

Arsenic Exposure: A Review of Health Risks in Latin America

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Abstract

Arsenic (As) contamination in drinking water poses significant health risks worldwide. Thirty-three peer-reviewed articles (i.e., studies and reviews) were identified and analyzed from three databases using keywords related to exposure and health impacts globally with a secondary focus on Latin America. The presence of As in groundwater and surface water due to both natural and anthropogenic sources has been well-documented, leading to severe health outcomes in affected populations, including cancers, adverse birth outcomes, and genetic susceptibility. There is also a significant correlation between As exposure and increased health risks, highlighting the need for effective short and long-term mitigation strategies. This review aims to synthesize existing literature on As in Latin America, with a focus on health implications, including cancer, cardiovascular diseases, cognitive impairments, and genetic susceptibility, along with mitigation strategies. This paper provides an overview of As in Latin America today and an understanding of how As research and mitigation should advance in the coming years.

Introduction

In 2006, the Mexican Government reported over 4 million Latin Americans drinking Arsenic (As) contaminated water; however, in recent years, efforts have been made to reduce exposure through improved water treatment, stricter regulations, and the use of home filters in communities on well water (M.L. Castro de Esparza, 2006). Many regions have seen improvements due to these interventions, but high levels of As contamination persists in areas with limited resources and infrastructure. Therefore, the overall trend in As exposure in Latin America varies by region and community, with both reductions and ongoing issues thus far.

Why should this matter? As is the 53rd most abundant element in the Earth's crust, while that may seem minuscule, if exposed via ingestion or inhalation, As can be detrimental to overall health (McClintock et al., 2012). As exposure can pose severe risks to human health across the life course, including but not limited to various cancers, adverse pregnancy and birth outcomes, respiratory diseases, neurological conditions, and increased risk of type 2 diabetes (Figure 1). Although emerging evidence suggests variability in the genetic expression of As exposure, there is limited understanding to date of the relationship between specific polymorphisms and their susceptibility to As exposure, which could, in the future, help target better health interventions (Faita et al., 2013).

This review addresses the research question: What are the health impacts of As exposure in Latin America? The study is significant because of the severe health implications associated with As exposure, impacting quality of life and consequential healthcare costs of these adverse health effects. Understanding the full scope of health impacts and identifying gaps in knowledge is essential for developing targeted strategies to reduce exposure and mitigate health risks. Furthermore, cost savings are even more meaningful to these communities, given their relative GDP compared to other regions of the world, with Latin American countries lower than the global average. Providing safe and clean water would allow these nations to save on healthcare costs from exposure to contaminated water sources (i.e., well water). These same saved resources could then be distributed towards alternate initiatives to further economic growth and sustainability (Economic Commission for Latin America and the Caribbean, 2024). The objective of this paper is to perform a literature review to synthesize current findings on health effects due to As exposure among communities in Latin America to identify knowledge gaps that can assist in mitigation strategy development.

Methods

Inclusion criteria:

Peer-reviewed articles published in English focusing on human As exposure were considered in the primary review to better understand the field. A secondary review focused on identifying the Latin American-specific articles. For the purpose of this study, Latin America was defined as countries in the American continent that spoke primarily Romance languages, including Mexico, Brazil, and many Caribbean nations. Studies focused on providing detailed data about the health impacts, genetic susceptibility, and mitigation strategies were included.

Exclusion criteria:

Studies not directly related to human health impacts or mitigation strategies were omitted from the primary review. Those not specific to Latin America were excluded in the secondary review, and non-peer-reviewed articles were excluded from both reviews. Studies with insufficient data or unclear methodologies were also omitted from both (the latter number of studies was not calculated).

Data acquisition methods/Keywords:

The search strategy included three databases: PubMed, ScienceDirect, and Google Scholar. "Arsenic exposure," "health effects," "Latin America," and "mitigation strategies," were four key terms used in the search. Data was organized into a table summarizing research aims, findings, and gaps in knowledge.

Data analysis:

A systematic approach was used to synthesize findings across studies. Data were categorized based on health impacts, genetic factors, and mitigation strategies. Chat GPT – a large language model (LLM) – was utilized to develop ‘tags’ for sorting through data after its compilation (OpenAI, 2024). Articles were then separated by geographical location: non-Latin American and Latin American studies. Using a thematic approach, major themes were identified for both groups of articles.

Results

The primary review included 33 human studies from a global geographic range to gain an understanding of As exposure on health impacts and mitigation strategies (Figure 2a).

The secondary review focused on 11 studies (included in the original 33) from various regions in Latin America and the Caribbean (Figure 2b). These articles highlighted significant health risks associated with As exposure and the effectiveness of different mitigation strategies.

1 | *Cancer*

The most common association with As contaminated drinking water is the increased risk of cancer. Whether bladder, respiratory, or skin cancers, the carcinogenic health implications of As exposure is severe but well-documented.

Bladder Cancers

Bladder cancer is one of the most frequently studied cancers in relation to As exposure. A systematic review by Saint-Jacques et al. (2014) summarized 30 years of epidemiological studies on As exposure in drinking water and the risk of bladder and kidney cancers. It is important to note this systematic review did not specifically pertain geographically to Latin America. Their analysis found a dose-response relationship between As exposure and bladder cancer, proving that even low to moderate levels of exposure can increase cancer risk.

In Latin American specific articles, the following studies were noted. In Northern Chile, a study assessed cancer mortality in a population exposed to high As levels in drinking water. The authors found an increase in bladder cancer mortality, with standardized mortality ratios (SMR) of 6.0 for men and 8.2 for women, significantly higher than the general population (Smith et al., 1998). This study provided strong evidence linking high long-term levels of As exposure to bladder cancer mortality from ingested contaminated water, especially for women.

In Argentina, a case-control study investigated the association between bladder cancer and long-term exposure to observe As levels in well water. This study, unlike many others similar to the one by Smith et al. did not find a significant association between bladder cancer risk and As levels in drinking water overall. However, it suggested that long-term consumption of well water for over 50 years may increase bladder cancer risk, particularly among smokers (Bates et al., 2004). The same study also suggested that

bladder cancers stemming from As exposure were found to be more lethal over less time. This disagreement of the association between bladder cancer risk and As levels is important to note for future research.

Lung and Respiratory Cancers

Lung cancer is another significant health risk associated with As exposure. The primary review identified a study by Lamm et al. (2018) which explored the relationship between low levels of As in drinking water and lung cancer risk across U.S. counties. This study found a negative association between low-level As exposure and lung cancer risk in the total and male populations, challenging the assumption that lower exposure levels are always safer. While this study is not Latin American-specific, it highlights the complexity of assessing cancer risks at different exposure levels and the need for more localized research in Latin America.

In the primary review, Yuan et al. (2018) conducted a dose-response meta-analysis to explore the relationship between inorganic As concentration in drinking water and lung cancer risk. To note, inorganic As (iAs) are As compounds that do not contain carbon. The most common forms are Arsenate and Arsenite, which come from both geological and anthropological sources. The study reviewed cohort and case-control studies, finding a significant association between high doses of iAs ($\geq 100 \mu\text{g/L}$) and increased lung cancer risk. Even at lower concentrations, the risk was elevated, with pooled relative risks (RRs) indicating a dose-response relationship. This analysis provided ample evidence for the carcinogenic effects of iAs at various exposure levels, reinforcing the need for stringent regulation of all forms of As in drinking water.

During the secondary review focusing on the carcinogenic nature of As, the same study in Northern Chile (as mentioned in the bladder cancer section) also found a substantial increase in lung cancer mortality. The SMR for lung cancer was 3.8 for men and 3.1 for women, indicating a strong link between As exposure and lung cancer risk (Smith et al., 1998). These findings suggest that As in drinking water significantly contributes to lung cancer mortality, independent of other factors such as smoking. It is also important to note the 0.7 difference of the SMR between As and lung cancer risk was slightly higher for men.

Skin Cancer

Chronic exposure to As-contaminated drinking water is also associated with an increased risk of skin cancers, including basal cell carcinoma and squamous cell carcinoma. As exposure can lead to skin lesions and hyperkeratosis, which are precursors to skin cancer. A systematic review by Karagas et al. (2015) examined the global evidence on the association between As contamination in drinking water and the incidence of skin lesions and malignancies. The review found that even low to moderate levels of As exposure can increase the risk of basal cell carcinoma and squamous cell carcinoma, with genetic factors influencing individual susceptibility.

In Latin America, the high prevalence of As-induced skin conditions has been reported in regions with significant As contamination. For example, in the same study from Northern Chile focused on Region 2, residents exposed to high As levels in drinking water showed a high incidence of skin lesions and cancers (Smith et al., 1998). These findings emphasize the importance of early detection and intervention to prevent the progression of skin lesions to malignant conditions.

2 | *Genetic Susceptibility of As Exposure*

Genetic susceptibility plays a crucial role in determining health outcomes of individuals exposed to As. Genetic factors influence how the body metabolizes As, leading to variations in susceptibility to its toxic effects. Understanding these genetic differences is essential for assessing individual and population-level risks, particularly in regions with high As exposure, such as Latin America. Moreover, understanding the effects of different enzymes on As metabolism may allow for future targeted interventions to be created.

Arsenic Metabolism and Genetic Factors

As metabolism in the human body primarily involves methylation, a process that converts iAs into less toxic, excretable forms (largely through the urine). The efficiency – metabolism – of this process can vary wildly among individuals, largely because of their genetic polymorphisms. One of the key enzymes involved in As methylation is As (+3 oxidation state) methyltransferase (AS3MT). Variations in the AS3MT gene can affect the enzyme's activity, altering the efficiency of As metabolism (Khan et al., 2020).

Studies like the one by Khan et al. (2020) have shown that individuals with certain polymorphisms in the AS3MT gene are more efficient at converting iAs to its less toxic methylated forms. Conversely, those with less favorable genetic variants may retain higher levels of As, increasing their risk of As-related diseases.

Health Implications of Genetic Susceptibility

Genetic susceptibility to As toxicity can influence the development of various health conditions. Research has shown that individuals with certain genetic traits are more susceptible to the carcinogenic and non-carcinogenic effects of As. For instance, genetic polymorphisms in AS3MT and other genes involved in As metabolism have been linked to an increased risk of cancers (such as bladder, lung, and skin cancers), cardiovascular diseases, and cognitive impairments (Sanyal et al., 2020).

The study by Khan et al. (2020) highlighted the significant role of genetic susceptibility in As toxicity. Their research indicated that genetic polymorphisms in the AS3MT gene were associated with increased health risks, though differentiated by emphasizing the need for personalized public health strategies that consider genetic factors in As exposure and risk assessment. This approach is particularly relevant in Latin America, where As exposure levels can vary widely based on geographic location, and genetic diversity among populations.

Case Studies from Latin America

Several studies across Latin America have explored the relationship between genetic susceptibility and As exposure, providing valuable insights into how genetic factors influence health risks in this region.

Northern Chile: Many studies have been based out of Northern Chile due to the high levels of As in drinking water. A study by Smith et al. (1998) discussed the increased mortality from bladder and lung cancers in the region. While the study largely focused on environmental exposure, it also suggested that genetic factors could play a role in the observed health outcomes. The high incidence of cancer in this population may be partly attributable to the diverse genetic makeup in the region and the variety in rates of As metabolism, highlighting the need for further research into genetic susceptibility.

Argentina: In Argentina, a case-control study investigated the association between bladder cancer and As exposure in well water. Bates et al. (2004) found no overall significant association between bladder cancer risk and As levels in drinking water. However, the study did indicate that

long-term consumption of well water, especially among smokers, might increase bladder cancer risk. This finding suggests that genetic factors, combined with other risk factors like smoking, could influence susceptibility to As-induced bladder cancer. Further research into genetic polymorphisms in the Argentine population could help clarify these associations.

Bolivia: A study titled "Human Adaptation to As in Bolivians Living in the Andes" by De Loma et al. (2022) explored genetic adaptation to As exposure among indigenous populations in the Bolivian Andes. The researchers focused on indigenous groups belonging to the Aymara-Quechua and Uru ethnicities, employing genome-wide selection scans, whole-genome sequencing, and genotype-phenotype association analyses to identify genetic variants associated with hyper-efficient As metabolism. The study found that these populations had developed a genetic adaptation to their high-As environment which is called the AS3MT gene. Genetic variants linked to differential expression of AS3MT were identified, providing insights into the mechanisms of As methylation in these populations (De Loma et al., 2022). The study in Bolivia provides a unique perspective on how human populations can adapt to environmental toxicants through genetic changes while also highlighting the potential for genetic resilience in high-risk areas.

Mexico: In Mexico, a study conducted by García Salcedo et al. (2022) focused on biomonitoring As exposure in mothers and their neonates in the Comarca Lagunera region. The study measured As levels in biological samples and highlighted significant exposure in this population. Although the study did not directly assess genetic susceptibility, the high levels of As found in neonates suggest potential genetic factors affecting As metabolism and retention. Understanding the genetic profiles of this population could provide insights into the observed high exposure levels and associated health risks.

3 | ***Birth Outcomes***

As exposure poses significant risks to maternal and child health, leading to severe health outcomes for both mothers and their children. Research indicates that chronic exposure to As-contaminated drinking water can result in adverse birth outcomes, including low birth weight, preterm delivery, and congenital anomalies (Bloom et al., 2014). In Peru, a study by George et al. (2014) found that a substantial percentage of groundwater samples exceeded World Health Organization (WHO) As guidelines, highlighting the widespread risk of exposure for pregnant women and children. Additionally, As can cross the placenta, exposing fetuses to this toxicant and leading to developmental and cognitive impairments

(Khan et al., 2021). High As levels in maternal blood and breast milk were reported in the Comarca Lagunera region of Mexico, posing ongoing exposure risks to neonates (García Salcedo et al., 2022). Ensuring maternal and child health in As-affected areas is crucial for preventing long-term health consequences and promoting healthy development.

Discussion

This review aims to summarize the scientific literature investigating As exposure in Latin American populations. The primary review of 33 reviewed studies showed significant differences based on geographical regions and population demographics. This information helped contextualize a secondary review focusing on 11 studies in Latin America, which revealed elevated health risks in areas with high As exposure. The search indicated that As exposure through drinking water in Latin America was largely associated with cancer risks (bladder, lung, skin, etc.) and poor maternal-child health outcomes. There was a significant emphasis on how an individual's genetic profile impacts their respective health outcomes.

While not well understood, it is hypothesized that As contamination, specifically in Latin America, is due to geogenic processes and, therefore, tectonic movement. One study cited that almost 90% of As contamination is related to these geological faults (Shaji et al., 2021). If one overlays the major convergent plate boundaries in Western Latin America to major concentrations of As globally, there is a strong trend. While this theory is promising it requires more research to determine the root cause of this contamination and how it has led to the varying health outcomes. This similarity also presents many areas of research, such as cross-examining As exposures in Latin America and As exposure in South Asia, where As is most prominent in groundwater. The literature shows that Latin America is similarly affected to South Asia in As contamination levels, both among the worst in the world (Shaji et al., 2021). To this end, a future area of study could involve the differences in how native communities in each respective region have evolutionarily adapted to metabolize the high As levels and how these diseases may manifest differently due to their differences in genetic makeup.

To that end, the examination of As as it reacts to individuals' respective genetic composition is also not fully understood. A study was conducted using mice to examine the relationship between the As3MT gene, its effects on As metabolism, and its relation to cardiovascular disease involving plaque buildup in the arteries (Negro Silva et al., 2021). The study reported reduced plaque build-up for mice with the

As3MT gene; these findings may point towards the use of animal models to further understand how genetic composition may affect an individual's health response, furthering the ability to create personalized medicine strategies. Such strategies that consider genetic factors can enhance effectiveness of interventions and reduce health disparities in As-exposed populations. As an example, genetic screening programs could identify individuals at higher risk, allowing for targeted interventions such as increased monitoring, dietary modifications, and access to alternative water sources.

The scientific community is beginning to learn the extent to which different combined pollutants affect the human body. For As exposure, there is very little data thus far analyzing co-exposures. Two studies identified as part of the secondary search examined the link between smoking and As and reported contradicting findings (Bates et al., 2004; Smith et al., 1998). Diseases are multi-factorial, and how these factors interact is not as well understood and further research on these subjects is necessary to develop preventive strategies.

This review should be considered in the light of its limitations. First, during the transition from the primary to secondary review, many of the studies were either non-geographically specific (i.e. many studies did not specify a geographic location or provide geographical context to the study) or not in Latin America, which may limit the validity of the findings specific to the Latin American region. Second, studies were not analyzed for the quality of evidence; however, human studies involving pollutants would not generally allow for randomized control trials, given the ethical challenges.

Conclusion

As exposure is a critical public health crisis in Latin America, accounting for approximately 7% of all deaths among those aged 30 years and over (Smith et al., 1998). This review underscores the severe health implications of As, including cancer (bladder, lung skin) and maternal-child health, all influenced by an individual's genetic profile. Clean drinking water is a human right; by integrating personalized health strategies, we can address the root causes of As contamination and provide these vulnerable populations with clean and affordable water. Furthermore, the promise of an epigenetic future offers hope for interventions that can convert this challenge into an opportunity for ensuring a healthier future for Latin American communities.

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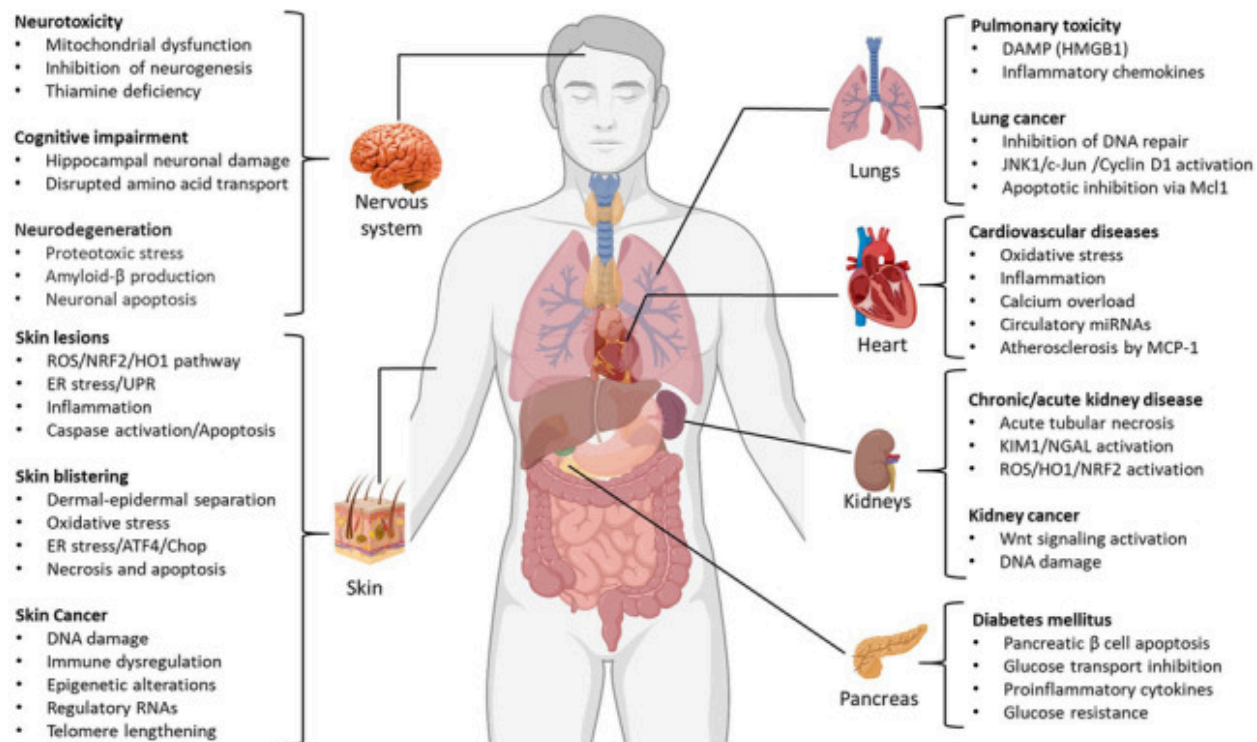
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Figure 1: Multi-Organ Systems Impacted by As Contamination*



*Muzaffar et al., 2023

Figure 2a: Dot Plot Distribution of Arsenic Related Research Articles By Year (n=33)

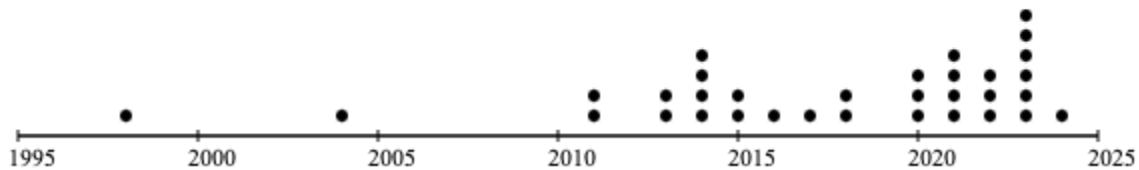


Figure 2b: Dot Plot Distribution of Arsenic Related Research Articles By Year Specific to Latin America (n=11)

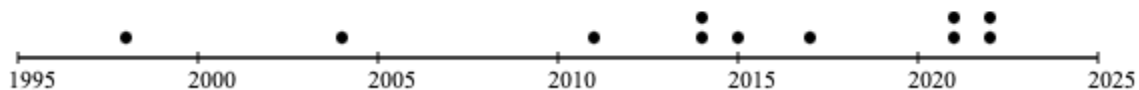


Table 1: Studies From the Primary Review

<https://1drv.ms/x/c/5b16afb730a0a710/EZSpwq6NHBIPqUeQ7RWAFWMBTjy-0CIrni-7-hylnvO3jg>

Table 2: Studies From the Secondary Review

<https://1drv.ms/x/c/5b16afb730a0a710/ET8iYhPGVZtBpi2eDhjST5QBgNIy3J820PhAJckE8iFfg>