

## Original Research Article

# Comparison of maternal serum and neonatal cord blood levels of zinc in relation to birth weight and period of gestation

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## ABSTRACT

**Background:** Women are at increased risk of zinc deficiency during pregnancy because of high fetal requirements for zinc. Severe maternal zinc deficiency has been associated with poor fetal growth, spontaneous abortion and congenital malformations (i.e., anencephaly), whereas milder forms of zinc deficiency have been associated with low birth weight (LBW), intrauterine growth retardation, and preterm delivery. However, the research relating maternal zinc status and birth weight has not produced consistent results. This study has been undertaken to confirm the association between maternal serum zinc concentration and birth weight and period of gestation in setting like India.

**Methods:** A total of 100 new-borns were included and divided into two groups, the 'study group' had babies with birth weight <2.5 kg and control group' with babies >2.5 kg birth weight. Cord blood from the new-borns and serum samples of mothers were collected and the zinc levels were measured.

**Results:** The correlation of cord blood and the maternal serum zinc levels were assessed in relation to birth weight and the gestational age. The results were compared between the two groups. The difference in values between the two groups was statistically significant, maternal serum zinc levels and birth weight ( $84.78 \pm 21.62$  vs  $66.04 \pm 18.66$ ) ('P' value 0.04), cord blood zinc levels and birth weight ( $98.44 \pm 22.59$  vs  $79.78 \pm 19.54$ ) ('P' value <0.001). The maternal serum and cord blood zinc was compared between the preterm and term; the results were statistically significant.

**Conclusions:** The maternal and cord blood levels of zinc are correlated well with the birth weight and the gestational age at delivery. Supplementation of zinc during gestation might help reduce the incidence of IUGR and the risk of prematurity.

**Keywords:** Birth weight, Cord blood zinc, Gestation, Maternal serum zinc

## INTRODUCTION

Zinc is known as one of the life's essential elements because of its vital role in a wide range of biological activities.<sup>1</sup> Although severe zinc deficiency is now considered rare, mild to-moderate zinc deficiency may be relatively common throughout the world. Women are at increased risk of zinc deficiency during pregnancy because of high fetal requirements for zinc.<sup>2</sup> Pre-term birth is often associated with nutritional compromise and

impaired growth. It is believed that the relation between nutrition and growth is mediated by the changes in the hormone and growth factor axis. These changes in the GH axis associated with malnutrition could be explained in part by zinc deficiency.<sup>3</sup> Zinc deficiency has a negative effect on the endocrine system, leading to growth failure.

Zinc is a key component of the cell architecture and function. Required for production of over 200 enzymes, including phosphatases, metallo-proteinases,

oxidoreductases, transferases, which are involved in protein synthesis, nucleic acid metabolism and immune function. In addition, it is a structural component of various proteins, hormones, nucleotides.<sup>3</sup> Severe maternal zinc deficiency has been associated with poor fetal growth, spontaneous abortion and congenital malformations (i.e., anencephaly), whereas milder forms of zinc deficiency have been associated with low birth weight (LBW), intrauterine growth retardation, and preterm delivery.<sup>3</sup> Importantly, milder forms of zinc deficiency have also been related to complications of labor and delivery, including prolonged or inefficient first-stage labor and protracted second-stage labor, premature rupture of membranes (PROM), and the need for assisted or operative delivery. These complications in turn impair maternal and perinatal health because they lead to increased risk of maternal infections, fetal distress, stillbirth, neonatal asphyxia (low Apgar scores), and neonatal sepsis.<sup>3</sup> The underlying mechanism whereby severe zinc deficiency causes developmental defects is not known with certainty however, it is likely to be the result of the impairment of several metabolic functions. Abnormal synthesis of nucleic acids and protein, impaired cellular growth and morphogenesis, abnormal tubulin polymerization with resultant reductions in cellular motility and development, chromosomal defects, excessive cell death, and excessive lipid peroxidation of cellular membranes may all occur in severe zinc deficiency and contribute to teratogenic effects.<sup>4</sup> Women are at increased risk of zinc deficiency during pregnancy in part because of high fetal requirements for zinc, and maternal zinc deficiency has been associated with poor fetal growth in both animal and human populations.<sup>5</sup> However, the research relating maternal zinc status and birth weight has not produced consistent results. Majority of these studies were performed in developed countries. The effects of zinc supplementation on duration of pregnancy and preterm delivery were examined in some trials.<sup>6-10</sup> These results indicate a consistent, albeit small, effect of zinc supplementation on the average duration of pregnancy. Thus, it may be true that increases in average birth weight observed with zinc supplementation occur not from improvements in fetal growth rates, but rather from prolongation of time spent in utero. Among Indian women, gestational age of the infant increased more with longer periods of supplementation.<sup>9</sup> Unlike in developed countries, where preterm is the main cause of low birth weight, in developing countries most low birth weight infants are small for gestational age. Low zinc concentrations in the cord blood of low birth weight newborns have been noted in a number of settings and birth weight has been shown to be highly correlated with cord zinc concentration. In India, where there is a high incidence of low birth weight,<sup>11,12</sup> it will be interesting to know the role of zinc in newborn and their mothers in relation to birth weight and significant predictor of low birth weight.<sup>13-16</sup> This study has been undertaken to confirm the association between maternal plasma or serum zinc concentration and birth weight and period of gestation in developing country like India.

## METHODS

Authors conducted a cross sectional prospective study at the tertiary hospital, over a period of one year during 2008-2009. Our inclusion and exclusion criteria were.

### *Inclusion criteria*

Term newborns, preterm newborns, IUGR babies, serum samples of mothers in good health were included.

### *Exclusion criteria*

Mothers on drugs (diuretics, anticonvulsants, anticoagulants), mothers with clinical conditions known to affect mineral metabolism such as severe malnutrition, severe anemia (hemoglobin <10 gm%), diabetes mellitus, parathyroid, bone and gastrointestinal diseases were excluded.

The gestational age in present study was calculated using the maternal dates and the Dubowitz scoring. Authors included 50 new-borns with a birth weight of <2.5 kg (included preterm, term IUGR) and their mothers. All the subjects in this group met the inclusion criteria, authors labelled this group as the 'study group'. Similarly, authors included new-borns with birth weight >2.5 kg and their mothers, who fulfilled the inclusion criteria, the subjects of this group were labelled as the 'control group'. At the time of admission to the labour ward, 2ml of blood was collected from the peripheral vein of the mother after consent; the samples were collected in a sterile EDTA container and labelled, the samples were immediately sent to the laboratory and centrifuged at 3000 rpm for 20 min. The supernatant serum was collected in a separate sterile polyethylene container and labelled; the sample was stored at -20°C until analysis. Similarly, the cord blood was collected immediately after the delivery and was sent to the laboratory in sterile EDTA vacutainer with labelling. The cord blood samples were centrifuged at 3000 rpm for 20 min and the supernatant serum was collected in a sterile polyethylene container and labelled. The samples were grouped with the maternal samples. The maternal serum samples and the corresponding cord blood samples were labelled as a set and were taken up for analysis. The analysis for the serum concentration of zinc was done using the atomic absorption spectrophotometric method (AAS), this method analytically is the most reliable for routine assessment of serum zinc levels. The results deduced from the analysis were accordingly grouped to the study group/control group. Authors had a sub-group analysis based on the gestational age, as preterm and term. The results obtained were correlated as per the objective of present study.

### *Statistical analysis*

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are

presented on Mean $\pm$ SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance. Student t-test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups Pearson correlation has been carried out to find the relationship between the pair of study variables. The statistical software namely SPSS 15.0, Stata 8.0, Med Calc 9.0.1 and Systat 11.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

## RESULTS

A prospective study conducted at the tertiary hospital over a span of one year. Authors had enrolled 100 newborns and the mothers as per our inclusion criteria. The newborns enrolled were randomized into two equal groups based on the birth weight. Newborns with a birth weight of <2.5 kg were categorized as the 'study group'. Among the 50 newborns in the study group authors had 20 preterm babies and the rest 30 newborns were term IUGR. 50 newborns with birth weight of >2.5 kg was included in the control group, the babies in the control group were term.

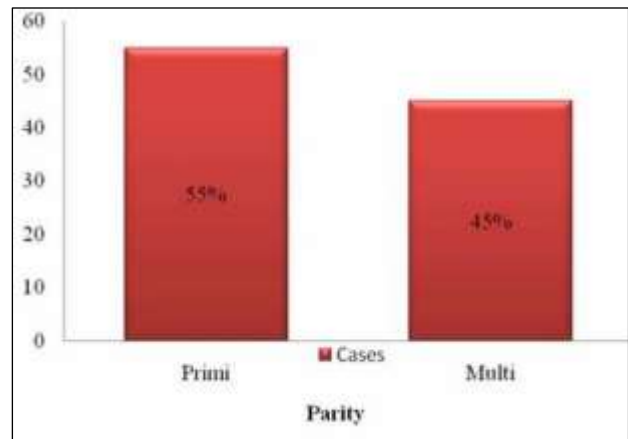
### Maternal demography

In present study most of the mothers were in the age group 21-25 years (48%), among the mothers included 55 (55%) were primigravida. 66 (66%) of the deliveries were normal vaginal delivery.

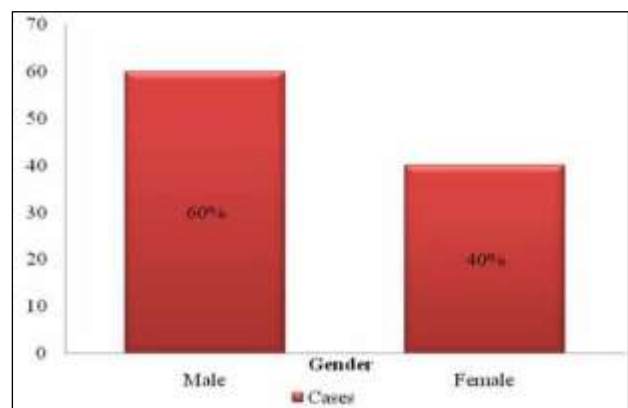
**Table 1: Maternal characteristics.**

	Number
<b>Mother details</b>	
18-20	7
21-25	48
26-30	34
>30	11
<b>Parity</b>	
Primi	55
Multi	44
<b>Mode of delivery</b>	
Normal	66
LSCS	34
<b>Gestational age in weeks</b>	
<37	20
>37	80
Total	100

Among the total babies included in the study, we had 60 male neonates (60%), and 40 neonates were females (40%). The male to female ratio was 3:2.



**Figure 1: Distribution of parity.**



**Figure 2: Gender distribution in the babies included in study.**

**Table 2: Gestational age and birth weight (kg).**

Gestational age (weeks)	Total		Birth weight
	Study	Control	
<37	20	0	20
>37	30	50	80
Total	50	50	100

In present study authors had a total of 50 babies included in the study group and 50 were the control group, the study group further consisted of 20 babies with gestation <37 weeks (40%) of the study group, the rest were term IUGR babies ( 60%) of the study group. In present study authors found that the mean maternal serum levels of zinc 66.04 $\mu$ g /dl $\pm$ 18.66, in the study group, was less as compared to the maternal serum levels of zinc in the control group with a mean level of 84.78 $\mu$ g/dl $\pm$ 21.62.

The 'P' value of 0.043 and the Pearsons correlation coefficient (r) of 0.44 was statistically significant. The results show a significant association between zinc levels and birth weight. These differences in the mean values were statistically significant and Pearson's correlation done showed a significant 'r' value of 0.42.

**Table 3: Zinc levels of maternal serum according to birth weight of baby.**

Birth weight (kg)	Maternal serum zinc ( $\mu\text{gm/dL}$ )			P value
	Min-Max	Mean $\pm$ SD	95% CI	
Study group	24-110	66.04 $\pm$ 18.66	60.73 $\pm$ 21.34	0.043
Control group	45-150	84.78 $\pm$ 21.62	78.63 $\pm$ 90.93	

**Table 4: Zinc levels of cord blood according to birth weight of baby.**

Birth weight (kg)	Cord blood -zinc ( $\mu\text{gm/dl}$ )			P value
	Min-Max	Mean $\pm$ SD	95% CI	
Study group	43-128	79.78 $\pm$ 19.54	74.24-85.35	<0.001
Control group	53-153	98.44 $\pm$ 22.59	92.02-104.86	<0.001

**Table 5: Zinc levels of maternal serum in relation to gestational age.**

Gestational age (weeks)	Maternal serum zinc ( $\mu\text{gm/dL}$ )			P value
	Min-Max	Mean $\pm$ SD	95% CI	
<37.0 weeks	36.0-89.0	65.60 $\pm$ 14.05	59.03-72.17	0.026
>37.0 weeks	24.0-150.0	77.86 $\pm$ 23.21	72.69-83.03	

**Table 6: Zinc levels of cord blood according to gestational age.**

Gestational age (weeks)	Cord blood-zinc ( $\mu\text{gm/dl}$ )			P value
	Min-Max	Mean $\pm$ SD	95% CI	
<37.0 weeks	46.0-98.0	79.80 $\pm$ 15.29	72.64-86.96	
>37.0 weeks	43.0-153.0	91.44 $\pm$ 24.09	86.07-96.97	

In present study authors compared the zinc levels of the cord blood with birth weight of the baby and we found that zinc levels of the cord blood in the control group (mean zinc levels-98.44 $\pm$ 22.59) were significantly higher than the study group (mean-79.78 $\pm$ 19.54). These differences in the mean values were statistically significant and Pearson's correlation done showed a significant 'r' value of 0.42.

In present study, we compared the zinc levels in the cord blood with relation to the gestational age, we found that the levels of zinc were lower in the babies born preterm as compared to the babies who were born at term. Mean cord blood zinc levels in gestation <37weeks was 79.80 $\pm$ 15.29 as compared to term newborns with mean zinc levels of 91.44 $\pm$ 24.09. The 'P' value of <0.001 and Pearson's correlation coefficient (r) of 0.20 was statistically significant.

## DISCUSSION

Zinc is a component of a large number of metalloenzymes and there is a high concentration of zinc in the brain. The consequences of zinc deficiency are several with severe impact on human health. Severe maternal zinc deficiency has been associated with poor fetal growth, spontaneous abortion and congenital

malformations (anencephaly), whereas milder forms of zinc deficiency have been associated with low birth weight (LBW), intrauterine growth retardation, and preterm delivery. Importantly, milder forms of zinc deficiency have also been related to complications of labor and delivery, including prolonged or inefficient first-stage labor and protracted second-stage labor, premature rupture of membranes (PROM). These complications in turn impair maternal and perinatal health because they lead to increased risk of maternal lacerations, high blood loss, maternal infections, fetal distress, stillbirth, neonatal asphyxia (low Apgar scores), respiratory distress, and neonatal sepsis.<sup>1</sup>

Unlike in developed countries, where preterm is the main cause of low birth weight, in developing countries most low birth weight infants are small for gestational age. Nutrient deficiencies during fetal development can cause this intrauterine growth retardation and may even compromise immune function after birth.

In India, where there is a high incidence of low birth weight it will be interesting to know the role of zinc in newborn and their mothers in relation to birth weight and gestation, especially when there have been studies suggesting zinc as one of the significant predictor of low birth weight.<sup>13-16</sup>



### **Demographic data**

In present study, most of the mothers included in the study were in the age group of 20-30 years, 55% were primigravida. The age group was in concordance with other studies by Neggers et al, Tamura et al, who in their studies included women in the age group comparable with present study.<sup>10</sup>

### **Baby characteristics**

In present study, authors randomized newborns into the control group and the study group, based on their birth weight. Control group consisted of babies >2.5 kg and study group consisted of babies <2.5 kg.

Authors included preterm and term IUGR in present study group. Other studies had similar groups and few other studies had categorized babies into different groups based on the birth weight and did not have any group as control.

### **Maternal risk factors**

In present study authors included women with no risk factors which could be a confounding factor affecting the birth weight of the newborn, authors excluded maternal illness (severe malnutrition, severe anemia (<10 gm%), diabetes mellitus, parathyroid diseases, bone and GI diseases) which could have an adverse effect on birth weight and the levels of zinc. Subjects included in present study had no history of drug intake during pregnancy, (diuretics, anti-convulsant, anti-coagulants) however mothers who had taken iron and folic acid supplements were included.

Tamura et al, Neggers et al, in their study had controlled for criteria which were confounding factors for birth weight and levels of zinc.<sup>10</sup> Anemia could be an important confounding factor for low birth weight, authors ruled out mothers with hemoglobin of <10 gm%.

### **Maternal zinc and birth weight**

In present study authors found the mean zinc levels in maternal serum in the 'study group' -66.04±18.66 µgm/dl, were less as compared to mean values of the 'control group' -84.78±21.62 µgm/dl. The difference in mean values was statistically significant.

Pearson's correlation done comparing the maternal serum zinc levels and birth weight, showed an 'r' (correlation coefficient) value of 0.44. The results were in concordance with other studies done by Neggers et al, Crosby et al, Bahl et al, Maral et al.<sup>10,11,17,18</sup> The results show, zinc levels have a positive association with birth weight and LBW babies had lower levels of zinc, which might be an independent factor influencing birth weight.

### **Cord blood levels of zinc and birth weight**

Authors correlated cord blood levels of zinc with the birth weight of the newborns. The mean cord blood levels of zinc in the study group -79.78±19.54 µgm/dl, was comparatively less than the control group -98.44±22.59 µgm/dl. The difference in values was statistically significant and had a Pearson's correlation value of 0.42. Our results were in conformity with other similar studies done by Bahl et al, Elizabeth et al, Iqbal et al, Jeswani et al.<sup>11,12,19,20</sup> The researchers in their study found a similar association between cord blood levels of zinc and low birth weight. The results of present study show, low serum zinc is a significant predictor of low birth weight, if the results are replicable, they will have important implications for both the prediction of low birth weight and possibly the prevention of low birth weight.

### **Maternal serum zinc levels and gestational age**

Authors did a sub-group analysis to correlate the maternal serum zinc levels with the gestational age, authors in present study found that mothers who delivered preterm had lower serum levels of zinc as compared to the mothers who delivered at term. The mean serum zinc levels in the preterm group was 65.60±14.05 µgm/dl, as compared to the mean zinc levels of 77.86±23.21 µgm/dl, in the term group. This difference in zinc levels was statistically significant, Pearson's correlation coefficient of 0.18. Present result show that low zinc levels are associated with preterm deliveries. Results were in concordance with other similar studies by Bahl et al, Iqbal et al, Jameson et al.<sup>3,11,19</sup> These studies showed a positive association of serum zinc levels with gestational age.

### **Cord blood levels of zinc and gestational age**

Authors in present study found a positive correlation between the cord blood levels of zinc and the gestational age at delivery. Mean cord blood zinc levels of preterm were 79.80±15.29 µgm /dl as compared to term newborns with mean zinc levels of 91.44±24.09 µgm/dl, the results were statistically significant. Pearson's correlation coefficient -0.26.

## **CONCLUSION**

Authors in present study found the observations which were the maternal serum zinc levels were significantly higher in the control group as compared to the study group, the cord blood levels of zinc were significantly higher in the control group as compared to the study group, mothers with preterm deliveries had significantly lower serum zinc levels as compared to mothers who delivered at term, babies born preterm had significantly lower cord blood levels of zinc as compared to babies born at term.

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*Ethical approval: The study was approved by the Institutional Ethics Committee*

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