Longitudinal Nephrotoxic Metal Exposure in a Cohort of Farm Workers in Sonora, Mexico

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Objective: Metal exposure among farmworkers along the US-Mexico border is understudied, despite links between certain metals and kidney injury or disease. We assessed seasonal metal exposure in agricultural workers in Sonora, Mexico, compared to office workers and other populations. **Methods:** Adult male agricultural and office workers provided urine samples and demographic data at the start and end of the work season. Urine was analyzed for specific gravity, creatinine, and metal(loid) concentrations. **Results:** Agricultural workers had significantly higher urinary arsenic, lead, nickel, and uranium than office workers. Uranium increased over time, whereas arsenic, lead, and nickel declined. Urinary metal levels exceeded those in NHANES Mexican Americans, with cadmium levels similar to other farmworker populations but higher arsenic and uranium. **Conclusions:** Findings enhance understanding of regional exposure, support global farmworker comparisons, and inform exposure modeling, mitigation strategies, and policy.

Keywords: agricultural worker, farm worker, Mexico, toxic metal exposure, toxic metal(loid) exposure, heavy metals

CME Learning Objectives

After completing this educational activity, the learner will be better able to:

- Outline the role of metal(loid) exposures in kidney disease etiology.
- Readers will be able to identify arsenic, lead, and mercury as potential contributors to acute kidney injury (AKI) and chronic kidney disease (CKD) in agricultural workers, advancing knowledge of environmental nephrotoxicants in occupational health.
- Differentiate occupational exposure profiles based on comparative data. This study enables readers to compare metal(loid) exposure patterns between agricultural workers with exposure levels in office workers, providing measurable insights into exposure disparities by occupation.
- Interpret exposure data from high-risk populations in northern Mexico by characterizing metal(loid) exposures in two distinct northern Mexico populations. Readers will gain the ability to contextualize environmental risk factors for CKD/AKI and apply this understanding to similar agricultural contexts globally.

Globally, outdoor workers have faced a rise in chronic kidney disease (CKD) in recent decades, which cannot be explained by the traditional risk factors associated with CKD, such as advanced age, hypertension, and diabetes.[1–3] Chronic and acute kidney damage as the result of metal and metal(loid) exposure has been investigated in various occupational and nonoccupational groups worldwide, with varied results.[4–7] Certain metal(loid)s can act as nephrotoxins, in part due to the kidney's ability to reabsorb and concentrate ions and metals.[8–15] Specific metal(loid)s, including arsenic (As), cadmium

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(Cd), chromium (Cr), lead (Pb), mercury (Hg), nickel (Ni), and uranium (U), have been hypothesized to be causal agents in the development of acute kidney injury (AKI) and/or CKD.[7,11,16–24]

Metal(loid)s are naturally occurring elements and are frequently added to industrial or agricultural products, such as pesticides and fertilizers.[7,12] Metals are elements with heat resistance, conductivity, malleability, and other unique properties, whereas metal(loid)s have a mix of properties typical of both metals and nonmetals. Humans can be exposed to metal(loid)s through a variety of routes and sources, including oral/ingestion via diet (eg, methylmercury in fish), drinking water (eg, As), and soil (eg, nondietary ingestion of Pb-contaminated soil); inhalation (eg, Cd in cigarette smoke); and, to a small extent, dermal absorption.[12] The primary route of exposure varies by element and its speciation state, and metal(loid)s have differing half-lives depending on the environmental matrix (eg, soil versus water).[7,11]

Metal(loid)s exist in the body in two forms that can affect the kidney: (1) a nondiffusible protein-bound form that can lead to chronic inflammation of the proximal tubule region of the kidney and (2) an ionized form that can affect the apical membrane of the proximal tubule, the loop of Henle, and terminal regions of the kidney.[15] Certain metal(loid)s can act as nephrotoxins, in part due to the kidney's ability to reabsorb and concentrate ions and metals.[15]

Globally, researchers have explored the connection between metal exposure and kidney damage, both chronic and acute, among different occupational and nonoccupational groups, yielding diverse findings.[7] In England, urinary Cd levels have been significantly associated with kidney injury in a population living near a closed Pb/zinc (Zn) smelter.[5] In Central Mexico, urinary As levels have been linked to tubular dysfunction. [20] A Swedish study found an association between erythrocyte Pb levels and end-stage renal disease (ESRD).[22] In Japan's Jinzu River Basin, elevated urinary Cd levels have been linked to a higher risk of mortality-related renal disease.[21] Studies from Sri Lanka have yielded mixed results on Cd exposure in farming communities linked to kidney disease, with some evidence of dietary exposure.[24,25] In Nicaragua, case-control studies among agricultural workers have revealed associations between Cd, Pb, and U with markers of kidney injury and/or decreased kidney function.[26] These varying results highlight the need to include metal(loid) exposure as a possible contributor to AKI and CKD, especially in areas where metal(loid)s are naturally present in drinking water and soils or used occupationally, such as in the Arizona-Sonora border region in Northern Mexico.[27–29]

Communities in Northern Mexico may be at higher risk for exposure to metal(loid)s due to high naturally occurring levels and the prevalence of deep wells combined with a lack of water treatment systems.[30] Mining and agricultural industries also contribute to human exposure in Sonora.[27] Agricultural workers are frequently exposed to metal(loid)s due to their proximity to soil, pesticides, fertilizers, manures, and wastewater.[31]

Objectives

To our knowledge, an assessment of metal(loid) exposure in agricultural workers in the US-Mexico border region has not been conducted. Therefore, the objective of this study is to characterize metal(loid) exposure in agricultural field workers by season and compare it to office workers. We hypothesize that samples collected from participants at the end of the work season will have significantly higher levels of metal(loid)s than samples collected at the beginning of the work season, as measured by urinary concentrations. Additionally, we hypothesize that agricultural workers will have significantly higher levels of urinary metal(loid) concentrations than office workers at the end of the work season and levels observed in the United States Nutrition and Health Examination Survey (NHANES).

METHODS

Study Design Overview and Study Population

All study protocols and written materials were approved by University of Arizona Human Subjects Protection Program (IRB no. 1810987689R001) before the study began. All recruitment methods and study details were communicated in Spanish, and informed written consent was acquired from all participants before their involvement. Participants were compensated with a monetary payment for their participation. Additional details on the population and recruitment strategy can be found in Lopez-Galvez et al 2021.[32]

Workers in this region are frequently recruited from their hometowns in southern Mexico (eg, Puebla, Chiapas, Oaxaca) and travel to Sonora for one or more crop seasons. We partnered with a table grape producer in Sonora that provides onsite housing, meals, water from an onsite well, and a snack bar for employees throughout their employment. A group of 77 adult males working in field positions (ie, nonpesticide applicators, nonsupervisors, nonengineers, etc) were recruited in March 2019. Only men were recruited for the cohort due to the overwhelming proportion of men working in this industry (>95% men). Field supervisors and farm doctors helped to recruit a convenience sample of workers expected to remain at the farm throughout the grape harvest season. Likewise, another group of 21 adult males engaged in nonagricultural office professions was recruited in Hermosillo, a neighboring city with similar climate conditions, during the same period. These individuals were recruited from a commercial business office and an academic institution with the support of local academic associates. Inclusion criteria for agricultural workers were 18 years old or above and intending to work on the farm until July, covering the grape harvest season. Office workers also had to be at least 18 years old. Agricultural workers and office workers were recruited in the spring, and agricultural workers were followed up in the summer.

We collected urine samples and questionnaires. Urine samples were analyzed for metal(loid) content and specific gravity. This exploration of metal(loid) exposure is part of a larger study on the effects of environmental and occupational exposures on kidney injury/function in agricultural workers. We have previously demonstrated decreased kidney function over time in this agricultural population.[32]

Questionnaires

Following the conclusion of the workday, a questionnaire was verbally administered to participants in Spanish, overseen by research personnel. The survey collected demographic information such as age, birthplace, education, and primary language spoken. The responses

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Ethical Approval: All study protocols and written materials were approved by the University of Arizona Human Subjects Protection Program (IRB no. 1810987689R001) before the study began. Additionally, the privacy rights of human subjects have been observed and that informed consent was obtained for research with human subjects.
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were transcribed electronically utilizing encrypted REDCap software hosted at the University of Arizona.[33]

Laboratory Analytical Methods for Urine Samples

Urine collection containers were given to workers the evening after the completion of a workday and were instructed to self-collect their first morning void, using sterile 120 mL metal-free polyethylene plastic containers. These samples were transported on ice to the University of Arizona within a 6-hour timeframe from collection and then stored at −80°C until analysis.

Urine samples were analyzed for metal(loid) concentration at the University of Arizona Laboratory for Emerging Contaminants via inductively coupled plasma - mass spectrometry (ICP-MS). A Perkin Elmer DRC-II ICP-MS (Perkin Elmer SCIEX, Shelton, Connecticut, USA) was used to quantify As, Cd, Cr, Pb, Ni, and U following US EPA Method 200.8.[34]

Urinary Adjustment

To compare our results to a variety of studies using different urinary correction methods, we present results that are unadjusted, specific-gravity factor adjusted, and creatinine adjusted. We used a digital and calibrated handheld refractometer (PAL-10S Specific Gravity Refractometer, Atago, China) on which a drop of urine was placed from each sample to measure urinary specific gravity within 1 hour of collection. The specific gravity factor (SGF) was computed using Eq. 1,[35]

$$\text{Specific Gravity Factor} = \mid (1.02-(\text{SG})-1) \mid \qquad (1)$$

where SG is urinary specific gravity. Specific gravity factor was chosen to address the limitations of creatinine adjustment, which has been shown in occupational biomonitoring studies to be influenced by physiological parameters. [35]

Urinary creatinine was measured using a commercially available assay (Parameter Creatinine Assay; R&D Systems, Inc, Minneapolis, MN; 2014). Frozen urine samples were thawed at room temperature and centrifuged at 15,000*g* for 10 minutes at 4°C. Supernatant was isolated and serial diluted 20-fold with DI water and tested in duplicate. Inter- and intra-assay variability and the limit of detection (LOD) were calculated following methods established by Masdor; LOD was calculated as three times the standard deviation of the lowest concentration.[36] The inter- and intra-assay coefficient of variation was less than 12%, and the LOD was determined to be less than 0.3 mg/dL across all plates (based on the calculated LOD of 0.282 mg/dL).

Data Analysis

Agricultural workers who remained at the farm throughout the harvest season (ie, for more than 4 months) were included in this study. All urine samples were analyzed in duplicate, and the arithmetic mean concentrations of biomarkers were used. Values below the LOD were substituted with the respective LOD/$\sqrt{2}$. The unadjusted and SGF-adjusted geometric mean, geometric standard deviation, 95% confidence intervals, and 25th, 50th, and 75th percentiles for each metal (loid) were calculated. Urinary metal(loid) data were assessed for normality using visual review of histograms and Shapiro-Wilk tests. Spring urinary metal(loid) concentrations among agricultural workers were compared to summer harvest season levels using a Wilcoxon signed-rank test. Similarly, spring urinary metal(loid) concentrations of agricultural workers were compared to office workers using Wilcoxon rank-sum tests. We used linear regression models to evaluate associations between SGF-adjusted urinary element concentrations at baseline with the following socioeconomic variables: age in years (continuous), body mass index in kg/m^2 (continuous), occupation (farmworker or office worker), primary language spoken (Spanish or Indigenous), state of origin (Sonora, Puebla, Chiapas, and other), highest level of education obtained (less than completion of high school or completed high school or higher), smoking (yes/no), and monthly income (<$200 USD or ≥$200 USD). All analyses were conducted in R (R Core Team 2023). Unadjusted element concentrations were compared to respective levels for Mexican Americans published in the 2017–2018 NHANES, an annual health examination and survey conducted by the United States Center for Disease Control and Prevention. Unadjusted and creatinine-adjusted results from this study were also compared to urinary element concentrations from other assessments of agricultural workers.

RESULTS

Study Population

Agricultural workers and office workers showed similar average ages (29 for agricultural workers, 31 for office workers; Table 1). However, statistically significant differences emerged in origin (predominantly Puebla and Chiapas for agricultural workers), primary language (more individuals reported speaking an Indigenous language among agricultural workers), education (mostly below high school for agricultural workers, high school or higher for office workers), and income (most agricultural workers earned less than $100 USD monthly, whereas none of the office workers did; Table 1).

Metal(loid) Exposure Levels

All urinary samples had detectable levels of As (LOD = 0.001 μg/L), Cr (LOD = 0.002 μg/L), Pb (LOD = 0.005 μg/L), Ni (LOD = 0.001 μg/L), and U (LOD = 0.138 ng/L; Table 2). Cd had a 98.3% detection rate (LOD = 0.001 μg/L). We observed statistically significant differences between office workers and agricultural workers for unadjusted and

TABLE 1. Participant Demographics by Occupation (n = 98), Sonora, Mexico, 2019

	Overall	Office Worker	Farmworker
	n = 98	n = 21 (21.4%)	n = 77 (78.6%)
Male, n (%)	98 (100%)	21 (100%)	77 (100%)
Age (y), mean (SD)	29.6 (9.4)	31.2 (8.6)	29.2 (9.6)
State of origin, n (%)			
Sonora	16 (16.3%)	16 (76.2%)	0 (0.0%)
Puebla	43 (43.9%)	2 (9.5%)	41 (53.2%)
Chiapas	37 (37.8%)	2 (9.5%)	35 (45.5%)
Other	2 (2.0%)	1 (4.8%)	1 (1.3%)
Primary language spoken, n (%)			
Spanish	70 (71.4%)	20 (95.2%)	50 (64.9%)
Indigenous or other	28 (28.6%)	1 (4.8%)	27 (35.1%)
Weight (kg), mean (SD)	74.3 (25.1)	88.0 (48.1)	70.5 (11.3)
Height (cm), mean (SD)	165.6 (8.7)	173.5 (12.0)	163.5 (6.1)
Body mass index (kg/m^2), mean (SD)	26.3 (4.0)	26.0 (4.9)	26.4 (3.7)
Education level, n (%)			
Less than high school	76 (77.6%)	4 (19.0%)	72 (93.5%)
Completed high school or higher	22 (23.7%)	17 (81.0%)	5 (6.9%)
Monthly income ($USD), n (%)			
<$100	50 (53.8%)	0 (0.0%)	50 (69.4%)
$100–$199	19 (20.4%)	3 (14.3%)	16 (22.2%)
$200–< $499	10 (10.8%)	5 (23.8%)	5 (6.9%)
$500–$1000	10 (10.8%)	9 (42.9%)	1 (1.4%)
>$1000	4 (4.3%)	4 (19.0%)	0 (0.0%)
Unknown	5 (5.1%)	0	5 (6.5%)
Smoking, n (%)*	57 (62.0%)	17 (81.0%)	40 (56.3%)
Alcohol consumption within previous 2 d†, n (%)	83 (89.2%)	13 (61.9%)	70 (97.2%)

*Six individuals declined to answer the question.
†Five individuals declined to answer the question.

SGF-adjusted urinary As, Pb, Ni, and U (Table 2). Similarly, we observed statistically significant differences between agricultural workers at baseline and agricultural workers at follow-up for unadjusted and SGF-adjusted urinary Pb, Ni, and U. As was significantly different only for the unadjusted samples, and Cr was significantly different only for SGF-adjusted samples (Table 2). As, Cr, Pb, and Ni concentrations decreased over time in the farmworker group, whereas U increased (Table 2).

Linear Regression Results

Education level was not included in final models due to significant overlap with occupation. Farmworker occupation was significantly associated with urinary As concentration (β: 0.80, 95% CI: 0.01–1.59; Table 3). Additionally, home residence in the state of Puebla was significantly associated with greater urinary concentrations of Cd (β: 0.70, 95% CI: 0.35–1.75), Pb (β: 0.99, 95% CI: 0.00–1.97), and Ni (β: 0.71, 95% CI: 0.04–1.39; Table 3).

DISCUSSION

Overview

This study assessed metal(loid) exposure in a group of agricultural workers in Sonora, Mexico, over time and compared these levels to a group of office workers living and working in the same area. Among agricultural workers, urinary As, Cr, Pb, and Ni decreased over time, whereas urinary U increased. We observed similar levels of urinary Cd in the farmworker group at both time points as those reported in agricultural studies from Guatemala and Nicaragua[26,38] (Table 4). However, we observed higher levels of As and U in the farmworker group at both time points than those reported in the aforementioned studies[26,38] (Table 4). Briefly, the 2012 study in Nicaragua included sugarcane workers followed over the course of a work season (ie, sampling before harvest and again in late harvest),[26] whereas the study in Guatemalan sugarcane cutters included urine collected at three time points during the harvest season.[38]

Similarly, we observed higher levels of creatinine-corrected urinary As than the concentrations reported in a US cohort of migrant agricultural workers from Mexico and sugarcane workers in Nicaragua (Table 5).[39] The creatinine-adjusted As concentrations observed in this study were also higher than the end of shift Biological Exposure Indices value of 15 μg/g set by the American Conference of Governmental Hygienists.[40] The creatinine-adjusted Cd levels at both baseline and follow-up in this study were similar to those reported in the US and Nicaraguan studies, whereas the levels of U were higher than those reported in the study of sugarcane workers in Nicaragua.[23] The US study included 258 farm workers from over 40 different residential sites in North Carolina, the majority (>90%) were male and from central Mexico (75.2%), and 36.8% worked in US agriculture for 8 years or

TABLE 2. Urinary Metal(loid) Concentrations by Occupation (Farmworkers [FW] and Office Workers [NFW]) and Time Point, Adjusted by a Specific-Gravity Factor (SGF), Sonora, Mexico, 2019

	Non-FW n = 21	FW Baseline n = 77	FW Follow-up n = 77	p Non-FW vs FW at Baseline	p FW Baseline vs FW Follow-up
Metal				*	†
Arsenic (μg/L)‡					
Unadjusted GM (GSD)	55.0 (2.09)	104 (2.35)	102 (2.04)	**0.01**	**<0.01**
25th, 50th, 75th percentile	33.3, 50.8, 103	63.0, 136, 195	81.9, 113, 155		
SGF-adjusted GM (GSD)	55.1 (2.10)	104 (2.36)	83.3 (3.41)	**<0.01**	0.13
25th, 50th, 75th percentile	33.4, 50.6, 104	63.6, 137, 195	82.3, 112, 156		
Cadmium (μg/L)§					
Unadjusted GM (GSD)	0.27 (1.91)	0.31 (2.52)	0.35 (3.32)	0.06	0.70
25th, 50th, 75th percentile	0.17, 0.28, 0.43	0.26, 0.34, 0.49	0.33, 0.44, 0.57		
SGF-adjusted GM (GSD)	0.27 (1.92)	0.31 (2.52)	0.29 (4.35)	0.14	0.07
25th, 50th, 75th percentile	0.17, 0.28, 0.43	0.26, 0.34, 0.50	0.26, 0.42, 0.56		
Chromium (μg/L)‡					
Unadjusted GM (GSD)	14.64 (1.66)	13.88 (1.53)	16.12 (1.56)	0.85	0.16
25th, 50th, 75th percentile	9.55, 16.0, 18.3	11.0, 13.5, 19.2	12.4, 17.5, 22.1		
SGF-adjusted GM (GSD)	14.66 (1.67)	13.93 (1.53)	z13.17 (2.80)	0.93	**0.04**
25th, 50th, 75th percentile	9.60, 16.2, 18.4	11.0, 13.5, 19.1	11.9, 17.5, 22.1		
Lead (μg/L)‡					
Unadjusted GM (GSD)	1.23 (1.56)	2.35 (3.44)	2.01 (2.89)	**0.01**	**<0.01**
25th, 50th, 75th percentile	0.743, 1.02 1.82	1.04, 2.44, 5.28	0.970, 2.07, 4.13		
SGF-adjusted GM (GSD)	1.23 (2.86)	2.37 (3.44)	1.65 (4.34)	**0.01**	**<0.01**
25th, 50th, 75th percentile	0.736, 1.03 1.83	1.04, 2.45, 5.28	0.901, 2.07, 4.17		
Nickel (μg/L)‡					
Unadjusted GM (GSD)	3.11 (2.11)	8.93 (1.71)	7.11 (1.98)	**0.01**	**<0.01**
25th, 50th, 75th percentile	1.54 2.89 4.07	6.61 9.27 13.3	5.37 7.41 10.6		
SGF-adjusted GM (GSD)	3.12 (2.12)	8.96 (1.71)	5.81 (3.00)	**<0.01**	**<0.01**
25th, 50th, 75th percentile	1.54, 2.92, 4.08	6.61, 9.19, 13.3	4.86, 7.33, 10.0		
Uranium (μg/L)‡					
Unadjusted GM (GSD)	0.02 (2.10)	0.05 (2.48)	0.27 (2.30)	**<0.01**	**<0.01**
25th, 50th, 75th percentile	0.02, 0.02, 0.04	0.03, 0.04, 0.09	0.16, 0.25, 0.46		
SGF-adjusted GM (GSD)	0.02 (2.10)	0.05 (2.48)	0.22 (3.82)	**<0.01**	**<0.01**
25th, 50th, 75th percentile	0.02, 0.02, 0.04	0.03, 0.04, 0.09	0.16, 0.25, 0.46		

Specific gravity correction factor = absolute value (1.02 − (1 × specific gravity) − 1).
Current study instrumentation limit of detections for total arsenic, cadmium, chromium, lead, nickel, and uranium: 0.0005, 0.0007, 0.002, 0.005, 0.001, and 0.0001 (μg/L), respectively.
GM, geometric mean; GSD, geometric standard deviation.
Statistical test performed: *Wilcoxon rank-sum, †Wilcoxon signed-rank. Bolded text represents statistically significant results.
‡100% detection rate.
§Cadmium had a 98.3% detection rate.

TABLE 3. Associations between Specific-Gravity Factor-Adjusted Urinary Metal Levels and Socioeconomic Factors in a Cohort of Migratory Farmworkers (n = 77) and Office Workers (n = 21) in Sonora Mexico in 2019 at Baseline

	Arsenic β Coefficient (95% CI)	Cadmium β Coefficient (95% CI)	Chromium β Coefficient (95% CI)	Lead β Coefficient (95% CI)	Nickel β Coefficient (95% CI)	Uranium β Coefficient (95% CI)
Occupation						
Office worker	Reference					
Farmworker	**0.80 (0.01–1.59)**	−0.23 (−1.12 to 0.65)	−0.32 (−0.76 to 0.11)	0.11 (−0.72 to 0.94)	0.44 (−0.13 to 1.00)	0.14 (−0.74 to 1.01)
Age (y)	−0.01 (−0.02 to 0.01)	0.01 (−0.01 to 0.03)	0.01 (0.00–0.02)	0.01 (−0.01 to 0.02)	0.00 (−0.01 to 0.02)	−0.01 (−0.03 to 0.01)
BMI	0.03 (−0.02 to 0.07)	−0.01 (−0.06 to 0.04)	−0.01 (−0.03 to 0.01)	−0.03 (−0.07 to 0.02)	−0.01 (−0.04 to 0.02)	−0.01 (−0.06 to 0.04)
Primary language spoken						
Spanish	Reference					
Indigenous	−0.17 (−0.56 to 0.23)	−0.16 (−0.61 to 0.28)	−0.03 (−0.25 to 0.19)	0.18 (−0.23 to 0.60)	0.04 (−0.24 to 0.32)	0.07 (−0.37 to 0.51)
State of origin						
Sonora	Reference					
Puebla	0.21 (−0.73 to 1.15)	**0.70 (0.35–1.75)**	0.41 (−0.11 to 0.93)	**0.99 (0.00–1.97)**	**0.71 (0.04–1.39)**	0.70 (−0.35 to 1.74)
Chiapas	−0.39 (−1.34 to 0.57)	0.37 (−0.70 to 1.43)	0.23 (−0.30 to 0.75)	−0.86 (−1.86 to 0.13)	0.61 (−0.07 to 1.29)	0.57 (−0.48 to 1.63)
Smoking						
No	Reference					
Yes	−0.20 (−0.58 to 0.19)	−0.24 (−0.68 to 0.19)	−0.06 (−0.28 to 0.15)	0.12 (−0.29 to 0.52)	−0.22 (−0.50 to 0.05)	0.10 (−0.33 to 0.53)
Monthly income (USD)						
Less than $200	Reference					
$200 or more	0.01 (−0.69 to 0.71)	−0.09 (−0.87 to 0.69)	−0.08 (−0.46 to 0.31)	−0.43 (−1.16 to 0.30)	−0.21 (−0.71 to 0.28)	−0.12 (−0.89 to 0.65)

All models: Multiple linear regression models were used to assess associations between urinary metal concentration with socioeconomic data. Bolded text represents statistically significant results.

Number of observations for all models = 93.

BMI, body mass index in kg/m^2; CI, confidence interval; USD, United States dollar.

more.[39] From regression models, the authors reported that age and pack years of cigarette smoking were associated with As and Cd exposure, whereas birth region in Mexico (ie, North, Central, Southern) was associated with Hg and Pb levels.[39] In the 2015 study of sugarcane workers and miners from Nicaragua, the majority were male, and the mean age was 32 years old.[23] The metal concentrations from the Nicaraguan sugarcane study were similar to those observed in the 2011–2012 NHANES for adult males and females, and the majority did not increase over the harvest season, whereas Cd and Pb decreased over time.[23] Outdoor workers had higher As concentrations than did indoor sugarcane factory workers, and males had blood Pb levels twice that of females.[23]

In comparison to studies in various populations from the US-Mexico border region, the levels of unadjusted As observed in our study were similar to levels of inorganic As seen in children living in southern Sonora[28] but higher than those reported in other populations and areas (Table 6). Our creatinine-adjusted geometric means of Cd, Cr, Pb, and Ni were generally similar to those reported in a 2022 case-control study of women in Northern Mexico (Table 6).[41] The authors reported positive associations between age, education, BMI, use of tobacco, and state of residence with concentrations of metal(loids),[41] similar to our observations of education and state of residence associated with increased urinary As, Cd, Pb, and/or Ni.

Urinary concentrations of U in our farmworker group increased over time (Table 2), suggesting increased exposure while living and working in Sonora. U, a radioactive metal, is primarily used in nuclear power and weaponry.[42] The state of Sonora contains several U deposits, such as El Horror located northeast of Hermosillo and Los Amoles, which may explain the increased exposure.[43,44] Exposure occurs through ingestion of contaminated food or water, inhalation of dust from mining and milling, and minimally through dermal absorption.[42,45] Around 0.5% to 5% of ingested U enters the bloodstream, with most being excreted via the kidneys within 24 hours, whereas the remainder accumulates in organs such as the kidneys, liver, and bones.[42] Outdoor work likely contributes to exposure in agricultural workers, through dust inhalation, nondietary ingestion, and potential contamination of the rural well used for drinking water.

Contrary to expectations, we observed a decrease in urinary concentrations of As, Pb, and Ni over time, suggesting reduced exposure with time. Agricultural workers in this study migrated to Sonora from various states in southern Mexico such as Chiapas, suggesting that exposure sources from their home states should be considered alongside those in Sonora. As exposure in Mexico stems from both natural sources (eg, geology affecting drinking water) and anthropogenic activities (eg, mining, smelting, pesticides, building materials).[46–49] Ni exposure, primarily from industrial uses and contaminated water, is a concern due to its prevalence in various applications and the recycling of Ni-containing products[50,51] Pb exposure occurs through air, soil, water, and consumer products, with industrial sources including smelting, mining, production and recycling of batteries, metal solder and pipes, ammunition, and pesticides.[52] The use of glazed stoneware containing Pb has been associated with increased exposure, particularly in the southern states of Mexico.[53–55] Although Mexico has phased out leaded gasoline and set limits for Pb in paints, exposure persists.[56–58] These findings highlight the need to consider multiple exposure sources and pathways, including those from occupational settings in workers' home states, when assessing toxic metal(loid) exposure and health impacts.

Strengths

A strength of this study was its longitudinal approach, with repeated measures of a migratory agricultural population within Mexico. Exposure misclassification was reduced by recruiting participants who worked at the same farm, were subject to similar occupational and environmental conditions, consumed water from a unified source, ate similar employer-provided meals, and resided in communal housing units on-site. These measures mitigate potential confounding variables and increase the reliability of the exposure assessment. Additionally, collecting first-morning void samples is a significant strength of this study, as few previous studies have successfully overcome the logistical challenges associated with this collection method. The study also fostered collaborative relationships with agricultural producers, which may translate into improving health outcomes for a vulnerable population and advancing public health initiatives in agricultural settings.

TABLE 4. Unadjusted Urinary Metal(loid) Concentrations of Study Participants in Comparison With Mexican Americans From the 2017–2018 US National Health and Nutrition Examination Survey (NHANES) and Other Studies From the United States, Guatemala, and Nicaragua

Study Authors, Year Country/Location Study and/or Worker Details Statistics Presented	Arsenic	Cadmium	Chromium	Lead	Nickel	Uranium
Current study, 2019	Baseline	Baseline	Baseline	Baseline	Baseline	Baseline
Sonora, Mexico	103 (85.6–125)	0.31 (0.25–0.38)	13.9 (12.60–15.30)	2.36 (1.79–3.11)	8.93 (7.91–10.10)	0.05 (0.04–0.07)
Grape workers at two time points†	Follow-up	Follow-up	Follow-up	Follow-up	Follow-up	Follow-up
Geometric mean (95% CI) (μg/L)[37]	102 (86.9–119.6)	0.35 (0.27–0.46)	16.10 (14.90–17.80)	2.01 (1.59–2.55)	7.11 (6.11–8.28)	0.27 (0.22–0.32)
2017–2018 NHANES	6.16 (5.23–7.26)	0.12 (0.11–0.14)	*	0.27 (0.24–0.30)	1.15 (1.04–1.28)	0.006 (0.005–0.007)
Mexican Americans						
Geometric mean (95% CI) (μg/L)						
McClean et al,[26] 2012	Time 1	Time 1	N/A	N/A	N/A	Time 1
Nicaragua	17 (2.0–110)	0.4 (0.1–0.82)				0.01 (0.01–0.09)
Various occupations at two time points‡	13 (1.3–71)	0.4 (0.1–0.80)				0.01 (0.01–0.02)
Geometric mean (range) (μg/L)	12 (2.7–52)	0.3 (0.1–0.68)				0.01 (0.01–0.03)
	8 (2.5–21)	0.3 (0.1–0.85)				0.01 (0.01–0.08)
	Time 2	Time 2				Time 2
	15 (4.3–74)	0.2 (0.1–0.7)				0.01 (0.01–0.1)
	11 (2.2–60)	0.3 (0.1–1.0)				0.01 (0.01–0.3)
	13 (2.2–48)	0.3 (0.1–1.2)				0.01 (0.01–0.04)
	13 (1.6–45)	0.3 (0.1–0.6)				0.01 (0.01–0.02)
	26 (6.3–180)					
Butler-Dawson et al,[38] 2022	Time 1: 6.88	Time 1: 0.14	N/A	N/A	Time 1: 1.40	10% detected,
Guatemala	Time 2: 7.13	Time 2: 0.10			Time 2: 1.80	unreported
Sugarcane workers at three time points§	Time 3: 8.05	Time 3: 0.09			Time 3: 2.20	results
Median (μg/L)						

CI, confidence interval; N/A, not applicable.
*Not calculated: Proportion of results below limit of detection was too high to provide a valid result.
†Data were collected at the following time points: March 2019 and July 2019.
‡Data were collected at the following time points: October to December 2010 and March to April 2011.
§Data were collected at the following time points: November 2017, January 2018, and July 2018.

TABLE 5. Creatinine-Adjusted Urinary Metal(Loid) Concentrations of Study Participants in Comparison With Mexican Americans From the 2017–2018 US National Health and Nutrition Examination Survey (NHANES) and Other Studies From the United States, Guatemala, and Nicaragua

Study Authors, Year Country/Location Study and/or Worker Details Statistics Presented	Arsenic	Cadmium	Chromium	Lead	Nickel	Uranium
Current study, 2019 Sonora, Mexico Grape workers at two time points* Geometric mean (95% CI) (µg metal per g of urinary creatinine)	Baseline 74.26 (62.17–88.70) Follow-up 62.71 (57.83–68.01)	Baseline 0.22 (0.19–0.26) Follow-up 0.22 (0.19–0.25)	Baseline 9.96 (9.33–10.63) Follow-up 9.92 (8.90–11.04)	Baseline 1.69 (1.30–2.20) Follow-up 1.24 (0.96–1.59)	Baseline 6.40 (5.85–7.01) Follow-up 4.37 (3.79–5.04)	Baseline 0.04 (0.03, 0.05) Follow-up 0.16 (0.13–0.21)
2017–2018 NHANES Mexican Americans Geometric mean (95% CI) (µg metal per g of urinary creatinine)	6.66 (5.62–7.88)	0.11 (0.09–0.12)	†	0.29 (0.26–0.031)	1.24 (1.16–1.33)	0.01 (0.01–0.01)
Quandt et al,[39] 2010 United States Mexican migrant farmworkers Geometric mean (95% CI) (µg metal per g of urinary creatinine)	13.23 (11.11–15.35)	0.20 (0.18–0.21)	N/A	1.26 (1.08–1.43)	N/A	N/A
Laws,[23] 2015 Nicaragua Sugarcane workers Geometric mean (µg metal per g of urinary creatinine)	14.80	0.22	N/A	N/A	N/A	0.01

CI, confidence interval; N/A, not applicable.
*Data were collected at the following time points: March 2019 and July 2019.
†Not calculated: Proportion of results below limit of detection was too high to provide a valid result.

TABLE 6. Creatinine-Adjusted Urinary Metal(loid) Concentrations in Populations along the US-Mexico Border Region

Study Authors, Year Location Study Details Statistics Presented	Arsenic	Cadmium	Chromium	Lead	Mercury	Nickel	Uranium
Current study, 2019 Sonora, Mexico Grape workers at two time points Geometric mean (95% CI) (µg metal per g of urinary creatinine)	Baseline 74.26 (62.17–88.70) Follow-up 62.71 (57.83–68.01)	Baseline 0.22 (0.19–0.26) Follow-up 0.22 (0.19–0.25)	Baseline 9.96 (9.33–10.63) Follow-up 9.92 (8.90–11.04)	Baseline 1.69 (1.30–2.20) Follow-up 1.24 (0.96–1.59)	N/A	Baseline 6.40 (5.85–7.01) Follow-up 4.37 (3.79–5.04)	Baseline 0.04 (0.03–0.05) Follow-up 0.16 (0.13–0.21)
Mérida-Ortega et al,[41] 2022 Northern Mexico Creatinine-adjusted levels in women, breast cancer cases, and controls Median (10th, 90th percentiles) (µg metal per g of urinary creatinine)	N/A	Cases: 0.53 (0.19, 1.48) Controls: 0.56 (0.22, 1.51)	Cases: 3.16 (1.27, 8.93) Controls: 3.00 (1.35, 7.97)	Cases: 2.71 (1.03, 7.33) Controls: 2.99 (0.93, 8.16)	N/A	Cases: 10.76 (4.86, 24.9) Controls: 10.72 (4.78, 26.6)	N/A

N/A, not applicable.

Limitations

The relatively small study population and the exclusion of women agricultural workers restrict the generalizability of the findings. Additionally, the small control group (n = 21) limits the power of comparisons and may not be representative of a true nonagricultural population from the region. Furthermore, the absence of environmental samples (eg, air, soil, sediment, water) prevents a source apportionment analysis, limiting insights into the origins of observed metal(loid) concentrations. The assessment of total urinary metal(loid) concentrations, rather than species-specific (eg, inorganic vs organic arsenic) concentrations for each element, limits the ability to assess risk for specific endpoints such as cancer. Samples were collected in 2019 and therefore may not accurately reflect current exposure levels. The utilization of urinary Pb measurements instead of blood samples presents another limitation for comparison to studies that used blood Pb, a more common measure of Pb exposure. The questionnaire utilized a general question about alcohol consumption but did not differentiate between types of alcoholic beverages consumed. This represents a potential limitation, as metals may be released into alcoholic beverages during production and storage, influencing potential exposure levels. Finally, we presented unadjusted, SGF-adjusted, and urinary creatinine–adjusted results in order to compare to other relevant studies. Although adjustments were made based on recommendations from previous studies, debate is ongoing regarding the optimal method for hydration adjustments in populations with extreme dehydration/hydration levels, which is a particular concern for the outdoor laborers such as those included in this study. These limitations underscore the need for cautious interpretation of the study findings. However, these data are useful for hypothesis generation to inform future studies.

Conclusions and Future Research

This study adds useful information regarding metal(loid) exposure data for migratory Mexican agricultural workers, a population that is both vulnerable and understudied. We observed exposure levels that were higher in agricultural workers than office workers in Sonora and also substantially higher than levels reported for Mexican Americans in the 2017–2018 NHANES. Future research should investigate sources of metal(loid) exposure and health consequences of exposures to develop effective interventions. For example, the consumption of unfiltered groundwater and chronic exposure to contaminated soil and airborne dust may contribute to agricultural workers' increased exposure to metal(loid)s. Future research should incorporate analysis of additional noninvasive biomarkers, such as hair, which would allow for comparisons between short- and long-term exposures. For example, analysis of hair via laser-ablation ICP-MS would facilitate interpretation of temporal exposure in Sonora versus earlier exposure in the home state from the same strand of hair.[59] Investigations into effects of environmental versus occupational exposures would facilitate the development of interventions (eg, drinking water filtration and use of PPE when in the fields) that could be implemented to improve renal function and broader health outcomes. Results such as ours could facilitate the development of agricultural-specific research and recommendations for the control of metal(loid) exposure. From a policy perspective, the establishment of a nationwide metal(loid) exposure surveillance database in Mexico is recommended. Such a database would facilitate comparisons between regions; inform the development of regulatory limits for drinking water, consumer products, food safety, pesticides, and fertilizers; and enable targeted allocation of public health funding to prioritize interventions where they are most needed. Finally, additional research is imperative to fully understand the connection between metal(loid) exposures and kidney diseases within agricultural communities.

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REFERENCES

1. Lunyera J, Mohottige D, Von Isenburg M, Jeuland M, Patel UD, Stanifer JW. CKD of uncertain etiology: a systematic review. *Clin J Am Soc Nephrol* 2016;11:379–385.
2. Chicas R, Mix J, Mac V, et al. Chronic kidney disease among workers: a review of the literature. *Workplace Health Saf* 2019;67:481–490.
3. Rango T, Jeuland M, Manthrithilake H, McCornick P. Nephrotoxic contaminants in drinking water and urine, and chronic kidney disease in rural Sri Lanka. *Sci Total Environ* 2015;518-519:574–585.
4. Zanoli L, Granata A, Dellaquila R, Castellino P, Lentini P, Signorelli SS. Kidney and heavy metals — the role of environmental exposure. *Mol Med Rep* 2017;15:3413–3419.
5. Thomas LDK, Hodgson S, Nieuwenhuijsen M, Jarup L. Early kidney damage in a population exposed to cadmium and other heavy metals. *Environ Health Perspect* 2009;117:181–184.
6. Barregård L, Svalander C, Schütz A, et al. Cadmium, mercury, and lead in kidney cortex of the general Swedish population: a study of biopsies from living kidney donors. *Environ Health Perspect* 1999;107:867–871.
7. Orr SE, Bridges CC. Chronic kidney disease and exposure to nephrotoxic metals. *Int J Mol Sci* 2017;18.
8. Gonick HC. Nephrotoxicity of cadmium & lead. *Indian J Med Res* 2008;128:335–352.
9. Robles-Osorio ML, Sabath-Silva E, Sabath E. Arsenic-mediated nephrotoxicity. *Ren Fail* 2015;37:542–547.
10. Sabath E, Robles-Osorio ML. Renal health and the environment: heavy metal nephrotoxicity. *Nefrologia* 2012;32:279–286.
11. Soderland P, Lovekar S, Weiner DE, Brooks DR, Kaufman JS. Chronic kidney disease associated With environmental toxins and exposures. *Adv Chronic Kidney Dis* 2010;17:254–264.
12. Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ, Kaufman JS. Chronic kidney disease associated With environmental toxins and exposures. *Adv Chronic Kidney Dis* 2010;17:254–264.
13. Sabolić I. Common mechanisms in nephropathy induced by toxic metals. *Nephron Physiol* 2006;104:107–114.
14. Vicente-Vicente L, Quiros Y, Pérez-Barriocanal F, López-Novoa JM, López-Hernández FJ, Morales AI. Nephrotoxicity of uranium: pathophysiological, diagnostic and therapeutic perspectives. *Toxicol Sci* 2010;118:324–347.
15. Barbier O, Jacquillet G, Tauc M, Cougnon M, Poujeol P. Effect of heavy metals on, and handling by, the kidney. *Nephron Physiol* 2005;99:105–110.
16. Wanigasuriya KP, Peiris-john RJ, Wickremasinghe R. Chronic kidney disease of unknown aetiology in Sri Lanka: is cadmium a likely cause? *BMC Nephrol* 2011;12.
17. Wanigasuriya K, Jayawardene I, Amarasiriwardena C, Wickremasinghe R. Novel urinary biomarkers and their association With urinary heavy metals in chronic kidney disease of unknown aetiology in Sri Lanka: a pilot study. *Ceylon Med J* 2017;62:210–217.
18. Kazancioğlu R. Risk factors for chronic kidney disease: an update. *Kidney Int Suppl* (2011) 2013;3:368–371.
19. Chandrajith R, Nanayakkara S, Itai K, et al. Chronic kidney diseases of uncertain etiology (CKDue) in Sri Lanka: geographic distribution and environmental implications. *Environ Geochem Health* 2011;33:267–278.
20. Robles-Osorio ML, Pérez-Maldonado IN, Martín del Campo D, et al. Urinary arsenic levels and risk of renal injury in a cross-sectional study in open population. *Rev Invest Clin* 2012;64(6 Pt 2):609–614.
21. Maruzeni S, Nishijo M, Nakamura K, et al. Mortality and causes of deaths of inhabitants with renal dysfunction induced by cadmium exposure of the polluted Jinzu River basin, Toyama, Japan; a 26-year follow-up. *Environ Health* 2014;13. Article 18.
22. Sommar JN, Svensson MK, Björ BM, et al. End-stage renal disease and low level exposure to lead, cadmium and mercury; a population-based, prospective nested case-referent study in Sweden. *Environ Health* 2013;12:1–10.
23. Laws RL. *Chronic Kidney Disease of Unknown Etiology in Nicaragua: Investigating the Role of Environmental and Occupational Exposures*. 2015. Available at: https://search.proquest.com/docview/1735800609?accountid=27931. Accessed April 9, 2024.
24. Bandara JM, Senevirathna DM, Dasanayake DM, et al. Chronic renal failure among farm families in cascade irrigation systems in Sri Lanka associated

with elevated dietary cadmium levels in rice and freshwater fish (Tilapia). *Environ Geochem Health*. 2008;30:465–478.
25. Jayatilake N, Mendis S, Maheepala P, Mehta FR. Chronic kidney disease of uncertain aetiology: prevalence and causative factors in a developing country. *BMC Nephrol* 2013;14:180.
26. McClean M, Amador JJ, Laws RL, et al. Boston University School of Public Health. *Biological Sampling Report: Investigating Biomarkers of Kidney Injury and Chronic Kidney Disease Among Workers in Western Nicaragua* Vol 8; 2012. Available at: https://aconsole-static.s3.amazonaws.com/media/public/cases/Biological_Sampling_Report_April_2012.pdf.
27. Gómez-Álvarez A, Valenzuela-García JL, Aguayo-Salinas S, Meza-Figueroa D, Ramírez-Hernández J, Ochoa-Ortega G. Chemical partitioning of sediment contamination by heavy metals in the San Pedro River, Sonora, Mexico. *Chem Speciation Bioavailability* 2007;19:25–35.
28. Maldonado Escalante JF, Meza Figueroa D, Dévora Figueroa AG, et al. An integrated health risk assessment of indigenous children exposed to arsenic in Sonora, Mexico. *Human Ecol Risk Assess* 2019;25:706–721.
29. Mendoza-Lagunas JL, Meza-Figueroa DM, Martínez-Cinco MA, et al. Health risk assessment in children by arsenic and mercury pollution of groundwater in a mining area in Sonora, Mexico. *J Geosci Environ Prot* 2019;07:90–105.
30. Mérida-Ortega Á, Rothenberg SJ, Cebrián ME, López-Carrillo L. Breast cancer and urinary metal mixtures in Mexican women. *Environ Res* 2022;210. 112905.
31. Alengebawy A, Abdelkhalek ST, Qureshi SR, Wang MQ. Heavy metals and pesticides toxicity in agricultural soil and plants: ecological risks and human health implications. *Toxics* 2021;9:1–34.
32. López-Gálvez N, Wagoner R, Canales RA, et al. Longitudinal assessment of kidney function in migrant farm workers. *Environ Res* 2021;202. doi:10.1016/j.envres.2021.111686.
33. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42: 377–381.
34. U.S. Environmental Protection Agency. *Method 200.8: Determination of Trace Elements in Waters and Wastes by Inductively Coupled Plasma-Mass Spectrometry*; 1994.
35. Sauvé JF, Lévesque M, Huard M, et al. Creatinine and specific gravity normalization in biological monitoring of occupational exposures. *J Occup Environ Hyg* 2015;12: 123–129.
36. Masdor NA. Determination of the detection limit using the four-parameter logistic model for the double-antibody sandwich ELISA for the rapid detection of *Bacillus cereus* in food. *J Environ Microbiol Toxicol* 2017;5:12–13.
37. U.S. Centers for Disease Control and Prevention. Biomonitoring Data Tables for Environmental Chemicals, Urinary Metals and Metalloids. Available at: https://www.cdc.gov/exposurereport/data_tables.html. Accessed September 3, 2025.
38. Butler-Dawson J, James KA, Krisher L, et al. Environmental metal exposures and kidney function of Guatemalan sugarcane workers. *J Expo Sci Environ Epidemiol* 2022;32:461–471.
39. Quandt SA, Jones BT, Talton JW, et al. Heavy metals exposures among Mexican farmworkers in eastern North Carolina. *Environ Res* 2010;110:83–88.
40. ACGIH. *American Conference of Governmental Hygienists Threshold Limit Values for Chemical Substances and Biological Exposure Indices*. American Conference of Governmental Industrial Hygienists; 2024.
41. Mérida-Ortega Á, Rothenberg SJ, Cebrián ME, Arias-Medellín LA, Salgado-Salgado AL, López-Carrillo L. Urinary concentrations of potentially toxic metals and metal(loid)s among women residing in northern Mexico. *Expo Health* 2022;14:857–870.
42. ATSDR. *Toxicological Profile for Uranium*. 2013. doi:10.1201/9781420061888_ch157.
43. Dahlkamp FJ. *Uranium Deposits of the World: USA and Latin America*. Springer Berlin, Heidelberg; 2010. Available at: https://link.springer.com/referenceworkentry/10.1007/978-3-540-78943-7_16#Fig1_16. Accessed April 9, 2024.
44. Grijalva-Rodríguez T, Valencia-Moreno M, Calmus T, Del Rio-Salas R, Balcázar-García M. The El horror uranium anomaly in northeastern Sonora, Mexico: constraints from geochemical and mineralogical approaches. *J South Am Earth Sci* 2017;80:107–119.
45. ATSDR. What Are the Routes of Exposure for Uranium? United States Centers for Disease Control Agency for Toxic Substances and Disease Registry Environmental Health and Medicine Education. 2023. Available at: https://www.atsdr.cdc.gov/csem/uranium/exposure_pathways.html. Accessed April 28, 2024.
46. Bundschuh J, Armienta MA, Morales-Simfors N, et al. Arsenic in Latin America: new findings on source, mobilization and mobility in human environments in 20 countries based on decadal research 2010–2020. *Crit Rev Environ Sci Technol* 2020;51:1727–1865.
47. Gutiérrez M, Alarcón-Herrera MT, Gaytán-Alarcón AP. Arsenic and fluorine in groundwater in northern Mexico: spatial distribution and enrichment factors. *Environ Monit Assess* 2023;195:1–12.
48. Litter MI, Armienta MA, Villanueva Estrada RE, Villaamil Lepori EC, Olmos V. Arsenic in Latin America: part II. *Arsenic in Drinking Water and Food* 2019;1: 113–157.
49. Ortiz Letechipia J, González-Trinidad J, Júnez-Ferreira HE, et al. Aqueous arsenic speciation with hydrogeochemical modeling and correlation with fluorine in groundwater in a semiarid region of Mexico. *Water (Switzerland)* 2022;14.
50. de León-Gómez H, Martin del Campo-Delgado MA, Esteller-Alberich MV, Velasco-Tapia F, Alva-Niño E, Cruz-López A. Assessment of nitrate and heavy metal contamination of groundwater using the heavy metal pollution index: case study of Linares, Mexico. *Environ Earth Sci* 2020;79:433.
51. Roberto Gutiérrez L, Rubio-Arias H, Quintana R, Ortega JA, Gutierrez M. Heavy metals in water of the San Pedro River in Chihuahua, Mexico and its potential health risk. *Int J Environ Res Public Health* 2008;5:91–98.
52. ATSDR. Toxicological Profile for Lead; 2020. Available at: https://www.atsdr.cdc.gov/toxprofiles/tp13.pdf. Accessed April 9, 2024.
53. Avila MH, Romieu I, Rios C, Rivero A, Palazuelos E. Lead-glazed ceramics as major determinants of blood lead levels in Mexican women. *Environ Health Perspect* 1991;94:117–120.
54. Azcona-Cruz MI, Romero-Placeres M, Rothenberg SJ, et al. Lead-glazed ceramic ware and blood lead levels of children in the city of Oaxaca, Mexico. *Arch Environ Health* 2000;55:217–222.
55. Téllez-Rojo MM, Bautista-Arredondo LF, Trejo-Valdivia B, et al. National report of blood lead levels and lead-glazed ceramics use in vulnerable children. *Salud Publica Mex* 2019;61:787–797.
56. Caravanos J, Dowling R, Téllez-Rojo MM, et al. Blood lead levels in Mexico and pediatric burden of disease implications. *Ann Glob Health* 2014;80: 269–277.
57. Flores J, Albert LA. Environmental lead in Mexico, 1990–2002. *Rev Environ Contam Toxicol* 2005;181:37–109.
58. UN. *Update on the Global Status of Legal Limits on Lead in Paint*. United Nations Environment Programme; 2020:2021. Available at: https://www.unep.org/resources/report/2020-update-global-status-legal-limits-lead-paint. Accessed April 9, 2024.
59. David GK, Hunter AH, Moromizato KH, et al. Pre-cleaning of hair is not beneficial in LA-ICPMS studies of chronic metal exposure. *PloS One* 2023;18:5–8.

