

RELATIONSHIP BETWEEN MATERNAL SERUM ZINC, CORD BLOOD ZINC AND BIRTH WEIGHT OF TERM NEWBORN INFANTS IN JOS, PLATEAU STATE, NIGERIA

Ofakunrin AOD,¹ John Collins,¹ Diala UM,¹ Afolaranmi TO,² Okolo SN.¹

¹Department of Paediatrics, University of Jos / Jos University Teaching Hospital, Jos.

²Department of Community Medicine, University of Jos/Jos University Teaching Hospital, Jos.

Corresponding Author:

Dr Ofakunrin AOD

Department of Paediatrics, University of Jos / Jos University Teaching Hospital, Jos

E-mail: aodofak@yahoo.com

Phone: +2348038345783

Abstract

Background: Adequate in utero supply of zinc is essential for optimal fetal growth because of the role of zinc in cellular division, growth and differentiation. Low maternal serum zinc has been reported to be associated with low birth weight and the later is associated with increased morbidity and mortality in newborns.

In Nigeria, where the prevalence rates of zinc deficiency among pregnant women, low birth weight and infant mortality are high; it will be useful to determine the relationship between maternal and cord serum zinc levels and birth weight.

Methods: A cross-sectional study of 190 mothers and their term babies. Blood samples were collected from the mothers and cord of the babies immediately after delivery for serum zinc analysis using atomic absorption spectrophotometry. Babies' weights were measured within thirty minutes post-delivery.

Results: The mean age of the mothers and gestational age of the babies were 28.29 ± 5.64 years and 39.2 ± 1.2 weeks respectively. The mean birth weight of the babies was 3106.7 ± 411.2 g; while the mean maternal and cord serum zinc concentrations were 48.5 ± 17.6 $\mu\text{g/dl}$ and 99.3 ± 21.5 $\mu\text{g/dl}$ respectively.

There was no association between the maternal serum zinc and cord serum zinc ($p = 0.62$); and likewise maternal serum zinc and birth weight ($p = 0.99$). However, there was a significant positive association between cord serum zinc and birth weight ($p < 0.001$, $r = 0.02$, $p = 0.04$).

Conclusion: The study outcome suggests that cord serum zinc but not maternal serum zinc predicts birth weight. In spite of low maternal serum zinc level, an adequate amount of zinc could be transferred to the babies thereby preventing zinc deficiency in the babies and aiding their growth. More studies are needed on the mechanism of placental zinc transfer.

Keywords: Maternal zinc, cord zinc, birth weight, Jos, Nigeria

INTRODUCTION

Zinc is one of the essential trace elements whose importance to human health is increasingly being recognized.¹ It is crucial for the activity of metalloenzymes involved in the synthesis of ribonucleic acid (RNA polymerase), deoxyribonucleic acid (DNA polymerase) and protein (thymidine kinase).² It therefore plays significant roles in the transcription process, gene expression and ultimately cellular division, growth, and differentiation.^{2,3} It is also involved in the expression of insulin-like growth factor 1 (IGF-1) which is a key regulator of embryonic growth and development.⁴ Impairment of these processes may retard fetal growth. Therefore, in order to ensure optimal fetal growth and development, an adequate supply of zinc from the mother to the fetus is essential.

Zinc deficiency is prevalent among pregnant women from the developing countries including Nigeria as a result of suboptimal dietary intake and a high fetal requirement for zinc.⁵⁻⁶ Maternal zinc deficiency in pregnancy has been reported to be associated with poor fetal growth and low birth weight (LBW).⁷ Low birth weight is estimated to account for about a third of all deaths in the first year of life in developing countries.⁸ The prevalence of LBW in Nigeria is about 14%⁹ and has undoubtedly contributed to the high infant mortality rate⁹ in the country.

In Nigeria, where the prevalence rates of zinc deficiency among pregnant women,⁵ low birth weight,⁹ and infant mortality are high,⁹ it will be useful to determine the relationship between maternal and cord zinc levels and birth weight. The findings of the work will add to the existing pool of knowledge on the association between zinc and birth weight. It could serve as the platform for conducting further research on the effect of zinc supplementation in pregnancy on birth weight which presently remains an unresolved issue.¹⁰

METHODS

A cross-sectional study carried out at the Jos University Teaching Hospital (JUTH), Plateau State, Nigeria from November 2013 to January 2014. The study population consisted of 190 mothers with uncomplicated pregnancy and their apparently healthy singleton term babies at the antenatal clinic and labour ward of the Jos University Teaching Hospital.

Personal data, medical and social information were obtained from the mothers using a predesigned

proforma.

Blood sample was collected from the mothers and cords of the babies immediately after delivery for serum zinc determination using Atomic Absorption Spectro-photometer (Perkin Elmer Analyst 400). Physical examination of the babies was done and maternal and baby's anthropometries were measured within thirty minutes post-delivery.

Definition of terms:

Birth weight of less than 2500g was classified as low birth weight, greater than or equal to 2500g but less than 4000g as normal birth weight and greater than or equal to 4000g as high birth weight (macrosomia). Maternal serum zinc was categorized as low if the level was less than 50µg/dl and normal or adequate if the level was above 50µg/dl.¹¹ Similarly, cord serum zinc was classified as low if the level was less than 65µg/dl and normal or adequate if the level was above 65µg/dl.¹²

Approval to conduct the study was obtained from the Ethics Committee of the Jos University Teaching Hospital and written informed consent was obtained from the mothers.

Data obtained was entered and analyzed using Epi info statistical software version 3.5.3. A 95% confidence interval was used and a p-value of less than or equal to 0.05 ($p = 0.05$) was considered statistically.

Results:

Socio-demographic characteristics of the mothers

One hundred and ninety mothers and their babies were recruited into the study. The mean age of the mothers was 28.29 ± 5.64 years (range 17- 43 years). Seventy four (39%) of the mothers were primiparous, while 16 (8.5%) were grand multiparous. The socioeconomic status of the women derived from their educational status and the occupational status of their husbands showed that more than half (56.3%) of the women were from middle socioeconomic class (Table 1).

Table 1: Socio-demographic characteristics of the mothers

Characteristics	Frequency	Percentage
Age group (years)		
15-19	9	4.7
20-24	39	20.6
25-29	66	34.7
30-34	49	25.8
35-39	19	10.0
40-44	8	4.2
Total	190	100.0
Mean age	28.29 ± 5.64 years	
Parity		
1	74	38.9
2	48	25.3
3	31	16.3
4	21	11.0
>4	16	8.5
Total	190	100.0
Tribe		
Indigenous Plateau tribe	124	65.2
Hausa	21	11.1
Igbo	13	6.8
Yoruba	10	5.3
Others	22	11.6
Total	190	100.0
Socioeconomic status		
Lower	43	22.6
Middle	107	56.3
Upper	40	21.1
Total	190	100.0

Characteristics and birth weight of the babies

A total number of 190 babies comprising 91(47.9%) males and 99(52.1%) females were recruited into the study with a male to female ratio of 1.0: 1.1. The mean gestational age was 39.2 ± 1.2 weeks (range 37 – 42 completed weeks). The mean birth weight of

the babies was 3106.7 ± 411.2g (range 1900-4100g). One hundred and seventy-four (92.6%) of the babies had normal birth weight (2500g - <4000g), 12(6.3%) had low birth weight (<2,500g) and four (2.1%) were macrosomic (=4000g). Table 2

Table 2: Characteristics and birth weight of babies

Variable	n	Percentage
Gender		
Male	91	47.9
Female	99	52.1
Total	190	100.0
Gestational age (weeks)		
37	14	7.4
38	42	22.1
39	54	28.4
40	54	28.4
41	18	9.5
42	8	4.2
Total	190	100.0
Classification of birth weight		
Low (<2500g)	12	6.3
Normal (>2500g -< 4000g)	174	92.6
High (4000g)	4	2.1
Total	190	100.0

Association between maternal and cord serum zinc

The mean maternal serum zinc concentration was $48.5 \pm 17.6\mu\text{g/dl}$ (range 12- 101 $\mu\text{g/dl}$). The prevalence of maternal serum zinc deficiency was 52.1% .). The mean cord serum zinc concentration was $99.3 \pm 21.5\mu\text{g/dl}$ (range 45- 158 $\mu\text{g/dl}$). The majority (96.8%) of the babies had normal cord serum zinc (>65 $\mu\text{g/dl}$).

Among the 99 mothers with low serum zinc level,

96 (97%) of their babies had normal cord serum zinc. Of the 91 mothers with normal serum zinc, three (3.3%) of their babies had low cord serum zinc. There was, therefore, no statistically significant association between the maternal and cord serum zinc ($p = 0.62$). Table 3.

Table 3: Association between maternal and cord serum zinc

	Classification of cord zinc level			2	df	p -
	Low	Normal	Total			
Maternal serum						
Zinc level value	Freq (%)	Freq (%)	Total			
Low	3(3.0)	96 (97.0)	99 (100.0)	-	-	0.62*
Normal	3(3.3)	88 (96.7)	91 (100.0)			
Total	6	184	190			

Association between cord serum zinc and birth weight

Three (50%) of the babies with low cord serum zinc level had low birth weight, while nine (4.9%) of the babies with normal cord serum zinc had low birth weight and none of the macrosomic babies had low

cord serum zinc. Low cord serum zinc was significantly associated with low birth weight ($p < 0.001$). Table 4.

Table 4: Association between cord serum zinc and birth weight

	Classification of birth weight			Total	2	df	P - value
	Low	Normal	High				
Cord serum Zinc level	Freq (%)	Freq (%)	Freq (%)				
Low	3(50.0)	3 (50.0)	0(0)	6 (100.0)	-	-	< 0.001*#
Normal	9(4.9)	171 (92.9)	4(2.2)	184 (100.0)			
Total	12	174	4	190			

*= Fisher's exact, #=statistically significant. Freq. = Frequency

Association between maternal serum zinc and birth weight

Out of the 99 mothers with low serum zinc, only six (6.1%) of them had babies with low birth weight; whereas, of the 91 mothers with normal serum zinc,

six (6.6%) of them also had babies with low birth weight. Therefore, the association between the maternal serum zinc and birth weight in this study was not statistically significant ($p = 0.99$, corrected chi-square = 0.03). See Table 5.

Table 5: Association between maternal serum zinc and birth weight.

Maternal serum Zinc level	Classification of birth weight			Total	2	df	P - value
	Low	Normal	High				
Low	6(6.1)	91 (91.9)	2(2.0)	99 (100.0)	0.03*	2	0.99
Normal	6(6.6)	83 (91.2)	2(2.2)	91 (100.0)			
Total	12	174	4	190			

*= corrected chi square, Freq = frequency

DISCUSSION

The mean maternal serum zinc level in this study is lower than the cut-off point (50µg/dl) for determining zinc deficiency in pregnant women at the third trimester by the International Zinc Nutrition Consultative Group (IZiNCG).^{11,13} The reason for the low mean maternal serum zinc could have been due to inadequate dietary intake of zinc by the women, though this was not assessed. The staple foods in Plateau state comprise primarily of cereals and tubers which are known to have low zinc content¹³ and contain a substantial amount of phytate, a compound known to inhibit zinc absorption and thereby causing zinc deficiency.^{13,14} Therefore, intake of the low zinc and high phytate-containing foods could have contributed to the low serum zinc level.

Furthermore, this inadequate dietary intake of zinc could have predisposed the women to have low pre-pregnancy serum zinc concentration (not determined in this study) which could have declined further during pregnancy as a result of plasma volume expansion (haemodilution) that is associated with pregnancy.¹⁵

The low mean maternal serum zinc is similar to those obtained by Okonofua et al¹⁶ in Ile-Ife and Iqbal et al¹⁷ in Bangladesh but lower than the values reported in studies in India¹⁸ and the United States.¹¹ The similarity in the mean maternal serum zinc obtained in this study with the studies in Ife and Bangladesh could be a reflection of the similarity among the study populations, all being from the developing countries where dietary intake of absorbable zinc has been documented to be low.^{19,20}

On the other hand, the higher mean maternal serum zinc concentration in the United States' study than this study may be a reflection of the high intake of absorbable zinc that has been reported among pregnant women in the developed countries.²¹

The mean cord serum zinc of the babies in this study is 99.3 ± 21.5µg/dl and it is of interest to note that despite the low mean serum zinc concentration of the mothers; the majority (96.8%) of the babies had normal cord serum zinc concentration (>65µg/dl).

The probable reason for the normal cord serum zinc of the babies could have been due to the maternal adaptive mechanisms in the use of zinc during pregnancy. The mechanisms involve increased intestinal absorption of zinc and a preferential active transfer of zinc across the placenta to the fetus.^{22,23} In addition, the babies could have been able to explore the "host-parasite relationship" that has been reported²⁴ to exist between mothers and their babies during pregnancy to extract sufficient quantities of zinc from the mothers.

The reason for the low cord serum zinc concentration among the remaining 3.2% of the babies is not clear but needs further evaluation.

The mean cord serum zinc concentration is in the same range with the studies done in Ile-Ife¹⁶, France²⁵ and Jordan²⁶ but higher than the value reported in Ibadan.²⁷ The similarity in the mean cord serum concentration with the studies in Ile-Ife, France, and Jordan could be due to the fact that all the studies were conducted among only term babies while the study in Ibadan recruited both term and preterm babies. Term babies have been reported to have

higher cord serum zinc concentration than preterm babies because of a longer period of zinc accretion in the term babies than the preterm babies.^{18, 28} Therefore, pooling the mean cord serum zinc concentration for term and preterm babies as was done in the study in Ibadan may have contributed to the mean serum zinc concentration value obtained. The higher level of cord serum zinc in this study than in the study conducted in Ibadan could also be a reflection of the socioeconomic status of the women as most of the women in this study belonged to middle socioeconomic class as against the majority of women in the study conducted in Ibadan belonging to the low socioeconomic class. Intake of food rich in zinc could be influenced by the socioeconomic status of the women.

As in other studies,^{23, 26, 29} the cord serum zinc concentration was higher than the maternal serum zinc concentration. This may be a reflection of active transfer of zinc from mothers to the fetuses which has been previously documented.²² However, the present study did not find any association between maternal serum zinc and cord serum zinc as mothers with low cord serum zinc also had babies with normal cord serum zinc. This observation may indicate that in spite of low mothers' serum zinc level, an adequate amount of zinc could be transferred to the babies thereby helping them to meet their zinc requirement since about 96.8% of the babies in this study had normal serum zinc concentration. The finding of no association between the maternal serum zinc and cord serum zinc is in tandem with the reports of some previous studies^{16,29} but it is in contrast to the findings of some other investigators^{18, 30} who found a positive association between maternal serum zinc and cord serum zinc concentrations.

This study has demonstrated a significant positive association between cord serum zinc concentration and birth weight. The positive association between cord serum zinc concentration and birth weight could be due to the adequate cord serum zinc concentration in the babies which may have been utilized for their growth. Zinc plays critical roles in cell division, differentiation, and function that are essential for tissue growth.²⁻⁴ The positive association between cord serum zinc concentration and birth weight found in this study is in agreement with the results of some previous studies,^{18,25-26,30}

The association between cord serum zinc and birth weight might be considered as a good indicator for the adequacy of zinc for fetal growth and development. Consequently, ensuring that adequate

concentration of zinc is transferred from pregnant mothers to their babies for optimal growth and development may be of utmost importance and this calls for further research to fully understand the mechanism of fetal accretion of zinc in pregnancy.

The study also did not show any significant relationship between maternal serum zinc and birth weight. As mentioned earlier, the babies in the study were thought to be able to extract an adequate quantity of zinc from the mothers for their growth despite the low zinc status of the mothers. This could have resulted in the present finding of no association between maternal zinc and birth weight. Perhaps, if the mothers were severely zinc deficient, the babies may not have been able to extract an adequate quantity of zinc to promote their growth which may translate into low serum zinc in the mothers causing low birth weight in the babies. Some previous studies^{16, 26, 29} have also reported no relationship between maternal serum zinc and birth weight; whereas, some other studies^{18, 30} found a positive relationship between maternal serum zinc and birth weight. The reason for the differences in the outcome of the above studies may be due to the influence of other determinants of birth weight apart from zinc. Birth weight is determined by both genetic and environmental factors.³¹ Therefore variation in these factors among the different studies could explain the differences found.

The finding in this study indicates that maternal serum zinc level (unlike cord serum zinc level) may not be a useful indicator for the assessment of fetal growth.

Conclusion

The outcome of the study suggests that in spite of low maternal serum zinc level, an adequate amount of zinc could be transferred to the babies thereby preventing zinc deficiency in the babies and aiding their growth. More studies are needed on the mechanism of placental zinc transfer.

Conflict of Interest: None

REFERENCES

1. Hambidge M. Human zinc deficiency. *J Nutr.* 2000; 130:1344s–1349s.
2. Mc Call KA, Huang C, Fierke CA. Function and mechanism of zinc metalloenzymes. *J Nutr.* 2000; 130:1437 – 1446.
3. Berg JM, Shi Y. The galvanization of biology: a growing appreciation of the role of zinc. *Science.* 1996; 271:1081-1085.
4. Fowden AL. The insulin-like growth factors and feto-placental growth. *Placenta* 2003; 24:803–812.
5. Ugwuja E, Akubugwo E, Ibiam U, Obodoa O, Ugwu N. Plasma Copper and Zinc among Pregnant Women in Abakaliki, Southeastern Nigeria. *Internet J Nutr Wellness.* 2010; 10:1-3
Mohamed B, Elhassan ME, Naji IA, Elfatih O, Khalid HB, Ishag IA. Anaemia, zinc and copper deficiencies among pregnant women in Central Sudan. *Biol Trace Elem Res.* 2010; 137 (3):255-261.
7. Jameson S. Zinc Status in pregnancy; the effect of zinc therapy on perinatal mortality, prematurity and placental ablation. *Ann NY Acad Sci.* 1993; 678:178-192.
8. Ferro-Luzzi A, Ashworth A, Martorell R, Scrimshaw N. Report of the IDECG working group on effects of IUGR on infants, children and adolescents: immunocompetence, mortality, morbidity, body size, body composition and physical performance. *Eur J Clin Nutr.* 1998; 52: 97-99.
9. National Population Commission (Nigeria) and ICF Macro. Nigeria Demographic and Health Survey 2008. p. 118 - 119. Available from: <http://www.nigeria.unfpa.org/pdf/nigeriadhs2008.pdf>. Last accessed 10/1/2014.
10. Saskia J M, Osendarp SJM, Clive E W, Robert E B. The need for maternal zinc supplementation in developing countries: An unresolved issue. *J Nutr.* 2003; 133:817s-827s.
11. Hotz C, Peerson JM, Brown KH. Suggested lower cutoffs of serum zinc concentrations for assessing zinc status: reanalysis of the second National Health and Nutrition Examination Survey data (1976–1980). *Am J Clin Nutr.* 2003; 78:756-764.
12. Lockitch G, Halstead AC: Reference (normal) values-zinc, In: Meites S, editor. *Paediatric clinical chemistry 3rd editor.* Washington: AACC Press, 1989; p. 297.
13. Brown KH, Rivera JA, Bhutta Z, Gibson RS, King JC, Lönnerdal B et al. International Zinc Nutrition Consultative Group technical document. Assessment of the risk of zinc deficiency in populations and options for its control. *Food Nutr Bull.* 2004; 25: 99–203.
14. Wise A. Phytate and zinc bioavailability. *Int J Food Sci Nutr.* 1997; 51(suppl):17-19.
15. Hambidge KM, Krebs NF, Jacobs MA, Favier A, Guyette L, Ikle DN. Zinc nutritional status during pregnancy: a longitudinal study. *Am J Clin Nutr.* 1983; 37:429–442.
16. Okonofua FE, Isinkaye A, Onwudiegwu U, Amole FA, Emofurieta WA, Ugwu NC. Plasma zinc and copper in pregnant Nigerian women at term and their newborn babies. *Int J Gynaecol Obstet.* 1990; 32:243–245.
17. Iqbal ASM, Shahidullah MD, Nurul I, Sohela A, Shahanara B. Serum zinc and copper levels in the maternal blood and cord blood of neonates. *Indian J Pediatr.* 2001; 68: 523-526.
18. Jeswani RM, Vani SN. A study of serum zinc levels in cord blood of neonates and their mothers. *Indian J Pediatr.* 1991; 58: 683-86.
19. Ferguson EL, Gadowshy SL, Huddle JM, Cullian TR, Lehrfield J, Gibbson RS. An interactive 24hr recall technique for assessing the adequacy of trace mineral intakes of rural Malawian women: its advantages and limitations. *Eur J Clin Nutr.* 1995; 49:565-578.
20. Lehti KK. Iron, folic acid and zinc intakes and status of low socio-economic pregnant and lactating Amazonian women. *Eur J Clin Nutr.* 1989; 43: 447s-463s.
21. Caulifield LE, Zavaleta N, Shankar AH, Merald M. Potential contribution of maternal zinc supplementation during pregnancy to maternal and child survival. *Am J Clin Nutr.* 1998; 68(suppl): 499s-508s.
22. Agett P. Neonatal trace element

- metabolism. In: Cowett R, ed. Principles of perinatal-neonatal metabolism. 2nd editor. New York: Springer Verlag; 1998: 909–942.
23. Zapata CL, Melo MR, Donangelo CM. Maternal, placental and cord zinc components in healthy women with different levels of serum zinc. *Biol Neonate*. 1997; 72: 84–93.
 24. Rossipal E, Krachler M, Li F, Micetic-Turk D. Investigation of the transport of trace elements across barriers in humans: studies of placental and mammary transfer. *Acta Paediatr*. 2000; 89: 1190-1195.
 25. Speich M, Bousquet B, Auget JL, Gelot S, Laborde O. Association between magnesium, calcium, phosphorus, copper, and zinc in umbilical cord plasma and erythrocytes, and the gestational age and growth variables of full-term newborns. *Clin Chem*. 1992; 38:141-143.
 26. Awadallah SM, Abu-Elteen KH, Elkarmi AZ, Qaraein SH, Salem NM, Mubarak MS. Maternal and cord blood serum levels of zinc, copper, and iron in healthy pregnant Jordanian women. *J Trace Elem Exp Med*. 2004; 17:1-8.
 27. Lasisi AO, Kuti MO, Adekunle AO. The association of maternal social factors and antenatal care with cord serum zinc in full – term neonates. *Afr J Biomed Res*. 2008; 11: 297-298.
 28. Zimmerman AN, Hambridge MK. Zinc levels in preterm babies. *Paediatrics* 1982; 69: 176-183.
 29. Bro S, Berendtsen H, Nørgaard J, Høst A, Jørgensen PJ. Serum zinc and copper concentrations in maternal and umbilical cord blood. Relation to course and outcome of pregnancy. *Scand J ClinLab Invest*. 1988; 48:805-811.
 30. Rwebembera AA, Munubhi EK, Manji KP, Mpembeni R, Philip J. Relationship between infant birth weight = 2000 g and maternal zinc levels at Muhimbili National Hospital, Dar Es Salaam, Tanzania. *J Trop Pediatr*. 2006; 52: 118–125.
 31. Johnston LB, Clark AJL, Savage MO. Genetic factors contributing to birth 8 6 : F2–F374