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Prenatal exposure to lead in relation to risk of preterm low birth weight: a matched case-control study in China

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Abstract

We investigated the association between prenatal exposure to lead (Pb) and the risk of preterm low birth weight (PLBW). Pb concentrations in maternal urine collected at birth from 408 subjects (102 cases and 306 matched controls) were analyzed and adjusted by creatinine. The median Pb concentration in the PLBW cases (10.60 μg Pb/g creatinine) was higher than that of the controls (7.28 μg Pb/g creatinine). An adjusted odds ratio (OR) of 2.96 (95% CI = 1.49-5.87) for PLBW was observed when the highest tertile was compared to the lowest tertile of Pb levels. The association was more pronounced among female infants (adjusted OR = 3.67 for the highest tertile; 95% CI = 1.35-9.93) than male infants (adjusted OR = 1.91 for the highest tertile; 95% CI = 0.74-4.95). Our study suggests that prenatal exposure to levels of Pb encountered today in China is associated with an elevated risk of PLBW.

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Conflict of interest

None

Keywords

Lead; Preterm birth; Prenatal exposure; Maternal urine

1. Introduction

About 15 million infants each year are born preterm (infants born alive prior to 37 completed weeks of pregnancy) worldwide, which equates to more than 1 in 10 born infants [1]. Moreover, infants born preterm account for about two-thirds of all low birth weight infants (< 2500 g) [2], in which case it is referred to as preterm delivery of low-birth-weight (PLBW). It is known that PLBW infants face a higher risk of serious health problems. Specifically, PLBW infants have a 40-fold greater risk of dying during the neonatal period and a 50 percent greater risk of having serious childhood development problems compared to normal weight infants [3]. To identify and analyze the factors affecting PLBW may help to prevent preterm labor and its associated adverse outcomes.

During the past decades, epidemiological studies have suggested the importance of environmental exposures as risk factors for preterm birth, particularly exposure to heavy metals. Lead (Pb), a widespread heavy metal, can easily across the placenta and affect the fetus [4]. Findings from studies evaluating prenatal exposure to Pb at community levels and preterm birth have been inconsistent. Some studies have showed a significant association with an increased risk of a preterm birth or a decreased total days of gestation [5-10], while other studies have observed no such association [11-16]. So far, no study has been conducted to investigate prenatal Pb exposure and risk of PLBW infants in Chinese women.

With the unprecedented economic development, China has become not only the largest producer of raw and refined Pb, but also the largest consumer [17]. As a result, Pb exposure and its associated health effects remain a serious public health issue [18], though Pb petrol has been forbidden in China since 2000. Given this background, we conducted a pair-matched case-control study in Hubei province, China, involving 408 pregnant women, including 102 cases that gave birth to PLBW infants and 306 matched controls, to investigate the relationship between prenatal Pb exposure and the risk of delivering PLBW infants.

2. Materials and Methods

2.1 Study population

This study was designed as a pair-matched case-control study. The subjects in the present study were derived from the prospective Hubei-Tongji birth cohort, which enrolled participants at the three hospitals in Wuhan, Ezhou, and Macheng cities, which are located in Hubei province, the central of People's Republic of China. Pregnant women, who came for their first examination in the first trimester or gave birth at one of the three hospitals, have been asked to participate in the study. Participants were invited to provide blood and urine samples and to participate in a face-to-face interview. Between November 2012 and April 2014, 16,293 women with a live singleton infant were recruited from the three study

hospitals (9,209 from Wuhan, 4,550 from Ezhou and 2,534 from Macheng). All participants in this study provided a written informed consent form at enrollment. The research protocol was reviewed and approved by the ethical committee of Tongji Medical College, Huazhong University of Science and Technology and the three study hospitals.

In this study, cases were mothers who delivered a live singleton infant with a gestational age < 37 weeks and weighing <2500 g (PLBW) in the obstetrics departments of the three hospitals. Three controls were matched to each case and included mothers who delivered a single live newborn with gestational age ≥37 weeks and weighing between ≥2,500 g and < 4,000 g. Potential cases and controls were excluded if they had multiple pregnancies, a stillborn infant, or an infant with a birth defect. Women without urine samples available for analysis were also excluded. Each case and control set had the same maternal age at conception (within 1-year interval), delivery of an infant of the same gender, and the same delivery hospital. A total of 102 cases and 306 controls were included in the analysis.

2.2 Data and sample collection

Standardized face-to-face interviews were conducted with the participants after delivery by specially trained nurses in the three hospitals. The interview collected a variety of information, including socioeconomic data (e.g., maternal age, education, reproductive history, occupation, and household income) and lifestyle factors during pregnancy (e.g., smoking, passive smoking, alcohol consumption, and multivitamin supplement use). The body mass index of mothers was calculated using the self-reported weight before pregnancy, as obtained from the interview, and height, which was measured using a stadiometer. Information about the mothers' history of pregnancy outcomes, disease, and information concerning the infants' birth date, gender, gestational age at birth, birth weight, and any apparent congenital malformations were retrieved from medical records. Gestational age was estimated using the date of the last menstrual period. Birth weight of nude infants was measured within one hour after birth by experienced obstetric nurses using standardized procedures.

The maternal urine samples were obtained during admission to the hospital as part of the preparation for delivery (within 3 days before delivery). All of the urine samples were collected in 50 mL polypropylene tubes, and frozen at −20 degrees Celsius (°C) until further processing.

2.3 Instrumental analysis

Pb concentrations in urine samples were measured by inductively coupled plasma mass spectrometry (ICP-MS) (Agilent 7700, Agilent Technologies, Santa Clara, CA, USA). Prior to the instrumental analysis, urine samples were thawed at room temperature, and then 1 mL of urine from the supernatant was introduced in 15 mL Kirgen polypropylene conical centrifuge tubes together with 3% HNO_3 to a final volume of 5 mL for overnight nitrification. The resulting sample was digested by ultrasound at 40 °C for 1 h. The operating parameters for ICP-MS were as follows: RF power, 1550 w; auxiliary gas flow, 0.9 L/min; carrier gas flow, 0.25 L/min; plasma gas flow, 15.00 L/min; resolution (peak high

10%), 0.65~0.80 amu; improve quantity of samples, 0.4 mL/min; unimodal residence time, 0.1 s; repetitions, 3 times; analysis of the time, 5 min.

To ensure the accuracy of the analytical methods and results, we applied stringent laboratory quality controls. Each sample was measured in triplicate. An external quality control sample (SRM2670a Toxic Elements in Urine, a standard reference material of National Institute of Standards and Technology, Gaithersburg, MD, USA) was analyzed in each batch to check for accuracy, and the concentrations measured were within the certified range (5%). A 3% HNO3 blank was processed in each batch of samples to control for possible contamination. The samples were analyzed with an external calibration method, using eight standard concentrations ranging from 0 to 5 μg/L. The limit of detection (LOD) of the urine Pb analysis in this study was 0.05 μg/L. The recovery of the quality control standard using this procedure was 99%. The intra-day coefficient of variation was 0.76 % and the inter-day CV was 2.99%. Field blanks were also included for quality control and the levels of Pb in the field blanks were < LOD. Pb measurements below the LOD were given values of 1/2 LOD.

Urine creatinine concentrations were measured by a creatinine kit (Mindray BS-200 CREA Kit, Shenzhen, China). Pb concentrations in urine (μg/L) were adjusted for creatinine, in order to account for variations in urine dilution in spot urine specimens, and results were expressed as μg Pb/g Creatinine.

Estradiol (E2), an important hormone for fetal development, was also measured in maternal urine by liquid chromatography-tandem mass spectrometry (ACQUITY UPLC H-Class System-TQD, Milford, MA) as previously described [19].

2.4 Statistical analysis

The distributions of Pb concentrations were tested by the Shapiro-Wilk normality test. The differences of Pb concentrations in maternal urine between cases and controls were evaluated using the Wilcoxon matched pairs signed rank test. Conditional logistic regression analyses were used to estimate the associations between the risk of PLBW and maternal urinary Pb levels by calculating matched odds ratios (OR) and 95% confidence intervals (CI). Models were fit using Pb measurements as categorical variables (the tertile distribution of urinary Pb concentrations in controls) and the lowest tertile was assigned as the referent group. Univariate analyses were carried out by computing crude ORs and 95% CIs. We tested for linear trends by modeling the median values of tertiles of Pb as a continuous variable and evaluated the statistical significance of this predictor using the Wald test. In this study, we selected household income to represent socioeconomic status, because inclusion of income, education, and occupation into the model did not produce significantly different results from addition of each individual variable into the model, and adjustment by income showed a larger impact on the estimate than the other two variables. In the final model, we adjusted for potential confounding factors, including household income (≥ 50,000, < 50,000 yuan per year), pre-pregnancy body mass index (<18.5, 18.5-23.9, ≥24), parity (1, ≥ 2), passive smoking (No, Yes), and hypertension during pregnancy (No, Yes). Additional adjustment for diabetes, heart disease, multivitamin supplement use during pregnancy, and delivery method did not result in material changes in the observed associations and thus were not included in the final models. Smoking and alcohol consumption during pregnancy

were not included in the model because very few Chinese women smoke and drink throughout life. The analyses were further stratified by infant gender and maternal age. The median age of the women at delivery (29 years old) was used as the cut-point for stratified analyses. All analyses were performed using SAS (version 9.2; SAS Institute Inc., Cary, NC, USA). All statistical tests were considered to be significant at an alpha level of 0.05 for a two-tailed test.

3. Results

Of the 102 PLBW cases and 306 controls, most of the participants were recruited from Wuhan (84%), while 9.4% were from Ezhou and 6.6% were from Macheng. There were 57 sets of boys and 45 sets of girls. Participating mothers had an average age of 28.9 ± 4.9 years old. The average gestational weeks of the cases and controls were 34.4±1.6 and 38.9±1.1, respectively.

Table 1 shows the distributions of selected characteristics in the PLBW case mothers and control mothers. Mothers who had PLBW deliveries were more likely to have lower educational attainment, be unemployed, have a lower household income, have a higher pre-pregnancy body mass index, and be parous. Mothers who were diagnosed with hypertension were also more likely to have a PLBW birth.

The detection rate for maternal urinary Pb was 99.1% in PLBW cases and controls. The median of the creatinine-adjusted Pb concentration in maternal urine was 10.60 μg Pb/g creatinine with a 95th percentile of 51.47 μg Pb/g creatinine in the cases, and a median of 7.87 μg Pb/g Cr with a 95th percentile of 43.25 μg Pb/g creatinine in the controls. The mothers in the PLBW case group had significantly higher urinary Pb levels compared to the control group ($p < 0.01$). In addition, case mothers had lower median levels of E2 in urine (113.4 vs. 158.1 μg/E2 g creatinine, $p < 0.01$). Urinary E2 levels was negatively associated with Pb levels ($r = -0.10$, $p = 0.16$).

Table 2 shows that increased creatinine-adjusted Pb levels in maternal urine was associated with an increased risk of PLBW. Specifically, compared to the lowest tertile of urinary Pb concentrations, a positive trend was found between PLBW risk and increasing levels of Pb in the unadjusted analysis [OR = 1.62 (95% CI = 0.85-3.08) for the medium tertile; OR = 2.29 (95% CI = 1.25-4.20) for the highest tertile; p trend < 0.01]. In the multivariable model, the association between PLBW risk and maternal urinary Pb levels was similarly significantly elevated [OR = 1.85 (95% CI = 0.91-3.73) and 2.96 (95% CI = 1.49-5.87) for the subsequent tertiles; p trend < 0.01].

Stratified results for these associations by maternal age are shown in Table 3, and the median age of women at delivery was used as the cut-point (< 29 and ≥ 29 years). Among younger mothers < 29 years old, a significant association was observed for higher Pb concentrations and risk of PLBW infants [adjusted OR = 2.58 (95% CI = 1.00-6.73) for the highest tertile; p trend = 0.05]. The associations were also significant among older women [adjusted OR = 2.97 (95% CI = 1.07–8.23) for the highest tertile; p trend = 0.04]. There was no significant interaction between maternal age and maternal urinary Pb levels (p heterogeneity = 0.94).

Results for stratified analyses by infant gender are shown in Table 4. The associations between PLBW risk and maternal urinary Pb levels were found to differ significantly across male and female infants (p heterogeneity = 0.01). Among female infants, mothers with urinary Pb levels in the highest tertile had a significantly higher risk of having PLBW infants compared to the lowest tertile (adjusted OR, 3.67; 95% CI, 1.35-9.93; p trend < 0.01). The adjusted OR was 1.91 (95% CI, 0.74-4.95) for mothers with urinary Pb levels in the highest tertile who delivered a male infant, but the association was statistically nonsignificant (p trend = 0.28).

4. Discussion

In this study, we measured the urinary Pb levels of mothers who gave birth to PLBW infants and control mothers, and analyzed the association between urinary Pb levels and PLBW risk with adjustment for known risk factors. We found that mothers with PLBW infants had significantly higher urinary Pb levels than did the control mothers. The risk of PLBW was significantly associated with increasing levels of maternal urinary Pb levels, and the mothers in the highest tertile of urinary Pb levels (≥ 11.67 μg Pb/g creatinine) had almost 3 times the risk of delivering PLBW infants as those in the lowest tertile (< 5.41 μg Pb/g creatinine). Our findings suggest that prenatal exposure to levels of Pb encountered today in China may be a risk factor for delivering PLBW infants.

In this study, Pb was detected in 99.1% of the maternal urine samples collected at the time of delivery, indicating a high prevalence of Pb exposure in our population. Urine, as a noninvasive sample, has been frequently used for assessing recent exposure to a variety of metals, and good correlation (0.72) between urine and blood Pb levels has been reported [20]. Table 5 shows a comparison of urinary Pb concentrations in women of the present study and previously published data from non-occupationally exposed populations worldwide [21-27]. The pregnant women in our study had higher levels of urinary Pb compared to other pregnant women in developed countries, such as in the USA (geometric mean 0.63 μg/L) [26], Japan (geometric mean 0.48 μg Pb/g creatinine) [22], and Australia (arithmetic mean 0.87 μg Pb/g creatinine) [23]. Few studies have investigated the urinary Pb concentrations of pregnant women in China. According to a recent survey of the general population in 8 provinces in central China, the geometric mean of the unadjusted urinary Pb levels was 2.85 μg/L [27], which is slightly lower than the observed levels in our study population who were also enrolled in Hubei Province, located in central China (geometric mean 3.35 μg/L). This may be explained by the increase in Pb mobilization from the bone tissues during pregnancy [28], which was supported by the observed higher levels of blood Pb in pregnant women compared to the general population in previous studies [26]. The maternal urinary Pb levels observed in our present study were lower than those reported in a study of 290 pregnant women (arithmetic mean 28.5 μg Pb/g creatinine) in Lagos, Nigeria, also a developing country in Africa where Pb gasoline has not been totally phased out [25]. The reported levels of urinary Pb in pregnant women worldwide indicates that environmental Pb exposure remains an important public health issue particularly in developing countries where data suggest that levels are the highest.

Pb derived from petrol used to be the main source of Pb exposure in the environment and was a significant contributor to the body Pb burden. Although Pb gasoline was banned officially in China in 2000, a significant reduction in blood Pb levels has not been observed, unlike the experience of developed countries [29, 30]. In recent decades, due to rapid economic growth in China, Pb emissions from industrial sources including mineral extraction and processing, smelting and refining, power generation, battery plants, and waste disposal have been increasing rapidly. Atmospheric Pb that is deposited in soil and dust have been identified as one of the major sources of Pb-related health threats [31]. Several studies conducted in large cities in China have revealed that the Pb levels in the soil and dust were significantly higher than those in many major cities in developed countries [30, 32]. Additionally, consumption of food and water contaminated with Pb is also a major source for human exposure. Our subjects were chosen from an area in Hubei province located near the Yangtze River. Several studies have reported that Pb contamination is increasing in the Yangtze River, and consequently residents who consume water or food from this area may be exposed to relatively high levels of Pb [33, 34].

The reported adverse effects of prenatal Pb exposure are concerning, our study provides evidence for an association between higher Pb exposure and an increased risk of PLBW. Consistent with our findings, Jelliffe-Pawlowski et al. [10], in a study of 262 mother-infant pairs in California, USA, reported that women with blood Pb ≥ 10 μg/dL were about three times as likely to experience a preterm delivery as women with Pb levels < 10 μg/dL (adjusted OR = 3.2; 95% CI, 1.2-7.4). In a recent study of 348 pregnant women conducted in Tehran, Iran, Vigeh et al. suggested that a 1 unit increase in maternal blood Pb levels led to an increased risk of preterm birth (adjusted OR = 1.41, 95% CI, 1.08-1.84) [6]. Also, in a case–control study of 620 pregnant women in Mexico City, compared with cord blood Pb < 5.1 μg/dL, the adjusted OR for preterm birth for Pb levels 5.1–9.0 μg/dL was 2.72 (95% CI, 1.03-7.19) among primiparous women [5]. This reported effect is similar to the one observed in our study in which mothers with urinary Pb levels in the highest tertile had a higher risk for delivering PLBW infants compared to mothers with Pb levels in the lowest tertile (adjusted OR=2.96, 95% CI = 1.49-5.87).

We found that the associations may vary by infant gender in our study, as the significant association between maternal urinary Pb levels and risk of delivering a PLBW infant was more pronounced in female infants than in males. Similarly, a previous study of 522 boys and 477 girls in Mexico city reported that maternal bone Pb tested after delivery was significantly associated with lower weight over time among female but not male children from birth up to 5 years of age [35]. Pb has the ability to decrease binding affinity of E2 to estrogen receptor (ER) [36]. Fetuses are exposed to E2 derived from their mother, but the expression of ER in cells was strikingly different among females and males [37]. Because a larger number of ER-positive cells were observed in females than in males [37], it is plausible that the risk of PLBW would have been more apparent in females. Further investigation of potential differences in the effect of prenatal Pb exposure on PLBW according to infant gender should be conducted in larger studies.

Pb exposure has been demonstrated to decrease serum E2 levels in animal studies [41], and lower E2 levels have been associated with increased risk of spontaneous preterm birth in

previous epidemiological studies [38]. In our study, we also found that the PLBW case mothers had lower levels of E2 in urine than that of the control mothers, and urinary E2 levels was negatively associated with Pb levels, though the correlation was weak. The results appear to support the hypothesis that low E2 contributes to PLBW. Since the effect of Pb on decreasing serum E2 levels was only reported in animal studies, whether or not the effect of Pb on the endocrine system in the pathway to preterm birth will require further epidemiological study. Several other mechanisms by which Pb exposure during pregnancy might result in preterm birth have been proposed previously. Rats exposed to Pb have altered growth plate morphology and increased activities of spontaneous uterine contraction [39]. Also, Pb can potentially suppress fetal growth and development by competing with calcium for deposition into bone to impair normal fetal bone growth [40].

Smoking has long been recognized as a risk factor for preterm birth/ low birth weight, and alcohol consumption has also been reported as a source of Pb intake [41]. However, these factors are very unlikely to explain the associations in our study, as only one mother in our study population reported smoking and two mothers reported alcohol consumption during pregnancy. While the presence of exposure to passive smoking during pregnancy was more common among the cases mothers than the control mothers in our study, which was consistent with previous studies [42], adjustment for this variable did not attenuate our findings. Further, the cases and controls were matched on potentially important aspects such as the age of mothers, gender of the infants, and residence, to exclude the influence of important confounding factors.

There are some limitations to this study. First, maternal urinary Pb levels were only measured at one spot time that may not accurately reflect Pb burden in pregnancy. There is a concern that measurements of Pb exposure at delivery are subject to distortion by the fetus's gestational age. Some studies have reported that the level of maternal blood Pb showed a U shaped pattern, i.e. a decline in Pb between weeks 12 and 20 followed by a rise that continued throughout the remainder of pregnancy [15, 43]. Therefore, further studies about Pb measurements in different trimesters may be required to analyze the relationship. Our study included preterm infants and it would also be of interest in future studies to evaluate whether similar associations with Pb are observed in term LBW infants. Finally, maternal diet and nutritional status has not been addressed in this study. While maternal nutrition could affect fetal development, the interrelationship between Pb exposure, nutrition, and pregnancy outcomes need to be more clearly defined.

In conclusion, our case-control study suggests that exposure to Pb in pregnant women may be an important risk factor in the etiology of PLBW. These data indicate that appropriate public health measures to decrease human exposure to Pb pollutants need to be implemented, particularly in developing countries where Pb levels have been reported to be the highest.

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Highlights

- Mothers with preterm low birth weight infants had higher levels of lead in urine.
- Prenatal exposure to lead was associated with preterm low birth weight.
- Female infants appeared to be more susceptible to lead than male infants.

Table 1

Basic characteristics of preterm low birth weight cases and controls [n (%)].

Characteristics	Cases (n = 102)	Controls (n = 306)
Maternal age		
<25	19 (18.6)	57 (18.6)
25-29	39 (38.2)	117 (38.2)
≥30	44 (43.1)	132 (43.1)
Education		
More than high school	38 (37.3)	178 (58.1)
High school	18 (17.7)	66 (21.66)
Less than high school	46 (45.1)	60 (19.6)
Missing	0 (0.0)	2 (0.7)
Occupational status		
Employed	74 (72.6)	252 (82.3)
Un-employed	28 (27.5)	47 (15.4)
Missing	0 (0)	7 (2.3)
Household income		
≥50,000 yuan per year	28 (27.5)	146 (47.7)
<50,000 yuan per year	66 (64.7)	138 (45.1)
Missing	8 (7.8)	22 (7.2)
Body mass index		
Normal (18.5-23.9)	58 (56.9)	195 (63.7)
Underweight (<18.5)	26 (25.5)	68 (22.2)
Overweight (≥24)	13 (12.8)	38 (12.4)
Missing	5 (4.9)	5 (1.6)
Smoking during pregnancy		
No	98 (96.1)	304 (99.4)
Yes	1 (10)	0 (0.0)
Missing	3 (2.9)	2 (0.7)
Passive smoking during pregnancy		
No	74 (72.5)	239 (78.1)
Yes	28 (27.5)	59 (19.3)
Missing	0 (0)	8 (2.6)
Alcohol use during pregnancy		
No	98 (96.1)	300 (98.0)
Yes	1 (1.0)	1 (0.3)
Missing	3 (2.9)	5 (1.6)
Parity		
1	76 (74.5)	248 (81.1)
≥2	26 (25.5)	58 (18.9)
Cesarean delivery		
No	11 (10.8)	37 (12.1)

Characteristics	Cases (n = 102)	Controls (n = 306)
Yes	91 (89.2)	269 (87.9)
Hypertension		
No	88 (86.3)	297 (97.1)
Yes	14 (13.78)	9 (2.9)
Diabetes		
No	100 (98.0)	292 (95.4)
Yes	2 (2.0)	14 (4.6)
Heart disease		
No	102 (100.0)	306 (100.0)
Yes	0 (0.0)	0 (0.0)
Multivitamin supplements during pregnancy		
Yes	45 (44.1)	124 (40.5)
No	56 (54.9)	179 (58.5)
Missing	1 (1.0)	3 (1.0)

Table 2

Association between risk of premature low birth weight and maternal urinary lead levels.

Pb (μg/g Pb creatinine)	Cases	Controls	OR[a] (95% CI)	OR[b] (95% CI)
Total (n=408)				
< 5.41	22	102	1.00	1.00
5.41-11.66	33	102	1.62 (0.85-3.08)	1.85 (0.91-3.73)
≥ 11.67	47	102	2.29 (1.25-4.20)	2.96 (1.49-5.87)
p for trend			< 0.01	< 0.01

Abbreviations: OR, odds ratio; CI, confidence interval.

[a] Crude odds ratio.

[b] Adjusted for gestational age, household income, maternal body mass index, parity, passive smoking, and hypertension during pregnancy.

Table 3

Risk of premature low birth weight associated with maternal urinary lead levels, stratified by maternal age.

Pb levels[a]	< 29 years (n = 200)			≥ 29 years (n = 208)			*P* for heterogeneity
	Ca/Co	OR[b] (95% CI)	OR[c] (95% CI)	Ca/Co	OR[b] (95% CI)	OR[c] (95% CI)	
T1	12/50	1.00	1.00	11/52	1.00	1.00	0.94
T2	15/50	1.32 (0.53-3.28)	1.56 (0.54-4.56)	17/52	1.60 (0.66-3.86)	1.71 (0.66-4.45)	
T3	23/50	1.93 (0.85-4.39)	2.58 (1.00-6.73)	24/52	2.37 (1.01-5.57)	2.97 (1.07-8.23)	
p for trend		0.10	0.05		0.05	0.04	

Abbreviations: ca/co, numbers of cases and controls; CI, confidence interval; OR, odds ratio; T, tertile.

[a] Lead levels (μg/Pb g creatinine): age < 29 years, T1 (< 4.92), T2 (4.92-10.03), T3 (≥ 10.04); age ≥ 29 years, T1 (< 6.33), T2 (6.33-13.08), T3(≥ 13.09).

[b] Crude odds ratio.

[c] Adjusted for household income, maternal body mass index, parity, passive smoking, and hypertension.

Table 4

Risk of premature low birth weight associated with maternal urinary lead levels, stratified by infant gender.

Pb levels[a]	Male (n=228)			Female (n=180)			*P* for heterogeneity
	Ca/Co	OR[b] (95% CI)	OR[c] (95% CI)	Ca/Co	OR[b] (95% CI)	OR[c] (95% CI)	
T1	12/57	1.00	1.00	12/45	1.00	1.00	0.01
T2	25/57	2.15 (0.96-4.78)	2.13 (0.89-5.08)	6/45	0.46 (0.15-1.45)	0.70 (0.20 - 2.45)	
T3	20/57	1.72 (0.74-4.00)	1.91 (0.74-4.95)	27/45	2.15 (0.96-4.85)	3.67 (1.35-9.93)	
p for trend		0.39	0.28		< 0.01	< 0.01	

Abbreviations: ca/co, numbers of cases and controls; CI, confidence interval; OR, odds ratio; T, tertile.

[a] Lead levels (μg/Pb g creatinine): male, T1 (< 5.86), T2 (5.86-13.12), T3 (≥ 13.13); female, T1 (< 4.96), T2 (4.96-10.11), T3(≥ 10.12).

[b] Crude odds ratio.

[c] Adjusted for household income, maternal body mass index, parity, passive smoking, and hypertension.

Table 5

Comparison of lead concentrations from the present study and previous studies.

Reference	Place	Sampling years	Numbers	Population	Arithmetic mean	Geometric mean
Present study	China	2012 - 2014	800	Pregnant women	6.35 μg/L 13.67 μg/Pb g creatinine	3.35 μg/L 7.99 μg/Pb g creatinine
Ding et al. 2014 [27]	China	2009 -2010	1647	General population	—	2.85 μg/L
Jain 2013[26]	USA	2003 - 2010	1565	Pregnant women	—	0.63 μg/L
Woodruff et al.2011 [21]	USA	2003 - 2004	268	Pregnant women	—	0.81 μg/L
Shirai et al. 2010 [22]	Japan	2007 - 2008	78	Pregnant women	1.19 μg/Pb g creatinine	0.48 μg/Pb g creatinine
Hinwood et al. 2013 [23]	Australia	2008 - 2010	157	Pregnant women	0.66 μg/L 0.87 μg/Pb g creatinine	—
Fort et al. 2014 [24]	Spain	2004 - 2006	657	Pregnant women	5.2 μg/Pb g creatinine	—
Adekunle et al. 2010 [25]	Nigeria	2006 - 2008	214	Pregnant women	28.5 μg/Pb g creatinine	—

—No data.