

Metal Exposure in Arica, Chile: Examining Toxic Elements

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Background: Bioaccumulation of toxic metals in the population is associated with adverse health effects. Although some elements are essential for humans, high levels of exposure can be dangerous. **Objective:** To describe the levels of Inorganic Arsenic (AsIn), Cadmium (Cd), Chromium (Cr), and Mercury (Hg) in urine, and Lead (Pb) in blood in the population of Arica, Chile. **Methodology:** Descriptive study. Beneficiaries of the Health Surveillance Program of Law 20.590 in sites of higher risk of exposure in the commune of Arica were considered eligible. The results of biological samples to measure their concentrations of AsIn, Cd, Cr, Hg in urine, and Pb in blood between August 2016 and May 2021 are described. **Results:** 9520 samples from a population with a mean age of 40.5 years were studied. 4.21% of the adult population and 6.57% of the children had AsIn values above 35 µg/L, while at least 95 % of the total samples had levels below 33 µg/L. At least 90 % of the samples had Cd levels below 1.1 µg/L, and 8.44 % had Cd levels above 2 µg/L, higher in males (11.67%). There were no values above the reference in children. 99.77% and 99.33% had Cr and Pb values below the reference limit, respectively (using the lowest reference range established by Chile Ministry of Health (MINSAL) < 5 µg/L). Children did not present risk values for Cr, and 0.16% presented Pb concentrations between 5-10 µg/dL. All samples presented Hg concentrations below risk levels (< 10 µg/L). **Conclusions:** The results of this study suggest that a small percentage of the samples analyzed in the beneficiary population of Arica register metal concentration levels above national reference levels established by MINSAL, mainly AsIn, Cd, and Pb. It is essential to continue biomonitoring to reduce and prevent exposure to these metals, which can have harmful effects on human health.

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Key words: Chile; Arsenic Poisoning; Cadmium; Mercury; Lead.

Análisis de exposición a metales en Arica, Chile: niveles de elementos tóxicos

Antecedentes: La bioacumulación de metales en la población está asociada a efectos adversos y pueden ser peligrosos. **Objetivo:** Describir los niveles de Arsénico Inorgánico (AsIn), Cadmio (Cd), Cromo (Cr), Mercurio (Hg) y Plomo (Pb) en la población de Arica, Chile. **Materiales y Métodos:** Estudio descriptivo. Se incluyeron todas las personas beneficiarias del Programa de Vigilancia de Salud de la Ley 20.590 en sitios de riesgo de mayor exposición en la comuna de Arica entre agosto 2016 y mayo 2021. **Resultados:** Se estudiaron 9.520 muestras provenientes de una población con una edad media de 40.5 años. 4.21% de la población adulta y el 6.57% de los niños presentaron valores

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de AsIn superiores a 35 µg/L y al menos el 95% de las muestras totales tenía niveles inferiores a 33 µg/L. Más del 90 % de las muestras tuvieron niveles de Cd menores a 1.1 µg/L y un 8.44% registró niveles de Cd superiores 2 µg/L. El 99.77% y 99.33% exhibieron valores normales de Cr y Pb, respectivamente. Todas las muestras presentaron concentraciones de Hg por debajo de los niveles de riesgo (< 10 µg/L). **Conclusiones:** Los resultados sugieren que un porcentaje pequeño de la población de Arica registra niveles de concentración de metales por sobre niveles de referencia nacional establecidos por el Ministerio de Salud de Chile, principalmente de AsIn, Cd y Pb. Es importante continuar con la vigilancia para reducir y prevenir la exposición a estos metales, que pueden generar efectos nocivos en la salud humana.

Palabras clave: Chile; Arsenic Poisoning; Cadmium; Mercury; Lead.

Metals correspond to a group of elements with a high density (greater than 4g/cm³) and a high molecular weight (between 63.55 and 200.59 g/mol). Some stand out because they can cause damage to the environment, such as Mercury (Hg), Lead (Pb), Cadmium (Cd), Thallium (Tl), Copper (Cu), Zinc (Zn), and Chromium (Cr)¹. These metals, which are the product of anthropogenic activity, such as mining, use of agricultural industries, and chemical fertilizers, move through the environment and reach rivers that irrigate vegetables and are consumed by animals. This scenario could lead to human exposition and potentially affect the population's health¹.

Chronic exposure to arsenic has been related to skin effects (hyperpigmentation and keratosis), increased cardiovascular risk (secondary to hypertension), respiratory systems, and increased risk of prostate, kidney, skin, lung, and liver cancer². Mercury exposure is related to neurological damage and renal and hepatic alterations. Chronic exposure to lead has been associated with hematological (anemia), immune, and asthma disorders³. Regarding Chromium, evidence indicates it increases the incidence of some human cancers, including lung, larynx, prostate, kidney, testicular, bone, and thyroid⁴.

In Chile, it has been described that there is a potential exposure to metals that could affect the population in areas with mining and industrial activity. The case of Arica, at the northern border of our country, exposed suspicion to metals for more than three decades due to 20,000 tons of mining liabilities (mud with mineral content) abandoned by the company Promel Ltda., mineral stockpiles from Bolivia, and mud with

minerals from Sweden, which were deposited in several points of the city between 1984 and 1985⁵.

The Chilean State has taken measures to guarantee and safeguard the rights of the population through Law 20.590, establishing an intervention program to address the presence of polymetals in the commune of Arica, which guarantees access to medical treatment, follow-up, recovery, and monitoring of residents and former residents exposed to metal contamination in the city who are beneficiaries of this Law⁶. In this process, three intervention sectors were defined in the commune, corresponding to the Port Sector, Maestranza Sector, and Sector F⁶.

After having measurements for a period of almost five years since the implementation (August 2016 to May 2021) and operation of this monitoring program in vulnerable populations in the commune of Arica, this article seeks to describe the level of the following metals, Inorganic Arsenic (AsIn), Cd, Cr, Hg, and Pb in the beneficiary population, as well as to compare the results of the program with the reference values in force in our country.

Methodology

A descriptive study of the AsIn, Cd, Cr, Hg, and Pb levels in the population benefited from the Health Surveillance Program of Law 20.590. The data on levels of heavy metals measured between August 2016 and May 2021 were provided by the Regional Ministry of Health Secretary (SEREMI) of Arica.

Requirements to obtain the benefits established by the Law are:

1. Beneficiaries for living in risk areas:

a) Over 18 years of age: To have resided for over three years, counted until May 29, 2012, within the zones established by the Regulation.

b) Under 18 years of age: Having resided six months or more, counted to May 29, 2012, within the polygon.

c) Children whose mother has spent at least three months of her pregnancy living within the polygon.

2. Beneficiaries with health effects: former residents or workers have health effects attributable to exposure to one or more pollutants in the Regulation.

3. Beneficiaries' former workers are occupationally exposed: workers who have accredited six months of permanence in companies in areas with any of the metals included in the Law.

4. Beneficiaries' occupational and non-occupationally exposed workers are workers or non-occupationally exposed former workers with a minimum exposure time of at least three years.

The data analysis was performed using the R program version 4.1.0⁷. The analysis plan considered the description of total metal levels over time (according to the month of sampling) and their stratification by age and sex category through percentiles. Chi-square tests were applied to evaluate

Table 1. Description of the samples studied in the beneficiary population of the commune of Arica (period from August 2016 to May 2021)

	Total (n = 9,520)		Female (n = 5,572)		Male (n = 3,948)	
	Mean	n	Mean	n (%)	Mean	n (%)
Age (years)	40.5	8.586	40.3	5.052 (58.5%)	40.7	3.534 (41.7%)

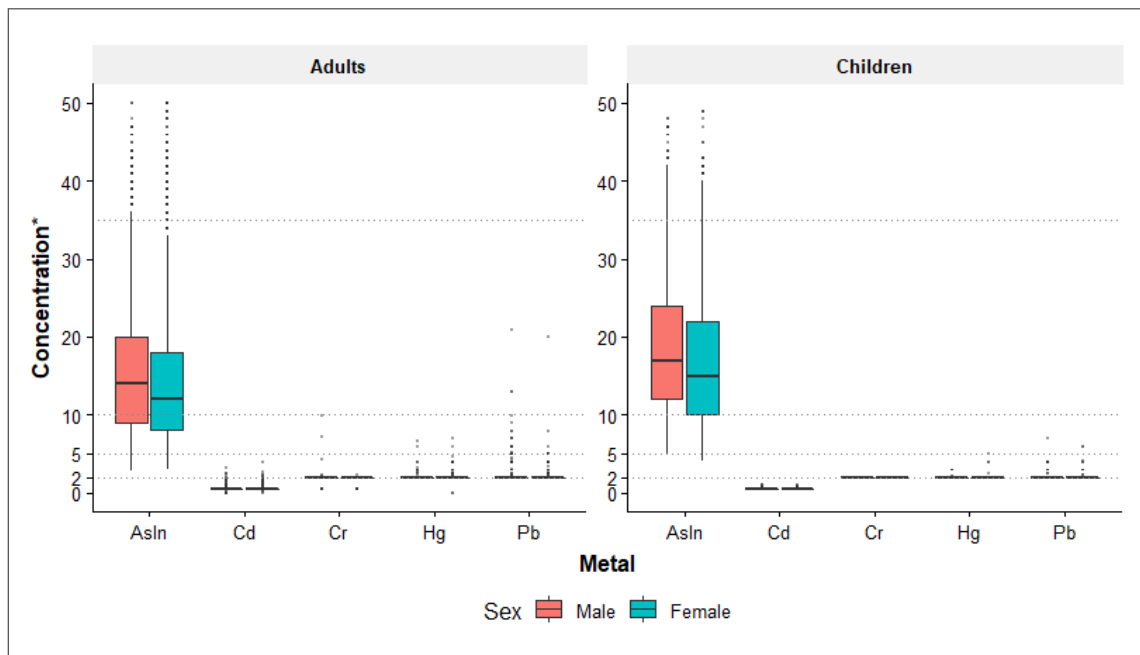


Figure 1. Distribution of metal concentrations in adults (n = 6.565) and children (n = 2.021) in the beneficiary population of Arica, according to age category and sex (between August 2016 and May 2021). Concentration*: in urine (ug/L) and blood (ug/dL). The blood concentration of Pb plotted is in ug/dL, unlike the other metals measured in urine (ug/L). The transverse lines represent the MINSAL reference value for each metal: AsIn 35 $\mu\text{g/L}$, Hg 10 $\mu\text{g/L}$, Pb 5 $\mu\text{g/dL}$, Cd and Cr 2 $\mu\text{g/L}$.

Table 2. Distribution by percentiles (p25, p50, p75, p90, and p95) of AsIn concentration in urine ($\mu\text{g/L}$; LoD = $5 \mu\text{g/L}$) in the beneficiary population of Arica, according to age and sex (period from August 2016 to May 2021)

Categories	p25	p50	p75	p90	p95	n
Total	7.0	13.0	19.0	27.0	33.0	9.181
Age Group						
0-5 years	7.0	15.0	20.0	28.8	30.4	13
6-11 years	11.0	16.0	23.0	32.0	38.0	682
12-19 years	11.0	16.0	23.0	30.0	37.0	1.239
20-39 years	10.0	15.0	21.0	29.0	36.0	2.082
40-59 years	8.0	13.0	19.0	27.0	32.0	2.242
≥ 60 years	7.0	11.0	16.25	24.0	30.0	2.020
Sex						
Female	7.0	12.0	18.0	26.0	32.0	5.293
Male	8.0	14.0	21.0	29.0	35.0	3.888

Table 3. Distribution by percentiles (p25, p50, p75, p90, and p95) of urinary Cd concentration ($\mu\text{g/L}$; LoD = $0.02 \mu\text{g/L}$) in the beneficiary population of Arica, according to age and sex (period from August 2016 to May 2021)

Categories	p25	p50	p75	p90	p95	n
Total	0.49	0.49	0.49	1.1	6.0	4314
Age Group						
0-5 years	-	-	-	-	-	0
6-11 years	0.49	0.49	0.49	0.49	0.548	217
12-19 years	0.49	0.49	0.49	0.49	0.602	497
20-39 years	0.49	0.49	0.49	0.6	0.733	915
40-59 years	0.49	0.49	0.51	0.854	1.084	917
≥ 60 years	0.49	0.49	0.49	0.77	0.947	867
Sex						
Female	0.49	0.49	0.49	0.9	5.0	2.514
Male	0.49	0.49	0.50	5.0	8.0	1.800

differences in proportions, and p-values less than or equal to 0.05 were considered significant.

This research was authorized by the Pontificia Universidad Católica de Chile Ethics Committee (ID: 211223002)

Results

Over 45 months - August 2016 to May 2021, 9520 blood and urine samples were recorded, corresponding to 5771 beneficiaries. The average age of the sample was 40.5 years, with no statistically significant differences according to sex. Most samples were from women (58.5%)

(Table 1).

The distribution of metal concentrations evaluated in the population tested using the 25th, 50th, 75th, 90th, and 95th percentiles, according to age category and sex, are shown in Tables 2 to 6 and plotted in Figure 1.

Inorganic Arsenic

The prevalence of inorganic arsenic (AsIn) exposure, taking as a cut-off point the reference values established by Chile Ministry of Health (MINSAL)⁵, 95.71% of the samples had normal AsIn levels ($< 35 \mu\text{g/L}$), 4.17% had AsIn levels between 35-100 $\mu\text{g/L}$ (362 people), and 0.12% levels $> 100 \mu\text{g/L}$ (11 people). The maximum value

Table 4. Distribution by percentiles (p25, p50, p75, p90, and p95) of Cr concentration in urine ($\mu\text{g/L}$; LoD = $0,59 \mu\text{g/L}$) in the beneficiary population of Arica, according to age and sex (period from August 2016 to May 2021)

Categories	p25	p50	p75	p90	p95	n
Total	1.9	1.9	1.9	1.9	1.9	3.455
Age Group						
0-5 years	-	-	-	-	-	0
6-11 years	1.9	1.9	1.9	1.9	1.9	217
12-19 years	1.9	1.9	1.9	1.9	1.9	497
20-39 years	1.9	1.9	1.9	1.9	1.9	914
40-59 years	1.9	1.9	1.9	1.9	1.9	918
≥ 60 years	1.9	1.9	1.9	1.9	1.9	867
Sex						
Female	1.9	1.9	1.9	1.9	1.9	2.032
Male	1.9	1.9	1.9	1.9	1.9	1.423

Table 5. Distribution by percentiles (p25, p50, p75, p90, and p95) of urinary Hg concentration ($\mu\text{g/L}$; LoD = $2 \mu\text{g/L}$) in the beneficiary population of Arica, according to age and sex (period August 2016 to May 2021)

Categories	p25	p50	p75	p90	p95	n
Total	1.9	1.9	1.9	1.9	1.9	3344
Age Group						
0-5 years	-	-	-	-	-	0
6-11 years	1.9	1.9	1.9	1.9	1.9	210
12-19 years	1.9	1.9	1.9	1.9	1.9	483
20-39 years	1.9	1.9	1.9	1.9	1.9	883
40-59 years	1.9	1.9	1.9	1.9	1.9	888
≥ 60 years	1.9	1.9	1.9	1.9	1.9	839
Sex						
Female	1.9	1.9	1.9	1.9	1.9	1.958
Male	1.9	1.9	1.9	1.9	1.9	1.386

observed was $239 \mu\text{g/L}$. Significant differences were recorded according to sex (levels $\geq 35 \mu\text{g/L}$ in 5.04% of men and 3.74% of women). It is also noteworthy that the proportion of people with values $\geq 35 \mu\text{g/L}$ was higher in children aged 0 to 19 years (6.57%) than in the population of adults over 20 years (4.21%). However, when reviewing the distribution by percentiles, at least 95% of the total population had levels below $33.0 \mu\text{g/L}$, indicating that only a small group had the highest levels. This higher concentration was reached at the 95th percentile only in 6-11, 12-19, and 20-39 years and in the male sex group (Table 2).

Cadmium

When examining the prevalence of cadmium (Cd) exposure, taking as a cut-off point the reference values established by MINSAL⁸, it stands out that 91.56% of the samples had normal Cd levels ($< 2 \mu\text{g/L}$), subtracting 8.44% of the samples with Cd levels greater than or equal to $2 \mu\text{g/L}$ (303 people). The maximum value observed was $26 \mu\text{g/L}$. Significant differences were recorded according to sex (levels $\geq 2 \mu\text{g/L}$ in 11.67% of men and 6.13% of women). No sample was recorded above the reference value in children (0-19 years). The distribution by percentile

Table 6. Distribution by percentiles (p25, p50, p75, p90, and p95) of Pb concentration in blood ($\mu\text{g}/\text{dL}$; LoD = $2 \mu\text{g}/\text{dL}$) in the beneficiary population of Arica, according to age and sex (period from August 2016 to May 2021)

Categories	p25	p50	p75	p90	p95	n
Total	1.9	1.9	1.9	1.9	2.0	9.056
Age Group						
0-5 years	1.9	1.9	1.9	1.91	1.96	10
6-11 years	1.9	1.9	1.9	1.9	2.0	658
12-19 years	1.9	1.9	1.9	1.9	1.9	1.217
20-39 years	1.9	1.9	1.9	1.9	1.9	2.089
40-59 years	1.9	1.9	1.9	1.9	2.0	2.221
≥ 60 years	1.9	1.9	1.9	2.0	3.0	1.976
Sex						
Female	1.9	1.9	1.9	1.9	1.9	5.285
Male	1.9	1.9	1.9	2.0	3.0	3.771

shows that at least 90% of the total population had Cd levels below $1.1 \mu\text{g}/\text{L}$ (Table 3), with the minimum accepted value being two $\mu\text{g}/\text{L}$.

Chromium

Regarding Chromium (Cr) levels, it is noteworthy that 99.77% of the samples exhibited values below the reference limit, according to those established in the MINSAL Clinical Guidelines⁹, with no significant differences according to sex. Only eight individuals recorded levels above $2 \mu\text{g}/\text{L}$, and no samples above $2 \mu\text{g}/\text{L}$ were recorded in children. The results of the distribution by percentiles reveal that at least 95% of the samples had Cr values less than or equal to $1.9 \mu\text{g}/\text{L}$ in all groups (Table 4). The maximum value observed was $10 \mu\text{g}/\text{L}$.

Mercury

When analyzing the urine samples, a situation similar to that described with the patients exposed to Chromium was observed in mercury (Hg) levels. 100% of the samples evaluated were within the recommended ranges according to clinical guidelines ($< 10 \mu\text{g}/\text{L}$)¹⁰, and the maximum value observed was $7 \mu\text{g}/\text{L}$ (Table 5).

Lead

Finally, when analyzing the prevalence of lead (Pb) exposure, 99.33% of the samples had blood Pb levels within the lowest range recommended by MINSAL ($< 5 \mu\text{g}/\text{dL}$)¹¹, evidencing

44 people who yielded values $\geq 5 \mu\text{g}/\text{dL}$ in the analysis period. 99.92% of the samples turned out to have concentrations within the World Health Organization (WHO) recommended range ($< 10 \mu\text{g}/\text{dL}$), with eight people exceeding this limit. In addition, a statistically significant difference was found in the proportion of people with levels above $5 \mu\text{g}/\text{dL}$ according to sex (levels $\geq 5 \mu\text{g}/\text{dL}$ in 1.17% of men and 0.32% in women) and by life cycle stage (children 0.16% and adults 0.64%). According to the distribution by percentiles, at least 95% of the population had values less than or equal to $2.0 \mu\text{g}/\text{dL}$ (Table 6), and the maximum value observed was $38.0 \mu\text{g}/\text{dL}$.

Figure 1 shows the distribution of metal levels (lead in blood and inorganic InAs, Cd, Cr, and Hg in urine) stratified by age category (children and adults) and sex; differences were observed between them, mainly in AsIn levels. Children showed higher levels of AsIn than adults ($p < 0.05$). Similarly, men showed higher concentrations than women ($p < 0.05$). In addition, a higher dispersion of AsIn concentrations was observed. The distribution of concentration values of the other metals was more homogeneous in the groups, presenting small interquartile ranges. However, the analysis of the samples of the other metals was not free of outliers, which were observed more frequently in the adult population than in the children.

Finally, the concentrations of the metals evaluated (mean and p50) were analyzed over time,

according to the month of sampling. These included no variations or special considerations, such as the p50 already detailed in the previous tables. The data are attached in the Annexes section.

Discussion

The information on the levels of metals contained in this study is highly relevant to public health since it allows us to know the level of this exposure in residents of Arica and beneficiaries of the Health Surveillance program of Law 20.590, as well as to determine the prevalence of people with levels of chemical substances above the reference levels established by MINSAL.

The first point to highlight is that, for almost all the metals monitored in the beneficiary population, the p95 without stratification is below the risk level, according to that established by MINSAL through the Polymetals Clinical Guidelines^{5,8-11}. Only Cd is the exception; however, when considering p90, Cd concentrations do fall below the risk level ($< 2\mu\text{g/L}$)⁸.

Additionally, the p95 of AsIn's concentration is above the reference level for specific subgroups (ages 6-39 years and male sex), and the p90 of Cd concentration was found above reference levels for males. All other subgroups presented metal concentrations below the reference limits established in their p90.

This finding is very relevant because, under these reference limits, it can be considered that during the time included in the study, the affected population of Arica had low exposure to the metals studied. Considering that the population benefiting from the monitoring program has the highest risk of exposure in Arica, according to the evaluation of the city due to incidents with hazardous waste collection, it can be assumed that the exposure in the entire commune of Arica should be considered low.

According to the Agency for Toxic Substances and Disease Registry (ATSDR), exposure to AsIn occurs mainly through diet, and the most important sources are fish and shellfish. At the same time, water has naturally high levels of this metal, according to the soil composition¹². In Chile, some regulations limit the amount of As that drinking water can contain (currently 0.01 mg/L)¹³, which reduces exposure through water

consumption. However, people not using the drinking water network could be more exposed to As. In the region, the use of rural drinking water is high in the valleys.

As for the other metals, the hypothesis that environmental exposure is low in the residents of Arica is notorious: more than 99% of the monitored population has levels below the reference for Cr, Hg, and Pb. The exception is Cd, which has 91.56% of people below the 2 ug/L reference level. However, this proportion does not discriminate between smokers and non-smokers, as this information is unavailable in the data provided. This point is relevant because smokers have exposure to Cd by this route, and their reference level is 4 ug/L . That said, there is a possibility that the proportion below the reference level is even more significant.

When comparing these results with other values reported by the CDC, similarities are observed with the results obtained in the United States. Exposure to Hg and Pb are similar, where the p95 is at 2.75 ug/dL for Pb in the blood (vs. 2 ug/dL) and 1.18 ug/dL for Hg in urine (vs. 1.9 ug/L). Regarding AsIn and Cd, the concentrations in both cases were higher in this study than in the USA. The p95 for AsIn in the USA is at 20.8 ug/L (vs. 33 ug/L), and Cd is 0.909 ug/L in the USA (vs. 6 ug/L)¹⁴.

The results can be compared with Antofagasta's biomonitoring program conducted in 2018, which also assessed the level of exposure to metals in a representative sample of that city. The authors found that the Cr, Cd, Hg, and Pb levels were like those in this study. However, levels were much higher in Antofagasta than in Arica: the p95 was 41.4 ug/L in Antofagasta vs 33.0 ug/L in Arica¹⁵.

Finally, in 1999, Tchernitchin et al. measured blood Pb concentration in 32 children from the Santa María de Arica population. The children from the Santa María site (9 in total) had an average of 21.8 mg/dL of Pb¹⁶. These alterations triggered the Arica Health Service to monitor Pb blood levels¹⁶.

In 2000, the local Health Service of Arica took 4990 blood samples from patients, consisting of 3240 children (65%) and 1750 adults (35%), for Pb measurement. The results showed that 4411 samples had $< 10\text{ }\mu\text{g/dL}$ (88%) and 579 $\geq 10\text{ }\mu\text{g/dL}$ (11.6%)¹⁷. Of the 579 subjects with

levels above 10 $\mu\text{g}/\text{dL}$, blood was drawn from 538 (92%). When the Pb levels were measured at the Public Health Institute (ISP) of MINSAL, 407 subjects had concentrations $< 10 \mu\text{g}/\text{dL}$ 75%, and 131 had concentrations $\geq 10 \mu\text{g}/\text{dL}$ (24%). Of the latter, 120 were children (< 15 years), and 11 were adults¹⁷.

The present study found a significantly lower proportion of people with blood Pb levels above 10 $\mu\text{g}/\text{dL}$ (0.09%) than previously cited evidence. In addition, the samples with levels $\geq 10 \mu\text{g}/\text{dL}$ in the present study were found only in adults, in contrast to previous publications, in which the most affected population was mainly children.

Health surveillance and biomonitoring programs for exposure to substances with toxic potential in humans generate helpful information to identify population groups that deserve further evaluation of exposure sources or health effects, and they allow tracking and monitoring trends in population exposure levels.

Although no significant exposure to metals was observed in the commune of Arica, it is recommended to continue with initiatives such as the biomonitoring program to identify early changes in exposure that could generate negative impacts on public health, in this case, in the population of Arica.

Referencias

1. Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ. Heavy Metal Toxicity and the Environment. In: Luch A, editor. *Molecular, Clinical and Environmental Toxicology*. Berlin, Germany: Springer; 2012.
2. Ratnaike RN. Acute and chronic arsenic toxicity. *Postgrad Med J*. 2003; 79: 391-936.
3. Londoño-Franco LF, Londoño-Muñoz PT, Muñoz-García FG. Risk of Heavy Metals in Human and Animal Health. *Biotechnología en el Sector Agropecuario y Agroindustrial*. 2016; 14(2): 146-53.
4. Deng Y, Wang M, Tian T, Lin S, Xu P, Zhou L, et al. The Effect of HEXavalent Chromium on the Incidence and Mortality of Human Cancers: A Meta-analysis Based on Published Epidemiological Cohort Studies. *Frontiers in oncology*. 2019; 9: 1-15.
5. Ministerio de Salud. *Guía Clínica: Vigilancia Biológica de la Población expuesta a Arsénico en la Comuna de Arica*. Santiago 2014.
6. Ley 20590: Establece un programa de intervención en zonas con presencia de polimetales en la comuna de Arica, (2012).
7. R Core Team. *R: A language and environment for statistical computing*. R Foundation for Statistical Computing. Vienna, Austria 2022.
8. Ministerio de Salud. *Guía Clínica: Vigilancia Biológica de la Población expuesta a Cadmio*. Santiago 2014.
9. Ministerio de Salud. *Guía Clínica: Vigilancia Biológica de la Población expuesta a Cromo en la Comuna de Arica*. Santiago 2014.
10. Ministerio de Salud. *Guía Clínica: Vigilancia Biológica de la Población expuesta a Mercurio en la Comuna de Arica*. Santiago 2014.
11. Ministerio de Salud. *Guía Clínica: Vigilancia Biológica de la Población Expuesta a Plomo en la Comuna de Arica*. MINSAL ed. Santiago 2014.
12. Agency for Toxic Substances and Disease Registry. *Toxicological profile for arsenic*. In: U.S Department of Health and Human Services, editor. Atlanta, Georgia 2007.
13. Norma Chilena Oficial: Agua Potable - Parte 1 - Requisitos, (2004).
14. Center for Disease Control and Prevention. *Fourth National Report on Human Exposure to Environmental Chemicals*. 2019.
15. Ríos JC, Villarroel L, Torres M, Astaburuaga JP, Leiva C, Cook P, et al. Estudio de metales urinarios y plomo en sangre: parámetros poblacionales en Antofagasta, 2018. *Rev Med Chile*. 2020; 148: 746-54.
16. Tchernitchin AN, Lapin N, Molina L, Molina G, Tchernitchin NA, Acevedo C, et al. Human Exposure to Lead in Chile. *Rev Environ Contam Toxicol*. 2005; 185: 93-139.
17. Ministerio de Salud. *Nómina de personas con muestras de Plomo en sangre con niveles $> 10\mu\text{g}/\text{dl}$ confirmada por I.S.P. Muestreo realizado en año 2000 y controles en 2001. Población industriales II, III y IV. Pob. Co. Chuño*. MINSAL. Arica: Servicio de Salud Arica, Subdirección Médica, Unidad de Epidemiología; 2001.