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ORIGINAL ARTICLE

Blood Lead Levels During Pregnancy and Its Influencing Factors in Nanjing, China

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Objective To investigate the blood lead levels (BLLs) in the duration of pregnancy and 6-12 weeks after delivery, and analyze the influencing factors of BLLs in healthy pregnant women.

Methods Pregnant women were recruited from September 2009 to February 2010 at the prenatal clinic in Nanjing Maternity and Child Health Care Hospital. Altogether 174 healthy pregnant women without pregnant or obstetric complications or abnormal pregnancy outcomes were enrolled as the gravida group, and 120 healthy non-pregnant women as the control group. BLLs during pregnancy were determined by flame atomic absorption spectroscopy.

Results BLLs in all the three pregnancy trimesters and postpartum were 59.8 ± 24.3 , 55.4 ± 20.1 , 55.9 ± 19.7 , and 67.6 ± 17.4 $\mu\text{g/L}$, respectively, and the mean BLL in control group was 67.5 ± 21.3 $\mu\text{g/L}$. BLLs during all the three trimesters were lower in the gravida group than in the control group ($P=0.043$, 0.021 , and 0.028). Furthermore, occupations, nutrients supplementation, and time of house/apartment painted were associated with BLLs in pregnant women. Lead-related occupations, cosmetics use, and living in a house painted less than 1 year before are risk factors of high BLLs among pregnant women, while calcium, iron, zinc, and milk supplements are protective factors.

Conclusion Supplementing calcium, iron, zinc, and milk, or avoiding contact with risk factors may help people, especially pregnant women, to reduce lead exposure.

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LEAD is a cumulative toxicant that adversely affects various organs and systems of human body. It can readily transfer into the fetus through the placenta,¹ and in the absence of efficient placental barrier, the fetus could be exposed to lead at a concentration very close to that in the mother's body. Fetal vulnerability may occur even if the mother's exposure had ceased many years earlier.^{2,3} Lead interferes with signal transmission at the synapse and cellular adhesion molecules, causing disruption in cell migration during critical times in the nervous system development.⁴ Other adverse effects related to prenatal lead exposure include reproductive effects, conduct disorder in children, cardiovascular functioning, and genomic methylation of DNA.⁵⁻⁸ Prenatal lead exposure forms a plumbeous environment for the fetus and newborns and may affect the fetus in a number of detrimental ways.^{9,10} Elevated blood lead level (BLL) during pregnancy are associated with an increased risk of preterm births, spontaneous abortion, and other anomalies.¹¹⁻¹³ Therefore, it is particularly important to reduce lead exposure in pregnant women for aristogenesis.

The BLL and the susceptibility to lead toxicity of pregnant women can be influenced by many factors such as environmental exposure, life styles, diet habits, and nutritional status.¹⁴ The living standards of pregnant women may vary largely along with geographical locations and uneven economic development. Similarly, lead exposure and the influencing factors may also differ greatly among women living in different areas and even among those in the same area but with different economic status. It is therefore essential to monitor the BLL and the influencing factors across or within different areas. China has been challenged with severe lead pollution.¹⁵ A previous research has found that the BLL in children in Chengdu, a city in southwest China, is different from the levels in other areas.¹⁶ To assess the level of lead poisoning in children in a given area, American Center for Disease Control divided the prevalence into three groups: (1) higher than 12% as high epidemic area; (2) 6%-12% as moderate epidemic area; (3) lower than 5.9% as low epidemic area. Chengdu is a moderate epidemic according to the criterion.¹⁶ To identify the BLL in pregnant women and its change during the whole gestation, we designed this prospective, longitudinal study, and investigated the influencing factors of BLL in pregnant women living in Nanjing at their early pregnancy (10-14 weeks) with a questionnaire.

MATERIALS AND METHODS

Study subjects recruitment

Pregnant women were recruited from September 2009 to

February 2010 at Nanjing Maternity and Child Health Care Hospital prenatal clinic. Of the 288 women assessed for eligibility, 18 did not meet the study criteria (at 10-14th gestation weeks; singleton pregnancy; well-developed fetus shown by ultrasonic examination). Of the remaining 270 eligible women, 250 (92.6%) agreed to participate in the study.

Then we excluded 31 women based on the following exclusion criteria: (1) body mass index (BMI) $>30 \text{ kg/m}^2$ or $<18 \text{ kg/m}^2$; (2) having a history of malignant tumor, systemic lupus erythematosus, diabetes mellitus, hypertension, pancreatitis, liver disease, kidney disease, or disease of the hematologic or metabolic system; (3) not living in Nanjing. A total of 219 blood specimens and questionnaires were obtained at early pregnancy of the included women. They were followed up at mid-pregnancy (20-24 weeks), late pregnancy (30-34 weeks), and 6-12 weeks after delivery. Seventeen participants withdrew due to abortion ($n=6$), transferred to another hospital ($n=10$), or withdrew voluntarily ($n=1$). After the 3-stage follow-up, we excluded the women who had obstetric complications or fetal abnormality and another 28 participants were excluded: 20 for obstetric complications, 3 for premature delivery, 2 for prolonged pregnancy, 1 for low birth weight, and 2 withdrew voluntarily. Finally 174 healthy pregnant women were included in the gravida group. Figure 1 outlines the screening process.

As controls, 120 healthy non-pregnant women were included after matching for age, BMI, and residence area. The women in the control group did not take any nutrients supplements. We also excluded those who were actresses or performers because they tended to use more cosmetics than those in other occupations. The study was carried out according to the principles of the Declaration of Helsinki. All the participants received a detailed explanation of the study objective, research procedure, and information on how to reduce environmental lead exposure.

Data collection

A screening questionnaire was employed to gather socioeconomic and demographic information, medical and reproductive histories, influencing factors for lead exposure of the women in the gravida group during pregnancy at first trimester. Those factors included occupations (such as painting workers, traffic policewomen, workers in irons, steel, and lead production, soldering, or smeltery, radiator repairwomen, battery manufacturers, welders of old painted metals, barbers, etc.), lifestyle (active/passive smoking, drinking), hair dyeing, cosmetics use, floor level of residence, time of house/apartment

painted, distance from residence to street, kitchen fuel, distance from a factory, existence of wall paint desquamating, and time of staying in the street. The dietary information focused on consumption of canned food, preserved eggs, milk, and Chinese herbal medicine. We also queried whether the pregnant women took Fe, Zn, or Ca supplements during gestation. Fasting blood samples were obtained from the antecubital vein in each pregnancy trimester and at the same period from the non-pregnant controls after a 30-minute rest in a sitting position. These blood samples were drawn into vacuum tubes (Becton-Dickinson, Franklin Lakes, NJ, USA) containing heparin lithium and sent to detect blood lead concentration by flame atomic absorption spectroscopy (BH-2100 atomic

absorption spectrometer, Bo Hui Company, Beijing, China) within 1 hour. Internal quality controls were taken both before and after the detection.

Statistical analysis

Data analysis was performed using SPSS version 13.0 (SPSS, Chicago, IL, USA). The BLLs were presented as means $\pm$ SD as Kolmogorov-Smirnov test showed normal distributions ($P>0.05$). The least significant difference t test of analysis of variance was used for the three trimesters and the postpartum in the gravida and the control group. The logistic regression was used for analyzing the possible influencing factors of BLLs at early pregnancy. $P<0.05$ was considered statistically significant.

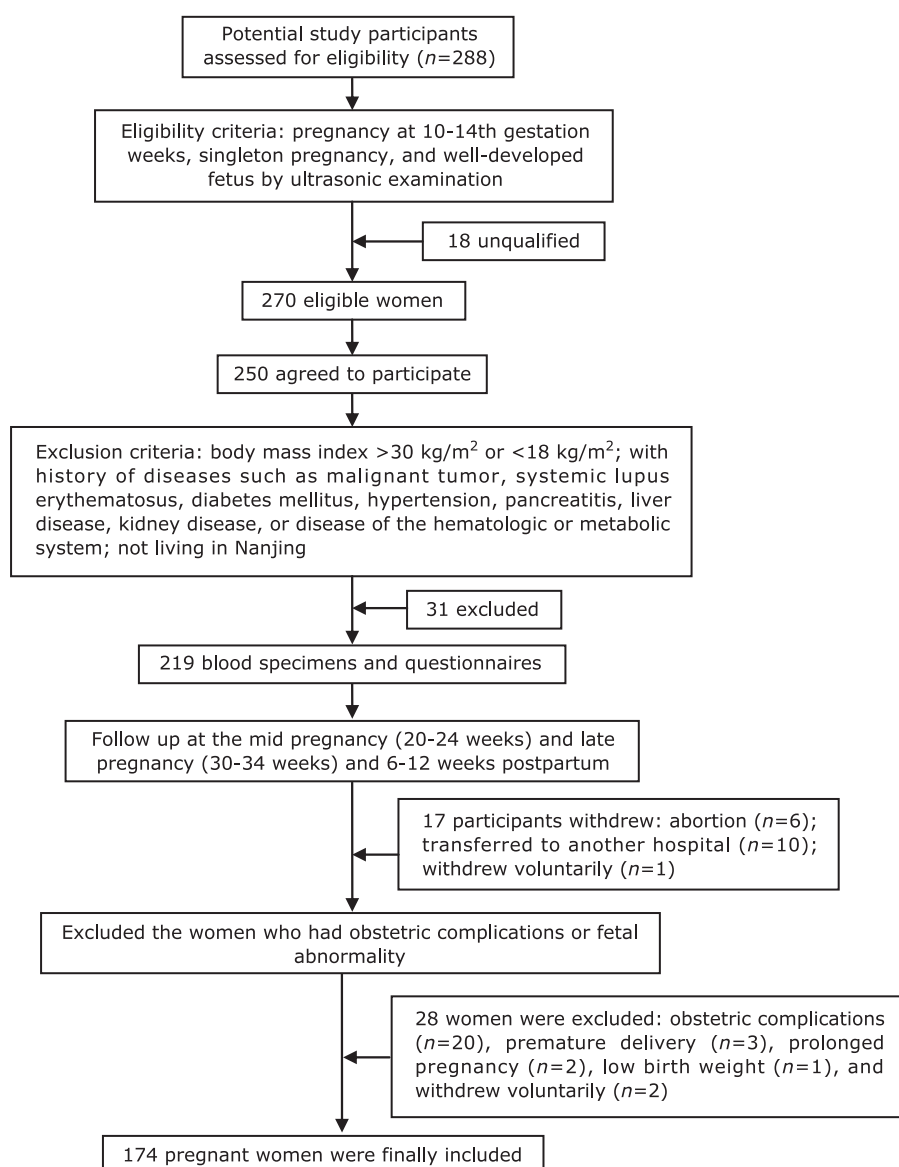


Figure 1. The flowchart of the screening of healthy pregnant women (gravida group)

RESULTS

The age of the recruited pregnant women ranged from 20 to 41 years with a mean age of 29 ± 3 years. There was no statistical difference between the gravida group and the control group in age, race, educational level, economic status, and living condition. The BLLs in all the pregnant women in the first trimester ranged from 17.4 to 120.0 $\mu\text{g/L}$, and in the control group ranged from 20.0 to 110.0 $\mu\text{g/L}$, there were 4 in the gravida group in the first trimester and 4 in the control group whose BLLs were greater than 100 $\mu\text{g/L}$ (Table 1). The mean lead concentrations in three trimesters in the gravida group were 59.8 ± 24.3 , 55.4 ± 20.1 , and 55.9 ± 19.7 $\mu\text{g/L}$, respectively, but rose to 67.6 ± 17.4 $\mu\text{g/L}$ in 6-12 weeks after delivery. The lead concentration of the control group was 67.5 ± 21.3 $\mu\text{g/L}$.

The BLLs in all the three trimesters were lower than those in the control group ($P=0.043$, 0.021 , and 0.028), but no statistical significance was found between each two trimesters ($F=9.55$, 8.74 , 8.89 ; $P>0.05$). After delivery, the BLLs of the pregnant women returned to the level in the control group. Logistic regression showed that age, active/passive smoking, hair dyeing, floor level of residence, distance from residence to street, kitchen fuel, distance from a factory, existence of wall paint desquamating, time of staying in street, consumption of canned food and preserved eggs, and use of Chinese herbal medicine had no correlations with BLLs in pregnant women ($P>0.05$, Table 2). The related occupations (including painting workers, traffic policewomen, radiator repairwomen, welders of old painted metals, barbers), of living in a house/apartment painted less than 1 year before, and cosmetics use were shown as risk factors of high BLLs in pregnant women, while consuming milk and Fe, Zn, or Ca supplements were protective factors (Table 3).

DISCUSSION

The possibility of intra-uterine lead exposure began to be addressed in the late 1970s. Correlations between maternal and umbilical cord BLLs confirmed the transfer of lead from the mother to the fetus.¹⁷ Elevated BLLs during pregnancy were also mentioned by Lagerkvist et al,¹⁸ while some other researchers found that BLLs dropped during pregnancy.¹⁹ Another study demonstrated a clear U-shaped curve of BLLs during pregnancy, with the lowest concentration at 20th gestation week.²⁰ The difference in BLLs in the duration of pregnancy may depend on various factors such as the time of sampling (different periods of

Table 1. Blood lead levels (BLLs) in 3 trimesters and postpartum 6-12 weeks of the gravida group and the control group ($\mu\text{g/L}$)

Groups	Mean $\pm$ SD	Minimum	Maximum
Gravida group ($n=174$)			
First trimester	59.8 ± 24.3	17.4	120.0
Second trimester	55.4 ± 20.1	20.1	100.0
Third trimester	55.9 ± 19.7	20.0	80.0
Postpartum	67.6 ± 17.4	30.0	110.0
Control group ($n=120$)	67.5 ± 21.3	20.0	110.0

Table 2. Factors which have no correlations with BLLs in pregnant women

Influence factors	P value
Age	0.287
Distance from a factory	0.507
Distance from residence to street	0.359
Kitchen fuel	0.473
Floor level of residence	0.204
Existence of wall paint desquamating	0.788
Time of staying in street	0.956
Hair dyeing	0.417
Active smoking	0.252
Passive smoking	0.874
Consumption of canned food	0.702
Consumption of preserved egg	0.402
Use of Chinese herbal medicine	0.840

Table 3. Influencing factors correlated with BLLs in pregnant women

Influencing factors	Coefficient (β)	P value	OR	95% CI
Lead-related occupations	1.38	0.021	4.032	1.112-13.324
House painted <1 year	1.04	0.029	2.641	1.045-6.323
Cosmetics use	1.134	0.043	3.109	1.044-9.252
Frequent consumption of milk	-1.302	0.021	0.234	0.081-0.744
Frequent supplement of Ca, Fe, or Zn	-1.042	0.020	0.317	0.147-0.841

OR: odd ratio; CI: confidence interval.

pregnancy), the method of sampling (venous blood or finger blood), maternal factors (parity and maternal lead burden), as well as environmental factors (place of residence, exposure level, and exposure duration). Several other factors (methods of analysis, contamination of the samples) might also interfere with the final results.²¹ In comparison to previous studies, the present study detected lower BLLs in different periods of pregnancy. In this study, BLLs in all the three trimesters in the gravida group were lower than that in the healthy control group and then returned to the control group level in 6-12 weeks after delivery. Because the concentration of red blood cells may decrease during pregnancy due to the increase of plasma volume, and the majority of blood lead is bound to red blood cells, a lower BLL is expected during pregnancy.¹⁵ That may be a possible explanation for the above-mentioned finding. Another influencing factor of BLLs in the present study was the interventions to evacuate lead from women who had high BLLs before conception.

Currently, the most common sources of lead exposure in the US are lead-based paint, contaminated soil, household dust, drinking water, lead crystal, and lead-glazed pottery. Historically, lead intake into the gastrointestinal tract was mostly from food and drinking water, into the lung through breathing, and into cutis or mucous membranes *via* contact.²² Canned food may be polluted during processing and storage, thus being a source of lead exposure.²³ Many traditional Chinese herbal medicines have been found to contain considerable amounts of heavy metals and studies showed that lead poisoning is associated with the application of Chinese herbal medicine.^{24,25} However, in the present study, we found that women who took canned foods and Chinese herbal medicine had indiscriminate BLLs compared with those did not. It was possible that in a few pregnant women in this study, consumption of canned foods and Chinese herbal medicine had little influence on their BLLs. Drinking water is a more common source of lead exposure. Lead leaches out from plumbing systems which contain lead pipes or lead solders, making the lead level higher in the tap water. The corrosiveness of the water, the quantity and surface area of the lead materials, the age of the lead components, and the temperature of the water also affect lead levels.^{23,26} Since all of the participants of this study were from urban area of Nanjing, where water was supplied through the same pipeline system, we did not consider water as an influencing factors for BLLs.

Lead may interact with various nutrients including calcium, iron, and zinc. Supplements of these nutrients could reduce the absorption of lead and release of it from

maternal bones.^{27,28} Milk contains abundant nutrients (proteins, calcium, iron) that could reduce lead absorption or facilitate lead excretion.²⁹ This may partly explain our finding that the women who regularly took calcium, iron, and zinc supplements or milk had lower BLLs. Leaded gasoline accounted for most of the airborne lead pollution in large cities.³⁰ Dust and soil are the final resting place for airborne lead from gasoline. Since the ban on leaded gasoline in 2000 in China, the influence of automobile exhaust on BLLs has been diminished, which may account for the result that the distance of residence from street was not correlated with BLLs in this study. The occupations related to metal processing are another source of lead pollution.^{14, 31} The present study also found that the women who were occupied with lead-related work had higher BLLs.

However, we found that distance from a factory (such as battery factory, iron and steel factory) had no correlation with BLLs in pregnant women. This may be interpreted that since many factories (such as iron and steel factory) had been removed to suburbs, most of our study subjects were not living near a factory.

In the present study, BLLs in the pregnant women who lived in a house/apartment painted less than 1 year before were higher, which may be due to the lead-containing paints and other decoration materials. Although using leaded paint in residential decoration was banned, no intervention has been made so far to remove existing lead-based paint from apartments constructed before this edict went into effect.³¹ The older the building is, the more leaded paint desquamating and plumbeous particulates there will be, hence the more harm to health.¹⁴ Nevertheless, this study detected no correlation between wall paint desquamating and BLLs, which may be because of the small number of pregnant women living in apartments having wall paint desquamating. Cosmetics are another common source of lead in daily life. This study found that the pregnant women who usually wore cosmetics had higher BLLs.

In conclusion, the present study demonstrated that BLLs in all the three trimesters in pregnant women were lower than that in non-pregnant controls, which returned to the level of control group in 6-12 weeks after delivery. Lead-related occupations, cosmetics use, and living in a house/apartment painted less than 1 year are risk factors, while calcium, iron, zinc supplementation, and milk consumption are protective factors for BLLs in pregnant women. Those influencing factors could be useful for enacting measures to reduce lead exposure for pregnant women. BLLs in pregnant women should be monitored. Health care organizations and government

bodies should carry out a series of measures to reduce lead exposure, including encouraging healthy diet and living habits in women of child-bearing age, educating people about lead poison, and maintaining a better environment.

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Notice of Retraction

The Editor of Chinese Medical Sciences Journal retracts the following article: Zhen Li, Zhong-gao Wang, Bian Ce, Chen Xiu, Han Bing, Gao-feng Hou, Chu Jian, and Cui Qi. Interferon Regulatory Factor-1 Exerts Inhibitory Effect on Neointimal Formation after Vascular Injury. *Chin Med Sci J* 2009; 24(2): 91-6. PubMed ID: 19618605. The reason was

that the first author, Zhen Li, used data contained in this article without permission of Dr. Masatsugu Horiuchi, Department of Molecular Cardiovascular Biology and Pharmacology of Ehime University. The first author admitted personal responsibility for the mistake.