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Genotoxicity in humans exposed to arsenic, lithium, and boron in drinking water in the Bolivian Andes—A cross sectional study

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Abstract

Elevated concentrations of arsenic, lithium and boron in drinking water have already been reported in Bolivia. Arsenic is known to cause genotoxicity but that caused by lithium and boron is less well known. The aim of the present cross-sectional study was to evaluate potential genotoxic effects of exposure to arsenic, while considering exposure to lithium and boron and genetic susceptibility. Women ($n = 230$) were recruited in villages located around Lake Poopó. Exposure to arsenic was determined as the sum of concentrations of arsenic metabolites inorganic arsenic, monomethylarsonic acid (MMA), and dimethylarsinic acid (DMA) in urine. Exposure to lithium and boron was determined based on their concentrations in urine. Genetic susceptibility was determined by *GSTM1* (glutathione S-transferase-mu-1) and *GSTT1* (glutathione S-transferase-theta-1) null genotypes and *AS3MT* (Arsenite Methyltransferase) rs3740393. Genotoxicity was measured in peripheral blood leukocytes using the comet assay. The geometric means of arsenic, lithium, and boron concentrations were 68, 897, and 3972 $\mu\text{g/L}$, respectively. *GSTM1* and *GSTT1* null carriers had more DNA strand breaks than gene carriers ($p = .008$, $p = .005$). We found no correlation between urinary arsenic and DNA strand breaks ($r_s = .03$, $p = .64$), and only a weak non-significant positive association in the adjusted multivariate analysis ($\beta = .09 [-.03; .22]$, $p = .14$). Surprisingly, increasing concentrations of lithium in urine were negatively correlated with DNA strand breaks ($r_s = -.24$, $p = .0006$), and the association persisted in multivariate analysis after adjusting for arsenic ($\beta = -.22 [-.36; -.08]$, $p = .003$). We found no association between boron and DNA strand breaks. The apparent protective effect of lithium merits further investigation.

KEYWORDS

arsenic, Bolivia, boron, genotoxicity, glutathione S-transferases, lithium

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1 | INTRODUCTION

High concentrations of arsenic have been documented in surface and groundwater in 14 out of 20 Latin American countries representing a health threat to 14 million people across the South American continent (Bundschuh et al., 2012). Elevated concentrations of arsenic, lithium and boron have also been reported in drinking water in Argentina, Chile and Bolivia, that is, in the southern part of the continent (Concha et al., 2010; Munoz et al., 2013; Ramos et al., 2012).

Chronic arsenic exposure is a risk factor known to have many adverse effects on health, including causing lung, bladder, and skin cancers (Rahaman et al., 2021). More recently, cohort studies reported cardiovascular diseases in adults (Balakumar & Kaur, 2009; Kuo et al., 2022) and immunotoxic effects in children (Raqib et al., 2009; Zheng et al., 2023). Less is known about the effects on health of chronic exposure to lithium and boron through water consumption (Cortes et al., 2011). Neither lithium nor boron have been classified by the International Agency for Research on Cancer (IARC). Genotoxicity data on lithium collected during in vitro, animal and human studies are unclear; several studies were negative, but some studies were positive and indicated a clastogenic effect, at least at high levels of exposure (Hadrup et al., 2022). Studies of newborns in the Andes have shown a negative impact of lithium on fetal growth and newborn weight potentially linked with impairment of thyroid and calcium homeostasis (Harari et al., 2016; Harari, Bottai, et al., 2015; Harari, Langeen, et al., 2015). Exposure to lithium in women in the Andes has been shown to impair thyroid function (Broberg et al., 2011). A recent review of studies of boron genotoxicity indicated that boron-containing compounds are not genotoxic (Hadrup et al., 2021), but postnatal exposure to boron in children in the Andes has been associated with impaired infant growth (Hjelm et al., 2019).

In the Bolivian highlands, geogenic arsenic is found in groundwater used for human consumption and concentrations as high as 500 µg/L have been measured in villages located around Lake Poopó (De Loma et al., 2019; Munoz et al., 2015; Ramos et al., 2014), much higher than the level recommended by World Health Organization (WHO) 10 µg/L. Groundwater in the Bolivian highlands was also found to contain elevated concentrations of lithium, frequently above 4300 µg/L (Lima et al., 2021; Munoz et al., 2013; Steinmetz, 2017). There are no international health based standards for lithium concentrations in drinking water, but the health based screening level used in the USA is 10 µg/L and the drinking-water only threshold is 60 µg/L (Lindsey et al., 2021). High concentrations of boron with a mean level in drinking water of around 1900 µg/L have been measured in the Bolivian highlands (Lima et al., 2021; Munoz et al., 2013). Health Canada proposes a maximum acceptable concentration of 2000 µg/L for drinking water (HealthCanada., 2020).

In previous studies in the Bolivian Andes, we already documented human exposure to arsenic (De Loma et al., 2019) plus associations with certain adverse biological effects such as increased oxidative stress and altered telomere length (De Loma, Kraiss, et al., 2022). We also identified a genetic adaptation to eliminate arsenic via efficient methylation driven by variants of the arsenic methylation

gene (*AS3MT*) in indigenous Andean populations, an adaptation that appears to modify susceptibility to arsenic toxicity (De Loma et al., 2019; De Loma, Vicente, et al., 2022; Li et al., 2012).

Metal and metalloid exposure can lead to oxidative stress, and hence to genotoxicity as evidenced by DNA strand breaks, which—as demonstrated by a recent meta-analysis—can be quantified using the comet assay (Qian et al., 2021). Still, very few studies have evaluated genotoxicity in relation to combined exposure to metals and metalloids. The aim of the present cross-sectional study was to evaluate the potential genotoxic effects of exposure to arsenic, considering simultaneous exposure to lithium and boron, as well as genetic susceptibility. We also assessed genetic variation in *AS3MT* and analyzed gene deletions involving the glutathione S-transferases *GSTM1* and *GSTT1* that have previously been correlated with increased genotoxicity linked to arsenic exposure (Fuciarelli et al., 2009; Jin et al., 2021).

2 | POPULATION AND METHODS

2.1 | Study participants and data collection

This study is nested in a project that started in 2015 including people from villages located around Lake Poopó in the southern part of Oruro administrative department in Bolivia to document the impact of chronic exposure to arsenic. The context and the population are described in detail in De Loma et al. (2019). Briefly, Lake Poopó is part of the endorheic basin of the Bolivian Altiplano and is surrounded by volcanoes of the Cordillera. Due to geogenic factors, the groundwater used by the population as a source of drinking water is contaminated by medium to high levels of arsenic, lithium, and boron (Lima et al., 2021; Munoz et al., 2013; Ramos et al., 2012). The 10 villages involved in this study were Poopó, Pampa Aullagas, Villañeque, Llapallapani, Bengal Vinto, Santuario de Quillacas, Sevaruyo, Puñaca, Crucero Belén and San Felipe de Chaytavi. With the help of health and local authorities and medical professionals, meetings were held before and during recruitment to provide information about the study.

Study participants came from two indigenous communities: one Uru Murato and the other Aymara-Quechua. The Aymara-Quechua population is much larger than the Uru Murato population, which explains the difference in sample size between the ethnic groups. Both ethnic groups depend on agriculture and trade in handcrafts.

The women recruited were a convenience sample from the study area. Our study focused on women because they spend more time at home and are less occupationally exposed to toxic metals than men due to other activities such as mining. After receiving information provided by a local physician about the objectives and methods of the project, women who lived permanently in the villages were invited to participate on a voluntary base. The sampling period was from 2015 to 2018 and included six successive field trips. All study participants gave their written informed consent to take part in the study. Ethical approval was obtained from *Comité Nacional de Bioética* in Bolivia and from the Regional Ethics Committee in Stockholm, Sweden (De Loma et al., 2019).

2.2 | Interviews and biological samples

After interviewing the women to collect information on their occupation, family status, life style, diet and health, we performed anthropometric measurements and collected biological samples. Two whole venous blood samples (approximately 3 mL each) were collected using BD Vacutainer EDTA tubes (Becton Dickinson, USA) for the assessment of genotoxicity and genotyping. Blood samples were labeled and stored at 4°C until they were transported to the Genetic Institute in La Paz, Bolivia, where they were prepared as described below. The urine samples were collected after explaining how the women should use dedicated wipes for local cleaning and how to collect midstream urine to avoid contamination. The midstream urine samples were labeled and immediately stored at -20°C in a portable freezer (ARB, Alice Springs, Australia) until our return from the field, when they were transported from Bolivia to Sweden frozen on dry ice. The samples were analyzed at the Institute of Environmental Medicine, Karolinska Institutet, Sweden, to determine the presence of trace elements. During each field trip, 3 days were dedicated to sampling making it possible to perform the comet assay back in the laboratory with a maximum time lag of 3 days.

2.3 | Genetic susceptibility

Genomic DNA was obtained from whole blood using Wizard Genomic DNA Purification Kit (Promega, Madison, WI). Isolated DNA was suspended in Tris-EDTA buffer (pH 8.0) and stored at -20°C. The null frequencies (referring to homozygous deletion of the gene) of *GSTM1* and *GSTT1* were analyzed simultaneously in a single assay using the multiplex PCR approach, as described by Abdel-Rahman et al. (1996) with some modifications (Cuenca et al., 2019). The *AS3MT* single nucleotide polymorphism (rs3740393), previously linked to arsenic metabolism (Engstrom et al., 2011), was genotyped as described in De Loma, Kraus, et al. (2022).

2.4 | Alkaline comet assay

The comet assay was performed in blood cells using established protocols (Liao et al., 2009; Tice et al., 2000). Briefly, microscope slides were covered with a thin layer of 1.5% agarose. For each sample, an aliquot of 30 µL of whole blood was mixed with 120 µL 0.5% low melting point agarose, loaded onto the slide, covered with a coverslip and stored at 4°C for 10 min. The coverslip was then removed and the cells were lysed in an ice-cold lysis buffer (2.5 M NaCl, 100 mM EDTA, 10 mM Tris-HCl, pH 10, 1% Triton X-100 and 10% DMSO) for 1 h at 4°C. The slides were then placed in alkaline buffer (1 mM EDTA, 300 mM NaOH, pH 13) for 20 min to allow unwinding of the DNA. Electrophoresis was performed at 4°C for 20 min (25 V, 0.66 V/cm), the slides were then washed 3 times for 5 min in a cold neutralization solution (0.4 M Tris-HCl, pH 7.5), immersed in absolute ethanol for 1 min and then dried at room temperature. The whole

procedure was carried out in dimmed light to minimize artifactual DNA damage. After staining with ethidium bromide (20 µg/mL, Sigma, St Louis, MO), 100 comets were scored per sample using a fluorescence microscope (Leica DMLB) and Comet assay IV software (Perceptive Instruments). The results are expressed as % DNA in tail and tail moment (tail length × % DNA in the tail), representing DNA strand breaks. Positive and negative controls were always included. For the positive control, the slides were exposed to hydrogen peroxide (50 µM), after layering of cells and before lysis. For the negative control, the cells were exposed to the solvent (Milli-Q water) with no added chemicals. Each electrophoresis run was only considered valid if the negative and positive controls yielded the expected results.

2.5 | Multi-element analysis

Trace elements in the urine samples were identified at the Institute of Environmental Medicine using ICPMS (Agilent 7700×, Agilent Technologies, Waldbronn, Germany). To guarantee the analytical accuracy of the measurements, commercial reference materials purchased from Seronorm™ and NIST were included in all runs. Detection limits and details concerning the analytical methodology are described in a previous publication (De Loma et al., 2019). Exposure to arsenic was determined as the sum of the concentration of arsenic metabolites, inorganic arsenic, monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) in the urine. The concentrations of arsenic metabolites in urine were determined using online high-performance liquid chromatography with hydride generation and ICPMS (HPLC-HG-ICPMS) (De Loma et al., 2019). To account for urine dilution, spot urine metal concentrations were adjusted to average urinary osmolality values (727 mOsm/kg).

2.6 | Statistical analyses

The DNA strand breaks measured as % DNA in tail and tail moment are the main outcome of this study. The distributions of both measurements were analyzed graphically as right skewed distributions that were closer to normal after log transformation. Arsenic, lithium and boron urinary concentrations also had right skewed distributions. For these reasons, in subsequent analyses, we decided to use the geometric means of these variables.

DNA strand breaks were evaluated relative to the characteristics of the study participants, life style and exposure (age, weight, height, number of children, food habits, occupation, concentrations of arsenic, lithium and boron, field trip, time lag (in days) between sampling and the comet assay) using *t*-tests, a Kruskal-Wallis test, Pearson *r* and Spearman *r_s* depending on data distribution.

The variables found to be statistically associated with DNA strand breaks with a *p*-value lower than .1 were included in the subsequent multivariate analysis. In addition, as the concentration of arsenic is known to be a potential determinant of genotoxicity in exposed populations, it was kept in all the models. We included a random effect in

TABLE 1 Characteristics of the women included in the study ($N = 202$).

	N or mean (SD or 95%CI)
Age years	38.17 (15.1)
Weight kg	62.14 (12.0)
Height cm	1.50 (0.057)
Number of children	2.97 (2.58)
Alcohol (yes/no)	67/135
Tobacco (y/n)	6/196
Coca mate (y/n)	135/65
Coca chewing (y/n)	146/54
Eat meat (y/n)	107/93
Eat fish (y/n)	93/106
Hemoglobin g/dL	15.1 (1.7)
Occupation	
Administrative staff	7
Farmer	56
House wife	57
Handicraft	25
Teacher	29
Health worker	27
Arsenic $\mu\text{g/L}^{*\S}$	67.9 (CI 61.5–74.9)
Lithium $\mu\text{g/L}^{\S}$	897 (811.1–992.1)
Boron $\mu\text{g/L}^{\S}$	3972 (3649–4324)
GSTM1 null genotype	72 (35.6%)
GSTT1 null genotype	167 (82.7%)
AS3MT rs3740393	
CC	111 (60.7%)
GC	67 (36.6%)
GG	5 (2.7%)
Comet tail %	8.69 (CI 7.81–9.68)
Comet tail moment %	1.43 (CI 1.18;1.72)

*Arsenic (sum of AsIII, AsV, MMA, DMA).

$\S\mu\text{g/L}$ adjusted for average urinary osmolality (727 mOsm/kg).

the models due to the fact that all the samples were collected during six separate field trips, in addition, not all samples were collected on the same day within each trip, all but one field trip took place at the end of the winter or in early spring. A parsimonious model was obtained using a supervised backward stepwise mixed regression model based on AIC criteria (Greenland et al., 2016). All statistical analyses were performed in R version 4.2.0.

3 | RESULTS

3.1 | Characteristics of the study participants

Of the 230 women who participated in the study, the comet assay was performed successfully on 202. The individual characteristics of

TABLE 2a DNA strand breaks, measured as %DNA in tail, in relation to individual characteristics (categorical variables).

	n	%DNA in tail	p value
Ethnicity			NS
Uru	33	10.90	
Aymara/Quechua	169	8.31	
Alcohol			.004
Yes	67	10.71	
No	135	7.83	
Tobacco			.03
Y	6	16.08	
N	196	8.53	
Coca mate			NS
Y	135	8.81	
N	65	8.16	
Coca chewing			NS
Y	146	8.29	
N	54	9.48	
Eat meat			.06
Y	107	7.83	
N	93	9.57	
Eat fish			<.0001
Y	93	11.26	
N	106	6.73	
Occupation			.002
Services*	63	11.06	
Others	138	7.80	
GSTM1			.004
Null genotype	72	10.60	
Gene carrier genotype	130	7.78	
GSTT1			.002
Null genotype	167	9.23	
Gene carrier genotype	35	6.52	
AS3MT rs3740393			NS
CC	111	9.22	
CG	67	8.61	
GG	5	8.10	

*Service work means administrative, education, health workers.

the 202 women are listed in Table 1. Of the 202 women, 169 identified themselves as Aymara-Quecha, and 33 as members of the Uru Murato ethnic group.

Geometric mean concentrations of arsenic, lithium and boron in urine were 67.9, 897.1, and 3972 $\mu\text{g/L}$, respectively (Table 1).

The geometric mean proportions of strand breaks, measured as the % of DNA in the tail or the tail moment were 8.7% (95% confidence interval, CI: 7.8–9.7) and 1.4 (CI95%: 1.2–1.7). The two measurements were strongly correlated (Pearson $r = .94$; CI: 92.5–95.6), which is why we only used the % of DNA in the tail in subsequent analyses.

3.2 | Univariate analysis

Null genotypes of *GSTM1* and *GSTT1* were both associated with a higher % of DNA in the tail. For *GSTM1* the geometric mean was 7.8% for gene carriers versus 10.6% ($p = .004$) for null carriers. Similarly, for *GSTT1* gene carriers, the geometric mean was 6.5% versus 9.2% ($p = .002$) (Table 2a). Age, alcohol consumption, smoking tobacco, eating fish and working in the service sector were found to be statistically correlated with the % of DNA in the tail (Table 2a). No correlation was found with weight, height, ethnic origin, the traditional use of coca leaves to make tea or to chew, or with the *AS3MT* genotype.

No correlations were found between arsenic or boron concentration in urine and the % of DNA in the tail ($r_s = .03$, $p = .64$; $r_s = -.11$, $p = .13$, respectively) (Table 2b). Surprisingly, we found lithium to be negatively correlated with the % of DNA in the tail ($r_s = -.24$; $p = .0006$) (Table 2b and Figure 1).

We observed a decrease in the proportion of strand breaks with an increase in the number of days between sampling in the field and

TABLE 2b DNA strand breaks, measured as %DNA in tail, in relation to individual characteristics (quantitative variables).

	Spearman Rho	<i>p</i>
Age (years)	-0.14	.04
Weight (kg)	0.02	NS
Height (cm)	0.11	NS
Number of children	-0.04	NS
Hemoglobin (g/dL)	-0.08	NS
Arsenic [§]	0.03	NS
Lithium [§]	-0.24	.0006
Boron [§]	-0.11	NS

[§]μg/L adjusted for average urinary osmolality (727 mOsm/kg).

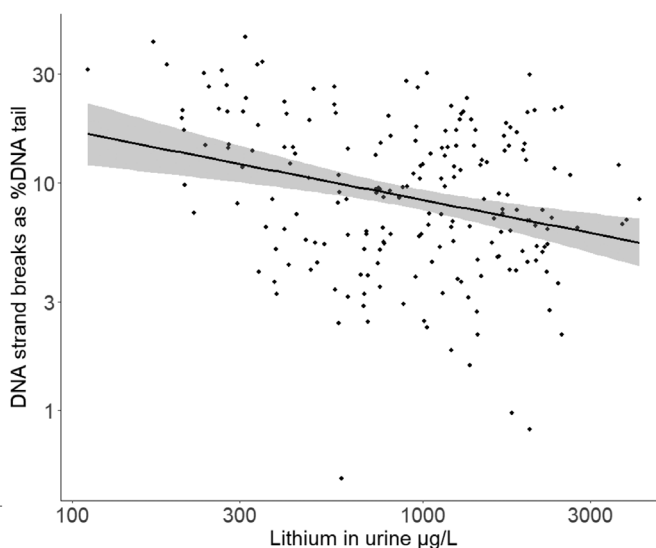
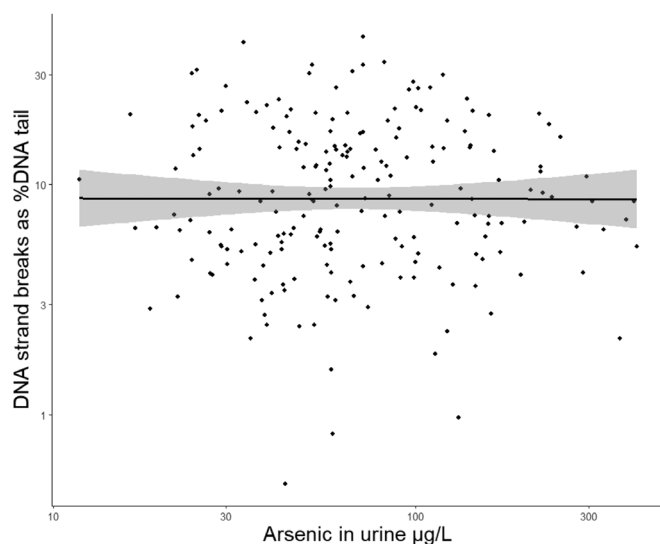


FIGURE 1 Scatter plot of the relation between arsenic (left panel) and lithium (right panel) concentrations in urine, and DNA strand breaks measured as %DNA tail with fitted regression line and 95% confidence intervals (both axes on log10 scale).

use of the comet assay (hereafter “day lag”) (Kruskal–Wallis test; $p < 10^{-3}$, Figure 2). We also observed a difference in the % of DNA in tail between the six different field trips ($p < 10^{-3}$).

3.3 | Multivariate analysis

To deal with the effect introduced by the different conditions related to field trips and to account for possible confounders, a mixed regression model including a random effect was used. This strategy considerably reduced the number of variables related to variations in the % of DNA in the tail. The results of the most parsimonious model, including arsenic concentrations, are listed in Table 3. Although not

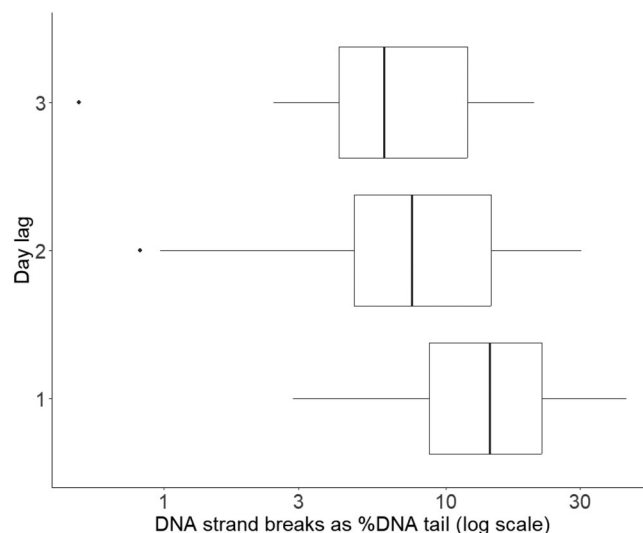


FIGURE 2 Boxplot of the comet tail proportion depending on the day lag between sampling and comet assay.

TABLE 3 Univariate and multivariate mixed regression model.

Determinants	Univariate analysis		Multivariate*	
	Beta (95%CI)	p-value	Beta (95% CI)	p-value
Arsenic	−0.002 (−0.15;0.15)	.97	0.09 (−0.03;0.22)	.14
Lithium	−0.30 (−0.44;−0.16)	<.001	−0.22 (−0.36;−0.08)	.003
Age	−0.01 (−0.02;−0.00)	.002		
Eat meat	−0.20 (−0.41;−0.01)	.062		
Eat fish	0.52 (0.31;0.72)	<.001		
Drink alcohol	0.31 (0.09;0.53)	.006		
Smoke tobacco	0.63 (0.01;1.26)	.045		
Occupation (services vs. others)	0.35 (0.12;0.58)	.002		
GSTM1 (null vs. positive)	0.31 (0.09–0.53)	.005		
GSTT1 (null vs. positive)	0.35 (0.07–0.62)	.014		
Day lag				
2	−0.53 (−0.79;−0.28)	<.001	−0.04 (−0.26;0.18)	.72
3	−0.71 (−0.99;−0.44)	<.001	−0.34 (−0.56;−0.12)	.003

*Mixed model with a random effect on field trip (conditional R^2 .52; marginal R^2 .059).

statistically significant, arsenic concentrations were weakly positively associated with the % of DNA in the tail ($p = .14$). The concentrations of lithium in urine and the time lag (in days) between sampling and the comet assay were associated with a reduction in the % of DNA in the tail. The variance explained by the fixed effects remained modest, with a marginal R^2 of 5.9%.

4 | DISCUSSION

To our knowledge, this is the first study to evaluate the genotoxicity of elements in drinking water in Bolivian populations. Surprisingly, we observed no strong link between exposure to arsenic and DNA damage. Arsenic causes DNA damage such as aneuploidy, micronuclei formation, chromosomal aberrations, deletions, sister chromatid exchange and DNA-protein cross-linking (Ozturk et al., 2022). Importantly, even at low concentrations, arsenic can induce DNA strand breaks (Martinez et al., 2005; Ozturk et al., 2022). Arsenic genotoxicity mechanisms include the formation of reactive oxidative species and inhibition of DNA repair, such as PARP-1 activity, an enzyme critically involved in oxidative DNA damage repair (Palma-Lara et al., 2020). As concluded in a meta-analysis (Qian et al., 2021), the alkaline comet assay on leukocytes or peripheral blood mononuclear cells could be an effective method to biomonitor genotoxicity in populations exposed to arsenic.

One possible explanation for the lack of arsenic genotoxicity in our study population could be that the women carry an *AS3MT* genotype linked to an efficient arsenic metabolism that reduces toxicity (De Loma, Kraiss, et al., 2022). Other studies have shown that carriers of *AS3MT* genetic variants—linked to efficient metabolism—have a lower risk of arsenic-related skin lesions (Pierce et al., 2012), and telomere or mitochondrial DNA alterations (De Loma, Kraiss, et al., 2022;

Li et al., 2012). We found no influence of *AS3MT* genotype in this analysis, which could be due to limited power, as 79% of the women were shown to carry the efficient metabolizing genotype (De Loma, Kraiss, et al., 2022). However, other, as yet unknown, factors that are specific to the Andes populations could also confer protection to DNA strand breaks. One such factor could be parallel exposure to lithium.

Increased concentrations of lithium—but not of boron—in urine were associated with fewer DNA strand breaks. We found no association between arsenic and DNA strand breaks in the non-parametric and univariate test, but when we included lithium in the multivariate analysis, arsenic in urine was weakly associated with more DNA strand breaks, suggesting that lithium mitigates the toxic effects of arsenic. Very few studies have been conducted on lithium and genotoxicity to date, and those studies included only a very small number of patients who were treated with lithium compounds at higher doses of lithium than in the present study (Hadrup et al., 2022). A recent review reported that some studies on humans provide evidence for an association between exposure to lithium substances and genotoxicity; however, whether the effect was actually due to lithium substances remains unknown, and better-designed human studies are required to enable firm conclusions to be drawn (Hadrup et al., 2022). Few studies have been conducted of the effect of lithium on DNA repair. Experimental studies detected a stabilizing effect of lithium on DNA, via promotion of the DNA strand NHEJ repair pathway by upregulating ligase IV (Yang et al., 2016).

As also reported by other authors, in the present study, the *GSTM1* and *GSTT1* null genotypes were both associated with more DNA strand breaks in the univariate analysis. The *GSTM1* null genotype has been suggested as a potential susceptibility biomarker to identify people who are not prone to arsenic poisoning (Jin et al., 2021). However, in our study, once adjustments were

made for lithium exposure and for the time lag (in days) between sampling and the comet assay in the lab, *GSTM1* and *GSTT1* genotypes were no longer statistically associated in the multivariate analysis.

The present study had several limitations as it was performed under difficult field conditions. Under the assumption exposure was chronic, we only collected spot urine samples. This assumption was supported by the interviews in which we asked how long the participants had been living in the area. We subsequently discovered that the time lag between when the samples were taken and when the comet assay was performed in the laboratory influenced the results. Longer time lags were associated with fewer DNA strand breaks. We are unable to find an explanation for this finding. The influence of the field trips on our results may be related to the environmental conditions or to laboratory batch effects, which are difficult to characterize in cohort studies and hence require follow up studies.

5 | CONCLUSION

This is the first study to investigate the impact of exposure to arsenic and lithium on genetic stability in humans in Bolivia that combines quantitative assessment of exposure and a comprehensive assessment of genotoxicity. The most significant finding was the absence of arsenic genotoxicity. Our observation of a reduction in the number of DNA strand breaks associated with exposure to lithium underlines the importance of including multiple element analysis when assessing genotoxicity in drinking water.

Our observations warrant more research into lithium exposure and more research on the impact of arsenic on the health of these specific populations in the Bolivian Andes.

Given the genotoxicity and potential adverse health effects related to arsenic in drinking water in our study region, immediate measures should be taken to reduce exposure, particularly that of vulnerable populations with a different and non-Andean origin, specifically children and pregnant women.

AUTHOR CONTRIBUTIONS

Noemi Tirado: Funding acquisition, investigation, formal analysis, visualization, writing—original draft. **Josué Mamani:** Investigation, writing—review & editing. **Jessica De Loma:** Writing—review & editing. **Franz Ascui:** Investigation, visualization, review & editing. **Karin Broberg:** Funding acquisition, conceptualization, formal analysis, writing—original draft, review & editing. **Jacques Gardon:** Formal analysis, writing—original draft, writing—review & editing.

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CONFLICT OF INTEREST STATEMENT

The authors confirm they have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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