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The Relationship between Cord Blood and Maternal Serum Zinc Levels and Birth Weight

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ABSTRACT

Background: Examining the relationship between cord blood and maternal serum zinc levels and birth weight.
Methods: A total of 127 infant-mother pairs were assigned to study (n = 58; with birth weight < 2500 g) and control (n = 69; with birth weight ≥ 2500 g) groups. Serum samples were collected from eligible mothers and cord blood of their low birth weight (LBW) or normal birth weight (NBW) healthy newborns. The inclusion criterion for the infant-mother pairs was lack of any medical complications. Serum zinc level was measured by using Inductively Coupled Plasma Mass Spectrometer method and the results were expressed in μg/dl. The two groups were compared in terms of maternal and cord blood serum zinc levels. Then, we evaluated their association with birth weight of neonates in both groups through Student's t-test and one-way analysis of variance using SPSS.
Results: The study protocol was reviewed and approved by the ethics committee of the Urmia University of Medical Sciences (Ir.umsu.rec.1393.108 1393/04/24). Participants were provided with detailed information about the study and were assured that confidentiality would be maintained at all times. Written consent was obtained prior to data collection. The mean age of the pregnant women was 26.1±5.8 years (age range: 18-40 years). The mean birth weight of the neonates in the two groups was 3275.9±552 kg. Pregnant women with serum zinc levels of higher than 70 μg/dl gave birth to neonates with birth weight higher than 3.5, whereas mothers with serum zinc levels of less than 60 μg/dl gave birth to infants with birth weight less than 3 kg (P=0.034). Mean serum zinc level in the cord blood of LBW group was 79.16±19.86 μg/dl, which was significantly lower than that in the NBW group (95.14±17.56 μg/dl; P<0.021). Similarly, mean maternal serum zinc level was 63.98±19.33 μg/dl in mothers who gave birth to LBW neonates, while it was 86.13±20.10 μg/dl in mothers with NBW neonates, indicating that serum zinc level was significantly lower in mothers with LBW infants than in those with NBW infants (P=0.017).
Conclusion: Maternal and cord blood zinc concentrations were shown to be associated with birth weight of the newborns.

Keywords: Low birth weight, Newborn, Pregnant, Serum zinc

Introduction

Low birth weight (LBW) is usually defined as birth weight less than 2500 g; it is an important risk for morbidity and mortality, especially in infants and children under 5 years of age and is a risk factor for morbidity in older age groups (1, 2).

Despite the significant improving trend in most health indicators in rural areas of Iran (3, 4), there is a slow increase in LBW among newborns. Based on the official data extracted form vital statistics of rural areas in Iran, LBW was 2.9% in 1994 with coverage of 83.9% in newborns. In 2004, LBW was 4.7% (coverage: 96.2%), and in 2009, it was 5.1% with a complete (100%) coverage of rural newborns (5). This growing trend of LBW was statistically significant (P=0.0001). LBW is a reliable indicator in assessing and monitoring maternal and child health and finding a rational reason for this increasing trend is critical (6). Other authors have reported increasing trends of LBW from other countries such as Turkey, Brazil, the United States, and the United Kingdom (7-10).

In addition, children with low birth weight are at considerable risk of morbidity; long-term effects of low birth weight affect not only the perinatal period, but also childhood and even adulthood (10). It has been argued that micronutrient deficiencies

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during pregnancy can lead to low birth weight (11). In particular, zinc deficiency is associated with abnormal conditions during pregnancy including congenital malformations (anencephaly), abortion, intrauterine

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; it is required for the production of several enzymes involved in protein synthesis, nucleic acid metabolism, and immune function. Low zinc concentrations of low birth weight newborns were noted in a number of settings in both animal and human populations (11, 12). In humans, however, the research relating neonatal zinc status and birth weight has not produced consistent results. A large number of studies established positive associations between neonatal serum zinc concentration and birth weight (13, 14), whereas some studies proposed negative associations (15) or did not find any significant relationships (16). However, meta-analysis on this issue did not indicate any association between maternal zinc level and birth weight as randomized controlled trials (RCTs) reported conflicting conclusions (17). Therefore, we conducted this study to examine the relation-nship between maternal zinc level and birth weight. Serum zinc level in LBW neonates was also examined and compared with that in term normal birth weight (NBW) infants.

Methods

This study was conducted in Ghamar Bani Hashem Hospital, the only referral obstetrics and gynecology hospital in Khoy, Iran, during 2009. The exclusion criteria for the pregnant women were diabetes mellitus, cardiovascular disease, parathyroid, thyroid, bone, and gastrointestinal disorders, receiving drugs (e.g., diuretics, anticoagulants, anticonvulsants, and antidiabetics), multiple pregnancies, placenta previa, and placental abruption. Further, neonates with history of perinatal insult or requiring admission to neonatal intensive care unit due to any reason were excluded. Venous blood specimens (2 ml maternal blood and 5 ml cord blood) were collected from the participating pregnant women at the end of the third trimester of pregnancy. Cord blood samples were collected from newborns before delivery of placenta. The collected blood was poured into metal-free plain tubes and was allowed to clot at room temperature. Plain tubes were centrifuged for 15 min at 3500 rpm and the serum was separated and kept in trace elements-free tubes and stored at -40°C until analysis. Finally, the samples were stored in dried ice and sent to Modarres University in Tehran for biochemical analysis. Zinc (μg/dl) levels were analyzed in both maternal and cord blood samples. Serum zinc was measured by Inductively Coupled Plasma Mass Spectrometer (18).

After delivery, neonatal weight was measured within 24 hours after birth using the standard procedure (19). Infants were weighed with minimum clothing while the child was restful.

The study was approved by the Human Research Ethics Committee of Urmia University of Medical Sciences and University of Mysore, India. Written informed consent was obtained from both parents or legal guardians of the eligible newborns.

The statistical differences between the two groups were analyzed by Student's t-test and one-way ANOVA followed by Bonferroni post hoc test and calculating the standard error of difference. P-value less than 0.05 was considered statistically significant.

Results

In general, 127 infant-mother pairs were enrolled in the present study. Out of the 127 cases, 58 newborns with birth weight < 2.5 kg were assigned to the study group and the remaining 69 NBW newborns (birth weight > 2.5 kg) were placed in the control group.
Demographic profiles of the infants and their mothers are presented in Table 1. The mean age of the pregnant women was 26.1±5.8 years (age range: 18-40 years). The majority (41%) of the pregnant women were within the age group of 26-36 years, followed by the age group of 20-26 years (36%). Among the subjects, high school and diploma education (55%) had the highest frequency, followed by academic education (34%).

The mean birth weight of the neonates in the two groups was 3275.9±552 g (2011±88 g in LBW neonates and 3101±19 g in the NBW group). Our

Table 1. Demographic information of the pregnant women (n=127)

	Category	N	Percent
Age group (year)	<20	23	18
	20-26	46	36
	26-36	52	41
	≥36	6	5
Mean age (yr)	26.1±5.8		
Educational level	≤Secondary	23	18
	High school and diploma	61	48
	College graduate	43	34
Financial status	No financial problems	25	20
	Moderate	65	51
	Insufficient	37	29

Table 2. Evaluation of the association between birth weight and maternal serum zinc level in the third trimester

Parameters	Reference values	Levels	Birth weight (kg)	F	P-value
Zinc (μg/dl)	66-110	<60	3.0a	24.6	0.034
		60-70	3.4b		
		>70	3.5b		

Note: Superscripts indicate significant difference at 5% level as shown by Bonferroni post hoc test

Table 3. Comparison of low birth weight and normal birth weight neonates regarding serum zinc levels in cord blood and maternal serum

	Weight (g)	N	Mean(SD) serum zinc level (μg/dL)	Range	95% CI	P-value
Neonates	Low birth weight (<2500)	58	79.16(19.86)	53-128	80.52-74.17	<0.021
	Normal birth weight (>2500)	69	95.14(17.56)	55-159	89.30-100.08	
Mothers	Low birth weight (<2500)	58	63.98(19.33)	42-110	59.91-69.97	<0.017
	Normal birth weight (>2500)	69	86.13(20.10)	49-138	80.01-90.02	

findings exhibited that pregnant women with serum zinc levels of higher than 70 μg/dl gave birth to neonates with birth weight higher than 3.5, whereas mothers with serum zinc levels of lower than 60 μg/dl gave birth to newborns with birth weight lower than 3 kg and neonates with birth weight of 3.4 kg had serum zinc levels of 60-70 μg/dl (P=0.034; Table 2).

Serum zinc levels in mothers and their newborns are demonstrated in Table 3. Mean serum zinc level in the cord blood of the LBW group was significantly lower than in the NBW group (79.16±19.86 μg/dl vs. 95.14±17.56 μg/dl; P=0.021). In addition, mean maternal serum zinc level was significantly lower in mothers with LBW infants than those with NBW neonates (63.98±19.33 μg/dl vs. 86.13±20.10 μg/dl; P=0.017; Table3).

Discussion

In the present study, we recognized that mothers of LBW newborns had significantly lower serum zinc levels compared to mothers who gave birth to NBW neonates. This finding is in agreement with those of Jyotsna et al. (14) and Gomez et al. (13) indicating higher serum zinc levels in mothers of NBW newborns compared to mothers of LBW infants. There was a positive relationship between maternal serum zinc level and neonatal birth weight. Zinc is essential for cellular division and differentiation and is an essential nutrient for normal embryogenesis. It is a cofactor for the synthesis of a number of enzymes, DNA, and RNA (20).

Zinc deficiency is linked with complications of pregnancy and delivery, as well as growth retardation, and fetal congenital abnormalities (21). Zinc deficiency during pregnancy may lead to growth retardation in infants by affecting the development of the immune system (22). It has been shown to regulate insulin-like growth factor I activity in formation of osteoblasts; thus, it particularly regulates bone growth (23). A wide range of enzymes and growth hormones, which play an important role in postnatal growth, require zinc during pregnancy (e.g., placental alkaline phosphatase that stimulates DNA synthesis and cell proliferation in pregnancy) (12). Our study results are in line with those of many studies conducted in different parts of the world showing a positive association between maternal zinc status and birth weight (12, 13, 21). Jyotsna et al. recognized that the rate of zinc deficiency was significantly higher in LBW neonates and their mothers as compared to term NBW neonates and their mothers (14). Gomez et al. found a significant positive association between serum zinc level and birth weight (13).

A recent study suggested that the majority of mothers receiving zinc supplementation gave birth to babies with normal birth weight compared to the mothers who did not receive zinc supplementation during pregnancy (24, 25). Another recent study showed a significant difference in plasma cord zinc levels between low and normal birth weight neonates (26). Likewise, the effect of prenatal zinc supplementation on birth weight is argumentative as a Cochrane review declined any significant relationship between prenatal zinc supplementation and delivery of LBW infants, preterm birth, small-for-gestational age, and stillbirth or neonatal death (24).

Our study was an observational study with a small number of cases and we did not study the effect of maternal zinc supplementation on birth weight. Birth weight is hinged upon a number other factors such as gender, gravidity, parity, race, body mass index, and maternal weight gain during pregnancy (27). We could not take into account all these factors and multiple regression analysis should have been performed to control for all these variables before recognizing zinc deficiency responsible for LBW. Despite these limitations, we successfully demonstrated a positive association between low maternal zinc level and low birth weight. Future studies are recommended to investigate ideal dosage, time of initiation, duration, and type or mode of zinc supplementation.

This study had some other limitations. First, the sample included pregnant women referring to one hospital in the northwest region of Iran; thus, the outcomes might not be representative of the whole population of pregnant women in Iran. To prevent such sample fluctuations, a large multicenter study is required. Second, birth weight depends on many other factors such as gravidity, parity, body mass index, and maternal weight gain during pregnancy (28). In addition, we did not control for the effects of sleep quality and stress management and other life style-related factors in our subjects, the impacts of which were proved on birth weight (29, 30). We could not consider all these factors, and multiple regression analysis should have been conducted to check for all of these factors before recognizing zinc deficiency responsible for LBW. These aspects have not yet been analyzed in this population. Moreover, food intake and the role of other micronutrients and vitamins during pregnancy were found to correlate with birth weight (31, 32), but they were not considered in this study. Third, the study had a cross-sectional design, which does not provide us with information about changes during pregnancy, and thus, it does not allow exploring causal pathways. Despite these limitations, we successfully demonstrated a positive relationship between low maternal zinc level and low birth weight.

Conclusion

Our findings illustrated that LBW neonates have significant zinc deficiency as compared to NBW infants. Additionally, mothers of LBW newborns had lower serum zinc levels than mothers of NBW neonates, and lower maternal serum zinc level was positively associated with lower birth weight. Future studies on birth weight should consider exploring life style factors, food intake quality, and role of micronutrients, particularly zinc, with more detail.

Conflicts of interests

None declared.

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