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Fetal exposure to lead during pregnancy and the risk of preterm and early-term deliveries

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ABSTRACT

Studies have reported the association between lead exposure during pregnancy and preterm birth. However, findings are still inconsistent. This prospective birth cohort study evaluated the risks of preterm and early-term births and its association with prenatal lead exposure in Hubei, China. A total of 7299 pregnant women were selected from the Healthy Baby Cohort. Maternal urinary lead levels were measured by the Inductively Coupled Plasma Mass Spectrometry. The associations between tertiles of urinary lead levels and the risks of preterm and early-term deliveries were assessed using multiple logistic regression models. The geometric mean of creatinine-adjusted urinary lead concentrations among all participating mothers, preterm birth, and early-term birth were 3.19, 3.68, and 3.17 μg/g creatinine, respectively. A significant increase in the risk of preterm births was associated with the highest urinary lead tertile after adjusting for confounders with odds ratio (OR) of 1.96. The association was more pronounced among 25–36 years old mothers with OR of 2.03. Though significant *p* trends were observed between lead exposure (medium and high tertiles) and the risk of early-term births, their ORs were not significant. Our findings indicate that the risk of preterm birth might increase with higher fetal lead exposure, particularly among women between the age of 25 and 36 years.

1. Introduction

Lead, to which the general population can be exposed easily through environmental sources due to its ubiquitous nature, is recognized as a widespread used heavy metal. With continued exposure, lead can accumulate in body tissues, especially bones (ATSDR 2007). Vulnerable fetus in utero is at particularly high risk to lead exposure because maternal lead can readily cross the placental barrier (Gundacker and Hengstschläger, 2012; Llanos and Ronco, 2009). Furthermore, maternal bone lead can be a risk factor to the fetus because of the increased bone turnover (Potula et al., 2005) due to calcium demands.

Many researchers have shown associations between fetal lead exposure and preterm birth (Torres-Sánchez et al., 1999), low birth weight (Min et al., 1996), and small for gestational age (Chen et al., 2006). A case–control study by Zhang et al. (2015) found elevated urinary lead levels in pregnant women delivered preterm low birth weight newborns. In general, epidemiological findings remain inconsistent. Some found adverse effects of lead on preterm birth (Falcón et al., 2003; Jelliffe-Pawlowski et al., 2006; Vigeh et al., 2011) while others not (Afkhami et al., 2012; Bloom et al., 2015; Zhu et al., 2010). Such findings' discrepancies might be partly due to under- and over-control of potential confounders or differences in the maternal lead body burdens, as well as study design, variations across different populations or risk factors.

Some researchers have highlighted the need to use different classification of term birth, because uncomplicated pregnancies delivered between $39^{0/7}$ weeks of gestation and $40^{6/7}$ weeks of gestation usually have the lowest frequency of adverse neonatal outcomes (Reddy et al., 2011; Tita et al., 2011). Sengupta et al. (2013) noticed that though early-term babies looked as healthy as their full-term counterparts, they were still physiologically immature.

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Table 1
Maternal urinary lead concentrations among all women, preterm, early-term and term birth.

Variables	n	Arithmetic mean	Geometric mean	Median	Interquartile range
Unadjusted lead (μg/L)					
Total	7299	2.40	1.82	1.94	1.80
Preterm birth[a]	283	2.60	2.13	2.20	1.66
Early-term birth	2145	2.34	1.80	1.90	1.77
Term birth[b,c]	7016	2.40	1.81	1.93	1.80
Creatinine-adjusted (μg/g Cr)					
Total	7299	6.38	3.19	2.97	2.89
Preterm birth[a]	283	6.40	3.68	3.44	4.13
Early-term birth	2145	5.23	3.17	2.97	2.97
Term birth[b,c]	7016	6.38	3.17	2.95	2.86

[a, b] Significant difference detected by Mann–Whitney test ($p < 0.01$).
[c] Including early-term birth.

Table 2
Multiple linear regression analyses of the association between maternal urinary lead as a continuous (Ln-lead) and categorical (tertiles) variable and gestational age in days.

Lead (μg/g Cr)	Gestational age (day)		
	n	β (95% CI)	
		Crude[a]	Adjusted[b,c]
All			
Continuous Ln-lead	7299	−0.24 (−0.48, −0.00)	−0.27 (−0.50, −0.03)
Low (≤2.29)	2439	Reference	Reference[b]
Medium (2.29–4.06)	2435	−0.36 (−0.85, 0.11)	−0.39 (−0.87, −0.11)
High (>4.06)	2425	−0.52 (−1.01, −0.04)	−0.58 (−1.06, −0.11)
p for trend[d]		0.02	0.03
Maternal age < 25			
Continuous Ln-lead	807	−0.01 (−0.79, 0.77)	0.33 (−0.49, 1.15)
Low (≤2.29)	275	Reference	Reference[c]
Medium (2.29–4.06)	273	−0.71 (−2.30, 0.87)	−0.46 (−2.04, 1.11)
High (>4.06)	259	−0.59 (−2.19, 1.01)	0.15 (−1.50, 1.81)
p for trend[d]		0.84	0.87
Maternal age 25–36			
Continuous Ln-lead	6250	−0.25 (−0.50, −0.00)	−0.29 (−0.55, −0.04)
Low (≤2.29)	2084	Reference	Reference[c]
Medium (2.29–4.06)	2092	−0.37 (−0.88, 0.13)	−0.38 (−0.89, 0.12)
High (>4.06)	2074	−0.51 (−1.02, −0.00)	−0.59 (−1.10, −0.09)
p for trend[d]		0.01	<0.01
Maternal age >36			
Continuous Ln-lead	242	−0.21 (−1.17, 1.31)	0.10 (−1.53, 1.74)
Low (≤2.29)	80	Reference	Reference[c]
Medium (2.29–4.06)	70	0.69 (−2.30, 3.68)	0.64 (−2.38, 3.67)
High (>4.06)	92	0.01 (−2.78, 2.81)	0.18 (−2.82, 3.18)
p for trend[d]		0.75	0.69

β, regression coefficient; CI, confidence interval.
[a] Unadjusted model for confounders.
[b] Adjusted model for maternal age, occupation status, pre-pregnancy BMI, parity, passive smoking, pregnancy-induced hypertension, and urinary concentrations of cadmium, arsenic, and thallium (μg/g Cr).
[c] Adjusted model for occupation status, pre-pregnancy BMI, parity, passive smoking, pregnancy-induced hypertension, and urinary concentrations of cadmium, arsenic, and thallium (μg/g Cr).
[d] p-Values for trend across tertiles of maternal urinary lead.

Based on these observations, a prospective birth cohort study was conducted to investigate the relationship between prenatal lead exposure and the risk of preterm and early-term births in Hubei, China. Since lead-based petrol was banned in China in 2000, a gradual drop in the blood lead levels of the Chinese population was observed (Li et al., 2014).

2. Methods

2.1. Study design and study population

Data of this research was obtained from the prospective Healthy Baby Cohort (HBC), conducted at the Wuhan Medical and Health Center for Women and Children, China. It was a longitudinal birth cohort study investigating the influence of the environmental factors exerted on children's development and health. During 2012–2014, 11,311 women were recruited, and asked to complete a questionnaire and provide blood and urine samples.

Inclusion criteria in this study were: (1) Residents of Wuhan City during pregnancy; (2) singleton live birth without congenital malformation, and (3) ability to understand Chinese in order to complete the questionnaire independently. Exclusion criteria for this study were missing urine samples or newborns with congenital heart defects (CHDs), cleft lip and cleft palate, anophthalmia and microphthalmia, gastroschisis, etc. Three women who had two times deliveries during the cohort study, the first delivery was chosen.

A total of 7299 women were chosen as our study population, and each participant signed a written informed consent at the time of enrollment. This research was approved by the ethics committee of the Tongji Medical College, Huazhong University of Science and Technology and the Women and Children Medical and Healthcare Center of Wuhan.