

The 2017 National Health Survey on Biomonitoring of Metals associates Higher Arsenic Levels with Age, Sex, Geography, and Fish Consumption

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La Encuesta Nacional de Salud 2017 sobre biomonitorización de metales asocia niveles más altos de arsénico con la edad, el sexo, la geografía y el consumo de pescado

ABSTRACT

*This study investigates the exposure of the Chilean population to heavy metals, specifically arsenic, lead, mercury, and cadmium, using data from the 2016-2017 National Health Survey (NHS). Chronic exposure to these metals poses significant health risks, including cancer, cardiovascular diseases, and neurological effects. **Aim:** The study aims to analyze metal levels across different demographics and identify factors associated with elevated exposure. **Methods:** A cross-sectional analysis was conducted using NHS data, which includes metal levels in blood and urine, alongside demographic, socioeconomic, and lifestyle information. The sample consisted of 3.600 participants aged 18 and older. Metal levels were measured using mass spectrometry and spectrophotometry. Statistical analyses, including quantile and logistic regression, were performed to assess the impact of various covariates on metal levels. **Results:** The study found that 91.04% of the population had arsenic levels below the reference value of 35 µg/L, while 8.45% had levels between 35 and 100 µg/L, and 0.51% exceeded 100 µg/L. Elevated arsenic levels were associated with younger age, male sex, rural residence, northern macrozone, and high fish consumption. Lead, mercury, and cadmium levels were generally within limits, with notable variations based on age, sex, and geographic region. **Conclusion:** The findings highlight significant arsenic exposure in certain demographics, necessitating targeted public health interventions. While lead, mercury, and cadmium levels are mostly within limits, ongoing biomonitoring and public awareness are*

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crucial to mitigate health risks. The study underscores the importance of tailored policies to reduce metal exposure and protect vulnerable populations in Chile.

Keywords: Arsenic; Cadmium; Lead; Mercury; Public Health; Toxicology.

RESUMEN

Este estudio investiga la exposición de la población chilena a metales pesados, específicamente arsénico, plomo, mercurio y cadmio, utilizando datos de la Encuesta Nacional de Salud (ENS) 2016-2017. La exposición crónica a estos metales supone riesgos significativos para la salud, incluyendo cáncer, enfermedades cardiovasculares y efectos neurológicos. **Objetivo:** Analizar los niveles de metales en diferentes demografías e identificar factores asociados con una exposición elevada. **Métodos:** Se realizó un análisis transversal utilizando datos de la ENS, que incluye niveles de metales en sangre y orina, junto con información demográfica, socioeconómica y de estilo de vida. La muestra consistió en 3.600 participantes de 18 años o más. Los niveles de metales se midieron utilizando espectrometría de masas y espectrofotometría. Se realizaron análisis estadísticos, incluyendo regresión cuantílica y logística, para evaluar el impacto de diversas covariables en los niveles de metales. **Resultados:** El estudio encontró que el 91.04% de la población tenía niveles de arsénico en orina por debajo del valor de referencia de 35 µg/L, mientras que el 8.45% tenía niveles entre 35 y 100 µg/L, y el 0.51% excedía los 100 µg/L. Los niveles elevados de arsénico estaban asociados con menor edad, sexo masculino, residencia rural, macrozona norte y alto consumo de pescado. Los niveles de plomo, mercurio y cadmio estaban generalmente dentro de los límites, con variaciones notables basadas en la edad, el sexo y la región geográfica. **Conclusión:** Los hallazgos destacan una exposición significativa al arsénico en ciertos grupos, lo que requiere intervenciones de salud pública específicas. Aunque los niveles de plomo, mercurio y cadmio están dentro de los límites considerados seguros de acuerdo a las guías de la autoridad sanitaria, el biomonitoreo continuo y la concienciación pública son cruciales para mitigar los riesgos para la salud. El estudio subraya la importancia de políticas adaptadas para reducir la exposición a metales y proteger a las poblaciones vulnerables en Chile.

Palabras clave: Arsénico; Cadmio; Mercurio; Salud Pública; Toxicología; Plomo.

Exposure to heavy metals such as arsenic, lead, mercury, and cadmium poses significant public health risks due to their toxicological effects. These metals can enter the human body through various environmental sources, including contaminated water, food, and air. Chronic exposure to these metals has been linked to numerous adverse health outcomes, including neurological, cardiovascular, and renal disorders, as well as increased cancer risk^{1,2}. Heavy metals are significant in toxicology due to their persistence in the environment and their ability to bioaccumulate in living organisms. Unlike organic pollutants, metals cannot be degraded and thus remain in the ecosystem, posing long-term health risks. Their toxic effects are often dose-dependent and can vary based on the form of the metal and the route of exposure.

Arsenic is a well-known carcinogen that can cause skin, lung, and bladder cancers. Chronic exposure to arsenic can also lead to cardiovascular disease, diabetes, and neurological effects³. The reference dose (RfD) for arsenic, established by the U.S. Environmental Protection Agency (EPA), is 0.0003 mg/kg/day, which represents the daily exposure level that is not expected to cause harmful effects over a lifetime. According to the "Guías Clínicas Polimetales" of MINSAL in Chile, the reference value for arsenic in urine is 35 µg/L⁴.

Lead exposure is particularly harmful to children, causing developmental delays, learning difficulties, and lower IQ. In adults, lead exposure can result in hypertension, renal impairment, and reproductive issues⁵. Lead disrupts the function of various enzymes and interferes with the synthesis of hemoglobin, leading to anemia. It also affects the nervous system by disrupting neurotransmitter release and causing oxidative stress. The EPA's RfD for lead is 0.0035 mg/kg/day, reflecting the level of exposure that is not expected to cause adverse health effects. The reference value for lead in blood, as per MINSAL guidelines, is 10 µg/dL⁴.

Mercury exposure, especially in the form of methylmercury, can impair neurological development in fetuses and young children. In adults, mercury exposure can lead to cognitive and motor dysfunction, as well as cardiovascular problems⁶. Mercury binds to sulfhydryl groups in proteins,

disrupting their function and leading to cellular damage. It can cross the blood-brain barrier and accumulate in the brain, causing neurotoxicity. The RfD for methylmercury is 0.0001 mg/kg/day, indicating the safe daily exposure level. The reference value for mercury in urine, according to MINSAL, is 10 µg/L.

Cadmium exposure is associated with kidney damage, bone demineralization, and an increased risk of cancer⁷. Cadmium accumulates in the kidneys, where it can cause tubular damage and impair renal function. It also interferes with calcium metabolism, leading to bone demineralization and increased risk of fractures. The EPA has set the RfD for cadmium at 0.0005 mg/kg/day, representing the daily exposure level that is not expected to cause harmful effects over a lifetime. According to the "Guías Clínicas Polimetales" of MINSAL in Chile, the reference value for cadmium in urine is 1 µg/L for non-smokers and 4 µg/L for smokers⁴.

Chile, with its diverse geography and industrial activities, presents unique challenges and opportunities for studying metal exposure. The country's extensive mining operations, particularly in the northern regions, have historically contributed to elevated levels of arsenic and other metals in the environment³. Additionally, dietary habits, such as high fish consumption, can influence mercury exposure levels⁸.

The National Health Survey (NHS) 2016-2017 provides a comprehensive dataset to analyze the exposure of the Chilean population to these metals. The National Health Survey (NHS) 2016-2017 provides a comprehensive dataset for analyzing the exposure of the Chilean population to these metals. The aim of this study is to analyze the levels of Arsenic, Lead, Mercury, and Cadmium among the Chilean population. We also explored the factors associated with levels above reference values and the impact of covariates on metal levels within the Chilean population.

Methodology

Study design

We conducted a cross-sectional analysis using data from the Chilean NHS 2016-2017, a public database released by the Ministry of Health,

which includes levels of Arsenic, Lead, Mercury, and Cadmium alongside demographics, socio-economic, smoking status, and geographic data. Also, we analyzed the prevalence of the population in the different exposure ranges established by the Ministry of Health to metals. We explored the effects of covariables for having a level above the reference value. The database is available on the Ministry of Health website⁹. The ENS 2016-2017 protocol was approved by the Ethics Committee of the School of Medicine of the Pontifical Catholic University of Chile, and all participants signed an informed consent.

Setting and participants

The NHS is an epidemiologic surveillance in health and health determinants focused on non-transmissible diseases in the population 15 years and older. It is representative of the Chilean population, men and women, living in rural and urban zones in all regions of the country. The data was collected between August 2016 and March 2017¹⁰.

The sample used in this study corresponds to a random subsample of individuals (RSI) who had already been part of the first selection of the ENS. The selection method is two-phase, in which the first phase selects the households that comprise the ENS's primary sample, and the second phase picks the homes that make up the RSI. In each house, one person was selected to be recruited in ENS randomly by The Kish Method. This sub-sample includes persons ≥ 18 years of age from rural and urban zones living in all regions¹⁰.

Data Sources/measurement and bias

The demographic information was collected through a questionnaire by trained nurses. The metal levels in blood or urine were determined at the Instituto Salud Pública de Chile. Arsenic, Cadmium, and Mercury were measured in urine, and Lead in blood samples. Arsenic, Lead, and Cadmium were analyzed by mass spectrometry coupled to plasma (ICP-MS), and Mercury in spectrophotometry (atomic absorption). The Limits of Quantification (LOQ) for Arsenic, Lead, Mercury, and Cadmium were 5 $\mu\text{g/L}$, 1 $\mu\text{g/dL}$, 2 $\mu\text{g/L}$ and 1 $\mu\text{g/L}$ respectively.

The NHS overestimated the sample size using the response rates from previous studies in Chile to reach the sample size in the first visit to homes. For selecting people in the homes, probabilistic methods were used (kish method), propensity stratification was used to identify homogenous groups in the probability of acceptance to participate in the ENS, and tried to adjust the bias for no response. Also, the ENS provided expansion factors for the calculation of prevalences¹⁰.

Sample Size

The RSI is expected to include 3,700 participants out of the 6,233 recruited in the NHS, and 3,600 participants had valid results. This sample size allows for estimates to be made with a 95% confidence interval and a relative error of less than 30% for national prevalences greater than 2%¹⁰.

Quantitative variables

For this analysis, the main variables were levels of Arsenic, Lead, Mercury, and Cadmium, expressed in their numeric value, and we categorized the levels according to the exposure vigilance guidelines published by the Ministry of Health in Chile⁴ as follows:

- a) Lead
 - a. Under 5 $\mu\text{g/dL}$
 - b. Between 5 y 10 $\mu\text{g/dL}$
 - c. Above 10 $\mu\text{g/dL}$
- b) Cadmium
 - a. Non-smokers
 - i. Under 2 $\mu\text{g/L}$
 - ii. Above 2 $\mu\text{g/L}$
 - b. Cadmium in Smokers
 - i. Under 4 $\mu\text{g/L}$
 - ii. Above 4 $\mu\text{g/L}$
- c) Mercury
 - a. Under 10 $\mu\text{g/L}$
 - b. Above 10 $\mu\text{g/L}$
- d) Arsenic
 - a. Under 35 $\mu\text{g/L}$
 - b. Between 35 y 100 $\mu\text{g/L}$
 - c. Above 100 $\mu\text{g/L}$

We considered as covariates the age range (18-24, 25-44, 45-64, >65), sex, zone (urban or rural), geographic macrozone (North, Center, South),

geographic region, educational level (<8 years, 8-12 years, 13 years or more), fish consumption (<3 times per month, 1 time per week, >1 time per week), and smoking (non-smoker, ex-smoker, active smoker).

Statistical methods

We characterized the sample by age average, age range, sex, educational level, smoking status, geographic macrozone, and zone. We described the Arsenic, Lead, Mercury, and Cadmium levels stratified by age range, sex, zone, macrozone, and educational level. The expansion factors corresponding to the RSI were considered and expressed as quantiles. Statistical measures are reported with their respective 95% confidence intervals.

Quantile regression was used to analyze the impact of smoking, age, sex, region of residence, and fish consumption on arsenic levels. Unlike traditional regression, which predicts the mean (or average) value of a dependent variable based on independent variables, quantile regression focuses on other points, such as the median (the middle point of the data) or any other quantile (portion of the data). This technique was performed for the 25th, 50th, 75th, 90th, and 95th percentiles of arsenic levels according to the covariables.

We described the levels according to each range of the exposure in the vigilance guidelines. For arsenic, we also built a logistic regression to adjust the odds ratio to have a value above 35 ug/L, the reference value according to the arsenic vigilance guideline published by the Ministry of Health in Chile.

For the statistical test performed, we considered p-values <0.05 as statistically significant. R software version 4.2.1 and STATA version 16 were used to obtain the statistical measures. We used the STROBE checklist to report this study¹¹.

Results

The sample had valid results for 3546 Arsenic, 3600 Lead, 3501 Mercury, and 3547 Cadmium. Table 1 summarizes the main characteristics of the population screened with metal levels in ENS. Of the valid results, 17.22% of the Arsenic

levels were <LOQ, 68.87% in Lead, 96.35% in Mercury, and 94.18% in Cadmium.

Table 2, Table 3, Table 4, and Table 5 summarizes the levels ordered by percentiles in the total sample and by stratus. Any of the values of Cadmium, Lead, and Mercury percentiles were above the reference values published by the Ministry of Health in their the vigilance guidelines. In Arsenic levels, all p95 values exceeded the reference values of 35 ug/L. In the stratified analysis, the people aged 15-25, men, rural, north macrozone, and educational level between 8-12 years, the values of p90 were above the reference value.

The quantile regression results that are detailed in Table 6 shows that age and geographic macrozone are related to statistically significant changes in arsenic levels in all the percentiles. Smoking status impacts in q25 and q50, and fish consumption in q50, q75, and q90. The magnitude of the impact depends on the percentile, which is higher at higher percentiles.

In the description per vigilance guidelines values in Chile (Table 7), on Cadmium levels, 99,60% (99,43-99,91) of the non-smokers were at normal levels and 100% in the smoker's strata. On mercury levels, 99,96% (99,74-99,99) were normal. 98,76% (97,98%-99,24%) of Lead was under 5 ug/dL, 0,99% (0,57-1,73) between 5 y 10 ug/L and 0,25% (0,09-0,65) above 10 ug/L. 91,04% of the Arsenic levels were under the reference value of 35 ug/L (89,2%-92,6%). 8,45% (6,91%-10,3%) of the levels were between 35 y 100 ug/L and 0,51% (0,26%-0,99%) above 100 ug/L.

Logistic regression made for the relationship of having an arsenic level above 35 ug/L with the covariables (Table 8) shows that having between 45-64 years reduces the chance in a 38% (OR 0.62; 95% CI 0.44 to 0.88), having >35 years reduces the chance in 41% (OR: 0.76; 95% IC= 0.60 to 0.96), female have 24% less chance (OR= 0.76; 95% CI= 0.60 to 0.96). Variables that are related to levels above 35 ug/L are fish consumption >1 time per week, which duplicates the chance (OR= 2.11; 95% CI=1.48 to 3.01), and living in the north macrozone, which triplicates the chance (OR= 3.78; 95% CI= 2.82 to 5.08).

Table 1. Sample demographic characteristics: age average, sex, educational level as years of study, geographic macrozone and proportion of urban and rural population.

| Variable | Unit | Value |
|----------------------|------------|---|
| Age average | Mean (SD) | 43.24 (42.75-43.72) |
| Sex | Mean (SD) | Male: 49.07 (46.48-51.67) Female: 50.92 (48.32-53.51) |
| Educational Level | % (CI95%) | <8 years : 16.68 (14.79-18.77) 8-12 years 56.59 (53.22-59.90) >13 years 26.71 (23.59-30.08) |
| Smoking status | % (CI 95%) | Active smoker: 34.33 (31.86-36.90) Ex smoker: 23.65 (21.51-25.94) Non Smoker: 42.00 (39.38-44.66) |
| Geographic Macrozone | % (CI 95%) | Metropolitana 38.92 (35.57-42.37) North 12.39 (11.48-14.53) Center 34.85 (31.99-37.82) South 13.29 (11.81-14.91) |
| Urban/rural | % (CI 95%) | Urban: 88.37 (86.82-89.76) Rural: 11.62 (10.23-13.17) |

Discussion

One of the most striking findings of the study is the elevated levels of arsenic exposure in certain segments of the population. Approximately 10% of the population has arsenic levels above the reference value of 35 µg/L, which is concerning given the toxicological effects of arsenic. Chronic exposure to arsenic is known to cause health issues, including skin, lung, and bladder cancers, cardiovascular diseases, diabetes, and neurological effects¹².

The study identifies several key factors associated with elevated arsenic levels. Younger individuals, particularly those aged 15-24, tend to have higher arsenic levels compared to older age groups. This trend could be attributed to differences in lifestyle, dietary habits, or environmental exposures that are more prevalent among younger people.

The northern macrozone of Chile shows significantly higher arsenic levels. This region has a history of extensive mining activities, which may have contributed to environmental contamination. The legacy of these industrial activities continues to impact the local population, leading to higher arsenic exposure¹³. Higher fish consumption is associated with increased arsenic levels. This finding reflects dietary exposure, as fish can accumulate arsenic from contaminated water sources. People who consume fish more frequently are at a higher risk of arsenic exposure⁸.

In contrast to arsenic, the levels of lead, mercury, and cadmium in the Chilean population are generally within limits as per the guidelines of the Chilean Ministry of Health. However, the study does highlight certain trends and demographic differences in exposure levels.

Table 2. Distribution of cadmium levels (ug/L) in the Chilean population obtained in the National Health Survey 2016-2017 and stratified by age, gender, and region of the country. LOQ: Limit of Quantification; MR: Metropolitan Region. G. Mean: Geometric Mean.

| Variable | Categories | G.Mean (ug/L) (CI 95%) | Q50th (ug/L) (CI 95%) | Q75th (ug/L) (CI 95%) | Q90 (ug/L) (CI 95%) | Q95 (ug/L) (CI 95%) | Sample size |
|-------------------|------------------|------------------------------|-----------------------------|-----------------------------|---------------------------|---------------------------|----------------|
| Total Population | - | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 3.547 |
| Age | 15-24 | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 467 |
| | 25-44 | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 997 |
| | 45-64 | 1,03 (1,02-1,04) | <LOQ | <LOQ | 1,02 (1,00-1,08) | 1,19 (1,02-1,04) | 1.204 |
| | >65 | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 879 |
| Sex | Female | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 2.223 |
| | Male | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 1.324 |
| Zone | Urban | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 2.977 |
| | Rural | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 570 |
| Macrozone | North | 1,02 (1,01-1,03) | <LOQ | <LOQ | <LOQ | <LOQ | 917 |
| | Center | 1,02 (1,01-1,03) | <LOQ | <LOQ | <LOQ | 1,02 (1,00-1,10) | 1.179 |
| | South | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 904 |
| | MR | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 547 |
| Educational Level | <8 years | 1,02 (1,01-1,03) | <LOQ | <LOQ | <LOQ | <LOQ | 838 |
| | 8-12 years | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 1.916 |
| | 13 years or more | 1,01 (1,00-1,02) | <LOQ | <LOQ | <LOQ | <LOQ | 764 |

Table 3. Distribution of lead levels (ug/dL) in the Chilean population according to demographic and socioeconomic variables. LOQ: Limit of Quantification. G. Mean: Geometric Mean.

| Variable | Categories | G. Mean (ug/dL) (CI 95%) | Q50th (ug/dL) (CI 95%) | Q75th (ug/dL) CI 95%) | Q90 (ug/dL) (CI 95%) | Q95 (ug/dL) (CI 95%) | Sample size |
|----------------------|---------------------|--------------------------------|------------------------------|-----------------------------|----------------------------|----------------------------|----------------|
| | Total Population | 1,16 (1,14-1,17) | <LOQ | <LOQ | 1,28 (0,92-1,64) | 1,77 (1,15-2,39) | 3.600 |
| Age | 15-24 | 1,07 (1,05-1,10) | <LOQ | <LOQ | 1,28 (0,92-1,64) | 1,77 (1,15-2,39) | 471 |
| | 25-44 | 1,11 (1,09-1,13) | <LOQ | <LOQ | 1,40 (1,20-1,60) | 2,08 (1,29-2,87) | 1.012 |
| | 45-64 | 1,22 (1,19-1,25) | <LOQ | 1,27 (1,16-1,38) | 1,87 (1,67-2,07) | 2,79 (2,06-3,52) | 1.214 |
| | >65 | 1,27 (1,23-1,30) | <LOQ | 1,40 (1,23-1,56) | 2,42 (2,01-2,83) | 3,03 (2,15-3,91) | 903 |
| Sex | Female | 1,08 (1,07-1,09) | <LOQ | <LOQ | 1,29 (1,18-1,40) | 1,77 (1,62-1,92) | 2.270 |
| | Male | 1,24 (1,22-1,27) | <LOQ | 1,30 (1,19-1,41) | 2,08 (1,66-2,50) | 3,19 (2,65-3,73) | 1.330 |
| Zone | Urban | 1,15 (1,14-1,17) | <LOQ | 1,08 (1,01-1,15) | 1,66 (1,51-1,81) | 2,37 (2,04-2,70) | 3.030 |
| | Rural | 1,20 (1,16-1,24) | <LOQ | 1,09 (1,00-1,38) | 1,89 (1,10-2,67) | 3,17 (1,00-6,93) | 570 |
| Macrozone | North | 1,23 (1,20-1,27) | <LOQ | 1,26 (1,06-1,46) | 2,14 (1,79-2,49) | 2,86 (1,79-3,93) | 944 |
| | Center | 1,15 (1,13-1,17) | <LOQ | 1,11 (1,01-1,21) | 1,61 (1,44-1,78) | 2,17 (1,78-2,56) | 1.170 |
| | South | 1,16 (1,14-1,19) | <LOQ | 1,09 (1,00-1,24) | 1,82 (1,26-2,38) | 2,83 (2,19-3,47) | 936 |
| | MR | 1,13 (1,10-1,16) | <LOQ | <LOQ | 1,57 (1,23-1,91) | 2,13 (1,17-3,09) | 550 |
| Educational Level | <8 years | 1,23 (1,20-1,27) | <LOQ | 1,23 (1,06-1,40) | 2,13 (1,46-2,80) | 3,14 (2,09-4,19) | 850 |
| | 8-12 years | 1,15 (1,14-1,17) | <LOQ | 1,10 (1,01-1,19) | 1,69 (1,54-1,84) | 2,20 (1,88-2,52) | 1.975 |
| | 13 years or more | 1,12 (1,09-1,14) | <LOQ | <LOQ | 1,57 (1,17-1,97) | 2,16 (1,15-3,17) | 774 |

Table 4. Distribution of mercury levels (ug/L) in Chilean population obtained in the National Health Survey 2016-2017 and stratified by age, gender, and region of the country. LOQ: Limit of Quantification. G. Mean: Geometric Mean.

| Variable | Categories | G.Mean (ug/L) (CI 95%) | Q50th (ug/L) (CI 95%) | Q75th (ug/L) (CI 95%) | Q90 (ug/L) (CI 95%) | Q95 (ug/L) (CI 95%) | Sample size |
|----------------------|---------------------|------------------------------|-----------------------------|-----------------------------|---------------------------|---------------------------|----------------|
| | Total Population | 2,02 (2,01-2,03) | <LOQ | <LOQ | <LOQ | <LOQ | 3.501 |
| Age | 15-24 | 2,04 (2,02-2,07) | <LOQ | <LOQ | <LOQ | <LOQ | 457 |
| | 25-44 | 2,03 (2,02-2,04) | <LOQ | <LOQ | <LOQ | <LOQ | 974 |
| | 45-64 | 2,01 (2,00-2,02) | <LOQ | <LOQ | <LOQ | <LOQ | 1.196 |
| | >65 | 2,01 (2,00-2,02) | <LOQ | <LOQ | <LOQ | <LOQ | 874 |
| Sex | Female | 2,03 (2,02-2,04) | <LOQ | <LOQ | <LOQ | <LOQ | 2.191 |
| | Male | 2,01 (2,00-2,02) | <LOQ | <LOQ | <LOQ | <LOQ | 1.310 |
| Zone | Urban | 2,03 (2,02-2,04) | <LOQ | <LOQ | <LOQ | <LOQ | 2.937 |
| | Rural | 2,01 (2,00-2,02) | <LOQ | <LOQ | <LOQ | <LOQ | 564 |
| Macro-zone | North | 2,04 (2,02-2,06) | <LOQ | <LOQ | <LOQ | 2,11 (2,00-2,32) | 893 |
| | Center | 2,02 (2,01-2,03) | <LOQ | <LOQ | <LOQ | <LOQ | 1.159 |
| | South | 2,01 (2,00-2,02) | <LOQ | <LOQ | <LOQ | <LOQ | 902 |
| | MR | 2,02 (2,01-2,03) | <LOQ | <LOQ | <LOQ | <LOQ | 547 |
| Educational Level | <8 years | 2,01 (2,00-2,02) | <LOQ | <LOQ | <LOQ | <LOQ | 839 |
| | 8-12 years | 2,02 (2,01-2,03) | <LOQ | <LOQ | <LOQ | <LOQ | 1.880 |
| | 13 years or more | 2,04 (2,02-2,06) | <LOQ | <LOQ | <LOQ | <LOQ | 754 |

Table 5. Distribution of arsenic levels (ug/L) in the Chilean population obtained in the National Health Survey 2016-2017 and stratified by age, gender, and region of the country. LOQ: Limit of Quantification.

| Variable | Categories | G.Mean (ug/L) (CI 95%) | Q50th (ug/dL) (CI 95%) | Q75th (ug/dL) (CI 95%) | Q90 (ug/dL) (CI 95%) | Q95 (ug/dL) (CI 95%) | Sample size |
|----------------------|---------------------|------------------------------|------------------------------|------------------------------|----------------------------|----------------------------|----------------|
| | Total Population | 12,63 (12,34-12,92) | 12,56 (11,77-13,35) | 19,54 (18,16-20,92) | 33,02 (30,31-35,73) | 43,86 (40,32-47,39) | 3.546 |
| Age | 15-24 | 15,52 (14,55-16,55) | 14,96 (13,25-16,67) | 26,49 (21,28-31,70) | 38,18 (33,43-42,92) | 44,21 (29,33-59,09) | 466 |
| | 25-44 | 13,30 (12,73-13,88) | 13,88 (12,71-15,05) | 20,13 (18,18-22,08) | 32,19 (26,32-38,06) | 45,06 (36,36-53,76) | 994 |
| | 45-64 | 11,94 (11,48-12,43) | 11,01 (9,90-12,12) | 18,42 (16,67-20,17) | 31,93 (27,84-36,02) | 41,53 (32,90-50,16) | 1.206 |
| | >65 | 9,39 (9,01-9,78) | 8,78 (7,74-9,81) | 13,21 (11,88-14,54) | 21,33 (18,02-24,63) | 28,15 (22,56-33,74) | 880 |
| Sex | Female | 11,46 (11,12-11,80) | 10,83 (9,97-11,69) | 17,69 (16,44-18,94) | 29,68 (25,94-33,41) | 42,5 (36,41-48,59) | 2.221 |
| | Male | 13,90 (13,39-14,42) | 13,86 (12,86-14,86) | 21,1 (31,72-40,05) | 35,87 (31,72-40,02) | 44,55 (38,03-51,07) | 1.325 |
| Zone | Urban | 12,52 (12,21-12,83) | 12,46 (11,60-13,32) | 19,23 (11,80-20,69) | 32,00 (29,22-34,78) | 43,63 (39,6) | 2.976 |
| | Rural | 13,52 (12,73-14,35) | 12,77 (11,56-13,98) | 21,61 (15,70-27,52) | 37,63 (29,98-45,28) | 46,47 (25,48-67,46) | 570 |
| Macrozone | North | 16,64 (15,87-17,44) | 16,84 (15,42-18,26) | 26,96 (24,55-29,37) | 42,43 (36,54-48,32) | 57,74 (50,43-65,05) | 914 |
| | Center | 12,32 (11,84-12,82) | 11,92 (11,15-12,69) | 17,92 (16,12-19,72) | 32,04 (26,49-37,59) | 42,5 (32,90-52,09) | 1.180 |
| | South | 12,61 (12,04-13,21) | 12,68 (11,62-13,74) | 19,09 (17,41-20,77) | 34,43 (30,21-38,64) | 48,55 (35,01-62,09) | 906 |
| | MR | 11,82 (11,17-12,52) | 11,53 (10,08-12,98) | 17,94 (15,46-20,41) | 30,64 (25,13-36,15) | 38,18 (31,85-44,51) | 546 |
| Educational Level | < 8 years | 10,81 (10,34-11,31) | 10,12 (9,16-11,08) | 16,02 (14,46-17,58) | 28,16 (23,67-32,65) | 36,35 (30,55-42,15) | 840 |
| | 8-12 years | 13,80 (12,80-13,65) | 13,08 (12,27-13,89) | 20,75 (18,71-22,79) | 35,7 (32,28-39,12) | 46,4 (40,11-52,82) | 1.914 |
| | 13 years or more | 12,59 (11,99-13,21) | 13,12 (11,80-14,44) | 19,26 (17,19-21,33) | 31,86 (25,80-37,92) | 43,63 (36,84-50,41) | 765 |

Table 6. Quantile regression to assess the impact of the variables smoking, age, sex, region of residence, and fish consumption on arsenic levels.

| Variable | Category | Coef | Q25 | IC95% | Coef | Q50 | IC95% | Coef | Q75 | IC95% | Coef | Q90 | IC95% | Coef | Q95 | IC95% | p-value |
|------------------|--------------------|------|--------|--------|-------|-------|-------|-------|--------|-------|-------|--------|--------|-------|--------|--------|---------|
| Age range | 18-25 | | Ref | | | Ref | | | Ref | | | Ref | | | Ref | | |
| | 25-44 | | -2.07 | -0.90 | 0.13 | -1.92 | -0.57 | 0.40 | -4.55 | -1.47 | 0.39 | -5.26 | 0.11 | 0.96 | -2.48 | 6.36 | 0.15 |
| | | | 0.26 | | | 0.77 | | | 1.61 | | | 5.49 | | | 15.20 | | |
| | 45-64 | | -3.15 | -2.07 | <0.05 | -4.16 | -3.13 | <0.05 | -7.46 | -4.74 | <0.05 | -10.07 | -5.69 | <0.05 | -10.03 | -2.33 | 0.55 |
| | | | -1.00 | | | -2.10 | | | -2.01 | | | -1.32 | | | 5.36 | | |
| | ≥65 | | -3.52 | -2.48 | <0.05 | -6.38 | -5.32 | <0.05 | -11.28 | -8.44 | <0.05 | -16.50 | -12.14 | <0.05 | -21.64 | -13.06 | <0.05 |
| | | | -1.43 | | | -4.26 | | | -5.60 | | | -7.78 | | | -4.47 | | |
| Sex | Male | | Ref | | | Ref | | | Ref | | | Ref | | | Ref | | |
| | Female | | -1.94 | -1.41 | <0.05 | -3.37 | -2.60 | <0.05 | -3.73 | -2.62 | <0.05 | -5.49 | -2.65 | 0.06 | -5.49 | -2.65 | 0.06 |
| Smoking | | | -0.88 | | | -1.84 | | | -1.51 | | | 0.17 | | | 0.17 | | |
| | No smoker | | Ref | | | Ref | | | Ref | | | Ref | | | Ref | | |
| | Ex-smoker | | -0.38 | -0.12 | 0.34 | -1.02 | -0.38 | 0.24 | -2.10 | -0.80 | 0.22 | -4.69 | -0.74 | 0.71 | -4.69 | -0.77 | 0.71 |
| | Active Smoker | | 0.13 | 0.76 | <0.05 | 0.25 | 1.40 | <0.05 | 0.49 | 1.37 | 0.11 | 3.20 | 2.94 | 0.12 | 3.20 | 2.94 | 0.12 |
| Fish consumption | | | 1.13 | | | 2.35 | | | 3.05 | | | 6.65 | | | 6.65 | | |
| | <3 times per month | | -0.21 | 0.70 | 0.62 | -0.82 | 0.43 | 0.17 | 0.78 | -1.09 | -1.13 | 0.59 | -5.35 | 1.16 | -4.84 | -4.84 | 0.70 |
| | 1 time per week | | 0.35 | 0.40 | 0.90 | 0.92 | 0.63 | 0.11 | -1.20 | 1.44 | 0.926 | -3.58 | 3.07 | 0.94 | 7.17 | 7.17 | 0.37 |
| | >1 time per week | | -0.002 | 0.329 | 0.52 | -0.15 | 2.63 | <0.05 | 1.32 | 0.06 | <0.05 | 3.34 | -12.26 | <0.05 | -7.51 | -2.33 | 0.06 |
| Macrozone | | | 0.82 | | | 1.31 | | | 2.09 | 5.61 | | 3.81 | 10.88 | | 2.84 | 14.56 | |
| | | | -0.33 | | | 0.95 | | | 9.12 | | | 17.96 | | | -0.91 | 30.05 | |
| | | | 0.99 | | | 4.31 | | | | | | | | | | | |
| | RM | | Ref | | | Ref | | | Ref | | | Ref | | | Ref | | |
| Macrozone | North | | 3.32 | 4.186 | <0.05 | 6.18 | 7.62 | <0.05 | 10.22 | 12.27 | <0.05 | 13.75 | 18.92 | <0.05 | 15.49 | 23.66 | <0.05 |
| | Center | | 5.04 | 0.27 | 0.11 | 9.07 | 0.13 | 0.78 | 14.33 | 0.08 | 0.90 | 24.09 | 0.23 | 0.91 | 31.82 | -0.02 | 0.99 |
| | South | | -0.06 | | | -0.83 | | | -1.30 | | | -3.99 | | | -6.76 | | |
| | | | 0.33 | | | 1.10 | | | 1.47 | | | 4.46 | | | 6.71 | | |
| | | | -0.34 | -0.004 | 0.98 | -1.93 | -0.88 | 0.10 | -2.60 | -0.97 | 0.24 | -3.25 | 1.73 | 0.49 | -4.73 | 3.19 | 0.43 |
| | | | 0.33 | | | 0.17 | | | 0.65 | | | 6.72 | | | 11.12 | | |

Table 7. Percentage distribution of population tested for results below and above the reference level established by the Chilean Ministry of Health, for lead, cadmium, mercury and arsenic.

| Metal | Value | Number of Persons | % | Confidence Intervals 95% Lower limit | Upper limit |
|------------------------|-----------------------|-------------------|-------|---|-------------|
| Lead | Under 5 ug/dL | 3.570 | 98,76 | 97,98 | 99,24 |
| | Between 5 y 10 ug/dL | 32 | 0,99 | 0,57 | 1,73 |
| | Above 10 ug/dL | 12 | 0,25 | 0,09 | 0,65 |
| Cadmium Non-smokers | Under 2 ug/L | 2.511 | 99,60 | 99,43 | 99,91 |
| | Above 2 ug/L | 11 | 0,40 | 0,09 | 0,57 |
| Cadmium in Smokers | Under 4 ug/L | 1.038 | 100 | - | - |
| | Above 4 ug/L | 0 | 0 | - | - |
| Mercury | Under 10 ug/L | 3.513 | 99,96 | 99,74 | 99,99 |
| | Above 10 ug/L | 1 | 0,04 | 0,01 | 0,26 |
| Arsenic | Under 35 ug/L | 3.206 | 91,04 | 89,2 | 92,6 |
| | Between 35 y 100 ug/L | 332 | 8,45 | 6,91 | 10,3 |
| | Above 100 ug/L | 21 | 0,51 | 0,26 | 0,99 |

Table 8. Logistic regression for risk of having an arsenic level above 35 ug/L.

| Variable | Category | OR | CI 95% | p-value |
|------------------|------------------------------|------|--------------|---------------|
| Age range | 18-25 | 0.99 | Ref | 0.98 |
| | 25-44 | | 0.71 1.38 | |
| | 45-64 | 0.62 | 0.44 0.88 | <0.05 |
| | ≥65 | 0.39 | 0.26 0.59 | <0.05 |
| Sex | Male | 0.76 | Ref | <0.05 |
| | Female | | 0.60 0.96 | |
| Smoking | No smoker | 0.91 | Ref | 0.58 |
| | Ex-smoker | | 0.67 1.25 | |
| | Active Smoker | 1.09 | 0.84 1.42 | 0.50 |
| Fish consumption | Less once per month or never | 0.92 | Ref | 0.625 0.28 |
| | <3 times per month | | 0.67 1.26 | |
| | 1 time per week | 0.85 | 0.63 1.14 | <0.05 |
| | >1 time per week | 2.11 | 1.48 3.01 | |
| Macrozone | Center | 3.78 | Ref | <0.05 |
| | North | | 2.82 5.08 | |
| | RM | 1.03 | 0.67 1.57 | 0.88 |
| | South | 1.11 | 0.78 1.59 | 0.53 |

The study finds that lead levels are higher in males and older age groups. This could be due to occupational exposures or lifestyle factors that are more common among these demographics. Lead exposure is associated with developmental delays, learning difficulties, and lower IQ. In adults, lead exposure can result in hypertension, renal impairment, and reproductive issues⁵.

The study observes higher mercury levels in individuals from the northern macrozone and those with higher fish consumption. This is consistent with the known sources of mercury exposure, such as industrial pollution and dietary intake from fish. Mercury exposure, especially in the form of methylmercury, can impair neurological development in fetuses and young children. In adults, mercury exposure can lead to cognitive and motor dysfunction, as well as cardiovascular problems⁶.

The study finds that smokers have higher cadmium levels compared to non-smokers, reflecting the impact of smoking on cadmium exposure. Cadmium accumulates in the kidneys, where it can cause tubular damage and impair renal function. It also interferes with calcium metabolism, leading to bone demineralization and increased risk of fractures.

The findings of this study have significant public health implications. The elevated levels of arsenic exposure in certain regions and demographics underscore the need for targeted public health interventions. Specifically, efforts should be made to reduce arsenic exposure in the northern regions and among younger populations. This could involve measures such as improving water quality, regulating industrial emissions, and promoting dietary changes to reduce arsenic intake.

The study also highlights the importance of ongoing biomonitoring to track exposure levels and identify emerging risks. Public health policies should be informed by the latest data on metal exposure to ensure that interventions are effective, and resources are allocated where they are most needed. Additionally, public awareness campaigns about the sources and risks of metal exposure are crucial. Educating the public about how to

minimize exposure, particularly through diet and environmental factors, can help reduce the health risks associated with heavy metal exposure.

When compared to data from the Centers for Disease Control and Prevention (CDC) in the United States, the Chilean population shows some interesting differences in metal exposure levels. The study finds that lead levels are lower in the Chilean population compared to the U.S. population. This could be due to differences in environmental regulations, industrial activities, or other factors that influence lead exposure. For cadmium and mercury, the exposure levels in the Chilean population are similar to those observed in the U.S. population. This suggests that the sources and pathways of exposure for these metals may be similar in both countries. However, the study finds that arsenic levels are higher in the Chilean population at the 50th and 75th percentiles. This highlights the need for continued monitoring and intervention to address arsenic exposure in Chile¹⁴.

The study underscores the importance of further research to explore the long-term health effects of metal exposure and to identify additional factors influencing exposure levels. Future studies should consider the impact of occupational exposure, lifestyle factors, and regional environmental policies on metal exposure. Additionally, research should focus on vulnerable populations, such as children and pregnant women, who may be more susceptible to the toxic effects of heavy metals. Longitudinal studies that track exposure levels over time and correlate them with health outcomes would provide valuable insights into the chronic effects of metal exposure.

The strengths of this study include its use of a large, nationally representative sample, which enhances the generalizability of the findings to the broader Chilean population. The comprehensive analysis of multiple metals and the consideration of various demographic and lifestyle factors provide a detailed understanding of exposure patterns. Additionally, the use of robust statistical methods, such as quantile regression and logistic regression, allows for a nuanced analysis of the data. However, the study also has some

limitations. The cross-sectional design limits the ability to infer causality between exposure and health outcomes. The reliance on self-reported data for certain variables, such as dietary habits and smoking status, may introduce reporting bias. Furthermore, the study does not account for potential confounding factors, such as occupational exposure, which could influence the observed associations.

Conclusion

This study demonstrates that the population's exposure to Cadmium, Lead, and Mercury is at percentile levels in the lowest range, below the reference value according to the exposure vigilance guidelines published by the Ministry of Health(4) (Table 2, Table 3, and Table 4). From the stratified analysis, no significant differences are observed for cadmium and mercury according to the socio-demographic variables in which stratified analysis was performed.

The study's comprehensive analysis of the levels of arsenic, lead, mercury, and cadmium in the Chilean population, and the identification of factors associated with elevated exposure levels, provide valuable insights for public health officials, policymakers, and researchers. The findings emphasize the importance of ongoing biomonitoring and public health interventions to protect the population from the harmful effects of heavy metal exposure. As Chile continues to develop and industrialize, it is crucial to address the environmental and public health challenges posed by metal exposure to ensure a healthy and sustainable future for all its citizens.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) used Copilot in order to improve the spelling to better readiness. After using this tool/service, the author(s) reviewed and edited the

content as needed and take(s) full responsibility for the content of the publication.

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