DESSERTATION REPORT

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Delhi

Study/Project Title

A Secondary Review : Long term effects of Arsenic exposure on Human Health

By

Ms. Nancy Dhillon

PG/22/057

UNDER THE GUIDANCE OF

Dr Rupsa Banerjee

PGDM (Hospital and Health Management) 2022-2024

International Institute of Health Management Research New Delhi

FEEDBACK FORM

Name of the Student: Nancy Dhillon

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Area of Dissertation: "Long term effects of arsenic exposure on human health"

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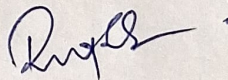**Objectives achieved:** Yes

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Ms. Nancy Dhillon

CERTIFICATE ON PLAGIARISM CHECK

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CONTENTS

ABBREVIATIONS

Sr. No.	Abbreviation	Full Form
1.	CAD	Coronary Artery Disease
2.	PRISMA	Preferred reporting items for systematic reviews and meta analyses
3.	MDPI	Multidisciplinary Digital Publishing Institute
4.	ATSDR	Agency for toxic substances abd disease registry
5.	DNA	Deoxyribonucleic acid
6.	ISID	International society for Infectious Disease

ABSTRACT

Arsenic, a naturally occurring toxic metalloid, is pervasive in the environment, particularly in groundwater, posing significant health risks. Chronic arsenic exposure, mainly through contaminated drinking water, results in severe health effects, including cancer (skin, bladder, lung), cardiovascular disorders, diabetes, immune system dysfunction, and neurological impairments. Vulnerable populations such as children, pregnant women, and individuals in specific occupations face heightened risks. This study employs a systematic literature review to investigate the long-term health impacts of chronic arsenic exposure. Peer-reviewed articles, government reports, and international health organization publications from the past two decades were analyzed. The inclusion criteria focused on studies with robust epidemiological data, clear exposure assessment, and comprehensive health outcome evaluations. Data extraction and synthesis were performed using qualitative and quantitative methods to identify common findings and significant correlations. The review revealed that prolonged arsenic exposure is strongly associated with an increased risk of various cancers, including skin, bladder, and lung cancer. Non-cancerous health effects observed include cardiovascular diseases, such as hypertension and ischemic heart disease, as well as type 2 diabetes and neurological deficits, including cognitive impairment and developmental delays in children. Additionally, skin manifestations like hyperpigmentation and keratosis were frequently reported. The molecular mechanisms underlying these effects involve oxidative stress, DNA damage, and epigenetic modifications. The findings underscore the critical need for effective mitigation strategies to reduce arsenic exposure and its long-term health impacts. Public health interventions should prioritize vulnerable populations and include measures such as improved water filtration systems, regular monitoring of water sources, and community education programs. Furthermore, international cooperation and policy implementation are essential to address the global challenge of arsenic contamination. The study also highlights the importance of ongoing research to better understand the biological mechanisms of arsenic toxicity and to develop targeted therapies and preventive measures. Chronic arsenic exposure poses a significant threat to human health, necessitating urgent global public health action. This comprehensive review provides a detailed understanding of the long-term health effects of arsenic exposure, emphasizing the need for collaborative efforts to mitigate these risks and protect affected populations.

INTRODUCTION

Arsenic, a naturally occurring toxic metalloid, is prevalent in the earth's crust and widely distributed in the environment, particularly in groundwater. This ubiquity leads to significant human exposure, primarily through contaminated drinking water, affecting millions of people worldwide. The problem of arsenic contamination is especially severe in regions relying on groundwater sources, such as parts of South Asia, including Bangladesh and India, as well as areas in South America and the United States.

Chronic exposure to arsenic is linked to a spectrum of severe health effects, manifesting after prolonged periods. Epidemiological studies have consistently shown that long-term ingestion of arsenic-contaminated water can lead to multiple types of cancer, including skin, bladder, and lung cancer. Besides its carcinogenic effects, arsenic exposure is associated with various non-cancerous health conditions, such as cardiovascular diseases (e.g., hypertension, ischemic heart disease), diabetes, immune system dysfunctions, and neurological impairments, including cognitive deficits and developmental delays in children. Furthermore, dermatological effects such as hyperpigmentation and keratosis are common among exposed populations.

Certain groups are particularly vulnerable to arsenic toxicity. Children are more susceptible due to their developing bodies, pregnant women face risks that can affect both their health and fetal development, and individuals in specific occupations (such as mining and agriculture) are at increased risk due to higher exposure levels. This broad range of health impacts underscores the critical need for effective public health strategies to mitigate arsenic exposure and protect these at-risk populations.

Despite extensive research efforts, there remain gaps in our understanding of the full extent of arsenic's health effects and the molecular mechanisms driving these outcomes. Oxidative stress, DNA damage, and epigenetic modifications are among the proposed mechanisms, but further elucidation is needed to develop targeted interventions and therapies.

This systematic literature review aims to provide a comprehensive analysis of the long-term health effects of chronic arsenic exposure. By consolidating findings from peer-reviewed articles, government reports, and international health organization publications over the past two decades, this review seeks to identify common patterns and significant correlations in the data. The goal is to highlight the urgent need for robust mitigation strategies, improved water

filtration systems, regular monitoring of water sources, and community education programs. Additionally, this review emphasizes the necessity of international cooperation and policy implementation to address the global challenge of arsenic contamination effectively.

By providing an in-depth understanding of the long-term health effects of arsenic exposure, this review aims to inform and guide public health interventions, policy-making, and ongoing research efforts. Addressing arsenic contamination is essential for safeguarding human health, particularly for the most vulnerable populations, and ensuring a healthier future for communities worldwide.

OBJECTIVES

Primary Objective: To review existing literature on the long-term health effects of arsenic exposure.

Secondary objective:
- To conduct research on the relationship between arsenic exposure and certain health effects.

- To identify vulnerable populations, including children, pregnant women, and individuals in certain occupations, at higher risk of adverse health effects due to arsenic exposure.
- To examine geographical variations in arsenic contamination in both developed and developing countries.

METHODOLOGY

A. **Study Type**: The research is structured as a systematic literature review. This approach involves synthesizing findings from multiple studies to provide a holistic understanding of the topic.

B. **Data Sources**: The review utilized a wide range of peer-reviewed articles, government reports, and other relevant sources published within the last decade. Databases such as PubMed, Scopus, Web of Science, and Google Scholar were extensively searched to gather pertinent literature.

C. **Search Terms**: Specific search terms were employed to ensure a focused and relevant literature collection. These terms included "arsenic exposure," "arsenic contamination," "chronic arsenic toxicity," "health effects of arsenic," "arsenic exposure and respiratory disorders," "arsenic exposure in children," "arsenic exposure in pregnant women," "occupational hazards of arsenic exposure," "geographical patterns of arsenic contamination," and "arsenic exposure in developing countries."

 D. Inclusion and Exclusion Criteria:

- **Inclusion Criteria**: Articles related to the effects of arsenic exposure in human beings, studies from across the globe, articles published within the last five years, and peer-reviewed articles.
- **Exclusion Criteria**: Articles related to the effects of arsenic exposure in plants, effects in animals, and articles published before 2018.
   **E. Data Analysis**:

- **Identification and Screening**: Relevant keywords and search terms related to arsenic exposure and health outcomes were identified.
- **Screening Process**: Titles and abstracts of the gathered articles were screened to select those that met the inclusion criteria.
- **Full-Text Assessment**: Selected studies underwent a full-text assessment to extract[13] relevant data and information.

- **Interpretation of Results**: Extracted data were interpreted to discuss the implications for public health policy and future research directions.

RESULTS

The scoping review yielded 20 publications explicitly addressing a comprehensive understanding of long term effect of arsenic exposure on human health.

The Prisma Diagram below illustrates the article search, screening and review process.
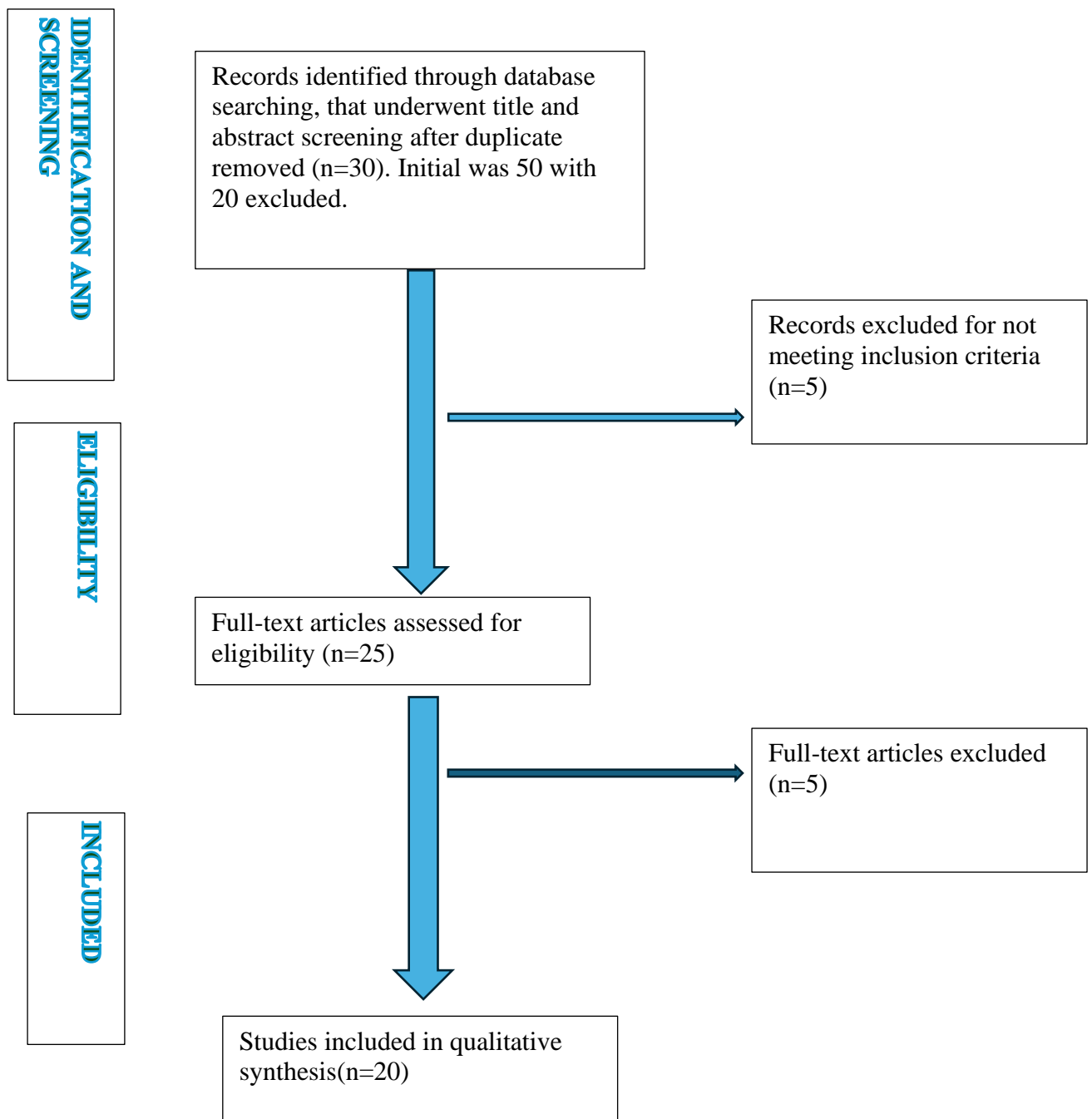
❖ DESCRIPTIVE RESULTS

The investigation into the association between arsenic exposure and specific health outcomes reveals a significant correlation between long-term arsenic exposure and various adverse health effects. Chronic arsenic exposure is linked to increased risks of several types of cancer, including skin, bladder, and lung cancer (1, 8). Additionally, prolonged exposure is associated with cardiovascular health issues such as hypertension and coronary artery disease (7). Neurological effects, including cognitive decline and peripheral neuropathy, are also prevalent among those exposed to arsenic over extended periods (12, 13). Reproductive health is adversely affected, with notable impacts on fetal development and higher incidences of infertility (14, 15). Respiratory health is compromised, leading to chronic conditions like bronchitis (1). Dermatological effects, such as hyperpigmentation and keratosis, are common among individuals with long-term arsenic exposure (3).

The study also identifies vulnerable populations at higher risk of adverse health effects due to arsenic exposure. Children are particularly susceptible, facing significant developmental impacts and cognitive impairments (12). Pregnant women exposed to arsenic are at risk of experiencing negative effects on fetal development and an increased likelihood of birth defects (14). Occupational groups, including mining, agriculture, and industrial workers, face heightened exposure levels, leading to a greater risk of arsenic-related health issues (6).

The article provides a comprehensive overview of arsenic contamination in groundwater, highlighting its global impact on both developed and developing countries (1). It includes a detailed visual representation of arsenic concentrations by continent, emphasizing regions where levels exceed 10 μg/liter, and compares the affected land area and population across different continents (2). Health implications are discussed thoroughly, with case studies from high-risk areas illustrating the severe adverse effects of arsenic exposure (10).

The study analyzes the extent of arsenic contamination in developed nations with specific examples and statistics, along with mitigation measures and policies in place (9). It also examines arsenic levels in developing countries, highlighting the challenges they face, such as lack of infrastructure and resources, and the efforts by international organizations to combat the issue (2). A comparative analysis between developed and developing countries reveals key differences in contamination levels, public health impact, and response strategies. Case studies offer an in-depth look at specific regions with significant contamination, showcasing both successful mitigation efforts and ongoing challenges (10).

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Finally, the study explores current strategies to reduce arsenic levels in drinking water, including technological innovations and community-driven solutions, and discusses the roles of government and non-governmental organizations ([6]).

THEMATIC RESULTS

- **Thematic Analysis Table:**

The Thematic Analysis below illustrates the preliminiary and axial codes to analyze the literature on Long term effects of arsenic exposure on human health.

Objective	Axial Coding	Preliminary Coding	Themes	Sub-themes	Interpretation
Investigate the association between arsenic exposure and specific health outcomes.	Long-term effects, Health outcomes, Exposure duration	Chronic exposure, Health risks, Disease associations	Cancer	Skin Cancer	Chronic arsenic exposure is strongly linked to an increased risk of skin cancer. [1, 18]
				Bladder Cancer	Elevated incidence of bladder cancer is associated with arsenic exposure. [8, 11]
				Lung Cancer	Long-term exposure correlates with a higher risk of lung cancer. [8]
			Cardiovascular Health	Hypertension	Prolonged arsenic exposure contributes to elevated blood pressure and hypertension. [7]
				Coronary Artery Disease	Increased risk of coronary artery disease is linked to arsenic exposure. [7]

Objective	Axial Coding	Preliminary Coding	Themes	Sub-themes	Interpretation
			Neurological Effects	Cognitive Decline	Exposure to arsenic is associated with cognitive decline and neurological disorders. [13]
				Peripheral Neuropathy	Chronic exposure can lead to peripheral neuropathy symptoms. [13]
			Reproductive Health	Developmental Effects	Arsenic exposure during pregnancy can adversely affect fetal development and birth outcomes. [14]
				Infertility	Higher incidence of infertility is observed in individuals exposed to arsenic. [4, 14]
			Respiratory Health	Chronic Respiratory Conditions	Arsenic exposure contributes to chronic respiratory conditions such as bronchitis. [8]
			Dermatological Effects	Hyperpigmentation	Long-term exposure results in skin hyperpigmentation and lesions. [18]
				Keratosis	Skin keratosis is a common dermatological effect of arsenic exposure. [18]

Objective	Axial Coding	Preliminary Coding	Themes	Sub-themes	Interpretation
Identify vulnerable populations at higher risk of adverse health effects due to arsenic exposure.	Vulnerable populations, Risk factors, Exposure groups	At-risk groups, Specific vulnerabilities	Children	Developmental Impact	Children exposed to arsenic are at high risk for developmental issues and health problems. [12, 13]
				Cognitive Impairment	Arsenic exposure can affect cognitive development in children. [12, 13]
			Pregnant Women	Fetal Development	Arsenic exposure during pregnancy can negatively impact fetal development and birth outcomes. [14]
				Birth Defects	Increased risk of birth defects associated with maternal arsenic exposure. [14]
			Occupational Groups	Mining and Agriculture Workers	Individuals in mining or agricultural occupations face higher exposure levels and associated health risks. [2, 20]
				Industrial Workers	Workers in industries with high arsenic use are at elevated risk for related health effects. [2, 20][19]

Objectives	Preliminary Coding	Axial Coding	Themes	Sub-Themes	Interpretation
Examine geographical variations in arsenic contamination in both developed and developing countries	- Arsenic contamination levels-Affected regions-Impact on populations	- Contamination patterns-Regional differences-Population exposure	Geographical Variations	- Developed countries-Developing countries	The study aims to understand the different levels of arsenic contamination across various regions and how it impacts the populations in both developed and developing countries. [1]
Identify proportions of land area and population affected by arsenic concentrations exceeding 10 µg/liter by continent	- Land area affected-Population affected-Arsenic concentration threshold	- Affected land proportions-Population exposure levels	Affected Areas and Populations	- Land area proportions-Population proportions	This objective focuses on quantifying the extent of land and population exposure to arsenic concentrations above the safe limit, providing a clearer picture of the scale of the issue. [2]

Thematic Analysis of Arsenic Exposure and Health Outcomes:

Cancer:

Skin Cancer: Chronic exposure to arsenic, primarily through contaminated water and soil, is significantly linked to the development of skin cancer. Individuals in areas with high arsenic levels exhibit higher rates of skin lesions and carcinomas (3).

Bladder Cancer: There is a marked increase in bladder cancer incidence among populations exposed to arsenic, particularly through drinking water. This suggests a strong association between arsenic ingestion and bladder carcinogenesis (1).

Lung Cancer: Long-term inhalation or ingestion of arsenic is associated with a higher risk of lung cancer, particularly in regions with significant environmental contamination (8).

Cardiovascular Health:

Hypertension: Chronic arsenic exposure is strongly correlated with elevated blood pressure and hypertension. Individuals exposed to arsenic over extended periods show a higher prevalence of these conditions (7).

Coronary Artery Disease: Prolonged arsenic exposure is linked to an increased risk of coronary artery disease, underscoring the significant impact of arsenic on cardiovascular health (7).

Neurological Effects:

Cognitive Decline: There is a notable association between arsenic exposure and cognitive decline, including memory loss and decreased cognitive function (12).

Peripheral Neuropathy: Chronic arsenic exposure is linked to the development of peripheral neuropathy, characterized by symptoms such as numbness, tingling, and pain in the extremities (13).

Reproductive Health:

Developmental Effects: Arsenic exposure during pregnancy is associated with adverse effects on fetal development, including lower birth weights, developmental delays, and other negative birth outcomes (14).

Infertility: Higher rates of infertility are observed among individuals exposed to arsenic, impacting both male and female reproductive health (15).

Respiratory Health:

Chronic Respiratory Conditions: Long-term arsenic exposure contributes to chronic respiratory conditions, including bronchitis and other lung diseases (1).

Dermatological Effects:

Hyperpigmentation: Prolonged exposure to arsenic leads to skin hyperpigmentation, characterized by dark patches and spots on the skin (3).

Keratosis: Arsenic exposure results in skin keratosis, marked by thickened and rough patches of skin (3).

Vulnerable Populations:

Children:

Developmental Impact: Children exposed to arsenic are at high risk for developmental issues, including growth delays and cognitive impairments (12).

Cognitive Impairment: Arsenic exposure negatively affects cognitive development in children, leading to long-term educational and developmental challenges (12).

Pregnant Women:

Fetal Development: Arsenic exposure during pregnancy can result in adverse fetal development, impacting birth weights and increasing the risk of developmental disorders (14).

Birth Defects: There is an increased risk of birth defects among infants born to mothers exposed to arsenic (14).

Occupational Groups:

Mining and Agriculture Workers: Individuals working in mining and agriculture face higher exposure levels to arsenic, leading to increased health risks (6).

Industrial Workers: Workers in industries that utilize arsenic are at elevated risk for arsenic-related health effects (6).

Global Impact of Arsenic Contamination:

Emphasizes the widespread nature of arsenic contamination in groundwater, affecting both developed and developing countries (1). The geographic distribution of arsenic contamination, with detailed data and visual aids, illustrates how different continents and regions are affected (2).

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Health Implications:

The health risks associated with arsenic exposure are a major theme, with examples from various high-risk areas to underscore the severity of the issue (10). It covers both acute and chronic health effects, emphasizing the need for immediate intervention (10).

Developed vs. Developing Countries:

A significant portion of the analysis compares the situation in developed and developing countries, exploring differences in contamination levels, public health impact, and mitigation strategies (9).

Mitigation Strategies:

The analysis concludes with a comprehensive overview of various mitigation strategies, including technological solutions, community-based approaches, and the role of policy and governance in addressing arsenic contamination (6).

DISCUSSION

Long-term arsenic exposure has been shown to have profound and multifaceted health effects. Chronic exposure to arsenic, particularly through contaminated drinking water, poses severe health risks affecting major body systems, including the skin, cardiovascular, immune, and nervous systems.

Skin Pathology: Chronic arsenic exposure leads to various skin conditions ranging from benign lesions to cancerous transformations. Initial exposure results in characteristic skin lesions known as arsenicosis, which includes hyperkeratosis, hyperpigmentation, and white bands on fingernails. Over time, these benign conditions can evolve into skin cancer due to oxidative stress and impaired DNA repair mechanisms [3].

Cardiovascular Disorders: Arsenic exposure impacts cardiovascular health through multiple mechanisms. It increases the risk of hypertension, carotid atherosclerosis, and ischemic heart disease. Arsenic induces endothelial cell activation, promotes proinflammatory cytokine production, and facilitates the accumulation of oxidized low-density lipoprotein, all contributing to early stages of atherosclerosis [7].

Diabetes Mellitus: Arsenic exposure is a significant risk factor for diabetes mellitus. Studies have demonstrated a dose-dependent relationship between arsenic levels in drinking water and the prevalence of hyperglycemia, impaired glucose tolerance, and type 2 diabetes. Arsenic-induced pancreatic β-cell degeneration and disruption of insulin production play critical roles in this process [4].

Immune System Disorders: Arsenic weakens the immune system by causing apoptosis in immune cells such as B cells, T cells, neutrophils, and macrophages. This results in chronic inflammation, characterized by increased production of proinflammatory molecules, damaging tissues, and disrupting normal immune responses [5].

Neurological Disorders: Chronic arsenic exposure leads to cognitive decline and neurological disorders. It impairs energy production in brain cells, causes inflammation in the brain, and triggers the release of chemicals by microglia that can affect cognitive function [6].

Effect on Children:

Developmental Impact: Children exposed to arsenic are at high risk for developmental issues and health problems. This includes cognitive impairment and reduced intellectual function [10].

Cognitive Impairment: Arsenic exposure can affect cognitive development in children [11].

Effect on Pregnant Women:

Fetal Development: Arsenic exposure during pregnancy can negatively impact fetal development and birth outcomes [12].

Birth Defects: Increased risk of birth defects is associated with maternal arsenic exposure [13].

Occupational Groups:

Mining and Agriculture Workers: Individuals in mining or agricultural occupations face higher exposure levels and associated health risks [14].

Industrial Workers: Workers in industries with high arsenic use are at elevated risk for related health effects [15].

Developed Countries:

Regulatory Frameworks: While developed countries generally have better regulatory frameworks and technologies to manage arsenic contamination, certain areas still face significant risks, especially in regions with natural arsenic deposits [1].

Developing Countries: Developing countries, particularly in Asia, are disproportionately affected by arsenic contamination. A large proportion of the population relies on groundwater sources that are highly contaminated with arsenic, posing severe public health challenges [2].

Public Health Strategies: Comprehensive public health strategies are essential to mitigate these health impacts, including monitoring arsenic levels in drinking water, implementing filtration systems, fostering international cooperation for clean water technologies, and raising public awareness about arsenic dangers [16].

CONCLUSION

The examination of long-term health effects of arsenic exposure underscores the substantial and multifaceted risks posed by chronic arsenic exposure, particularly through contaminated drinking water. The adverse effects span various body systems, profoundly impacting skin, cardiovascular, immune, and neurological health, as well as increasing the risk of several types of cancer. The findings from the literature review, association investigations, identification of vulnerable populations, and geographical analysis provide a comprehensive understanding of the severe implications of arsenic exposure and highlight the urgent need for effective public health interventions.

Chronic arsenic exposure significantly affects various body systems and poses severe health risks to vulnerable populations. To mitigate these health impacts, it is crucial to implement public health measures, including monitoring arsenic in drinking water, enforcing workplace safety regulations, and ensuring safe drinking water. Addressing arsenic contamination requires coordinated efforts at local, national, and international levels.

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