Comparison of blood lead levels of mothers and cord blood in intrauterine growth retarded neonates and normal term neonates

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ABSTRACT

Objectives: To compare the blood lead levels of mothers and cord blood in intrauterine growth retarded (IUGR) neonates and normal term neonates.

Methods: From April to December 2005, we carried out a cross-sectional, prospective study in Isfahan University of Medical Sciences, Isfahan, Iran. Blood lead levels were measured in the umbilical cord and maternal venous blood samples in 32 mother-infant pairs with IUGR full term neonates, and 34 mother-infant pairs with normal full term neonates. Blood-lead levels were analyzed by atomic absorption spectrometry.

Results: The mean lead concentration in neonates of IUGR and normal groups was not significantly different (107.47 ± 16.75 versus 113.08 ± 19.08 µg/L, p=0.2). The mean lead concentration in mothers of IUGR group was lower than normal groups, but this difference was not significant (124.56 ± 19.71 versus 135.26 ± 26.91 µg/L, p=0.07). Maternal lead levels were strongly related with cord blood in both IUGR and normal groups (r=0.8, p<0.0001). Maternal and cord blood lead levels was not correlated with birth weight of newborns in either group. Overall, 65.6% of IUGR neonates and 76.4% of normal neonates was above the critical level defined for lead poisoning as >100 µg/L by the centers for disease control; however, this was not statistically different between the groups.

Conclusion: Our results indicate that the mean lead level was not higher in IUGR neonates, and the whole blood lead was not related to the birth weight. In addition, maternal and cord blood lead levels were strongly correlated, and there were remarkable lead burdens on both the mothers and their neonates in this industrial area.

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Determining whether a fetus is at risk for sub-optimal growth is a major focus of effective prenatal care.[1] Intrauterine growth retardation (IUGR) is an important cause of prenatal mortality and morbidity.[2] The sequelae of IUGR include stillbirth, failure to thrive and neurodevelopment delay in childhood. In addition, IUGR appears to be an antecedent to some degenerative diseases such as hypertension, vascular disease, and diabetes in adulthood.[3,4] The fetal growth restriction may be caused by fetal, placental or maternal factors.[5,6] Environmental factors may play an important role in this regard.[7,8] Maternal lead is transferred to the fetus via the placenta, and some studies reported higher levels of lead in mothers with IUGR neonates.[7,9] It seems that lead is not necessary for any physiologic function in the body, and prenatal exposure to lead produced toxic effects in the fetus, including pre-term delivery, low birth weight, and impaired mental development.[10] However, several studies in humans have not consistently demonstrated an inverse relationship between lead exposure and birth weight,[11,12] perhaps due to the numerous factors that can influence birth weight and to the difficulty of accurately assessing prenatal lead exposure. The present study was designed in order to control one of the possible environmental risk factors of IUGR in an urban area of Isfahan, an industrial city in the central part of Iran. The aim of this study was to compare the blood lead levels of maternal-cord pairs, in normal and IUGR term neonates.

Methods. From April to December 2005, 66 full-term neonates and their mothers who delivered at Shahid-Beheshti Hospital, a Teaching Hospital affiliated to Isfahan University of Medical Sciences, Iran, were enrolled in this study. Based on birth weight, we divided neonates into 2 groups: the first group (n=34), included normal deliveries at term, (gestational age is >37 weeks) and birth weight is ≥2500 gm; and the second group (n=32), consisted of IUGR neonates, which included term neonates (gestational age is >37 weeks) and birth weight ≤ 2500 gm. The Ethics Committee in Isfahan University of Medical Sciences approved the study, and informed written consent was obtained from mothers before their accouchement. The anthropometric data from mother and newborn pairs, as well as, umbilical cord and maternal venous blood samples were gathered within 12 hours of delivery. Information on estimated gestational age, based on the date of last menstrual period, and characteristic of the birth and newborn period was extracted from the medical records. The exclusion criteria included premature neonates (gestational age <37 weeks), medical conditions that could cause low birth weight, such as multiple gestation, pre-eclampsia, psychiatric, kidney, or cardiac disease, gestational diabetes, history of repeated urinary infections, seizure disorders requiring daily medication, ingestion of corticosteroid, or blood pressure (140 mm Hg systolic or >90 mm Hg diastolic). Blood samples was collected from each mother-infant pair in trace metal free tubes. The venous maternal blood was obtained within 12 hours of delivery. Placental blood from the umbilical vein was taken from the newborn at delivery time. Heparinized blood samples was kept at 40ºC until being analyzed. Blood samples were analyzed using an atomic absorption spectrophotometer instrument (Perkins-Elmer 3030, USA) equipped with a graphite furnace at the Clinical Toxicology Laboratory in Emam-Reza Hospital in Mashad city.

In the statistical analysis, data were stored in a computer database, and analyzed after data management for excluding outliers. All analysis was performed using SPSS for windows version 10.5 (Chicago Inc., USA). The difference between means was assessed by independent samples t-test. Bivariate correlation between quantitative variables was tested by Spearman's coefficient. A *p*-value of less than 0.05 was considered significant.

Results. Clinical characteristics of newborns and their mothers in both groups are shown in **Table 1**. As presented in **Table 2**, the mean lead concentration in mothers of the IUGR group was lower than in normal weight groups, but this difference was not significant. The mean lead concentration in neonates of the IUGR and normal weight groups was not significantly different. Maternal lead levels were strongly correlated with cord blood in both the IUGR and normal weight groups (r=0.8, $p<0.0001$, and r=0.82, $p<0.0001$). There was no significant relationship between cord blood lead levels and birth weight of newborns in IUGR and normal weight groups (r=-0.36, $p=0.84$, and r=0.19, $p=0.26$). The results also showed no significant correlation between lead levels of

Table 1 - Characteristic (mean ± SD) of newborns and mothers.

Characteristic	Case (IUGR)	Control (normal)	*P*-value
Newborn characteristic (n=66)	32	34	
Female n (%)	23 (71.87)	16 (47)	0.04
Male n (%)	9 (28.15)	18 (53)	
Birth weight (g)	2150.94 ± 314.28	3144.12 ± 262.99	<0.0001
Head circumference (cm)	33.21 ± 0.99	35.01 ± 1.06	<0.0001
Length (cm)	46.95 ± 2.61	50.70 ± 1.09	<0.0001
Maternal characteristic (n=66)	32	34	
Age, years	27.31 ± 5.78	24.73 ± 4.41	0.045
Pre-pregnancy, BMI (kg/m^2)	22.95 ± 3.47	22 ± 2.58	0.23
Weight gain during pregnancy (kg)	11.06 ± 2.85	14.98 ± 3.39	<0.0001
Height (cm)	162.32 ± 6.83	167.26 ± 7.85	0.005

IUGR - intrauterine growth retardation, BMI - body mass index

Table 2 - Maternal and newborn whole blood lead concentration in the intrauterine growth retardation (IUGR) and normal groups (N=66).

Parameters	Lead level (µg/L)			
	Mother		Newborns	
	IUGR	Normal	IUGR	Normal
Number	32	34	32	34
Mean value	124.56	135.26	107.46	113.08
SD	19.71	26.91	16.75	19.08
Range	95-172	99-258	71-146	71-180
95% (CI)	-22.36, 0.96		-14.47, 3.23	
P-value	0.07		0.20	

SD - standard deviation, CI - confidence intervals

mothers and the birth weight of neonates in the IUGR and normal groups (r=-0.24, p=0.17, and r=0.18, p=0.3). Overall, 65.6% of IUGR neonates and 76.4% of normal neonates had lead levels above the critical level defined for lead poisoning as >100 µg/L by the centers for disease control,[13] but this was not statistically different between groups (p=0.49).

Discussion. In this study conducted in an industrial city, we found very high levels of lead in mothers and neonates. However, the mean lead level was not higher in the IUGR neonates. We also did not found any significant association between the cord blood lead level of neonates in both groups and their birth weight.

Prenatal lead exposure has been found to be associated with IUGR, some congenital anomalies, neurodevelopment deficit such as intelligence, information processing, memory and verbal skills, as well as behavior problems.[14-17] Some recent studies suggest an inverse relation between maternal lead burden, estimated by bone lead concentrations, and birth size in offspring for women with relatively low blood lead burden, estimated by bone lead concentrations, and birth size.[7,18] Controversial reports exist about a consistent association of maternal blood lead levels with pre-term delivery, fetal growth parameters such as birth weight and head circumference.[19] However, increased risk of low birth weights suggest that lead exposure may affect birth weights through IUGR rather than prematurity.[7] Such inconsistent findings may be due to differences in the study population and research methodologies.[19] The results of previous studies vary greatly when maternal and cord blood lead were used as the biologic marker of intrauterine lead burden. One study from India, reported that both maternal and cord blood lead levels were significantly higher in IUGR than in normal neonates.[20] Despite this, the other studies,[11,21,22] including the current one, did not confirm this association, or have found an association in the opposite direction.[12]

Our study revealed no association between the values of blood lead level and the somatometric variables of newborn infants. Probably the best explanation for finding no relation of cord blood lead level and any growth parameters of the neonates in some reports, such as our research, may be due to the use of blood lead as the biomarker to assess lead burden or due to the numerous factors that can influence birth weight and the difficulty to control all independent causes of size at birth. Gonzalez-Cossio et al[7] showed that maternal bone-lead burden, but not a maternal whole blood lead levels or umbilical cord blood lead levels, have been related to lower birth weights. More than 95% of lead in whole blood is bound to red cells.[23] The lead that is available to cross the placenta is derived from lead that is in free state in plasma.[24] Plasma lead levels may fluctuate significantly without a discernible change in whole blood lead levels; moreover, plasma lead seems to have a positive correlation with levels of lead in bone.[25] As pregnancy and lactation stimulate increased bone turnover, mobilization of lead from bone into plasma constitutes a significant threat to the fetus that is not well estimated by measuring lead in whole blood.[7] Bone lead is an indicator of cumulative rather than recent lead exposure and might be a better biomarker of plasma lead.[26] In addition, placenta lead was used as a biomarker of prenatal lead exposure in previous studies.[27] However, Iyengar and Rapp,[27] believe that placental lead could be a good biomarker of fetal lead exposure in a way that adequately reflects fetal lead toxicity, at least one study reported that higher placental lead levels were not related to a smaller weight, head and abdominal circumference or shorter length at birth.[10] Therefore, bone lead might be a better biomarker for evaluation of the association between maternal lead burden and birth weight.

Our results confirm the previously reported finding that maternal lead burden is an important determinant of infant lead levels at birth. It has generally been assumed that there is no general enhancement or barrier to transfer.[28] Although, maternal blood lead levels are on average approximately 30% higher than that of her infant.[29] In the current study, the mean maternal lead level was approximately 30% higher than their neonates in both groups. Although, our data did not show any relation of a whole blood lead level in the mother and their neonates birth weight, but a remarkable percent (approximately 2/3) of mothers and their neonates in both groups were above the critical level defined for lead poisoning as >100 µg/L by the Centers for Disease Control.[13] More than 95% of body lead burden is stored in the bones. The lead accumulation in bones is related to calcium. Due to the increased demand for calcium during the periods of increased bone turnover such as growth, pregnancy and lactation, lead is mobilized from the bones.[26] The inverse relation between calcium consumption and blood lead level is well-documented in both animal and other human populations.[18] In our study, which may be due to not giving enough calcium supplements to pregnant mothers, the high frequency of mother in both groups had remarkable blood lead level with no significant difference in the IUGR and normal groups. However, environmental contamination and poisoning must be considered for these high levels of whole blood lead in our study.

In conclusion, our results indicate that the mean blood lead level was not higher in IUGR neonates and in their mothers. Whole blood lead was not related to the

birth weight in IUGR and normal infants. In addition, due to remarkable lead burdens on both the mothers and their neonates in this industrial area, preventive strategies must be conducted against air pollution in our country. Additional research in this area is needed to seek the association of other biomarkers such as the bone lead level and the placenta lead level with birth weight. Calcium supplementation may decrease fetal lead exposure and the effect of giving calcium supplement to pregnant mothers in order to decrease the fetal lead exposure and should be evaluated in future studies.

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