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The Time Trend of Blood Lead and Cadmium Levels in Rural Chinese Children: China Nutrition and Health Survey 2002 and 2012

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Abstract

This study was to investigate blood lead (Pb) and cadmium (Cd) levels and time trend in rural Chinese children derived from the China Nutrition and Health Survey 2002 and 2012 (CNHS 2002, CNHS 2012). In total, 1698 and 1581 of rural Chinese children were selected from the CNHS 2002 and the CNHS 2012 databases, respectively. The blood Pb and Cd levels were determined by inductively coupled plasma mass spectrometer (ICP-MS), whilst the prevalence of blood Pb levels >5 μg/dL and blood Cd levels >0.5 μg/L and the corresponding reference values (RV_{95}s: the upper limit of 95% confidence interval of 95th percentile) were together calculated. From the CNHS 2002 to the CNHS 2012, median concentrations in blood were severally decreased from 6.3 to 3.1 μg/dL for Pb and from 0.64 to 0.39 μg/L for Cd. The prevalence of blood Pb levels >5 μg/dL had decreased from 63.6 to 14.2%, together with blood Cd levels >0.5 μg/L prevalence from 62.7 to 33.5%, respectively. The RV_{95}s of blood Pb and Cd levels were 15.2 μg/dL and 1.54 μg/L in the CNHS 2002, as well as 6.3 μg/dL and 1.12 μg/L in the CNHS 2012. In conclusion, blood Pb and Cd levels had been obviously improved in rural Chinese children during the past 10 years. However, the risks of Pb and Cd exposure are still serious and required to have continuous health monitoring and evaluation, even call for greater collaboration of the government and society.

Keywords Lead · Cadmium · Human biomonitoring · Exposure risk · Reference value

Introduction

Lead (Pb) and cadmium (Cd) are two ubiquitous heavy metals that have great toxicological significance in the general population [1, 2]. Excess Pb and Cd exposure has been widely recognized to have a range of adverse health effects, including neurological, cardiovascular, hematological, nephrotoxic, carcinogenic, and genotoxic effects [3, 4]. Nevertheless, a considerable amount of industrial pollutants containing Pb and Cd have been discharged so far and persistently stayed in the environment. With advanced industrialization and urbanization, further aggravation of bioaccumulation in food chains reaches humans.

Children appear to be the most susceptible to adverse effects from Pb and Cd exposure and have a higher health burden as compared to other groups in the population [5], due to higher basal metabolic rate, larger food uptake, and lower toxin elimination rate. In children, excess Pb and Cd exposure can cause numerous negative effects, including impaired neurodevelopment, developmental delay, reduced intelligence quotient, and serious adverse outcomes on bone composition and development [6, 7]. From the viewpoint of public health, there is a pressing need for adequate information regarding adverse events from Pb and Cd exposure. Thus, as an effective tool, human biomonitoring is progressively playing an essential role in identifying and targeting high-risk groups, evaluating interventions, and tracking exposures over time [8].

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Blood samples are currently one of the most common choices in laboratory analyses for assessing recent and past exposures to chemical pollutants. Reference values (RVs) are currently recommended to detect the levels in individuals with higher exposures to a substance of interest [9]. Thus, RV_{95}s were further defined as the 95th percentile's upper limit of the 95% confidence interval (CI) of the measured pollutants, indicating the upper margin of the current background exposure of the general population to a given pollutant at a given time [10]. To date, several reference values for blood Pb and Cd levels have been successively established in some countries, such as the USA [11], Canada [12], Germany [13], Belgium [14], and Korea [15]. However, there is still a paucity of national data on blood Pb and Cd levels in Chinese children, especially those living in rural areas. Coincidently, the conduction of the China Nutrition and Health Survey in 2002 and 2012 (CNHS 2002 and CNHS 2012) provided the valuable opportunities to evaluate and understand pollutant exposure implications in rural Chinese children in the past and in future.

Therefore, the purpose of this study was to investigate national data of blood Pb and Cd levels from the CNHS 2002 and CNHS 2012 databases and delineate the time trend in rural Chinese children. Furthermore, it could be used for the exposure risk assessments for the formulation of public health policies and their management.

Materials and Methods

Study Population

This study was carried out from the CNHS in 2002 and 2012, both covering 31 provinces, autonomous regions, and municipalities in China (Hong Kong, Macao, and Taiwan were excluded). A detailed description of the CNHS 2002 and CNHS 2012 survey designs and sampling strategies has been reported elsewhere [16]. The recommended sample size for determining the reference value was at least 120 according to the International Federation of Clinical Chemistry (IFCC) guidelines; the sample size of each survey was estimated to be at least 1440, for an alpha level of 0.05, when considering residence region (general, poor), sex (male, female), and age group (6–7 years, 8–9 years, 10–11 years). All participants were then selected based on the CNHS 2002 and CNHS 2012 databases using a multistage stratified random sampling method. Information from included children was retrieved and reviewed, and signed consent forms were also examined. The study protocol was approved by the Ethics Committee of the National Institute for Nutrition and Health of the Chinese Center for Disease Control and Prevention.

Collection and Determination of Blood Samples

Blood samples were drawn from each participant after a fasting period of over 8 h using a BD vacutainer blood collection tube containing heparin lithium for venipuncture in the CNHS 2002 and CNHS 2012. Blood samples were stored frozen at −70 ℃ in the biobanks of the CNHS 2002 and CNHS 2012 without freeze-thawing, until analysis. In this study, blood samples were chosen based on the inclusion of children with a strict one-to-one association. Blood samples (100 μL) were melted, vortexed, and diluted in a 1:25 (v/v) solution of 0.5% (v/v) HNO_3 and 0.05% (v/v) Triton X-100 (Sigma, USA). Blood Pb and Cd levels were determined using a triple quadrupole inductively coupled plasma mass spectrometer (Q-ICP-MS, PerkinElmer, NexION® 350D, USA) equipped with an autosampler (PerkinElmer, model AS-93 plus, USA). Daily analytical conditions were optimized to meet the requirements of the analysis.

For quality control, the certified reference materials (Seronorm™ Trace Elements Whole Blood Level-2 and Level-3, Norway) were run with prepared blood once every 20 samples, to assess the accuracy and precision of the method. The limits of detection (LOD) and quantification (LOQ) of the method were calculated as 3- and 10-fold the standard deviation of the concentrations of 11 independent blank replicates multiplied by the corresponding dilution multiple. In this study, the LOD for the method was 0.24 μg/L for Pb and 0.02 μg/L for Cd, and the LOQ for the method was 0.79 μg/L for Pb and 0.06 μg/L for Cd, respectively. The intra- and inter-day precisions were 1.0% and 4.8% for Pb, and 1.3% and 5.0% for Cd. The recoveries of Pb and Cd in whole blood with level-2 and level-3 reference materials were 96.7% and 106.7%, respectively. Sample preparations and analysis were performed in an ISO class 6 clean room at the Key Laboratory of Trace Element Nutrition of the National Health Commission of the National Institute for Nutrition Health at the Chinese Center for Disease Control and Prevention.

Statistical Analysis

All statistical analyses were conducted using SAS 9.3 (SAS Institute, Cary, NC, USA). Categorical variables were analyzed using the χ^2 test and continuous variables were assessed using the Kolmogorov-Smirnov (K-S) test. Subgroups were classified according to residence region, sex, age group, and BMI status. BMI status was divided by the Z scores of the BMI-for-age growth reference for 5–19 years (thinness was defined as <-2 SD, overweight >1 SD, and obese was considered >2 SD) as suggested by the World Health Organization (WHO). Blood Pb and Cd levels were described in terms of median (M_0), interquartile range (IQR), and 95% reference intervals (2.5th to 97.5th percentile). The following values (5 µg/dL for Pb and 0.5 µg/L for Cd) were selected as the cutoff values [17, 18], justifying the threshold for determination of "elevated" levels. The prevalence of elevated blood Pb and Cd was further calculated. In addition, the RV_{95}s of blood Pb and Cd levels were estimated using the CNHS 2002 and CNHS 2012. Differences between subgroups were compared using the Mann-Whitney or Kruskal-Wallis tests. $P<0.05$ was considered significant.

Table 1 Sampling characteristics of study population in China Nutrition and Health Survey 2002 and 2012

Variables		CNHS 2002		CNHS 2012	
		N	Percent (%)	*N*	Percent (%)
		1698	-	1581	-
Residence	General	1300	76.6	960	60.7
	Poor	398	23.4	621	39.3
Gender	Boys	844	49.7	785	49.6
	Girls	854	50.3	796	50.4
Age	6–7 years	504	29.7	486	30.7
	8–9 years	589	34.7	510	32.3
	10–11 years	605	35.6	585	37.0
BMI status	Thinness	592	34.9	419	26.5
	Normal	860	50.6	647	40.9
	Overweight	99	5.8	123	7.8
	Obese	147	8.7	392	24.8

CNHS, China Nutrition and Health Survey; *N*, number; BMI status was classified as by *Z* score: thinness <−2SD, −2SD < normal <1SD, overweight >1SD, obese >2SD

Results

Characteristics of Study Population

For the included children, average age was 8.6 ± 1.7 years and 9.1 ± 1.8 years; average height was 127.6 ± 11.3 cm and 132.2 ± 12.5 cm; average weight was 25.6 ± 6.5 kg and 30.0 ± 10.1 kg; and BMI was 15.5±1.9 and 16.8±3.2. The sampling characteristics of the children included in the CNHS 2002 and CNHS 2012 are presented in Table 1. In total, 3279 (1698 versus 1581) rural Chinese children were included in the statistical analysis. There were no significant differences in the demographic characteristics between the CNHS 2002 and CNHS2012 ($P>0.05$).

Blood Pb and Cd Levels

Table 2 shows that median blood Pb concentration had decreased from 6.3 µg/dL in the CNHS 2002 to 3.1 µg/dL in the CNHS 2012. The overall change in blood Pb levels is shown in Fig. 1. Significant differences were observed in residence region, sex, age group, and BMI status ($P<0.001$). In the CNHS 2002, median blood Pb concentration was significantly higher in boys (6.6 µg/dL) than girls (6.0 µg/dL) ($P<0.05$), as well as in the general (6.8 µg/dL) than poor rural areas (4.6 µg/dL) ($P<0.05$). In the CNHS 2012, median blood Pb concentration was significantly higher in boys (3.3 µg/dL) than girls (2.9 µg/dL) ($P<0.05$), but significantly lower in the general (3.0 µg/dL) than poor rural

Table 2 Blood Pb concentrations (µg/dL) in the Chinese rural children from the CNHS 2002 and the CNHS 2012

Variables		CNHS 2002			CNHS 2012		
		M_0	P_{25}–P_{75}	$P_{2.5}$–$P_{97.5}$	M_0	P_{25}–P_{75}	$P_{2.5}$–$P_{97.5}$
Total		6.3	4.4–9.1	1.6–16.5	3.1	2.3–4.2	1.1–6.5
Residence	General	6.8[a]	4.8–9.4	2.0–16.7	3.0[a]	2.2–3.9	1.2–6.3
	Poor	4.6[b]	3.1–7.2	0.8–14.9	3.5[b]	2.4–4.9	0.9–6.8
Gender	Boys	6.6[a]	4.6–9. 5	1.9–16.7	3.3[a]	2.5–4.52	1.3–6.6
	Girls	6.0[b]	3.9–8.7	1.5–16.2	2.9[b]	2.2–3.9	1.0–6.5
Age groups	6–7 years	6.4	4.4–9.6	1.6–16.2	3.2	2.3–4.4	1.1–6.6
	8–9 years	6.3	4.5–8.8	1.9–15.8	3.1	2.3–4.2	1.1–6.6
	10–11 years	6.1	4.1–9.1	1.5–16.8	3.0	2.3–4.0	1.1–6.5
BMI status	Thinness	6.2	4.2–8.8	1.5–16.4	3.3	2.3–4.3	0.8–6.7
	Normal	6.3	4.4–9.2	1.8–17.1	3.2	2.4–4.4	1.1–6.6
	Overweight	6.1	4.4–9.2	2.1–13.1	2.8	2.2–3.9	1.2–6.0
	Obese	6.6	4.7–9.0	1.3–15.1	3.0	2.3–4.0	1.2–6.5

CNHS, China Nutrition and Health Survey; M_0, median; a and b mean significant difference; P_{25}, 25th percentiles; P_{75}, 75th percentiles; $P_{2.5}$, 2.5th percentiles; $P_{97.5}$, 97.5th percentiles; BMI status was classified as by *Z* score: thinness <−2SD, −2SD < normal <1SD, overweight >1SD, obese >2SD

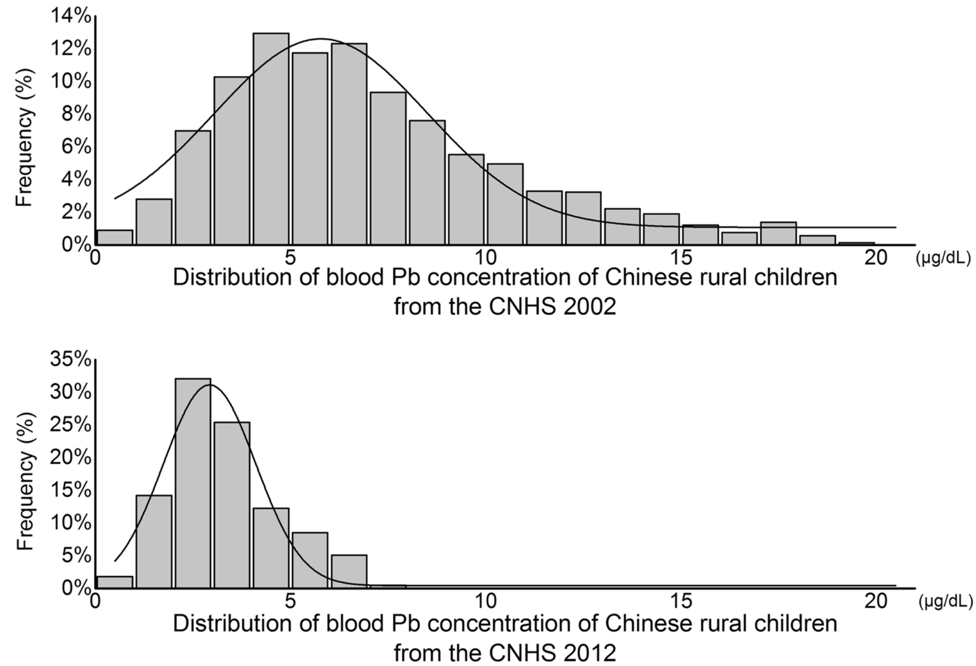

Fig. 1 The time change of blood Pb levels in rural Chinese children between 2002 and 2012

areas (3.5 μg/dL) ($P<0.05$). In addition, the median blood Pb concentration changed slightly with increased age and BMI. Of these, the overweight subgroup had the lowest blood Pb levels among the BMI groups.

As presented in Table 3 and Fig. 2, median blood Cd concentration was 0.64 μg/L in the CNHS 2002 and 0.39 μg/L in the CNHS 2012. There was a significant decrease in the CNHS 2012 as compared with the CNHS 2002 ($P<0.05$). In the CNHS 2002, a significant difference was observed in the blood Cd levels for residence region and sex ($P<0.01$). It was fluctuated slightly with increased age and BMI status, but without a significant difference ($P>0.05$). There was no significant difference in residence region or age group in the CNHS 2012 ($P<0.01$), but it was different for the residence regions during the CNHS in 2002.

Assessment for Pb and Cd Exposure

As shown in Table 4, there was a distinct decline in the overall or subgroup in the last 10 years. The prevalence of blood Pb levels >5 μg/dL decreased from 63.6% in the CNHS 2002 to 14.2% in the CNHS 2012. The percentage

Table 3 Distribution of blood Cd concentrations (μg/L) for Chinese rural children in the CNHS 2002 and the CNHS 2012

Variables		CNHS 2002			CNHS 2012		
		M_0	P_{25}–P_{75}	$P_{2.5}$–$P_{97.5}$	M_0	P_{25}–P_{75}	$P_{2.5}$–$P_{97.5}$
Total		0.64	0.42–0.91	0.09–1.69	0.39	0.20–0.60	0.02–1.21
Residence	General	0.63	0.43–0.89	0.09–1.68	0.47[a]	0.29–0.69	0.02–1.21
	Poor	0.66	0.38–0.97	0.12–1.73	0.25[b]	0.13–0.49	0.02–1.18
Gender	Boys	0.64	0.42–0.90	0.09–1.66	0.39	0.20–0.60	0.02–1.20
	Girls	0.63	0.42–0.93	0.09–1.74	0.40	0.20–0.61	0.02–1.21
Age groups	6–7 years	0.59	0.40–0.90	0.07–1.69	0.38[a]	0.17–0.59	0.02–1.15
	8–9 years	0.63	0.41–0.86	0.09–1.63	0.36[a]	0.19–0.58	0.02–1.21
	10–11 years	0.67	0.45–0.97	0.13–1.74	0.44[b]	0.22–0.65	0.02–1.22
BMI status	Thinness	0.66	0.42–0.98	0.11–1.78	0.40	0.21–0.59	0.02–1.24
	Normal	0.63	0.41–0.90	0.07–1.69	0.38	0.17–0.60	0.02–1.17
	Overweight	0.54	0.36–0.77	0.02–1.53	0.37	0.21–0.60	0.02–1.12
	Obese	0.64	0.46–0.87	0.13–1.38	0.41	0.23–0.61	0.02–1.21

CNHS, China Nutrition and Health Survey; M_0, median; a and b mean significant difference; P_{25}, 25th percentiles; P_{75}, 75th percentiles; $P_{2.5}$, 2.5th percentiles; $P_{97.5}$, 97.5th percentiles; BMI status was classified as by Z score: thinness <−2SD, −2SD < normal <1SD, overweight >1SD, obese >2SD

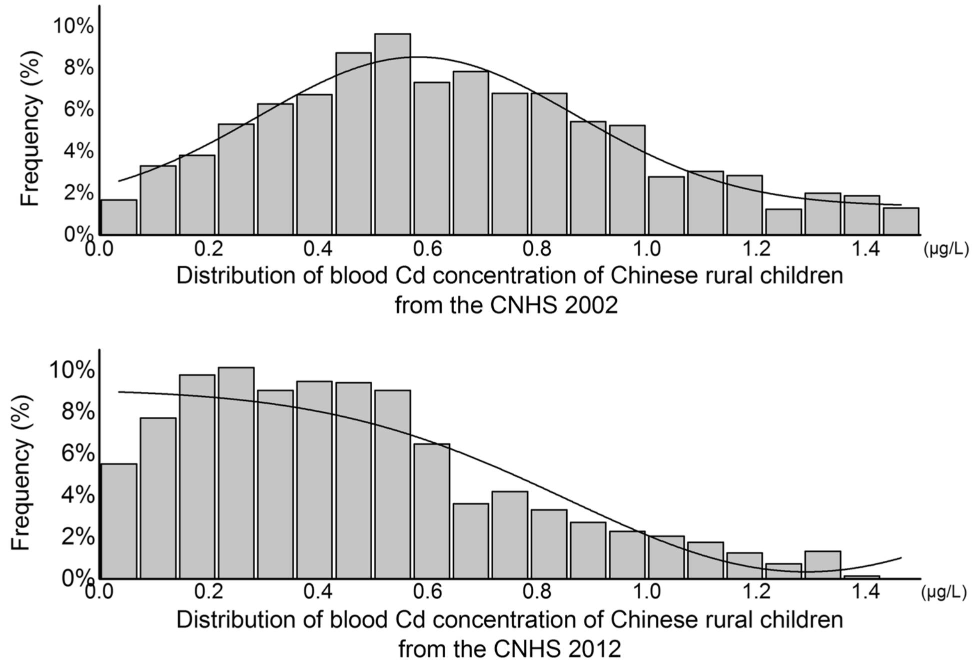

Fig. 2 The time change of blood cadimum levels in rural Chinese children between 2002 and 2012

Table 4 Prevalence of blood Pb and Cd concentration > 5μg/dL and > 0.5 μg/L for Chinese rural children in the CNHS 2002 and the CNHS 2012

Variables		CNHS 2002		CNHS 2012	
		Prevalence Pb > 5 μg/dL	Prevalence Cd > 0.5 μg/L	Prevalence Pb > 5 μg/dL	Prevalence Cd > 0.5 μg/L
Total		63.6	62.7	14.2	33.5
Residence	General	69.7[a]	63.3	9.1[a]	41.1
	Poor	44.3[b]	60.6	21.6[b]	21.7
Gender	Boys	67.0	63.3	17.5	31.5
	Girls	60.5	62.0	10.9	35.4
Age groups	6–7 years	64.3	59.5	15.8	32.3
	8–9 years	64.9	64.2	14.1	30.8
	10–11 years	61.8	63.8	13.3	36.8
BMI status	Thinness	64.0	63.2	16.9	34.6
	Normal	63.0	62.9	14.8	33.1
	Overweight	61.6	54.6	7.3	28.5
	Obese	66.7	64.6	13.0	34.4

CNHS, China Nutrition and Health Survey; *P*, percent; a and b mean significant difference; BMI status was classified as by *Z* score: thinness <−2SD, −2SD < normal <1SD, overweight >1SD, obese >2SD

of samples with blood Cd levels of >0.5 μg/L had also diminished from 62.7 to 33.5%. In the CNHS 2002, the prevalence of blood Pb levels of >5 μg/dL was significantly higher in the general than in the poor rural areas ($P<0.05$). However, no significant difference was observed in sex, age group, or BMI status ($P>0.05$). In the CNHS 2012, there was no significant difference in sex, age group, or BMI status for the prevalence of samples with blood Pb levels >5 μg/dL ($P>0.05$).

Reference Values for Blood Pb and Cd

According to the estimation, the RV_{95}s of blood Pb and Cd levels were 15.2 μg/dL and 1.54 μg/L, respectively in the CNHS 2002, as well as 6.3 μg/dL and 1.12 μg/L, respectively in the CNHS 2012 (Table 5). Regardless of the overall or subgroup analyses, a declining trend of RV_{95}s of blood Pb and Cd levels was observed in the CNHS 2012 as compared with the CNHS 2002.

Table 5 Reference values of blood Pb (μg/dL) and Cd (μg/L) for Chinese rural children in the CNHS 2002 and the CNHS 2012

Variables		CNHS 2002		CNHS 2012	
		P_{95} for Pb (95% CIs)	P_{95} for Cd (95% CIs)	P_{95} for Pb (95% CIs)	P_{95} for Cd (95% CIs)
		14.5 (14.0–15.2)	1.46 (1.41–1.54)	6.2 (6.0–6.3)	1.07 (1.02–1.12)
Residence	General	14.9 (14.3–15.8)	1.45 (1.37–1.54)	5.6 (5.3–5.9)	1.09 (1.06–1.15)
	Poor	13.0 (12.0–14.9)	1.48 (1.43–1.69)	6.5 (6.3–6.7)	0.97 (0.86–1.11)
Gender	Boys	15.0 (14.4–15.9)	1.44 (1.38–1.55)	6.3 (6.1–6.5)	1.05 (0.98–1.12)
	Girls	14.0 (13.0–14.8)	1.49 (1.40–1.61)	5.9 (5.7–6.3)	1.08 (1.04–1.16)
Age	6–7 years	15.0 (14.1–15.9)	1.41 (1.38–1.66)	6.2 (6.0–6.5)	1.01 (0.96–1.09)
	8–9 years	14.1 (13.4–15.2)	1.44 (1.34–1.54)	6.1 (5.8–6.6)	1.07 (0.99–1.20)
	10–11 years	14.4 (13.7–16.4)	1.53 (1.43–1.69)	6.2 (5.9–6.4)	1.10 (1.05–1.21)
BMI status	Thinness	14.7 (13.7–15. 8)	1.56 (1.44–1.69)	6.3 (5.9–6.6)	1.10 (1.02–1.21)
	Normal	14.9 (14.1–15.8)	1.45 (1.38–1.54)	6.3 (6.1–6.5)	1.07 (1.00–1.13)
	Overweight	12.6 (11.4–17.0)	1.25 (0.99–1.55)	5.7 (4.8–6.2)	1.01 (0.91–1.31)
	Obese	14.1 (12.5–17.7)	1.35 (1.17–1.69)	6.2 (5.8–6.5)	1.05 (0.95–1.21)

P_{95}, 95th percentiles; 95% confidence intervals (CIs)

Discussion

Reliable data on blood Pb and Cd levels were obtained in rural Chinese children derived from the CNHS in 2002 and 2012. The median blood Pb and Cd levels had greatly decreased from 6.3 to 3.1 μg/dL for Pb and from 0.64 to 0.39 μg/L for Cd. The prevalence of blood Pb levels >5 μg/dL and Cd levels >0.5 μg/L had 4.5 times (63.6 to 14.2%) and 1.9 times (62.7 to 33.5%) decrease, respectively. In addition, the RV_{95}s of blood Pb and Cd levels were 15.2 μg/dL and 1.54 μg/L in the CNHS 2002, respectively, as well as 6.3 μg/dL and 1.12 μg/L in the CNHS 2012, respectively. From a public health research perspective, the time changes in blood Pb and Cd levels could embody an inspiring improvement toward a healthy living environment and awareness.

To date, human biomonitoring has been conducted and documented in certain populations [19, 20]. Given that Pb and Cd exposure is mainly derived from contaminated air, dust, food, water, or jewelry, inhalation of cigarette smoke, or improper handling of the metal itself [21]. Several effective interventions have been implemented, such as bans on lead-based paint and gasoline, tobacco control, good hygiene, and dietary habits. Our findings confirm that exposure levels of Pb and Cd in rural Chinese children are gradually declining. Nevertheless, blood Pb levels (6.3 μg/dL or 3.1 μg/dL) were still higher in rural Chinese children as compared with Americans at 1.2 μg/dL [11] or Australian's 1.5 μg/dL [22]. It was only similar to the Italian's 3.4 μg/dL [23], even approaching half of the Brazilian's 6.5 μg/dL [24] while the literature reported a level of 8.9 μg/dL in China [25]. By contrast, blood Cd levels (0.64 μg/L or 0.39 μg/L) were relatively consistent with Cd exposures in Korea (0.30 μg/L) [26] and Brazil (0.48 μg/L) [27], but far higher than the German levels (<0.06 μg/L). From the above comparison, we illustrate that Pb and Cd exposure is still of great concern, although blood Pb and Cd levels have decreased considerably in just the last 10 years.

A 10% significantly higher blood Pb level was observed in boys compared to girls. This subtle difference was in line with previous studies from Korea [28], Germany [17], and the USA [29]. This may be explained by more sources of Pb exposure and higher hematocrit levels in boys [30]. Notably, the contrasting blood Pb and Cd levels were observed in the residence regions between the CNHS 2002 and the CNHS 2012. Blood Pb and Cd levels were positively associated with increased age and BMI. The distribution and time trend could be attributed to the socioeconomic factors and bioaccumulation in adipose tissue. In addition, Cd exposure in Asia is generally higher than in Europe or the USA due to higher daily intake of rice and vegetables grown in locally contaminated soil [31]. The RV_{95}s of Pb and Cd blood levels are regularly regarded as convenient tools for early warnings in public health. We tentatively estimated the RV_{95}s of blood Pb and Cd levels in rural Chinese children. They were indeed different in the CNHS 2002 versus the CNHS 2012, and out of line with other countries and regions. As previously reported, the RV_{95}s of blood Pb and Cd levels could be variable and will play an important role in future risk assessments.

This study was the first nationwide population-based study derived from the CNHS 2002 and the CNHS 2012 and reported reliable data on blood Pb and Cd levels in rural Chinese children. However, this study had some limitations. First, the gap between the two surveys should be prudently considered when comparing residential regions, because of the non-one-to-one correspondence in rural areas and only a little in the readjustment district. Second, the RV_{95}s of blood Pb and Cd levels always fluctuate with changes in population, and they are also determined by the ambient environment and monitoring times. Blood Pb and Cd levels in excess RV_{95}s only indicate elevated risks in advance. Third, there is still a lack of information on sociodemographic and environmental factors, and a longitudinal and professional correlation analysis could not be performed.

Conclusions

This study obtained reliable data on Pb and Cd exposures in rural Chinese children derived from the CNHS 2002 and the CNHS 2012. These findings indicate that the exposure risks of Pb and Cd in rural Chinese areas significantly decreased from the CNHS 2002 to the CNHS 2012. Nevertheless, regardless of the RV_{95}s of Pb and Cd exposures, the exposure risks are still rather high, and it is necessary to focus continuous attention, provide in-depth monitoring, and conduct health evaluations, together with greater collaboration between the government and society.

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Author Contribution Xiaobing Liu and Xiaoguang Yang conceived and designed the conduction of this study; Xiaobing Liu, Huidi Zhang, Yu Zhang, Jun Wang, Hongxing Tan, and Lichen Yang performed the experiment; Xiaobing Liu wrote the manuscript; Xiaoguang Yang and Jianhua Piao reviewed the manuscript.

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Data Availability The data used to support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Competing interests The authors declare no competing interests.

Conflict of Interest The authors declare no competing interests.

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