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Research Article

Zinc and copper levels in preeclampsia: a study from coastal South India

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ABSTRACT

Background: Preeclampsia is one of the major causes of maternal and fetal morbidity and mortality. Though the etiology is obscure, studies indicate the role of oxidative stress and antioxidants may have a role in the prevention of preeclampsia. Micronutrients such as copper and zinc are involved in the antioxidant defense mechanism.
Methods: The present study was undertaken in a medical college hospital in coastal South India to assess the serum levels of zinc and copper in women with preeclampsia and to compare them with normal pregnant women. The blood samples from 60 preeclamptic women and an equal number of controls were analyzed for zinc and copper levels. Outcome of pregnancy was analyzed and compared. Data were expressed as mean ± standard deviation. Comparison of levels of the elements between the two groups was performed by independent t test and Chi square test and P value of <0.05 was considered as statistically significant.
Results: The serum zinc and copper levels were significantly lower in the preeclamptic group compared to the normotensives. Also preeclamptic women were older, their BMI was higher and birth weight of babies lower compared to normotensives.
Conclusions: Increased knowledge about the importance of specific antioxidant micronutrients and their part in successful pregnancy outcome should be the focus for future health strategies. Low levels of maternal copper and zinc are related to preeclampsia and might have a causal role in this disease. Further investigation is needed to establish the role of these elements in this dangerous condition of pregnancy.

Keywords: Copper, Micronutrients, Nutrition, Preeclampsia, Zinc

INTRODUCTION

Preeclampsia is one of the important diseases of pregnancy. It complicates 7% to 10% of all pregnancies and is a leading cause of both maternal and perinatal morbidity and mortality worldwide.[1] Preeclampsia is defined as a combination of high blood pressure (hypertension), swelling (edema) and protein in the urine (proteinuria) developing after the 20th week of pregnancy.[2] The etiology of this relatively common medical complication of pregnancy however remains unknown.[2] Hypertensive disorders account for 40000 maternal deaths annually.[3] It stands next to hemorrhage and embolism among pregnancy related cause of death.[4] The greatest impact is in developing countries, where it accounts for 20 - 80% of the strikingly increased maternal mortality.[5]

Preeclampsia is more common in developing countries due to their low dietary intake of essential minerals and vitamins. Pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins.[6] An inadequate dietary intake might be

harmful not only for the mother but also for the growing fetus.[1]

The pathogenesis of adverse pregnancy outcomes including preeclampsia and fetal growth restriction has been shown to be associated with oxidative stress.[7] Micronutrients such as copper, zinc, magnesium, manganese and selenium are involved in the antioxidant defense as cofactors of enzymes.[8] Superoxide dismutase is an antioxidant enzyme that contains the trace elements zinc and copper.[9] The present study was undertaken to assess the serum levels of zinc and copper in women with preeclampsia and to compare them with normal pregnant women. This study focuses on the role of copper and zinc in preeclampsia.

METHODS

This was a case-control study conducted to investigate the levels of serum zinc and copper in pregnant women with and without preeclampsia. The study population was pregnant women attending the antenatal clinic in the department of obstetrics and gynecology in a teaching hospital in coastal South India. India is a developing country where the nutrition of pregnant women is a matter of concern. 120 women were included in the study of whom 60 were with preeclampsia and the other 60 were normal pregnant women without preeclampsia who were taken as controls. All participants were in the third trimester of pregnancy with a single fetus and gestational age beyond 32 weeks. Preeclampsia was defined as a blood pressure of 140/90 or more on two occasions each 6 hours apart associated with proteinuria of at least 300 mg per 24 hours or at least 1+ on dipstick testing. Severe preeclampsia was defined as a blood pressure of 160/110 mmHg or above measured on two occasions each 6 hours apart.

Informed consent was obtained from each of the subjects before recruiting in to the study. Ethical committee clearance was obtained from the institution.

Patients with history of chronic hypertension, renal disease, cardiovascular disease, liver disease, diabetes, multiple gestations were excluded from the study. A detailed family and medical history were taken. Thorough clinical examination was done in all the subjects. Systolic and diastolic blood pressure was carefully recorded. Urine analysis was done in all subjects to measure the degree of proteinuria. Blood was taken from the ante cubital vein using a sterile needle and syringe in the fasting state. Blood samples were allowed to clot and then centrifuged at 3000 revolutions per minute for 10 minutes. Serum zinc and copper levels were measured by atomic absorption spectrometry. Whenever possible, the analysis was done immediately. When there was a delay, the samples were stored at -20 degree Celsius till further analysis. Data were expressed as Mean ± Standard deviation. Data analysis was done by SPSS version 20. Comparison of serum levels of the elements between the two groups was performed by independent t test and Chi square test and P value of <0.05 was considered as statistically significant.

RESULTS

The present study enrolled 120 pregnant women. No significant differences in demographic characteristics were present between the preeclamptic subjects and the healthy controls. There were no cases of maternal or fetal death or of maternal renal or hepatic insufficiencies. The clinical characteristics of the participants are shown in Table1. The mean age of women with preeclampsia was higher than normotensive controls. The mean BMI (Body Mass Index) was significantly higher in preeclamptics than normotensives. The systolic and diastolic blood pressure was significantly higher in cases compared to controls. The period of gestation was significantly higher in the normotensives compared to preeclamptics. The fetal birth weight was significantly less in women with preeclampsia than normal pregnant women.

Table 1: Clinical characteristics of cases and controls.

Clinical characteristics	Cases (n=60)	Controls (n=60)	Significance level (P value)
Age (years)	27.45 ± 4.33	25.87 ± 3.11	0.023*
BMI (kg/m^2)	27.07 ± 3.07	24.9 ± 2.32	<0.001*
Gestational age (weeks)	36.9 ± 0.9	38.21 ± 0.85	<0.001*
Systolic BP (mm Hg)	155.50 ± 12.18	108 ± 6.50	<0.001*
Diastolic BP (mm Hg)	108.18 ± 10.89	68.69 ± 8.19	<0.001*
Birth weight (kg)	2.61 ± 0.53	2.98 ± 0.36	<0.001*

Values are given as mean ± SD (Standard Deviation), *P <0.05 - Statistically Significant, BMI - Body Mass Index BP - Blood Pressure

Table 2 shows the comparison of levels of serum zinc and copper in both the groups. The serum zinc and copper levels were significantly lower in the preeclamptic group compared to the control group which was statistically significant.

Table 2: Comparison of serum zinc and copper levels in cases and controls.

Parameters	Cases (n=60)	Controls (n=60)	Significance (P value)
Zinc (µmol/L)	8.84 ± 0.87	14.87 ± 0.89	<0.001*
Copper (µmol/L)	6.53 ± 0.65	15.87 ± 0.72	<0.001*

Values are expressed as mean ± SD (Standard Deviation), *P<0.05 – Statistically Significant, NS - Not Significant

DISCUSSION

Women with greater Body Mass Index (BMI) in pregnancy are more likely to become hypertensive than those with lower BMI.[10] In our study, women with preeclampsia had a significantly higher BMI than normotensives.

We observed a significant decrease in zinc and copper levels in preeclamptic women compared to the control group.

Increased load of oxidative stress or excessive lipid peroxidation may act as an attributing factor in the pathogenesis of preeclampsia.[4] Many studies have reported an increase in lipid peroxidation and a decrease in antioxidant capacity in preeclampsia.[9] A number of micronutrients and vitamins are known to serve as antioxidants or be essential cofactors for antioxidant enzymes; these include copper, selenium, zinc, manganese and vitamins C and E.[7] They are involved in the antioxidant defense as cofactors of enzymes (i.e. zinc in metallothionein, copper in ceruloplasmin, copper-selenium-zinc in super oxide dismutase.[8,9]

Zinc counteracts oxidation through binding sulphydryl groups in proteins and by occupying binding sites for iron and copper in lipids, proteins and DNA.[8] Zinc is also involved in the synthesis of deoxyribonucleic acid and ribonucleic acid.[6,11]

Copper, an essential component of numerous metalloenzymes and cofactor for the antioxidant enzyme superoxide dismutase, catalase and cytochrome oxidase is known to affect the level of norepinephrine and dopamine in the brain.[7,12]

Deficiency of these elements may withdraw the effect of antioxidant potential of cells leading to increase in blood pressure.[4] Zinc deficiency causes an increase in lipid peroxidation.[11] Increased oxidative stress, ongoing excessive lipid peroxidation, endothelial dysfunction, vasospasm which results from the imbalance of vasodilators and vasoconstrictors in these micronutrient deficient environments may progress towards the development of preeclamptic pregnancy.[4]

It was estimated in 2002 by the World Health Organization that suboptimal zinc nutrition effected nearly half the world's population.[13] The requirement of zinc during the third trimester is approximately twice as high as that in non-pregnant women.[14]In developing countries, nutritional deficiencies of both macro and micro nutrients are common health problems among women of reproductive age. The risk is further increased with pregnancy because of increased requirements of various nutrients like zinc, copper, etc. to satisfy the needs of the growing fetus.[1] It has been reported that 82% of the pregnant women worldwide are likely to have inadequate dietary intake of zinc.[4] The dietary intake of copper in women aged between 19 and 24 years is generally below the recommended levels which may cause problems during pregnancy when requirements increase.[15] Deficiencies of trace elements such as zinc, copper, selenium and magnesium have been implicated in various reproductive events like infertility, pregnancy wastage, congenital anomalies and have been reported to correlate with pregnancy complications such as prolonged labor, hypertension, premature rupture of membranes, preterm delivery, placental abruption, still births fetal growth retardation, low birth weight and post-partum hemorrhage.[3,5,12,16]

Trials with zinc supplementation during pregnancy have shown to improve the immune system of the developing fetus and reduce the incidence of pregnancy induced hypertension, preterm delivery and low birth weight.[1]

Studies on zinc supplementation from developing countries where incidence of zinc deficiency is high showed that benefits of supplementation include reduced incidence of pregnancy induced hypertension and low birth weights[17] and suggest that supplementation in developing countries is beneficial.[1]

Despite several studies on preeclampsia, its etiology has not yet been fully elucidated; some studies have shown that changes in the levels of blood trace elements in preeclamptic patients may implicate its pathogenesis while others do not show an association of blood levels of trace elements and prevalence of preeclampsia.

Kumru et al., in their study found significantly lower levels of copper (68%) and lower zinc and calcium levels (43% and 10%) in preeclamptic women compared to healthy controls. They concluded that measurement of these elements may be useful for the early diagnosis of a preeclamptic condition.[11] Ugwuja et al. in a study from Nigeria found lower plasma zinc and copper levels in preeclamptics than normotensives with a significantly lower copper levels.[18] Similarly, Akinloye et al. in a study from western Nigeria found significantly lower levels of zinc and copper in women with preeclampsia.[6]

Ikgoz et al. found zinc and copper concentrations in the placental tissues of preeclamptic women to be lower than those in healthy pregnant women.[9]

Jain et al. showed that the mean zinc levels were significantly reduced in preeclamptic group when compared with healthy group.[1] Whereas Golmohammad et al. did not find much difference in the serum levels of copper and zinc in women with preeclampsia compared to healthy normotensive pregnant women.[19]

We have found in our study that zinc and copper levels are significantly lower in the preeclamptic women compared to the healthy controls.

To conclude, increased knowledge about the importance of specific antioxidant micronutrients and their part in successful pregnancy outcome should be the focus for

future health strategies. Only by fully understanding the requirements of micronutrients during pregnancy will we be able to evaluate the use of these supplements in preventing adverse pregnancy outcomes. Low levels of maternal serum copper and zinc are related to preeclampsia and might have a causal role in this disease. Further investigation is needed to establish the role of these elements in this dangerous condition of pregnancy.

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