The Relationship between Maternal and Neonatal Umbilical Cord Blood Lead Levels and their Correlation with Neonatal Anthropometric Indices

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Abstract

Background: Lead is an element, which can cross the placenta and enter the fetus during pregnancy if present in the blood of the expectant mother. Therefore, in this study, the level of lead in maternal and umbilical cord blood of neonates was determined, and its relationship with weight at birth, gestational age, height, and head circumference was investigated.

Methods: In this cross sectional study, a total of 70 pregnant women and their newborns were selected at Mousavi Hospital of Zanjan, Iran, based on the inclusion criteria. The level of lead in the umbilical cord blood of newborns and mothers was evaluated, and its correlation with birth weight, gestational age, height, and head circumference was assessed.

Results: The average level of lead in the maternal and cord blood was 11.01 μg/dL and 9.54 μg/dL, respectively, which indicates a significant difference (P < 0.001). In addition, there was a significant inverse linear relationship between the level of lead in maternal blood and birth weight; therefore, an increase in the maternal blood lead level resulted in the lower weight of neonates at birth. However, there was no significant correlation between lead level and gestational age, height, or head circumference.

Conclusions: In this study, the average lead level of pregnant women was 11.01 μg/dL in Zanjan, which is higher than the global standard (10 μg/dL). The birth weight of newborns, whose mothers had higher blood lead levels, was lower than that of other neonates. Therefore, more attention should be paid to the level of lead by the healthcare system in order to take effective measures and reduce lead pollution.

Keywords: Umbilical Cord, Neonates, Lead, Birth Weight, Maternal

1. Background

Epidemiological studies have unveiled the harmful reproductive effects of fetal lead exposure through maternal blood, including sudden miscarriage, preterm labor, congenital anomalies, negative effects on mental and physical growth, and differentiation of the newborn (1). Lead is an element, which can cross the placenta through mother's blood during pregnancy and enter the fetus body; therefore, the level of this element is equal in maternal and cord blood (2).

In highly polluted areas, the umbilical cord blood lead level (BLL) reaches 1.13 ng/mL, which is much lower than its level in the placenta (0.5 μg/mL) (3). This finding indicates the cumulative effect of this element in the body, which can cause several problems for the fetus in the womb due to its teratogenic properties (4). Several factors contribute to the increasing risk of high maternal BLL, including maternal age below 21 years, low economic status, high body mass index (BMI), smoking, and low blood calcium level (5).

Lead is absorbed through ingestion, inhalation, skin contact, and serous or synovial membranes or veins. Overall, exposure to lead in dust is the most important source of contamination (6-9). Adults and children absorb 5% - 15% and 30% - 40% of lead entered into the gastrointestinal tract, respectively (10, 11). The half-life of lead is 25 days in blood, 40 days in soft tissues, 7 years in kidneys, and 25 - 32 years in bones (12). Lead precipitates in the bone marrow and replaces calcium due to the similar size of Pb^{2+} and Ca^{2+} cations (13, 14). In pregnant women, absorption of calcium from the digestive tract and its retention in the kidneys increase because of the growing need for calcium, which augments the activity of bone tissues and increases lead turnover in the blood, as well as BLL (15, 16).

Lead in maternal blood can be transmitted to the fetus

through the placenta from 12 weeks of gestation until birth (17). It first enters soft tissues, such as liver and kidney, infiltrates into the bones, hair, and teeth, and is also excreted in breast milk, causing numerous side effects. Acute encephalopathy is the most serious complication of lead. Behavioral changes, vomiting, abdominal pain, constipation, concentration problems, anemia, growth and mental retardation, reduced IQ, fatigue, headache, weakness, metallic taste in mouth, lead lines in gums, irritability, increased blood pressure, seizure, coma, and even death are the most important complications of lead (10, 11, 18-21).

Although previous studies have indicated the impact of lead at concentrations above 10 μg/dL on pregnancy outcomes (22, 23), recent studies suggest that maternal BLL below 10 μg/dL can also cause symptoms, such as low weight at birth, birth of small for gestational age (SGA) newborns, decreased duration of pregnancy, premature rupture of membranes, and increased blood pressure during pregnancy (4, 24).

Considering the correlation between maternal and umbilical cord BLL, lead transmission to the fetus from the cord blood, and harmful effects of lead exposure on the fetus during pregnancy, it seems necessary to assess umbilical cord BLL and to determine its correlation with neonatal anthropometric indices, such as weight, height, head circumference at birth, and gestational age (15).

2. Methods

2.1. General Description

This descriptive, cross sectional study was performed on 70 pregnant women, admitted to Mousavi Hospital of Zanjan, Iran in 2016. After obtaining permission from the ethics committee of Zanjan University of Medical Sciences (code, ZUMS.REC.1393.125), the necessary explanations were presented to pregnant women, and written consents were obtained. Women were enrolled in the study if they met the inclusion criteria: 1) absence of diseases such as chronic hypertension, preeclampsia, and renal failure; 2) consumption of lead-based drugs; 3) cervical disorders; and 4) uterine anatomical abnormalities according to previous studies. After delivery, newborns, who did not meet the exclusion criteria, i.e., multiple pregnancy, placenta previa, and placental or neonatal anomalies, were entered into the study. Then, 3 mL of maternal and cord blood samples was drawn.

2.2. Serum Isolation from Whole Blood

Blood samples were poured into EDTA anticoagulant tubes to separate the serum from whole blood and to prevent the formation of clots. Then, they were placed in a cen-

trifuge (model 5702; Eppendorf) for 5 minutes at 3000 rpm to isolate the serum from whole blood.

2.3. Serum Digestion by a Microwave Digestion System

After separation, 1 mL of serum sample, together with 8 mL of 65% Suprapur nitric acid (Merck KGaA, Darmstadt, Germany), was poured into the cells of a microwave digest device (Microwave Digestion and Extraction-10; China) to digest organic materials and leave minerals intact. After 25 minutes, the samples were digested and removed. The method used to determine the minerals was based on the standard procedures presented by Metrohm AG (Switzerland) in Bulletin No. 231.2 to measure zinc, cadmium, lead, and copper levels in water; the only difference was that our samples were collected from blood, which was digested by the digestion system for measurements (Table 1).

Table 1. The Process of Blood Digestion in the Digester

Step	Temperature, °C	Time, min	Power, W
1	130	10	400
2	150	5	400
3	180	10	400

2.4. Determination of Minerals Via Polarographic Analysis

For this purpose, 0.5 mL (500 μL) of digested serum sample was poured into the cell, along with 1 mL of buffer solution and 9.5 mL of deionized water. The cell was placed in a polarographic device (model VA797), and the lead level was measured twice (25). In the first step, nitrogen was blown into the sample for 300 seconds to completely withdraw oxygen and eliminate its interfering effects. After measurements in duplicate, 0.1 mL of standard solution was added, and level of lead was measured twice. Then, the same amount of standard solution was added for the second time, and analysis was completed. In each measurement, peak of Pb^{2+} cation was recorded.

2.5. Data Analysis

Data were entered into SPSS version 18 and analyzed at a significance level of 0.05 for all analyses. Descriptive statistics were reported as mean and standard deviation for continuous variables, as percentage for nominal variables, and as T frequency in table formats. In inferential statistics, the distribution of data was evaluated using Kolmogorov-Smirnov test, which showed a normal distribution, and parametric tests were accordingly used to analyze the data. Independent t test was used for comparison of means in the groups. Pearson's correlation coefficient test was also

used to determine the relationship between continuous variables, as the data showed a normal distribution. Also, partial correlation test was used to eliminate the effects of other variables. Finally, a regression model was used to determine the correlation of maternal and umbilical cord BLL with weight, head circumference, and height through eliminating the effects of other variables.

3. Results

3.1. Evaluation of Data Distribution

The distribution of data was first assessed by Kolmogorov-Smirnov test, and the data on maternal and umbilical cord BLL were evaluated using this test. The test was not significant for maternal (P = 0.082) and umbilical cord (P = 0.467) BLL, which shows that these variables had a normal distribution.

3.2. Comparison of Maternal and Umbilical Cord BLL

The umbilical cord BLL of male and female neonates was 9.16 ± 1.90 µg/dL and 10.1 ± 1.18 µg/dL, respectively, and the mean umbilical cord BLL was 9.54 ± 1.7 µg/dL (maximum, 20 µg/dL; minimum, 4 µg/dL). The maternal BLL of male and female newborns was 10.53 ± 2.27 µg/dL and 11.2 ± 1.10 µg/dL, respectively, and the mean maternal BLL was 11.2 ± 1.10 µg/dL (maximum, 30 µg/dL; minimum, 7.9 µg/dL). A significant difference was found in lead level between the umbilical cord and maternal serum samples (P < 0.001) (Table 2).

Table 2. The Basic Characteristics of Male and Female Newborns Under study

Variables	Male (n, 42)	Female (n, 28)	P Value
Mean gestational age, w	39.29 ± 1.01	39.04 ± 1.10	0.334
Mean weight, kg	3.32 ± 0.38	3.17 ± 0.41	0.120
Mean height, cm	49.60 ± 1.76	49.08 ± 2.38	0.300
Mean head circumference, cm[a]	35.32 ± 1.58	34.27 ± 1.18	0.018
Mean maternal BLL, µg/dL[a]	10.53 ± 2.27	11.72 ± 1.77	0.022
Mean umbilical cord BLL, µg/dL[a]	9.16 ± 1.90	10.1 ± 1.18	0.024

[a] Head circumference and maternal and umbilical cord blood lead levels (BLLs) were significantly different in male and female neonates.

3.3. Relationship Between Maternal BLL and Weight, Height, Head Circumference, and Gestational Age of Neonates

The correlation between maternal BLL and weight at birth was also examined, which showed a significant correlation between these variables (P < 0.001). Therefore, an increase in maternal BLL was expected to significantly reduce

the newborn's weight at birth. When the neonates were examined in terms of gender, a correlation was found in both genders. This correlation was also significant in a regression model, which included gender, occupation, age, pregnancy term, and gravidity as the predictive variables, in addition to maternal BLL. Among the variables, maternal BLL had a significant inverse correlation with birth weight (P < 0.001).

The correlation between maternal BLL and neonate's height and head circumference was also assessed. No significant relationship was observed between maternal BLL and neonate's height (P = 0.367), while a significant relationship was found between maternal BLL and head circumference (P = 0.017). In the partial correlation analysis, which considered the impact of other variables, such as gender, parental occupation, gestational age, and gravidity, the relationship was not significant (P < 0.104). Moreover, analysis of the relationship between maternal BLL and gestational age showed no significant correlation between these variables (P < 0.090) (Table 3).

3.4. Relationship Between Umbilical Cord BLL and Neonates' Weight, Height, head Circumference, and Gestational Age at Birth

The correlation between umbilical cord BLL and weight of neonates was examined, which showed a significant correlation between these variables (P = 0.002); therefore, a significant reduction in the neonate's weight was expected by increasing the umbilical cord BLL. However, when the newborns were assessed in terms of gender, this relationship was more significant in male newborns. This association was also significant in a regression model in which variables of gender, occupation, gestational age, and gravidity were entered as predictive variables, in addition to umbilical cord BLL; the umbilical cord BLL had a significant inverse correlation with birth weight (P = 0.008).

The correlation between umbilical cord BLL and head circumference of newborns was also assessed, and no significant correlation was found between umbilical cord BLL and the newborns' height (P = 0.251) and head circumference (P = 0.088). Similarly, there was no significant correlation between umbilical cord BLL and gestational age (P = 0.580). The partial correlation between birth weight and umbilical cord and maternal BLL was assessed by eliminating the effects of gestational age, sex, gravidity, and parents' occupation (correlation coefficient, -0.328 and significance level, 0.008; correlation coefficient, -0.454 and significance level < 0.001, respectively) (Table 4).

Table 3. The Correlation Coefficients Between Maternal Blood Lead Level (BLL) and Weight, Head Circumference, Height, Gestational Age, and Umbilical Cord BLL in Male and Female Newborns

Variables	Gender			
	Male		Female	
	Correlation Coefficient	Significance Level	Correlation Coefficient	Significance Level
Birth weight	-0.504[a]	0.001	-0.445[a]	0.018
Head circumference	-0.298	0.055	-0.034	0.864
Height	-0.166	0.292	0.041	0.835
Age at birth	-0.189	0.232	0.168	0.393
Umbilical cord BLL	0.857[a]	< 0.001	0.376[a]	0.049

[a]The neonates' birth weight had a significant inverse correlation with maternal BLL in both genders. Also, maternal BLL had a significant correlation with umbilical cord BLL in both genders.

Table 4. The Correlation Coefficients Between Umbilical Cord Blood Lead Level (BLL) and Neonates' Weight, Head Circumference, Height, Gestational Age, and Maternal BLL in Male and Female Newborns

Variables	Gender			
	Male		Female	
	Correlation Coefficient	Significance Level	Correlation Coefficient	Significance Level
Birth weight	-0.475[a]	0.002	-0.053	0.789
Head circumference	-0.263	0.093	0.260	0.181
Height	-0.193	0.220	0.019	0.923
Age at birth	0.149	0.347	0.209	0.286
Maternal BLL	0.654[a]	< 0.001	0.476[a]	0.038

[a]The weight of male neonates had a significant inverse correlation with umbilical cord BLL. Also, maternal BLL had a significant correlation with umbilical cord BLL in both male and female neonates.

4. Discussion

In this study, 70 pregnant women and their newborns were examined, and a significant correlation was observed between maternal and umbilical cord BLL. Furthermore, maternal and umbilical cord BLL showed a significant correlation with the newborns' weight. Based on the findings, an increase in maternal and umbilical cord BLL resulted in a reduction of birth weight; however, no significant relationship was found with variables of gestational age, height, and head circumference of newborns.

In this regard, Andrews et al. in a review study examined the relationship between prenatal lead exposure and low birth weight of newborns. Their results confirmed the relationship between these variables in line with our study, although the findings vary with respect to the study design, sample size, and control level (26). Moreover, in a study by Pawlowski et al. in USA in 2006, it was reported that BLL higher than 10 μg/dL in the placenta increases the risk of preterm labor and birth of SGA newborns (27). In our study, a significant relationship was found between these variables, and an increase in umbilical cord BLL significantly reduced the weight of newborns.

Another study from Mexico by Afieche et al. showed that prenatal exposure to lead can not only result in the lower birth weight of newborns, but also lead to the progression of weight loss in female newborns until early childhood. However, in this study, lead exposure was assessed through analysis of lead in maternal bones (28). In another study, the researchers also showed a significant relationship between birth weight and prenatal exposure to lead (29).

A study by Chen et al. showed a significant relationship between maternal exposure to lead (through measurement of lead in the mother's blood) and birth of SGA newborns (30). Also, in a study by Kaul et al. from India in 2002, it was reported that the rate of pregnancy complications in women having a high BLL was higher than that of other women, which largely affects the weight of neonates and can explain the significant relationship between the umbilical cord BLL of newborns and their weight in our

study (31).

Although lead is one of the most toxic studied metals for the fetus during pregnancy, there are studies reporting no effects on the outcomes of pregnancy. In this regard, Mirghani examined the relationship between lead exposure and pregnancy outcomes, including gestational age, premature rupture of membranes, and even birth weight, and found no significant relationship between exposure to lead and these pregnancy outcomes (32).

In another study on 1578 mothers (age, 16 - 50 years), performed at Al-Kharj hospital of Saudi Arabia during 2005 - 2006, the levels of lead, cadmium, and mercury were measured in maternal blood, umbilical cord blood, and placenta, and their effects on birth weight, SGA, and thickness of placenta were assessed. The results showed that unlike other heavy metals, lead only affects the thickness of placenta and has no impacts on the weight and SGA of newborns, while in our study, an increase in maternal BLL reduced the weight of neonates (33). Additionally, in a case report of lead poisoning, a 33-year-old woman at the gestational age of 19 weeks was referred for pregnancy care with a history of pica. In the primary test, BLL was 26 μg/dL. She gave birth at the gestational age of 38 weeks and delivered an infant with a normal birth weight (34).

In another study by Iranpour et al. from Isfahan, Iran in 2007 on the comparison of maternal and umbilical cord BLL between neonates with intrauterine growth retardation (IUGR) and healthy newborns, BLLs were measured in the umbilical cord and maternal venous blood samples of 32 IUGR and 34 healthy newborns. According to the results, the mean BLL in the cord blood of IUGR newborns was not significantly different from that of normal newborns, whereas maternal BLL of IUGR neonates was lower than that of term and normal mothers; however, the difference was not significant. The maternal BLL was strongly associated with umbilical cord BLL in both groups of neonates. Nevertheless, umbilical cord and maternal BLL were not associated with low birth weight (35).

As birth weight is one of the most important health indicators in neonates and largely reflects sufficient fetal growth, the impact of lead on this indicator should be identified, and independent analyses should be conducted on both genders. In this study, the mean umbilical cord BLL of male and female neonates was 9.169 μg/dL and 10.1 μg/dL, respectively.

4.1. Conclusions

The elderly, children, cardiopulmonary patients, and in particular pregnant women and their fetuses, are vulnerable to environmental pollution. Low birth weight is among the outcomes of environmental pollution, which threatens pregnant mothers and their fetuses. Many studies have been conducted worldwide to reduce low birth weight and prematurity, and various factors, including effects of metals (e.g., lead, copper, and zinc) on the weight of neonates, have been taken into account. The results of our study showed that BLL of pregnant women was 11.06 μg/dL on average in Zanjan, which is higher than the maximum global standard (10 μg/dL), and the neonates of these mothers had a lower birth weight, compared to those of other mothers. Since low birth weight is an indicator of poor health at the community level and imposes medical expenses and mental burdens on families and societies, it seems that pregnant mothers should be screened for BLL, given the impact of lead on neonatal birth weight.

4.2. Limitations

The main limitation of this study was inadequate funding for recruiting a larger sample size.

Acknowledgments

Footnotes

Conflicts of Interest: The authors declare no conflicts of interest.

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