Letter to the Editor

A Comparative Study of Blood Lead Levels in Urban Children in China: The China Nutrition and Health Survey (CNHS) 2002 and 2012*

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Pb is a well-known toxic metal that has attracted considerable attention because of its ubiquitous distribution in the environment owing to the recent industrialization and rapid urbanization in China. In general, Pb from contaminated food, water, and dust enters the body through different channels, spreads throughout the body, combines with multiple amino acids, and interferes with normal physical activity. Chronic Pb exposure can affect the hematological, cardiovascular, renal, reproductive, and nervous systems[1], and has aroused serious concern. From the perspective of risk management, timely monitoring and assessment of Pb exposure is urgently required.

Children, particularly those living in urban regions, are the most sensitive group owing to their special physiological traits and living habits. Pb exposure can cause various adverse effects in children, including injury to the hematopoietic system, neurocognitive and behavioral dysfunctions, and potential health risks in adulthood[2]. To avoid health risks, several steps have been taken in China, such as prohibition of the use of leaded gasoline in 2000 and reduction in Pb content in processed foods and packaging materials.

Human biomonitoring is a reliable approach for assessing pollutant exposure and has been widely adopted worldwide. Whole-blood samples are commonly used for the assessment of Pb exposure in the population. In this context, the notion of reference values (RVs) was first proposed[3], and RV_{95} was further defined as the 95th percentile of measured target pollutant in the population within the 95% confidence interval (*CI*)[4]. RV_{95} indicates the individuals who are highly exposed to the substance of interest and need increased attention. To date, similar RVs for blood Pb levels (BLLs) have been established in several developed countries, and 100 μg/L, 50 μg/L, and < 35 μg/L have been proposed as safe thresholds[5]. Regional BLLs have been investigated in China, but few population-based national surveys have reported RVs and RV_{95}s in children.

To address this gap, we determined BLLs in urban Chinese children from the biobanks established as part of the China Nutrition and Health Survey (CNHS) in 2002 and 2012. Furthermore, we assessed Pb exposure and estimated the national RV_{95}s of BLL to facilitate decision and policy making on public health.

This study used data from CNHS 2002 and CNHS 2012, which were both conducted at > 200 monitoring sites across 31 provinces (except Hong Kong, Macau, and Taiwan, China) in China to assess dietary intake, health status, and behavioral habits. Participants were selected using multistage stratified cluster random sampling and probability proportionate to the population size. Written informed consent was obtained from the participants in the two surveys. The protocols of both surveys were approved by the Ethics Committee of the Chinese Center for Disease Control and Prevention. In the current study, urban children (boys and girls) aged 6–11 years were selected, and corresponding whole-blood samples were simultaneously selected from the CNHS 2002 and CNHS 2012 biobanks. According to the International Federation of Clinical Chemistry guidelines, the sample size for determining RV should be at least 120 individuals; thus, the total number of included participants should be considered when RVs are calculated in targeted individuals. The detailed plan of

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this study was approved by the Ethics Committee of the National Institute of Nutrition and Health of the Chinese Center for Disease Control and Prevention.

In the two surveys, venous blood samples were drawn from each participant after a fasting period of > 8 h using a BD vacutainer blood collection tube containing heparin lithium. Blood samples were stored at −70 °C in the biobanks of CNHS 2002 and CNHS 2012 without thawing until analysis. In the current study, the blood samples of the included participants were selected based on a one-to-one correspondence from the biobanks of CNHS 2002 and CNHS 2012. Blood samples (100 µL) were slowly thawed at room temperature, vortexed, and diluted in a 1:25 (v/v) solution of 0.5% (v/v) high-purity nitric acid (Beihua, China) and 0.05% (v/v) Triton X-100 (Sigma, USA). Participants' BLLs were determined using a triple quadrupole inductively coupled plasma mass spectrometer (Q-ICP-MS, PerkinElmer, NexION® 350D, USA) equipped with an auto-sampler (PerkinElmer, model AS−93 plus, USA).

For quality control, certified commercial reference materials (Seronorm™ Trace Elements Whole Blood Level-1, Level-2, and Level-3, Norway) were used after each batch of 50 samples to monitor the accuracy and precision of the analytical method. The limits of the method for detection and quantification of Pb are calculated as 3- and 10-fold of the standard deviation (SD) of the corresponding concentration of 11 independent blank replicates multiplied by the dilution factor, respectively. In this study, the limits of detection and quantification of the method were 0.24 µg/L and 0.79 µg/L, respectively. The intra- and inter-day precisions of the method for Pb detection were between 1.0% and 4.8%, and recoveries with Level-1, Level-2, and Level-3 reference materials were 88.2%, 92.3%, and 106.7%, respectively. Blood samples were prepared and analyzed at the National Institute for Nutrition Health at the Chinese Center for Disease Control and Prevention.

All statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, NC, USA). Differences in categorical variables were analyzed using the χ^2 test, and continuous variables were examined using the Kolmogorov–Smirnov test. Participants were classified according to sex (boy or girl), age group (6−7 years, 8−9 years, and 10−11 years), race (Ethnic Han or Ethnic minority), residence region (South or North), and body mass index (BMI) (Underweight, Normal, Overweight, and Obese). The Qinling–Huaihe line was considered the dividing line between South and North China. The Z scores of the BMI-for-age growth reference for 5–19 years were used to classify participants according to BMI (underweight, overweight, and obese was defined as < SD−2, > SD+1, and > SD+2, respectively) as suggested by the World Health Organization. The BLLs of urban children are presented as the median, interquartile range, and RV_{95}. In this study, 100 µg/L and 50 µg/L were selected as the BLL threshold. The RV_{95}s of BLLs and the prevalence of elevated BLLs were estimated. Differences between subgroups were compared using the Mann–Whitney or Kruskal–Wallis tests. Statistical significance was set as $P < 0.05$.

This study aimed to determine blood Pb concentrations and describe the changes based on data from CNHS 2002 and CNHS 2012. In total, 2,182 urban children (1,036, CNHS 2002; 1,146, CNHS 2012) were included (Table 1). The average age and BMI in CNHS 2002 and CNHS 2012 were 8.7 ± 1.8 years and 16.2 ± 1.8 and 9.2 ± 1.8 years and 17.1 ± 3.4, respectively. There were no significant differences according to sex (P = 0.735 > 0.05) and

Table 1. The characteristics of participants in the China Nutrition and Health Survey (CNHS) 2002 and the CNHS 2012

Variables	CNHS 2002	CNHS 2012
	Number (%)	Number (%)
Total	1,036 (100.0)	1,146 (100.0)
Sex		
Male	510 (49.7)	578 (50.4)
Female	516 (50.3)	568 (49.6)
Age group (years)		
6–7	337 (32.5)	264 (23.0)
8–9	323 (31.2)	371 (32.4)
10–11	376 (36.3)	511 (44.6)
Race		
Han	962 (94.9)	1,084 (94.6)
Other	52 (5.1)	62 (5.4)
Residence region		
South	178 (17.2)	678 (59.2)
North	858 (82.8)	468 (40.8)
BMI status		
Thinness	229 (22.1)	235 (20.5)
Normal	545 (52.6)	478 (41.7)
Overweight	128 (12.4)	110 (9.6)
Obese	134 (12.9)	323 (28.2)

race (P = 0.769 > 0.05) between CNHS 2002 and CNHS 2012, but significant differences were observed according to age group (P < 0.0001), residence region (P < 0.0001), and BMI (P < 0.0001).

Table 2 shows the BLLs and RV_{95}s of urban children in CNHS 2002 and CNHS 2012. Overall, BLLs noticeably decreased over 10 years, as did the RV_{95}s. The median BLL and RV_{95} was 67.4 μg/L and 149.1 μg/L and 36.9 μg/L and 107.9 μg/L in CNHS 2002 and CNHS 2012, respectively. Significant differences were observed according to sex (P < 0.0001), race (P < 0.0001), and residence region (P < 0.0001) between CNHS 2002 and CNHS 2012. There was a significant difference in BLL between the age groups in CNHS 2002 (P < 0.0001), but no significant difference was observed in CNHS 2012 (P > 0.05). Furthermore, the median BLL was significantly higher in boys than in girls (P < 0.0001), and in the ethnic Han group than in the ethnic minority group (P < 0.0001), but presented as an inverse distribution in the South compared with the North (P < 0.0001).

Pb exposure risks according to the threshold in urban children in CNHS 2002 and CNHS 2012 are shown in Table 3. The Pb exposure risk clearly decreased in 10 years, in the overall sample and in each subgroup. In CNHS 2002, the prevalence of BLLs > 50 μg/L and > 100 μg/L was 74.0% and 18.2%, respectively, while the corresponding prevalence dropped to 28.4% and 5.2% in CNHS 2012, respectively. In CNHS 2002, a significant difference in the prevalence of BLL > 50 μg/L was observed according to race alone (P = 0.0015). In contrast, significant differences were observed in the prevalence of BLL > 50 μg/L according to the residential region (P = 0.0007) and in the prevalence of BLL > 100 μg/L according to race (P = 0.0141 < 0.05) and residence region (P = 0.0407 < 0.05) in CNHS 2012.

With rapid industrialization and urbanization, the adverse effects of chronic Pb exposure have caused extensive concern. This study showed that compared with CNHS 2002, BLLs in CNHS 2012 significantly decreased by nearly half from 67.4 μg/L to 36.9 μg/L, and the RV_{95}s declined from 149.1 μg/L to 107.9 μg/L. In addition, the prevalence of BLL

Table 2. The blood lead levels (BLLs) and reference values (RVs) (μg/L) of urban children in the China Nutrition and Health Survey (CNHS) 2002 and the CNHS 2012

Variables	CNHS 2002			CNHS 2012		
	M_0	IQR	RV_{95}s	M_0	IQR	RV_{95}s
Total	67.4	49.6–90.8	149.1	$36.9^{†}$	27.6–52.6	107.9
Sex						
Boys	72.5^{a}	52.9–96.4	167.6	$38.4^{†a}$	28.6–53.8	112.2
Girls	63.7^{b}	47.5–85.3	133.3	$35.2^{†b}$	26.5–51.1	117.3
Age group (years)						
6–7	71.6^{a}	53.8–93.1	147.8	$35.7^{†}$	27.0–48.3	110.8
8–9	69.6^{a}	50.8–95.6	170.7	$37.7^{†}$	28.7–54.8	115.6
10–11	63.0^{b}	46.1–85.8	157.5	$37.2^{†}$	27.1–54.1	122.9
Race						
Han	66.7^{a}	48.8–90.4	147.7	$36.4^{†a}$	27.2–52.3	105.9
Other	79.7^{b}	59.4–106.3	146.2	$43.1^{†b}$	35.6–58.5	187.2
Residence region						
South	61.4^{a}	43.4–82.2	139.8	$40.5^{†a}$	28.1–63.1	108.2
North	69.5^{b}	51.8–93.6	152.9	$34.2^{†b}$	27.2–43.8	69.9
BMI status						
Thinness	64.7	48.6–86.2	127.4	$37.3^{†}$	26.8–52.3	102.4
Normal	66.3	49.6–90.4	105.0	$35.7^{†}$	26.9–51.3	90.0
Overweight	70.3	48.7–90.0	149.8	$36.8^{†}$	27.7–47.5	139.7
Obese	78.0	54.2–99.0	155.4	$38.9^{†}$	29.4–56.7	150.3

Note. M_0, median; IQR, interquartile range; RV_{95}s, reference values; [†]Means significant difference between the CNHS 2002 and the CNHS 2012; Values sharing the different superscript letter (a and b) denote a significant difference between the subgroup such as sex, age group, race, region, and BMI status.

> 50 μg/L and > 100 μg/L decreased from 74.0% and 18.2%, respectively, in CNHS 2002 to 28.4% and 5.2 %, respectively, in CNHS 2012. The results of this study indicate that the BLLs in urban Chinese children remained relatively high, despite a noticeable decrease from 2002 to 2012.

Chronic Pb exposure in urban children requires extra attention compared to that in children living in rural areas because exposure sources such as traffic, architectural coatings, and possible contact through parental occupational exposure, are more frequent in urban areas. The distinct decline in BLLs in CNHS 2012 compared with those in CNHS 2002 (from 67.4 μg/L to 36.9 μg/L) is undoubtedly attributable to national efforts, including the phase out of leaded gasoline, a transition from coal fuel to clean energy alternatives, and closure of heavily polluting enterprises. However, BLLs in urban children remain higher in China than in developed countries. The median BLLs (67.4 μg/L, and 36.9 μg/L) for urban Chinese children are almost thrice those synchronously reported from Germany (9.5 μg/L)[6] and Korea (12.3 μg/L)[7], but slightly lower than those in Egypt (90 μg/L)[8], and consistent with those in rural China (63−31 μg/L)[9] and South Africa (64 μg/L)[10]. The differences in BLLs could be related to the living environment, dietary habits, demographic characteristics, and socioeconomic status.

In this study, among urban children, BLLs were significantly higher in boys than in girls ($P < 0.05$), which is consistent with similar reports from Korea[7]. This could be attributed to the higher hematocrit level or a higher exposure chance in boys, due to greater contact with polluted soil, air, or Pb-based toys or paints, and reluctance to maintain personal hygiene as compared with girls. In addition, Pb exposure increases with age in children because of the more frequent hand-to-mouth and outdoor activities in older children. However, the results of our study were not consistent with those of previous studies, even with slight fluctuations. This difference can be attributed to the growing knowledge on Pb hazards. Among urban children, BLLs were lower in

Table 3. Assessment of blood lead levels (BLLs) of urban children using the recommended threshold (50 μg/L and 100 μg/L) in the China Nutrition and Health Survey (CNHS) 2002 and the CNHS 2012

Variables	CNHS 2002				CNHS 2012			
	P^1	95% *CI*	P^2	95% *CI*	P^1	95% *CI*	P^2	95% *CI*
Total	74.0	71.4–76.7	18.2	15.9–20.6	28.4†	25.8–30.9	5.2†	3.8–6.6
Sex								
Male	78.0	74.5–81.6	22.2	18.6–25.8	31.1†	27.4–34.9	5.7†	3.8–7.6
Female	70.2	66.2–74.1	14.0	11.0–16.9	25.5†	22.0–29.1	4.6†	2.9–6.3
Age group, (years)								
6–7	78.3	73.9–82.7	19.0	14.8–23.2	22.7†	17.7–27.8	4.2†	1.8–6.6
8–9	75.5	70.9–80.2	20.7	16.3–25.2	30.2†	25.5–34.9	5.9†	3.5–8.3
10–11	68.9	64.2–73.6	15.4	11.8–19.1	29.9†	25.9–33.9	5.1†	3.2–7.0
Race								
Han	73.1^a	70.3–75.9	17.6	15.2–20.0	28.1†	25.5–30.8	4.7^{†a}	3.4–6.0
Other	90.4^b	82.4–98.4	28.9	16.5–41.2	32.3†	20.6–43.9	12.9^{†b}	4.6–21.3
Residence region								
South	76.1	73.3–79.0	19.8	17.2–22.5	37.0^{†a}	33.3–40.7	8.1^{†a}	6.1–10.2
North	64.0	57.0–71.1	10.7	6.1–15.2	15.8^{†b}	12.5–19.1	0.9^{†b}	0.0–1.7
BMI status								
Thinness	71.6	65.8–77.5	17.5	12.6–22.4	29.8†	23.9–35.6	6.0†	2.9–9.0
Normal	74.1	70.5–77.8	16.9	13.7–20.0	25.9†	22.0–29.9	6.1†	3.9–8.2
Overweight	73.4	65.8–81.1	21.1	14.0–28.2	20.9†	13.3–28.5	4.6†	0.7–8.4
Obese	78.4	71.4–85.3	22.4	15.3–29.5	33.4†	28.3–38.6	3.4†	1.4–5.4

Note. *P*, prevalence; P^1, means the prevalence of BLL > 50 μg/L; P^2, means the prevalence of BLL > 100 μg/L; *CI*, confidence interval; †Means significant difference between the CNHS 2002 and the CNHS 2012; Values sharing the different superscript letter (a and b) denote a significant difference between the subgroups such as sex, age group, race, region, and BMI status.

the ethnic Han than in the ethnic minorities in both CNHS 2002 and CNHS 2012. The different dietary habits are considered the major reason, and the smaller sample size likely increased the uncertainty of variation. In this study, a reverse distribution of BLLs was observed in the residential regions (South and North) between the two surveys. This variation might be ascribed to the transition of regional economics, industrial production, and environmental pollution during the intervening 10 years. In addition, the change in Pb status according to BMI status might indicate a disparity in Pb accumulation.

The Pb poisoning thresholds are inconsistent between countries. It should be noted that RVs are established according to local exposure levels; thus, it might be time to consider establishing the RV for BLLs in Chinese children. The new RV for BLLs would help identify children with BLL > RV_{95} as having higher Pb exposure and requiring increased attention. Accordingly, to avoid the adverse effects of Pb exposure, our efforts should focus on preventing children from being exposed to high Pb levels, while maintaining resources to respond quickly when children have been exposed.

Our findings should be interpreted in light of the strengths and limitations of the study. First, this was a national population-based study that used data from CNHS 2002 and CNHS 2012. The two cross-sectional datasets provide the RVs for BLLs in urban children and depict a real change in the trend for Pb exposure risk. The findings in this study could strongly assist in understanding the necessity and feasibility of Pb-restrictive measures. Second, the sample size of this study might be too small to draw reliable conclusions from some subgroup analyses. Moreover, because some socioeconomic factors were missing, the findings do not provide a clear picture of Pb exposure. Third, a single blood sample was used to assess Pb exposure risk in this study. BLLs may fluctuate over time in one day, even in a short time; thus, the use of a single blood sample to assess Pb exposure is based on the assumption that a single measure represents the usual exposure levels.

In summary, nationally representative data on Pb exposure in urban Chinese children aged 6–11 years were obtained from the CNHS 2002 and CNHS 2012 databases. The findings of our study indicate that BLLs in urban Chinese children improved during the 10-year study period, but Pb exposure remains a serious public health threat. Therefore, it is imperative to understand the ongoing surveillance of Pb exposure, continue to implement public health interventions, and protect Chinese children from the harmful effects of Pb toxicity.

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