

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20240453>

Original Research Article

## Association of maternal serum zinc and cordblood zinc with neonatal birth weight

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Received: 14 January 2024

Accepted: 03 February 2024

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### ABSTRACT

**Background:** Zinc is essential for optimal fetal growth because of the role of zinc in cellular division, growth and differentiation. Low maternal serum zinc and cord blood zinc has been reported to be associated with low birth weight and, a risk factor for neonatal morbidity and mortality. The aim of this study was to evaluate the association of maternal serum zinc, cord blood zinc with neonatal birth weight.

**Methods:** This case-control study was conducted in department of obstetrics and gynecology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from November 2020 to October 2022. A total of 60 women in their postnatal period were included in this study.

**Results:** In the present study, none of the socio-demographic characteristics in both case and control groups were statistically significant ( $p>0.05$ ). Mean BMI was  $23.88\pm 1.36$  kg/m<sup>2</sup> in cases and  $24.39\pm 1.39$  kg/m<sup>2</sup> in controls, with 16.7% of cases overweight ( $p>0.05$ ). Cases had lower maternal serum zinc ( $58.33\pm 27.63$  µg/dl) than controls ( $82.96\pm 16.94$  µg/dl), significantly affecting neonatal birth weight ( $p=0.001$ ,  $r=+0.406$ ). Low zinc levels ( $<68$  µg/dl) increased the risk of birth weight  $<2.500$  kg by nearly six times (OR 5.67, 95% CI 1.84-17.49;  $p=0.002$ ).

**Conclusions:** Low birth weight neonates and their mothers have significant zinc deficiency as compared to term neonates and their mothers and this deficiency is correlated with zinc deficiency in mothers of these low-birth-weight neonates.

**Keywords:** Association, Maternal serum zinc status, Neonatal birth weight

### INTRODUCTION

Birth weight is the first weight of the baby at delivery, which is a strong predictor of prenatal growth and newborns future chances of survival and is dependent on maternal health and nutrition during pregnancy.<sup>1</sup> Low birth weight (LBW) is defined as a birth weight of less than 2500 grams (up to and including 2499 grams). Compared to normal birth weight infants, LBW neonates experience increased morbidity, including acute neonatal complications as well as childhood stunting and risk of adult-onset chronic conditions (e.g. cardiovascular disease).<sup>2</sup> LBW continues to be one of the most important causes of death during the first year of life in both developed and developing countries. In Bangladesh,

nearly half of newborns are not weighed at birth. According to the multiple indicator cluster survey (MICS) 2019, the percentage of children weighed at birth is only 52% in Bangladesh.<sup>3</sup> The mean birth weight of infants in Bangladesh was recorded as 2,898 gm, average for boys was higher than girls and average weight more in non-slum than slum newborns. The LBW rate was 22.6% and more among girls and in slums.<sup>4</sup> Pregnancy is a period of fetal growth and development which necessitates an increase in nutrients.<sup>5</sup> Maternal micronutrients especially zinc deficiency are one of the contributing factors for the higher incidence of FGR and LBW neonates in developing countries.<sup>6</sup> The estimated average requirement of zinc during pregnancy ranges from 10.0 to 12.0 mg/day.<sup>7</sup> Zinc deficiency is one of the common micronutrient

deficiencies in developing countries, where multiple micronutrient deficiencies often present concomitantly as a result of diets with limited diversity, poor bioavailability, and limited micronutrient content, in addition to poor hygiene and infections.<sup>8</sup> Serum zinc is considered the best biochemical indicator of zinc status in a population. A major consideration for use of serum zinc is the fact that it is a negative acute phase reactant, and therefore declines in response to inflammation.<sup>9</sup> Reference ranges is defined as 70-120 µg/dl, while the values lower than 70 µg/dl is defined as zinc deficiency.<sup>10</sup> Zinc deficiency affects around 17% of the world's population but mainly embraces sub-Saharan Africa and South Asia.<sup>11</sup> Zinc is intimately linked to bone metabolism, thus, zinc acts positively on growth and development. Zinc concentration in bone is very high compared with that in other tissues, and it is considered an essential component of the calcified matrix. Zinc also enhances vitamin D's effects on bone metabolism through the stimulation of DNA synthesis in bone cells.<sup>12</sup> Moreover, an optimum level of zinc concentration helps in the secretion of the growth hormone.<sup>13</sup> Severe maternal zinc deficiency has been associated with poor fetal growth, spontaneous abortion, and congenital malformation. Whereas milder forms of zinc deficiency have been associated with LBW, fetal growth restriction, and preterm delivery. Maternal complication includes pregnancy-induced hypertension, pre-eclampsia, intrapartum haemorrhage, infection, and prolonged labor.<sup>14</sup> Maternal nutrition, therefore, is an important factor for fetal development and pregnancy outcome including birth weight. Particularly the babies born with low birth weight remain vulnerable to which many researchers have found a correlation with maternal zinc deficiency, while others didn't.<sup>14,15,16</sup> Therefore, considering the inconsistent previous study findings, the current study on maternal serum zinc status in pregnancy might clarify its potential relationship with birth weight.

## METHODS

Author conducted a case control study at the obstetrics and gynecology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, during the period from November 2020 to October 2022. A total of 60 women at their 37-40 weeks of gestation were included in this study among which 30 women who had just given birth to a baby weighing <2.5 kg were considered as the cases and the rest of the 30 delivered babies weighing ≥2.5 kg were enrolled as the controls. Women with multiple gestation, pre-existing hypertension, chronic renal failure or cardiovascular disease were excluded. The reference range for normal serum zinc level is 68-107 µg/dl. Maternal zinc level is considered as low if the serum level is <68 µg/dl. At the time of admission to the labour ward, 2 ml of blood was collected from the peripheral vein of the mother after consent. Similarly, the cord blood was collected immediately after the delivery and was sent to the laboratory in sterile EDTA vacutainer for serum zinc determination. Then samples were sent for analysis in the laboratory of the department of biochemistry and

molecular biology, BSMMU. Serum zinc concentration was measured using a fully automated Thermo Scientific™ Indiko™ Plus Clinical Chemistry Analyzer (Thermo Scientific, USA) using a colorimetric method. Personal data, medical and social information were obtained from the mothers using a predesigned proforma. The birth weight of the neonates was measured immediately after birth (within hours) without any clothing by the electronic baby weighing scale. Maternal serum zinc level and cord blood zinc level was categorized based on the cut off value. To understand the relationship between case and control variables Pearson's correlation coefficient (r) test was done. The strength of association was determined by estimating the odds ratio (OR) and their 95% confidence interval (CI). The p value <0.05 was considered statistically significant.

## RESULTS

Sixty mothers and their babies were recruited into the study. In this present study, it was observed that half (50.0%) of the cases and three-fifths (60.0%) of the control group of respondents aged were between 21-29 years. But these differences in distribution were statistically not significant (p=0.714). The socioeconomic status of the women derived from their educational status and the occupational status of their husbands showed that more than half of the women were from middle socioeconomic class. In regards to participants' occupations, homemakers comprised 73.3% of the cases and 66.7% of the control group of respondents (66.7%). Majority of the participants monthly family income was 10,000-25,000 Tk (cases: 63.3% versus controls: 70.0%). None of these differences in the distribution of respondents according to their socio-demographic characteristics in both case and control groups were statistically significant (p>0.05). The gestational age of the respondents was taken matched in this study where there mean±SD gestational age in the cases was 39.00±0.83 weeks and in the control group was 38.87±0.86 weeks, which was statistically non-significant (p=0.544). In this study, the mean body mass index (BMI) of the case and control group of respondents were 23.88±1.36 and 24.39±1.39 kg/m<sup>2</sup>, whereas only 16.7% of the cases were observed overweight. These were not statistically significant (p>0.05).

**Table 1: Distribution of mean±SD maternal zinc level by group (case=30, control= 30).**

Maternal serum zinc level (µg/dl)	Case (N=30)	Control (N=30)	P value
Maternal serum zinc level	58.33±27.63	82.96±16.94	0.001 <sup>c</sup>

Table 1 demonstrates the distribution of mean (±SD) maternal zinc level by group. Lower maternal serum zinc level was observed in the cases (58.33±27.63 µg/dl) compared to the control group of respondents (82.96±16.94 µg/dl), which was statistically highly significant (p=0.001).

**Table 2: Odds ratios (OR) and 95% confidence intervals (CI) for neonatal birth weight according to serum zinc level in pregnancy (case =30, control =30).**

Maternal serum zinc level ( $\mu\text{g/dl}$ )	Case (N=30)	Control (N=30)	P value	OR	(95% CI)
<68	19 (63.3)	7 (23.3)	0.002 <sup>a</sup>	5.67	1.84-17.49
$\geq$ 68	11 (36.7)	23 (76.7)			

<sup>a</sup>Chi-square test was done to measure the level of significance. CI=confidence interval

**Table 3: Distribution of mean $\pm$ SD cord blood zinc level by group (case =30, control =30).**

Cord blood zinc level ( $\mu\text{g/dl}$ )	Case (N=30)	Control (N=30)	P value
Cord zinc level	51.42 $\pm$ 23.67	85.42 $\pm$ 16.74	0.001 <sup>c</sup>

**Table 4: Odds ratios (OR) and 95% confidence intervals (CI) for neonatal birth weight according to cord blood zinc level in pregnancy (case =30, control =30).**

Cord blood zinc level ( $\mu\text{g/dl}$ )	Case (N=30)	Control (N=30)	P value	Odds ratio	(95% CI)
<68	22 (73.3)	11(36.7)	0.002 <sup>a</sup>	4.98	2.01-16.51
$\geq$ 68	08 (26.6)	19 (63.3)			

<sup>a</sup>Chi-square test was done to measure the level of significance. Figure within parenthesis indicates in percentage.

Table 2 represents the odds ratios (OR) and 95% confidence intervals (CI) for neonatal birth weight according to serum zinc level in pregnancy. The risk of birth weight of <2.500 kg was almost six times (OR 5.67, 95% CI 1.84-17.49;  $p=0.002$ ) more with low maternal serum zinc levels (<68  $\mu\text{g/dl}$ ). Serum cord zinc levels in study population are given in Table 3. Mean neonatal serum zinc level in the study group (51.42 $\pm$ 23.67  $\mu\text{g/dl}$ ) was comparatively lower than in control group (85.42 $\pm$ 16.74  $\mu\text{g/dl}$ ), which was statistically significant ( $p$  value <0.05). Table 4 represents the odds ratios (OR) and 95% confidence intervals (CI) for neonatal birth weight according to cord zinc level in pregnancy. The risk of birth weight of <2.500 kg was almost five times (OR 4.98, 95% CI 2.01-16.51;  $p=0.002$ ) more with low cord blood zinc levels (<68  $\mu\text{g/dl}$ ).

## DISCUSSION

In this present study, it was observed that half (50.0%) of the cases and three-fifths (60.0%) of the control group of respondents aged were between 21-29 years. None of the differences in the distribution of respondents according to their socio-demographic characteristics in both case and control groups were statistically significant ( $p>0.05$ ). These findings were consistent with the study of Wang et al.<sup>17</sup> They demonstrated that majorities belonged to the 25-29 years age group in maternal zinc level deficient and sufficient group, 60.7% and 62.9% respectively. Similarly, middle-income participants were 49.8% in the maternal zinc deficiency group and 52.3% in the adequate respondents. While Rwebembera et al conferred that maternal age of <19 years was associated with low infant birth weight and low maternal zinc levels.<sup>18</sup> In a similar study by Rwebembera et al, all infants in the control group were full term.<sup>18</sup> The mean gestational age was 36.16 $\pm$ 2.67

weeks for cases and 39.19 $\pm$ 0.93 weeks for controls. In the current study, multigravida participants were observed in 50.0% of cases and 43.3% of the controls. This difference was statistically non-significant ( $p=0.760$ ). Endalamaw et al, in a systematic review and meta-analysis, illustrated that women with higher gravidity and short pregnancy interval (<24 months) are more likely to experience LBW compared with lower gravidity counterparts due to malnutrition which is highly related to frequent pregnancy with short inter pregnancy interval.<sup>19</sup> This difference in the findings was probably due to variation in the study design and geographical location. In this study, the mean body mass index (BMI) of the case and control group of respondents were 23.88 $\pm$ 1.36 and 24.39 $\pm$ 1.39  $\text{kg/m}^2$ , whereas only 16.7% of the cases were observed overweight. These were not statistically significant ( $p>0.05$ ). A similar observation was enumerated by Maamouri et al, who demonstrated the mean maternal weight in the case and control groups were 54.41 kg and 60.0 kg, respectively, and there was no significant difference for mother's BMI ( $p=0.11$ ) between two groups.<sup>20</sup> Lower maternal serum zinc level was observed in the cases (58.33 $\pm$ 27.63  $\mu\text{g/dl}$ ) compared to the control group of respondents (82.96 $\pm$ 16.94  $\mu\text{g/dl}$ ), which was statistically highly significant ( $p=0.001$ ). This deficiency can be due to expanded blood volume, increased demands, and poor intake or bio-absorption, though this was not assessed. Maternal serum zinc level was found positively correlated with neonatal birth weight ( $r=+0.406$ ,  $p=0.001$ ), and the risk of birth weight of <2.500 kg was almost six times (OR 5.67, 95% CI 1.84-17.49;  $p=0.002$ ) more with low maternal serum zinc levels (<68  $\mu\text{g/dl}$ ). This was similar with the study by Maral et al, where they found that the mean zinc level of women with LBW infants was significantly lower than that of their counterparts with normal birth weight infants (58.6 $\pm$ 11.2  $\text{mg/dl}$  versus

70.6±23.3 mg/dl,  $p < 0.05$ ).<sup>21</sup> Of the 20 women with LBW infants, 18 (90.0%) had low serum zinc levels, whereas of the 40 women with normal birth weight infants, 22 (52.5%) had normal serum zinc levels (odds ratio = 7.36). Jyotsna et al found that serum zinc level of mothers of LBW newborns was significantly low, and this deficiency was correlated with zinc deficiency in their neonates (Pearson correlation value- 0.938).<sup>22</sup> Bellad et al conferred that the mean zinc levels in maternal serum in the study group: 67±16.6 µg/dl, were less as compared to mean values of the control group: 82.35±19.45 µg/dl.<sup>23</sup> The difference in mean values was statistically significant. They also showed a positive correlation of maternal zinc levels with birth weight and prematurity. Ahmed et al found that the mean maternal serum levels of zinc 66.04±18.66 µg/dl 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±21.62 µg/dl.<sup>24</sup> Pearson's correlation done comparing the maternal serum zinc levels and birth weight showed an 'r' value of 0.44. Cord blood zinc levels in study population are given in Table 3. Mean neonatal serum zinc level in the study group (51.42±23.67 µg/dl) was comparatively lower than in control group (85.42±16.74 µg/dl), which was statistically significant ( $p$  value <0.05). Table 4 represents the odds ratios (OR) and 95% confidence intervals (CI) for neonatal birth weight according to cord zinc level in pregnancy. The risk of birth weight of <2.500 kg was almost five times (OR 4.98, 95% CI 2.01-16.51;  $p=0.002$ ) more with low maternal serum zinc levels (<68 µg/dl). The mean cord blood zinc concentration is in the same range with the studies done in Ile-Ife, France and Jordan but higher than the value reported in Ibadan.<sup>25-27</sup> 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. Zinc plays critical roles in cell division, differentiation, and function that are 2-4 essential for tissue growth. 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.<sup>25-27</sup> 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.

This study has some limitations. The study population was relatively small and pregnant women were chosen from BSMMU, Dhaka; so, the results of this study may not reflect the exact picture of the whole country. The present study was conducted in a short period of time. The sample was taken purposively. So, there may be a chance of bias that can influence the results. Therefore, the study findings cannot be generalized to the entire population.

## CONCLUSION

In this prospective observation study, we showed that low birth weight neonates have significant zinc deficiency as compared to term neonates. Also, the mothers of LBW newborns have lower serum zinc levels than the mothers of the normal birth newborns and lower maternal serum zinc level was positively correlated with lower birth weight. This suggests the need to advocate zinc intake by pregnant women, either in the diet or in the form of supplements. It is recommended to undertake further prospective study with a larger sample size to find out the validity of the findings of the present study.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh*

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**Cite this article as:** Mahmood S, Deeba F. Association of maternal serum zinc and cordblood zinc with neonatal birth weight. *Int J Reprod Contracept Obstet Gynecol* 2024;13:548-52.