Examining The Effects Of Arsenic In Drinking Water On Human Health By Understanding Its Chemistry, Metabolism, And Toxicity

Dr. Ashutosh Kumar Shukla[1]*, Dr. Niranjan Kumar[2], Dr. Hansnath Tiwari[3], Badshah Alam[4]

[1]*Assistant Professor, Amity School of Engineering & Technology, Amity University Patna, Bihar
E-mail:- akumar1@ptn.amity.edu, https://orcid.org/0000-0001-6685-2124
[2]Assistant Professor, Department of Physics, Amity University Patna, E-mail:- Niranjan_sinha786@rediffmail.com, https://orcid.org/0000-0003-0680-0466
[3]Assistant Professor, Department of Chemistry, Motilal Nehru National Institute of Technology, Allahabad
E-mail:- hansnathtiwarigf@mnnit.ac.in, https://orcid.org/0000-0003-1955-0937
[4]Assistant Professor, Amity University Patna, Bihar, E-mail:- balam@ptn.amity.edu

***Corresponding Author: -**Dr. Ashutosh Kumar Shukla
*Assistant Professor, Amity School of Engineering & Technology, Amity University Patna, Bihar, E-mail:- akumar1@ptn.amity.edu, https://orcid.org/0000-0001-6685-2124

Abstract

Arsenic pollution in India, particularly in Bihar, is a significant public health issue. The main source of contamination is geological, as naturally existing arsenic from rocks and sediments leaches into aquifers. High levels of arsenic in wells make drinking water unsafe and pose health hazards to millions of people. Exposure to arsenic-contaminated drinking water can lead to skin lesions, malignancies, cardiovascular ailments, and neurological abnormalities. Vulnerable groups like youngsters and pregnant women are particularly at risk. Public relations efforts and educational initiatives have also been launched to alert the public about the dangers of drinking water tainted with arsenic and to promote behavioural changes. Arsenic contamination has been addressed, but there are still big obstacles to overcome. Many affected regions still have limited access to clean drinking water, particularly in rural areas. Large-scale arsenic mitigation strategies, such the construction of community-level arsenic removal plants, call for ongoing financial support and technical know-how. This paper attempts at understanding the chemistry of arsenic, its metabolism in human body, its toxicity and underlying health implications.

Keywords:- Arsenic, Groundwater, Surface Water Contamination, Metabolism, Toxicity, Health Implication

INTRODUCTION

In many regions of the world, drinking water poisoning with arsenic is a serious public health issue. Arsenic is a substance that naturally occurs in rocks and soil. It can enter groundwater because of geological processes or human activity like mining and the disposal of industrial waste. Numerous health issues, including skin lesions, cancer (including skin, lung, bladder, and kidney cancer), cardiovascular illness, and neurological impacts have been associated to prolonged exposure to high amounts of arsenic in drinking water. Arsenic is listed by the World Health Organization (WHO) as a Group 1 human carcinogen.

Arsenic in drinking water, primarily found in groundwater sources, poses a significant health risk in Bihar. Groundwater is the primary source, accounting for over 90% of rural drinking water sources. Contamination is a major issue due to urbanization, population growth, industrialization, and unrestricted extraction for domestic, industrial, and agricultural purposes. In Bihar, arsenic was discovered in the groundwater at levels exceeding the WHO guidelines, or 10 ppb (parts per billion) or 0.01ppm (parts per million), in the early 2000s. According to studies by Kumar et.al (Kumar, 2023), nearly 10 million residents of the northern Bihar Gangetic plains drink water with an arsenic content of more than 10 ppb and more than 40% of the population of Bihar was affected by arsenic, and that the southern bank of the river Ganga was more susceptible to it than the northern bank. They observed that only two districts were afflicted by arsenic in 2002, but that by 2023, 18 districts had drinking water with more than 50 ppm of arsenic.

A metalloid found in soil and aquifers; arsenic (As) may pose serious health hazards when present in drinking water at amounts above the recommended limit. Most of the arsenic that finds its way into water sources comes from either natural earth deposits or pollution from industry and agriculture. Although most surface water is regarded as safe for drinking, groundwater sources are arsenic contaminated between 14 and 49 meters below the surface.

In Bihar's groundwaters, arsenic was first discovered in 2002. While the number of districts with arsenic at more than 50 mg/L has climbed from two in 2003 to eighteen in 2023 (Kumar, 2023), the spread of arsenic in the southern bank of the Ganges is greater than on the northern bank, and about 40% of the population is susceptible to exposure.

MATERIALS AND METHOD

This work has tried to comprehend the chemistry of arsenic from a chemist's perspective, as well as its distribution in various habitats, metabolism in the human body, health consequences of arsenic toxicity, and the mechanism of arsenic toxicity, with the aid of currently accessible literature. We looked for scholarly literature on the various facets of arsenic chemistry in the online database 'Google Scholar' and 'PubMed'. It came to our notice that there is exponential increase in number of papers if we search terms like 'arsenic', 'metabolism of arsenic' in PubMed. Results from the search went as far back as 1960 and as recently as 2023. Metabolism, health consequences, arsenic dispersion, toxicity, and skin problems were some of the search terms/phrases used. After carefully reading and evaluating the chosen articles, we organize the papers by generating subtopics and looking for trends, also a hand search and another search using the "related articles" option were done to finish the literature survey. Personal visits to the affected districts were done and natives were interviewed on the severity of the crisis. It came to our notice that despite government efforts, the problem persists and propagates.

Chemistry of Arsenic

The study of arsenic's chemistry is highly comprehensive. The only thing covered in this section is a description of the chemistry of arsenic compounds that may be significant for the environment. Arsenic is rarely found as a free element in the natural world. It is most usually found in sulfidic ores, where it manifests as metal arsenides such as nickel diarsenide, cobalt diarsenide, nickel arsenide, cobalt arsenide sulfide, copper arsenide sulfide, and iron diarsenide. Other naturally occurring arsenates include those of aluminum, barium, bismuth, calcium, cobalt, copper, iron, lead, magnesium, manganese, uranium, and zinc. Arsenic trioxide is also produced as a result of the weathering of arsenides (Frankenberger, 2001).

There have been a tremendous number of arsenic compounds created that include one or more arsenic-carbon bonds. The ability of the arsenic atom to form bonds with aromatic or aliphatic organic groups of one to five makes a wide range of compounds conceivable. Organic groups can be joined to other atoms and groups using the valences that aren't used in their bonds.

Arsenic was probably used for the first time by Romans during 164 BC when they unintentionally destroyed the agriculture of ancient city Carthage by repeatedly using salts of copper and arsenic (Markham, 2019). They were slowly poisoning their crops. The unfortunate event is eerily like what happened in the ancient city of Pompei where they used lead (pb) in plumbing thus slowly poisoning and annihilating themselves. History is full of such events which point towards the ill-effects of 'Law of Unintended Consequences ("Unintended Consequences")'.

Organic arsenic compounds are extensively used as herbicides and pesticides. The first known use of arsenic-based compound in India was in year 1937 in Punjab district. In the following table, name of arsenic based herbicides, as issued by Indian Council of Agricultural Research (ICAR) year-wise (Choudhury, 2016), has been listed in Table1.

Table1: Different herbicides, as approved by ICAR, containing arsenic, with issued year. Source: ICAR, Government of India

Herbicide	Chemical Nomenclature	Year of introduction
DSMA	Disodium methanearsonate	1956
Cacodylic acid	Hydroxydimethylarsine oxide	1961
MSMA	Monosodium methanearsonate	1963
Methylarsonic acid	Methylarsonic acid	1994

These chemicals can have major negative influence on adjacent water supplies, especially through runoff and leaching. Herbicides are substances created specially to eradicate or manage undesirable plants (weeds). These chemicals may enter surrounding water bodies, such as rivers, lakes, and groundwater, when they are used on crops, lawns, gardens, or other plants. Herbicides can be transported from the treated area into surrounding surface water bodies by precipitation or irrigation runoff after application. Runoff can happen when the soil is already saturated with water, blocking further absorption of the herbicides, or when the herbicides have not yet been absorbed into the soil. Leaching is when herbicides can potentially leak into groundwater through the soil, particularly if they are water-soluble (Jones, 2007). They might eventually get to surface water sources or contaminate drinking water wells once they are in the groundwater. Herbicides in aquatic bodies can have several negative effects:

Distribution of Arsenic in Environment

I. Rocks and Soil:

Arsenic is the twentieth most prevalent element in the crust of the planet. Arsenic concentrations in the earth's continental crust are typically estimated to be between 1.5 and 2 ppm. As a result, it is relatively rare. Arsenic is found in high concentration in sulfide deposits, where it is present as the native element or alloys (four minerals), arsenides (27 minerals), sulfides (13 minerals), sulfosalts (sulfides of arsenic with metals, such as lead, copper, silver, and thallium, 65 minerals), and the oxidation products of the foregoing (two oxides, 11 arsenites, 116 arsenates, and seven silicates). Arsenopyrite is by far the most typical of these minerals. In the middle Gangetic plain of Bihar, India, groundwater, agricultural soils, and subsurface sediment concentrations of the inorganic forms of arsenic (As) [arsenite, As(III), and

arsenate, As(V)] were measured. As(III) is the dominating species in about 73% of the groundwater samples (n = 19), while As(V) is the dominant species in about 27% of the samples (Kumar, 2016).
The two rivers Ganges and Brahmaputra contribute to the lush Bengal Delta Plains (BDP), which are made up of riverine deposits. The Indian Plate, Chota Nagpur Plateau, Shilong Plateau, and Naga Lusai orogenic belt, which are all extremely neotectonic, border the BDP from the west to the northeast (Shrivastava, 2015). The local vegetation and climate have an impact on the deposition of sediment in these areas. As a result, the distribution of organic matter, oxic-anoxic conditions, and local microbial flora play major roles in determining the sources and distribution of arsenic in these plains.

II. Arsenic in plants:
In the world of plants, arsenic is found everywhere. Its dry-weight basis concentration ranges from less than 0.01 to roughly 5 ppm. Species differences in plants and, in a broader sense, environmental and edaphic conditions in a specific geographic area are likely the causes of variations in arsenic content. Plants growing in arsenic-contaminated soils have greater residue levels than plants growing in regular soils.
An issue with food safety could arise from agricultural plants absorbing too much arsenic. Recent discoveries that rice (Oryza sativa) is particularly effective at absorbing arsenic from paddy soil serve as an illustration of this. Arsenic accumulates in rice grains at concentrations that may be harmful to humans who consume significant amounts of rice in their diet. The development of mitigation strategies to address the issue of arsenic contamination in the food chain depends on an understanding of how plants absorb and metabolize the metal. In the meantime, the discovery of arsenic-hyperaccumulating fern species has drawn considerable attention and prompted more investigation into the mechanisms underlying this exceptional phenomenon as well as an assessment of the phytoremediation capacity of different arsenic hyperaccumulators.

III.Human and animals:
Every living thing has arsenic. Coelenterates, some molluscs, and some crustaceans may have higher arsenic concentrations more than marine fish, which may have up to 10 ppm. Although most readings are less than 1 ppm, freshwater fish can have up to roughly 3 ppm. On a wet-weight basis, domestic animals and people typically possess less than 0.3 ppm. Between 3 to 4 mg make up the entire human body, and this amount tends to rise with age. Analyses have shown that most bodily tissues, except for hair, nails, and teeth, contain less than 0.3 ppm.

IV. Arsenic in air:
Numerous natural and human activities have the potential to release arsenic into the atmosphere. A few of the sources of airborne arsenic include:
a. Volcanic activity: When volcanoes erupt, arsenic is released into the atmosphere.
b. Industrial processes: Because of their operations, some businesses, including mining, smelting, and coal-fired power plants, can emit arsenic into the air.
c. Fossil fuel combustion: Burning fossil fuels, such as coal, oil, and natural gas, can release chemicals containing arsenic into the atmosphere.
d. Agriculture: The use of pesticides and fertilizers that contain arsenic can cause the emission of arsenic into the air.
e. Residential sources: Burning wood that has been treated with arsenic-based preservatives for building or other uses can produce arsenic emissions in some places.

Arsenic can travel a great distance after being discharged into the air and finally be deposited onto soil and water surfaces through rain or dry deposition. Arsenic in the air can be absorbed by both people and animals, which can be harmful to their health.
The recommended exposure limit set by the National Institute for Occupational Safety and Health (NIOSH) is 2 microgram per cubic meter of air for no more than a 15-minute period, based on classification of arsenic as a potential human carcinogen (Muller, 2022; U.S. Department of Labor, 1975).

V. Arsenic in Water:
Arsenic exposure to humans and animals is mostly facilitated by contaminated water. Several Indian states, including West Bengal, Bihar, Uttar Pradesh, Assam, and portions of Punjab, have recorded elevated groundwater arsenic concentrations. Natural geological processes are frequently blamed for this contamination because over time, rocks rich in arsenic release the element into the water. Since many rural people rely on groundwater for daily needs like drinking and sanitation, this has a significant impact on them.
In Bihar, currently18 districts have drinking water with more than 50 ppb arsenic (Fig1, Fig2). This includes about 50 blocks from 15 districts that encompass more than 1590 habitations around the state. More than 100 million people are impacted in India and Bangladesh if the WHO limits of 10 ppb are considered, with over 30 million people in Bihar (Ravenscroft, 2011) and West Bengal, India, being at danger due to drinking water contamination (Chakraborti, 2003; Hossain, 2013).

Fig2. Data in columnar form that depicts the picture of severity of arsenic affected districts in Bihar. It's evident that districts sprawled on the either side of river Ganga are most affected which points towards water-born infection and causes.

Fig1. Geospatial map of arsenic affected districts of Bihar. Source: PHED Bihar

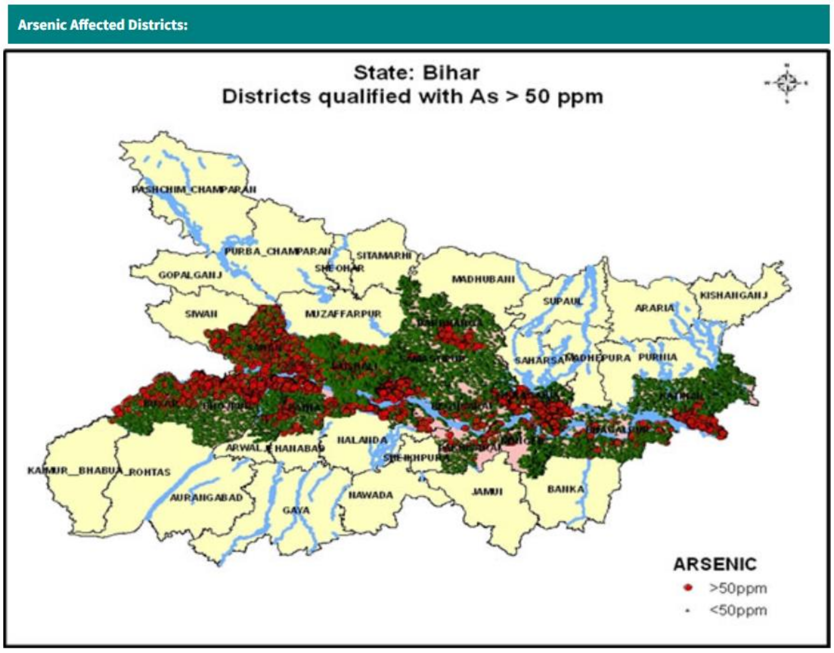

Fig2. List of districts with number of affected blocks by arsenic contamination. Source: PHED Bihar

SL	District Name	Total Blocks	Total Affected Blocks	Total Affected Habitations
1.	Begusarai	18	4	84
2.	Bhagalpur	16	4	159
3.	Bhojpur	14	4	31
4.	Buxar	11	4	385
5.	Darbhanga	18	1	5
6.	Katihar	16	5	26
7.	Khagaria	7	4	246
8.	Lakhisarai	7	3	204
9.	Munger	9	4	118
10.	Patna	23	4	65
11.	Samastipur	20	4	154
12.	Saran	20	4	37
13.	Vaishali	16	5	76
	Total	**195**	**50**	**1,590**

Metabolism of Arsenic in Human Body

Humans undergo a multi-step, multi-pathway process known as arsenic metabolism. Arsenic is a poisonous metalloid that occurs naturally in the environment. It can be ingested through contaminated food, drink, or air. Arsenic's metabolism affects its toxicity and potential health impacts, therefore understanding it is crucial (Drobna, 2010). Following are the steps involved in its metabolism when ingested by mammalian, particularly human:

1. **Absorption:** Arsenic can enter the body through several different pathways, but the two most typical are ingestion and inhalation (Vahter, 1983). Arsenic can be absorbed through the digestive system after consumption. The liver, kidneys, lungs, skin, and hair are just a few of the organs and tissues it can reach once inside the body.

2. **Biotransformation:** Arsenic goes through biotransformation in the body, particularly in the liver, where it is digested by enzymes (Kumagai, 2007). Inorganic arsenic (iAs) and organic arsenic (primarily arsenobetaine and arsenocholine), which are both important for human metabolism, are the two main types of arsenic of importance.
3. **Methylation:** Methylation is a critical stage in the metabolism of arsenic. This procedure transforms the arsenic molecule into a variety of methylated metabolites by adding methyl groups (CH3) (Aphoshian, 1997). Arsenite methyltransferase (AS3MT) and other methyltransferases are the main enzymes involved in the methylation of arsenic.
4. **Arsenic metabolites:** Monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) are two of the methylated metabolites of arsenic (Tseng, 2007). In general, these methylation forms of arsenic are less poisonous than inorganic arsenic, while some research indicates that MMA may be more harmful than DMA.
5. **Excretion:** The methylated arsenic metabolites, left over after the amount absorbed by body, are eliminated from the body through the urine after methylation (Lai, 2004). Individual differences in methylation and excretion efficiency can be attributed to both hereditary and non-genetic factors, such as exposure levels and dietary status.

It's crucial to remember that certain individuals may have genetic variations in the genes in charge of metabolism of arsenic (such as the AS3MT gene), which may affect their capacity to metabolize and eliminate arsenic. Individual sensitivity to arsenic toxicity may vary because of this.

Associated Health Implications

Environmental arsenic poisoning, especially in drinking water and food, can have detrimental effects on health (Kazi, 2009). Even though arsenic occurs naturally, human activities like mining and industrial processes can cause it to be released into the environment. Chronic exposure to high quantities of arsenic can cause several health issues, including:

1. **Skin Problems:** Prolonged contact with arsenic can lead to hyperpigmentation, hyperkeratosis (skin thickening), and skin sores. It might occasionally cause the growth of skin cancer. Following skin-related health issues have been observed due to arsenic contamination:

1.1 **Hyperpigmentation**: Hyperpigmentation, or the darkening of regions of skin, can be brought on by long-term exposure to arsenic (Walvekar, 2007). Due to its distinctive appearance, this condition is sometimes known as "raindrop" hyperpigmentation.

1.2 **Hypopigmentation:** Arsenic exposure can cause areas of depigmentation or whitening of the skin in addition to black patches (Saleem, 2019).

1.3 **Hyperkeratosis:** Skin thickening, especially on the palms and soles of the feet, can result from exposure to arsenic. Hyperkeratosis is the name of this disorder, which can be both painful and unsightly (Baker, 2005).

1.4 **Skin Lesions:** Prolonged exposure to arsenic can cause skin lesions including warts, nodules, and corns to appear (Mazumdar, 2008).

1.5 **Skin cancer:** The International Agency for Research on Cancer (IARC) has categorized arsenic as a Group 1 carcinogen. The chance of acquiring skin cancer, including basal cell carcinoma, squamous cell carcinoma, and melanoma, is significantly raised by chronic exposure to arsenic (Astolfi, 1981).

2. **Peripheral vascular disease:** a condition that affects the blood vessels and blood circulation in the extremities, can be brought on by prolonged exposure to arsenic (Yu, 2002). In extreme circumstances, this could lead to gangrene and ulceration.

3. **Bowen's disease:** a form of squamous cell carcinoma in situ that manifests as red, scaly spots on the skin, has been connected to exposure to arsenic (Graham, 1961).

4. **Respiratory Issues:** Breathing in dust or fumes containing arsenic can cause respiratory problems, including respiratory tract inflammation (Islam, 2007) and a higher risk of lung cancer. Chronic exposure to arsenic has been associated with an increased risk of cancer. Islam et.al in their seminal paper in 2007 found that ‘Arsenic patients had highly significantly elevated levels of serum immunoglobulins that positively correlated with respiratory complications, urinary excretion of arsenic, and duration of exposure’.

5. **Cancer:** Long-term exposure to arsenic has been associated with a higher risk of developing several cancers (Smith, 1992), including skin, lung, bladder, liver, and kidney cancer. Study of Kumar et.al. (Kumar, 2021) found that the raised blood arsenic concentration in the cancer patients strongly correlates the relationship of arsenic with cancer especially the carcinoma type which is more vulnerable. They also created a geospatial map which correlates the blood arsenic with cancer types and the demographic area of Gangetic plains (Fig1).

6. **Cardiovascular Effects:** Exposure to arsenic has been linked to a higher incidence of heart attacks, hypertension, and atherosclerosis, among other cardiovascular illnesses (Islam, 2007; Wang, 2007; Alissa, 2011; Navas, 2005). Epidemiological studies have demonstrated dose-response correlations between numerous cardiovascular illnesses and chronic arsenic poisoning, which is caused by consuming arsenic-contaminated water. These cardiovascular conditions include carotid atherosclerosis, which can be detected by ultrasonography, impaired microcirculation, a prolonged QT interval and increased QT dispersion on electrocardiography, as well as clinical outcomes like

hypertension, coronary artery disease, cerebral infarction, and blackfoot disease, a rare peripheral vascular disease that is endemic to southwestern Taiwan. An independent risk factor for cardiovascular disease is chronic arsenic exposure.

7. **Effects on the Nervous System**: According to some studies, long-term exposure to arsenic may have negative effects on the nervous system, including neurological symptoms like tingling and numbness as well as cognitive deficits (Kumar, 2022; Rodriguez, 2003). The mechanisms of oxidative stress, apoptosis, thiamine shortage, and decreased acetyl cholinesterase activity are responsible for arsenic-induced neurotoxicity. Peripheral nerves and sensory fibres are more commonly affected by the observed neurotoxicity (Mochizuki, 2019). Natives which were interviewed during this research complained of sharp, jabbing pain in foot, back, thigh and hands with tingling sensation that is consistent with the symptoms of peripheral neuropathy.

8. **Reproductive Problems:** Exposure to arsenic may harm the reproductive system, resulting in issues with fertility and a higher likelihood of unfavourable pregnancy outcomes (Mukherjee, 2023; Neeti, 2013).

8.1 Reproductive health of female:

8.1.1 Menstrual irregularities: Exposure to arsenic can alter the body's normal hormonal balance, which may result in irregular menstrual cycles and fertility problems.

8.1.2 Reduced Fertility: Women who are exposed to arsenic have been shown to have lower fertility. It may have an impact on ovulation, egg quality, and general reproductive health.

8.1.3 Pregnancy Complications: During pregnancy, exposure to arsenic increases the chance of miscarriages, stillbirths, preterm births, and low birth weight newborns. Birth defects and abnormal development may also be affected by it.

8.1.4 Impaired Ovarian Function: Exposure to arsenic can have a deleterious effect on ovarian function, which can damage both the development of eggs and the ovaries' general health (Barbhuiya, 2021).

8.2 Reproductive health of male:

8.2.1 Reduced sperm quality: Arsenic exposure can result in lower sperm counts, decreased sperm motility (movement), and altered morphology (shape), all of which can have an influence on male fertility.

8.2.2 Hormonal Disruption: Arsenic can disrupt the endocrine system, which controls hormone production and balance, resulting in hormonal disruption. The production of testosterone and other hormones necessary for healthy male reproduction may be impacted by this imbalance.

8.2.3 Erectile Dysfunction: Due to its detrimental effects on blood vessel health and hormone control, some research point to a possible association between arsenic exposure and an increased risk of erectile dysfunction (ED).

8.2.4 Genetic Damage: Sperm cells exposed to arsenic may sustain DNA damage, which may result in genetic changes that could be passed on to progeny and raise the risk of birth abnormalities and developmental problems (Zargari, 2022).

9. **Diabetes**: There is evidence to suggest that a person's chance of getting type 2 diabetes may rise if they are exposed to arsenic on a regular basis (Lai, 1994). It's crucial to remember that the connection between diabetes and arsenic poisoning is convoluted and poorly understood. Nonetheless, an outline of how diabetes may be impacted, based upon the status of current research, by arsenic exposure is given below:

9.1 Insulin Resistance: It has been established that exposure to arsenic contributes to the onset of insulin resistance. The main cause of type 2 diabetes, when the body's cells become less receptive to the actions of insulin and rising blood sugar levels result, is insulin resistance. Exposure to arsenic can disrupt glucose metabolism and alter insulin signalling pathways, which can result in insulin resistance.

9.2 Beta Cell Dysfunction: The pancreatic beta cells, which oversee making and releasing insulin, may also be affected by exposure to arsenic. Beta cell dysfunction can result in insufficient insulin synthesis, which aggravates diabetes.

9.3 Inflammation and oxidative stress: Exposure to arsenic can cause these conditions in the body. Both diabetes and its consequences are accompanied with oxidative stress and chronic inflammation. These procedures may affect diabetes control and increase insulin resistance.

9.4 Impaired glucose regulation: Arsenic exposure may interfere with the body's ability to regulate glucose, which can lead to swings in blood sugar levels. For people with diabetes who must closely monitor and control their blood sugar levels, this can be very challenging (Farkhondeh, 2019).

To properly comprehend the mechanisms through which arsenic exposure affects diabetes, it is important to note that research on the connection between arsenic poisoning and the disease is still in progress. Arsenic's effects on diabetes can also differ depending on the degree and length of exposure, a person's vulnerability, and general health.

10. **Impaired Immune Function**: Exposure to arsenic can impair immunity, leaving people more prone to infections and other illnesses (Islam, 2015). Following are some effects of arsenic poisoning on the immune system in people:

10.1 Immunosuppression: Long-term exposure to high quantities of arsenic has been associated with immunosuppressive effects, which can impair the immune system's capacity to fight off infections. The formation and function of immune cells like T cells and B cells, which are essential for identifying and warding off infections, can be decreased because of exposure to arsenic. An increased susceptibility to infections may come from this.

10.2 Changes in Cytokine Production: Cytokines are immune response-controlling signalling molecules that can change because of arsenic exposure. The balance between pro-inflammatory and anti-inflammatory responses can be upset by these changes in cytokine levels, which may result in chronic inflammation or autoimmune reactions.

10.3 Impaired phagocytosis: Phagocytes, immune cells that are essential for capturing and eliminating foreign substances like bacteria and viruses, have impaired phagocytosis. It has been demonstrated that exposure to arsenic interferes with the phagocytic function of immune cells like macrophages, reducing their capacity to remove infections from the body.

10.4 Genotoxic effects: Arsenic is well known for causing DNA damage and having genotoxic consequences. Immune cells may generate mutations because of DNA damage, which may impair how well they function and contribute to the emergence of immune-related illnesses.

10.5 Increased Propensity for Allergic Reactions: According to certain research, exposure to arsenic may be linked to a higher risk of allergic reactions. Arsenic can modify immune responses by interfering with the balance of various immune cell types and changing the release of histamine and other molecules involved in allergic responses.

10.6 Immune Dysregulation: Exposure to arsenic may impair the immune system's ability to respond appropriately, which may result in autoimmune disorders, persistent inflammation, and dysregulated immunological responses.

The consequences of arsenic poisoning on the immune system might differ based on several variables, including the degree and length of exposure, a person's sensitivity, and general health. Arsenic exposure over an extended period is more likely to produce negative long-term effects on the immune system. Seminal work by Kozul et.al. on arsenic poisoning in rats suggests that immune response expression is altered (Kozul, 2009).

Health implication of arsenic poisoning in Bihar is shown in Fig3. It points towards different types of skin infections and cancer that can be caused due to arsenic-poisoning. A lot of remedial and awareness measures has been taken by Bihar Government in recent times and that is shown in Fig4 (PHED, 2018).

It's vital to remember that the effects of arsenic pollution on one's health can change based on the degree and length of exposure as well as one's own sensitivity. The poisonous effects of arsenic are particularly harmful to unborn babies and pregnant women.

Mechanism of Toxicity of Arsenic in Human

Arsenic pathogenesis is characterized by oxidative damage caused by reactive oxygen species (ROS). Arsenic also causes morphological abnormalities in the mitochondria's structural integrity. Cells are more susceptible to the harmful effects of arsenic because of glutathione-depleting substances paired with cascade mechanisms of free radical generation resulting from the superoxide radical (Jomova, 2011). The formation of ROS/RNS, including peroxyl radicals (ROO•), the superoxide radical, singlet oxygen, hydroxyl radicals (OH•) via the Fenton reaction, hydrogen peroxide, the dimethylarsenic radical, the dimethylarsenic peroxyl radical, and/or oxidant-induced DNA damage, is increased in arsenic-exposed humans and animals (Obinaju, 2009). Arsenic poisoning in humans is caused by several routes, including:

1. **Inhibition of enzyme:** Arsenic inhibits the activity of several enzymes that are involved in vital metabolic reactions. The pyruvate dehydrogenase complex, which is essential for cellular energy synthesis, is one of the most notable enzymes affected (Hughes, 2002). Arsenic alters the cellular energy metabolism by blocking this enzyme, which has a few negative effects.
2. **Production of Reactive Oxygen Species (ROS**): Cells that have been exposed to arsenic may produce reactive oxygen species (ROS). ROS are very reactive chemicals that can harm biological elements like proteins, lipids, and DNA (Obinaju, 2009; Hughes, 2002). It is possible for this oxidative stress to cause tissue damage, inflammation, and cell death.
3. **DNA damage**: Arsenic can harm DNA through several different methods, including direct DNA binding and interfering with DNA repair processes (Hughes, 2002). This raises the risk of developing cancer and other diseases by causing mutations and chromosomal abnormalities.
4. **Impairment of cell signalling**: Apoptosis (planned cell death) and other cellular signalling pathways can all be affected by arsenic, including those involved in cell proliferation, differentiation, and apoptosis (Rahaman, 2021). These disturbances can trigger unchecked cell growth and aid in the development of cancer.
5. **Epigentic changes:** Exposure to arsenic can cause epigenetic changes, which are variations in gene expression patterns without underlying DNA sequence modifications (Obinaju, 2009; Hughes, 2002; Rahaman, 2021). Numerous diseases, including cancer, may evolve differently because of these modifications.
6. **Cellular Membrane Disruption**: Arsenic can alter the permeability and structural integrity of cellular membranes, impairing ion transport and cell activity (Biswas, 2008).
7. **Impact on Immune System:** Exposure to arsenic can depress the immune system, increasing a person's susceptibility to illnesses and reducing their body's capacity to fight off diseases (Bellamari, 2018).

Arsenic's toxicity is dose-dependent, with chronic exposure to low levels occurring more frequently than not in many areas. Skin lesions, cardiovascular problems, respiratory ailments, and an elevated risk of cancer (such as lung, skin, bladder, and liver cancer) have all been associated to prolonged exposure to low amounts of arsenic.

Fig3: Severity of arsenic pollution on human. Source: PHED, Bihar

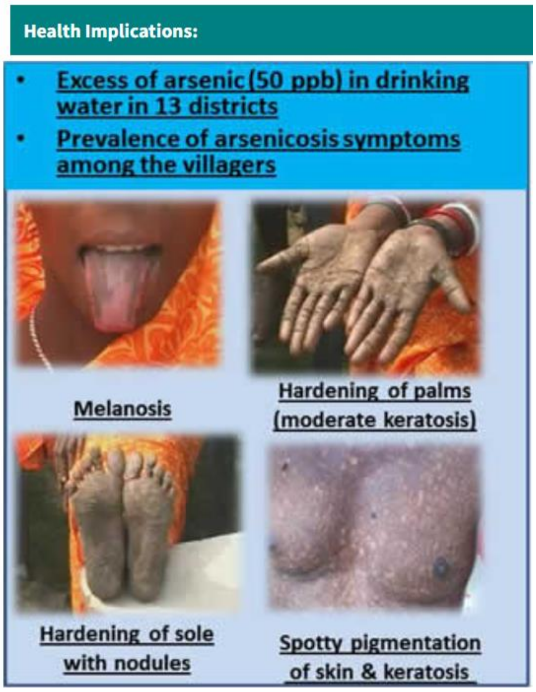

Fig4: Awareness campaign against arsenic pollution of groundwater. Source: PHED, Bihar

CONCLUSION

Research on arsenic in drinking water is crucial as it poses significant health risks, including skin lesions, cardiovascular disorders, respiratory problems, and increased risk of malignancies. Arsenic contamination affects many areas globally, particularly in developing nations with limited access to clean water. Understanding the distribution, occurrence, and health hazards of arsenic contamination can help develop effective mitigation methods and regulations. Groundwater contamination, a major source of drinking water for millions, can occur due to geological processes or human activities like mining and industrial waste discharge. Understanding arsenic pollution in drinking water is essential for developing successful mitigation and cleanup plans. Researchers can investigate strategies like filtration, adsorption, and advanced treatment techniques to reduce arsenic levels in water sources. Understanding the effectiveness, viability, and long-term sustainability of these methods is crucial for implementing safe drinking water access. Arsenic contamination research provides a scientific foundation for establishing regulatory criteria and guidance, which can be used by governments and regulatory organizations to set maximum contamination levels and implement monitoring mechanisms to ensure compliance. These regulations protect public health, direct water treatment procedures, and ensure the security of drinking water supplies.

DECLARATIONS:

Availability of data and materials:

The data on usage of herbicides is freely available on the website of Indian Council of Agricultural Research (ICAR) and can be downloaded following the link - https://shorturl.at/ipNQ7 .

Important information materials, viz. Fig1, Fig2, Fig3 and Fig4 has been taken from the website of Public Health Engineering Department of Bihar (https://phedbihar.gov.in/WaterQuality.aspx) and can be freely accessed and downloaded from the website mentioned in parenthesis.

Funding:
Not Applicable

Conflicts of interest:
The study was done on constrained individual budget and reflects no conflict of either financial or academic nature. The authors declare that they have no conflict of interest.

Author's contributions:
Both authors, AK, NK, HT and BA have contributed equally to the development of this paper and research.

Acknowledgement:
Ak acknowledges the infrastructure and academic support provided by Amity University Patna along with long discussions held with the esteemed and erudite colleagues there-in on the issue of air, soil, and water pollution, not only on local but related repercussions on global scale. AK also acknowledges numerous unknown natives he interviewed to understand the severity of crisis.

Tables: - 01

Figures: - 04

REFERENCES:
1. Alissa, Eman M., and Gordon A. Ferns. "Heavy metal poisoning and cardiovascular disease." *Journal of toxicology* 2011 (2011).
2. Aposhian, H. Vasken. "Enzymatic methylation of arsenic species and other new approaches to arsenic toxicity." *Annual review of pharmacology and toxicology* 37.1 (1997): 397-419.
3. Astolfi, E., et al. "Relation between arsenic in drinking water and skin cancer." *Biological Trace Element Research* 3 (1981): 133-143.
4. Baker, Beth A., et al. "Persistent neuropathy and hyperkeratosis from distant arsenic exposure." *Journal of agromedicine* 10.4 (2005): 43-54.
5. Barbhuiya, Sweety Nath, Dharmeswar Barhoi, and Sarbani Giri. "Impact of arsenic on reproductive health." *Environmental Health* 89 (2021).
6. Bellamri, Nessrine, et al. "Arsenic and the immune system." *Current Opinion in Toxicology* 10 (2018): 60-68.
7. Biswas, Debabrata, et al. "Mechanism of erythrocyte death in human population exposed to arsenic through drinking water." *Toxicology and applied pharmacology* 230.1 (2008): 57-66.
8. Chakraborti, Dipankar, et al. "Arsenic groundwater contamination in Middle Ganga Plain, Bihar, India: a future danger?." *Environmental health perspectives* 111.9 (2003): 1194-1201.
9. Choudhury, Partha P., et al. "Herbicide use in Indian agriculture." ICAR - Directorate of Weed Research, Jabalpur, Madhya Pradesh, 110 (2016).
10. Drobná, Zuzana, et al. "Metabolism of arsenic in human liver: the role of membrane transporters." *Archives of toxicology* 84 (2010): 3-16.
11. Farkhondeh, Tahereh, Saeed Samarghandian, and Mohsen Azimi-Nezhad. "The role of arsenic in obesity and diabetes." *Journal of cellular physiology* 234.8 (2019): 12516-12529.
12. Frankenberger Jr, William T., ed. *Environmental chemistry of arsenic*. CRC Press, 2001.
13. Graham, James H., Giovanna R. Mazzanti, and Elson B. Helwig. "Chemistry of Bowen's disease: Relationship to arsenic." *Journal of Investigative Dermatology* 37.5 (1961): 317-332.
14. Hossain, M. Amir, et al. "Water consumption patterns and factors contributing to water consumption in arsenic affected population of rural West Bengal, India." *Science of the Total Environment* 463 (2013): 1217-1224.
15. Hughes, Michael F. "Arsenic toxicity and potential mechanisms of action." *Toxicology letters* 133.1 (2002): 1-16.
16. Islam, Laila N., et al. "Association of respiratory complications and elevated serum immunoglobulins with drinking water arsenic toxicity in human." *Journal of Environmental Science and Health, Part A* 42.12 (2007): 1807-1814.
17. Islam, Laila N. "Immunotoxic effects of arsenic exposure." *Handbook of arsenic toxicology*. Academic Press, 2015. 493-519.
18. Jomova, K., et al. "Arsenic: toxicity, oxidative stress and human disease." *Journal of Applied Toxicology* 31.2 (2011): 95-107.
19. Jones, F. T. "A broad view of arsenic." *Poultry science* 86.1 (2007): 2-14.
20. Kazi, Tasneem Gul, et al. "The correlation of arsenic levels in drinking water with the biological samples of skin disorders." *Science of the Total Environment* 407.3 (2009): 1019-1026.

21. Kozul, Courtney D., et al. "Chronic exposure to arsenic in the drinking water alters the expression of immune response genes in mouse lung." *Environmental health perspectives* 117.7 (2009): 1108-1115.
22. Kumagai, Yoshito, and Daigo Sumi. "Arsenic: signal transduction, transcription factor, and biotransformation involved in cellular response and toxicity." *Annu. Rev. Pharmacol. Toxicol.* 47 (2007): 243-262.
23. Kumar, Manoj, et al. "Concentrations of inorganic arsenic in groundwater, agricultural soils and subsurface sediments from the middle Gangetic plain of Bihar, India." *Science of the Total Environment* 573 (2016): 1103-1114.
24. Kumar, Arun, et al. "Arsenic exposure in Indo Gangetic plains of Bihar causing increased cancer risk." *Scientific Reports* 11.1 (2021): 2376.
25. Kumar, Shishu Kesh, and Das Ambika Bharti. "Is Stress, Anxiety and Depression Salient in Arsenic-Induced Cancer?." *Indian Journal of Clinical Psychology* 49.1 (2022): 23-27.
26. Kumar, Arun, Chandrajeet Kumar, and Yerravarapu Vamsi Krishna. "Blood Arsenic Contamination Causing Breast Cancer Risk in Exposed Population of Bihar." *Health Science Journal* 17.5 (2023): 1-6.
27. Lai, Mei-Shwu, et al. "Ingested inorganic arsenic and prevalence of diabetes mellitus." *American Journal of Epidemiology* 139.5 (1994): 484-492.
28. Lai, Vivian W-M., et al. "Arsenic speciation in human urine: are we all the same?." *Toxicology and applied pharmacology* 198.3 (2004): 297-306.
29. Markham, Adam C. *A brief history of pollution*. Routledge, 2019.
30. Mazumder, DN Guha. "Chronic arsenic toxicity & human health." *Indian Journal of Medical Research* 128.4 (2008): 436-447.
31. Mochizuki, Hitoshi. "Arsenic neurotoxicity in humans." *International journal of molecular sciences* 20.14 (2019): 3418.
32. Mukherjee, Anirban Goutam, and Abilash Valsala Gopalakrishnan. "The interplay of arsenic, silymarin, and NF-κB pathway in male reproductive toxicity: A review." *Ecotoxicology and Environmental Safety* 252 (2023): 114614.
33. Müller, L., et al. "Human health risk assessment of arsenic in a region influenced by a large coal-fired power plant." *International Journal of Environmental Science and Technology* (2022): 1-8.
34. Navas-Acien, Ana, et al. "Arsenic exposure and cardiovascular disease: a systematic review of the epidemiologic evidence." *American journal of epidemiology* 162.11 (2005): 1037-1049.
35. Neeti, Kapoor, and Tiwari Prakash. "Effects of heavy metal poisoning during pregnancy." *Int Res J Environ Sci* 2.1 (2013): 88-92.
36. Obinaju, Blessing Ebele. "Mechanisms of arsenic toxicity and carcinogenesis." *Afr. J. Biochem. Res* 3.5 (2009): 232-237.
37. PHED, 2018, *Public Health Engineering Department, Government of Bihar,* https://phedbihar.gov.in/WaterQuality.aspx
38. Rahaman, Md Shiblur, et al. "Environmental arsenic exposure and its contribution to human diseases, toxicity mechanism and management." *Environmental Pollution* 289 (2021): 117940.
39. Ravenscroft, Peter, Hugh Brammer, and Keith Richards. *Arsenic pollution: a global synthesis*. John Wiley & Sons, 2011.
40. Rodrıguez, V. M., Maria E. Jiménez-Capdeville, and Michele Giordano. "The effects of arsenic exposure on the nervous system." *Toxicology letters* 145.1 (2003): 1-18.
41. Saleem, Mohammed D., et al. "Acquired disorders with hypopigmentation: A clinical approach to diagnosis and treatment." *Journal of the American Academy of Dermatology* 80.5 (2019): 1233-1250.
42. Shrivastava, Anamika, et al. "Arsenic contamination in soil and sediment in India: sources, effects, and remediation." *Current Pollution Reports* 1 (2015): 35-46.
43. Smith, Allan H., et al. "Cancer risks from arsenic in drinking water." *Environmental health perspectives* 97 (1992): 259-267.
44. Tseng, Chin-Hsiao. "Arsenic methylation, urinary arsenic metabolites and human diseases: current perspective." *Journal of Environmental Science and Health Part C* 25.1 (2007): 1-22.
45. "Unintended Consequences." *Wikipedia*, Wikimedia Foundation, 7 Aug. 2023, en.wikipedia.org/wiki/ Unintended_ consequences. Accessed 8 Aug. 2023.
46. U.S. Department of Labor. Occupational Safety and Health Administration. Inorganic arsenic. Proposed exposure standard. Fed. Reg. 40:3392–3404, 1975.
47. Vahter, M. A. R. I. E. "Metabolism of arsenic." *Biological and environmental effects of arsenic* 6 (1983): 171-198.
48. Walvekar, R. R., et al. "Chronic arsenic poisoning: a global health issue–a report of multiple primary cancers." *Journal of cutaneous pathology* 34.2 (2007): 203-206.
49. Wang, Chih-Hao, et al. "A review of the epidemiologic literature on the role of environmental arsenic exposure and cardiovascular diseases." *Toxicology and applied pharmacology* 222.3 (2007): 315-326.
50. Yu, Hsin-Su, Chih-Hung Lee, and Gwo-Shing Chen. "Peripheral vascular diseases resulting from chronic arsenical poisoning." *The Journal of dermatology* 29.3 (2002): 123-130.
51. Zargari, Felor, et al. "Arsenic, oxidative stress and reproductive system." *Journal of Xenobiotics* 12.3 (2022): 214-222.