Maternal and Neonatal Zinc and Copper Levels and Birth Weight

Gholamali Maamouri MD[1], Hassan Boskabadi, MD[1*] Mehran Noria, MD[1]
Hosein Ayatollahi, MD[2] Majid Ghayour-Mobarhan, MD, PHD[3] Abbas Heshmati MD[4]
Zohre Samirad, BC[5] Hosein Mohsenzadeh MD [6]

1,2-Neonatal Research Center, School of Medicine, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Iran
3-Department of nutrition and biochemistry, Mashhad University of Medical Sciences, Mashhad, Iran.
4-Cardiovascular Research Center, Avicenna (Bu-Ali) Research Institute,
Mashhad University of Medical Sciences, Mashhad, Iran
5-Head of Educational and Student Services
6-Resident of pediatrics, Mashhad University of Medical Sciences, Mashhad, Iran

Abstract

Introduction

Minerals and trace elements such as zinc and copper have significant influence on development and growth of the fetus and newborn. The purpose of this study was to determine the relationship between low birth weight and maternal and neonatal zinc, copper levels.

Materials and Methods

This case – control study was done from September 2006 to Sep 2007 consisted of 65 infants with birth weight < 2500 g and 65 infants weighing ≥ 2500g. Cord and maternal blood samples collected at delivery were analyzed by atomic absorption spectrophotometry for zinc and copper levels.

Results

Mean serum zinc levels in maternal (P=0.001) and the cord blood (P=0.49) were 6.35 ± 2.09 µmol/l, 12.77±3.83 mol/l and 7.57±1.75 µmol/l , 13.18±2.69 µmol/l of cases and control groups ,respectively.The mean copper levels in maternal (P=0.62) and cord blood (P=0.005) were 21.82±4.45 µmol/l, 5.12±1.54 µmol/l and 21.19 ± 5.34 µmol/l and 3.65±2.04 µmol /l of control and case group, respectively.

Conclusion

This study indicated that there is a relationship between birth weight less than 2500 gr and maternal zinc levels (P<0.001). Mothers with zinc levels less than 6.4 mol/l were 3.8 time more at risk of having an infant with birth weight less than 2500 g. Lower maternal weight (less than 55kg), was associated with 4.2times increase risk of having low birth weight infants.

Key Word

Neonate, Mother, Copper, Zinc, Low Birth Weight

Introduction

Low birth weight (LBW), cause increase rate of death and long-term complications. Minerals and trace elements such as zinc and copper have significant influence on development and growth of the fetus and neonate. LBW neonates accounted for around 10% of all births in Iran [(1)]. The importance of zinc during infancy and zinc deficiency in adults were first founded in the 1970s.[(2)] Pregnancy is accompanied with increase need for micronutrients, such as copper (Cu) and zinc (Zn)[(3)], and decrease can affect the prognosis of pregnancy. Essential trace elements have many functions and are indispensable for life.[(4)] Zinc and copper play a key role in health.[(5)] There are data showing that mild to moderate zinc and copper deficiency (as assessed by available indicators) is quite common in the developing world.

Different studies on animals indicate that, copper and zinc deficiency have accompanied congenital anomalies and fetal growth restriction (FGR).[(6)] Growth is a basis biological function in neonates and infants and a reflection of their general status of nutrition and health.[(7)]

At the cellular level, zinc is used for nucleic acid

*Address for Correspondence: Dr.Hassan Boskabadi, Mashhad University of Medical Science, Mashhad, Iran.
Tel: +98-511-8783210, Fax: +98-511-8425878, E-mail: BoskabadiH@mums.ac.ir

synthesis, cell division, protein digestion, bone metabolism and protection against free radicals. Copper is also an essential component of many organic complexes such as metalloenzymes.

Also decrease in the plasma zinc levels of the study pregnant mothers elevates probability birth of LBW neonates; this suggested fetal growth restriction.[7] The relationship of zinc to copper ratio between mother and birth weight is not clear.[8-10] The status of the trace elements copper and zinc has been evaluated in maternal and cord blood of neonates and assessed the relationship between blood levels of these trace elements and infant weight.

The purpose of this study, was to estimate, seral zinc and copper levels in the maternal blood and cord blood of newborns, to correlate the trace elements in LBW neonates and their mothers in comparison with the values of normal neonates(weight>2500 g) and their mothers.

Material and methods

Subjects

This is a case-control-cross sectional study, which was done in the obstetric ward and toxicology department from September 2006 until September 2007 included 170 mothers and neonates. Inclusion criteria included neonates from healthy mothers, without a history of underlying disease.

Mothers with evidence of identified underlying disease (preeclampsia, gastrointestinal disease, hypertention, infections, malignancy, osteoprosis, endocrinal disorders, incompetent cervix, use of zinc containing drugs, anticonvulsants drug (antiepileptic drugs-AEDs) and Antineurological) multiparus neonates, neonates who were very ill on the first day, severe asphyxia, incompelete history and probable contamination of test tubes were excluded from the study; 2580 infants were born at the this Ghaem Hospital from September 2006 to September 2007; 130 mothers and neonates were evaluated; 40 of were excluded from study and 130 neonates were recruited. They were divided into 2 groups according to birth weight: ≥2500 g (control) and <2500 g (case) and each group included 65 infants. Written consent to participate in the study approved by our ethics committee was obtained.

Clinical investigation

Complete gestational and obstetric histories were taken from recruited neonates. Both case and control groups were selected homogenous in social status, race, mother's nutrition, history of LBW, anemia, mother's age, sexual disease, parity, smoking, prenatal care and weight gain during pregnancy.

Sample collection

Cord and maternal blood samples were collected at delivery (5cc). After seral separation (allowed to clot and then serum removed), blood samples were collected into vacutainer® tubes and transmitted to the laboratory for measuring of zinc and copper concentrations. Before sampling, serum tubes were rinsed by acid and de-ionized water until they were free of trace elements and after 10 min were centrifuged (1000 rpm). Sera were accumulated in poly-ethylene tubes which were rinsed by acid and aliquots of serum were frozen at -20ºC until analysis.

Serum Zinc and Copper analysis

Zinc and copper levels were analyzed by atomic absorption spectrophotometery with air-acetylene fuel.

Statistical analysis

All statistical analyses were performed with SPSS software. Statistical interpretation of the data was performed by frequency table and data analyzing was done with chi-square and student's t test and one way ANOVA analysis. Confounding variables were controlled using logistic regression and general linear models.

Parametric and non-parametric correlations were assessed using Pearson's correlation coefficients and Spearman's correlation coefficients, respectively. Operating curve was utilized to determine cut-off point.

Results

Demographic data

Mean mother's age (year), mother's weight (Kg), birth number, neonate's weight (Kg), neonate's height (cm), head circumferences (cm), sex (male/female) and Apgar score in total study were 25.4, 57, 1.84, 2.627, 46.9, 33, 72.58 and 8.3, In control group were 25.5, 60,1.90, 2.2, 49.3, 34.47, 34.32 and 8.6. In case group were 25.1, 54.41, 1.74, 1.94, 45.05, 31.2, 38.26 and 8, (Fig.1). Mean mother's zn values (mmol/l), neonate's Zn (mmol/l), mother's Cu (mmol/l) and neonate's Cu (mmol/l) in total study were 6.97, 12.98, 21.52, 4.57 and in control group were 7.61, 13.2, 21.83, 5.93 and in case group were 6.43, 12.9, 20.79, 3.71, respectively (Table1); 25.8% (16 cases) of neonates of study group required to be confined to bed. But this rate in control group was 6.5% (P=0.006). Mother's education in both groups was homogenous (P=0.49). There was no significant difference for income (P=0.35) and mother's BMI (P=0.11) between 2 groups.

LBW and mother's age and gravity were not significantly different in our study.

History of LBW existed in 4 infants of the case group and 3 infants of the control group (P=0.31). Pregnancy care was present in 95% of case group and 96.9% of the control group (P=0.68).

Neonatal weight and head circumferences and trace elements

Mean mother's zinc did differ significantly between the 2 groups (P=0.001). Neonate's Cu did differ significantly between 2 groups (P=0.005). Comparison of zinc to copper ratio of neonates in both case and control group were significantly different (P ≤0.0001). The neonate's weight and neonate's head circumferences were significantly related to maternal zinc level (P =0.027,P=0.016). Furthermore, weight and head circumferences of neonates in the total population differed significantly with neonate's Cu level and also with zinc to copper ratio of neonates.

There was significant correlation between total Apgar score of neonates and neonatal Zn and Cu levels (P =0.045).

Neonate's height correlated significantly with neonate's Cu and zinc to copper ratio (P=0.001). Gestational age of neonates was also significantly correlated to neonate's serum level of Cu and zinc to copper ratio (P = 0.001).

Zinc, Copper and LBW infants

Mean values of Cu in neonate's mother was 5.4 18.9 SGA and 4.9 22.4 AGA, which was significant (P<0.013).

Logistic analyzing indicated that elevation of mother's weight and mother's serum Zn, decrease LBW probability. On the other hand, elevated Zn/Cu ratio, increase LBW probability (Table 2).

Using operating curve and determining zinc and copper cut-off point demonstrated that neonate's with ≤4.3 ,serum level of Cu elevate the probability of LBW about 18 times; mothers with serum levels of zinc <6.4 increase probability of birth of LBW neonates about 3.8 times (Table 3).

Discussion

This study indicated that, there is a significant difference between maternal zinc of case and control groups and also Cu and Cu/Zn ratio of neonates of both case and control groups.

Thus, higher maternal weight and maternal zinc level, lower LBW probability. Maternal weight less than 55 Kg, elevate risk of LBW 4 times (P<0.001). Low income mothers are 6.8 times more susceptible for LBW in comparison to moderate income mothers. Our study exhibited that zinc level of neonates were more than their mothers (similar to other studies) which could be caused by active transport of zinc from mother to fetus through placenta as a result of high zinc requirement in the fetus, sufficient transport from mother to the fetus and increased absorption in the fetus. On the other hand, it could be caused by band valency reduction of maternal zinc during pregnancy and physiologic dilution because of

Table 1.Mean, standard deviation of Zn and Cu in mothers and neonates, in both case and control groups

Group Variable	Control	Case	P-value
Zn Maternal $(\mu mol/L)$	7.57±1.75	6.35±2.09	0.001
Cu Maternal $(\mu mol/L)$	21.82±4.45	21.19± 5.34	0.62
Zn Neonatal $(\mu mol/L)$	13.18±2.69	12.77± 3.83	0.49
Cu Neonatal $(\mu mol/L)$	5.12±1.54	3.65± 2.04	0.005
Maternal $\frac{zn}{cu}$ $(\mu mol/L)$	0.36±0.11	0.32 ±0.17	0.21
Neonatal $\frac{zn}{cu}$ $(\mu mol/L)$	2.61±0.89	4.40 ±2.56	<0.001

enhanced maternal blood volumes. This could be due to rising neonatal zinc level as compared to their mothers (P <0.01).
We could not found any significant difference between zinc cord blood level of LBW neonates with neonates weighing more than 2500 g (P=0.49). However, the plasma zinc level of mothers in LBW group were lower (P=0.001) which suggested zinc has a role in fetus growth. In another study, serum zinc level of mothers who gave birth to preterm neonates, were lower.[11] Also another study[11], found a positive relationship between gestational age and serum zinc level of umbilical cord and maternal zinc. On the other hand, Iqbal et al. in bangladesh[13] did not indicate any significant relationship between serum zinc level of umbilical cord and maternal zinc and gestational age. Low serum zinc of mothers could be a cause of preterm birth.
Rwebembera et al.[14] found obvious relationship between newborn's weight and maternal zinc serum level (P=0.002) and mothers with zinc serum level less than 9.1 were 5.2 time more at risk of having infant with birth weight less than 2000 g. Our study demonstrated that, enhanced zinc seral level of mothers, lowered the probability of LBW neonate; zinc level less than 6.4 mol/l causes a 3.8 fold increase of having a LBW neonate. This risk rate in Rwebembera's study[14]was 3 fold.
Rwebembera found a significant relationship between LBW and neonatal zinc, which was in contrast with our study. Maternal and neonatal zinc values in this study were similar to Sakha et al. study but it was lower in comparison to other parts of the world.
It was demonstrated that subjects with mild zinc deficiency did not affect fetal weight. Subjects with moderate to severe zinc deficiency influenced infant weight.
Among the LBW neonates 25% had SGA and their maternal copper levels were significantly different from controls (P= 0.014) but there were no significant difference in maternal zinc serum levels. This suggested that the difference between zinc level of LBW and normal neonates were mainly because of gestational age rather than the difference of neonate`s weight, however more studies need to be done in order to prove this hypothesis because of our small sample size. Kappar and Sakha[11] reported a positive relationship between gestational age and zinc level of umblical cord and maternal serum. Saleh et al. study[14] found no significant relation between maternal and neonate`s cord blood zinc serum levels and gestational age.
In one other study there were no positive or negative relations between maternal Zn, Cu and Fe serum levels and birth weight.
In this study maternal copper serum level was not significantly different in both groups but the neonatal serum copper level was lower in LBW group, which discloses the role of copper in fetal growth. Copper transport is done actively from mother to fetus through the placenta as a result of fetal need. In one study maternal copper serum level was obviously higher than umbilical cord serum level which was similar to our study [15].
Conclusion In this study maternal zinc level (Zn < 6.4) demonstrated a 57.4 % sensitivity, 79.7 % specificity, 72.9% positive predict value and 66.2 % negative predict value in prediction of LBW neonate upon delivery.
In this study maternal copper level (Cu < 4.3) demonstrated a 75 % sensitivity, 64% specificity, 75% positive predict value and 76 % negative predict value in prediction of LBW neonates upon delivery.
This study indicated that there is a relationship between low birth weight (weight<2500 g) and maternal zinc levels (P<0.001).
Mother's with zinc levels <6.4 mol/l were 3.8 time more at risk of having newborns with LBW and neonates with ≤ 4.3, serum level of Cu, have around an 18 fold increase probability of LBW.

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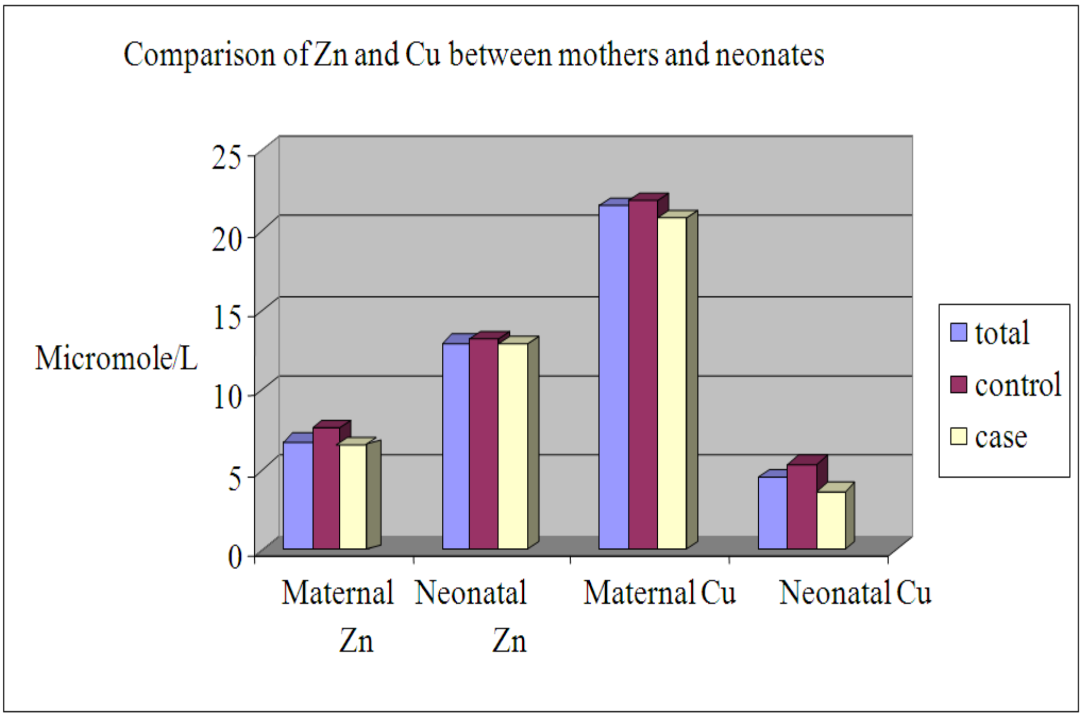
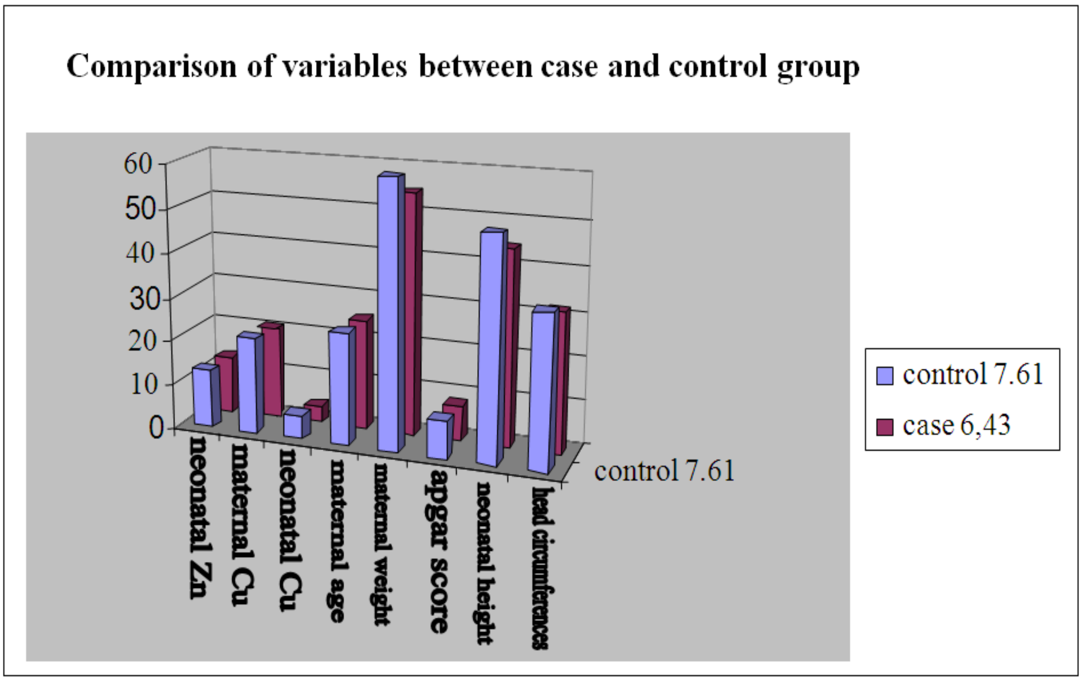
Table 2. Coefficients of logistic regression model of influential variables on LBW

Variables	Regression coefficient	P-value
Maternal weight	0.08 -	0.003
No need to take care and to confine to bed	1.322 –	0.057
Maternal zinc	0.35 –	0.008
Neonate $\frac{zn}{cu}$	0.730+	<0.001

Table 3. Logistic regression coefficients

Variables	Regression coefficient	OR	Confidence interval 95%	P-value
Neonatal Cu $4/3 \geq$	2.89	18.02	5.42-59.96	<0.001
Zn Maternal $6/4 \geq$	1.16	3.19	1.11-9.16	0.031


Comparison of Zn and Cu between mothers and neonates
Micromole/L
25
20
15
10
5
0
Maternal Zn
Neonatal Zn
Maternal Cu
Neonatal Cu
total
control
case


Comparison of variables between case and control group
60
50
40
30
20
10
0
neonatal Zn
maternal Cu
neonatal Cu
maternal age
maternal weight
apgar score
neonatal height
head circumferences
control 7.61
control 7.61
case 6,43