

## Association of Cord Blood Zinc Level and Birth Weight in a Sample of Iranian Neonates

### Abstract

**Background:** In addition to its short-term effects, low birth weight increases the risk of noncommunicable diseases (NCDs) in adult life. The quality of maternal diet including the macronutrient intake is very important in this regard. This study aims to evaluate the possible associations between maternal zinc and neonatal anthropometric measures. **Method:** This cross-sectional study was conducted on 226 pairs of mothers-neonates in Isfahan, Iran. Maternal characteristics including the history of the disease, age, preconceptional weight, weight gain during pregnancy, as well as, anthropometric characteristics of neonates such as weight, height, length, and circumferences of head, belly, chest, and thigh were documented. Cord blood zinc was measured by atomic absorption spectrophotometer in three groups of neonates depending on their weights. **Results:** The gestational age of neonates was 35 to 38 weeks with a mean weight of  $3.13 \pm 0.42$  kg. The mean of zinc concentration was  $0.81 \pm 0.18$  and it was higher in neonates with appropriate weight than in those with high or low birth weight ( $0.82 \pm 0.18$ ,  $0.75 \pm 0.19$ , and  $0.65 \pm 0.12$  ng/ml, respectively). Bivariate correlation analysis showed significant weak correlation between cord blood zinc and neonatal weight ( $r = 0.16$ ,  $P = 0.04$ ). **Conclusions:** The cord blood zinc concentration of normal-weight neonates was higher than others. Our findings suggest that maternal zinc may influence neonatal birth weight, and it should be considered in the primordial prevention of NCDs.

**Keywords:** Birth weight, fetal blood, preventive medicine, zinc

### Introduction

Low birth weight (LBW) is a major health problem in developing countries.<sup>[1]</sup> LBW is known as a risk factor for adverse growth and neurodevelopment in early childhood and chronic diseases in adolescence.<sup>[2,3]</sup>

According to the studies, one-half of all LBW infants in developed countries are born preterm (less than 37-week gestation). Unlike developed countries, most of the low-birth-weight children in developing countries are born at term ( $\geq 37$  weeks and gestation).<sup>[4-7]</sup> It is evident that poor nutrition during pregnancy is an important cause for low birth weight, particularly in developing countries.<sup>[8]</sup> Some studies show that deficiencies in micronutrients like zinc, iron, folic acid, and iodine during pregnancy can lead to low birth weight.<sup>[9-11]</sup>

Zinc is one of the most essential metals which can be transferred through the placenta to the fetus.<sup>[12]</sup> Zinc is important

and necessary for normal growth and development. It is essential for cellular growth, division, and differentiation.<sup>[13]</sup> Zinc is more required in some periods such as periods of pregnancy, infancy, and puberty.<sup>[14]</sup>

Studies have shown that low birth weight is associated with an increased risk of obesity, chronic diseases such as type-2 diabetes mellitus, in later life. On the other hand, the role of micronutrients in pregnancy has always been of much concern,<sup>[15,16]</sup> hence the effects of micronutrients especially zinc on neonates is investigated.

In this study, we examined the possible associations between cord blood zinc as an important element for growth and health of fetus and mothers and characteristics of neonates, as predisposing factors for noncommunicable diseases (NCDs) in adulthood.

### Method

This cross-sectional study was approved by the research and Ethics Committee

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of Faculty of Medicine, Isfahan University of Medical Sciences. After an explanation of objectives of the study, pregnant mothers signed a written informed consent for involvement in the project. Approval code of this project is 394633 in November 2015.

Overall, 226 pairs of mothers and neonates were included in this study conducted in Isfahan, Iran. Mothers who lived less than a year in one region prior to the delivery date, those who had a history of long term medication use or chronic diseases including diabetes, ischemic heart disease, cerebrovascular diseases, chronic liver, and kidney diseases were not enrolled in the study. Moreover, neonates who were delivered after 38<sup>th</sup> or before 35<sup>th</sup> week of pregnancy, twins, stillbirths, or neonates who needed progressive resuscitation at birth, were excluded. The date of delivery; mother's demographic data including age, weight before pregnancy, total pregnancy weight gain; and anthropometric characteristics of neonates including weight, height, length, and circumference of head, belly, chest, and thigh were obtained from checklists. Newborns were divided into three groups: newborns who are small for gestational age (SGA; birth weight [BW] <10<sup>th</sup> percentile), newborns who are appropriate for gestational age (AGA; BW at 1–90<sup>th</sup> percentile), and newborns who are low for gestational age (LGA; BW >90<sup>th</sup> percentile). For biochemical tests, 10 ml cord blood sample was taken after birth and serum were isolated immediately. For atomic absorption spectroscopy, all chemical substances used were of highest purity analytical-reagent grade (Sigma-Aldrich St. Louis, MO. USA). All lab tools were rinsed and scrubbed with adequate deionized water, then soaked and rinsed in 20% nitric acid solution. After that, all tubes were washed again and dried with deionized water.

Zinc concentration was determined by Perkin Elmer 2380 apparatus flame atomic absorption spectrophotometer (Perkin Elmer, Waltham, MT. USA) at the wavelength of 213.9 nm. Samples were prepared according to details in the operating manual. Each measurement was made in triplicate and the mean of the three values was taken.

Normality of variables was tested by the Kolmogorov-Smirnov test. Comparing mean values between groups were analyzed statistically by analysis of variance (ANOVA) test. Pearson correlation coefficient test was used to evaluate the association between variables. Association between zinc, zinc quartiles and other parameters were examined by multiple linear regression models. For statistical analysis, the SPSS software (ver. 18.0, Inc., Chicago, IL) was used. *P* value less than 0.05 was considered significant.

## Results

The mean (SD) age of mothers was 27.66 (5.36) years and the means (SD) of the weight before pregnancy and total pregnancy weight gain were 62.51 (12.74) kg and 13.02 (4.36) kg, respectively.

Among neonates, the mean (SD) of the Apgar score was 9.41 (0.32). Overall 112 (49.8%) of neonates were boys and, the mean (SD) of weight, height, and head circumference of neonates was 3.13 (0.42) kg, 50.02 (2.30) cm, and 34.66 (1.42) cm, respectively.

The mean (SD) of zinc concentration was 0.81 (0.18) ng/ml, and it was higher in AGA 0.82 (0.18) ng/ml than in the LGA 0.75 (0.19) ng/ml and SGA 0.65 (0.12) ng/ml groups, and in the LGA than in the SGA group. There was a significant difference between AGA and SGA groups (*P* = 0.002).

Bivariate correlation analysis showed a significant correlation between zinc and neonates' weight and head circumference (*P* = 0.042 and 0.039 respectively). Table 1 presents the zinc correlations with characteristics of mothers and neonates.

The results of linear regression analysis showed that the zinc concentration has no significant association with other parameters except the weight of neonates (Beta = 0.178, *P* = 0.022) [Table 2]. Moreover, we did not find any significant difference between birth weights across quartiles of zinc levels when Q1 was chosen as reference. (*P* = 0.373) [Figure 1].

## Discussion

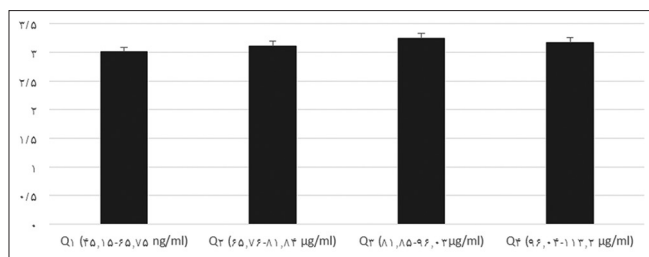
In this study, we investigated the association of cord blood zinc level with birth weight and found a significant

**Table 1: Correlation of maternal cord blood serum zinc with mothers and neonates characteristics**

Parameters	R	P
Mothers characteristics		
Age	0.010	0.899
Weight before pregnancy	0.066	0.419
Pregnancy weight gain	-0.032	0.699
Neonates characteristics		
Sex	0.038	0.632
APGAR	0.073	0.437
Length	0.051	0.526
Weight	0.158	0.042
Abdomen circumference	0.043	0.694
Head circumference	0.165	0.039
Chest circumference	0.047	0.628

**Table 2: Results of linear regression of cord blood zinc level with neonatal characteristics**

Parameters	Beta	P
Weight	0.178	0.022
Height	0.156	0.792
Abdominal circumference	0.03	0.785
Head circumference	0.157	0.697
Chest circumference	0.066	0.498
APGAR	0.03	0.673



**Figure 1: Weight of neonates across quartiles of zinc level quartiles. Standard error of mean (SEM) presented as Error bars. ( $P = 0.374$ )**

association between cord blood zinc level and normal birth weight. This finding is important for the prevention of low and high birth weights, and therefore in the primordial prevention of NCDs.

The mean concentration of cord blood zinc in our study was slightly lower than the normal range in plasma (0.66–1.10 mcg/ml). Some other studies have reported the mean maternal zinc level as  $0.70 \pm 0.11$ <sup>[17]</sup> and  $1.03 \pm 0.17$  mcg/ml<sup>[18]</sup> in India,  $0.47 \pm 0.24$  mcg/ml in Bangladesh,<sup>[19]</sup>  $1.14 \pm 0.23$  mcg/ml in Jordan,<sup>[20]</sup> and  $0.83 \pm 0.21$  mcg/ml in a previous study in Iran.<sup>[21]</sup> These levels show a wide range of zinc concentration in different population; the level documented in the current study is placed at about the average level of this range. We did not have the information about the amount of zinc intake of mothers to evaluate the correlation between zinc levels and diet but the nutritional status of subjects should be considered seriously in this regard.

Moreover, we found that maternal age, weight before pregnancy, the pregnancy weight gain, Apgar score, and anthropometric measures of neonates had no correlation with cord blood zinc concentration. However, normal birth weight was positively correlated with cord blood zinc level.

Some studies from developing countries like Tanzania<sup>[22]</sup> and India<sup>[23]</sup> showed a positive correlation between zinc level and birth weight. However, there was not any association between maternal blood zinc levels and birth weight in some studies.<sup>[24,25]</sup> Also, there was no significant difference between zinc supplemented group compared with the placebo group in term of birth weight among Iranian pregnant women.<sup>[26]</sup> A cohort study in Ethiopia showed prenatal zinc deficiency was not significantly associated with LBW too.<sup>[27]</sup> These controversial findings might be because of differences in the study design and in the populations studied.

Moreover, the role of other minerals and their conjugative or cumulative effects, as well as their interactions with zinc in this regard, should be investigated.

By considering that birth weight is one of the most important health indicators; confirmation of the association of this factor and zinc concentration, and depletion of zinc during pregnancy, it seems follow-up of zinc concentration among pregnant mothers and administration of this element

to zinc-deficient mothers is necessary and will have a dominant effect on maternal and fetus health.

The main limitation of this study is its cross-sectional design. The other limitation is that we did not determine details of maternal lifestyle habits during pregnancy and could not assess their associations with the cord blood zinc level.

## Conclusions

Our findings showed a significant correlation for cord blood zinc level and birth weight. Since the cord blood zinc concentration of normal-weight neonates was higher than those with low and high birth weight, screening of pregnant women for zinc deficiency and designing more interventional clinical trials would be helpful for evaluation of the effectiveness of zinc supplementation or consequences of zinc deficiency or on the outcome of pregnancy, as well as, primordial prevention of NCDs.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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