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DECIPHERING THE EARTH'S ARSENIC ENIGMA: A COMPREHENSIVE EXAMINATION OF GLOBAL GROUNDWATER CONTAMINATION

Comprehensive Review

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ABSTRACT

Background: Arsenic contamination in groundwater is a major global environmental and public health issue, affecting over 150 million individuals across more than 70 countries. Toxic inorganic arsenic species, arsenite (AsIII) and arsenate (AsV), significantly disrupt cellular processes, causing oxidative stress and leading to severe health risks such as arsenicosis, cardiovascular diseases, neurotoxicity, and multiple cancers. Major river basins and deltas, including the Bengal and Mekong Deltas, exhibit arsenic levels exceeding World Health Organization (WHO) guidelines of 10 ppb, impacting vulnerable populations disproportionately.

Objective: To comprehensively examine the sources, health effects, and mitigation strategies for arsenic contamination in groundwater on a global scale, with a focus on current challenges and regional disparities.

Methods: A systematic review was conducted, synthesizing data from over 100 peer-reviewed studies published in the last decade. Arsenic concentration data from affected regions were evaluated, alongside epidemiological studies on health outcomes. Mitigation strategies, including deep groundwater extraction, well switching, and oxidation methods, were analyzed for effectiveness and limitations based on field trials and global implementation reports.

Results: Groundwater arsenic levels varied widely, with concentrations ranging from <0.5 ppb to over 5000 ppb globally. In Bangladesh, over 45 million people are exposed to arsenic levels exceeding 50 ppb, compared to 20% of deep wells in Vietnam exceeding WHO guidelines. Health effects included a 30% increase in cardiovascular dysfunction and a 25% higher incidence of neurotoxicity in regions with elevated arsenic exposure. Mitigation strategies demonstrated regional variability, with deep tube wells reducing arsenic levels below 10 ppb in 95% of tested wells in Bangladesh, while oxidation achieved up to 99% arsenic removal under controlled laboratory conditions.

Conclusion: Arsenic contamination in groundwater remains a critical threat to global public health. Although existing mitigation strategies show promise, their effectiveness is challenged by high costs, regional variability, and socioeconomic disparities. Ongoing research, adaptive solutions, and international collaboration are essential to reducing the health and environmental impacts of arsenic exposure.

Keywords: Arsenic poisoning, Cardiovascular diseases, Groundwater, Neurotoxicity, Oxidative stress, Public health, Water pollution.

INTRODUCTION

A significant environmental issue in many regions of the world is currently the contamination of groundwater, originating from either human activities or natural sources, which has various socioeconomic consequences. The use of groundwater with high concentrations of arsenic (As) exposes millions of individuals in several nations to elevated amounts of this element. Background studies have extensively recorded high concentrations of arsenic in groundwater in Chile, China, Mexico, USA, Argentina, and Hungary (1, 2) as well as in the Indian State of West Bengal, Vietnam, Bangladesh.(2–6). The estimated number of afflicted individuals round the globe is roughly 150 million, and this number is expected to rise as additional impacted regions are consistently identified. (7).

Arsenic is a notable example of heavy metals that typically contaminate groundwater resources. Arsenic sources associated with water bodies of geothermal entities have been discovered in various geographical divisions which include thermal springs from parts of Japan, Dominica, France, USA, New Zealand, Argentina and Chile (8). Arsenic's (As) has an atomic number of 33. and has only one naturally occurring isotope with an atomic mass of 75. It has four different oxidation states which include -3, 0, +3 and +5. The most prevalent states are +3 and +5 which occur as oxyanions arsenite and arsenate (8). Additionally, arsine gases (containing As-3) are found in soil and are usually produced by fungi and other microbial species (9). Gases containing arsine are considered to be the most harmful (10).

A widely recognised carcinogen, arsenic is regarded as one of the most dangerous substances globally (11). Chronic and prolonged (5–10 years) human use of hazardous inorganic substances Consuming water and food contaminated with arsenic can lead to arsenicosis, a term commonly used to describe health issues associated with arsenic such as skin diseases, skin cancers, internal cancers (bladder, kidney, and lung), diseases of the blood vessels in the legs and feet, potentially diabetes, elevated blood pressure, and reproductive problems (12–14). Generally, the inorganic forms of arsenic (such as trivalent arsenite (AsIII) and pentavalent arsenate (AsV)) are more common and harmful than the biological forms in terrestrial ecosystems. The compound exhibits deleterious effects on overall protein metabolism with significant toxicity by interacting with sulfhydryl groups present in cysteine residues (15). The occurrence of arsenicosis has severe implications for the means of subsistence, familial relationships, and financial capacity of affected persons. Implementing the WHO provisional guideline of 10–50 ppb of Arsenic in water used for drinking puts over 100 million people globally at risk. Among this group, more than 45 million people, mostly in developing Asian countries, are particularly vulnerable to being exposed to more than 50 ppb of Arsenic, which is the maximum concentration limit in drinking water in most Asian countries (7). Current estimates indicate that over 150 million individuals globally are affected by the rising levels of arsenic in drinking water (17). The primary regions affected by arsenicosis are found in expansive deltas and principal river basins worldwide, (18) including Paraiba do Sul Delta, Brazil (19), Bengal Delta (20–22), Mekong Delta, Cambodia (23), Danube river basin, Hungary (24), Hetaoriver basin, Mongolia (25), Duero Cenozoic Basin, Spain (26), Zenne river basin, Belgium, and Tulare Lake, USA (27). The persistent presence of arsenic in the food chain will continue to pose a long-term threat to both human and natural systems (28). Given that water is the primary source by which arsenic (As) is ingested in human body (29), it is necessary to have knowledge about the mechanisms of arsenic contamination in groundwater, the related health hazards, and strategies to reduce the problem of As emissions.

This analysis provides a comprehensive summary of potential sources of arsenic pollution in groundwater, using a worldwide perspective on groundwater. Analysis of As contamination, related health hazards, the cellular processes impacted by As-toxicity, and the most effective existing approaches for reducing As pollution in groundwater.

GLOBAL DISTRIBUT|ION

Arsenic (As) pollution can be erroneously transmitted into the structure of groundwater due to the mobilisation of As in underground water and aquifers, such as through hydraulic fracturing. Hence, its toxicity can impact a substantial number of individuals (30). Documented in the literature, the groundwater content of arsenic (As) covers a wide range from less than 0.5 to 5000 parts per billion (ppb), indicating natural As pollution in over 70 nations (7). Table 1 cites some of the most well-documented and severe instances of groundwater poisoned with arsenic seen in aquifers worldwide. Commonly, preliminary guideline standards for arsenic (As) content in groundwater are established at 10 parts per billion (ppb), however it might potentially exceed 50 ppb. The findings of this study confirm that As-contamination is a pervasive worldwide phenomena and sufficiently severe.

Table 1: Documented reports of As-contamination of groundwater resources across different countries

Sr. No	Country	As-level (ppb)	Citation
1	Afghanistan	10 - 500	(24)
2	Australia	1 - 12	(20, 24)
3	Bangladesh	<1 - 4730	(21, 24)
4	Brazil	0.4 - 350	(20)
5	Cambodia	1 - 1610	(23, 24)
6	Canada	1.5 - 738.8	(20, 24)
7	China	50 - 4440	20, 24)
8	Finland	17 - 980	(87)
9	Greece	<10,000	(20)
10	India	10 - 3200	(87)
11	Japan	1 - 293	(20)
12	Mexico	8 - 620	(1, 24)
13	Nepal	<2620	(24, 87)
14	Pakistan	<906	(20, 25)
15	Taiwan	10 - 1820	(1, 24)
16	Thiland	1 - >5000	(1, 24)
17	USA	<2600	(21, 27)
18	Vietnam	<1 - 3050	(1, 87)

HEALTH EFFECTS OF ARSENIC POISONING

Arsenic-Induced Cardiovascular Dysfunction

Esophageal atherosclerosis, ischaemic heart disorders, hypertention, and ventricular arrhythmias are consequences of prolonged exposure to arsenic (31-33, 34) Arsenite induces the increase of reactive oxygen species (ROS) in the plasma membrane of vascular smooth muscle cells and vascular endothelial cells by stimulating Nicotinamide Adenine Dinucleotide Phosphate (NADPH) (35, 36). These ROS combine with nitric oxide (NO) to produce peroxynitrite, a potent oxidic compound associated with the upregulation of cyclooxygenase-2, an inflammatory mediator (37). ROS increases the expression of genes associated to atherosclerosis, including heme oxygenase-1 (HO-1), interleukin-6 (IL-6) and monocyte chemo-attractant protein (MCP-1), thereby facilitating the adhesion, penetration, and migration of monocytes in vascular smooth muscle cells (VSMC) (38). The proliferation and migration of vascular smooth muscle cells (VSMCs) are induced by the modification of focal adhesion proteins by arsenic (39). Moreover, blood vessels undergo neurogenic inflammation by the increase of endothelial neurokinin-1 in response of arsenic trigger (40). Moreover, arsenic stimulates protein kinase C alpha, leading to the phosphorylation of beta-catenin. This phosphorylation then reverses the interaction between vascular endothelial cadherin and beta-catenin. Additionally, it induces the development of actin stress fibres, which in turn generates more intercellular gaps and increases the permeability of the endothelium (41). Reports indicate that arsenite reduces the activity of endothelial nitric oxide synthase (eNOS) and Akt/protein kinase B, thereby reducing the availability of nitric oxide (NO), which might result in vascular endothelial dysfunction and related cardiovascular problems (42, 43). Through phosphorylation of myosin light chain kinase (MLCK), arsenite induces vasoconstriction of the blood vessels and enhances calcium sensitisation, resulting in hypertension (44). Prolonged exposure to arsenic causes oxidative stress and impacts the secretion of vasoactive substances in blood vessels, resulting in increased blood pressure (45). The induction of extended Q-T interval and action potential duration by arsenic trioxide leads to the development of ventricular arrhythmia (34, 46).

Arsenite-Induced Neurotoxicity

As arsenic readily traverses the blood-brain barrier, the brain is particularly susceptible to its harmful effects (46, 47). Arsenic exposure in humans is linked to several neurological problems including memory impairment, diminished focus, Parkinson's disease, Guillain-Barre-like neuropathy, deficits in verbal comprehension, encephalopathy, and peripheral neuropathy
(48-53). Arsenic-induced neurotoxicity mostly causes oxidative stress characterised by elevated levels of reactive oxygen species (ROS) and lipid peroxides, as well as a declining superoxide dismutase activity and reduced glutathione levels (54). Potential effects of arsenic

exposure include modifications in the metabolic processes of neurotransmitters including monoamines, acetylcholine, gamma amino butyric acid, and glutamate (55). In a recent study, chronic arsenic exposure was found to cause a substantial decrease in monoamines, including adrenaline, nor-adrenaline, dopamine, and serotonin, in the corpus striatum, frontal cortex, and hippocampal regions of the brain. (46) Arsenite-induced neurotoxicity triggers apoptosis in cerebral neurones via activating the p38 nuclear mitogen-activated protein kinase (p38MAPK) and JNK3 pathways. (56) Furthermore, the exposure to arsenic causes neurotoxicity by causing instability and disorder in the cytoskeletal structure, ultimately resulting in the degeneration of axons (57). Significantly, arsenic induces thiamine (vitamin B1) insufficiency and hinders pyruvate decarboxylase, resulting in increased blood pyruvate levels and provoking encephalopathy (52). Arsenic-induced oxidative stress in the brain leads to oxidative DNA damage, apoptosis, and the deterioration of dopaminergic neurones, which in turn causes symptoms similar to those of Parkinson's disease (50, 51). Acute arsenic poisoning reduces the activity of acetylcholinesterase, resulting in cholinergic crisis-like episodes characterised by changes in mental state and neurological symptoms related to peripheral neuropathy, neuropsychiatric pathologies, and extrapyramidal illnesses (59). Prolonged exposure to arsenic and its byproducts, monomethyl arsenic acid and monomethyl arsonous acid, inhibits the NMDA receptors in the hippocampus. These receptors are crucial for synaptic plasticity, learning, and memory, and their suppression results in neurobehavioral problems and cognitive impairment. (60, 61).

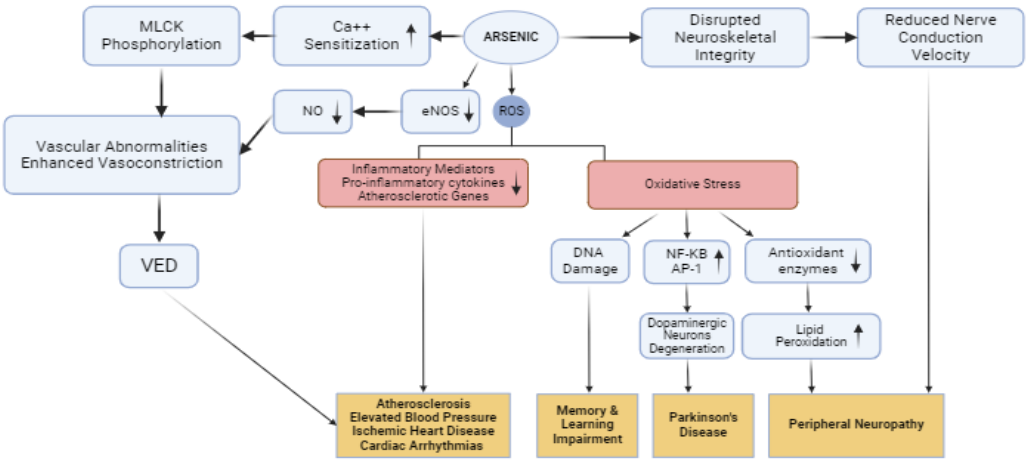

Figure 1 Schematic Illustration of Arsenic-induced subcellular abnormalities resulting in cardiovascular dysfunction and Neurotoxicity

Arsenic-Induced Carcinogenicity

Due to its high cellular uptake, the trivalent form of arsenic has more pronounced genotoxic effects than its pentavalent equivalents (62). Arsenic is hypothesised to trigger MAPK signal transduction, which in turn stimulates AP-1 and NF-kB transcription factors to modify different gene expression patterns that contribute to the carcinogenicity associated with arsenic (63). Arsenic induces the activation of focal adhesion kinase, which in turn activates certain signalling pathways including integrin, Src, Rho, Grb2, EGFR, ERK, and cadherins. These pathways play a role in cell adhesion, cell migration, cell survival, cell cycle regulation, carcinogenesis, and pathogenic cell death (64). The compounds DMA(V) and TMAO(V) create oxidative stress and increase 8-hydroxydeoxyguanosine, a detectable indicator of oxidative DNA damage. This, in turn, promotes cell proliferation and has carcinogenic effects (65, 66). The presence of arsenic stimulates the growth of bladder epithelial cells and increases the expression of proto-oncogenes including c-fos, c-jun, and EGR-1. These factors may all lead to the development of bladder cancer (67). Arsenic causes skin cancer by reacting synergistically with sunlight to inhibit DNA repair, promote angiogenesis, modify DNA methylation patterns, disrupt cell cycle regulation, and impede natural apoptosis (68). The primary cause of carcinogenicity caused by arsenic is oxidative stress, which can be mitigated by antioxidants including vitamin E, curcumin and melatonin (69, 70).

PREVENTION AND TREATMENT STRATEGIES

Arsenic can be eliminated from groundwater systems by a range of treatment methods utilizing either laboratory or site-scale experiments. The primary principles behind these technologies include oxidation, sorption, co-precipitation, ion exchange and filtration.

Deep Groundwater

Literature evaluations from the Bengal and the Mekong deltas suggest that shallow groundwater is predominantly contaminated with arsenic (As), whereas groundwater from deeper aquifers is nearly devoid of As. For instance, the research conducted by BGS found that just 5% of the waters from deep tube wells (>150m deep) had arsenic (As) contents over 10 parts per billion (ppb), and 1% surpassed 50 ppb. Therefore, water supply from manually operated deep tube wells (DTW) might be a suitable source (71). Yet, the depth of aquifers without arsenic varies across the different places. In the Bengal Delta, water extraction below 150/200m depth is conventionally classified as a deep aquifer. However, it is worth noting that in many instances, this depth might be as little as 200m (72). Nevertheless, the concentration of arsenic (As) is very low at depths above 50 m and 70 m in the Red River and the Mekong deltas (73). An inherent limitation of the deep water extraction method is its expensive installation, which limits its suitability for community-level implementation. Additional disadvantages of this choice include the dependence on the As-free deep aquifer, the unpredictability of the groundwater replenishment process, the potential for saltwater infiltration in coastal regions (74), and the presence of extremely high levels of dissolved iron and manganese (75).

Well Switching

The less deep groundwater doesn't contain constant levels of As toxicity. (1) A countywide study conducted by the British Geological Survey in Bangladesh and cross-checked by Chakraborti et al (76) found that the amount of arsenic (As) contamination in tube wells in the Ganga-Meghna-Brahmaputra plain ranges from 20% to over 50%. Therefore, it is often feasible to find uncontaminated tube wells in many areas within reasonable distances. Switching to an uncontaminated shallow tube well can be a viable alternative. Well-change to shallow tubewell has been identified as the most favoured mitigation technique among the several attempted approaches, with a preference rate of 29% (77). An inherent limitation of the well-switching approach is the significant scope of regional and temporal fluctuations in arsenic (As) concentration in groundwater, which poses challenges and uncertainties for its dependability. Subsequent investigations have shown that the concentration of arsenic (As) in the tube wells varies over time, with higher levels observed during the monsoon season in comparison to the dry winter season (78, 79). This implies that it may be necessary to monitor each well and conduct a long-term study to ensure that the tube wells will continuously be free from arsenic.

Oxidation

The critical purpose achieved by oxidation is to obtain AsV by the transformation of soluble AsIII after which precipitation of AsV is carried out. The presence of AsIII is crucial for anoxic groundwater since it is the dominant form in nearly neutral pH conditions (80). AsV has greater adsorption affinity for solid surfaces compared to AsIII. Consequently, the process of oxidation followed by adsorption is very efficient for the elimination of As (81, 82). For the oxidation, several oxidants have been employed. The reaction kinetics with O3, H2O2, Cl2, NH2Cl, and ferrate are first-order processes involving both AsIII and oxidants. Therefore, the concentrations of AsIII and the oxidant are crucial requirements for efficient removal of As from an aqueous solution. Permanganate, chlorine, and ozone have a much faster reaction rate compared to hydrogen peroxide and chloramine when used for the oxidation of AsIII to AsV (82–84). Bajpai and Chaudhuri (85) found that Air and pure oxygen may oxidize 54-57% of AsIII to AsV in polluted groundwater, whereas ozone can achieve 100% oxidation of AsIII. Manganese dioxide polished sand is a dual-purpose oxidizing agent and adsorbent, making it a valuable oxidizing catalyst. Integrating manganese dioxide polished sand with Fe-containing compounds enhances the efficacy of its application, resulting in treated products that are more filterable and manageable (85). Recently,Criscuoli etal. (86) investigated the oxidation of AsIII using MnO2-coated PEEC-WC nanostructured capsules. They found that these capsules exhibit superior efficiency compared to traditional oxidation techniques, particularly when the water includes a low concentration of AsIII. An oxidation rate over 99% was achieved within the range of 100 to 300 parts per billion of initial arsenic concentration. Nevertheless, when the concentration was raised to 700 and 1000ppb, just 90% and 73% of AsIII underwent oxidation, suggesting a decline in the oxidation efficiency of the particle as the initial AsIII concentration increased.

DISCUSSION

The review provided a comprehensive synthesis of arsenic contamination in groundwater, shedding light on its pervasive impact on global health and the environment. By examining diverse geographical regions and exploring the biochemical pathways of arsenic toxicity, the study reinforced the pressing need for robust mitigation strategies. The strengths of this review lie in its detailed exploration

of arsenic's cellular effects and its global distribution, which integrates data from over 70 countries. This breadth highlights the alarming scale of the issue while offering a solid foundation for developing targeted interventions. Additionally, the review demonstrated how chronic arsenic exposure contributes to systemic dysfunctions such as cardiovascular and neurological disorders, as well as its carcinogenic potential. However, limitations include a lack of detailed exploration into socioeconomic barriers and regional disparities that hinder the implementation of mitigation measures. Such challenges underscore the necessity of adaptive, region-specific approaches. Despite its depth, the review could have delved further into emerging technologies for arsenic mitigation and the role of global policy frameworks in addressing this crisis. For instance, while oxidation methods and well-switching were briefly discussed, advanced approaches such as nanotechnology and community-based participatory research were omitted, both of which show promise in addressing arsenic contamination sustainably. Furthermore, insufficient emphasis on the synergistic impact of arsenic with other pollutants in water systems left a critical gap in understanding cumulative toxicity. Overall, the synthesis of biochemical, environmental, and health-related aspects provided a robust narrative; however, integrating policy, economics, and innovative solutions would strengthen the discussion further. Such inclusivity would ensure not only the mitigation of existing contamination but also the prevention of future outbreaks, safeguarding public health and environmental integrity on a global scale.

Recent comparative research conducted by Rahman et al. (2021) in Bangladesh and Vietnam highlighted critical regional disparities in arsenic contamination mitigation strategies. The study evaluated the effectiveness of deep groundwater extraction and well-switching in reducing arsenic exposure in rural communities. In Bangladesh, deep tube wells (>150 m) were found to be more effective, with arsenic concentrations below 10 ppb in over 90% of the wells tested. Conversely, in Vietnam, the variability in aquifer depth made deep groundwater extraction less reliable, with arsenic levels exceeding safe limits in 20% of wells despite their depth. Interestingly, well-switching proved to be a more practical solution in Vietnam, given its lower cost and adaptability to local hydrological conditions. The findings underscored the importance of tailoring mitigation strategies to local geological and socioeconomic contexts rather than relying on uniform solutions. This comparative approach strengthens the case for region-specific interventions to effectively combat arsenic contamination worldwide (87).

CONCLUSION

A worldwide scale issue of great concern is the pollution of groundwater by arsenic. The dissolution of naturally existing arsenic into groundwater has been seen in several regions of the world due to biogeochemical processes. The objective of this study was to provide a detailed analysis of several natural and human-induced origins of arsenic (As) in groundwater, including its classification and distribution pattern in groundwater. In addition, we have examined the issue of arsenic (As) pollution in groundwater across various regions globally, followed by a comprehensive analysis of the epidemiology and toxicity mechanisms of As in animals and humans. The persistent exposure to arsenic through polluted water may be responsible for a range of health problems. Arsenic elevation of oxidative stress leads to the upregulation of proinflammatory cytokines and inflammatory mediators, deactivation of eNOS, and phosphorylation of MLCK, therefore inducing cardiovascular problems. The pathological processes in arsenic-induced carcinogenicity are associated with the development of arsenic-induced diabetes. Furthermore, oxidative stress, suppression of pyruvate decarboxylase, and acetylcholinesterase appear to be crucial factors in the neurotoxicity caused by arsenic. Furthermore, arsenic causes kidney and liver damage by enhancing oxidative stress and programmatic cell death. In addition, exposure to arsenic can trigger carcinogenesis by promoting oxidative DNA damage and chromosomal abnormality and disrupting cellular signalling pathways. Novel pharmaceutical therapies to stop diseases linked to arsenic exposure may be achieved by targeting and regulating the specific pathogenic signalling systems described above.

Author Contribution

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Muhammad Abubakar*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Hina Kausar	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sarmad Habib Khan	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Uzair Rabbani	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muzammil Khalid	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published

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