

Parity-related Changes in Body Weight May Influence the Zinc and Copper Status of Urban Pregnant Women: A Report from South Eastern Nigeria

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ABSTRACT

Background: Micronutrient replacement is done indiscriminately, without recourse to peculiar socioeconomic and sociodemographic variables. Particularly, the relationship between parity, body weight, and some micronutrients has received minimal attention in Nigeria. **Aim:** To determine the relationship between parity, body weight, and some micronutrients during pregnancy. **Subjects and Methods:** This is a cross-sectional study involving 130 pregnant women and 30 nonpregnant control. They were recruited from two health care facilities in Nigeria and grouped into nulliparous and multiparous. After a 24-h dietary recall, the weight (W) and height (H) were measured. The body mass index (BMI) (W in kg/ H in m^2) was calculated. Serum copper and zinc were estimated using flame atomic absorption spectrophotometer. **Results:** Multiparous nonpregnant subjects parity=3.0 (0.58) had higher weight ($P=0.037$) and BMI ($P=0.035$) than their nulliparous counterparts (parity=0). In addition, there were no significant difference in Cu and zinc levels between the two groups ($P=0.243$ and 0.402 , respectively). Expectedly, weight and BMI increased as pregnancy progressed. There was no significant difference in Cu levels between the three trimesters in the nulliparous pregnant and multiparous pregnant subjects. In the pregnant nulliparous subjects, the Zn levels of the 2nd and 3rd trimesters were significantly lower than that of the nonpregnant nulliparous subjects ($P<0.001$ and 0.039 , respectively). However, in multiparous pregnant subjects, only the 3rd trimester Zn level was significantly lower than that of the nonpregnant controls ($P=0.017$). **Conclusion:** Pregnancy weight gain is more pronounced in multiparous than nulliparous women. This parity-related pattern only affects the serum zinc levels, a situation that should be taken into consideration when formulating policies for nutritional replacement.

KEY WORDS: Africa, body mass index, copper, parity, pregnancy, zinc

INTRODUCTION

Body mass index (BMI) is a universally accepted indicator representing obesity by measuring weight in kilograms and dividing by height in meter square.^[1] It has been classified that the BMI for normal weight in adults is 18.5-24.9 kg/m²; underweight is less than 18.5 kg/m²; overweight is 25.0-29.9 kg/m², while obese is greater than 30.0 kg/m².^[2] Obesity has been classified as a modern epidemic. It has been described as the fastest growing health problem in the United State of America, where approximately one-third of all US women are obese.^[3] Several criteria have been used to

define obesity in pregnancy. These include; increase of 110% to 120% of ideal body weight, absolute weight of >91 kg or BMI >30 kg/m².^[4] Overweight and obesity in pregnancy may be associated with some pregnancy-related complications. However, modification could be done to improve pregnancy outcome. Some of the complications include: birth defects, especially neural tube defects,^[5,6] complications during labor and delivery,^[7] fetal and neonatal death,^[8] hypertensive disorders in pregnancy, gestational diabetes,^[9] and delivery of large for gestational age infants.^[7,9]

It is beyond dispute that the regulation of body weight requires a balance between food intake and energy expenditure. Since the discovery of the adipocyte-derived hormone, leptin, in the early 1990s,^[10] evidence has accumulated to support the existence of a physiological

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system that is responsible for the long-term regulation of food intake and energy balance. Leptin is a potent satiety factor^[11,12] that circulates in plasma in proportion with body adiposity.^[13] Several workers have observed that the administration of leptin increases energy expenditure and decreases appetite^[11,14-16] through a decrease of the orexigenic neurotransmitters in hypothalamus.^[16,17] Leptin is essential for the establishment of pregnancy.^[18] It has also been reported that it is a fundamental fetal growth promoting factor^[19,20] independent of insulin-like growth-promoting factors^[21] as reduced placental transport of leptin from mother to the fetus is associated with fetal growth retardation.^[18]

Zinc (Zn) plays a significant role in the regulation of the appetite.^[22-24] A widely accepted mechanism for Zn-induced regulation of appetite is changes in the metabolism of the hypothalamic neurotransmitters.^[23,25] The existence of a link between zinc-induced appetite regulation and leptin-induced appetite regulation was suggested by Mantzoros *et al.*,^[26] and Mangian *et al.*,^[27] when they observed that, in humans and rodents, zinc deficiency decreases, while Zn supplementation increases leptin levels. This suggests a positive correlation between leptin and Zn levels.^[24]

Copper (Cu) is a trace element that regulates the functions of several cuproenzymes that are essential for life^[24] and plays a significant role in antioxidant defense and immune development.^[28]

Zn and Cu are beneficial during pregnancy. Both excesses and deficiencies have been reported to have profound and sometimes persistent effects on many fetal tissues and organs in the absence of clinical signs of deficiency in the mother. These effects have been reported to be through alterations in maternal and fetal metabolism; as a consequence of their essential role in enzymes and transcription factors and through their involvement in signal transduction pathways that regulate development.^[29]

The relationship between body fat, BMI, leptin, and some micronutrients has received attention in some settings. The reports showed that plasma leptin level correlates positively with BMI^[13,24,30] and plasma zinc level.^[24] Furthermore, Cu competes with Zn at absorptive sites, suggesting a role for Cu in the regulation of Zn level.

In Nigeria, despite the enormous resources from oil, poverty level remains remarkably high. Micronutrient supplementation is, therefore, routinely advocated. As a result, several micronutrient formulations (including copper and zinc) have flooded the Nigerian market with various unsubstantiated claims of superiority. It is exceedingly

unfortunate, that these formulations were done without scientific evidence. Indeed, economic, geographical, sociocultural, and patient demographic peculiarities were not considered. Consequently, maternal mortality and morbidity has remained embarrassingly high,^[31] and the attainment of the Millennium Development Goals is in doubt. Unfortunately, there is a dearth of information on the relationship between some micronutrients (Cu and Zn) status, parity, and obesity indices in pregnant and nonpregnant women. The present study was designed to investigate this in eastern Nigerian women and form the basis for more specific and detailed investigation.

SUBJECTS AND METHODS

Study area

The study was done in Enugu state in Southeast Nigeria between January and October 2009. The state is located in the hilly tropical rain forest about 230 m above sea level. The average annual temperature is between 23.1 and 31°C with a rainfall of 1520-2030 mm. It has a mixed rural and urban population with the majority being Igbo's, with a projected population of 3.3 million out of which slightly more than 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 51 years.^[32] The maternal mortality rate ranges between 750 and 850 per 100,000 live births.^[33,34] 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 involving 130 normal pregnant women at various trimesters (34 in the first trimester, 44 in the second trimester, and 52 in the third trimester) attending antenatal clinic at University of Nigeria Teaching Hospital (UNTH) and Kenechukwu specialist hospital in Enugu. The control group consists of 30 nonpregnant women recruited from the staff of the above-named institutions. Subjects with febrile conditions, multiple pregnancy, preeclampsia, diabetes mellitus, and chronic renal disease, sickle cell anemia, and HIV infections were excluded from the study. Ethical approval was obtained from UNTH ethical review board. After obtaining informed written consent, the subjects that met the above criteria were recruited. Personal history, history of present pregnancy, obstetric history, medical history, family and social history, and review of systems were obtained. The gestational age was assessed from the last normal menstrual period. Trimester was defined as the first trimester (<14 weeks), second (14-27 weeks), and third (>27 weeks). All the women were on routine iron and folic acid supplementation as recommended in Nigeria, but not on copper and zinc. The socioeconomic class was determined by the method

of Szreter.^[35] All the subjects belonged to the middle class. A 24-h dietary recall dialogue was conducted to estimate their dietary copper, zinc, and calorie intake. In this method, the subjects were required to recall the individual's exact food intake during the previous 24-h period or 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 zinc contents, was estimated using the nutrient composition of commonly eaten staple foods in Nigeria,^[36] and other parts of the world.^[37]

Medical and obstetric examinations were performed. The weight was measured to the nearest 0.1 kg using a standard weighing scale (Stadiometer, Seca, Model 220, and Germany). The height was measured with the same instrument, to the nearest 0.1 cm, without shoes, with the feet together, standing as tall as possible with the eyes level and looking straight ahead. All subjects and controls were subjected to the same instrument and method of measurement.

BMI was calculated from the formula: Weight in kg divided by height in m² (after converting the centimeter to meter and recorded as kg/m²).

Estimation of copper and zinc; Five (5 mL) of venous blood was collected from the antecubital vein from the subjects using sterile, disposable syringes. The samples were transferred into sterile, anticoagulant-free glass sample containers (plain tubes). Blood samples of the nonpregnant group were collected on the 5th day of their menstrual cycle and analyzed after a negative pregnancy test. The blood samples were allowed to stand for about 30 min to clot and then centrifuged at 3,500 (rpm) for 15 min. The serum was collected and kept frozen at -20°C until analyzed. flame atomic absorption spectrophotometer (AAS); (Buck Scientific AAS/AES Model 205, United States of America) was used to assay the trace elements.

Statistical analysis

Statistical analysis was done using SPSS version 15.0 (Chicago, Illinois, USA) values were recorded as mean and standard deviation. The test for significance was done using student's *t*-test and one-way analysis of variance, followed by multiple comparisons using Tukey's honestly significant post hoc test.

RESULTS

BMI and weight

Results show that the mean (SD) BMI of the multiparous nonpregnant subjects (parity=3.0 (0.58)) was significantly higher than that of the nulliparous nonpregnant

subjects (parity=0) $P=0.035$ [Table 1]. The BMI for the nulliparous pregnant women was significantly different when compared with the nonpregnant nulliparous counterparts ($P<0.001$). However, the nonpregnant versus 1st trimester ($P=0.106$) and the 1st trimester versus 2nd trimester, ($P=0.312$) did not contribute to this change. This significant difference is mainly due to differences between the 2nd and 3rd trimesters. The BMIs of the 2nd and 3rd trimesters of the nulliparous pregnant subjects were significantly higher than that of the nulliparous nonpregnant subjects ($P=0.014$ and $P=0.002$, respectively) [Table 2].

For the multiparous pregnant subjects, only the 3rd trimester BMI was significantly higher than the nonpregnant multiparous ($P=0.032$), whereas the BMI of the 1st and 2nd trimesters was not significantly different from that of the nonpregnant multiparous subjects ($P=0.463$ and $P=0.223$, respectively) [Table 3]. The changes in weight are also recorded in the tables.

Table 1: Some mean anthropometric data and Cu and Zn status of nonpregnant subjects

	Nonpregnant (N=30)		P values
	Parity=0 (N=12)	Parity=3.0 (0.58) (N=18)	
Age (years)	24.67 (1.63)	32.14 (2.54)*	0.018
Weight (kg)	60.5 (2.38)	70.86 (4.37)*	0.037
Height (M)	1.64 (0.03)	1.65 (0.02)	0.390
BMI (kg/m ²)	22.45 (0.76)	25.99 (1.49)*	0.035
Cu (µmol/L)	15.20 (1.40)	18.0 (3.3)	0.243
Zn (µmol/L)	4.74 (0.50)	4.43 (1.04)	0.402

* $P<0.05$ versus nulliparous (parity=0); BMI – Body mass index; Cu – Copper; Zn – Zinc

Table 2: Some mean anthropometric data and Cu and Zn status of nulliparous pregnant and nonpregnant subjects

	Nulliparous (N=66)			
	Nonpregnant (N=12)	Pregnant (N=54)		
		1 st trimester (N=20)	2 nd trimester (N=22)	3 rd trimester (N=12)
Age (years)	24.6 (1.6)	29.4 (1.6)*	26.27 (1.13)	28.17 (1.01)*
Weight (kg)	60.5 (2.4)	71.9 (5.1)	69.82 (4.31)	79.17 (3.19) [†]
Height (M)	1.6 (0.03)	1.68 (0.02)	1.61 (0.02)	1.64 (0.03)
BMI (kg/m ²)	22.5 (0.8)	25.57 (1.8)	26.82 (1.24)*	29.53 (1.68)*
Cu µmol/L	15.20 (1.40)	15.9 (1.6)	14.6 (2.3)	18.6 (4.1)
Zn µmol/L	4.74 (0.50)	4.32 (0.46)	2.64 (0.26)*	3.31 (0.53)*

* $P<0.05$ versus nonpregnant; BMI – Body mass index; Cu – Copper; Zn – Zinc

Table 3: Some mean (SD) anthropometric data and Cu and Zn status of multiparous pregnant and nonpregnant subjects

	Multiparous parity=3.48 (0.54) (N=94)			
	Nonpregnant (N=18)	Pregnant (N=76)		
		1 st trimester (N=14)	2 nd trimester (N=22)	3 rd trimester (N=40)
Age (years)	32.14 (2.54)	32.8 (3.25)	31.57 (2.35)	30.67 (1.06)
Weight (kg)	70.86 (4.37)	65.6 (5.31)	72.0 (6.9)	83.07 (3.07)*
Height (M)	1.65 (0.02)	1.59 (0.05)	1.60 (0.03)	1.67 (0.01)
BMI (kg/m ²)	25.99 (1.49)	25.76 (1.75)	27.90 (1.89)	29.96±1.19*
Cu µmol/L	18.0 (3.34)	17.1 (2.3)	12.4 (2.1)	15.0± (3.1)
Zn µmol/L	4.43 (1.04)	4.27 (0.66)	2.76 (0.28)	2.67 (0.24)*

* $P<0.05$ versus nonpregnant; BMI – Body mass index; Cu – Copper; Zn – Zinc

Copper

Although the serum copper level was higher in the multiparous nonpregnant subjects than the nulliparous nonpregnant subjects: 18.0 (3.3) versus 15.2 (1.4) $\mu\text{mol/L}$. The differences were not statistically significant ($P=0.243$) [Table 1]. For the pregnant subjects, there was a tendency toward a peak at the 3rd trimester for the nulliparous patients, while the peak occurred in the first trimester, and there after declined for the multiparous women. Again these differences were not significant ($P>0.05$) [Tables 2 and 3].

Zinc

There was no significant difference between the Zn levels of the multiparous nonpregnant subjects and the nulliparous nonpregnant subjects ($P=0.402$) [Table 1]. The Zn levels of the 2nd and 3rd trimesters of the pregnant nulliparous subjects were significantly lower than that of the nonpregnant nulliparous subjects ($P<0.001$ and $P=0.039$, respectively) [Table 2], whereas that of the 1st trimester was not significantly different from that of the nonpregnant nulliparous subjects ($P=0.283$). The Zn levels of the 1st and 2nd trimesters of the pregnant multiparous subjects were not significantly different from that of the nonpregnant multiparous subjects ($P=0.455$ and $P=0.074$, respectively) [Table 3]. Only the Zn level of the 3rd trimester multiparous pregnant subjects was significantly lower than that of the nonpregnant multiparous subjects ($P=0.017$) [Table 3]. Table 4 shows the parity-related differences in copper and zinc levels between pregnant and nonpregnant women.

DISCUSSION

This study investigated the possible interrelationships between body weight, Zn, and Cu. Body weight has been reported to be positively correlated with serum leptin.^[13,24,30] Leptin and Zn are both involved in the physiological regulation of energy homeostasis. While leptin stimulates energy expenditure and inhibits appetite through altering hypothalamic neuropeptide concentrations,^[13,16,17] Zn stimulates appetite by altering the concentrations of neurotransmitters either in the circulation or locally in the hypothalamus.^[38-40]

The interrelationship between leptin and Zn in humans has

been reported by Mantzoros *et al.*,^[26] who observed that serum leptin concentration was significantly affected by Zn status. More specifically, some reports show that leptin levels decreased in response to Zn depletion and increased after Zn supplementation. Similar findings in rodents had earlier been reported.^[27] The mechanism by which Zn level affects leptin level is known to be through body fat and leptin synthesis.^[41] More recently, Ozdemir *et al.*,^[24] reported a positive correlation between maternal serum leptin and maternal BMI and Zn levels. Furthermore, it has been observed that maternal Zn, but not Cu level, affects maternal serum leptin level.

In the present study, a significantly increased BMI was observed in the multiparous nonpregnant subjects compared with the nulliparous nonpregnant subjects. According to WHO¹ and NIH² classification, the BMI for the nulliparous was normal, whereas the BMI for the multiparous showed that these subjects were overweight. This may suggest a parity-related predisposition to obesity. The effects of prepregnancy overweight and obesity on pregnancy outcome are well- documented.^[6,42] This has led to the clamor for women of child-bearing age and their healthcare providers to work together to assess and address the weight issue before, during and after pregnancy.

The copper level was biochemically higher, while the zinc level was lower (though statistically nonsignificant) in the multiparous than the nulliparous nonpregnant women. This observation was a bit surprising as a statistically significant parity-related increase in Zn status similar to BMI was expected, as BMI has been reported to be positively correlated with serum leptin^[13,24,30] and leptin in turn has been reported to be positively correlated with Zn status.^[24] This may suggest that the relationship that exists between leptin and Zn may be lost in overweight and obese subjects, since it is well-established that these subjects are leptin resistant.

In this study, there was a progressive, parity-related increase in body weight and BMI as pregnancy progressed. This was expected because of the increasing growth of the fetus. In pregnancy, BMI is not valid for use in weight classification because the increased weight gain, which is expected in pregnancy, is due to the growth of the products of conception and not necessarily accumulation of fat. This means that the positive correlation between leptin and BMI may not exist in pregnancy.

The copper levels in the present study increased in the nulliparous but decreased in multiparous women as pregnancy progressed. Although these changes were not statistically significant, the biochemical difference is glaringly obvious. There have been reports of variations

Table 4: Parity-related differences in mean (SD) copper and zinc levels between pregnant and nonpregnant women

	Nulliparous women (N=66)			Multiparous women (94)		
	Nonpregnant (N=12)	Pregnant (N=54)	P values	Nonpregnant (N=18)	Pregnant (N=76)	P values
Cu $\mu\text{mol/L}$	15.20 (1.40) ^a	15.98 (1.61) ^b	0.399	18.0 (3.34) ^c	14.69 (2.34) ^d	0.210
Zn $\mu\text{mol/L}$	4.74 (0.50) ^e	3.41 (0.210) ^f	0.001 ^{evsf}	4.43 (1.04) ^g	2.99 (0.20) ^h	0.019 ^{gvsh}

b versus d, $P=0.291$; f versus h, $P=0.113$. P values comparing the nonpregnant nulliparous and multiparous (a vs. c and e vs. g) were noted in Table 1

in copper levels during pregnancy. While some studies reported increasing levels as pregnancy progressed,^[43-45] others reported high prevalence of copper deficiency.^[46,47] However, these studies did not take parity into consideration while making such assumptions. Since micronutrient malnutrition is prevalent in the developing countries,^[48] the observed change in Cu level in the subjects in this study maybe a contributory factor in the physiological homeostatic mechanism protecting fetal growth.

In the multiparous and nulliparous pregnant women, zinc levels decreased as pregnancy progressed. Also noted was lower biochemical level of zinc in the multiparous pregnant group, though statistically nonsignificant. The decrease in the Zn status of the pregnant subjects in the 2nd and 3rd trimesters was not progressive. This was not surprising because Zn requirement increases during pregnancy mainly because of its utilization during embryogenesis and fetal development.^[49] This was similar to the observation of Hambidge *et al.*,^[50] and Ejezie and Nwagha^[51] where a progressive decrease in Zn level during pregnancy was reported.

There is no doubt that obesity and overweight is highly prevalent in pregnancy in our environment.^[52] Indeed, there appeared to be a parity-related increase in body weight and BMI in nonpregnant and pregnant women. The parity-related changes in copper during pregnancy although statistical insignificant showed some biochemical relevance.

Routine supplementation during pregnancy has been the usual practice in Nigeria and indeed many developing countries. This has been indiscriminately undertaken without recourse to the peculiar micronutrient needs in a varied geographic and socioeconomic situation. Indeed it seems plausible, from this preliminary study that parity may influence maternal micronutrient composition. Consequently, it may not be totally absurd to advocate that parity be considered as a critical variable in the formulation of micronutrient replacement policies during pregnancy and lactation. The composition and quantity of micronutrient required during pregnancy should not be the same for all pregnant women. Body weight and parity should play a significant role in making the appropriate choices.

The cross-sectional and hospital-based nature of the study may have limitations over the findings. Again, the small sample size and the nonconsideration of age as a confounding variable may have affected the outcome. Indeed, it would have been more appropriate to use the Esha Pro software (ESHA Research, USA) to aid the assessment of total energy and micronutrient intake. Further studies, which must, be longitudinal, with higher sample size should be instituted to enable a clear understanding on the effect of parity on

micronutrients stores. Indeed, studies should include serum leptin levels to determine its relationship with serum zinc, copper, and BMI.

The results of this study further highlight the importance of assessment of weight and micronutrient status before, during, and after pregnancy. This will enable the institution of the appropriate measures to ameliorate maternal micronutrient deficiency, avoid micronutrient overdose, and achieve optimal fetomaternal outcome.

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