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Full Length Research Paper

Assessment of serum calcium, magnesium, copper and zinc levels in Sudanese pregnant women with pre-eclampsia

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Pre-eclampsia is the most common medical complication of pregnancy associated with increased maternal and infant mortality and morbidity. Its exact etiology is not known, although several evidences indicate that various elements might play an important role in pre-eclampsia. This study was carried out to analyze and to compare the concentration of calcium, magnesium, copper, and zinc in the serum of women with pre-eclampsia and in normal pregnant women. seventy five clinically diagnosed patients with pre-eclampsia and 74 normal pregnant controls were enrolled in this study. The serum calcium, magnesium, copper, and zinc levels were estimated using spectrophotometer and atomic absorption spectrophotometer. The mean serum levels of calcium, magnesium, were significantly lower in pre-eclamptic pregnant group 7.56 ± 0.82 mg/dl, and 1.75 ± 0.11 mg/dl, respectively when compared with normal pregnant women 8.69 ± 0.34 mg/dl, 1.87 ± 0.11 mg/dl, respectively, P.values < 0.05 , while serum levels of copper and zinc were insignificantly lower 0.47 ± 0.14 μ g/l, and 0.76 ± 0.25 μ g/l, when compared with normal group, 0.79 ± 0.14 μ g/l, and 1.05 ± 0.23 μ g/l, respectively, P.values > 0.05 . These results indicate that reduction in serum levels of calcium and magnesium, during pregnancy might be possible contributors in etiology of pre-eclampsia.

Keywords: Pre-eclampsia, Calcium, Magnesium, Copper, Zinc

INTRODUCTION

Pre-eclampsia is a multi-system disorder of pregnancy, which is characterized by new onset hypertension (systolic and diastolic blood pressure of ≥ 140 and 90 mm Hg, respectively, on two occasions, (at least 6 hours apart) and proteinuria (protein excretion of ≥ 300 mg in a 24 h urine collection, or a dipstick of $\geq 2+$), that develop after 20 weeks of gestation in previously normotensive women (Sibai et al., 2005). Pre-eclampsia is a transient

and serious complication of pregnancy that approximately affects 3-5% of pregnancies (Sarsam et al., 2008). It is a major cause of maternal and perinatal morbidity and mortality worldwide, particularly in developing countries (Sibai, 1998). The etiology of this disease is not fully elucidated and placental ischemia is considered to have a major role in the pathogenesis of these complications (Dekker and Sibai, 1998). Some studies have reported that changes in levels of blood metals such as calcium and magnesium observed in pre-eclamptic patients may contribute to the pathogenesis of pre-eclampsia (Yazbeck et al., 2009).

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Calcium plays a critical role in the function of the cardiac and vascular smooth muscles (Morgan and Morgan, 1984). It is known that the deficiency of calcium may lead to irritable nervous muscular symptoms, even tetanic convulsions, bleeding diathesis, capillary haemorrhages, tissue exudation and osteomalacia (Bera et al., 2011).

Magnesium is a unique calcium antagonist as it can act on most types of calcium channels in vascular smooth muscle and as such would be expected to decrease intracellular calcium. One major effect of decreased intracellular calcium would be arterial relaxation. The theory of cerebrovascular vasospasm as the etiology of eclampsia seemed to be reinforced by transcranial doppler (TCD) studies which suggested that MgSO₄ treatment caused dilation in the cerebral circulation (Euser and Cipolla MJ, 2009). However, a vasodilator such as MgSO₄ would seem to be a paradoxical treatment choice for eclamptic encephalopathy (Euser and Cipolla MJ, 2009).

Copper participates in multiple enzymatic reactions with varied physiological roles from melanin production to wound healing to electron transport (Roberts and Schilsky, 2008). Ceruloplasmin represents 90% of circulating copper, and excesses are excreted into bile. It stimulates the absorption of iron and is required for the synthesis and function of hemoglobin. It is also involved in the production of elastin and collagen which contribute to the structural stability of bone, cartilage, and tendons (Roberts and Schilsky, 2008). Serum copper values can be used as an indicator of the condition of pregnancy and fetoplacental unit, and could be introduced into the protocol of routine prenatal diagnostics as a simple, cheap and accurate method (Vukelic et al., 2012).

Zinc is the second main element in the body after iron. The importance of zinc in pregnancy is due to its role in DNA and protein synthesis and as a result the necessity of its availability for the appropriate growth and development of the fetus and neonate. Zinc deficiency, in addition to reducing cell proliferation, protein synthesis, or rate of tubule polymerization, decreases growth in embryonic and fetal periods (Norrozi et al., 2012).

A study was carried out to analyze and to compare the concentration of calcium, magnesium, and zinc in the serum of women with pre-eclampsia and in normal pregnant women. The results indicate that reduction in serum levels of calcium, magnesium, and zinc during pregnancy might be possible contributors in etiology of preeclampsia, and supplementation of these elements to diet may be of value to prevent pre-eclampsia (Jain et al., 2010).

Sandip S et al. evaluated and compared serum calcium and magnesium, copper, zinc and uric acid in pre-eclamptic women and normal pregnant women. They found that significantly high uric acid level in pre-eclamptic women as compare to normal pregnant women ($p < 0.05$). Also there is significantly low serum magnesium

and serum calcium level in severe pre-eclamptic women as compare to normal pregnant and mild pre-eclamptic women ($p < 0.05$). There was no significant difference found in copper and zinc obtained between normal and mild pre-eclamptic women (Punthumapol and Kittichotpanich, 2008). So the aims of this study were to measure serum levels of calcium, magnesium, copper and zinc in pre-eclamptic pregnancies and to compare them with those in normal pregnancies.

MATERIALS AND METHODS

This is a cross sectional case control study conducted in Khartoum state during the period from May 2013-September 2013. The study was approved by Alneelain University Ethics Committee and all subjects gave informed consent (Based on Helsinki Declaration).

The case group was composed of 75 pregnant women with pre-eclampsia, confirmed by elevated blood pressure and proteinuria, while the control group was composed of 74 women with normal pregnancy. None of the case or control subjects was in a supplement that included calcium, magnesium, copper or zinc.

A coded enrollment number was given for each enrolled subject. The data were collected by using a direct interviewing questionnaire. Medical information was collected from the patient with help of the physician. The questionnaire was used to collect data regarding name, age, gender and blood pressure and proteinuria.

Five ml venous blood were collected from each enrolled subject and poured into plain containers, left at room temp for one hour and centrifuged at 3200 rpm for three minutes to obtain sera. Sera obtained were analyzed for calcium, magnesium using advanced clinical chemistry analytical system, cobas integra (Roche, Germany), at Omdurman Military hospital. Copper and zinc were determined by flame atomic absorption spectrophotometry at Academy of Science and technology-Khartoum-Sudan.

The data were analyzed using the statistical software package SPSS, version 16.0 (SPSS Inc., Chicago, IL).

RESULTS

The provided results are obtained from 149 individual. The mean age of case group was 29 years, and the mean age of control group was 28 years. This study estimated the serum concentrations of Ca, Mg, Cu and Zn in 149 in case and control subjects. The statistical findings showed that serum Ca levels in pre-eclamptic women were significantly lower than those of control, 7.57 vs. 8.6 mg/dl, respectively, ($P = 0.000$). The mean value of Mg in cases was 1.7 vs. 1.87 mg/dl in control group. Although this difference is small in parts of one but the difference is statistically significant ($P = 0.038$).

Table 1. The mean of calcium, magnesium, copper and zinc levels in studied group

| Parameter | Study Group (n=149) | | 95% confidence interval for mean in pre-eclamptic group | | P. value |
|-------------------|----------------------------------|-----------------|---|-------|------------------|
| | Women with pre-eclampsia (n =75) | Control (n =74) | Lower | Upper | |
| | Mean±SD | Mean±SD | | | |
| Age (years) | 29.5±5.1 | 28.7±5.0 | 21 | 39 | <i>P</i> = 0.56 |
| Calcium (mg/dl) | 7.56 ±0.82 | 8.69 ± 0.34 | 5.0 | 8.6 | <i>P</i> = 0.000 |
| Magnesium (mg/dl) | 1.75 ± 0.11 | 1.87 ± 0.11 | 1.0 | 2.0 | <i>P</i> = 0.030 |
| Copper (µg/l) | 0.47 ± 0.14 | 0.79 ± 0.14 | 0.38 | 1.4 | <i>P</i> = 0.322 |
| Zinc (µg/l) | 0.76 ± 0.25 | 1.05 ± 0.23 | 0.25 | 0.99 | <i>P</i> = 0.311 |

The mean values serum levels of Cu and Zn in cases were 0.47 and 0.77 µg/l and in control subjects were 0.79 and 1.05 µg/l. However these differences were not statistically significant. The mean values of Ca, Mg, Cu and Zn were illustrated in table 1.

DISCUSSION

Preeclampsia, as a risky pregnancy, is the commonest cause of prenatal and maternity related death in the world. In the developing countries, women lost their lives due to pre-eclampsia every year and the risk of infants' mortality in pre-eclampsia is 4 times higher than that in normal pregnancies (Bahadoran et al., 2010). It is the third common cause of mothers' mortality in the world. Diagnosis of pre-eclampsia is considered in women whose blood pressure increases to 90/140 mmHg for the first time after the 20th week of pregnancy while they have proteinuria (Turner, 2010). The high prevalence of pre-eclampsia in developing countries have derived some researchers to conclude that malnutrition is a risk factor in the etiology of pre-eclampsia and implicate it by deficit intake of calcium and zinc (Caughey et al., 2005). Several results reported that deficiencies of some minerals are associated with pre-eclampsia (Sarwar et al., 2013; Hassan et al., 1991), whereas, other studies have failed to show an association between the serum concentrations of these elements and occurrence of pre-eclampsia (Gabbe and NJSJ, 2002).

The results of the present study showed significant differences in the serum levels of calcium and magnesium between pre-eclampsia group and healthy pregnant individuals, with reduction in levels of serum calcium and magnesium. This is compatible with the findings in other studies (Sarwar et al., 2013; Hassan et al., 1991). This may potentiate the results of Levine R et al. which reported that dietary calcium deficiency has been contributed to pre-eclampsia (Levine et al., 1997). Regarding calcium we are in agreement with the study that recommended prophylactic magnesium sulphate should be considered for women with severe pre-

eclampsia for whom there is concern about the risk of pre-eclampsia (Weeks and Ononge, 2002).

The results of this study showed that the serum zinc level in pre-eclampsia group was lower than that in normal pregnancy group, but the difference was not statistically significant. In the study of Adam et al also the mean serum zinc in pre-eclampsia was lower than that in normal pregnancy. This is in agreement with the previous study of Adam's et al (Adam et al., 2001). Controversial to the results of the present study, in a study by Ilhan et al the mean serum zinc level was significantly higher in normal pregnancy group than pre-eclampsia group (Ilhan et al., 2002).

There are reports that maternal serum copper level is lower in pre-eclamptic women as compared to healthy controls (Kumru et al., 2003; Orhan et al., 2001). The results of this study revealed that the level of serum copper is not associated with pre-eclamptic pregnancy.

CONCLUSION

The findings of this study showed that the hypocalcaemia and lower levels of serum magnesium were associated with pre-eclampsia and may be used as predictor risk factors for pre-eclampsia. The assessment of serum zinc level and copper do not have any association for preeclampsia. Supplementation of calcium and magnesium in pregnant women may reduce the risk of preeclampsia. We recommend assessment of serum calcium and magnesium concentration as an index for predicting the pre-eclampsia.

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