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Low serum selenium concentration is associated with preeclampsia in pregnant women from Bangladesh

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ABSTRACT

Objectives: Preeclampsia is a hypertensive disorder of pregnancy which is one of the leading causes of maternal and perinatal mortality and pre-term delivery, especially in low and middle income countries. Selenium is an important constituent of selenoproteins that act as antioxidant and have several metabolic functions. The present study was conducted to determine serum selenium concentration in preeclampsia patients in order to find out the role of selenium in preeclampsia.
Methods: This study was conducted as case-control study with 74 preeclampsia patients as cases whose gestation were ≥20 weeks (52 mild and 22 severe patients) and 118 normotensive pregnant women as controls from same gestational period. Detailed patient history was recorded during routine hospital visits. Serum selenium concentration was determined by using atomic absorption spectroscopy. Independent sample *t*-test and Pearson's correlation test were done for the statistical analysis using the statistical software package SPSS, version 16.
Results: Our study found that mean serum concentration of selenium in preeclampsia patients was significantly lower than that of healthy pregnant women ($p < 0.05$). Further analysis for selenium concentration with disease severity explored that selenium concentration was significantly lower in severe preeclampsia in comparison to mild preeclampsia ($p < 0.05$). We found no significant difference for selenium concentration between rural and urban preeclampsia patients ($p > 0.05$). Pearson's correlation analysis reveals significant negative correlation of selenium with systolic blood pressure ($r = -0.419$, $p = 0.001$), diastolic blood pressure ($r = -0.392$, $p = 0.001$), and gestational period ($r = -0.218$, $p = 0.001$).
Conclusion: Our study found that preeclampsia patients have decreased serum selenium concentration than the healthy pregnant women.

1. Introduction

Preeclampsia is a human pregnancy specific multisystem disorder which is characterized by hypertension and significant proteinuria in a previously healthy woman on or after 20th week of gestation [1,2]. It is characterized by systolic blood pressure of 140 mmHg or more and diastolic blood pressure of 90 mmHg or more on at least two measurements within 6 h [3]. Hypertension can be seen as late as six weeks after delivery of the child. It is the most common medical complication of pregnancy and is associated with significant maternal morbidity and mortality, accounting for about 50,000 deaths worldwide annually [4]. Although the main cause of preeclampsia is still unknown, it is considered as a disorder with two components, an abnormal placentation coupled with endothelial dysfunction [5,6]. Abnormal placentation occurs between 8 and 18 weeks of gestation due to remodeling of spiral arteries followed by dysregulation of placental perfusion, development of placental oxidative stress, and release of syncytiotrophoblast pro-inflammatory factors [7]. Poor placentation results in placental ischemia and oxidative stress [8], which further results in formation of endothelin, thromboxane and superoxide [9].

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Superoxides react with polyunsaturated fatty acids and produce lipid peroxides. Lipid peroxides increase thromboxane synthesis by stimulating prostaglandin synthase and they inhibit prostacyclin synthesis by inhibiting prostacyclin synthase. Thromboxane is a potent vasoconstrictor and stimulator of platelet aggregation, whereas prostacyclin inhibits platelet aggregation. An imbalance between thromboxane and prostacyclin causes increased blood pressure [10,11]. Peroxynitrite is a potential oxidizing and nitrating agent produced in vivo from superoxide and nitric oxide in endothelium [12]. It is produced at significantly higher rate in preeclampsia patients than the healthy pregnant women [13] and being potential oxidizing and nitrating agent, peroxynitrite causes vasoconstriction, platelet aggregation and thrombus formation [8].

Selenium is an essential component of selenoproteins that play important role in several major metabolic pathways, including thyroid hormone metabolism, antioxidant defense systems, immune function and act antagonistically to heavy metals such as lead, mercury, arsenic and cadmium [14]. It is incorporated as selenocysteine at the active site of proteins. In human body, over 25 selenoproteins have been identified that play significant role in cellular redox system [15]. Selenoproteins such as glutathione peroxidases, thioredoxin reductases, and iodothyronine deiodinases are involved in redox reactions [16]. Ionized selenium in selenocysteine is the main biological catalyst [15]. Glutathione peroxidases (GPxs) are major antioxidative enzymes that protect cell membrane from detrimental effect of hydrogen peroxide and lipid peroxides [17]. There are five selenocysteine containing GPxs in human body: the ubiquitous cytosolic GPx (GPx1), the gastrointestinal specific GPx (GPx2), the plasma GPx (GPx3), the ubiquitous phospholipid hydroperoxide GPx (GPx4), and the olfactory epithelium and embryonic tissue specific GPx (GPx6), among which GPx1–3 catalyzes the reduction of hydrogen peroxide and organic hydroperoxides, whereas GPx4 can directly reduce phospholipids. On the other hand, GPX3 is extracellular and require glutathione in plasma or serum for its activity [16]. Selenoprotein-P (SelP) is an extracellular glycoprotein that is rich in selenocysteine containing 60% plasma selenium. They contain 10 selenium atoms per molecule and the main transport protein for selenium. Moreover, they prevent endothelial oxidative damage by reducing cytokine-induced adhesion molecule expression and by reducing inflammation [18,19]. Albumin plays an important role in transporting Se from gastrointestinal tract to live, where it is metabolized and produce SelP, which is then released into blood [14]. Selenoprotein-P scavenges peroxinitrites from endothelial surface and prevents endothelial dysfunction [8]. Considering all these facts, the present study was designed to explore the serum selenium status in preeclamtic pregnant women in Southern region of Bangladesh.

2. Materials and methods

2.1. Study design

This case-control study was carried out in the Department of Obstetrics and Gynecology, Noakhali Medical College Hospital; from June 2013 to January 2014. Ethical permission was taken from hospital ethical committee. In this case control study, 74 diagnosed cases of preeclampsia (52 mild and 22 severe) with gestational period ≥20 weeks were recruited and for comparison 118 normotensive pregnant women were randomly selected as control subjects. Patients with blood pressure 140/90 mmHg or higher on 2 occasions at least 6 h apart were categorized as mild preeclampsia and patients with blood pressure 160/110 mmHg or higher on 2 occasions at least 6 h apart were categorized as severe preeclampsia. An obstetrician and gynecologist conducted the diagnosis of preeclampsia. Then detailed patients history was taken using a structured questionnaire. Each and every patient was briefed about the purpose of this study prior to data collection and written informed consent was obtained from them. Subjects with history of diabetes mellitus, renal, cardiovascular, liver disease, endocrine disorder, any chronic illness, were excluded from the study.

2.2. Blood sample collection

5 mL of venous blood was collected from each diagnosed patient in metal free tube after 8 h overnight fasting condition. The blood samples were kept at room temperature for 30 min and allowed to clot and then centrifuged at 3000 rpm for 10 min to extract serum. The serum was the stored at −80 °C until analysis.

2.3. Analytical procedure

Selenium concentration in blood serum was determined by using flame atomic absorption spectrometry (Shimadzu AA 6800). A software package, WizAArd AA was used to calculate concentration. In brief, selenium metal granules (99.99%) was dissolved in 0.1N hydrochloric acid to prepare the standard solution in the concentrations of 2000, 4000, 6000 and 8000 μg/L. 0.1N hydrochloric acid was used as a blank solution. A stock solution having concentration of 10,000 μg/L was prepared by using Merck standard solution of 1×10^6 μg/L. 4 mL of the stock solution was taken in 10 mL volumetric flask and volume up to 10 with 0.1N hydrochloric acid, so the concentration was 4000 μg/L. In another 10 mL volumetric flask, 50 μl of blood serum and 4 mL of 10 μg/mL solution was taken, and diluted up to 10 mL with 0.1N hydrochloric acid. Absorbance of 4000 μg/L solution and sample solution was measured, and determined the serum Se concentration by subtracting absorbance of 4000 μg/L solution to sample solution. To verify the assay accuracy and to maintain quality, the standard solution was run for every 10 test samples and to avoid carryover the blank solution were run for every 5 test samples. For this analysis wave length of 196 nm, slit width of 1.0 nm and N_2O–C_2H_2 flame was used.

2.4. Statistical analysis

All data were expressed as mean ± standard error mean (mean ± SEM). Statistical analysis was performed using the statistical software pack-age SPSS, version 16.0 (SPSS Inc., Chicago, IL). Comparison of trace elements between patient and control groups was performed using independent sample *t*-test. Pearson's correlation analysis was used to find the correlation among various study parameters.

3. Results

Obstetric and socio-demographic features of the patients and controls are represented in Table 1. The mean maternal age of the patients and controls were 27.51 ± 0.98 and 24.59 ± 0.51 years respectively and the mean gestational period at diagnosis were 31.02 ± 0.71 and 25.98 ± 0.55 weeks respectively. The comparative percentages of primigravida and multigravida pregnancy were 73% vs. 27% and 59% vs. 41% for cases and controls respectively. The mean age of primigravida and multigravida preeclampsia patients were 27.80 ± 5.81 and 26.91 ± 6.48 years respectively. Most of the preeclampsia patients were from rural area (56% vs. 44%) which was 59% vs. 41% for healthy pregnant women. And majority of them were of lower (62% vs 47%) economic class followed by medium (33% vs. 29%) and high (3% vs. 24%) economic class.(Table 2)

Fig. 1 represents distribution of serum selenium concentration in preeclampsia patients and healthy pregnant women. Mean serum concentration of selenium in cases and controls