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Comparison of Plasma Copper, Iron and Zinc Levels in Hypertensive and Non-hypertensive Pregnant Women in Abakaliki, South Eastern Nigeria

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Abstract: With the increasing speculations of the involvement of nutrition, particularly trace elements in the pathogenesis of preeclampsia, a comparative study of plasma copper, iron and zinc levels was carried out between preeclamptic and non-eclamptic Nigerian women living in Abakaliki, Southeastern Nigeria. Data for 40 preeclamptic and 40 non-eclamptic women matched for age, gestational age, Body Mass Index (BMI), parity and socioeconomic status from a cohort of 349 pregnant women recruited at gestational age ≤25 weeks for the assessment of impacts of trace elements' status on pregnancy outcomes were analyzed. In addition to trace elements which were determined by Atomic Absorption Spectrophotometer (Buck Scientific, Model AVG 210), Total White Blood Cell Count (TWBC) and Haemoglobin Concentration (HbC) were determined using standard laboratory techniques. The preeclamptic and the non-eclamptic women had comparable TWBC and HbC with the former having significantly ($p < 0.05$) higher blood pressure. However, although, the preeclamptic women had lower plasma copper, iron and zinc levels than the non-eclamptic women, only copper was found to be statistically significant (6.02±7.23 vs. 10.23±9.84 µmol/l, $p<0.05$). It is thus concluded that preeclampsia is associated with significant decrease in plasma copper. Further research is desired to elucidate the role of trace elements, especially copper in the pathogenesis of pregnancy induced hypertension.

Key words: Pregnancy-induced hypertension, trace elements, proteinuria, oedema, ceruloplasmin, Abakaliki

INTRODUCTION

Pregnancy-induced hypertension (otherwise known as pre-eclampsia), characterized by persistently elevated blood pressure of greater than 140/90 mmHg, proteinuria and oedema (ACOG, 2002) during pregnancy has been described as a transient but potentially dangerous complication of pregnancy that affects approximately 5-10% of pregnancies worldwide (Skjaerven *et al*., 2002; Sarsam *et al*., 2008; Cunningham *et al*., 2007). Pregnancy induced hypertension has been associated with adverse course and outcomes of pregnancy (Dekker and Sibai, 1998; Ziaei *et al*., 2006). For instance, in developing countries, pre-eclampsia accounts for 20-80% of the strikingly increased maternal mortality (Roberts, 1998) and 15% of preterm deliveries (Belizan *et al*., 1983). Although many pathophysiologic factors such as inflammation, cytokine production, dyslipidaemia (Hube, 1998), elevated homocysteine (Laivuori *et al*., 1999), oxidative stress (Roberts and Hubel, 2004), reduced calcium intake and excretion and an imbalance between thromboxane and prostacyclin (Paknahad *et al*., 2008; Williams *et al*., 1999) have been implicated in the aetiology of pre-eclampsia, the complete aetiologies have not been fully elucidated (Golmohammad *et al*., 2008). Although the high rate of pre-eclampsia in developing countries has forced some authors to propose the involvement of nutrition, especially the trace elements in the aetiology of the disorder (Caughey *et al*., 2005; Golmohammad *et al*., 2008), studies on the relationship between maternal plasma trace elements concentrations and pre-eclampsia have produced inconsistent results (Harma *et al*., 2005; Atamer *et al*., 2005; Ilhan *et al*., 2002). For example, while

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Golmohammad *et al*. (2008) reported non-significant difference in the mean serum levels of calcium, magnesium, copper and zinc between non-eclamptic and preeclamptic pregnant women, Paknahad and colleagues (2008) reported increased urinary excretion of copper in preeclamptic women in comparison to their non-eclamptic counterparts. The present study is aimed at comparing the plasma levels of copper, iron and zinc in hypertensive and non-hypertensive pregnant women in Abakaliki, a semi-urban setting with high prevalence of trace element deficiencies (Ugwuja *et al*., 2010a,b).

MATERIALS AND METHODS

This study which was part of a larger study that investigated the impact of plasma copper, iron and zinc status on pregnancy outcomes was carried out among pregnant women attending antenatal clinic of the Department of Obstetrics and Gynaecology of the Federal Medical Centre, Abakaliki, one of the referral tertiary health institutions in the South eastern part of Nigeria. The protocol for this study was approved by the Ethics and Research Committee of the Hospital. The approval was based on the provision of Helsinki Declaration (2000) and on the agreement that patient anonymity must be maintained, good laboratory practice/quality control ensured and that every finding would be treated with utmost confidentiality and for the purpose of this research only. Informed consent of the participants was sought and obtained after which recruitment was carried out. Subjects' selection and detailed methodology has been previously described (Ugwuja *et al*., 2010a,b). Data for forty hypertensive and forty non-hypertensive pregnant women matched for age, gestational age, parity, anthropometrics and socioeconomic status were analyzed. While plasma copper, iron and zinc were determined by Atomic Absorption Spectrophotometer (Buck Scientific, model AVG 210), haemoglobin concentration was determined by Cyanmethaemoglobin method while total white blood cell count was estimated as in a standard haematology textbook (Dacie and Lewis, 1994).

Data analysis: Data were analyzed for mean and standard deviation while comparison between subjects and controls were analyzed using Student's t-test with statistical significance set at $p<0.05$.

RESULTS

From Table 1, the hypertensive and the non-hypertensive pregnant women had comparable ($p>0.05$) Body Mass Index (BMI), gestational age and number of antenatal attendance. Although the hypertensive women appeared to be older (29.45±3.70 vs. 27.55±4.23) than their non-hypertensive counterparts, this was not statistically significant ($p>0.05$). The haematological parameters (haemoglobin concentration and total white blood cell counts) were also comparable ($p>0.05$) between the groups. However, the blood pressure was significantly ($p<0.05$) higher in the hypertensive than in the non-hypertensive pregnant women.

Table 2 shows that hypertensive pregnant women had significantly ($p<0.05$) lower plasma copper when compared with the non-hypertensive women (6.02±7.23 vs. 10.17±9.84). Lower plasma levels were also observed for iron and zinc in the hypertensive women in comparison to the non-hypertensive group, although these were not statistically significant ($p>0.05$).

Table 1: Comparison of maternal characteristics between hypertensive and non-hypertensive pregnant women[1]

Parameters	Non-hypertensive (n = 40)	Hypertensive (n = 40)	p-values
Age (yrs)	27.55±4.23	29.45±3.70	0.076
BMI (kg/m^2)	28.79±3.99	29.19±4.76	0.145
Gestational age (Wks)	21.53±3.73	21.40±3.22	0.873
Parity (n)	1.45±1.40	1.95±1.55	0.134
Number of antenatal attendance	6.88±2.90	6.35±2.42	0.383
HBC (g/dl)	10.24±1.28	10.44±0.97	0.444
TWBC (x 10^9/l)	5.12±1.37	5.48±1.38	0.255
Blood pressure (mmHg)			
Systolic	119.00±23.3	147.00±19.1	0.049*
Diastolic	78.00±12.7	96.00±9.3	0.031*

BMI: Body Mass Index; HBC: Haemoglobin Concentration; TWBC: Total White Blood Cell Count.
[1]Values are mean ± standard deviation, *$p<0.05$

Table 2: Comparison of plasma copper, iron and zinc between hypertensive and non-hypertensive pregnant women[1]

Parameters	Non-hypertensive (n = 40)	Hypertensive (n = 40)	p-values
Copper (µmol/l)	10.17±9.84	6.02±7.23	0.041*
Iron (µmol/l)	11.63±11.03	9.92±7.80	0.430
Zinc (µmol/l)	10.87±10.28	9.97±9.74	0.686

[1]Values are mean ± standard deviation, *$p<0.05$

DISCUSSION

Although study has shown that women with greater Body Mass Index (BMI) in pregnancy are more likely to become hypertensive than those with lower BMI (Pipkin, 2001), the comparable Body Mass Index (BMI), gestational age and number of antenatal attendance observed in the hypertensive and the non-hypertensive pregnant women in the present study ruled out the influence of these parameters on the aetiology or severity of hypertension in the two groups. This study had documented lower plasma copper, iron and zinc in hypertensive pregnant women in comparison to their non-hypertensive counterparts, although only plasma copper was found to be statistically significant ($p<0.05$) between the two groups. The non significant lower plasma zinc in preeclamptic women in comparison to non-eclamptic women recorded in the present study contrast earlier findings (Kumru *et al*., 2003) where serum zinc level was 43% lower in the preeclamptic women. It is also in contrast with 31% higher median leucocyte zinc concentrations in preeclamptic women when compared with controls (Mohamed *et al*., 2000). However, it corroborated the findings of Golmohammad *et al*. (2008) where the difference in serum level of zinc between preeclamptic and non-eclamptic women was found to be non-significant. Zinc insufficiency has been recognized by a number of experts as an important public health issue, especially in developing countries (Prasad, 1998). Zinc has been found to be involved in a number of metabolic processes that are essential for growth and development (WHO, 1996) and zinc deficiency has been associated with a number of chronic diseases such as diabetes (Ugwuja *et al*., 2010a,b), increased prevalence of Coronary Artery Disease (CAD), as well as other risk factors including hypertension and dyslipidaemias (Singh *et al*., 1998). Like zinc, non-significantly lower plasma iron concentration in preeclamptic women when compared to their non-pre-eclamptic controls in the present study suggest a role for iron in the pathophysiology of pregnancy induced hypertension. Although iron deficiency can be a major contributory factor to severe anemia with adverse pregnancy outcomes, such as low birth weight, premature birth and maternal mortality, evidence that iron-deficiency anemia is a causal factor in poor pregnancy outcomes is still lacking (Conlan *et al*., 1990; Eaton-Evans *et al*., 1996). However, elevated hemoglobin, especially in later pregnancy, has been associated with poor pregnancy outcomes. Although we did not encounter any study on plasma iron in pregnancy complicated with hypertension, it is interestingly to note that elevated hemoglobin rather than anaemia in pregnancy was linked to underlying conditions like pregnancy induced hypertension or preeclampsia, which are well known to contribute to poor pregnancy outcomes (Eaton-Evans *et al*., 1996). In the present study, although plasma copper concentration in preeclamptic women was found to be significantly lower than that of the non-eclamptic women, study has shown that while severe copper deficiency results in heart abnormalities and damage (cardiomyopathy) in some animal species, the pathology differs from atherosclerotic cardiovascular disease that is prevalent in humans (Institute of Health, 2001). Although studies in humans have produced inconsistent results and their interpretation is hindered by the lack of a reliable marker of copper nutritional status, outside the body, free copper is known to be a pro-oxidant and is frequently used to produce oxidation of Low Density Lipoprotein (LDL) in the test tube. Moreover, the copper-containing protein ceruloplasmin has been found to stimulate LDL oxidation in the *in vito* (Fox *et al*., 2000), leading some scientists to propose that increased copper levels could increase the risk of atherosclerosis by promoting the oxidation of LDL. However, there is little evidence that copper or ceruloplasmin promotes LDL oxidation in the human body. Additionally, the cuproenzymes, superoxide dismutase and ceruloplasmin, are known to have antioxidant properties, leading some experts to propose that copper deficiency rather than excess copper increases the risk of cardiovascular diseases (Jones *et al*., 1997). However, both epidemiological (Malek *et al*., 2006; Leone *et al*., 2006) and experimental studies (Turley *et al*., 2000; Rock *et al*., 2000) have failed to unequivocally confirm the role of copper in the aetiopathology of pregnancy-induced hypertension. It is therefore concluded that pregnancy-induced hypertension is associated with significant reduction in plasma copper level without significant effect on plasma iron and zinc status. Further research is desired to explain the roles of trace elements, particularly copper in the pathogenesis of preeclampsia.

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