuria is defined when ≥300 mg protein in 24-hours urine collection or urinary dipstick reading 1+ or protein creatinine ratio ≥ 0.3 mg/dl.[1] Preeclampsia is associated with fetal growth restriction, low birth weight, preterm birth, respiratory distress syndrome, and admission to a neonatal intensive care unit.[2] In Bangladesh the incidence of preeclampsia and eclampsia is alarmingly high and is considered as second common direct cause of maternal death after post-partum hemorrhage. Although this disorder is decreasing in developed countries, it is still

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responsible for 20% of maternal death in developing countries like Bangladesh.[3] Therefore, to reduce maternal mortality and to achieve Sustainable Development Goal 2030, it is necessary first to eliminate the preventable cause of maternal mortality like preeclampsia and eclampsia.[4,5] There are many theories about the etiology and pathogenesis of preeclampsia. Endothelial dysfunction, inflammation and angiogenesis are the most explainable theories about the etiology and pathogenesis.[6]

Folate (B9) is a member of B vitamin family. Our body needs folic acid for cell division and it is specially needed during pregnancy and infancy. Folic acid is crucial for proper brain functioning and plays an important role in mental and emotional health. It helps in the production of DNA and RNA, the body's genetic material, especially when cells and tissues are growing rapidly, such as during infancy, adolescence, and pregnancy.[7]

Humans are entirely dependent on dietary source or dietary supplements for their folate supply. A significant proportion of women of reproductive age have low dietary folate intake and do not use folic acid containing supplements or eat fortified cereals. [7]

The major food sources of folate include spinach, dark leafy greens, asparagus, turnip, beets, and mustard greens, Brussels sprouts, lima beans, soybeans, beef liver, brewer's yeast, root vegetables, whole grains, wheat germ, bulgur wheat, kidney beans, white beans, salmon, orange juice, avocado, and milk. All grain and cereal products in the US are fortified with folic acid.[7]

Maternal folate deficiency remains a frequent and mostly unrecognized disorder and is associated with the recurrent miscarriage, placental abruption and intrauterine growth restriction. In addition, folic acid supplementation improves the function of endothelial cells and may reduce the risk of developing preeclampsia.[8]

METHODS

This cross-sectional comparative study was carried out in the department of Biochemistry, Dhaka Medical College, Dhaka from July 2018 to June 2019. 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 appendorp 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 folate level by Chemi-

luminescent Microparticle Immune Assay (CMIA) technology.

We defined PE as a blood pressure (BP) of 140/90 mm Hg or above, measured two times within 4 hours.

After meticulous checking all the data were entered in SPSS. Continuous variables were expressed as mean ± SD between groups of patients by unpaired t-test. Correlation was done with serum folate and SBP and DBP. All p values were two-tailed with significance defined as $p < 0.05$ at the level of 95% confidence interval (CI).

RESULTS

A total of 60 subjects, all of which were pregnant women, were included in the study. The subjects were divided into two groups. In group A thirty pregnant women with preeclampsia were selected while in group B age & gestational age matched thirty healthy pregnant women were taken.

Concentration of serum folate in different groups were expressed in ng/ml.

Table 1: shows the mean ± SD of serum folate in both groups. Serum folate was 5.50 ± 2.11 ng/ml in preeclamptic pregnant women &14.15 ± 3.13 ng/ml in healthy pregnant women.

Table 1: Comparison of serum folate level in study subjects

	Preeclampsia (n=30) Mean ± SD	Healthy pregnant (n=30) Mean ± SD	p value
Serum folate (ng/ml)	5.50 ± 2.11	14.15 ± 3.13	<0.001

Table 1: shows the mean ± SD of serum folate in both groups. Serum folate was significantly low in preeclamptic pregnant women compared to healthy pregnant women.

Table 2: Correlation of serum folate with systolic and diastolic BP

Serum folate	r value	P value
Systolic BP	-0.732	<0.001
Diastolic BP	-.743	<0.001

Table 3: Linear regression of serum folate with systolic and diastolic BP:

Serum folate	β coefficient	P value
Systolic BP	-1.181	0.002
Diastolic BP	-1.082	0.001

DISCUSSION

According to the findings from this current study, mean ± SD of serum folate was 5.50 ± 2.11 and 14.15 ± 3.13ng/ml in preeclampsia and healthy pregnant group respectively. So, the mean value of serum folate level was found decreased in patients with preeclampsia than healthy pregnant, which is statistically significant ($p<0.001$). Mean levels of serum folate were significantly found low in the preeclamptic patients (9.28 ± 1.96ng/ml v/s 15.48 ± 2.47ng/ml) in a case control study done by Paul and Dabla .[9]Shahbazian, Zafari and Hagnia also found significantly decreased serum folate level in case group.[10] Similar findings obtained by Serrano, et al. where they also found decreased serum folate level in preeclampsia group.[11]

According to the study negative correlation of serum folate with systolic and diastolic blood pressure was observed. Folate showed significant negative correlation with

systolic (r=-0.732) and diastolic BP (r= 0.74). Serum folate was significantly associated with SBP (β= -1.181) and DBP (β= -1.082) on linear regression (p<0.001). The finding is suggestive that reduced folate level might be associated with the development of preeclampsia.

Conclusion: This study established the relationship of lower level of folate in preeclampsia compared with normal pregnancy. We suggest the regular supplementation of folate in antenatal period.

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