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Umbilical Cord-blood Lead Levels and Pregnancy Outcome

Ibrahim Ramadan El Sawi and Mahmoud Helmy El Saied
Department of Obsteric and Gynecology and Forensic Medicine and Clinical Toxicology, Al-Azhar Faculty of Medicine, Egypt

Corresponding Author: Ibrahim Ramadan El Sawi, Department of Obsteric and Gynecology and Forensic Medicine and Clinical Toxicology, Al-Azhar Faculty of Medicine, Egypt

ABSTRACT

Lead is a toxic metal for which it is hard to avoid exposure, due to its widespread distribution in the environment. Numerous activities involving lead and its products are carried out in Egypt. The present study was designed to investigate the status of prenatal lead exposure and birth outcomes. It included 100 pregnant females in their third trimester of pregnancy that underwent blood sampling for lead concentration in the cord blood at delivery; and these levels were estimated to be lower or higher than 10 μg dL^{-1}. Adverse maternal outcome and Neonatal anthropometric measurements were correlated with cord plasma lead levels. There was significant decrease of hemoglobin, gestational age at delivery, gestational weight, height and head circumference in cases with higher lead in comparison to cases with lower lead. In addition, there was increase of previous abortions, Cesarean Section (CS), Preterm Premature Rupture of Membranes (PPROM) and preterm delivery, in cases with higher lead in comparison to lower lead. There positive correlation between gravidity and abortion with lead concentration. On the other hand, there was inverse correlation between baby weight and lead concentration. There is an association between cord blood lead concentration and adverse pregnancy outcome. It was associated with increased rate of CS, PPROM and preterm labor and decreased anthropometric measurement of the neonate.

Key words: Lead, toxic metal, pregnant females

INTRODUCTION

Worldwide increase of industrial pollution and manmade or natural combustion activities leads to voluntary or involuntary exposure to environmental pollutants such as heavy metals, from various sources. The most sensitive stage of human development is the prenatal life, as there is a high degree of fetal cellular division and differentiation. Compared to adults, the fetus is highly susceptible to teratogens, even at low exposure levels that do not harm the mother (Wells *et al.*, 2010). Effects of prenatal exposure to different pollutants may be expressed as a chronic diseases either immediately or later in life (Silbergeld and Patrick, 2005).

Timing of exposure has a determinant role on the consequences of the exposure (e.g., If exposure occurs during the time when organogenesis, permanent structural abnormalities might occur, while exposure after organogenesis is complete might lead to only functional abnormalities) (Sly and Flack, 2008).

Intrauterine exposure to heavy metals has been studied but there is a growing concern about the effects on pregnancy outcomes at levels lower than international guidelines

(Holmes *et al.*, 2009). Heavy metals reached the fetus by trans-placental transfer. Placenta is a barrier that permits nutritional substances and oxygen to reach the fetus and prevent toxic compounds (Carter, 2009).

Lead is a multi-target toxin that affects the gastrointestinal, hematopoietic, cardio-vascular, nervous, immune, reproductive and excretory system (Lanphear *et al.*, 2005; Herman *et al.*, 2007).

Although, it is well known for a long time, that, lead (Pb) is reproductive toxicant that crosses the placenta (Gardella, 2001), questions remain about the association between prenatal Pb exposure and pregnancy outcomes. In addition, previous studies examining the association between prenatal Pb exposure, birth weight, length of gestation and intrauterine growth have differed in their conclusions (West *et al.*, 1994; Sowers *et al.*, 2002).

The present work was designed to investigate the relation between umbilical cord blood lead levels and pregnancy outcome.

MATERIALS AND METHODS

Patients: The study was carried out in Antenatal Clinic of Obstetrics and Gynecology Department, Al-Azhar Faculty of Medicine, New Damietta, during the period from 1st, July 2012 till the end of December 2012. It included 100 pregnant women in their third trimester of pregnancy.

Inclusion criteria: Healthy pregnant women with singleton pregnancy and at third trimester.

Exclusion criteria:

- Women with BMI>30 or <18 kg m^{-2}
- Women having a psychiatric disorder
- Women with daily consumption of alcoholic beverages
- Women with addiction to illegal drugs
- Smokers
- Women with high-risk pregnancy as preeclampsia, renal or circulatory disease
- Women with seizures under medical treatment

Methods: All women were inquired about socio-demographic data and lifestyle issues. In addition, there were asked about current and previous pregnancies, medical history, occupation and environmental exposures.

Furthermore, all women were examined clinical in a systematic manner. Ultrasound examination was done to estimate Fetal Birth Weight (FBW), Amniotic Fluid Index (AFI) and Intrauterine Growth Restriction (IUGR). Routine antenatal care was applied during third trimester to report any complications as preterm labor or Premature Rupture of Membranes (PROM).

Venous blood sample of 5 mL were drawn from cord blood and collected in heparinized tube directly after delivery of the fetus and were immediately centrifuged (800×g, 6 min) to separate plasma from whole blood, thus avoiding transfer of lead from erythrocytes. Each plasma fraction was then pipetted into two ultra-cleaned Eppendorffs tubes (2 mL) and levels of lead are determined immediately if possible or plasma samples were stored at -20°C, till the time of analysis. For each sample, lead concentration was measured using atomic absorption spectrophotometery as described by Sakai *et al.* (1998). According to ATSDR (2007), the cutoff levels of lead ≥10 μg dL^{-1}

was considered to be excessive for infants, children and women of child-bearing age. Thus, in the present study, cases were divided into two groups, the first included cases who had lead ≥10 μg dL^{-1} (30 cases) and the second who had lead concentration <10 μg dL^{-1} (70 cases).

For each mother, the following were searched for: premature rupture of membranes, preterm delivery and mode of delivery.

For each neonate, the following data were collected: Anthropometric measurements at the moment of birth (weight, height and head circumference) and values of the APGAR scores at 1st and 5th min.

The main sources of lead exposure in subjects of the present study are believed to be air pollution, cosmetic use, drinking water and the food chain. Contamination of agricultural water by industrial sewage and lead washed out of the air by rain, leading to entering of lead food chain.

Statistical analysis of data: All statistical analyses will be performed using SPSS software version 16.0 for Windows. A $p \leq 0.05$ was set as the level of statistical significance. Descriptive statistics were reported as an arithmetic Mean±SD. Categorical variables were expressed as frequency and percent distribution. Comparison between groups was done using student (t) test or Chi square test. For correlation between two parameters, Pearson's correlation coefficient (r) was calculated. It was mild if r <0.3, if it was between 0.3 and 0.7, the correlation is moderate and if >0.7 the correlation is powerful.

RESULTS

In the present study, there was significant decrease of hemoglobin concentration and gestational age at delivery in cases with higher lead in comparison to lower lead (9.79±0.48, 34.23±1.27 vs 10.63±0.57, 36.92±2.03, respectively). On the other hand, there was significant increase of previous abortions in higher lead in comparison to lower lead (0.43±0.56 vs 0.14±0.35, respectively). In addition, there was significant increase of CS in higher lead in comparison to lower lead (56.7 vs 18.6%, respectively). In addition, there was significant increase of PPROM and Preterm delivery in higher lead in comparison to lower lead (30.0, 33.3% vs 0.0, 0.4%, respectively) (Table 1).

Table 1: Comparison between higher and lower lead groups as regard to clinical data of studied mothers

Parameters	Higher lead (n = 30)	Lower lead (n = 70)	Test	p-value
Age (years) (Mean±SD)	26.40±2.83	27.27±1.69	1.76	0.08ns
BMI (kg m^{-2})	26.86±1.37	27.17±1.02	1.27	0.21ns
Pulse (beat min^{-1})	80.90±4.55	79.05±4.19	1.96	0.52ns
Systolic BP (mm Hg)	118.67±8.89	117.14±6.73	0.93	0.35ns
Diastolic BP (mm Hg)	77.33±5.97	75.50±5.59	1.47	0.14ns
Hemoglobin concentration (g dL^{-1})	9.79±0.48	10.63±0.57	6.95	<0.001*
Gestational age	34.23±1.27	36.92±2.03	6.70	<0.001*
Previous abortions	0.43±0.56	0.14±0.35	3.11	0.002*
CS delivery	17.0 (56.7%)	13.0 (18.6%)	12.32	<0.001*
Associated morbidity				
PPROM	9.0 (30.0%)	0.0 (0.0%)	50.49	<0.001*
Preterm labor	10.0 (33.3%)	1.0 (0.4%)		

ns: Non-significant, *Significant, SD: Standard deviation, BMI: Body mass index, CS: Cesarean section, PPROM: Preterm premature rupture of membranes

Table 2: Comparison between higher and lower lead groups as regard to gender and anthropometric measurements of studied neonates

Parameters	Higher lead	Lower lead	Test	p-value
Male gender	11.0 (36.7%)	40.0 (57.1%)	3.52	0.061ns
Anthropometric measurements				
Weight	2.51±0.20	3.09±0.31	9.40	<0.001*
Length	40.70±1.96	44.32±2.14	7.94	<0.001*
HC	32.13±1.13	33.97±1.19	7.16	<0.001*

ns: Non-significant, *: Significant, HC: Head circumference

Table 3: Correlation between different parameters and lead concentrations

	Lead concentrations	
Variables	Pearson correlation (r)	p-value
Age	-0.187	0.062
BMI	-0.078	0.439
Gravidity	0.280	0.004*
Abortion	0.290	0.005*
Baby weight	-0.630	<0.001*

In the present work, there was non-significant difference between higher lead and lower lead as regard gender (males represent 36.7% in higher lead vs 57.1% in lower lead). On the other hand, there was significant decrease of gestational weight, length and head circumference in higher lead in comparison to lower lead (Table 2).

In the present study, there was mild, significant, positive correlation between both gravidity and abortion (r = 0.28, 0.29; p = 0.004; 0.005, respectively) and lead concentration. On the other hand, there was moderate (r = -0.630), inverse, significant (p<0.001) correlation between baby weight and lead concentration (Table 3).

DISCUSSION

Lead is a widespread environmental pollutant associated with adverse health effects in humans. It is likely that lead impairs child growth and development, especially when lead exposure occurs in the prenatal period (Needleman, 2004).

There are many epidemiologic studies on the adverse effects of prenatal lead exposure on children's health, that focused on populations with relatively high lead levels (Opler *et al.*, 2008; Rahman *et al.*, 2012; Xu *et al.*, 2012), although blood lead levels below 10 μg dL^{-1} are much more common in the general population (Wells *et al.*, 2011).

According to researchers best of knowledge, few studies have estimated the relationship between low-level prenatal lead exposure and birth outcomes. Thus, the present study was designed to investigate the status of prenatal lead exposure and birth outcomes.

It the present study, cord blood lead is used as it is considered a potential predictor of child development and has been used in many studies as an indicator of prenatal lead exposure (Gomaa *et al.*, 2002).

Mean plasma lead concentration in the present study (8.77±4.03 μg dL^{-1}; 14.23±2.60 in higher lead group and 6.42±1.40 in lower lead group) was higher than the reference data from the NHANES study from 1999 to 2002 (Mean: 1.52 mg dL^{-1}; n = 4525) (Crinnion, 2010); a study in France (1.9 mg dL^{-1}; n = 1017) (Yazbeck *et al.*, 2009); and Shanghai (5.61 mg dL^{-1}; n = 400) (Zhu *et al.*, 2011). On the other hand, Rahman *et al.* (2012) reported that, the Mean±SD, cord blood lead concentration was 12.05 mg dL^{-1} in Kuwait.

In the present study, there was non-significant difference between higher and lower lead as regard mother's and BMI, pulse or blood pressure. Vigeh *et al.* (2006) reported that, there was no significant difference between cases with higher and those with lower lead concentration as regard weight, height or BMI, systolic or diastolic blood pressure, although they used lower limit values.

In the present work, there was significant decrease of hemoglobin concentration and gestational age at delivery and increase of previous abortions, caesarean deliveries, PPROM and preterm deliveries in cases with higher lead in comparison to lower lead. These results are in agreement with that reported by Naicker *et al.* (2010) who found that, higher parity and abortion levels ($p = 0.01$) was also significantly associated with higher cord blood lead levels. In addition, Vigeh *et al.* (2006) reported that, blood lead concentrations were higher in PROM deliveries than in non-PROM deliveries. Also, early fetal membrane rupture has been shown in subjects at higher blood lead concentrations (>13 mg dL^{-1}).

Furthermore, a group of complicated pregnancies, including eight PROM cases, was found to have higher placental lead concentrations than a group of 53 normal deliveries (154 and 103 ng g^{-1}, respectively) (Falcon *et al.*, 2003). However, old study has failed to find significant relationships between increased lead concentrations and the risk of PROM delivery (McMichael *et al.*, 1986). Since, PROM is a multifactorial problem, individual susceptibility and/or other environmental or laboratory factors could influence the results.

In the present study, non-significant difference between higher lead and lower lead as regard gender. On the other hand, there was significant decrease of gestational weight, length and head circumference in higher lead in comparison to lower lead. These results are in agreement with Xie *et al.* (2013) who reported that the square root of maternal blood levels were associated with a small but statistically significant decrease in birth weight.

In the present study, there was mild, significant, positive correlation between both gravidity and abortion from one side and lead concentration from the other side. On the other hand, there was moderate, inverse (negative), significant correlation between baby weight and lead concentration. These results are similar to previous studies conducted in New York (Zhu *et al.*, 2010) and in Austria (Gundacker *et al.*, 2010). Similarly, Osman *et al.* (2000) reported that cord blood lead was negatively correlated with child's birth weight, length and head circumference. Another study conducted in Beijing found a negative link between cord blood lead level and birth length (Tao *et al.*, 2001).

CONCLUSION

There is an association between cord blood lead concentration and adverse pregnancy outcome. It was associated with increased rate of CS, PPROM and preterm labor and decreased anthropometric measurement of the neonate.

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