

## ARTÍCULO ORIGINAL

# PREVALENCE OF ARTERIAL HYPERTENSION AND CARDIOVASCULAR RISK FACTORS IN A RURAL POPULATION EXPOSED TO ARSENIC IN ARGENTINA

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This study was presented at the XXXV Congreso Nacional de Cardiología (Rosario, 2017); 72.º Congreso Argentino de Bioquímica (Buenos Aires, 2017); Congreso de las Enfermedades Cardiovasculares SEC 2018 (Sevilla, España); XXVI Congreso Nacional de Medicina (Buenos Aires, 2018); XXXVII Congreso Nacional de Cardiología de la Federación Argentina de Cardiología (Rosario, 2019).

## ABSTRACT

**Objective.** To determine the prevalence of arterial hypertension and cardiovascular risk factors (CRF) in a rural population exposed to arsenic (As) in drinking water in the province of Tucumán, Argentina. **Materials and methods.** A total of 352 adult inhabitants participated. Consumption of arsenic in drinking water was measured. Blood pressure, smoking, risk and harmful alcohol consumption, salt intake, physical activity, body mass index, glycemia and dyslipidemia were evaluated. Cardiovascular risk was calculated using the Framingham score. **Results.** The population was divided into Exposed Group (EG) n=90 and Non-Exposed Group (NEG) n=262. The prevalence of hypertension was 48.9 and 51.1% in each group, respectively; for smoking it was 31.1 and 39.7%; for risky alcohol consumption, 22.2 and 17.9%; for harmful alcohol consumption, 36.6 and 36.6%; for salt intake, 100 and 100%; for physical activity, 16.7 and 18.7%; for being overweight, 43.3 and 43.9%; for obesity, 25.5 and 25.6%; for diabetes, 24.4 and 32.8%; and for dyslipidemia, 58.9 and 66.4%. The scores for low, moderate, or high-risk were 50; 21.1; and 28.9% in the EG, and 54.6; 19.1 and 26.3% in the NEG, respectively. **Conclusions.** Exposure to As does not affect the prevalence of CRFs. We identified a rural population in a vulnerable condition with high CRFs. The National Risk Factor Survey does not reflect what happens in rural areas. The Framingham scale is consistent with the found CRFs. The implementation of health promotion policies is required to improve the prognosis of suffering cardiovascular events in the short and medium term.

**Keywords:** Arsenic, Cardiovascular Risk Factors, Rural Population, Argentina. (Source: MeSH NLM).

## INTRODUCTION

According to the World Health Organization (WHO), cardiovascular disease (CVD) is one of the major public health concerns worldwide and is the leading cause of mortality<sup>(1)</sup>. Cardiovascular risk factors (CRF) are conditions present in an individual that increase the probability of suffering a CVD, including arterial hypertension (HT), smoking, hypercholesterolemia, etc. In Argentina, one out of every three adults have HT, however, four out of ten are unaware of their condition, which makes it the main CRF. It is also the most important cause of stroke and the leading cause of death, disability and cognitive impairment, which causes high healthcare costs<sup>(2)</sup>.

Arsenic (As) and other metals are considered to be among the ten chemicals of major public health concern by the WHO, and some authors have linked them to cardiovascular disease. As it is a natural contaminant found in air, soil and water<sup>(3)</sup>. The Argentine Republic has natural waters with As contents exceeding 0.05 mg/L, as established by the Argentine Food Code (CAA), with an exposed population of approximately 1 million inhabitants living in rural

**Cite as:** Soria AG, Guber RS, Tefaha LM, Aragón FF, Romero CJ, Toledo RV, Sandoval NG, Áleman MN. Prevalence of arterial hypertension and cardiovascular risk factors in a rural population exposed to arsenic in Argentina. *Rev Peru Med Exp Salud Publica.* 2021;38(4):530-6. doi: <https://doi.org/10.17843/rpmesp.2021.384.9402>.

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**Received:** 02/09/2021  
**Approved:** 09/12/2021  
**Online:** 22/12/2021

areas<sup>(4)</sup>. The toxic effects of As depend on exposure, sex, age, genetic factors, among others. In addition, socioeconomic conditions may increase the susceptibility of the population to environmental toxicants<sup>(5)</sup>.

Several studies suggest that As exposure is associated with an increased risk of developing CVD<sup>(6)</sup>. Prolonged exposure to this metalloid may produce persistent and/or irreversible adverse cardiovascular effects. The main effects have been established in areas with high exposure; in contrast, the evidence for low-dose effects remains controversial regarding CVD. Also, pleiotropism of health effects has been reported, including hypertension, microcirculation damage, coronary and peripheral arterial disease, among others<sup>(7)</sup>.

The province of Tucumán, located in northwestern Argentina, is one of the most affected by As contamination in drinking water. The Graneros department is located in the southeast of the province, 120 km from San Miguel de Tucumán, the provincial capital. In a previous study, it was reported that the concentration of As in drinking water in this province fluctuates between 0.05 and 0.97 mg/L, as minimum and maximum values, respectively<sup>(8)</sup>. However, there is no information in our region on the relationship between As exposure and CRFs. The aim of this study was to determine the prevalence of arterial hypertension and cardiovascular risk factors (CRF) in a rural population exposed to As in drinking water in the province of Tucumán (Argentina).

## MATERIALS AND METHODS

### Study design and population

Descriptive, cross-sectional study that was conducted between February 2017 to December 2019. The calculated sample size was 322 considering a population of 1975 adults over 30 years old, according to the last Municipal Diagnosis of Graneros of 2015, with a confidence level of 95% and a power of 90%. In order to take an effective sample, 352 inhabitants of both sexes were included by simple random sampling.

We included people over 30 years of age, of both sexes, asymptomatic, who had been drinking water from wells for over 10 years, as long as the wells were dug by hand, since they generally have depths of less than 10 m (where arsenic is naturally present in shallow aquifers)<sup>(9)</sup>. We excluded individuals with preexisting cardiovascular disease such as coronary, cerebral, or peripheral atherosclerosis and pregnant women, in whom hypertensive disorders are multicausal. Individuals with partial residence in the area or who refused to sign the informed consent form were also excluded.

### KEY MESSAGES

**Motivation for the study:** In Graneros (Tucumán, Argentina), chronic arsenicism and cardiovascular disease are a public health problem that affects poor communities without access to the healthcare system.

**Main findings:** In this study we determined that there is a high prevalence of arterial hypertension (HT) and other cardiovascular risk factors, that exposure to As consumption does not affect HT prevalence and that the National Survey of Risk Factors does not reflect what occurs in rural areas such as Graneros.

**Implications:** The implementation of health promotion strategies with a multidisciplinary approach is required to improve the quality and prognosis of life of these inhabitants.

### Study variables and procedure

The complete medical history of each participant was registered and a manual sphygmomanometer (Silfa, CABA, Argentina) was used to measure blood pressure (BP). HT was defined as BP values  $\geq 140/90$  mm Hg and/or when the participants were currently using antihypertensive drugs (values according to the cut-off points established in the latest National Consensus between the Argentine Society of Arterial Hypertension, the Argentine Society of Cardiology, and the Argentine Federation of Cardiology)<sup>(10)</sup>.

Diabetes was registered by self-report or according to WHO diagnostic criteria. Physical activity was measured with a questionnaire following the WHO recommendations on healthy physical activity in adults aged 18 to 64 years.

Smoking was also registered, and individuals were categorized into nonsmokers and smokers. Alcohol consumption was classified according to regular daily consumption into: risky consumption: 20 to 40 g of alcohol per day in women, 40 to 60 g of alcohol per day in men; and harmful consumption: average regular consumption greater than 40 g of alcohol per day in women and more than 60 g per day in men<sup>(11)</sup>. Salt consumption was assessed by questions that inquired about the number of salt packets used per month, how many people eat, and whether they use the salt shaker at the table to add salt to food.

The weight and height of the individuals were determined using a Health-o-Meter Professional (USA) scale-measuring device with a capacity of 180 kg. Each subject was evaluated standing upright, with ankles together, shoulders relaxed and both arms at the sides of the body. Using the weight and height measures we calculated the body mass index

(BMI), and the nutritional status was categorized according to WHO criteria as: normal weight ( $BMI \geq 18.5 \text{ kg/m}^2 < 25 \text{ kg/m}^2$ ); overweight ( $BMI \geq 25 \text{ kg/m}^2 < 30 \text{ kg/m}^2$ ) and obese ( $BMI \geq 30 \text{ kg/m}^2$ )<sup>(10)</sup>.

Venous blood samples were collected after fasting for 10 hrs. to obtain serum, which was stored at  $-20 \text{ }^\circ\text{C}$  until its use for the determination of laboratory parameters. Glucose dosing was conducted using the optimized colorimetric method (Wiener Lab, Rosario, Argentina) following the manufacturer's instructions. For total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG), we used the optimized colorimetric method (Wiener Lab, Rosario, Argentina). Normal fasting glycemia was considered at glucose concentrations  $\leq 100 \text{ mg/dL}$ . Triglyceridemia was considered normal at values  $\leq 150 \text{ mg/dL}$  regardless of sex. Cholesterolemia was considered normal at values  $\leq 200 \text{ mg/dL}$  regardless of sex. Participants with values  $> 40 \text{ mg/dL}$  in men and  $> 50 \text{ mg/dL}$  in women were considered to have normal c-HDL.

Cardiovascular risk stratification was calculated using the Framingham score, which estimates the risk of ischemic heart disease in the next 10 years. This score takes into account seven variables: sex, age, BP, TC, LDL-C, smoking and diabetes. Three categories were considered:  $<10\%$  low risk; between 10 and 20% moderate risk; and  $> 20\%$  high risk<sup>(12)</sup>.

### Assessment of arsenic exposure

The participants attended with a water sample from the household well. Prior to collection, they were asked to wash a small plastic bottle with water three times, taking care not to expose the bottle to heat or sunlight. The As concentration was determined by the silver diethyldithiocarbamate method (AQAssay, GT Lab, Rosario Santa Fe, Argentina)<sup>(13)</sup>. The exposed group (EG) participants were considered as those with levels in drinking water higher than  $0.05 \text{ mg/L}$ , and those in the unexposed group (UEG) when the levels were lower than  $0.05 \text{ mg/L}$ <sup>(4)</sup>. These cut-off values are those established by the FAC, based on the fact that there are other regions in the world where arsenic concentrations in water are high (above the reference value of  $10 \text{ } \mu\text{g/L}$  recommended by the WHO), but are lower than  $50 \text{ } \mu\text{g/L}$ , and in these cases, the incidence of cancer attributed to arsenic consumption is difficult to detect in epidemiological studies<sup>(14)</sup>.

### Statistical analysis

The analysis was conducted using SPSS ver. 23.0 (IBM Co., Armonk, NY, USA) for Windows. The Kolmogorov-Smirnov test was used to determine the distribution of quantitative

variables. Qualitative variables were presented as relative frequencies with their respective 95% confidence intervals; the chi-square test was used to compare proportions. Quantitative variables were expressed as mean  $\pm$  standard deviation. Student's t-test was used to establish comparisons between two variables. A statistically significant association was established for a value of  $p < 0.05$ .

### Ethical considerations

The study was endorsed by the Research Ethics Committee of the National University of Tucumán and the National Council for Scientific and Technical Research Scientific and Technological Center CONICET-TUCUMAN (Resol. 7/2017). All participants signed the informed consent in which the details concerning the study and the procedures were explained, guaranteeing the anonymity and voluntariness of their participation.

## RESULTS

The population was invited to the Primary Health Care Center of Graneros (Tucumán, Argentina). According to the levels of As in drinking water, they were divided into two groups: EG ( $n=90$ , 37 females and 53 males) and UEG ( $n=262$ , 103 females and 159 males). The average As level measured in water was  $0.180 \pm 0.36 \text{ mg/L}$  (range:  $0.05\text{-}3.16 \text{ mg/L}$ ).

The demographic and social characteristics of the studied rural population are shown in Table 1. The age distribution in both groups was similar; approximately two thirds of the participants were over 50 years of age. The level of education was similar for both the EG and the UEG; approximately half of the participants were illiterate and almost half had only basic education. Informal work in primary activities (agriculture, livestock) was the main economic activity. These data show that the subjects are in a vulnerable situation.

Table 2 shows the analysis of the prevalence of risk factors for cardiovascular disease in the EG and UEG. The percentage of subjects with HT was high in both groups and no significant differences were found according to As exposure. Approximately one third of the surveyed subjects reported smoking habits in both EG and UEG. Regarding alcohol consumption, our results showed that half of the entire studied population ingested alcohol at levels corresponding to risky and harmful consumption, regardless of As exposure in drinking water. In addition, 100% of all participants claimed to consume table salt in excess. The analysis of metabolic variables showed a high prevalence of overweight and obesity (according to the BMI values

**Table 1.** Sociodemographic characteristics of the study population.

Variables	EG (n=90)		UEG (n=262)		p-value
	Absolute frequency	% (95% CI)	Absolute frequency	% (95% CI)	
Sex					
Male	53	58.9 (48.7-69.1)	159	60.7 (54.8-66.6)	
Female	37	41.1 (30.9-51.3)	103	39.3 (33.4-45.2)	0.764
Age (years)*	90	56.0 ± 13.58	262	57.67 ± 9.26	0.302***
Marital status					
Single	40	44.9 (34.6-55.2)	137	52.3 (46.3-58.3)	
Married	50	55.1 (44.8-65.4)	125	47.7 (41.7-53.7)	0.230**
Educational level					
None	40	44.7 (34.4-55.0)	107	40.8 (34.8-46.8)	
Primary school	41	45.9 (35.6-56.2)	120	46.0 (40.0-52.0)	0.723**
Secondary school / Higher	8	9.4 (3.4-15.4)	35	13.2 (9.1-17.3)	
Employment					
Laborer	46	51.2 (40.9-61.5)	87	33.3 (27.6-39.0)	
Retired/Pensioner	23	25.6 (16.6-34.6)	77	29.3 (23.8-34.8)	
Unemployed	10	11.8 (5.1-18.5)	19	7.3 (4.2-10.4)	0.002**
Several	11	12.2 (5.4-19.0)	79	30.1 (24.5-35.7)	

EG: exposed group, UEG: unexposed group. \* Mean ± standard deviation. \*\* Chi-square test. \*\*\* Student's t test.

established by the WHO), both in the group that ingested As in levels above those allowed by the FAC, and in the group that did so within acceptable values. On the other hand, no differences were found in the prevalence of physical activity among the groups studied. The prevalence of diabetes in the EG was similar to that reported by the UEG, and no significant differences were found. After the dyslipidemia analysis, we found that around 60% of the subjects in the EG and UEG presented some type of alteration of the lipid profile. The levels found were: TC 213.5 ± 46.8 mg/dL, LDL-C 143.0 ± 33.0 mg/dL, HDL-C 54.5 ± 10.5 mg/dL and TG 185.6 ± 56.2 mg/dL in the EG; and TC 207.2 ± 39.9 mg/dL, LDL-C 145.4 ± 32.4 mg/dL, HDL-C 49.9 ± 11.9 mg/dL, TG 206.4 ± 83.8 mg/dL for the UEG.

The results presented in Figure 1 show the percentages of the groups that had low, moderate or high risk according to the Framingham score: 50% (95% CI: 39.7-60.3), 21.1% (95% CI: 12.7-29.5) and 28.9% (95% CI: 19.5-38.2) of the EG and 54.6% (95% CI: 48.6-60.6), 19.1% (95% CI: 14.3-23.9) and 26.3% (95% CI: 21-31.6) of the UEG, respectively. No statistically significant differences were found between the two groups.

## DISCUSSION

In Graneros (Tucumán, Argentina), chronic arsenicism and cardiovascular disease are a public health problem

that affects poor communities without access to the health system. In this study we determined that in this population of northwestern Argentina there is high prevalence of arterial hypertension and other cardiovascular risk factors, and that exposure to consumption of water contaminated with As does not affect the prevalence. However, the National Survey of Risk Factors (ENFR) conducted by the National Institute of Statistics and Census of the National Secretariat of Health does not reflect what happens in vulnerable rural areas.

The sociodemographic indicators for the town of Graneros showed that approximately 50% of the population is poor and has low-skilled jobs. Other countries with impoverished rural populations showed similar indicators<sup>(15)</sup>. Water contaminated with As represents an important public health problem at the international level, especially in poor areas, with Argentina being one of the most affected countries<sup>(4)</sup>. Our results showed a high concentration of As in drinking water, which reveals that the population studied is susceptible to the toxic effects of chronic consumption of this metalloid, a situation that coincides with previous studies carried out in the area<sup>(10)</sup>.

One of the most interesting findings of this study was to demonstrate that the population presents high prevalence of CRF regardless of the exposure to elevated As levels. The prevalence of HT was similar in the EG and UEG and higher than what was found by the fourth ENFR published in 2019 in Argentina<sup>(16)</sup> and what was found in countries such as Mexico and Colombia<sup>(2,17,18)</sup>.

**Table 2.** Prevalence of cardiovascular risk factors in a rural population exposed to arsenic in northwestern Argentina.

Variables (%)	EG (n=90)		UEG (n=262)		p-value*
	Absolute frequency	% (95% CI)	Absolute frequency	% (95% CI)	
Arterial hypertension	44	48.9 (38.6-59.2)	134	51.1 (45.0-57.2)	0.712
Smoking	28	31.1 (21.5-40.7)	104	39.7 (33.8-45.6)	0.147
Risky alcohol consumption	20	22.2 (13.6-30.8)	47	17.9 (13.3-22.5)	0.336
Harmful alcohol consumption	33	36.6 (26.6-46.6)	96	36.6 (30.8-42.4)	0.716
Salt consumption	90	100	262	100	
Physical activity	15	16.7 (9.0-24.4)	49	18.7 (14.0-23.4)	0.666
Body mass index					
Overweight	39	43.3 (33.1-53.5)	115	43.9 (37.9-49.9)	0.913
Obesity	23	25.5 (16.5-34.5)	67	25.6 (20.3-30.9)	0.953
Diabetes	22	24.4 (15.5-33.3)	86	32.8 (27.1-38.5)	0.137
Dyslipidemias	53	58.9 (48.7-69.1)	174	66.4 (60.7-72.1)	0.198
Total cholesterol	41	45.5 (35.2-55.8)	126	48.1 (42.0-54.2)	0.678
Low density lipoproteins	84	93.3 (88.1-98.5)	230	87.8 (83.8-91.8)	0.143
High density lipoproteins	82	91.1 (85.2-97.0)	230	87.8 (83.8-91.8)	0.391
Triglycerides	63	70.0 (60.5-79.5)	193	73.7 (68.4-79.0)	0.501

EG: exposed group, UEG: unexposed group. \*Chi-square test.

In the literature, the association between As exposure and HT is not conclusive, due to the limited number of studies and because the dose-response relationship between the two variables is not clear. In a study conducted in Bangladesh with 1004 participants living in a rural area, with inclusion criteria similar to those of this study, no association was found between As consumption in drinking water and HT<sup>(19)</sup>. In contrast to these findings, there is empirical research that supports a relationship between As consumption and HT<sup>(20)</sup>.

Smoking and salt consumption are important CRFs for cardiovascular disease and HT. The prevalence of tobacco use in this population was greater than 30%, exceeding what was published in the ENFR (22%); salt consumption was highly prevalent. These findings are similar to those from a study on rural populations in northern India where higher tobacco consumption was found in association with low educational level and low family income<sup>(21)</sup>. As for salt consumption, although there was an intake decrease at the national level, when comparing the ENFR conducted in 2005 and the one published in 2019, it was not evident in the rural population studied<sup>(22)</sup>.

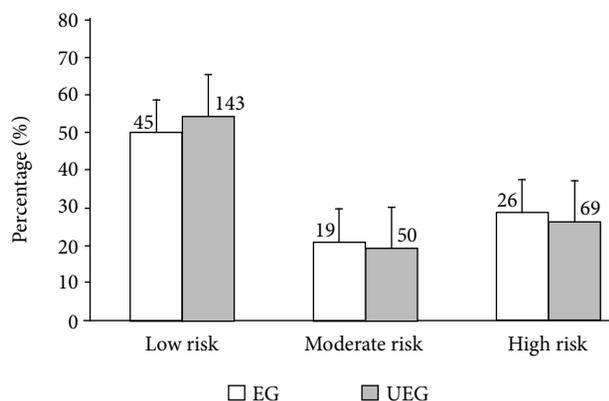
Uruguay and Argentina are the countries with the highest alcohol consumption in the region and projections indicate that it will continue to increase. The high percentage of individuals in both groups who consumed both risky and harmful levels of alcohol was noteworthy. Doval *et al.* in a

study on slum dwellers in Buenos Aires, reported that the alcohol problem was ten times higher than that published by the ENFR (8.4%), reaching values similar to those found in our study<sup>(23)</sup>. Other rural populations with similar characteristics also showed higher tobacco and alcohol consumption, related to a low socioeconomic status<sup>(21)</sup>.

The prevalence of physical activity was lower than that found by the ENFR (44.2%). On the other hand, the prevalence of overweight and obesity in this community was notably high with no differences in prevalence between the EG and UEG. Numerous studies document an increase of HT prevalence in overweight and obese individuals<sup>(24)</sup>.

Patients with diabetes may have multisystemic, microvascular and macrovascular complications. In addition, between 20-60% of people with diabetes have concomitant HT. The prevalence of diabetes in both groups was double of what published in the ENFR (12.7%), and was similar in the groups with or without arsenic exposure. The results are consistent with papers that document high prevalence of diabetes in populations with low education levels and low income<sup>(23)</sup>.

It is known that dyslipidemias are associated with an increased risk of cardiovascular events and that hypertensive patients with dyslipidemias tend to present greater arterial stiffness. Abnormal lipid profiles were detected in this population, being similar in the EG and UEG. The prevalence was approximately 60%, similar to what was found in



**Figure 1.** Percentages of subjects with low, moderate or high risk according to the Framingham score in the exposed (EG) and unexposed (UEG) groups. The numbers above the bars indicate the frequency for each one.

Vietnam and lower than what was reported in Colombia (87.7%), being more common in rural regions and in those with a low socioeconomic level<sup>(25, 26)</sup>.

The Framingham scale was used to identify the probability of experiencing a cardiovascular event in the following 10 years. Approximately 50% of both groups showed moderate and high risk, figures higher than those documented in studies carried out in a rural population in India, which was between 30-35%<sup>(27)</sup>.

This study has some limitations, it is a cross-sectional design that only allows establishing prevalence, but not causality, so the findings cannot be generalized. Therefore, further studies are needed to confirm the results, such as establishing the relationship between CRFs and the association with arsenic levels in urine as a marker of recent exposure, or in hair and nails, these samples being the only

evidence that the patient was chronically exposed to this metalloid. Furthermore, despite the precautions taken in the selection of the population with stable residence, it is difficult to ensure that there was no recall bias.

In conclusion, these results suggest that exposure to As in drinking water does not affect the prevalence of CRFs. It also identifies a rural population with a limited educational level and in a situation of social vulnerability with high prevalence of CRFs. In this context, the results of the ENFR carried out by the National Institute of Statistics and Census of the National Secretariat of Health do not reflect what happens in rural areas such as those of the Graneros Department of the province of Tucumán. On the other hand, the Framingham scale turned out to be an easily accessible instrument in primary health care, which reflects the CRFs found in a concordant manner. For this reason, the high prevalence of harmful habits requires the implementation of health promotion strategies, as well as treatment strategies with a multidisciplinary approach to improve both, the quality of life of these inhabitants and the prognosis of suffering cardiovascular events in the short and medium term.

**Author contributions:** SAG participated in the conception and design of the article. SAG, GRS, TLM, AFF, RCJ, TRV, SNG and AMN participated in data collection and analysis, review of drafts and the final version of the article. SAG, GRS and AMN participated in the statistical analysis and writing of the article.

**Funding:** This work was funded by the Secretaría de Ciencia y Técnica de la Universidad Nacional de Tucumán (SCAIT). Code D633.

**Conflicts of interest:** The authors declare that they have no conflicts of interest.

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