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Arsenic and fifteen other metal (loid)s exposure of children living around old mines in the south of France

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A R T I C L E I N F O

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A B S T R A C T

As many countries plan to resume mining for the energy transition, assessing the health impacts of past activities is crucial. This cross-sectional study investigated whether children living near four old mines in southern France were exposed to higher levels of arsenic and 15 other metal(loid)s compared to those in unexposed areas. Arsenic, a prevalent contaminant, was used as an indicator to explore exposure in relation to children's lifestyles (housing, activities, diet) and their environments (soil, dust, water). The study included 240 children—138 from exposed areas and 102 from control areas. Urine samples were analyzed for inorganic arsenic, its metabolites, and other trace elements. No significant difference was found in average age, BMI, or parental education between groups. Urinary arsenic levels were similar for children living near mines and those in control areas (6.4 vs. 7.0 µg/g; $p = 0.152$). Proximity to mining sites did not increase arsenic exposure (r Pearson = 0.142). Instead, factors like age, seafood consumption, and environmental conditions were more influential. Children who ate seafood had higher arsenic levels in urine ($p < 0.001$). In a subgroup near mines, arsenic in soil and dust was significantly linked to increased exposure ($p < 0.001$). Overall, metal exposure levels were comparable to or lower than national averages. Access to clean water, mine closures, and health awareness likely kept exposure low. Ongoing biomonitoring is crucial for identifying and mitigating health risks in communities living near former mining areas.

1. Introduction

Metallic mining is essential for the transition to clean energy, as it supplies the essential metals needed for green technologies (EC, 2020). However, this reliance on mining increases consumer countries' dependence on producer countries and exacerbates social and environmental injustices in developing nations. In response, France and other industrialized countries are considering reopening mines to support the energy transition. The EU, for example, aims to produce over 10 % of its metals domestically by 2030 (EC, 2023). Yet, the resurgence of mining in regions where it has nearly vanished presents significant challenges. Abandoned or poorly rehabilitated mining sites pose health risks to nearby communities, with insufficient health monitoring even years after closure, complicating efforts to establish new mining projects in these countries.

Health surveillance in mining communities faces challenges due to the lack of specific effects, latency of health effects, and low incidence rates in affected populations (Núñez et al., 2017). Environmental health risk assessments are often misunderstood, as the distinction between contaminant presence, risk modeling, and actual risk can be blurred (Tubis et al., 2020; Cáceres et al., 2021). This can lead to heightened perceptions of danger that don't always align with actual health risks in these industrialized countries where mines have been abandoned, often rehabilitated, and where the population has limited exposure to the environment (Trumbo et al., 2007). Consequently, biomonitoring has become essential to assess community exposure levels, yet existing studies are limited in scope, often focusing on only a few metals or single sites without a reference population (Zota et al., 2016; Rakete et al., 2022). Children in these communities are particularly vulnerable, as behaviors like hand-to-mouth contact and frequent outdoor play increase their exposure to contaminants. Besides dietary intake, soil or dust ingestion is their primary exposure route to metal(loid)s (EPA, 2008). Additionally, children's physiological capacities differ from those of adults (greater digestive absorption, immature metabolic and

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excretory mechanisms), which increases their vulnerability to harmful substances (Dauphiné et al., 2011). Yet, some studies have shown a higher risk of exposure to certain metals in young children in mining environments (Bose-O'Reilly et al., 2018; Piñeiro et al., 2021).

Thus, this study seeks to assess biomonitoring of polymetallic exposure in communities residing near multiple former mining sites, focusing on children. Southern France's mining region is an ideal study site, due to its history of significant metal extraction activity over the past century (Bril and Floc'h, 2001). These mines have caused extensive soil and water contamination with metal sulfide minerals, leading to environmental contamination by metal(loid)s such as Pb, Cu, Zn, Cd, Bi, Ag, and Sb (BRGM, 2019). Acid drainage from the mines is a major environmental issue (U.S. EPA., 2000). The released metal(loid)s pose long-term health risks, including cancers and various diseases (Nordberg et al., 2014). Arsenic, especially prevalent in public areas with concentrations ranging from 50 to 5000 mg/kg of soil, remains a primary concern due to its chronic health risks including skin, cardiovascular, and neurological issues, increased cancer risk, and higher mortality rates (Flora, 2014). Consequently, local residents are deeply concerned about the ongoing health effects of this exposure.

Therefore, it is imperative to conduct thorough biomonitoring studies in such regions to accurately assess the health risks posed by historical mining activities, ensuring the safety and well-being of current and future generations. This cross-sectional study aims to compare children's exposure levels in various mining sites with those in control populations from uncontaminated areas. Arsenic, the most prevalent environmental contaminant on these former mining sites, was used as a tracer for exposure. Specific objectives include estimating arsenic exposure levels, identifying risk factors of exposure within population, assessing environmental quality, and documenting exposure to other metallic elements.

2. Materials and methods

2.1. Study area and participation

The research program comprised a cross-sectional study of exposure levels in children living within 3 km of a mining site or experiencing significant metallic contaminations from the mining site. The selected sites were located in France (Fig. 1), in the mountainous mining regions of the southern Massif Central, where arsenic was still present in significant quantities in soil (arsenic concentrations range from 50 to 1000 mg/kg). The study focused on two former mining areas: the Orbiel Valley and the Gard, selected for their high arsenic contamination, as documented in databases and reports, but also for the health and social concerns these sites generate, making them points of focus for French public organizations (BRGM, 2019; BRGM; Delplace et al., 2022). The Orbiel Valley was home to the Salsigne mine, Europe's largest gold mine, closed in 2004, with significant contamination from arsenic-rich arsenopyrite and other metals (As, Pb, Zn, Sb) extending to nearby areas (BRGM, 2019). Between 1968 and 1975, a significant increase in mortality from all types of cancer (+17 %) and respiratory tract cancers (+112 %) was observed. After 1975, these figures declined and were no longer evident following the mine's complete closure in 2004 (Santé publique France, 2019). The Gard region contained several lead, zinc, and silver mines, including three studied sites—Saint-Félix-de-Pallières, Saint-Sébastien-d'Aigrefeuille, and Saint-Laurent-Le-Minier—closed in the 1970s and also contaminated with metals (As, Pb, Zn Cd). Control sites, over 5 km from mining areas and free from industrial mining, showed arsenic levels below 100 mg/kg, a threshold distance consistent with similar studies (Fernández-Navarro et al., 2012; García-Pérez et al., 2010). The choice of these two mines for the study was based on the fact that despite the different closure times, the exposure risks to the surrounding populations may not differ significantly due to the persistent nature of the contaminants.

The inclusion criteria were children aged 3–12, living in one of the study areas for at least 6 months, without urinary incontinence or treatment for it. Sample and questionnaire collection occurred simultaneously in exposed and control areas: March to November 2021 in the Orbiel Valley, March to November 2022 in Gard, and May to July 2023 in St-LM. The French ethics committee (CPP) approved the research protocol (CPP ref: 07,09,20, RCB ID: 2020-A02164–35), and only data essential to the research objectives were collected.

2.2. Biological samples and questionnaires collection

Local authorities were informed about the study, its objectives, and its procedures. Their collaboration and support were sought.

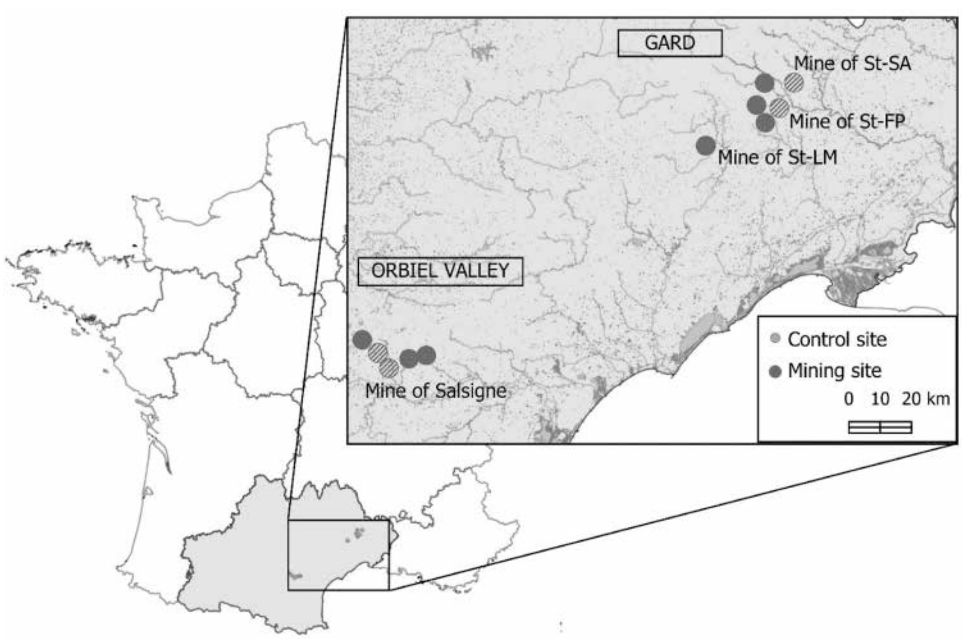

Fig. 1. Location of study areas, including the Orbiel Valley (Salsigne mine) and the Gard region (St-FP: Saint-Félix-de-Pallières, St-SA: Saint-Sébastien-d'Aigrefeuille, and St-LM: Saint-Laurent-Le-Minier mines).

Recruitment was conducted randomly by door-to-door visits to meet families, with at least one child per household enrolled in the study. During recruitment, the investigator provided families with detailed information about the study's objectives and procedures, supplemented by a written document. Families were then asked to sign an informed consent form. A urine collection kit was provided to them to collect a morning urine sample from their child. Families were advised to eliminate seafood (fish, algae, mollusks, crustaceans) and rice from their child's diet three days prior to sample collection to minimize dietary arsenic intake (Kales et al., 2006). The child's first-morning urine was collected mid-stream and stored at -20 °C by the families. The researcher later retrieved the urine samples, transported them in a frozen state (-20 °C), and ensured their storage at -20 °C in the laboratory until analysis. The researcher also administered or reviewed the questionnaire during the sample collection visit. Questionnaires were structured into multiple sections, they gathered detailed information on household sociodemographic, housing, health status, behaviors, and usual activities of the child, as well as their dietary and beverage consumption.

2.3. Arsenic measurement in urine

Only the inorganic forms of arsenic (AsIII and AsV, with the sum noted as Asi) as well as the methylated metabolized forms (MMA and DMA) were considered in the overall calculation: $\sum$Asi-MMA-DMA (WHO, 2001). The analytical method, adapted from Schramel et al. (2002), allowed for the rapid measurement of the 6 species of arsenic (AsIII, AsV, MMA, DMA, arsenocholine, and arsenobetaine) by high-performance liquid chromatography (HPLC ICS-5000, Thermo-Scientific) coupled with inductively coupled plasma mass spectrometry (ICP-MS single quadrupole iCAP-Qc, ThermoScientific). Urine samples were diluted 1/5 with distilled water (>18 mΩ.cm^{-1}) and placed in 2 mL polypropylene analysis tubes. Analyses were performed by injecting 50 µL of sample into the HPLC system. Chromatographic separation was performed on a strong cation exchange resin (PRP-X-100, 250 × 4.1 mm, 10 µm, Hamilton) at a flow rate of 1.5 mL/min using mobile phase A (4 mM NH_4NO_3, 2 % isopropanol, pH 9.2 adjusted with NH_4OH) and mobile phase B (10 mM NH_4NO_3, 10 mM $NH_4H_2PO_4$, 2 % isopropanol, pH 8.6 adjusted with NH_4OH) in gradient mode (0–2 min: A 100%; 2–7.5 min: B 100 %; 7.5–10 min: A 100%). ICP-MS conditions were optimized daily. A germanium solution at 50 µg/L was used as an internal standard. Calibration curves were generated using 6 concentration points with mixed standards at concentrations ranging from 0.125 to 16 µg/L, with $R^2 > 0.999$. External certified reference materials (P-CU-S2103, INSQP, Canada) were added during analysis to identify major sources of error. Bias accuracy was established using certified urine samples (SRM 2669, NIST), with biases being less than 5 % for the 4 concentration levels. Fidelity biases had coefficients of variation lower than 7 % for repeatability and 6 % for intermediate fidelity. The measured LOD and LOQ were 0.05 and 0.18 µg/L respectively.

2.4. Trace metal(loid)s measurement in urine

The analysis was performed after diluting the urine at a 1/20 ratio in a 1 % nitric acid solution (metal-free nitric acid and distilled water>18 mΩ.cm^{-1}) in 10 mL polypropylene tubes, and after an external calibration using mixed metal standard solutions. ICP-MS conditions were optimized daily. A germanium solution at 50 µg/L was used as an internal standard for ICP-MS analysis. Calibration curves were generated using 5 concentration points with mixed standards at concentrations ranging from 0.1 to 20 µg/L. For each element, R^2 values exceeded 0.999. Samples were analyzed in random order, with a blank analyzed every 10 samples to check for contamination of the analytical system. An external certified reference material (ClinChek-Control, 8847/8849–1227, Recipe, Germany) was analyzed at the beginning, middle, and end of the analysis to identify and correct major sources of error, biases being less than 15 % for the 2 concentration levels. Previously quantified replicas were blindly introduced into the analytical series to assess intermediate fidelity between different sets of analyses. For each element, fidelity biases had coefficients of variation lower than 10 %. The LOQ for each element was as followed (µg/L): Al (0.420), Ba (0.004), Cd (0.0006), Co (0.001), Cr (0.005), Cu (0.009), Mn (0.008), Mo (0.058), Ni (0.022), Sb (0.003), Sn (0.029), Tl (0.0007), U (0.0002), V (0.002), Zn (0.023).

2.5. Urinary dilution measurement

Urinary creatinine analysis was conducted using spectrophotometry, following the Jaffé method. The intensity of coloration of the complex formed between picric acid and creatinine is measured in an alkaline medium. The assay was performed in a 96-well plate format with a spectrophotometer at 490 nm (SPECTROstar Nano; BMG Labtech, France), using absorption kinetics. Urine samples were diluted at a 1/20 ratio. Calibration curves were generated using 6 concentration points ranging from 5 mg/L to 100 mg/L, with a correlation coefficient exceeding 0.99. The limits of detection and quantification (LOD and LOQ) were 1.1 and 3.5 mg/L, respectively.

2.6. Environmental analysis

Samples were collected from outdoor soil, indoor dust, and drinking water near the residences of some children. Soil samples around the homes were collected at a depth of 0–5 cm, homogenized, heated, and sieved (<63 µm) to retain only the fraction with the highest risk of adhering to hands and being ingested or inhaled (Choate et al., 2006). Dust was collected from vacuum cleaner bags, heated, and sieved (<63 µm). These samples were then mineralized by microwaves according to the US EPA 3051 method and analyzed by ICP-MS. Water samples were collected directly from kitchen taps and other domestic water sources using clean, metal-free containers to prevent contamination. The samples were preserved in 1 % nitric acid and analyzed directly by ICP-MS. The analytical procedure was carefully adapted from the ISO 17294-2 standard, which is widely recognized for the determination of metals in water quality assessments.

2.7. Data management and statistics

When urinary creatinine values were outside the range of 0.3 g/L to 3 g/L, these urine samples were considered unusable, accounting for less than 3 % of the samples (WHO, 1996). Out of the 240 sampled children, 8 had creatinine values lower than 0.3 g/L or higher than 3 g/L and were excluded from the biomonitoring results. Values below the limit of quantification (LOQ) were replaced by: (LOD+LOQ) /2 (Baccarelli et al., 2005). The substituted values represented less than 1 % for arsenic and less than 3 % for trace elements. The distribution of urinary concentration is described in percentiles (25, 50, 75, and 95), minimum and maximum values, and geometric mean (GM). A 95 % confidence interval is provided for the geometric mean (CI95 % GM) and the 95th percentile (CI95 % P95). The graphical distribution of these levels is described in the form of a frequency histogram or boxplot, with outliers defined as values more than 1.5 times the interquartile range (IQR) from the quartiles.

Depending on distributions, univariate parametric and non-parametric statistics were used with individual and environmental characteristics to test for association with arsenic exposure, following verification of the necessary conditions for their application. All tests were two-sided with an alpha at 5 %. During multiple analyses, p-values are adjusted using the Bonferroni method. Databases were created using Microsoft Access software, and statistical analysis was performed using R-Studio software (version Ri386 4.1.3). The QuantilCI package was used to calculate 95th percentile confidence intervals by an interpolation procedure. The distance from each residence to the mining site was calculated using geolocation coordinates to the nearest point of either the main historical mine or a mining waste storage area, utilizing the Geosphere package in R. Multivariable-adjusted linear regression analyses were conducted to identify factors predicting urinary arsenic concentration. A backward selection approach was employed, beginning with significant variables (p-value < 0.1). The Akaike information criterion (AIC) was calculated for these models.

3. Results

The study included 240 children: 108 from the Orbiel Valley (66 exposed, 42 controls) and 132 from Gard (72 exposed, 60 controls). Table 1 shows the general characteristics of the participating populations in the mines of the Orbiel Valley and Gard. For the Orbiel Valley, no significant difference was observed in the average age of children between the exposed area (mean 7.8 years) and the control area (mean 7.2 years), nor in the distribution by age groups or gender. For the Gard site, an average difference of 1.2 years was noted between the exposed population (mean 8.7 years) and the control group (mean 7.5 years), with an overrepresentation of boys in the mining area. No disparity was found between the two groups for BMI, parents' education level, or their occupation. However, in the Gard site, the control area had a higher density of inhabitants and had smaller garden areas than the exposed area. Regarding dietary habits, particularly the removal of seafoods and rice from the diet before sampling, no disparities were noted between exposed and control populations for the two sites.

The results regarding exposure by inorganic arsenic and its two metabolites in children showed a comparable distribution between the entire exposed and control populations (Fig. 2.a). The means were not statistically different (exposed vs. control: 6.4 vs 7.0 μg/g; p-value = 0.152). High values were comparable between the groups (P95 [95 % CI] exposed vs. control: 16 (BRGM, 2019; U.S. EPA., 2000; Nordberg et al., 2014; Flora, 2014) vs. 14 (Piñeiro et al., 2021; Bril and Floc'h, 2001; BRGM, 2019; U.S. EPA., 2000; Nordberg et al., 2014; Flora, 2014; BRGM; Delplace et al., 2022; Santé publique France, 2019) μg/g), and the proportion of children exceeding the exposure limit of 10 μg/g of creatinine was similar (17 % vs. 18 %, respectively). When comparing children's exposure based on the exposure zone (Fig. 2.b), comparable values were found between exposed and control populations, with similar means for Gard and the Orbiel Valley (respective p-values: 0.19 and 0.50), comparable high values (P95[95 % CI] Gard: 16 (Bril and Floc'h, 2001; BRGM, 2019; U.S. EPA., 2000; Nordberg et al., 2014; Flora, 2014) vs 14 (Piñeiro et al., 2021; Bril and Floc'h, 2001; BRGM, 2019; U.S. EPA., 2000; Nordberg et al., 2014; Flora, 2014; BRGM; Delplace et al., 2022; Santé publique France, 2019) μg/g – Orbiel Valley: 15 (Piñeiro et al., 2021; Bril and Floc'h, 2001; BRGM, 2019; U.S. EPA., 2000; Nordberg et al., 2014; Flora, 2014) vs 12 (EPA, 2008; Dauphiné

Table 1
Description and comparison of the participating populations. N represents the number of participants, and values are means with their 95 % confidence intervals. p-values less than 0.05 are in bold.

	Orbiel Valley			Gard		
	Exposed area (N = 66)	Control area (N = 42)	*p-value (exposed/control area)*	Exposed area (N = 72)	Control area (N = 60)	*p-value (exposed/control area)*
Gender (N)						
Boys	42	26	0.929	44	27	0.08
Girls	24	16		28	33	
Age (years [CI 95 %])	7.8 [7.1–8.4]	7.2 [6.4–8.0]	0.261	8.7 [8.0–9.3]	7.5 [6.8–8.2]	**0.016**
Age group (N)						
2–6 years	20	16	0.671	13	25	**0.007**
6–9 years	23	14		24	18	
9–12 years	23	12		35	17	
BMI (kg/m² [CI 95 %])						
Boys	16.5 [15.9–17.2]	16.0 [16.7–15.3]	0.268	16.6 [15.7–17.5]	16.3 [15.2–17.3]	0.677
Girls	16.0 [16.7–15.3]	15.9 [16.9–14.9]	0.903	16.4 [15.2–17.6]	16.0 [15.1–16.9]	0.643
Parental education level (N)						
Primary or no diploma	10	5	0.563	10	5	0.379
Secondary	78	42		48	36	
University	29	22		60	59	
Employment Status (N)						
Employees	66	28	0.468	41	30	0.109
Workers	13	8		10	7	
Executives and higher professions	12	9		16	29	
Don't know/Other	34	23		12	12	
Type of housing (N)						
House	65	40	0.65	69	52	0.698
Apartment	1	2		3	4	
Housing area (m² [CI 95 %])	110 [100–120]	110 [99–122]	0.969	115 [106–125]	120 [110–132]	0.475
Garden area (m² [CI 95 %])	228 [149–349]	276 [197–386]	0.48	503 [355–714]	189 [108–331]	**0.004**
Bare soil in the garden (N)						
Yes	27	13	0.315	31	21	0.375
No	39	29		41	39	
Consumption of seafood (N)						
Yes	5	4	0.598	1	4	0.148
No	58	34		70	53	
Don't know	3	4		1	3	
Consumption of rice (N)						
Yes	13	7	0.766	16	17	0.35
No	50	32		54	39	
Don't know	3	3		2	4	
Consumption of spring or well water (N)						
Yes	2	0	0.52	9	2	0.063
No	64	42		63	58	

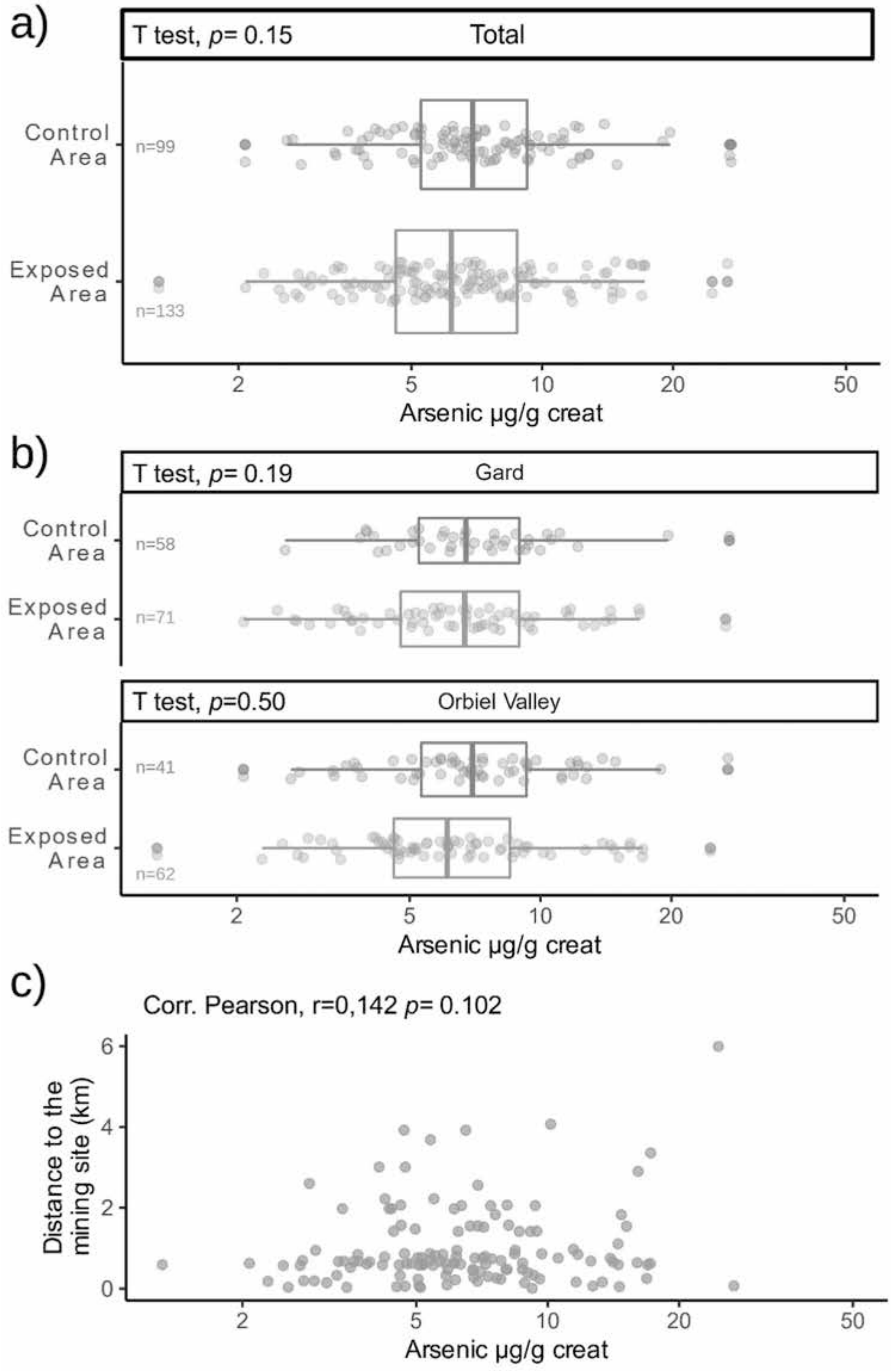

Fig. 2. Arsenic level in children: a) overall (N = 232); b) by mining area (Gard, N = 129; Orbiel Valley, N = 103); c) in relation to the distance between home and the nearest mining site (exposed children only, N = 133).

et al., 2011; Bose-O'Reilly et al., 2018; Piñeiro et al., 2021; Bril and Floc'h, 2001; BRGM, 2019; U.S. EPA., 2000; Nordberg et al., 2014; Flora, 2014; BRGM; Delplace et al., 2022; Santé publique France, 2019; Fernández-Navarro et al., 2012; García-Pérez et al., 2010; Kales et al., 2006; WHO, 2001; Schramel et al., 2002; Choate et al., 2006; WHO, 1996) µg/g), and comparable proportions of children exceeding the exposure limit value (Gard: 16 % vs 14 %, Orbiel Valley: 18 % vs 15 %). When comparing the level of exposure based on the distance of children's homes to the nearest mining site, the data displayed in Fig. 2.c showed an absence of increased exposure among children residing near the mining sites in both areas (r Pearson = 0.142, p-value = 0.102).

Table 2 presents the influence of various variables of interest on the increase in urinary arsenic, first in an univariate analysis, and then in a multilinear model. *Living Context:* In univariate analysis, living in a mining area was not associated with an increase in arsenic exposure, nor was associated with the distance to the mining site. Multivariate analysis (Table 2) confirmed these results, showing no statistical relationship between the mining areas and the levels of arsenic in children.

Table 2
Univariate and multivariate analysis of factors associated with urinary arsenic (log As μg/g creatinine) in children (N = 232). p-values less than 0.1 are in bold.

Predictor	Univariate analysis		Multivariate analysis	
	Beta (CI 95 %)	p-value	Beta (CI 95 %)	p-value
Intercept			2.33 (2.09 to 2.57)	**< 0.001**
Age (years)	-0.04 (-0.06 to -0.01)	**0.002**	-0.04 (-0.07 to -0.02)	**< 0.001**
Genre				
Boys	Ref.			
Girls	-0.02 (-0.15 to 0.11)	0.761		
Living area				
Control area (Gard)	Ref.			
Control area (Orbiel Valley)	-0.31 (-2.37 to 1.75)	0.768		
Mine of Salsigne (Orbiel Valley)	0.28 (-1.56 to 2.13)	0.762		
Mine of St-FP (Gard)	0.25 (-2.11 to 2.61)	0.835		
Mine of St-SA (Gard)	-0.13 (-2.36 to 2.09)	0.907		
Mine of St-LM (Gard)	-3.34 (-6.55 to -0.14)	**0.041**		
Distance from the old mining site (km)	0.02 (-0.00 to 0.04)	**0.074**		
Garden area (log m^2)	0.05 (-0.01 to 0.09)	**0.009**	0.06 (0.02 to 0.09)	**0.002**
Presence of bare soil				
No	Ref.			
Yes	0.08 (-0.06 to 0.21)	0.269		
Consumption of spring or well water				
No	Ref.			
Yes	0.17 (-0.11 to 0.46)	0.233		
Consumption of rice				
No	Ref.			
Don't know	0.21 (-0.10 to 0.52)	0.190		
Yes	0.13 (-0.03 to 0.28)	0.115		
Consumption of seafood				
Non	Ref.		Ref.	
NSP	0.12 (-0.19 to 0.44)	0.445	0.12 (-0.17 to 0.42)	0.414
Yes	0.41 (0.14 to 0.69)	**0.003**	0.32 (0.07 to 0.58)	**0.014**
Urinary arsenobetaine (log μg/L)	0.06 (0.03 to 0.10)	**< 0.001**	0.06 (0.03 to 0.10)	**< 0.001**
Observations	232			
Multivariate regression model: R^2 /adjusted R^2	0.166/0.147			

Regarding residential gardens, both univariate and multivariate analyses revealed a correlation between garden size and increased exposure levels.

3.1. Children's age

In multivariate analysis, after considering all variables of interest, increasing age was associated with a decrease in urinary arsenic. Younger children (aged 3–6 years) had higher exposure averages, reaching 7.4 μg/g, compared to their older peers (6–9 years: 6.7 μg/g; 9–12 years: 6 μg/g – p-value 0.039). When these results are expressed in concentration not adjusted to creatinine, the differences between age groups diminish (3–6 years: 5.7 μg/L; 6–9 years: 6.36 μg/L, 9–12 years: 6.7 μg/L – p-value 0.144).

3.2. Seafood consumption and presence of arsenobetaine

Univariate and multivariate regressions reveal that children who reported consuming seafood 3 days before sampling (6 % of children) had significantly higher arsenic levels compared to those who did not (mean: 9.7 vs 6.4 μg/g, p-value 0.001), with a higher proportion of children exceeding 10 μg/g of creatinine (50 % vs 14 %). Seafood consumption was also evidenced by the measurement of urinary arsenobetaine (AsB), which is a non-toxic form of arsenic derived from marine foods. The distribution of arsenobetaine for children had a median of 5 μg(AsB)/L with an interquartile range between 1 and 15 μg(AsB)/L. Univariate and multivariate regressions reveal an increase in arsenic level linked to the quantity of arsenobetaine. Children with higher levels of arsenobetaine in urine (>15 μg(AsB)/L) showed a significant increase in arsenic concentration compared to others: 8.3 μg/g versus 6.1 μg/g (p-value <0.001). These children also exhibited notably higher maximum values (P95: 19.9 μg/g vs 12.8 μg/g) and an increased frequency of exceeding the reference exposure value of 10 μg/g of creatinine (37 % vs 11 %, p-value <0.001).

3.3. Arsenic in the living environment

The living environment of a sub-sample of 18 children residing in the exposed area of the Orbiel Valley was assessed (Fig. 3). To eliminate the inherent noise associated with dietary exposure to seafood products, children who reported consuming seafood were excluded from this group, as well as those with the highest concentrations of arsenobetaine in urine (> third quartile, or >15 μg (AsB)/L). Outdoor residential soils exhibit heterogeneity in metal concentrations, with arsenic levels ranging from 5 to 850 mg/kg of soil (mean: 132, 95 % CI: 30–234). Elevated arsenic levels in outdoor soil were associated with increased arsenic exposure in children (Spearman's Rho = 0.555, p-value < 0.050). Similarly, arsenic-rich indoor dust (mean: 70 mg/kg, 95 % CI: -7–148) showed a strong correlation with outdoor soil arsenic concentrations (Spearman's Rho = 0.619, p-value < 0.010) and was further linked to higher arsenic exposure in children (Spearman's Rho = 0.757, p-value < 0.001). In contrast, no correlation was observed with drinking water, where arsenic concentrations consistently remained below the reference value of 10 μg/L (mean: 1.8 μg/L, 95 % CI: 0.6–3.1). Of particular concern was one child presenting elevated urinary arsenic levels (28 μg/g creatinine) despite no dietary co-exposure (no fish consumption, moderate arsenobetaine concentration: 7 μg(AsB)/L). This child lived in an area with a history of ore processing, characterized by highly contaminated soil (mean: 842 mg/kg of arsenic) and indoor dust containing elevated arsenic concentrations (683 mg/kg). The residence was also situated near a mine tailings site. For other metal(loid)s in soils, chromium (mean: 74 mg/kg, 95 % CI: 62–85) and cadmium (mean: 0.7 mg/kg, 95 % CI: 0.6–0.8) were moderately elevated, while copper (mean: 1.4 g/kg, 95 % CI: 0.3–2.5), zinc (mean: 0.9 g/kg, 95 % CI:

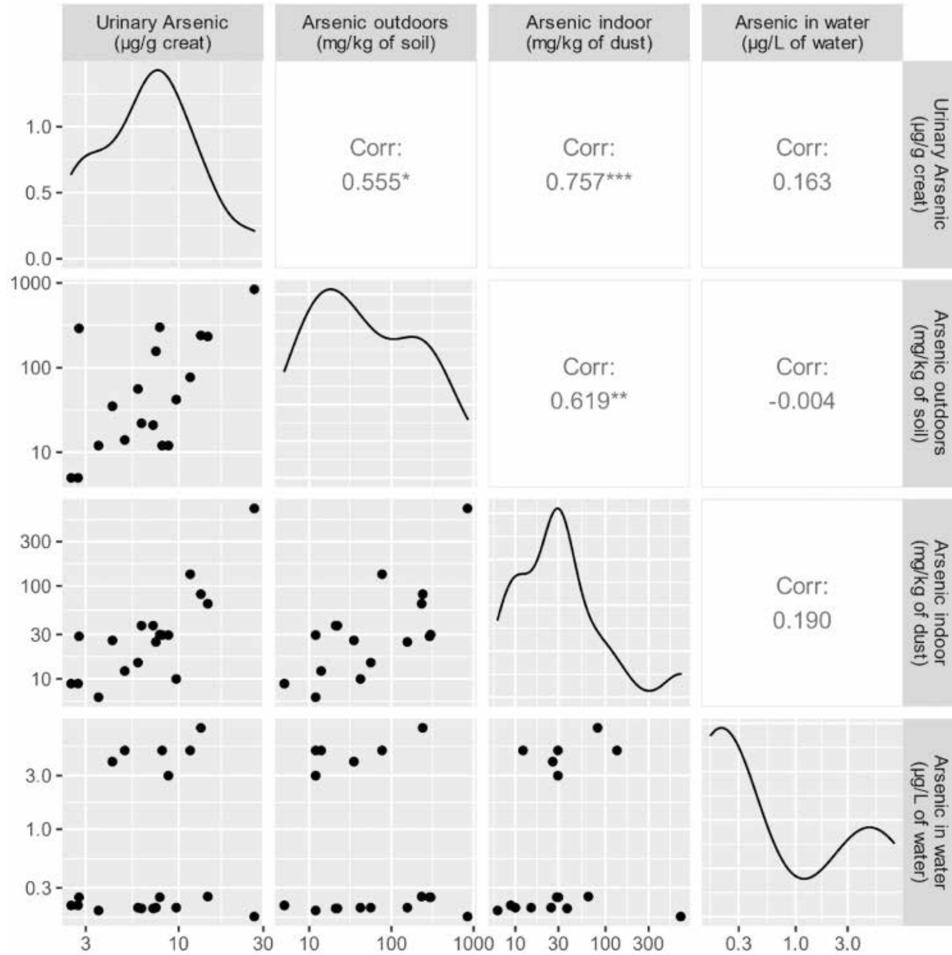

Fig. 3. Correlation matrix between urinary arsenic concentration (log µg/g of creatinine) and arsenic concentrations in various components of the home environment: garden soil around the residence (soil As, log mg/kg), settled respirable dust inside the residence (dust As, log mg/kg), and drinking water at the residence (water As, log µg/L). (Spearman correlation, N = 18). "*" for p-value < 0.05, "**" for p-value < 0.01, "***" for p-value < 0.001.

0.3–1.5), and lead (mean: 140 mg/kg, 95 % CI: 70–200) were highly elevated compared to typical values in French soils (Baize, 1997). However, with the exception of lead, which was not assessed, none of these metals exhibited a significant correlation with children's exposure levels (adjusted p-values > 0.1 for Spearman correlation).

The data Table 3 indicates that, for 15 other metal(loid)s, urinary levels in children from mining areas were similar to those in the control group. Furthermore, levels of copper, thallium, and zinc were lower in children from mining areas. A correlation analysis between each metal (loid) revealed no significant relationships between arsenic exposure and other metal(loid)s (adjusted p-values > 0.1 for Pearson correlations). Compared to French national reference data (Santé publique France, 2021), exposure levels in all children were similar (Al, Ba, Sb, Mo, Tl, U) or lower (Cd, Cr, Sn, Ni, V, Zn). However, cobalt (1.35 µg/g vs. 1.0 µg/g), copper (16.9 µg/g vs. 12.9 µg/g), and manganese (0.61 µg/g vs. 0.3 µg/g) were significantly higher (p-value < 0.001) in both mining and control areas. Metal(loid)s exposure levels showed no significant correlations with the proximity of children's homes to mining sites (adjusted p-value > 0.1 for Pearson correlations). Similarly, no significant associations were observed with living environment factors (e.g., housing size, garden size, bare soil presence), dietary habits (e.g., seafood, rice, or spring/well water consumption), or gender for most metal(loid)s (adjusted p-values > 0.1 for Pearson correlations or ANOVA tests). An exception was aluminum, with boys exhibiting lower levels than girls (11.5 vs. 14.9 µg/g; adjusted p-value = 0.05). Age, however, showed negative correlations with urinary concentrations of most elements (-0.15 to -0.30; adjusted p-values < 0.05 for Pearson correlations).

4. Discussion

4.1. Main results

While previous studies have documented significant environmental pollution (Delplace et al., 2022; Saunier et al., 2013), our cross-sectional, multisite study found no significant difference in arsenic exposure between children residing in former mining areas and those in control areas. The distribution pattern, means, and high values of exposure were comparable. These results were observed for all mining sites as well as for each site individually. Even when considering the proximity of children's homes to former mining sites, we did not observe higher arsenic exposure levels. When compared to other exposure studies on children living in mining areas (Cochet et al., 2018; Occitanie, 2019) or in the general population in France (Santé publique France, 2021a), similar averages arsenic exposure levels were observed, ranging between 6.2 and 7.8 µg/g, regardless of the exposure context. This suggests that current environmental contamination levels may not pose an immediate increased risk for arsenic exposure in these regions. Despite these results, overexposure risks still exist in certain areas, particularly where there are high natural or anthropogenic arsenic concentrations in soil. Higher arsenic levels in household dust and larger gardens also increase daily exposure risk for children. For example, a

Table 3
Distribution of concentrations in metal(loid)s (µg/g of creatine) for the population living in the exposed and control zones (N = 232), and comparison with national data (Ref.: ESTEBAN Study – SPF, 2021 – – children aged 6–10). p-values less than 0.05 are in bold.

Biomarker*	Population	N	GM	CI95 % GM	p-value * *	P25	P50	P75	P95
	Exposed area	133	12.1	[10.5 - 13.9]	0.152	7.1	11.1	19.9	48.3
Aluminum	Control area	99	13.9	[12.1 - 16.0]		8.3	13.7	20.7	50.6
	Ref.	477	12.7	[11.5 - 14.1]		5.0	7.4	12.0	23.1
	Exposed area	133	0.1	[0.1 - 0.1]	0.107	0.1	0.1	0.2	0.4
Antimony	Control area	99	0.1	[0.1 - 0.1]		0.0	0.1	0.2	0.5
	Ref.	477	0.1	[0.1 - 0.1]		0.1	0.1	0.1	0.3
	Exposed area	133	6.4	[5.8 - 7.0]	0.152	4.6	6.2	8.8	16.1
Arsenic (∑Asi-MMA-DMA)	Control area	99	7.0	[6.4 - 7.7]		5.3	6.9	9.2	14.0
	Ref.	251	7.1	[6.5 - 7.9]		4.7	6.7	10.5	21.2
	Exposed area	133	3.8	[3.5 - 4.3]	0.089	2.7	3.8	6.0	10.7
Barium	Control area	99	4.5	[3.9 - 5.2]		2.9	4.2	6.9	13.2
	Ref.	477	4.6	[4.1 - 5.1]		2.6	4.4	7.8	16.5
	Exposed area	133	0.1	[0.1 - 0.1]	0.333	0.1	0.1	0.1	0.2
Cadmium	Control area	99	0.1	[0.1 - 0.1]		0.1	0.1	0.1	0.3
	Ref.	477	0.3	[0.3 - 0.4]		0.2	0.3	0.5	1.3
	Exposed area	133	0.8	[0.7 - 1.0]	0.136	0.5	0.7	1.1	4.4
Chromium (total)	Control area	99	0.7	[0.6 - 0.8]		0.4	0.7	1.2	2.0
	Ref.	477	1.5	[1.3 - 1.6]		0.9	1.4	2.1	4.7
	Exposed area	133	1.3	[1.1 - 1.4]	0.172	0.8	1.3	2.0	3.6
Cobalt	Control area	99	1.5	[1.2 - 1.7]		1.0	1.4	1.9	4.9
	Ref.	477	1.0	[0.9 - 1.1]		0.6	1.0	1.5	3.1
	Exposed area	133	15.6	[14.6 - 16.8]	0.004	12.0	14.9	20.1	31.4
Copper	Control area	99	18.9	[17.0 - 21.0]		14.2	17.4	24.7	38.8
	Ref.	477	12.9	[12.2 - 13.7]		9.9	13.1	17.2	23.8
	Exposed area	133	0.6	[0.5 - 0.7]	0.097	0.3	0.5	0.9	2.3
Manganese	Control area	99	0.7	[0.6 - 0.8]		0.4	0.6	1.1	2.2
	Ref.	477	0.3	[0.3 - 0.3]		0.2	0.3	0.5	1.5
	Exposed area	133	73.0	[65.6 - 81.3]	0.100	45.1	68.2	123.0	175.9
Molybdenum	Control area	99	84.3	[73.7 - 96.4]		56.0	86.4	125.8	243.8
	Ref.	477	78.1	[71.9 - 84.8]		52.6	7.5	109.6	228.8
	Exposed area	133	1.2	[1.0 - 1.5]	0.999	0.5	1.7	2.7	6.0
Nickel	Control area	99	1.2	[0.9 - 1.7]		0.2	1.8	3.0	11.4
	Ref.	477	2.3	[2.1 - 2.5]		1.6	2.4	3.6	6.1
	Exposed area	133	0.3	[0.2 - 0.3]	0.040	0.2	0.3	0.4	0.6
Thallium	Control area	99	0.3	[0.3 - 0.3]		0.2	0.3	0.4	0.7
	Ref.	477	0.3	[0.3 - 0.3]		0.2	0.3	0.4	0.7
	Exposed area	133	0.6	[0.5 - 0.8]	0.833	0.3	0.7	1.4	3.6
Tin	Control area	99	0.6	[0.5 - 0.8]		0.3	0.7	1.4	3.0
	Ref.	477	1.1	[1.0 - 1.2]		0.6	1.0	1.9	5.7
	Exposed area	133	0.0	[0.0 - 0.0]	0.180	0.0	0.0	0.0	0.0
Uranium	Control area	99	0.0	[0.0 - 0.0]		0.0	0.0	0.0	0.0
	Ref.	477	0.0	[0.0 - 0.0]		0.0	0.0	0.0	0.0
	Exposed area	133	0.3	[0.2 - 0.3]	0.253	0.2	0.2	0.3	0.6
Vanadium	Control area	99	0.3	[0.3 - 0.3]		0.2	0.3	0.4	0.7
	Ref.	477	0.3	[0.3 - 0.0]		0.2	0.3	0.5	0.8
	Exposed area	133	493	[447 - 543]	**0.018**	346	531	719	1165
Zinc	Control area	99	592	[526 - 665]		412	577	740	1292
	Ref.	477	592	[560 - 626]		450	616	797	1204

* Exclusion of children with a creatinine level < 0,3 g/L or> 3 g/L. ** Mining area vs. Exposed area. Ref.: ESTEBAN Study (SPF, 2021) – children aged 6–10.

child residing near a former ore processing site and a mine tailing, where soil arsenic levels exceeded 800 mg/kg, exhibited an exposure level of 28 µg As/g of creatinine. While such cases are rare, they require further investigation by health authorities to identify and inform residents in higher-risk areas.

This study not only assessed exposure to arsenic, the primary contaminant, but also evaluated exposure to other, less prevalent metal (loid)s, some of which were found at elevated concentrations in soils, exceeding national soil reference values (Pb, Cd, Cr, Cu, Zn) (Baize, 1997). For these metal(loid)s, urinary exposure levels were similar between children living in former mining areas and those in control areas, as well as with the general French population of the same age (Santé publique France, 2021b). Regarding other environmental exposure factors, including proximity to former mines, housing characteristics (e.g., housing size, garden size, presence of bare soil), and dietary habits (e.g., seafood, rice, or spring/well water consumption), no significant associations were observed. The only exception was higher exposure to aluminum in girls, which appeared unrelated to the specific context of the study. Additionally, no correlation was found between arsenic exposure and exposure to other metal(loid)s, emphasizing the lack of a direct relationship between the environmental concentrations of these elements and those found in the children.

These findings highlight that, although arsenic and other metals are present in these environments, their current levels may not pose an immediate health risk. This contrasts with much of the existing literature, which often associates living near metal mining sites with increased exposure risks for children. Such risks include elevated concentrations of metals in residential areas (Loh et al., 2016) and in children's bodies—such as lead in blood and arsenic in urine—exceeding reference values (Piñeiro et al., 2021; Loh et al., 2016). Several factors may contribute to these differences. First, the cessation of mining activities limits metallic contamination and the generation of new exposures, particularly through the air, where metal(loid)s can be rapidly transported by atmospheric dust and aerosols, as is still the case in countries with active mines (Csavina et al., 2012). For example, at the Salsigne mine, which has been closed for over 20 years, air contamination levels are low (average 0.27 (As)ng.m^{-3}), and atmospheric pollution indexes are minimal (Calas et al., 2024). Water contamination remains a critical issue linked to mining activities, posing additional risks to children who may consume contaminated water or engage in recreational activities near polluted water bodies. For example, a study examining arsenic contamination from an abandoned metal mine in South Korea found a high urinary arsenic concentration of 149 μg/L, which decreased to 32 μg/L following the implementation of a multi-regional water supply that restricted arsenic exposure through drinking river water (mean As in water: 0.2 mg/L) (Chang et al., 2019). In our study, the use of well or surface water for drinking is rare, as most residents rely on tap or bottled water, which is subject to strict safety standards (<10 μg/L, as observed in our results), significantly mitigating the most critical exposure risks (Peter et al., 2009). Finally, residents' awareness of environmental risks, reinforced by health messages from authorities, has led to effective avoidance strategies that can significantly reduce exposure risks. Many people have adopted practices such as consuming less homegrown produce to limit their contact with contaminated environments. Additionally, in these mining regions, the most contaminated sites are often situated distant from residential areas or are inaccessible to the public, further minimizing exposure.

4.2. Exceedance of reference values

The low levels of exposure observed in our study contradict public perceptions and assessments by health agencies. In the Orbiel Valley and Gard, previous screenings (without comparison to a control population) showed 15–30 % of children had arsenic levels above the French reference value of 10 μg/g of creatinine (Cochet et al., 2018; Occitanie, 2019). Our study found comparable results: 17 % in the exposed population and 18 % in the control group, aligning with the 25–30 % range in the general French population (Santé publique France, 2021a). This indicates that in this context, comparisons with a control population are essential, as relying solely on a reference value is insufficient to accurately determine overexposure.

In France, the arsenic exposure reference value in urine is set at 10 μg/g. This value was derived from the 95th percentile of a non-seafood-consuming adult population's distribution (8.9 μg/g or 10.7 μg/L) (Fréry et al., 2017). Internationally, this value is on the lower range for adults (P95 in Germany: 17.9 μg/L, in the United States: 14.2 μg/L, in Canada: 27 μg/L, in the United Kingdom: 15.8 μg/L. For children, the 95th percentile typically ranges between 15 and 20 μg/g of creatinine (P95 in this study: 15.5 μg/g or 16.2 μg/L; in the general French population aged 6–10 years: 21.2 μg/g or 17.7 μg/L; in the United States aged 6–11 years: 17.8 μg/g or 11.4 μg/L; in Canada aged 6–11 years: 18 μg/g or 14 μg/L) (Santé, 2019; CDC, 2019). These data indicate that the current limits may be overly conservatives explaining their frequent exceedance. The implications for contaminated sites include the erroneous belief that a high proportion of the population is overexposed, when in reality, their exposure may be within normal ranges.

4.3. Environmental factors influencing arsenic exposure

This study also found higher arsenic levels in young children compared to older ones. This can be attributed to behaviors like hand-to-mouth contact, common in young children who frequently mouth toys, objects, and their hands. The US-EPA estimates soil ingestion rates of 60 mg/day for infants under one year and 100–200 mg/day for children aged 1–6 years (EPA, 2008)., thereby heightening environmental exposure risks. A more likely explanation is lower urinary creatinine levels in younger children (Remer et al., 2002), which can impact reported arsenic levels when adjusted per gram of creatinine. Our findings support this trend for arsenic and other metal(loid)s, showing a decrease in exposure with age when concentrations are adjusted for creatinine, whereas these values remain stable when not adjusted. Similar observations in France, Canada, and the USA have documented higher metal(loid)s exposure in younger children compared to older ones, with less variation noted when creatinine adjustment is not applied (Santé publique France, 2021a; CDC, 2019; Canada, 2021). This indicates creatinine adjustment may artificially elevate values in younger children. Alternative correction methods less influenced by age, gender, or diet, such as adjustment by urinary density and urinary osmolality, are less commonly used in public health settings but present viable alternatives (Muscat et al., 2011; Hsieh et al., 2019).

The study notably highlighted the issue of dietary co-exposure to seafood products. This observation was made possible by measuring urinary arsenobetaine, rather than relying on questionnaire-based reporting. Arsenobetaine is a non-toxic arsenic compound exclusively introduced through the consumption of seafood, along with other arsenic compounds (particularly DMA, MMA, and Asi) (Molin et al., 2012). Its high presence in urine directly indicates past seafood consumption and may therefore indicate dietary co-exposure to arsenic through exposure to other arsenic compounds. In this study, over 25 % of children had arsenobetaine concentrations exceeding 15 μg/L (median 4.5 μg/L), and 10 % had concentrations exceeding 44 μg/L. These children with high levels of arsenobetaine also exhibited high levels of arsenic, confirming the role of seafood consumption as a co-exposure to arsenic. This finding aligns with results from other studies on the significant role of seafood consumption in increasing arsenic concentration in children's urines (Jones et al., 2016). For adults, recommendations to refrain from consuming these products for 3 days before testing help limiting this co-exposure (Molin et al., 2015). However, children are likely to be exposed differently, perhaps through their eating behaviors. They may consume these foods outside the home without their parents' knowledge (e.g., school canteen, childcare, other parents), or consume processed foods containing seafood that may go unnoticed by families (e.g., surimi, condiments, Asian sauces, prepared dishes, broths, etc.). It is also conceivable that arsenic elimination in children is slower than generally described; indeed, in children, mechanisms for metabolizing and eliminating toxins are not yet fully mature, increasing their vulnerability to harmful substances (EPA, 2008; Dauphiné et al., 2011), potentially prolonging their presence in the body beyond the usual 3-day window. Finally, the communication of instructions to avoid consuming seafood products to families, as well as the diligence of these families in adhering to them, may also play an important role in the risk of co-exposure.

4.4. Study limitations

Our study has several limitations. The sample size was small, but the low population density in these areas makes it difficult to achieve larger sample sizes. We used door-to-door recruitment, which resulted in over 80 % participation, helping to maximize the number of participants and demonstrating residents' willingness to contribute. However, this approach risked selection bias due to refusals, especially in municipalities where the issue causes significant tension, particularly when the authorities do not understand the value of prevention strategies. The populations residing in the control area in Gard had a higher density compared to the exposed municipalities in the site, resulting in a disparity in garden size between the two groups. While these variations are not substantial, they could potentially lead to a slight underestimation of exposure in the control population due to less environmental exposure. Moreover, homes with larger gardens are often located outside urban areas and closer to former mining sites. This proximity could explain the higher exposure levels observed in children with larger gardens. The study also observed a male overrepresentation, with a sex ratio of 1.37, differing from the actual demographic values (1.15) (INSEE data 2021–2022). However, this imbalance was consistent across both control and exposed groups, minimizing its potential impact on exposure assessment. Additionally, biological samples were collected between spring and early summer, a time when children typically spend more time outdoors and consume more homegrown foods.

Furthermore, these former mining sites may also contain other elements like rare earths or lead, which were not documented in this study and are poorly researched in mining areas. Measuring lead requires blood samples, often not well accepted by families, creating a barrier to screening (Bretin et al., 2008). For rare earths, measurement protocols are still needed to compare exposure data between the general and mining populations. Future research is needed to evaluate the presence of these elements at former mining sites more comprehensively.

5. Conclusion

In conclusion, this study demonstrated that children living near abandoned mines in France were not significantly overexposed. Several factors may have contributed to this low exposure, including access to non-contaminated water, the long-term closure of the mines, and the population's awareness of health risks. These factors were likely shaped by the country's economic development and the health concerns stemming from the region's mining history.

Despite the low exposure levels, anxiety remains prevalent in these communities, primarily due to the lack of routine biomonitoring by health authorities. Urinary biomonitoring is a simple and effective method to assess exposure to multiple metals and better understand potential health impacts. Such studies are vital for refining risk assessments and developing effective measures to reduce exposure risks, especially in areas affected by past and potential future mining activities.

CRediT authorship contribution statement

Igor Pujalté: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Zeno Loi:** Validation, Resources. **Alice Bernard:** Validation, Resources. **Lionel Moulis:** Validation, Resources. **Sophie Delpoux:** Validation, Methodology. **Jacques Gardon:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

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Conflict of Interest Declartion

It is important to note that there are no conflicts of interest associated with this research. The authors declare that they have no financial or personal relationships that could potentially bias their work or influence the interpretation of the results presented in this article. This study was conducted with the sole purpose of advancing scientific knowledge and contributing to the understanding of environmental and public health issues. All research procedures and methodologies were carried out with integrity and transparency, adhering to the highest ethical standards in scientific inquiry.

Data availability

Data will be made available on request.

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