Original Article

Reduced Maternal Selenium levels in Pregnant and Lactating Nigerian women: Should Routine Selenium Supplementation be advocated?

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ABSTRACT

BACKGROUND: Deficiencies in micronutrients are common in our environment, leading to indiscriminate replacement strategies. Selenium is an antioxidant micronutrient that may undergo depletion during pregnancy and lactation. Regrettably, information in this matter is scanty in Nigeria.

OBJECTIVES: To determine maternal selenium concentration during pregnancy and lactation.

METHODS: This was a cross-sectional research involving 120 pregnant women, 40 in each trimester. They were attending antenatal clinic of one tertiary and two secondary health care facilities in Enugu, Southeastern Nigeria. Control subjects constitute age, parity and socioeconomic matched 35 apparently healthy, non pregnant women. Serum selenium concentration was measured during pregnancy and postpartum. Breast milk selenium concentration was also determined by Atomic Absorption Spectrophotometer (AAS).

RESULTS: The mean serum selenium levels were significantly decreased (P<0.0001) in pregnancy when compared with non-pregnant control subjects; also as pregnancy progressed. However, there was a non significant increase immediately after birth. In the breast milk, selenium concentration significantly decreased (P<0.0001) as lactation progressed.

CONCLUSION: The observed significant decreases in the levels of selenium during pregnancy and breast milk may leave the mothers and their neonates at risk and, therefore, may necessitate maternal supplementation. Dietary intervention such as food diversification and bio-fortification is recommended to improve dietary selenium intakes in pregnant and lactating mothers, and infants in this region.

KEY WORDS: Selenium, pregnancy, postpartum, breast milk, mothers, Enugu Nigeria.

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Synopsis; Serum selenium levels decline in pregnancy and as pregnancy progresses. Immediately post-partum, the levels rise, nevertheless, there is consistent reduction in breast milk levels.

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INTRODUCTION

Maternal under nutrition is one of most neglected aspects of nutrition in public health globally. Although relatively few indicators are systematically tracked, recent reports on the global burden of maternal under nutrition concluded, despite limited information, that some 10%19% of women of reproductive age are critically undernourished.[1] Indeed, a significant proportion of women of reproductive age also have insufficient micronutrients levels.[2] Deficiencies in micronutrients may be associated with low maternal age, poverty and poor diets or food faddism. In much of the developing world, such deficiencies are exacerbated by malnutrition, repeated pregnancies and short intervals between pregnancies.[3]

Selenium is an essential trace element for animals and humans, with protective properties against endogenous or exogenous aggression, initiated largely by the hyper-production of highly reactive oxygen derivatives. It is an antioxidant, also an effective 'scavenger', regularly mopping up noxious free radicals and reactive oxygen species.[4] This unique role in human physiology has been found to include; the prevention of a number of degenerative conditions, atherosclerosis, specific cancers, arthritis, diseases of accelerated aging, central nervous system pathologies, infertility, inflammatory diseases, thyroid function, preeclampsia, cardiovascular disease, infections and altered immunological function.[5] In recent years, selenium deficiency in humans has been implicated as a risk factor for recurrent pregnancy loss, abortions and retention of the placenta.[6] Undeniably, selenium is involved in a variety of selenoproteins that include, but not limited to, the glutathione reductases.[7]

It is beyond uncertainty that micronutrient deficiency is particularly prevalent among pregnant women in developing countries like ours; and these deficiencies could have a detrimental effect on the fetus and neonate.[8] During pregnancy, the need for optimal fetal growth necessitates increased demand for selenium, which consequently manifests as decreased maternal blood and tissue concentrations.[8]

Placental hormones play a key role in selenium homeostasis during pregnancy. This is accomplished by the simultaneous effort to preserve selenium via a decrease in selenium urinary excretion. This unique placental induced homeostatic mechanism is more pronounced in late than in early pregnancy.[9]

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The human breast milk is a complex fluid, rich in nutrients, non-nutritional bioactive components; also a powerful antimicrobial agent[10]. In our environment, maternal malnutrition is particularly prevalent, and this has led to wild spread suggestions that routine micronutrient supplementation should suffix[2]. The Nigerian drug market has, therefore, been flooded with several multivitamin and trace element preparations, with each company claiming advantage of its products over the others. Unfortunately, information on maternal selenium status during pregnancy and lactation is scanty in our environment. We are, therefore, poorly equipped to determine whether to advocate increased intake of selenium rich food or outright supplementation. Consequent to this confusion, practitioners have used different types of formulations with varied micronutrient types and amount. These compositions are utterly alien to our distinctive geographic and socioeconomic needs and may be detrimental to feto-maternal health. It thus became essential to determine the baseline selenium level of our pregnant and lactating mothers and support policy makers in accurately determining the selenium needs and profer optimal replacement strategies.

SUBJECTS AND METHODS

Study Area

Enugu State is one of the 36 states of the Federal Republic of Nigeria. It has an approximate land mass of 8727.1km$_2$. It shares borders with Abia state to the south ,Ebonyi state to the East, Benue state to the North East, Kogi state to the North West and Anambra state to the West. It has a mixed rural and urban population with the majority being Igbos, with a projected population of 3.3 million out of which about 50% 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 51years[11]. The maternal mortality rate ranges from 750 to 850 per 100,000 life births[12, 13]. Enugu city is located in the hilly tropical rain forest about 230 m above sea level. The average annual temperature is between 23.1^{o}c and 31^{o}C with a rainfall of 1520 to 2030mm.There are two main seasons, the rainy season (April to October) and dry season (November to February). The city has a population of about 464,514 inhabitants. Commonly eaten foods in Enugu include; rice, yam, cassava, beans, corn food, egusi, ogbono, orah and vegetable soups.

Study design and setting

This is a cross sectional study, undertaken between March and December 2009. After obtaining ethical approval and written consent of 120 pregnant women; 40 in each trimester, first (0-13 weeks), second (14-27 weeks) and third (= 28weeks) were randomly recruited. They were attending the ante-natal clinic of one tertiary and two secondary health care facilities in Enugu, South-eastern Nigeria. Thirty-five (35) age, parity and socioeconomic status matched non-pregnant and non-lactating; apparently healthy mothers were used as control subjects. The selection was based on lucky dip of "YES" or "NO". The exclusion criteria include; multiple pregnancies, obstetric hemorrhage, deliveries by cesarean section. Other exclusions included women on selenium supplements, anemia, fever, HIV positive patients, sickle cell disease, diabetes mellitus, smokers, malignancy, chronic alcoholics, tuberculosis, hypertension and any diagnosed inflammatory disease in pregnancy. The age range of the pregnant women was 19-42 years. Among those recruited, only 80 had hospital delivery. Twenty two (22) from the 1st trimester, 31 from the second trimester and 27 from the 3rd trimester.

Approval for the study was granted by the Ethics committee of the Hospital (ref: UNTH/CSA.329/Vol.6).

Socio-economic Status of Subjects

Information on the socio-economic status was obtained by the administration of a pre-tested, semi-structured, self-administered questionnaire. The socio-economic rating was determined by the method of Szreter,[14] and both pregnant and control subjects belonged to the middle class.

Anthropometric/Socio-demographic Characteristics

The anthropometric/socio-demographic characteristics were obtained from the medical history, obstetric profile and folders. The weight was measured to the nearest 0.5 kilogram using a standard weighing scale **(STADIOMETER, SECA, MODEL 220, GERMANY).** The height was measured in meters, with the same equipment without shoes, with the feet together, standing as tall as possible with the eyes level and looking straight ahead. Clinical examinations, routine laboratory investigations and ultrasonography, were performed.

Dietary Assessment of Subjects

A 24-hour dietary recall interview was conducted for all the pregnant subjects and controls to evaluate their dietary selenium and calorie intake. In this method, the subjects were required to recall the person's correct food intake during the last twenty-four-hour period or preceding day. Detailed descriptions of all foods and beverages consumed, including cooking methods and brand names (where possible) were recorded. The amount of nutrient intake was calculated based on the nutrient composition of commonly eaten foods in Nigeria and other parts of the world.[15,16]

Blood Specimen Collection

About 5ml of fasting venous blood from the antecubital vein was collected from subjects at each period (pregnancy, and postpartum), using sterile, disposable syringes. The samples were transferred into sterile, anti-

coagulant-free glass sample containers (plain tubes). Samples for the non pregnant group were collected on the 5th day of their menstrual cycle after a negative serum pregnancy test. The blood samples were allowed to stand for about thirty (30) minutes to clot and then centrifuged at 3,500 (rpm) for 15 minutes to separate cells from serum. The serum was collected and kept frozen at -20°C until analyzed.

Breast Milk Sample Collection

Breast milk sample collection was carried out on the 3rd, 6th, 9th, 12th and 15th day after birth since lactation did not commence on the day of delivery for most of the mothers. Breast milk samples (10ml) were collected from the postpartum/lactating mothers by manual expression of the milk directly from the breast into sterile, plastic sample containers. After collecting the first 5ml, the child was breastfed for 15 minutes and then, an equal amount of hind-milk from the same breast was collected. After mixing thoroughly, the samples were immediately stored and frozen at -20°C prior to analysis. All the milk samples were collected within the same period of the day (9.00 11.00 am) to avoid any possible diurnal changes.

Sample Analysis

Analyses (serum and milk) were done within two weeks of sample collection. Serum and breast milk samples were analyzed for the antioxidant micronutrient mineral (Selenium) levels by Atomic Absorption Spectrophotometer (AAS) method (Buck Scientific AAS/AES Model 205, United States of America).

Statistical Analysis

Analysis of data was done using Graph Pad prism version 5.02. Values were recorded as mean and standard deviation. D'Agostino & Pearson omnibus normality test was performed and data assumed Gaussian distribution. Consequently, a one way analysis of variance (ANOVA) followed by Tukey's honestly significant difference post hoc tests was done. P values < 0.05 were considered significant.

RESULTS

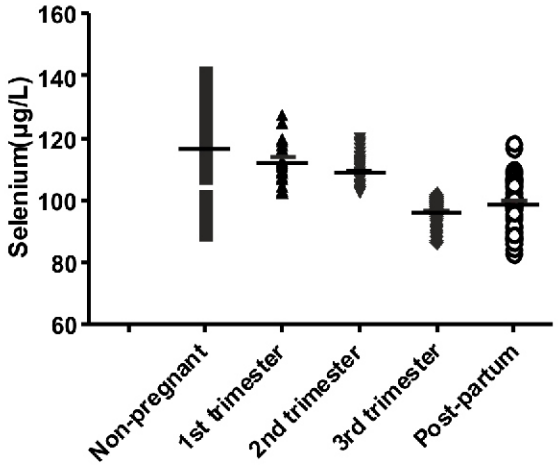
Table 1 represents the mean values of some anthropometric/sociodemographic characteristics of the subjects. Further more, the estimated mean daily selenium and caloric intake of the subjects did not differ significantly (P=0.58 and 0.66 respectively). The mean selenium level (µg/L) in the control subjects was 116.28 ± 13.66.This reduced to 112.48 ± 7.78 in the 1st trimester, 108.59 ± 4.90 in the 2nd trimester and 96.04 ± 4.21 in the 3rd trimester. However, immediately after delivery, the value rose to 98.45 ± 7.88. These values are statistically significant. (P<0.0001).

On the other hand, post hoc analysis did not show any significant changes between Control versus1st trimesters (p=0.40), 1st trimester versus second trimester (p=0.41) and 3rd trimester versus postpartum (p=0.98). (Figure 1). The level of selenium (µg/L) in the breast milk was 70.9 ±3.08 (0-3rd day); 65.2 ± 2.95 (4th-6th day); 61.00 ± 2.11(7th-9th day); 58.81 ± 4.23(10th-12th day) and 52.07 ± 3.14 (13th-15th day). These changes are statistically significant (P<0.0001), however, post hoc analysis did not observe any significant differences between days 7-9 and days 10 -12 post partum levels (p=

Table 1. Some anthropometric/socio-demographic characteristics and estimated daily calorie (EDCI) and selenium (EDSeI) intake.

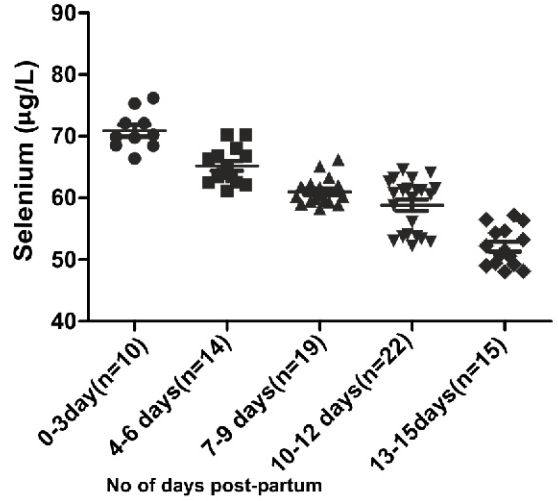
Variable	*1st trimester*	*2nd trimester*	*3rd trimester*	*Control*
Mean age (years)	30.12±5.60	28.23±5.47	29.04±4.04	28.20±6.30
Mean gestational age (weeks)	9.94±1.75	21.27±3.83	34.42±2.90	0.000
Mean parity	1.00±1.41	1.23±1.74	1.85±1.46	1.53±1.77
Height(m)	1.65±.07	1.60±.08	1.66±.05	1.64±.05
Mean weight (kg)	69.71±14.1	71.14±14.77	81.46±10.35	64.60±10.62
EDCI (kcal/day)	2130110	2200110	2210100	2100108
EDSeI (µg/day)	53.27±6.7	52.34±6.8	51.42±6.6	49.69±6.2

Figure 1: Mean serum selenium concentrations (µg/L) in pregnancy and postpartum periods



One way ANOVA (P<0.0001)

Figure 2: Mean breast milk selenium concentrations (µg/L) at different days postpartum



One way ANOVA (P<0.0001)

0.997). (Figure 2)

DISCUSSION

Mean serum selenium levels were significantly decreased in pregnancy when compared with non-pregnant control subjects. The levels decreased as gestation progressed, with the lowest concentration of serum selenium obtained during the third trimester. This finding may be due to its utilization as defense mechanisms against reactive oxygen species/free radicals during the oxidative stress of pregnancy[17]. Additional factors include hemodilution of pregnancy, when plasma volume may increase by 40-50%[18, 19], and active transport of selenium from mother to fetus[20]. Furthermore, normal physiologic adjustments to pregnancy and response to hormonal changes may also contribute to the decline in serum selenium during pregnancy[19]. This result is supported by the earlier report which revealed that normal pregnancies had lower plasma levels of selenium than non-pregnant women [21,22]. However, conflicting information on Spanish women acknowledged that no significant differences in the selenium levels either among pregnant women according to the trimester of pregnancy or in the group of non-pregnant women.[23]

In this study, the serum selenium levels which decreased in pregnancy, increased non-significantly in mothers after the baby was delivered. Understandably, this could be due to expulsion of the baby and placenta, with the gross reduction in the active transfer of selenium from the mother. The finding is consistent with a previous work that also suggested that placental secretions might be involved in the control of serum selenium content during pregnancy[20].

A progressive decline in the selenium concentration of breast milk as the duration of lactation increased, with the highest concentration in colostrum (day 0-3 postpartum) and the least in mature milk (day 13-15 postpartum) was also demonstrated. This is consistent with reports from other studies, which showed that the mineral and trace element composition of breast milk varied greatly as the duration of lactation increased.[24, 25]. Indeed, it has also been demonstrated that the mammary-gland regulating process controls the synthesis and secretion of seleno-compounds throughout lactation, with a high total Selenium status in colostrum that decreases as lactation progresses.[26] Selenium levels in humans vary widely between geographical areas. This depends on soil content, intake of selenium in diet and its bioavailability.[27] This is also reflected in diverging breast milk selenium levels which depends on stage of lactation, breastfeeding routine/pattern, parity, age, and other maternal characteristics.[28]

This study forms a cornerstone in the establishment of serum selenium reference levels in pregnancy, postpartum and breast milk of mothers in this region. It should, therefore, form the basis for the formulation of adequate and optimal micronutrient supplementation strategies for our pregnant and lactating women. On the other hand, it would have been more appropriate if we had recruited all the women in the first trimester and followed them up until birth. Besides, one month dietary recall, where feasible gives better dietary overview than a 24 hour recall. Furthermore, this study did not evaluate the impact of short birth to pregnancy interval on the levels of the micronutrients. In addition, it may be possible that conventional iron and folic acid taken by these women may have affected selenium absorption. These issues, as well as determining the reference values for our environment need to be addressed in future studies.

Appropriate strategy for the prevention and management of maternal undernutrition and micronutrient deficiencies in developing countries is recommended to be a priority. These strategies may require different interventions. Selenium concentration is low during pregnancy and lactation. Our poor socioeconomic circumstance may militate against advocating only dietary replacement as it is glaringly obvious that selenium reach foods are unaffordable by majority of pregnant women in Nigeria and indeed many developing countries. Routine selenium supplementation is, therefore, advocated in addition to evidence-based interventions that can improve maternal nutritional status and fetal growth. This should include fortified food supplements or conditional cash transfers to address household food insecurity.In addition, there should be micronutrient interventions that address selenium and other micronutrient deficiencies, and measures to reduce the burden of maternal and infant morbidity and mortality.

Conflict of Interest: None

Authors Contribution

1).FEE was involved in the conception and design of the study, micronutrient estimation, analysis and interpretation of data, drafting of the manuscript, revising the article for intellectual content and giving final approval of the version to be sent for publication.

2).ANCO was involved in the design of the study, the analysis and interpretation of data, revising the article for intellectual content and giving final approval of the version to be sent for publication.

3) UIN was involved in the conception and design of the study, history taking and clinical examination of the subjects, analysis and interpretation of data, revising the article for intellectual content and giving final approval of the version to be sent for publication.

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