Biological monitoring and health assessment of 21 metal(loid)s in children and adolescents in Liuzhou City, Southwest China

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Received: 1 June 2021 / Accepted: 5 October 2021 / Published online: 25 October 2021
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Abstract
Exposure to metal(loid)s is associated with adverse effects on human health, especially for children and adolescents. This study was designed to evaluate metal(loid)s exposure in 2050 children and adolescents aged 6–18 years from Liuzhou City, Southwest China. The detection rates of 21 elements were all above 99%. We found that age was an important predictor for most elements, and that children exhibited more exposure than adolescents, expect for strontium (p < 0.05). Interestingly, urinary levels were higher in girls for 13 of our study elements. Multiple regression models also showed that dietary habits also affected the distribution of elements. Moreover, we estimated exposure risk by generating the hazard quotient (HQ) for single metal and the hazard index (HI) for the co-occurrence of metals. The HQ of cadmium was > 1 at the P95 value and that the risk of the mixed effect of cadmium, mercury, and thallium was not negligible, and indicated that the associated risk was of concern. Our results provide basic data on the reference values of urinary metal(loid) levels and an assessment of health risks for children and adolescents that reside in industrial areas.

Keywords Metal(loid)s · Children and adolescents · Exposure · Biomonitoring · Predictors · Health assessment

Introduction
Metal(loid)s are existing widely in the air, drinking water, and foods encountered in daily life. These compounds gain entry into the body through the respiratory and digestive tract, as well as through dermal absorption (Nordberg et al. 2014). Some metals are essential and are needed only in trace amounts, while in excess can be harmful. Arsenic and most heavy metals are directly toxic and adversely affect the central nervous system, the cardiovascular and hematopoietic systems and the gastrointestinal tract (Diyabalange et al. 2017; Roca et al. 2016). Children and adolescents are particularly susceptible to the effects of these elements because of the fragility of the developing nervous system (Sughis et al. 2014). These age groups also exhibit higher rates of intestinal absorption and lower rates of renal excretion than do adults (Ilimiwati et al. 2015; Molina-Villalba et al. 2015).

Exposure to metal(loid)s is generally measured in urine and this type of biomonitoring has demonstrated widespread human exposure to elements (CDC 2021; Godebo et al. 2019; Lewis et al. 2018; Roca et al. 2016; Zhang et al. 2017). For instance, the National Health and Nutrition Examination Survey (NHANES) reported that children and adolescents in the USA have detectable concentrations of a variety of metal(loid)s (CDC 2021). Another study that screened for the presence of 23 elements in urine from Ethiopian Rift populations aged 10–50 years found that arsenic, boron, molybdenum, manganese, thallium,
lithium, and zinc exceeded that of the reference population (Godebo et al. 2019). In China, a study that monitored 9 urinary metal(loid)s in 210 children aged 2–12 years and reported the creatinine-adjusted concentrations of aluminum, barium, cerium, and vanadium in urine was significantly correlated to one another (Zhang et al. 2017). These biomonitoring studies from different countries investigated a variety of influencing factors, including diet, lifestyle, and geographical characteristics. The demographic characteristics varied from region to region; therefore, further research is required to determine whether metal(loid)s accumulation is linked to demographic characteristics and dietary habits.

Liuzhou is the second largest industrial city in Guangxi Province of Southwest China, with a large population and a strong economy. It has a population of 1.6 million and includes more than 3400 companies and 11 large state-owned enterprises (Miao et al. 2018). The expansion of industry, increases in population, the growth of transport networks, and increases in vehicle emissions are all potential sources of metal pollution. The biomonitoring of metal(loid)s is necessary to assess environmental pollutants in the general population. To the best of our knowledge, no biomonitoring data have been established regarding the reference concentration ranges of urinary metal(loid)s in this representative city of Southwest China. In this study, we investigated the profile of metal(loid) exposure, identified possible predictors of these pollutants, assessed their potential risks to human health, and provided basic data for public health policies by collecting urine samples from 2050 children and adolescents in Liuzhou City.

Materials and methods

Design and study population

We adopted baseline data from a cross-sectional study conducted from February 2018 to July 2018 in Liuzhou City (southwestern China). We selected schools in 4 districts of Liuzhou City (Cheng-zhong District, Yu-feng District, Liu-nan District, and Liu-bei District) that included grades 1–12 (Fig. 1). Trained interviewers provided each subject with questions in face-to-face interviews and questionnaires that included demographic and dietary habits were obtained from the parents or guardians. Data were collected on age, sex, maternal education, passive smoking, and the consumption frequency of milk, eggs, fish, meat, vegetables, and fruits. All participants were selected randomly but were required to have been living for at least 1 year continuously in good health in any of the study areas. A total of 2050 children and adolescents aged 6–18 years who were eligible and provided spot urine samples. All participants and parents or guardians provided informed consent and the study protocol was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology.

Sample collection and detection

Spot urine samples were collected into tubes by the students and transported to the laboratory and stored at −20 °C. Before testing, frozen urine samples were thawed at room temperature (22 ± 2.0 °C) and centrifuged. A 0.5-mL urine sample was transferred to a 10-mL pre-cleaned digestion
tube and 20-μL 67–70% ultrapure nitric acid (Fisher Chemical, Pittsburg, PA, USA) was added and then placed in a 4 °C refrigerator for overnight digestion. The samples were then allowed to stand at room temperature for 30 min and 4.48 mL of 1% nitric acid was added and mixed by ultrasonication for 30 min.

We measured the concentrations of urinary metal(loid)s using previously published methods with some modifications (Heitland and Köster 2006). An ICP-MS instrument (Agilent 7700, Agilent Technologies, Santa Clara, CA, USA) was used for all measurements. The operation conditions for ICP-MS were as follows: plasma gas flow 15.00 L/min, auxiliary gas flow 0.8 L/min, carrier gas flow 0.8 L/min, increase in the quantity of samples of 0.4 mL/min, and unimodal residence time of 0.1 s. Twenty-one elements were analyzed, including aluminum (Al), vanadium (V), chromium (Cr), manganese (Mn), iron (Fe), cobalt (Co), nickel (Ni), copper (Cu), zinc (Zn), arsenic (As), selenium (Se), rubidium (Rb), strontium (Sr), silver (Ag), cadmium (Cd), cesium (Cs), barium (Ba), mercury (Hg), thallium (TI), lead (Pb) and uranium (U).

Quality control

The SRM1640A quality control reagent (National Institute of Standards and Technology, Gaithersburg, MD, USA) was determined after every 20 samples using 6 repetitions. SRM1640A provides a confirmed urinary metal concentration that can be used for quality control if the measured metal concentration is at levels comparable with the given reference value. The limits of detection (LOD) for the urinary metals were in the range 0.0001–0.2546 μg/L. The spiked recoveries of the 21 metal(loid)s were in the range 78.3–113.2%.

The metal(loid) concentrations were normalized to the levels of urine creatinine, that was measured using a commercial kit and biochemical analyzer (Mindray BS-200 CREA Kit, Mindray Biomedical Electronics, Shenzhen, China). The corrected concentrations were in units of μg/g creatinine.

Exposure assessment and risk calculation

The hazard quotients (HQ) were calculated as the ratio of the metal(loid) concentrations to the chemical-specific value of the biomonitoring equivalent (BE) or human biological monitoring (HBM) for noncancer endpoints. The HQ was defined as follows:

\[
HQ = \frac{[\text{Metal(loid)}]}{\text{BE}/\text{HBM}}
\]

where metal(loid) was the value of P50 or P95 for urinary metal(loid)s observed in the population. HBM is an effective tool to assess the actual dose absorbed in the environment (internal exposure dose) by measuring element levels of reactive chemicals or their metabolites in biological substrates (blood, urine, and breast milk) (Schulz et al. 2011). The values of HBM-I (control level) and HBM-II (action level) determined by the HBM committee of Germany include cadmium, mercury, and thallium (Apel et al. 2017). The BE is defined as the concentration of a substance in the biological matrix that is consistent with the reference dose (RfD) established by the US Environmental Protection Agency (EPA) and used in urine for cadmium (Bocca et al. 2016). If the HQ value was >1, exposure to metals at or above the current exposure guidelines may have adverse health effects.

The hazard index (HI) assesses the overall potential risk of noncarcinogenic effects of multiple elements (Saha and Zaman 2013). The formula for HI is as follows:

\[
HI = \sum_{i=1}^{n} \text{HQ}_i
\]

HI > 1 indicates an unacceptable risk of noncarcinogenic effects in a health assessment, while HI < 1 shows an acceptable risk.

Statistical analysis

Statistical analysis was performed using SPSS version 25.0 and R software (Version 3.6.1, R foundation for Statistical Computing, Vienna, Austria). Geometric means (GM) and medians were calculated for descriptive statistical analysis. Levels below the LOD were allocated as the square root of LOD values over 2 (Health et al. 2009). In addition, Spearman’s test was used to study correlations between sample components.

The concentrations of metal(loid)s are not normally distributed; hence, nonparametric tests, including the Mann–Whitney and Kruskal–Wallis tests, were used to assess the differences in element levels and the potential effects of confounding factors such as sex, maternal education, passive smoking, and dietary habits. Predictor variables of interest were selected according to the results of the univariate analysis (p < 0.2), as well as those identified in previous studies. Accordingly, the multivariate analyses were adjusted for the following independent variables: (a) demographic factors of age, sex, maternal education, and passive smoking, and (b) diet including frequency of milk, egg, fish, meat, vegetable, and fruits consumption.

The multivariate linear regression model was used to evaluate the relationship between the concentration of metal(loid)s corrected for natural logarithmic transformation.
and factors with a significance level of \( p < 0.05 \). The models were built following a forward stepwise variable selection procedure. Residual analysis was used to test the independence, normality, and homogeneity of variance once the model was established. The regression coefficients and confidence levels at 95% significance were calculated for the multivariate models.

**Results**

A total of 2050 students (1016 boys and 1034 girls) were included in this research. Information about the demographic characteristics and dietary intake habits of the participants was shown in Table 1. The ages ranged from 6 to 18 years, and 54.0% of mothers had an education level below high school.

**The concentrations and correlations of metal(loid)s**

The distribution of elements in the urine of the study population was presented in Table 2 (in μg/L and μg/g creatinine). The detection frequencies (DFs) were all above 99%. We found significant positive correlations between the test metal(loid)s (\( p < 0.05 \)). For instance, there were strong correlations \([r = 0.78 (Al \text{ and Mn}), 0.87 (Rb \text{ and Cs}), 0.80 (Mn \text{ and Ba}), 0.79 (Rb \text{ and Tl})]\). The correlations between Cd and the other elements were generally weak or moderate with \( r \) values < 0.5 (Fig. S1).

**Predictors of metal(loid)s**

The urinary concentrations of our test compounds and their relationships with the main characteristics and dietary habits of the study population were shown in Table S1. Table S2 displayed the multivariate log-linear regression analysis of element levels in urine with influencing factors. We used these numbers to calculate the multivariate log-linear regression and corresponding 95% confidence intervals (CIs). Our regression models indicated that age was an important predictor of element levels and that children exhibited higher metal(loid) exposure levels than adolescents, with the exception of Sr. The concentrations of 13 elements (Al, V, Cr, Mn, Fe, Co, Ni, Rb, Sr, Ba, Tl, Pb and U) were higher in girls (\( p < 0.05 \)). We also found two different tendencies that were correlated with maternal education: the levels of Co, Sr, Cd, and Pb in urine were lower in the more educated group, but the converse was true for Cr and Se. The levels of Cr, Co, and Ni were elevated for passive smokers (\( p < 0.05 \)). We also identified significant positive relationships between vegetable intake and Al, Cr, Mn, Fe, Co, Ni, Rb, Sr, Ba, Tl, Pb and U) and various metals (Fig. 2).

**Risk assessment of metal(loid) exposure**

Human biomonitoring (HBM) data was available for evaluating health risks to particular environmental chemicals (Organization 2012). The limits of urinary levels that are higher than HBM-II indicated that immediate measures should be taken to reduce exposure; values above HBM-I but lower than HBM-II require a reduction of specific exposure sources in an appropriate manner. Additionally, urinary element levels above biomonitoring equivalents (BE) suggest that further study on the exposure source is needed. Table 3 showed the human biomonitoring assessment values for cadmium, mercury, and thallium. The data indicated that 31.8% of the population had Cd levels between HBM-I and HBM-II, 1.4% (\( n = 28 \)) of the population had urinary cadmium levels above HBM-II and 3.4% had urinary Cd levels above BEs. Seven of the subjects had Hg levels between HBM-I and HBM-II and
one sample had a Tl concentration exceeding 5 μg/L. The threshold value for total arsenic is 50 μg/l (Caldwell et al. 2009) and 11.6% of our samples exceeded this level. However, As can be present in a number of chemical complexes and further investigations are needed to assess the exposure for this element.

HBM-I and BE values were only applicable to Cd, Hg, and Tl so that only the hazard quotient (HQ) values of these metals could be calculated. We used the HQ to evaluate whether children and adolescents’ exposure levels exceeded the exposure risk values. The HQ values of all three metals were less than 1 using the P50 value of the population. However, the HQ value of urinary Cd alone was above 1 at the P95 value, suggesting that there may be health risks for a small number of the study population. When evaluating the joint effect of multiple metals, we presumed that all metals presented synergistic effects, and the HI was calculated from the sum of the HQ of each metal. The combined exposure to Cd, Hg, and Tl showed an HI value above 1 when the P95 value was used, while at the P50 value, the HI value was close to 1 in this study (Fig. 3).

### Table 2

| Element | LOD (µg/L) | N (%) < LOD | Unadjusted (µg/L) | Cr-adjusted (µg/g creatine) |
|---------|------------|-------------|-------------------|-----------------------------|
|         |            |             | AM    | Median | GM    | AM    | Median | GM    |
| Al      | 0.2546     | 1 (0.05)    | 20.1  | 16.7   | 17.3  | 55.4  | 29.0   | 32.1  |
| V       | 0.0005     | 1 (0.05)    | 0.853 | 0.845  | 0.745 | 1.94  | 1.35   | 1.38  |
| Cr      | 0.0036     | 20 (0.98)   | 1.53  | 0.864  | 0.825 | 3.61  | 1.47   | 1.53  |
| Mn      | 0.0023     | 2 (0.10)    | 0.931 | 0.682  | 0.706 | 2.24  | 1.22   | 1.31  |
| Fe      | 0.0261     | 1 (0.05)    | 28.9  | 16.7   | 17.6  | 62.2  | 30.6   | 32.6  |
| Co      | 0.0005     | 7 (0.34)    | 0.687 | 0.425  | 0.417 | 1.41  | 0.749  | 0.774 |
| Ni      | 0.0126     | 2 (0.10)    | 5.72  | 4.81   | 4.72  | 12.6  | 8.49   | 8.76  |
| Cu      | 0.0161     | 1 (0.05)    | 26.6  | 9.59   | 10.9  | 73.7  | 15.1   | 20.2  |
| Zn      | 0.1739     | 6 (0.29)    | 451   | 312    | 276   | 853   | 526    | 514   |
| As      | 0.0070     | 12 (0.59)   | 28.6  | 19.8   | 17.7  | 49.2  | 33.4   | 32.9  |
| Se      | 0.0146     | 3 (0.15)    | 24.1  | 19.8   | 17.8  | 41.4  | 33.8   | 33.1  |
| Rb      | 0.0007     | 0 (0.00)    | 1536  | 1334   | 1166  | 2846  | 2157   | 2177  |
| Sr      | 0.0036     | 1 (0.05)    | 81.9  | 61.1   | 55.4  | 159   | 110    | 103   |
| Ag      | 0.0376     | 0 (0.00)    | 1.30  | 0.821  | 0.811 | 3.01  | 1.47   | 1.50  |
| Cd      | 0.0006     | 8 (0.39)    | 0.634 | 0.359  | 0.335 | 1.16  | 0.617  | 0.620 |
| Cs      | 0.0004     | 1 (0.05)    | 8.51  | 7.80   | 6.90  | 15.9  | 12.8   | 12.8  |
| Ba      | 0.0239     | 1 (0.05)    | 3.85  | 3.32   | 3.25  | 10.4  | 5.87   | 6.03  |
| Hg      | 0.0001     | 9 (0.44)    | 0.699 | 0.477  | 0.449 | 1.41  | 0.852  | 0.834 |
| Tl      | 0.0002     | 1 (0.05)    | 0.535 | 0.446  | 0.415 | 1.04  | 0.765  | 0.769 |
| Pb      | 0.0026     | 13 (0.63)   | 1.69  | 1.25   | 1.16  | 3.87  | 2.14   | 2.14  |
| U       | 0.0002     | 17 (0.78)   | 0.0255| 0.0149 | 0.0151| 0.0664| 0.0251 | 0.0279|

**LOD**, limits of detection; **AM**, arithmetic mean; **GM**, geometric mean; **Al**, aluminum; **V**, vanadium; **Cr**, chromium; **Mn**, manganese; **Fe**, iron; **Co**, cobalt; **Ni**, nickel; **Cu**, copper; **Zn**, zinc; **As**, arsenic; **Se**, selenium; **Rb**, rubidium; **Sr**, strontium; **Ag**, silver; **Cd**, cadmium; **Cs**, cesium; **Ba**, barium; **Hg**, mercury; **Tl**, thallium; **Pb**, lead; **U**, uranium

### Discussion

This study assessed exposure to metalloid(s) among children and adolescents in Liuzhou City, Southwest China. We measured concentrations of urinary metalloid(s) and assessed correlations among different elements. According to the World Health Organization recommendations, urine samples with creatinine values below 0.3 g/L or above 3 g/L were unrepresentative and were not included in the following statistical analysis in order to reduce the possibility of overestimation or underestimation in calculating concentrations. In our study population, 4 samples had creatinine levels above 3 g/L and 21.5% of samples showed levels below 0.3 g/L. We performed a sensitivity analysis by removing samples with creatinine levels without in the range of 0.3 g/L–3 g/L in order to compare the coefficients of the regression models. No significant changes were observed in the regression coefficients comparing to the whole analysis that requires the conclusions of the study to be changed. In addition, our values for our test metalloid(s) were within the range of values usually
reported in other studies in Europe, the USA, and Canada for Al, V, Co, Ni, Cu, Zn, As, Se, Rb, Sr, Ag, Cs, Ba, Hg, and U or even lower for Mn. In contrast, the average levels of Cr, Cd, Tl and Pb in our study were slightly higher than those in other countries (Table 4).

The geometric mean (GM) for Cr found (1.53 μg/g creatinine) was close to the GM of 1.57 μg/g creatinine in China (Xu et al. 2020) but lower than the GM of 2.15 μg/g creatinine in southern Brazil (Rocha et al. 2016). The level was higher than those in Spanish children aged 5–17 years (0.43 μg/g creatinine) (Aguilera et al. 2010) and in French adults (0.33 μg/g creatinine) (Nisse et al. 2017). Cr enters the brain through the olfactory pathway and this results in a detrimental effect on experimental ethology and memory processes and retention (Singh and Chowdhuri 2017). Cr in the environment primarily originates from the production of metal alloys, leather, and steel (ATSDR & asp 2012). Automobile manufacturing and steel production are major industries in Liuzhou City, and previous studies have reported high Cr levels in the Liujiang River flowing through Liuzhou City (Miao et al. 2020). The Cr levels for our study subjects were high and may be harmful to their health, growth, and development.

The Cd levels in our study subjects were 0.620 μg/g creatinine and higher than those found in Spain (0.41 μg/g creatine) (Aguilera et al. 2010) and Japan (0.34 μg/g creatine) (Ilmiawati et al. 2015), but lower than that found in the industrial area of Spain (0.75 μg/g creatinine) (Molina-Villalba et al. 2015). Wastewater, waste gas, and residues from industrial sites increase the Cd load in the local populations.

The GM of urinary Pb measured in this study was 2.14 μg/g creatinine, higher than that in Spain (1.16 μg/g creatine) (Roca et al. 2016) and similar to that in industrial areas of Spain (2.22 μg/g creatinine) (Molina-Villalba...
et al. 2015). In addition, Pb levels in our study were higher than that of adults reported in rural areas along the Yangtze River (1.51 μg/g creatinine) (Cui et al. 2017). Pb could hinder the absorption of trace elements in the human body and affect growth and development; long-term exposure to low doses of lead could also cause immune disorders such as alterations in disease resistance (Fleisch et al. 2013). Pb originates from car and truck pollution even though leaded gasoline was phased out in China since 2001 (Zhou et al. 2016). Other agents in unleaded gasoline could still introduce a certain amount of Pb into the atmosphere, especially in areas where there are more gasoline-based motor vehicles and motorcycles on (Li et al. 2012). In addition, population growth and industrial expansion are potential sources of lead pollution that may contribute to the increased concentration of urinary Pb.

Mn is an element that is closely related to human health; either its excess or deficiency can lead to disease, and low levels of manganese can adversely affect neurodevelopment (Riojas-Rodríguez et al. 2010). Our study showed that the GM for Mn (1.31 μg/g creatinine) was higher than that in Spain (0.48 μg/g creatinine) (Perez et al. 2018), but lower than those reported in Italy (7.52 μg/g creatinine) (Pino et al. 2012) and the industrial area of China (6.37 μg/g creatinine) (Zhang et al. 2017). Urinary concentrations in the range of 1 μg/L to 8 μg/L are considered to fall within the reference range; only 6 of our subjects had Mn exceeding 8 μg/L, while more than 40% of our subjects had Mn levels below 1 μg/L (Godebo et al. 2019).

Urinary concentrations of Co, Ni, and Ba were comparable to those found in Mexican children aged 8–14 years (0.8 μg/L, 9.27 μg/L and 3.09 μg/L, respectively) (Lewis et al. 2018) and were slightly higher than the concentrations in Belgian adults (0.15 μg/g creatinine, 1.73 μg/g creatinine, and 1.68 μg/g creatinine, respectively) (Hoet et al. 2013). Zn and Hg levels in our study subjects were comparable to those of Spanish children aged 6–11 years (515 μg/g creatinine and 0.73 μg/g creatinine, respectively) (Molina-Villalba et al. 2015). In contrast, Tl levels were higher than that in several other countries (CDC 2015; Roca et al. 2016). Current studies of the health effects of Tl are limited, but they may be related to headache, anorexia as well as arm, thigh, and abdominal pain (Peter and Viraraghavan 2005). The high levels of some elements may occur because Liuzhou City has a large number of factories. Industrial pollution is a major potential source of metal exposure and may also be a source of surrounding bioavailable metal(loid)s, making metal(loid)s more accessible to humans through water, food, and air particles. We found significant correlations were observed between almost all metal(loid)s, suggesting possible similar sources. The relationship between Mn and Cu (r = 0.47) and Hg and Se (r = 0.44) in our study was similar to those reported among Spanish children (Roca et al. 2016). Moderate to strong relationships were found between urinary Al and Cd (r = 0.38) and As and Se (r = 0.66) and a study of Mexican children revealed a moderate relationship between urinary Al and Cd (r = 0.38) in Mexican children (Lewis et al. 2018).

Regarding predictors of exposure to metal(loid)s, we found that age was an important predictor of element levels and that children exhibited higher metal(loid) exposure levels than adolescents, expect for Sr. Previous reports also found that older people present lower levels of metal(loid)s (Godebo et al. 2019; Rocha et al. 2016). Other studies also demonstrated that age was one of the most important

Table 3 Human biomonitoring assessment values for cadmium, mercury, and thallium

| Metals | Population group | HBM-I (% of subjects between HBM-I and HBM-II) | HBM-II (% of subjects > HBM-II) | BE (% of subjects > BE) | Reference |
|--------|------------------|---------------------------------------------|--------------------------------|------------------------|-----------|
| Cd     | Children and adolescents | 0.5 μg/L (31.8%) | 2 μg/L (1.4%) | 1.5 μg/L (3.4%) | (Schulz et al. 2011) |
| Hg     | Children and adults | 7 μg/L (0.3%) | 25 μg/L (0.1%) | (Schulz et al. 2007) |
| Tl     | General population | 5 μg/L (0.1%) | | (Apel et al. 2017) |

HBM-I, human biomonitoring value I; HBM-II, human biomonitoring value II; BE, biomonitoring equivalent; Cd, cadmium; Hg, mercury; Tl, thallium
| Reference | Site        | Age     | Number | Value | Concentration |
|-----------|-------------|---------|--------|-------|---------------|
| Present study | China | 6–18  | 2050 | GM<sup>a</sup> | 32.1 | 1.38 | 1.53 | 1.31 | 0.774 | 8.76 | 20.2 | 514 | 32.9 | 33.1 | 0.620 | 12.8 | 6.03 | 0.834 | 0.769 | 2.14 | 0.0279 |
| (Zhang et al. 2017) | China | 2–12  | 210   | Median<sup>a</sup> | 29.0 | 1.35 | 1.47 | 1.22 | 0.749 | 8.49 | 15.1 | 526 | 33.4 | 33.8 | 0.617 | 12.8 | 5.87 | 0.852 | 0.765 | 2.14 | 0.0251 |
| (Zhang et al. 2019) | China | 3–4  | 55    | Median<sup>a</sup> | 358.67 | 1.79 | 6.37 | 12.21 | 26.62 | 14.75 |
| (Feng et al. 2015) | China | 18–80 | 2004 | GM<sup>b</sup> | 338.6 | 0.51 | 2.83 | 1.22 | 2.47 | 35.0 | 515 | 33.3 | 55.7 | 0.176 | 5.40 | 0.18 | 0.02 | 6.09 |
| (Roca et al. 2016) | Spain | 6–11  | 125   | GM<sup>a</sup> | 0.223 | 0.430 | 1.41 | 4.27 | 35.0 | 515 | 33.3 | 55.7 | 0.176 | 5.40 | 0.18 | 0.02 | 6.09 |
| (Molina-Villalba et al. 2015) | Spain | 6–11  | 261   | GM<sup>a</sup> | 0.42 | 2.438 | 0.747 | 1.059 | 2.22 |
| (Aguilera et al. 2010) | Spain | 5–17  | 196   | GM<sup>a</sup> | 0.43 | 1.61 | 11.46 | 1.6 | 0.41 |
| (CDC 2015) | United States | 6  | 2502  | GM<sup>a</sup> | 0.140 | 0.370 | 7.77 | 0.176 | 4.33 | 1.35 | 0.367 | 0.168 | 0.141 | 0.91 |
| (Health and Services 2018) | United States | ≥6 | 2502  | GM<sup>b</sup> | 0.123 | 0.391 | 8.63 | 0.124 | 0.141 | 0.277 | 0.005 |
| (Haines et al. 2017) | Canada | 6–79 | 1869  | GM<sup>b</sup> | 0.081 | 0.23 | 1.1 | 9.0 | 250 | 12 | 49 | 0.34 | 4.60 | 0.23 | 0.48 |
| (Schulz et al. 2009) | Germany | 3–14 | 1790  | GM<sup>b</sup> | 1.26 | 4.40 | 0.068 | <LOQ |
| (Nisse et al. 2017) | France | 20–59 | 1910  | GM<sup>a</sup> | 1.61 | 0.21 | 0.33 | 0.24 | 0.53 | 1.75 | 278 | 16.1 | 0.33 | 0.75 | 0.19 | 0.91 |
| Reference | Site    | Age  | Number | Value | Concentration |
|-----------|---------|------|--------|-------|---------------|
|           |         |      |        |       | Al  | V  | Cr | Mn | Co | Ni | Cu | Zn | As | Se | Cd | Cs | Ba | Hg | Tl | Pb | U  |
| (Hoet et al. 2013) | Belgium | 18–80 | 1022   | GM   | 2.03 | 0.223 | 0.101 | 0.150 | 1.73 | 6.94 | 229 | 21.3 | 0.228 | 1.68 | 0.238 | 0.169 | 0.73 |
| (Santos et al. 2018) | Brazil  | 6–11 | 96     | GM   | 25.0 | 0.8  | 6.9  | 25.0 | 1.05 | 6.95 | 5.21 | 283 | 10.0 | 0.228 | 0.169 | 0.73 |
| (Godebo et al. 2019) | Ethiopia | 10–50 | 386   | GM   | 25.0 | 0.8  | 6.9  | 25.0 | 1.05 | 6.95 | 5.21 | 283 | 10.0 | 0.61 | 1.44 | 0.21 |
| (Lewis et al. 2018) | Mexico  | 8–14 | 250   | GM   | 17.7 | 1.26 | 0.80 | 9.27 | 408 | 15.5 | 0.14 | 3.09 | 2.3 |
| (Aprea et al. 2018) | Italy   | 18–60 | 260   | GM   | 0.099 | 0.218 | 0.298 | 0.420 | 1.48 | 11.5 | 0.255 | 0.202 | 0.644 |
| (Park et al. 2016) | South Korea | >19  | 6311 | GM | 35.0 | 0.58 | 0.53 |

GM, geometric mean; Al, aluminum; V, vanadium; Cr, chromium; Mn, manganese; Co, cobalt; Ni, nickel; Cu, copper; Zn, zinc; As, arsenic; Se, selenium; Cd, cadmium; Cs, cesium; Ba, barium; Hg, mercury; Tl, thallium; Pb, lead; U, uranium

*μg/g creatinine b μg/L
predictors among most metal(loid)s, possibly because younger children were more exposed to external substances through hand-to-mouth activity (Roca et al. 2016).

Our study subjects were also grouped according to sex and in general, most urinary element levels were higher in girls and 13 elements reached the level of statistical significance ($p < 0.05$). Girls were more exposed to metal(loid)s in beauty products such as nail polish and hand cream and continued use of these products increases the absorption of metal(loid)s, which is particularly harmful to children. For instance, Pb and Cd have been found in white cosmetics such as creams and lotions (Orisakwe and Otaraku 2013). In relation to maternal education, children whose mothers reported higher education levels showed lower concentrations of Co, Sr, Cd, and Pb, while a positive correlation was found in the levels of Cr and Se. This finding may be due to the association between family status and other variables potentially associated with exposure to metal(loid)s. The concentrations of Cr, Co, and Ni were also significantly elevated in passive smokers ($p < 0.05$). Many metals found in cigarette smoke, tobacco, and cigarette paper, such as Cr, Ni, Cu, Cd, and Pb, are potential health threats (Bernhard et al. 2005). These passive-smokers also possessed higher Cd levels, although there was no significant association with passive smoking. Smoking by family members is more likely to be inhaled by student groups in an indoor environment with poor ventilation, and attention should be given to passive smoking in children in this region.

Dietary habits may also affect the distribution of various metal(loid)s. Milk, vegetables, and fish were important factors in assessing the source of metal(loid) exposure in our study. People who ate fish, the main dietary source of As, showed higher levels of arsenic in their urine. Other studies observed that elevated As levels were related to frequent consumption of fish (Bocca et al. 2016; Schulz et al. 2011). Studies showed a significant correlation between urinary arsenic concentrations and total protein intake, and fish are rich in protein (Kordas et al. 2016). People with higher dairy intake had lower urinary levels of V, Co, Ag, Cd, and Tl, as in previous studies (Ashrap et al. 2020; Roca et al. 2016). Regarding Cd, these results may be related to the inverse ratio between the presence of large amounts of minerals in dairy products and the absorption of Cd, as previously reported (Castaño et al. 2012). Higher vegetable consumption was also associated with higher levels of Al, Cr, Mn, Zn, Rb, Cs, Ba, and Tl. Vegetables contain essential trace elements but may also contain heavy metal residues (Zeinali et al. 2019). Accordingly, higher meat consumption was associated with higher levels of Zn. Due to lifestyle changes and increased demand for fast food based on meat, meat consumption has increased in recent years. This food source also results in increased exposure to metal(loid)s that may lead to neurological problems, headaches, and liver dysfunction (Farmer et al. 2011). Although this work was a cross-sectional study, the food intake and urine metal content for the study participants remained in long-term equilibrium, and was therefore a reliable assessment of the role of food in metal(loid) exposure.

In our study subjects, 31.8% of the population had urinary Cd levels between HBM-I and HBM-II levels, and only the HQ of Cd was $> 1$ at the P95 value, indicating that exposure to this metal may pose a health risk to a small number of people. Similar tendencies were found in a previous biomonitoring study carried out in Italy (Bocca et al. 2016). Another study of wild fish in the Liujiang River also found that the potential health risks were primarily the results of Cr and Cd in the river water and sediments (Miao et al. 2020). The HI of multiple metals was near 1 at the P50 value and above 1 at the P95 values, indicating that the joint toxicity of multiple metals could not be ignored and that noncancer health consequences are likely to occur in children and adolescents exposed to metals in the relevant study areas. However, this algorithm may be affected by many parameters. The mechanism of action and toxic effects of these metals in the human body may not be the same, and there may be antagonistic or synergistic effects among them. More data, including information on socioeconomic, personal care products, and environmental conditions, are essential to determine the real effects of metal exposure.

**Strengths and limitations**

This is the first study to provide valuable information on metal exposure in Liuzhou City, Southwest China, based on a large sample size. This study also provided information on potential predictors including sociodemographic and dietary habits. However, our study also has some limitations. First, urinary metal levels were only measured at one spot time. Urine is the preferred matrix in metal biomonitoring, and previous studies showed that spot urine could reflect both short- and long-term exposure to metals in situations with similar lifestyles. Second, the amount of dietary intake was not included in the questionnaire in detail, and we were unable to assess the effect of unmeasured confusing information. Third, the area is historically industrial and we could not ignore the metal exposure from particulate matter, dust, and drinking water. In the future, studies should be designed to collect more detailed and comprehensive questionnaire information, duplicate biological samples to explain exposure levels in children and adolescents.

**Conclusion**

In the present study, we evaluated 21 urinary metal(loid) concentrations from children and adolescents in Liuzhou City, Southwest China, analyzed the potential predictors of
metal(loid) exposure, and assessed the potential health risks. In general, we found that children had higher metal(loid) exposure levels than adolescents. The multiple regression models also revealed that dietary habits may affect the distributions of metal(loid)s. It is particularly noteworthy that 31.8% of the population had Cd levels between HBM-I and HBM-II, and the potential health risks of the mixed effects of Cd, Hg, and Tl exposure were not negligible. In the future, more comprehensive investigations are warranted in this industrial area to protect children and adolescent health.

**Supplementary Information** The online version contains supplementary material available at [https://doi.org/10.1007/s11356-021-16953-1](https://doi.org/10.1007/s11356-021-16953-1).

**Acknowledgements** We acknowledge the participants in the study.

**Author contribution** Yaping Li: conceptualization, investigation, writing original draft. Yu Zhang: investigation, validation, methodology. Meng Yu: investigation, validation, methodology. Liqin Hu: investigation, validation, methodology. Ting Zeng: investigation, validation, methodology. Ling Liu: data curation, software, validation. Limei Wang: data curation, software, validation. Liangqiong Deng: data curation, software, validation. Xiang Li: data curation, software, validation. Ping Liu: investigation, methodology, data curation. Dingyuan Zeng: project administration, resources, supervision. Surong Mei: conceptualization, funding acquisition, project administration, resources, supervision. All authors read and approved the final manuscript.

**Funding** This research was funded by the National Key R&D Program of China (2017YFC0212003) and the National Natural Science Foundation of China (No. 42077397).

**Availability of data and materials** The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

**Declarations**

**Ethics approval and consent to participate** This study was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology.

**Consent for publication** Not applicable.

**Competing interests** The authors declare no competing interests.

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