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Review Article

Public Health Section

Arsenic Exposure and Non-Communicable Diseases: A Review on Mechanisms and Global Impact

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ABSTRACT

Arsenic is a naturally occurring metalloid that poses a significant public health concern due to its widespread contamination in the groundwater and food chain globally. Prolonged exposure to arsenic through consumption of contaminated drinking water and foods has been identified as a major risk factor in development of a number of Non-Communicable Diseases (NCD), mostly Diabetes Mellitus (DM), heart disease, a number of cancers (skin, bladder, lung, liver) as well as respiratory and skin diseases. Epidemiological and laboratory experiments repeatedly show that arsenic has its toxic effects due to some complicated biochemical mechanisms, oxidative stress, chronic inflammation, endocrine and the immune system dysfunction, alterations in the genes and epigenetic alterations. The problem of arsenic contamination is becoming a global crisis which is affecting both developing and developed countries, with South and Southeast Asian countries severely impacted. Millions of people remain at risk despite growing awareness. In this review, available scientific information on arsenic-induced NCDs is presented in the most elaborate manner with the dire need for a community health response from the global community, including adequate surveillance of water and food security, implementation of efficient arsenic-control technology, and area-specific community-based responses to this ever-increasing menace that is arsenic-induced NCDs.

Keywords: Chronic inflammation, Environmental exposure, Heavy metals, Oxidative stress, Public health

INTRODUCTION

Arsenic is a metalloid that is widely found in the crust of the earth and has both metallic and non-metallic characteristics. It has a variety of oxidation states, including -3 to +5, and occurs either in the organic or the inorganic form in nature. The reaction of inorganic arsenic with oxygen and sulphur produces various derivatives, and its reaction with carbon and hydrogen yields organic arsenic forms [1].

Human exposure to arsenic is through both its organic compounds like Monomethylarsonic Acid (MMA) and Dimethylarsinic Acid (DMA) as well as more toxic inorganic forms [2]. Inorganic arsenic (iAs) exists almost exclusively in trivalent (arsenite, As (III)) and pentavalent (arsenate, As (V)) states, and is a frequent groundwater contaminant. The United States Environmental Protection Agency (EPA) and the World Health Organisation (WHO) recognising its toxicity, have set a maximum allowable limit of 10 µg/L (10 parts per billion) in drinking water [3].

In particular, inorganic forms of groundwater arsenic can biologically transform into less toxic organic species like arsenobetaine and arsenosugars [4]. Apart from natural processes, human activities such as mining, smelting, burning coal, farming, and industrial operations have also contributed to an increase in arsenic contamination [5].

Arsenic release into the environment can also be caused by natural events, such as earthquakes and volcanic eruptions. However, consuming food and water contaminated with arsenic is the most common way for humans to be exposed. Many detrimental health effects have been linked to chronic arsenic exposure, which is defined as consuming arsenic-contaminated water every day for six months or more [6].

The aim of the review is to explain the recent evidence on the possibility of the exposure to arsenic in contributing to the occurrence of several NCDs. It is a discussion of the relationship between arsenic and DM, various types of cancer, chronic respiratory illnesses, skin diseases, and Cardiovascular Diseases (CVDs).

CURRENT INSIGHTS INTO GLOBAL ARSENIC EXPOSURE

Arsenic toxicity has become a growing public health issue in most countries across the globe and long-term exposure to large levels of arsenic by oral route, mainly in food and drinking water, have been attributed to various systemic manifestation [5,6].

Global Groundwater Arsenic Contamination

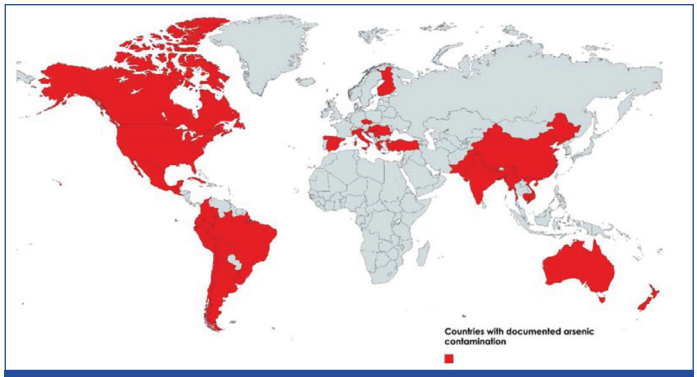
Naturally occurring arsenic in groundwater, particularly in unconsolidated sediment aquifers, poses a significant global health threat. An estimated 500 million people worldwide are affected by arsenic-contaminated ground-water, with long-term exposure linked to dermatological manifestations, various cancers, and damage to the liver, kidneys, lungs, and cardiovascular system [7].

Because of its high population density and geogenic sources of arsenic, Southeast Asia continues to be the most severely affected region. Arsenic contamination of groundwater is a persistent problem in nations like China, Bangladesh, and India, as illustrated in [Table/Fig-1] [8-12]. As a major public health concern, arsenic has been found in 17 out of 29 states in India alone since the 1980s, and the number of impacted districts and people is continuously rising [8].

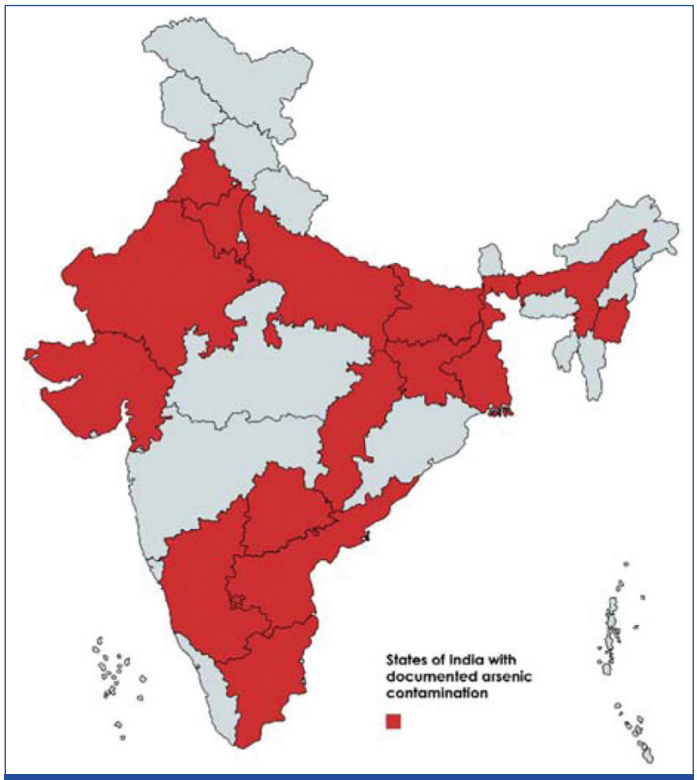
In India, arsenic contamination occurs primarily in two types of geographies: alluvial plains (e.g., West Bengal, Uttar Pradesh, Bihar, Jharkhand, Assam, Manipur, Punjab, and Haryana) and hard-rock terrains (e.g., Karnataka and Chhattisgarh) as shown in [Table/Fig-1] and [Table/Fig-2]. Additional cases have also been reported in Rajasthan, Andhra Pradesh, Telangana, Tamil Nadu, and Gujarat, shown in [Table/Fig-2] [9].

Across South Asia, the issue is widespread, affecting around 110 million people. Countries such as Pakistan, Bangladesh, Nepal, Vietnam, Cambodia, Myanmar, and China have groundwater arsenic concentrations that exceed the World Health Organisation (WHO) guideline of 10 µg/L, as illustrated in [Table/Fig-1] [10].

Beyond Asia also arsenic contamination is a global concern. In North America, parts of Canada and the United States have



[Table/Fig-1]: Global distribution of arsenic-contaminated groundwater [8-12].



[Table/Fig-2]: State-wise distribution of arsenic-contaminated groundwater in India [9].

reported groundwater arsenic contamination [8]. Latin American countries have also documented arsenic presence in both surface and groundwater, primarily due to natural geogenic sources with some anthropogenic contributions, as shown in [Table/Fig-1] [11].

Over 600,000 people are affected in the Pannonian Basin by groundwater arsenic contamination, which includes Hungary, Serbia, and Romania. Other European nations that are impacted include Greece, Italy, Spain, Turkey, Finland, Croatia, and the Czech Republic. Geogenic sources and human activities like mining, pesticide use, timber treatment, and waste disposal are the main causes of arsenic contamination in Oceania, which includes Australia and New Zealand, as illustrated in [Table/Fig-1] [12].

Sources and Routes of Arsenic Exposure Worldwide

Arsenic exposure in humans occurs through various environmental and dietary routes. Besides contaminated drinking water, dietary intake particularly rice consumption serves as a major source of inorganic arsenic, due to its ability to accumulate arsenic from soil and water during cultivation [13]. This is of growing concern, as rice remains a dietary staple in many arsenic-endemic regions. Inorganic and methylated arsenic in food comes from natural soil and water contamination, past or current use of arsenic-based pesticides, and arsenic-containing drugs used in poultry farming [14].

Another significant exposure route is consumption of fish and shellfish, which can accumulate significant amounts of arsenic, although primarily organic forms are less harmful than inorganic forms [15,16]. Similarly, consumption of cow milk, eggs, poultry, and crops grown in arsenic-contaminated areas can cause health issues for the general public [17]. The concentrations of arsenic in water consumed by cows, goats, buffaloes, sheep, and camels and the concentrations of arsenic in their milk were found to be highly correlated in a study done by Kazi TG et al., in the year 2016 [18].

Vegetables which are irrigated with arsenic-laden groundwater also contribute significantly to dietary exposure often exceeding national as well as international safety limits [19]. A US based market study by Nachman KE et al., reported that use of arsenic-based feed additives in poultry farming has been linked to elevated levels of inorganic arsenic in chicken meat, further amplifying dietary exposure risks [20].

Electronic cigarettes have gained popularity as a safe alternative to conventional smoking. However, recent evidence has shown that e-cigarettes may expose users to toxic metals, including arsenic, posing a new and poorly understood health risk [21].

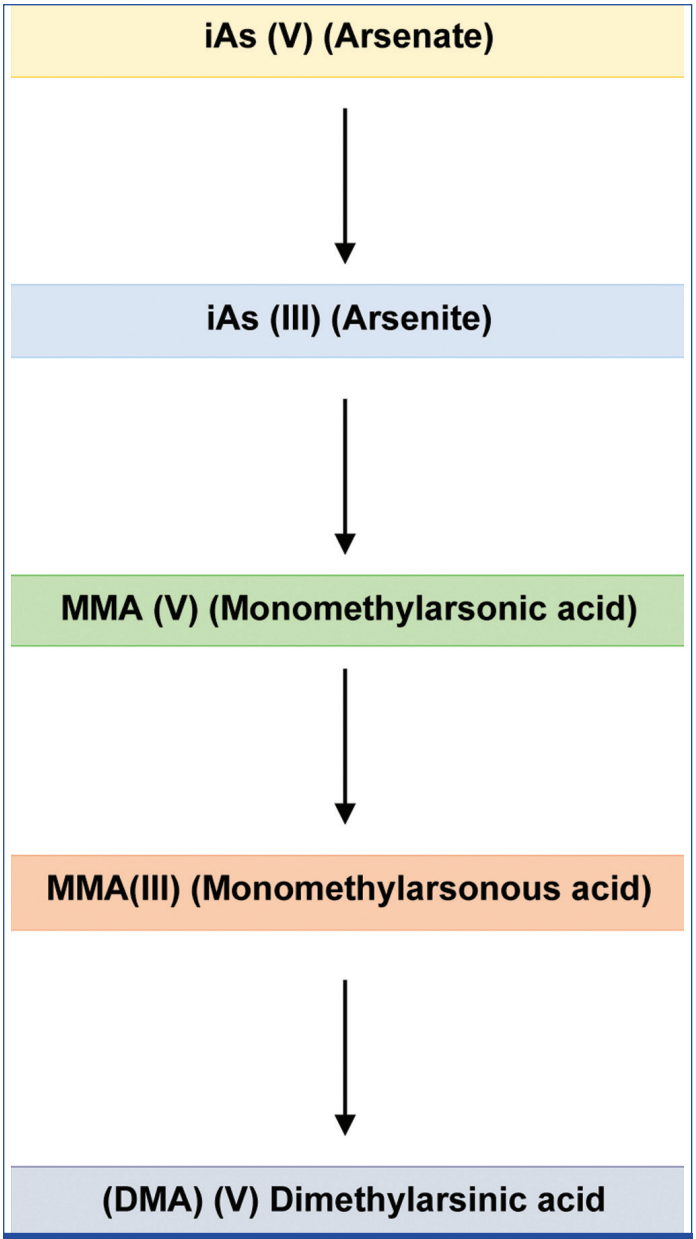
BIOTRANSFORMATION AND TOXICOLOGICAL MECHANISMS OF ARSENIC

Human exposure of arsenic occurs primarily through the consumption of contaminated water and food materials, inhalation of airborne particles in the atmosphere and through the skin. Once inside the body, arsenic is easily transported to other organs in the body through the blood stream. Toxicity of arsenic is dependent on chemical form, route of exposure, dose and duration of exposure, which cause cellular responses that include adaptive stress response to apoptosis and tissue damage [1]. The long-term exposure to inorganic arsenic causes a number of molecular processes, such as oxidative stress, inflammation, and cytotoxicity resulting in structural and functional damage of various organs [3]. Inorganic arsenic is biotransformed in the liver of humans primarily by methylation to form metabolites, including MMA and DMA, which are considered as biomarkers of exposure to arsenic and due to which arsenic-induced toxicity occurs [5].

Biotransformation of Arsenic

Arsenic exposure arises from both natural and anthropogenic sources, primarily through ingestion, inhalation, and skin contact. Both pentavalent and trivalent arsenic forms are rapidly and extensively absorbed via the gastrointestinal tract [22]. The digestive tract and lungs are effective in the absorption of most arsenic into the bloodstream after its ingestion and inhalation. The respiratory system is the major organ that is being affected by airborne arsenic trioxide in the industrial areas. After getting absorbed inside the body, arsenic comes into the blood circulation where 95-99% of it forms complex with haemoglobin and is transported to organs like liver, lungs, kidney and skin. Arsenic that is ingested is excreted more quickly than arsenic that is inhaled because of increased rate of processing in the liver. Around 70% is excreted in urine, but arsenic can take longer time from the skin to get removed as compared to other organs [5]. Unlike organic arsenic, inorganic Arsenic (iAs) persists longer in the body [22].

The liver is central site of arsenic methylation after oral dose as revealed in experimental studies. It is found that among the various tissues the testes have the maximum methylation activity and the kidneys, the liver and the lungs come next [23]. Inorganic arsenic is arsenic that, in mammals, is principally metabolised to MMA and DMA by the process of methylation, although a portion of the inorganic arsenic (iAs) is not metabolised, illustrated in [Table/Fig-3] [24,25]. These biotransformation reactions are sequential and include reduction of pentavalent arsenic, {iAs (V)} to trivalent arsenic {iAs (III)} and oxidative methylation. Of particular interest is the fact that methylarsonous acid {MMA (III)} exhibit substantially stronger cytotoxicity than most other varieties of arsenic and the order of Arsenic (As) toxicity is MMA (III) > iAs (III) > iAs (V) > DMA (V) > MMA (V) [26].



[Table/Fig-3]: Arsenic metabolic pathway [24,25].

Mechanism of Arsenic Toxicity

There has been epidemiological and experimental evidence that associates the exposure of arsenic with the occurrence of cancer and other diverse NCDs. Toxicity of arsenic and its metabolites is mainly the results of binding to cysteine residues, zinc finger motifs, and RING finger structural regions causing impairment in important protein functions. These molecular interactions also lead to the disrupted functioning of the important cellular processes, such as epigenetics, hormone signaling, DNA repair, and gene expression, facilitating diseases progression [27].

The process of oxidative stress is one of the most well-known arsenic toxicity mechanisms, which is mainly due to the production of Reactive Oxygen Species (ROS) [28]. Arsenic disrupts mitochondrial respiration and mitochondrial energy production by blocking major enzymes in Tricarboxylic Acid (TCA) and inhibits NADH generation via Nicotinamide Adenine Dinucleotide (NAD^+) reduction, increasing ROS production [29]. Arsenic also has an effect of inhibiting mitochondrial complex I and III in the electron chain to aid the production of superoxide (O_2^-). It also blocks succinate dehydrogenase and interferes with oxidative phosphorylation, further increasing ROS production. Arsenite (As^{3+}) and arsenite metabolites (MMA, DMA) inhibit the production of succinyl-CoA, interfere with ATP by forming unstable arsenate bonds that break down very quickly and disturb cellular energy processes [30].

Hu Y et al., in their study in 2020 have demonstrated that the physiological process of oxidation of As (III) to As (V) play a role in hydrogen peroxide (H_2O_2) generation. H_2O_2 is not a radical but accumulation persists to be dangerous in the presence of free iron (Fe^{2+}) which is abundant in cases such as haemochromatosis or haemodialysis. In Fenton reaction, iron catalyses formation of highly reactive hydroxyl radicals [31].

Exposure to arsenic also depletes antioxidant defense in the body, by decreasing the activity of antioxidant enzymes Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPx), Glutathione Reductase (GR), glucose-6-phosphate dehydrogenase, and levels of reduced Glutathione (GSH). The result of this imbalance is dysfunction of the mitochondrial membrane, the subsequent release of cytochrome c, resulting in activation of caspase-dependent apoptosis pathways, particularly caspase 9, 3, 6, and 7 [32].

In an animal study, Bhadauria S and Flora SJS in the year 2007 reported that Wistar rats exposed to 25 ppm arsenic for 10 weeks exhibited reduced levels of δ-Aminolevulinic Acid Dehydrogenase (ALAD), GSH, Red Blood Cells (RBCs), haemoglobin, haematocrit, and SOD activity. Moreover, there was a significant increase in hepatic and renal oxidative stress markers such as Thiobarbituric Acid Reactive Substances (TBARS), a lowered GSH: GSSG ratio, and elevated metallothionein expression in hepatic tissue [33].

ARSENIC TOXICITY AND ASSOCIATED NON-COMMUNICABLE DISEASES (NCDS)

Arsenic is increasingly recognised as a major environmental contributor to the burden of NCDs [34]. These diseases affect individuals across all age groups and are particularly prevalent in regions impacted by mining activities and groundwater arsenic contamination [7,35].

Exposure to humans is generally through contact with arsenic contaminated water or food, inhalation of airborne particles, and absorption of the contaminants through the skin. Keratosis, which is the occurrence of skin lesions, is among the most well-known and early non-cancerous effects of chronic arsenic exposure and may occur at even lower drinking water arsenic concentrations (5-10 µg/L) [36]. Gastrointestinal symptoms may be present in case of acute exposure to inorganic arsenic (iAs) which includes nausea, diarrhoea, abdominal pain, and vomiting [3]. On the other hand, prolonged exposure to arsenic is associated with chronic arsenic poisoning which increases the risk of developing cancer (especially skin, lungs, bladder), CVDs, type 2 diabetes, gastrointestinal disorders [37].

Arsenic and Diabetes Mellitus (DM)

The DM is a serious health issue in the world and emerging data suggest that chronic arsenic exposure may be associated with the development of type 2 DM, with some evidence also implicating type 1 DM, though the latter remains less established. According to experimental and epidemiological observations, arsenic may cause development of DM through alteration of the immune system functionality [38]. The suggested mechanisms are oxidative stress, inflammation and apoptosis [39]. Exceptionally low levels of arsenic as little as 0.4 µg/L have been found to contribute to increased likelihood of diabetes type 2 through exceedingly long periods of getting exposed to arsenic contaminated drinking water [40].

Experiments have proved that insulin secretion and cell survival are hampered by arsenic accumulation in the pancreas [41]. Although the risks of diabetes due to high amounts of exposure to arsenic are well established, data on low-to-moderate levels show mixed results. Arsenic metabolism is individually varied to some degree due to genetic makeup and nutrition, including B vitamin content, which modulates the toxicity of arsenic [42].

Although there is no direct connection between the relationship of arsenic and obesity in humans, however, exposure to arsenic might

result in the development of obesity, and obese persons are more susceptible to arsenic-related illnesses [43]. A study done by Hong YS et al., (2014) reported an association between inorganic arsenic exposure and the onset of type 2 diabetes in obese people with the age of 40 and older. The association was significant after controlling age, sex, body mass index, and activity level at work through multiple logistic regression analysis yielding a multivariate-adjusted odds ratio of 6.61 and 10.05, respectively, among individuals with cumulative arsenic exposures equivalent to 0.1-15.0 ppm-years and >15.0 ppm-years. These findings indicate that the DM on human beings could be induced by chronic exposure to arsenic [44].

A study in Taiwan supports the association between chronic consumption of inorganic arsenic and prevalence of DM [45]. Likewise, a study conducted in Bangladesh examined how exposure to arsenic is related to the outcome of diabetes. The research results revealed that people who were exposed to arsenic especially those with skin lesions caused by arsenic were much more affected by diabetes and glucosuria than their unexposed counterparts. Also, a distinct dose-response association was demonstrated that states that the more the exposure to arsenic, the higher the risk of developing diabetes related conditions ($p<0.001$) [46].

Arsenic and Skin Diseases

The exposure to arsenic is linked to a number of acute and chronic health conditions of which the first signs are usually related to dermatological manifestations. They are pigmentary change, nail abnormalities, arsenic-induced keratosis, and skin cancers [47].

In a cross-sectional study in the Adami Tulu Jido Kombolcha district of Ethiopia, arsenic skin lesions (arsenicosis) were found in 2.2 percent of the population. The most common among the affected individuals was keratosis (55.6%), then hyperpigmentation (33.3%) and hyperkeratosis (11.1%). The consumption of well water was noted as one of the key risk factors [48].

Long-term arsenic exposure was further explored in Jiaole village in Xingren County, Guizhou Province in China, over a period of 22 years. The study revealed a close connection between skin damage and arsenic exposure where heightened hair arsenic concentrations and cumulative arsenic were significant predictors of skin lesions in coal-burning regions [49].

In their study, Zeng Q and Zhang A in the year 2020 compared the skin samples of 106 participants from reference and arsenic exposure groups that were collected over 20 years. The arsenic group was further divided into non-cancerous (hyper pigmentation, hyper keratosis) and cancerous (Bowen disease, basal cell carcinoma, squamous cell carcinoma) subgroups. The miR-155-5p, Krt1, Krt10, and Krt6c were highly upregulated in the arsenic-exposed group, whereas the immune markers of NF-AT1, IL-2, and IFN-γ were downregulated in the arsenic-exposed group and indicate immune dysfunction. It was confirmed in the lab that miR-155-5p could have a role in developing a NF-AT1-mediated immune dysregulation due to arsenic exposure [50].

Arsenic and Cardiovascular Diseases (CVDs)

Arsenic exposure has been increasingly recognised as one of the key factors to CVDs. Despite the fact that high levels of arsenic, unquestionably, are linked to a greater risk of CVDs, there is also new evidence that links the low-to-moderate level of exposure to adverse cardiovascular outcomes. The suggested mechanisms include oxidative stress, epigenetic changes, chromatin instability, and accelerated platelet aggregation [51,52].

Arsenic can damage endothelial cells, change the activity of enzymes and the intracellular pathway, which increase the risk of CVDs, including coronary artery disease, stroke, high blood pressure, cardiomyopathy, and microvascular complications. Genetic susceptibility, nutritional status and lifestyle factors such as smoking and alcohol consumption modulate these effects [53].

There are significant long-term health risks associated with exposure to inorganic arsenic through drinking water at levels within current regulatory limits and this has been found in a study conducted in California where there is an increased risk of ischemic heart disease, and it is therefore indicative that exposure even to low levels can be harmful [54]. Correspondingly, exposure to arsenic has been said to be linked to elevated blood pressure as well as atherosclerosis of the carotid arteries, with an oxidative injury perpetrated by ROS being an underlying mechanism [55].

In addition, Schmidt S in the year 2024 presented evidence of the Strong Heart Study, a cohort study of the Native American communities, which demonstrated that arsenic exposure is a biological accelerator of aging, by assessing DNA methylation clocks. The researchers concluded that about 20 percent of the CVD-related incidence in arsenic-exposed populations might be explained by the accelerated epigenetic aging, which may imply that the epigenetic aging can play the role of an early biomarker for assessing cardiovascular risk in the populations exposed to arsenic [56].

Arsenic and Cancers

Arsenic is recognised as Group-1 carcinogen worldwide and it is a major threat to the health of the population predominantly because of the variety of cancers that are related to it, among which skin cancer, lung cancer, liver cancer and even bladder cancer are predominant. Its carcinogenicity is mediated by various mechanisms that include oxidative stress, DNA repair, epigenetic alterations, protein malfunction, and the stimulation of cancer stem cells, although the complete molecular processes are not completely elucidated [57].

Kidney cancer incidence and mortality have been found to be significantly elevated in epidemiological studies in areas of high arsenic levels (approximately 100 µg/L) in drinking water as observed in southwest Taiwan, Niigata (Japan), Argentina and northern Chile [58]. Moreover, a recently conducted meta-analysis demonstrated that even low-to-moderate exposure to arsenic (<150 µg/L) is associated with increased risk of lung cancer incidence and mortality, prompting calls for stricter regulatory thresholds [59].

A population-based study on Hamadan Province, Iran, evaluated the association between levels of arsenic in groundwater and mortality caused by different diseases relying on 8,042 reported deaths between 2016 and 2020. The results revealed that there was a great positive relationship between arsenic contamination and the mortality caused by various forms of cancers such as breast cancer, leukaemia, stomach cancer, liver cancer, and brain cancer. The study conducted on the Poisson regression analysis ($p<0.05$) showed that cancer-related mortality was strongly related to an elevated concentration of arsenic in drinking water. Another importance that was pointed out by the study was the necessity to come up with efficient arsenic mitigation methods and enhance water treatment in the affected regions [60]. Complementing this, a systematic review has highlighted that the effects of exposure to low arsenic concentrations in drinking water (as low as 10 µg/L) significantly increased the probabilities of developing bladder and kidney cancer and thereby emphasising the need to conduct extensive surveillance and management of arsenic in the drinking water supply [61].

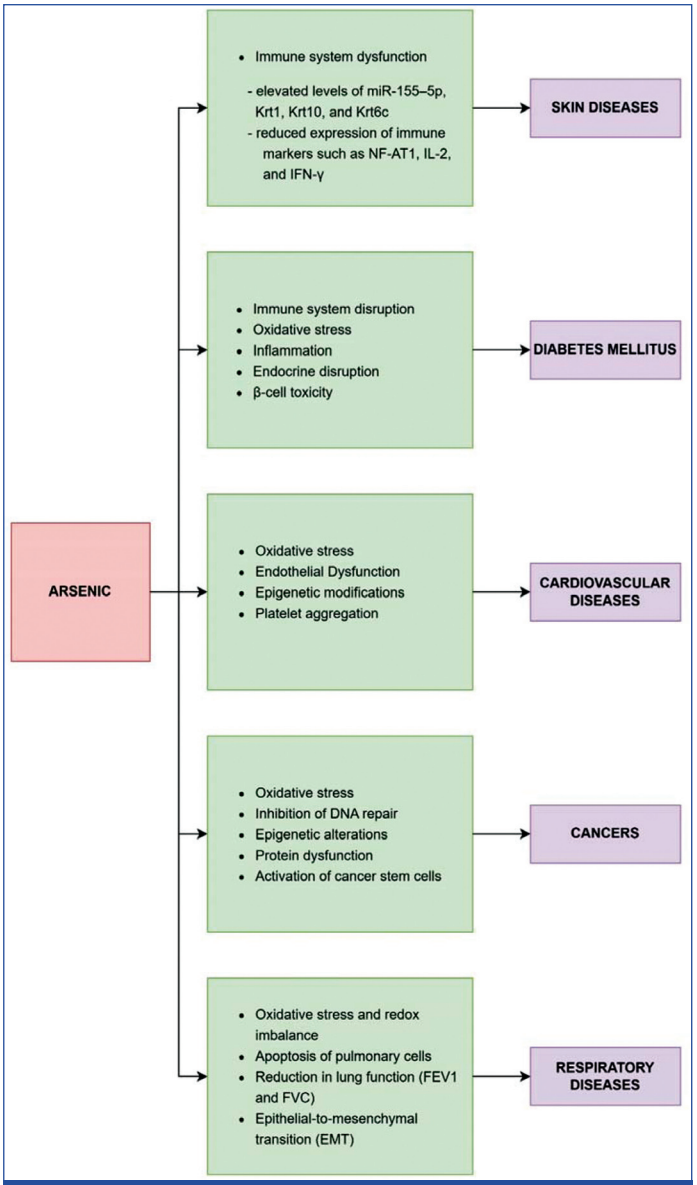
Arsenic and Respiratory Diseases

Chronic ingestion of arsenic in drinking water, especially in India and Bangladesh, has been associated with non-malignant severe respiratory effects besides the typical skin effects. These includes chronic bronchitis, Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Disease (ILD), and bronchiectasis, which indicate that arsenic is a strong respiratory toxicant, even in cases of exposure through ingestion [62].

A cross-sectional study was carried out between 1995 and 1996 in an arsenic affected region of West Bengal, India that involved

6,864 non-smokers and reported a considerable impact of arsenic on the respiratory system. Chronic arsenic exposure was strongly associated with respiratory morbidity, with the prevalence of cough, shortness of breath, and abnormal chest sounds (crepitations/rhonchi) increasing with the level of arsenic in drinking water; significant associations were found at concentrations above 500 µg/L. The Prevalence Odds Ratios (POR) for respiratory symptoms were significantly greater in high-arsenic-exposed individuals (≥500 µg/L) than the low-arsenic-exposed individuals (<50 µg/L). The age-adjusted cough POR was 7.8 in females (95% CI: 3.1-19.5) and 5.0 in males (95% CI: 2.6-9.9); for abnormal chest sound it was 9.6 in females (95% CI: 4.0-22.9) and 6.9 in males (95% CI: 3.1-15.0); and for shortness of breath it was 23.2 in females (95% CI: 5.8-92.8) and 3.7 in males (95% CI: 1.3-10.6), indicating a strong association between arsenic exposure and respiratory morbidity [63].

The Health Effects of Arsenic Longitudinal Study (HEALS) in Bangladesh showed dose response association between the concentration of arsenic in drinking water and symptoms of respiratory diseases. Using a cohort of 11,746 individuals monitored during a 4-year period, the exposure to arsenic was also found to be significantly linked with increased risk of persistent cough, difficulties in breathing, and haemoptysis even with low to moderate levels of exposure, indicating its greater implications on the health of the general population [64]. A study in 2013 highlighted the biggest analysis of lung functioning using a population-based cohort, revealing significant associations between arsenic levels in both water and urine and reduced Forced Expiratory Volume in 1 second (FEV1) and Forced Vital Capacity (FVC) values [65]. In another study, a small number of children who were prenatally and early-postnatally exposed to high arsenic (>500 µg/L) were found to have high chronic respiratory symptoms, such as wheezing and dyspnea during routine physical activity [66]. Experimental and clinical knowledge of the mechanism behind respiratory dysfunction led to the conclusion that the mechanism is driven by the arsenic-induced redox imbalance, apoptosis, inflammatory signaling mechanism, and Epithelial-to-Mesenchymal Transition (EMT). It also alters the normal development of the lungs by interfering with the important intracellular signaling pathways [67]. [Table/Fig-4] provides an outline of the mechanisms of arsenic-induced Non-Communicable Diseases (NCD) [38-41,50-53,55-57,65,67].



[Table/Fig-4]: Mechanisms of arsenic-induced Non-Communicable Diseases (NCDs) [38-41,50-53,55-57,65,67].

DISCUSSION

Arsenic is a ubiquitous environment metalloid that causes a serious global health risk, and there are more than 500 million individuals affected by groundwater contamination, mainly in the Southeast Asian area where levels are frequently above the WHO limit of 10 µg/L [1,3,7,8,10]. In addition to drinking water, the dietary sources of exposure include rice and contaminated crops, and emerging risks, including e-cigarettes [13,19,21]. Methylation of inorganic arsenic (iAs) occurs in the liver to methylarsonous acid {MMA(III)} which is highly toxic, but the toxicity hierarchy is MMA (III) > iAs (III) > iAs (V) > DMA (V) > MMA (V) [5,24,26]. The pathophysiology of arsenic toxicity is in many ways mediated by the stimulation of oxidative stress and the generation of ROS that prevents mitochondrial respiration and damages key antioxidant defence mechanisms such as SOD and GSH [28,29,32]. These molecular alterations promote the onset of various NCDs, such as Type 2 diabetes due to disrupted insulin release and pancreatic cell survival, CVDs associated with endothelial damage and rapid epigenetic aging, and severe respiratory pathologies, including COPD, chronic bronchitis, ILD and bronchiectasis [41,44,51,56,62,65]. Being a Group-1 carcinogen, chronic exposure is also marked by greater mortality due to skin, lung, bladder, and kidney cancer, which requires strict surveillance of the environment and prevention or control interventions on the population [57,59,61]. Moreover, a widespread occurrence of arsenic in groundwater indicates the need to combine environmental monitoring with the national surveillance systems of health. The prevention of the long-term health risks is important through the early identification of arsenic pollution and timely mitigation measures which can be achieved by implementing arsenic-removal technologies and supplying safe drinking water. Community awareness, nutritional intervention beneficial in the support of the arsenic metabolism, and regular health screening of the affected populations can also be significant in reducing the disease burden. It will be necessary to strengthen the environmental regulations and encourage interdisciplinary research to create sustainable solutions to address the global challenge of arsenic exposure.

CONCLUSION(S)

Arsenic exposure to humans is a serious global public health issue, especially in areas where food and groundwater are contaminated with arsenic. Numerous NCDs, such as heart disease, diabetes, cancer, respiratory ailments, and skin disorders, are closely linked to long-term exposure to arsenic. Mechanisms like inflammation, oxidative stress, immune dysfunction, and genetic and epigenetic changes are the main causes of these health effects. Therefore, to lessen the burden of diseases linked to arsenic, efficient mitigation techniques, routine food and water source monitoring, and public health initiatives are crucial.

Authors' contribution: PB: Performed drafting, formal analysis, and methodology; RRSP: Participated in validation, supervision, methodology, and writing-review and editing; VS: Performed conceptualisation, validation, and supervision, as well as writing-review and editing. All the authors have read and approved the final manuscript.

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