Copper and selenium status of healthy pregnant women in Enugu, southeastern Nigeria

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Abstract

Background: Copper and selenium are important trace elements in man. They function as antioxidants and play roles in oxido-reductase reactions. Several imported multivitamin preparations are given to our women during pregnancy and lactation to correct possible deficiencies.

Objective: The aim of the study is to determine the serum level of these micronutrients (selenium and copper) in a cross section of pregnant women in Enugu, southeastern Nigeria.

Materials and Methods: A cross section of 130 healthy pregnant women at different trimesters of pregnancy and 30 non-pregnant controls were selected from two health facilities in Enugu, southeastern Nigeria. Serum from the samples collected was assayed for copper and selenium using atomic absorption spectrophotometer.

Results: The mean copper level increased ($P = 0.018$), while the selenium level decreased ($P < 0.0001$) as pregnancy advanced.

Conclusion: High copper levels indicate that supplementation should not be undertaken during normal pregnancy. Dietary intake should be modified to ensure optimal selenium levels during pregnancy.

Key words: Copper, Nigeria, pregnancy, selenium

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Introduction

Copper is an essential trace element, which has been found to be an important constituent of vital enzymes, especially those functioning as antioxidants and as oxido-reductases.[1,2] Copper deficiency is rare, but cases have been identified in humans, which manifested as neutropenia,[3] anemia and skeletal abnormalities,[4] with atherogenic and electrocardiographic irregularities,[5] and is linked to low birth weight of neonates.[6] Different studies have reported high serum copper levels during normal pregnancy.[7,8] These changes are steady and consistent from the first trimester to third trimester.[9,10]

Selenium is an essential antioxidant trace mineral for the human body. It is a component of selenoproteins such as the antioxidant enzyme glutathione peroxidase (GSHPx), which protects human tissue from damage by hydrogen peroxide, lipid peroxides and free radicals.[11] Thus, it is invaluable in the protection of the tissues against oxidative stress. Furthermore, it is very useful for healthy human growth and reproduction, and is important in the metabolism of thyroid hormones.[12] Wide variations in selenium levels occur in humans. Geographical location, soil content, intake of selenium in diet and its bioavailability significantly affect selenium status.[13] There have been varying reports on the selenium status during pregnancy, with various studies showing lower levels in pregnancy.[14,15] However, studies in Spain and Japan observed no differences in serum

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selenium levels between healthy pregnant and non-pregnant women.[16,17]

Low selenium status has been associated with pre-eclampsia,[18,19] increased incidences of intrahepatic cholestasis,[20] gestational and pre-gestational diabetes,[21] and recurrent pregnancy loss.[22,23] Indeed, low selenium status is associated with an acceleration of HIV disease progression among HIV-1 infected pregnant women.[24] In addition, a low plasma selenium level is associated with increased risk of fetal death, child death and increased risk of intrapartum mother-to-child transmission of HIV.[25]

In our environment, there is no doubt that nutritional deficiency is prevalent in pregnancy. It thus became a common practice to routinely supplement iron and folic acid with the aim of preventing anemia in pregnancy. However, the role of other micronutrients in the prevention of anemia and oxidative damage to red cell membrane has received little attention. Consequently, maternal and perinatal mortality and morbidity remained unacceptably high despite global efforts to curb the trend. In an attempt to improve the situation, our caregivers resorted to the practice where all sorts of micronutrient replacements are administered, without recourse to the peculiar micronutrient needs necessitated by our varied socioeconomic, cultural and geographic environment. The resultant effect was the infiltration of the Nigerian market with numerous multivitamin and mineral preparations with diverse and varying compositions. It thus became pertinent that we should determine the serum level of some of the micronutrients (copper and selenium) in our healthy pregnant women to assist in the optimal formulation of micronutrient needs suitable for our environment.

Materials and Methods

Study area

The study was done in Enugu, the capital of Enugu State in southeastern Nigeria, between January and October 2009. The city of Enugu is situated at about 230 m above sea level. The population of the city is about 464,514 of which 52.1% are females. Enugu State has a crude birth rate of 45 per 1000, crude death rate of 18 per 1000 of the population and a life expectancy of 51 years.[26] The maternal mortality rate ranges between 750 and 850 per 100,000 live births.[27,28] Commonly eaten foods in Enugu include rice, yam, cassava, beans, corn food, egusi, ogbono, orah and vegetable soups.

Study population/subjects

This was a cross-sectional study involving 130 healthy pregnant women in various trimesters of pregnancy (34 in first trimester, 44 in second trimester and 52 in third trimester), attending antenatal clinic at two health care facilities in Enugu (one secondary and one tertiary). The control group was made of 30 healthy non-pregnant women recruited from the staff of the health institutions. All the subjects were selected by simple random sampling using a lucky dip of YES or NO. They were matched for age and social class. The parity range was between zero and four. Subjects with febrile conditions, multiple pregnancy, pre-eclampsia, diabetes mellitus, chronic renal disease, sickle cell anemia and HIV infections were excluded from the study. After obtaining ethical clearance and informed verbal consent, healthy pregnant women were recruited. Medical and obstetric histories were obtained. The gestational age was assessed from the first day of the last normal menstrual period in completed weeks of gestation. Trimester was defined as first trimester (<14 weeks), second (14–27 weeks) and third (>27 weeks). All the women were on routine iron and folic acid only, but not on copper and selenium supplementation. The socioeconomic class was determined by the method of Szreter.[29] All the subjects belonged to the middle class. A 24-hour dietary recall dialog was conducted to estimate their dietary copper, selenium and calorie intake. In this method, the subjects were required to recall their individual exact food intake during the previous 24-hour period or the preceding day. Also recorded were detailed descriptions of all foods and beverages consumed, including cooking methods and brand names (where possible). The amount of caloric as well as copper and selenium contents were estimated using the nutrient composition of commonly eaten staple foods in Nigeria[30] and other parts of the world.[31] Medical and obstetric examinations were performed. The weight was measured to the nearest 0.5 kg using a standard weighing scale. All the subjects and controls were subjected to the same instrument and method of measurement.

Sample collection/preparation

About 5 ml venous blood from the ante-cubital vein was collected from the subjects using sterile, disposable syringes into sterile, plain tubes. Samples for the non-pregnant group were collected on the 5th day of their menstrual cycle after an early morning negative pregnancy test. The blood samples were allowed to stand for about 30 minutes to clot and then centrifuged at 3500 rpm for 15 minutes. The serum was collected and kept frozen at −20°C until analyzed.

Biochemical measurements

Analyses were done within 2 weeks of sample collection using atomic absorption spectrophotometer (AAS/AES Model 205) (Buck Scientific , East Norwalk, Conneticut USA).

Statistical analysis

Values were recorded as mean and standard deviation. Comparison of mean was by one-way analysis of variance (ANOVA) followed by multiple comparisons with Tukey's honestly significant *post-hoc* test.

Ethical considerations

Ethical clearance was obtained from the university hospital ethical committee and verbal informed consent was got from all participants.

Results

Table 1 shows some demographic characteristics and estimated daily calorie, copper and selenium intake of the women. They were approximately on same nutrient intake. There were no statistically significant differences in parity ($P = 0.542$). Table 2 shows the mean copper and selenium levels in the control and across the three trimesters of pregnancy. The mean copper level increased ($P = 0.018$), while the selenium level decreased ($P < 0.0001$) as pregnancy advanced. Table 3 shows Tukey's honestly significant *post-hoc* test multiple comparisons.

Discussion

Progressive rise in concentrations of maternal serum copper from first trimester to third trimester was observed in this study, with statistically significant difference observed only between the third trimester and the controls. This trend has been shown in many other studies from different countries[32-34] and has been associated with increase in blood estrogens and decreased biliary excretion which is common in pregnancy.[8,35]

The relationship between copper and iron has been a subject for debate. It has been shown that iron supplementation in pregnant women (with hemoglobin greater that 13.2 g/dL) significantly reduced serum copper concentrations in both second and third trimesters.[36] Furthermore, Ghosh *et al.*[37] reported higher serum copper concentration in anemic pregnant women than in non-anemic ones in both second and third trimesters. This supported the view that iron has the potency of inducing negative copper concentrations or limiting its bioavailability in pregnancy. This phenomenon should be taken into cognizance during the treatment of iron deficiency anemia.

The selenium levels seen in this study indicate the selenium status of women in southeast Nigeria to be adequate when compared to other studies.[17,19] However, the serum selenium concentration decreased linearly from non-pregnant controls and as pregnancy progressed. Studies have shown that selenium levels are significantly lower in healthy pregnant women (especially in the second and third trimesters) than in healthy non-pregnant women.[20,38] Some studies have however produced conflicting reports.[16,17] Several reasons may be responsible for the lower levels found in this study. Active transfer of selenium from maternal blood to the tissues of the developing fetus has been advocated.[39] Indeed, hemodilution due to increased plasma volume in pregnancy further depletes selenium concentration. Additionally, inadequate intake and storage in the maternal tissues and increased demand by the growing fetus invariably leads to low maternal levels during pregnancy.

While this study population consists mainly of urban

Table 1: Some demographic characteristics/Estimated daily nutrient intake

Variable	1st trimester	2nd trimester	3rd trimester	Control
Mean age (years)	30.12 ± 5.60	28.23 ± 5.47	29.04 ± 4.04	28.20 ± 6.30
Mean gestational age (weeks)	9.94 ±1.75	21.27 ± 3.83	34.42 ± 2.90	0
Mean parity	1.00 ± 1.41	1.23 ± 1.74	1.85 ± 1.46	1.53 ± 1.77
Social Class	III	III	III	III
Mean weight (kg)	69.71 ± 14.1	71.14 ± 14.77	81.46 ± 10.35	64.60 ± 10.62
EDCI (kcal)	2130	2200	2210	2100
EDCoI (mg)	1.3	1.2	1.1	1.1
EDSeI (mg)	0.1	0.11	0.12	0.11

EDCI (kcal); estimated daily calorie intake, EDCoI (mg); estimated daily copper intake, EDSeI (mg); estimated daily selenium intake

Table 2: Mean serum selenium and copper levels in different trimesters

	Trimester							
	1st trimester		2nd trimester		3rd trimester		Control	
	N	Level	N	Level	N	Level	N	Level
Selenium (μmol/L)	34	1.36 ± 0.20[a]	44	1.05 ± 0.22[b]	52	1.01 ± 0.24[c]	30	1.38 ± 0.18[d]
Copper (μmol/L)		22.41± 15.17[e]		25.78± 7.55[f]		26.44± 11.80[g]		19.11± 7.54[h]

ANOVA; abcd; $P<0.0001$, efgh; $P=0.018$

Table 3: Multiple comparisons of differences of means between the variables (Turkey, s honestly significant post hoc)

Subjects	*P* value	
	Copper	Selenium
Control/first trimester	0.626[ns]	0.981[ns]
Control/second trimester	0.054[ns]	0.000*
Control/third trimester	0.021*	0.000*
First trimester/second trimester	0.537ns	0.000*
First trimester/third trimester	0.347ns	0.000*
Second/third trimester	0.991ns	0.000*

*(significant);ns (not significant); The significant differences seen in the copper levels is mainly due to differences between the control vs third trimester. For selenium, the differences between the control vs first trimester and second trimester vs third trimester had no significant effect on the results

dwellers who may have a varied diet including bread from imported wheat, the results may not be the same for rural dwellers where poor farm practices, heavy tropical rains, and erosion may cause trace elements to be leached out of the soil. In addition, the staple foods in the rural areas are mainly tubers (especially cassava) which are not known to contain high levels of selenium. However, a study in Anambra State, also in southeast Nigeria,[40] comparing Oba town to Nanka (a town prone to erosion), did not show statistically different mean values for selenium in both communities.

High copper levels, as observed in this study, had led to the recommendation by the Institute of Medicine of Washington DC, USA, that copper supplementation should not be undertaken during normal pregnancy.[41] Low levels of selenium suggest that dietary modification be advocated to meet the needs of pregnant and lactating mothers. Where dietary modifications are not possible, supplementation may be advocated. Despite this, majority of the prenatal drugs used in our environment still contain copper in appreciable amounts with little or no selenium.

In developing countries, it seems maternal malnutrition will continue to be a key contributor to unpleasant reproductive outcomes, in spite of efforts to fortify foods or distribute medicinal supplements to pregnant women.[42] Consequently, all forms of micronutrient supplementation have been advocated. These formulations come in all forms of sizes and shapes, with various and varying micronutrient compositions, and with diverse claims of superiority among the competing importers and manufacturers. As a result, our pregnant women ingest all forms of chemicals in the name of routine drugs.

Currently, practitioners are advocating the use of a single daily dose micronutrient supplement in order to enhance compliance. Good as this maybe, allowing drug manufacturers and importers to indiscriminately compound drugs, without recourse to peculiar socioeconomic, geographical and biochemical variables, may spell doom for feto-maternal health. Our practitioners and caregivers should thus discourage our pregnant women from taking those supplements that contain copper as this may provoke overload. Conversely, selenium-rich foods or, when applicable, supplements, should be encouraged while formulating nutritional policies during pregnancy and lactation.

This study did not evaluate the effect of short birth to pregnancy interval on the levels of the micronutrients. In addition, it may be possible that routine iron and folic acid taken by these women will have affected selenium absorption. These issues, as well as determining the reference values for our environment, need to be addressed in future studies. Indeed, larger longitudinal studies in pregnant Nigerian women would also be needed to further validate our findings. Additionally, the effect of these biochemical changes on pregnancy outcome needs further investigation. A 1-month dietary recall gives a better dietary history than a 24-hour method; however, this is very cumbersome and difficult to comply by the subjects.

Maternal malnutrition has attracted little concern from the authorities and this attitude may not be unrelated to the continued adverse feto-maternal outcomes in our environment. Nutritional needs of our pregnant women should be streamlined to enable optimal replacements if we must attain the millennium developmental goals.

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