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The relationship between maternal serum zinc level and cord serum zinc

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ABSTRACT

Zinc deficiency in neonates is a common finding in the developing world. The serum zinc level of neonates is affected by the maternal serum zinc level and conditions leading to decreased absorption of ingested zinc as well as increased loss from the body. The purpose of this study was to determine the relationship between maternal serum zinc level and cord serum zinc.Three hundred and thirty mother-neonate pairs who met the inclusion criteria were consecutively recruited; one hundred and eighty (54.5%) of the neonates were males while 150(45.5%) were females. Serum zinc was assayed using Flame Atomic Absorption Spectrophotometer (AAS). The cord serum zinc level of neonates was normal in 51.5% of cases but low in 48.5% of cases.There was a significant positive association between cord blood serum zinc and maternal serum zinc. The conclusion from this study included that the prevalence of hypozincemia was high in neonates delivered at FMC Owerri, maternal serum zinc is a strong factor influencing cord serum zinc. In conclusion result from this study has revealed that maternal serum zinc level is a strong factor influencing neonatal serum zinc level.
Keywords: Maternal, serum, zinc level and cord

INTRODUCTION

Low serum zinc in the mother has been associated with hypozincemia in the neonate. This is because the cord zinc level of the neonate is totally dependent on the amount of zinc transferred from the mother to the foetus [1,2,3,4]. This transfer is maximal in the third trimester of pregnancy. Low serum zinc in the mother has been found to predispose to the delivery of LBW neonates; this fact has been supported by studies like that by [5]. The authors reported that the higher the severity of the zinc deficiency,(severity classified according to serum zinc level measured), the higher the risk of the mothers having LBW neonates [6]. The researchers documented that the overall prevalence of zinc deficiency in neonates was 11.9%; severe zinc deficiency was found in 3.7% (serum zinc ≤60 µg/dl) while mild to moderate zinc deficiency was noted in 8.3% of neonates (serum zinc 60.1-70µg/dl). Studies have also shown that preterm delivery can be caused by low maternal serum zinc in the United Statesof America reported that there was a 14% reduction in incidence of prematurity in zinc- supplemented women and that low maternal serum zinc has also been associated with adverse maternal outcomes [7,8,9,10]. [11,12,13], also reported that mothers with low serum zinc had preterm deliveries. In contrast, [14,15] in Birmingham stipulated that there was no relationship between plasma zinc of the mother and birth weight, head circumference, crown heel length,APGAR at 1 and 5 minutes and gestational age at birth. Supplementation of zinc in preterms has been shown to improve growth and development. In a study by [16,17],an increased weight and length in supplemented preterms as opposed to the control group was reported; they also noted that the increase in weight for age was higher in girls than in boys. [18,19] in Brazil reported the effect of zinc supplementation on the morbidity, immune function and growth of LBW infants. They reported that zinc supplementation was associated with 28% reduction in diarrhoea prevalence and 33% decrease in cough prevalence and these supplemented LBW patients also had positive immune response after injection of purified phytohemagglutinin antigen in the flexor surface of the right forearm done at 8 weeks of age as evidenced by induration measuring ≥5mm afer 20- 30 hours of its injection [20,21,22]. A study by [23,24,25] in America reported that zinc supplementation in small for gestational age infant results in a substantial reduction in infectious diseases and mortality. Another study on zinc supplementation in very low

birth weight infants reported that inadequate zinc intake may lead to poor growth and development outcome in very low birth weight infants as there was improved linear growth velocity and higher motor developmental scores on those that were supplemented. [26,27,28,29,30] reported that zinc supplementation reduced the occurrence of morbidities like necrotizing enterocolitis and reduced mortalities as well, however, daily weight gain surprisingly was similar in both subjects and controls.

The World Health Organization (WHO), International Atomic Energy Association (IAEA), and the United Nations Children's Fund (UNICEF) recommended the use of biochemical, dietary, or functional indicators in assessing zinc status [31]. The biochemical method (serum or plasma) of zinc estimation is the most reliable means of assaying zinc. The biochemical indicators are measured and compared to reference values or an established cut-off for the sample to be assayed. Serum zinc has been found to be the best biomarker of the risk of zinc deficiency; the reason is because it reflects dietary intake, and has reference data for sex and age; and responds consistently to zinc supplementation. Dietary assessment of zinc status involves the use of Estimated Average Requirement (EAR) of zinc in a population. In this case, intakes below the EAR or the probability of zinc intake falling below the EAR is used to assess zinc status. The risk of zinc deficiency using this method is said to be of public health importance when inadequate intake is seen in more than 25% of the population [32,33,34,35]. Functional indicators of zinc status involves use of indicators such as height/lenght for weight and weight for age. However the use of height/ length for age is the best known functional indicator for zinc deficiency because it is responsive to supplemental zinc, has standardized method of measuring the outcome and has a readily-available reference data. Serum zinc in this study was measured using Flame atomic AAS which is a machine that uses the Beer-Lambert principle to determine the concentration of an analyte in a sample [36,37,38,39,40].

MATERIALS AND METHODS

STUDY AREA

The study was carried out at the delivery room and Obstetrics theatre of FMC Owerri. The population of Imo state is about 3.93 million with about 401,873 people living in Owerri. Most of those living in Owerri are civil servants while traders and artisans constitute a small percentage of the population. The inhabitants of Owerri are predominantly of Igbo tribe. Federal Medical Centre Owerri is the foremost tertiary health institution in Imo state. It however provides primary, secondary and tertiary healthcare services in Paediatrics, Obstetrics and Gynaecology, Internal Medicine, and Surgery. It provides healthcare for patients from Imo state and parts of Abia, Anambra and Rivers states. The Paediatrics department is made up of the children's emergency, the children's ward, the children's outpatient department and the special care baby unit.The SCBU cares for sick neonates.It has two sections; the inborn and the out born units. The Obstetrics department conducts an average of 1500 deliveries yearly.The delivery room has 8 beds and is opposite the prenatal ward which has 12 beds while the Obstetrics theatre is situated between SCBU and the delivery room.

STUDY DESIGN

This was a cross-sectional study.

STUDY POPULATION

This consisted ofneonates delivered at FMC Owerri within the study period and their respective mothers.

ETHICAL CONSIDERATION

Ethical approval (Appendix 1) for this proposal was obtained from the research and ethics committee of FMC Owerri.

INCLUSION CRITERIA

1 Neonates delivered at FMC Owerri within the study period.

2 Mothers who gave consent.

EXCLUSION CRITERIA

1 Neonates whose mothers were placed on zinc supplements during pregnancy
2 Neonates with gross congenital anomalies.
3 Neonates whose mothers had preeclampsia and eclampsia in pregnancy.
4 Neonates whose mothers suffered severe heart or lung diseases during pregnancy.

INFORMED CONSENT

A written informed consent was obtained from the mothers once labour was established or as soon as she came in for caesarean section.The informed consent was obtainedafter providing information to parents regarding the study particularly benefits and risks involved in doing this study.

RECRUITMENT OF STUDY SUBJECTS

Mothers who met the inclusion criteria wererecruited as soon as labour was established oras soon as they came for caesarean section and a proforma was administered to her. This included her personal data, parity, socio-economic indices, nutrition while pregnant and medications taken while pregnant.All live neonates delivered in the labour ward and obstetrics theatre of FMC Owerri who met the inclusion criteria wereconsecutively recruited until the desired sample size was achieved. A quick general examination was carried out on the neonate before blood sample was collected from the umbilical cord. A more detailed examination was carried out on the neonate after sample collection. Warmth was provided using the resuscitaire for those that needed warmth.

SAMPLE SIZE ESTIMATION

The sample size for this study was calculated using the formula for calculating sample size when the study population is less than 10,000.

$$nf = \frac{n}{1+\left(\frac{n}{N}\right)}$$

nf=the desired sample size when population is less than 10,000
n=desired sample size when the population is more than 10,000.
N= the estimate of the population size

To calculate n, the formula $n = \frac{z^2 pq}{d^2}$

n=minimum sample size
z= normal standard deviation set at 1.96 which corresponds to the 95% confidence interval.
P= prevalence of zinc deficiency in Nigerian neonates. In this study,a prevalence of 39.6%
q= 1.0-p
d=degree of accuracy desired (considered significant at the 0.05 level).
Therefore n= $(1.96)^2$ (0.39) (0.61)/$(0.05)^2$
= 0.9139/0.0025
= 366

$$nf = \frac{366}{1+\left(\frac{366}{1500)}\right)}$$

$$= \frac{366}{1.244}$$

=294
Giving room for 10% attrition=29
Calculated sample size= 294+29= 323 neonates.

The respective mothers (323) of these neonates were also recruited and their serum zinc also assayed.

SAMPLING METHOD

The neonates and their mothers were recruited consecutively until the desired sample size was attained.

STUDY PROCEDURE

The mother was counselled on the procedure and a written informed consent obtained from her. The study proforma was used to record the mother's biodata, parity, origin, address, phone contact. Other information recorded in the proforma includedmaternal intake of zinc-rich foods during pregnancy,number of antenatal visits and gestational age at delivery. Her height and weight were also measured and her HIV status wasalso recorded. Then 3millilitres of venous blood was collected from a prominent vein on the mother's upper limb after cleaning the area with a combination of 2% chlorhexidine and isopropyl alcohol. The sample was put in a pre-labelled sterile anticoagulant free bottle that had been immersed in 10% nitric acid and rinsed in deionized water to make it free from trace elements. Samples were transported in vaccine-rush containers with ice- gel packs (to prevent hemolysis of red cells) to the hematology department of FMC Owerri where samples were centrifuged for 10 minutes by the laboratory scientist and researcher. After centrifugation, the serum was separated from the cells with a bulb pipette and stored in a Thermocool® freezer at a temperature of -20◦c until enough samples were pooled for analysis. Upon delivery of the neonate and before delivery of the placenta, the cord wasdouble –clamped and the severed end (also known as the placental end) of the cord was cleaned with a sterile gauze to reduce contamination by wharton's jelly and maternal blood and was placed into the barrel of a 20 millilitres syringe and the clamp wasreleased to allow the flow of cord blood from the cord to the barrel of the syringe and the blood (3 millilitres) was subsequently transferred to the specimen bottle from the syringe. This was done after ensuring that the neonate did not have any gross congenital anomaly. The sample wasalso put into atrace- element decontaminated container, taken to the hematology laboratory for centrifugation and separation of serum from the blood cells, stored in Thermocool® freezer at -20°c same way with the mother's sample. Meanwhile the neonate was dried, provided with warmth on the resuscitaire (for those that needed it) and within this period, the neonate was examined mainly for the weight, length, occipitofrontal circumference; presence or absence of skin changes, palor and jaundice. The New Ballard scoring for preterm neonates was also done and the neonates were classified using the relationship between birth weight and gestational age on a standard growth chart (Colorado). All these measurements and examination findings were recorded in the study proforma. These samples (mothers' and neonates') that had been stored at -20°C were transported by road to the research laboratory at Nnamdi Azikiwe University Awka, Anambra Statein vaccine rush containers with ice gel packs. In the research laboratory, the samples were also stored at the same temperature of -20◦c before analysis.The researcher and the laboratory scientist analysed the samples using the Flame AAS machine. The serum was diluted five-fold with deionized water and passed through the Atomic Absorption Spectrophotometer; the diluted solution was compared against standards prepared to approximate viscosity in glycerol. The electrons of the atoms in the atomizer (a component of the AAS) were promoted to higher orbitals by absorbing a defined quantity of energy (radiation) in a process called atomization; the wavelength it travels corresponded to only one element giving the technique its elemental selectivity .The radiation flux with the standard was compared with that of the sample and the ratio between the two also known as the absorbance was converted to the concentration of the analyte(sample). The maternal serum zinc level was low when values below 49.9µg\dl are recorded while the cord serum zinc level was said to be low when values less than 64.7µg\dl are recorded. The cord blood

serum zinc level of the neonate and serum zinc level of the mother were recorded in the proforma. The mothers of the zinc- deficient neonates were contacted to bring their neonates to the neonatology follow-up clinic for treatment;the zinc-deficient mothers were also contacted and referred to the gastroenterology clinic for treatment.

QUALITY CONTROL

Samples were collected from the cord immediately the umbilical cord was severed. These samples were centrifuged at the FMC Owerri laboratory, separated with a bulb pipette and then stored in the Thermocool® freezer at -20 degrees Celsius. This was ensured by keeping a dedicated freezer under lock and key at one end of the SCBU call room which had a constant light supplyto power the incubators. These stored samples were transported to Awka in ice pack using a private vehicle inorder to shorten the time spent on the road thereby avoiding temperature alterations. At the laboratory the samples were also transferred into a freezer for storage before analysis. Before analyzing the samples, standards were prepared and were run at intervals to ensure similar results were obtained.

DATA ANALYSIS

Data wasanalysed using Statistical Package for Social Sciences (SPSS) version 20.0. Descriptive analysis such as mean and standard deviation were calculated for continuous variables like cord serum zinc levels; frequency distribution tables and percentages were used for variables like gender and mode of delivery of neonate whilebar chart was used to demonstrate the relationship between categories ofgestational age, birth weight and cord serum zinc. Chi-Square wasused to determine association between categorical variables like association between cord serum zinc and gender whilePearson's Correlation was used to test for strength and direction of association between cord serum zinc and maternal serum zinc; p-value ≤ 0.05 was regarded significant.

RESULTS AND DISCUSSION

THE RELATIONSHIP BETWEEN MATERNAL SERUM ZINC LEVEL AND CORD SERUM ZINC

Linear relation in the cord serum zinc level was found to increase with increase in maternal serum zinc level as displayed by the positive scatter plot below $R^2 = 0.154$, figure 1.

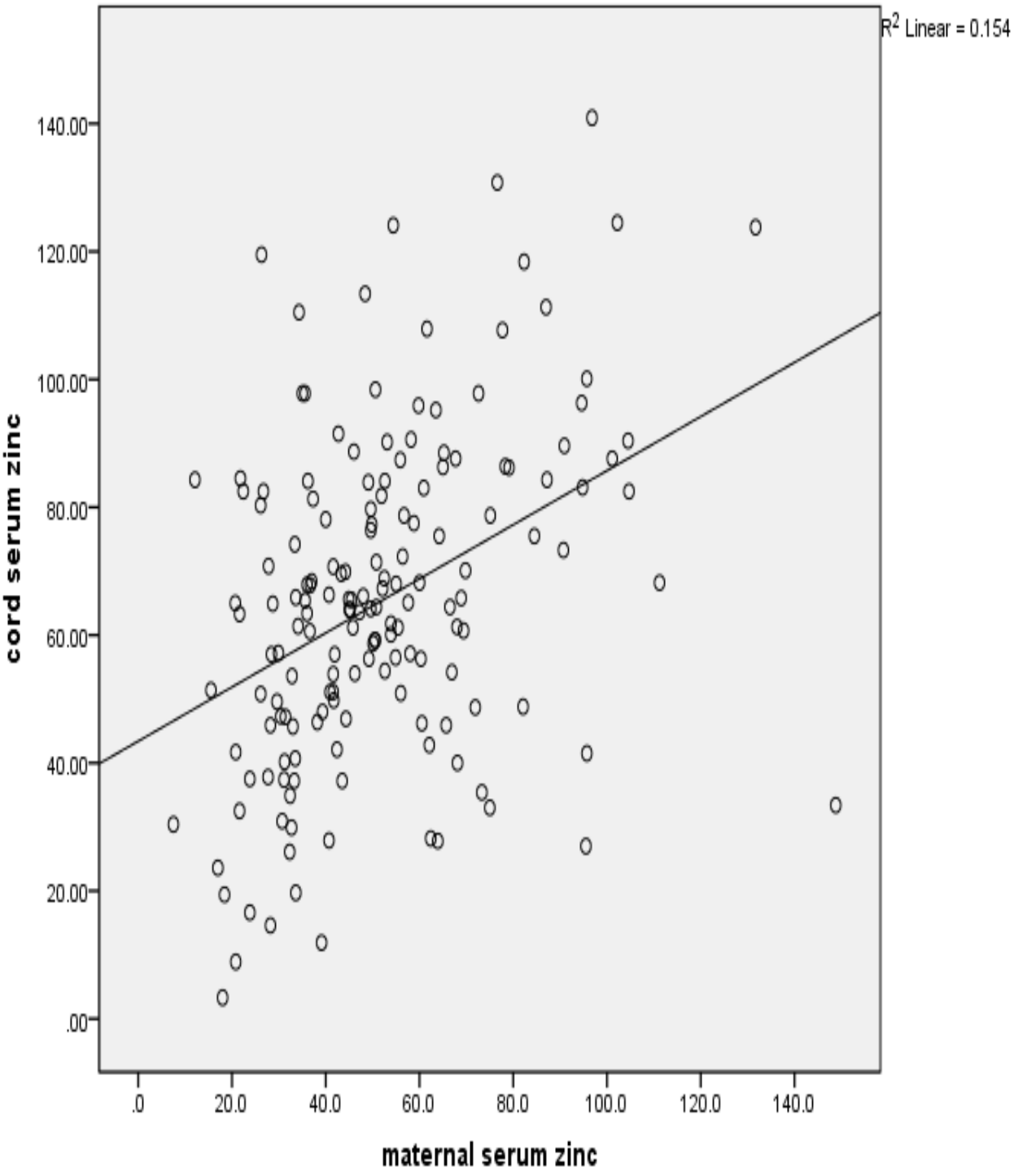

Figure 1 Scatterplot showing the relationship between maternal serum zinc level and cord serum zinc level.

RELATIONSHIP BETWEEN CORD SERUM ZINC AND MATERNAL SERUM ZINC

Pearson correlation showed a significant positive relationship between maternal serum zinc level and cord serum zinc level, p – value <0.001. As the maternal serum zinc increased, the cord serum zinc also increased. Also a significant positive correlation was found between gestational age at delivery and maternal serum zinc Level, p – value 0.014 as shown in table below.

Table 1 Pearson Correlation between Maternal Serum Zinc Level and Cord Serum Zinc Level.

Variables (N =330)		Maternal serum zinc	Cord Serum Zinc	Birth Weight	Gestational Age
Maternal	r	1	0.392	0.110	0.190
Serum Zinc	p-value		<0.001	0.159	0.014
Cord Serum	r		1	-0.001	-0.065
Zinc	p-value			0.987	0.404

r = Pearson Correlation Coefficient

DISCUSSION

The cord serum zinc of neonates delivered at FMC Owerri was found to be low in 48.5% of cases while the mean cord blood serum zinc level in neonates was 65.29±25.7µg/dl. The prevalence of zinc deficiency reported by investigators in Iran, Ghana, Abuja Nigeria, Brazil and Kenya ranged from 6% to 56.6% while the mean cord serum zinc ranged from 60µg/dl to 108.7µg/dl [10, 14, 30]. The prevalence of low cord serum zinc level of 39.6% found by [29] in South West Nigeria was lower than that found in the present study.This could be explained by the fact that [29] did not recruit preterms who are more likely to have lower serum zinc than term neonates. However, the mean serum zinc measured by [29] was 60µg/dl which is lower than that found in this study and this can be explained by the fact that these studies were carried out in different geographical regions with different soil and water zinc content from that in the present study. [10] in Iran documented a lower prevalence of 11.9% and a higher mean plasma zinc of 108.57±33µg/dl and these findings can be explained by the fact that this Iranian study excluded anaemic women in their study. A group of investigators from Jordan have found a statistically significant relationship between anemia and low serum zinc in pregnant mothers. Although [10] in Iran studied plasma zinc in neonates as against serum zinc in the present study; [30] in America had documented that there was no difference between plasma and serum zinc levels as a linear relationship was observed when the concentration of the two elements was plotted on a graph. An even lower prevalence of 6% was documented in Ghana by [14] in a study of 50 neonates with seizures and 50 age and sex-matched controls. The differences in the prevalence could be explained by the fact that [13] recruited neonates aged 1-28 days who had been priviledged to benefit from exogeneous intake of zinc in their diets when compared to the present study where cord blood samples were collected before the neonate initiated feeding. So even with a higher cut-off of 70µg/ dl, these invesigators documented a lower serum zinc than that in the current study. [40], documented a prevalence of low cord serum zinc of 36.8% in HIV-exposed neonates which is lower than the prevalence of 48.5% found in the index study and a mean serum zinc of 74.9 mg/dl which is higher than that documented in this study. This however can be explained by the fact that all mothers recruited by [41] in Brazil were on HAART which reduces the disease burden of HIV-positive patients as HIV has been reported to be associated with hypozincemia [16].

The index study found a significant positive relationship between cord serum zinc and maternal serum zinc and that the mean cord blood serum zinc is higher than the mean maternal serum zinc. The significant positive relationship between cord serum zinc and maternal serum zinc found in this study agrees with the findings of [29] in

South West Nigeria. Both studies were hospital-based and used AAS to assay serum zinc. However, [42] documented no statistically significant relationship between cord blood serum zinc and maternal serum zinc, this can be explained because [42] recruited only term neonates. The mean cord blood serum zinc measured in the index study was higher than the mean maternal serum zinc; this finding was also corroborated by [29] in South West Nigeria and [40] in Jordan. This can be explainedby increased uptake of maternal zinc by the foetus and placenta, expansion of maternal plasma volume, decreased availability of serum albumin which binds zinc in the mother and increased transfer of serum zinc to maternal erythrocytes [9].

CONCLUSION

In conclusion result from this study has revealed that maternal serum zinc level is a strong factor influencing neonatal serum zinc level.

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