Influence of Maternal Trace Elements Status of Zinc, Copper and Iron on Some Neonatal Parameters

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Abstract

Background: *Birth weight is important to infant survival and later health as Low birth weight is still a major health problem in developing countries like Nigeria.*

Aim: This study aimed to determine the relationship between maternal serum zinc, copper and iron concentrations and neonatal parameters (birth weight, length and head circumference).

Methods: *A Case-Control study was conducted on women who delivered low birth weight infants (cases) and normal birth weight infants (controls). One hundred women volunteered to be part of this research which was conducted from the 1st June to 12th July, 2016.*

Results: *50 cases of infants with low birth weight [2.01 (1.5) Kg] and their mothers were the case group while 50 infants with normal birth weight [3.12 (2.3) Kg] and mothers were controls. Maternal serum zinc [9.1 (1.8) µmol/L vs 12.4 (3.3) µmol/L], copper [14.3 (2.2) µmol/L vs 17.9 (3.7) µmol/L] and iron [21.3 (1.7) µmol/L vs 27.8 (3.2) µmol/L], concentrations were significantly lower in case group than in control group, $p < 0.05$. There were significant direct correlations between neonatal parameters (birth weight, length and head circumference) and maternal serum zinc levels however, no correlation was observed in copper and iron concentrations.*

Conclusion: *These findings suggest that maternal zinc status affects birth weight and prematurity.*

Keywords: Low birth weight, Zinc, Copper, Iron, Maternal, Trace elements, neonates

Introduction

Pregnancy is a period of increased metabolic demand with changes in maternal physiology and requirement by the growing fetus[1]. It is associated with increased demand of all nutrients-macronutrients and micronutrients. Interactions of micronutrients are particularly important during pregnancy when the developing fetus is very vulnerable to inappropriate micronutrient levels[2]. Deficiency of these nutrients could adversely affect pregnancy, delivery and outcome of pregnancy[3], resulting in stillbirth, low birth weight babies, preterm delivery, intrauterine growth retardation, congenital malformation, reduced immunocompetence and abnormal organ development[4].

Birth weight defined as the first weight of an infant obtained within the first hours after birth is important to infant survival and later health of a child. It is one of the best markers of a favourable pregnancy outcome and determinant of prognosis of neonatal morbidity. Babies with birth weight of less than 2500 grams are considered as Low birth weight (LBW) regardless of gestation age[5]. Maternal micronutrient deficiency is one major contributing factor for the high incidence of LBW infants in developing countries[6].

Zinc (Zn) is an essential trace mineral important for normal metabolic and physiological processes. Pregnant women are prone to Zn deficiency due to the fetus need of Zn for its growth[7]. Severe maternal Zn deficiencies during pregnancy has been associated with poor fetal growth, congenital malformation and spontaneous abortions[8]. Even moderate forms of Zn deficiency can result in LBW infants and preterm delivery[8]. It is further possible that maternal Zn status during pregnancy influence infant growth and morbidity beyond the neonatal period through its effect on the development of the immune system[9].

During pregnancy, the needs of the growing fetus and placenta as well as the increasing maternal blood volume and red cell mass, impose such a demand on maternal iron (Fe) stores that iron supplementation at daily doses between 18 mg and 100 mg from 16 weeks gestation does not completely prevent the depletion of maternal iron stores at term[10]. In humans, iron deficiency anemia during pregnancy is common and is associated with adverse birth outcomes such as low-birth weight[10].

Copper (Cu) is important for haemopoiesis and it is essential for normal growth and development of human fetuses, infants, and children[11]. The human fetus accumulates copper rapidly from its mother during the third trimester of pregnancy, apparently to ensure that it will have adequate supplies to carry out metabolic functions after birth such as cellular respiration, connective tissue synthesis, iron metabolism, free radical defense, gene expression and proper functioning of the heart and immune system[11]. Studies have shown that maternal deficiency of Cu during pregnancy can result in the delivery of low-birth weight babies[12].

Materials and Methods

The study area of this research was in Sagbama, which is one Local Government Area of Bayelsa West Senatorial District. It is made up of 38 communities and has a population of about two hundred and forty nine thousand seven hundred (249,700). There is one general hospital, several primary health care centers and private hospitals evenly distributed within the communities.

A total of 100 eligible subjects volunteered for this study from the Antenatal Clinic of the Department of Obstetrics and Gynecology, General Hospital mile 2, Sagbama, Bayelsa State, Nigeria, after informed consents were obtained.

A case-control analytical study was adopted to determine the influence certain trace elements on birth weight. The study was carried out within a six week period; 1st June to 12th July. The subjects had their routine multivitamins as prescribed by the doctors and were followed-up until after delivery, healthy Low birth weight (LBW) infants (birth weight less than 2500 grams) and their mothers were recruited as Cases while normal weight newborns (birth weight of 2500 grams or greater) and their mothers were included as Controls. Infants of mothers with HIV/AIDS, diabetes mellitus, pre-eclampsia and those who did not give consent were excluded from the study. Hundred newborn-mother pair were enrolled in the study as per our inclusion criteria. Out of the 100 cases, 50 mothers and their infants with birth weight < 2.5 Kg were enrolled in the Case group and 50 mothers and their infants with birth weight ≥ 2.5 Kg were the Control group.

Demographic characteristics of the subjects were obtained from the administration of a semi-structured questionnaire and anthropometric measurements-weight and height were measured while Body Mass Index (BMI) was calculated. Neonatal parameters (birth weight, head circumference and length) of babies were measured. Head circumference in centimeters (cm) was

measured at the level of occipital protuberance and frontal bone. The body weight of each subject was measured with a standard scale to an accuracy of 0.1 grams.
Maternal venous and cord blood samples were collected and serum extracted for the measurement of Zn, Fe and Cu by atomic absorption spectrophotometry[13] while total protein and albumin were determined by Biuret method[14] using reagent kit by DIALAB Laboratory, United Kingdom and bromocresol green (BCG) method[15] using reagent kit produced by Span Diagnostics Limited respectively.
Data were analyzed statistically using SPSS version 15 to determine relationships and associations. Student t-test was used to find out significant differences between the means and Pearson's co-efficient was used to find out associations between quantitative variables. Data are expressed as the Mean (SD), and $p < 0.05$ was considered statistically significant.

Results
Demographic profile of babies and their mothers are shown in Table 1. The age range of the subjects was from 18 years to 45 years, with mean age of 31 ± 3.1 years at 38 to 42 weeks' gestation. The mean birth weight of low birth weight babies was 2.01 ± 1.5 Kg while that of normal birth weight babies was 3.12 ± 2.3 Kg.
Maternal serum Zn concentration (µmol/L) differed between Cases and Controls; 9.1 (1.8) µmol/L vs. 12.4 (3.3) µmol/L respectively. Similarly, maternal serum Cu and Fe concentrations were also found to be significantly lower in the case groups compared to the control group as shown in Table 2. Mean cord Zn [11.3 (1.5) µmol/L vs. 16.8 (2.0) µmol/L] and Cu [8.7 (2.4) µmol/L vs. 11.3 (3.8) µmol/L] concentrations in the Case group were comparatively lower than in the Control group.
In Table 3, there were significant direct correlations between maternal Zn concentration and birth weight (r = 0.735, $p < 0.001$), head circumference (r = 0.635, $p < 0.002$) and length (r = 0.635, $p < 0.002$) in the case group. Similarly, cord Zn concentrations were also positively correlated with birth weight (r = 0.689, $p < 0.002$), head circumference (r = 0.587, $p < 0.003$) and length (r =0.715, $p < 0.000$). However, no correlation was found between maternal Cu and Fe concentrations and neonatal parameters.

Discussion
Pregnant women are susceptible to deficiency of trace elements such as Zn, Cu and Fe due to the requirements of the growing fetus and placenta, expanded blood volume, increased demands and poor intake or bio-absorption[6]. This study demonstrated that there were significant differences between serum concentrations of trace elements Zn, Cu and Fe of mothers who delivered LBW infants and mothers who had normal weight babies.
Zinc deficiency during pregnancy has been associated with a number of feto-maternal complications such as low birth weight, spontaneous abortion, congenital malformations and premature delivery[8]. In this study, those mothers who delivered babies with low birth weight were observed to have lower serum Zn levels and lower cord serum Zn levels were found in the newborns with low birth weight. This results is in agreement with previous studies which demonstrated that serum Zn levels of women with low birth weight neonates were significantly lower than those with normal birth weight babies[16-18]. Furthermore, babies from women with lower levels of essential trace elements were found to have significantly lower neonatal parameters (head circumference and length). We found a positive correlation between maternal Zn levels and neonatal parameters (birth weight, head circumference and length) which corroborate many reports[19-20] and those neonates with low birth weight had lower Zn levels indicating that Zn status influences birth weight.
In this study, there was no significant difference between maternal serum levels of Cu in the case and control groups. However, infants with low birth weight had lower serum cord concentrations

compared with those babies with normal birth weight, indicating the role of copper in fetal growth. There was no correlation between maternal serum levels of Cu and neonatal birth weight which is in agreement with our previous studies[17].
Results from this studies also showed that those mothers who delivered low birth weight babies had slightly lower serum Fe levels compared with those with normal birth weight babies, however there was no positive or negative correlation between maternal serum levels of Fe and neonatal birth weight which is contrary to the findings of Milman *et al.*

Conclusion: In this study, maternal serum essential trace elements (Zn, Cu, and Fe) concentrations were found to play significant roles in fetal growth and development. There was no correlation between maternal serum levels of Cu and Fe on neonatal birth weight. Maternal serum levels of Zn were found to have a strong relationship with neonatal birth weight as deficiency of Zn led to the delivery of babies with lower birth weight. Therefore, it is recommended that supplements of essential trace micronutrients be given to women during pregnancy especially in women from rural communities.
Maternal serum trace element status has been reported to influence neonatal birth weight, this study further confirms the relevance of maternal Zn concentration in the determination of neonatal parameters.

References

1. Black, R.E. Micronutrient in pregnancy. *British. Journal of Nutrition*. 2001;**85**(2):S193-197.
2. Gambling, L., Danzeisen, R., Fosset, C., Andersen, H.S., Dunford, S., Srai, S.K., *et al.*, Iron and Copper Interaction in Development and the Effect on Pregnancy Outcome. *Journal of Nutrition*. 2003;**133**(5):1554-1556.
3. Naeye, R., Blanc, W., Paul, C. Effects of maternal nutrition on human fetus. *Pediatrics.* 1973;**52**:494-503.
4. Aggat. Current status of Zinc in health and disease states. *Arch. Dis. Chil.*, 1994;**54**:909-917.
5. Bhargava, M., Iyer, PU, Kumar R., Ramji, S., Kapani, V., Bhargava, S.K. Relationship of maternal serum ferritin with foetal serum ferritin, birth weight and gestation. *Journal of Tropical Pediatrics* 1991;**37**:149-52.
6. Prentice AM. Variation in maternal dietary intake, birth weight and breast milk output in the Gambia. In: Aebi H, Whitehead RG, editors. Maternal Nutrition during Pregnancy and Lactation. 1991. p. 167-83.
7. Shah D, Sachdev HP. Effect of gestational zinc deficiency on pregnancy outcomes: summary of observation studies and zinc supplementation trials. *British Journal of Nutrition*. 2001;**85**:S101–108. doi: 10.1079/BJN2000301.
8. Aydemir, F., Cavdar, A. O., Soylemez, F., Cengiz, B. Plasma zinc levels during pregnancy and its relationship to maternal and neonatal characteristics: a longitudinal study. *Biological Trace Element Research*. 2003;**91**:193–202.
9. Shankar, A.H., Prasad, A.S. Zinc and immune function: the biological basis of altered resistance to infection. *American. Journal of Nutrition*. 1998; **68**:447S-463S.
10. Milman N, Ibsen KK, Christensen JM. Serum ferritin and iron status in mothers and newborn infants. *Acta Obstetrica Gynecologica Scandinavica*.1987;**66**:205–11
11. Krachler, M., Rossipal, E., Micetic-Turk, D. Trace element transfer from mother to the newborn: investigations of triplets of colostrum, maternal and umbilical cord. *European Journal of Clinical Nutrition*. 1999;**53**:486-494.
12. Kantola, M., Purken, R., Kroger, P. Accumulation of cadmium, Zinc and Copper in maternal blood and the development of the placenta tissue: differences between Finland, Estonia and St. Peterburg. *Environmental Research*. 2000;**83**:54-66.

13. Fernandez, F.J., Kahn, L. Graphite atomic absorption spectrophotometry for metals. Atomic Absorption, *News letter* 1971;**10**:65.
14. Henry, R.J., Cannon, D.C., Winkelman, J.W. Clinical Chemistry: Principles and Techniques, 2nd ed. New York: Harper and Row Publishers; 1974.
15. Doumas, B.T., Watson, W.A., Biggs, H.G. Albumin standards and the measurement of serum albumin with bromcresol green. *Clinical Chimica Acta* 1971;**31**:87-96.
16. Elizabeth, K. E., Krishnan,V., Vijayakumar, T. Umbilical cord blood nutrients in low birth weight babies in relation to birth weight & gestational age. *Indian Journal of Medical Research*. 2008;**128**:128–33.
17. Ikeh-Tawari, E.P., Anetor, J.I., Charles-Davies, M.A. Cadmium level in pregnancy, influence on neonatal birth weight and possible amelioration by some essential trace elements. *Toxicology International* 2013;**20**:108-12.
18. Ashraf, M., Ahmad, Z., Khan, M.N., Khawaja, T.F., Khan, M.A., Salam, A. Relationship of maternal serum zinc levels to the birth weight of the infants. *Professional Medical Journal*. 2005;**12**:336–39
19. Castillo-Duran, C., Marin, V.B., Alcazar, L.S., Iturralde, H ., Ruz, M. Controlled trial of zinc supplementation in Chilean pregnant adolescents. *Nutrition Research*. 2001;**21**:715–24.
20. Naher, K., Nahar, K., Aziz, M.A., Hossain, A., Rahman, R., Yasmin, N. Maternal serum zinc level and its relation with neonatal birth weight. *Mymensingh Medical Journal*. 2012; **21**:588–93.

Table I
General and Clinical characteristics of Participants and their infants

Parameter	Cases (n =50)	Control (n = 50)	t-value	p-value
Age (years)	29.3 (1.1)	30.1 (2.2)	0.49	0.78
Parity	2.1 (1.6)	2.2 (1.5)	0.28	0.37
Height (m)	1.6 (4.7)	1.5 (4.9)	0.43	0.74
Weight (Kg)	60.1 (2.3)	68.7 (1.5)	0.99	0.00*
BMI(Kg/m^2)	23.5 (2.6)	30.7 (2.1)	1.99	0.02*
Total Protein(g/L)	60.9 (1.0)	65.0 (1.2)	0.98	0.01*
Albumin(g/L)	32.0 (1.8)	36.0 (2.7)	0.90	0.02*
Neonatal Birthweight (kg)	2.01 (1.5)	3.13 (2.3)	7.95	0.00*
Head circumference(cm)	30.6 (3.8)	35.3 (2.2)	4.68	0.00*
Neonatal Length (cm)	45.1 (2.6)	52.6 (3.4)	5.22	0.00*

*= significant at $p < 0.05$, BMI= Body mass index, Kg = Kilogram, m = meters, cm = centimeter, n = number

Table II
Trace Element Status of Participants and their infants

Parameter	Cases (n =50)	Control (n = 50)	p-value
Maternal Zn (µmol/L)	9.1 (1.8)	12.4 (3.3)	0.00*
Maternal Cu (µmol/L)	14.3 (2.2)	17.9 (3.7)	0.00*
Maternal Fe (µmol/L)	21.3 (1.7)	27.8 (3.2)	0.00*
Neonatal Zn (µmol/L)	11.3 (1.5)	16.8 (2.0)	0.00*
Neonatal Cu (µmol/L)	8.7 (2.4)	11.3 (3.8)	0.00*
Neonatal Fe (µmol/L)	17.2 (2.1)	21.4 (4.2)	0.00*

*= significant at $p < 0.05$, Zn = Zinc, Cu = Copper, Fe = Iron, n = number

Table III
Correlation of Trace Element Status and Neonatal Parameters in Case Group

Parameter	**Neonatal birthweight (Kg) (r, *p* value) (n =50)**	**Head Circumference (cm) (r, *p* value) (n =50)**	**Length (cm) (r, *p* value) (n =50)**
Maternal Zn (µmol/L)	0.74, 0.00*	0.63, 0.00*	0.76, 0.00*
Maternal Cu (µmol/L)	0.02, 0.54	0.05, 0.61	0.01, 0.44
Maternal Fe (µmol/L)	-0.29, 0.08	-0.31, 0.08	-0.37, 0.06
Neonatal Zn (µmol/L)	0.68, 0.00*	0.58, 0.00*	0.71, 0.00*
Neonatal Cu (µmol/L)	0.06, 0.77	0.08, 0.85	0.08, 0.78
Neonatal Fe (µmol/L)	-0.37, 0.90	-0.41, 0.90	-0.43, 0.80

*=significant at p<0.05, Zn = Zinc, Cu = Copper, Fe = Iron, n = number