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Arsenic contamination in rice and drinking water: An insight on human cognitive function

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ABSTRACT

Arsenic, a prevalent environmental contaminant in drinking water and rice, poses significant health risks, especially in Southeast Asia. Emerging evidence suggests that even low-level arsenic exposure may contribute to neurodevelopmental disorders such as autism spectrum disorder (ASD). However, evidence linking low-level arsenic exposure in water and rice to neurobehavioral dysfunctions are often underestimated, neglecting the risks to children. This review aims to explores arsenic contamination in rice and drinking water across Southeast Asia, comparing it with Bangladesh, India, and China—three of the world's largest rice producers and consumers. It focuses on prenatal and postnatal exposure, exploring potential impacts on cognitive function related to ASD traits. Bangladesh, India, and Indonesia consistently report arsenic levels in rice above the 0.2 mg/kg safety threshold, while Malaysia, Vietnam, Myanmar, and Thailand generally remain below this limit. Seven studies reported noncarcinogenic risks (HQ > 1), while nine studies found carcinogenic risks (CR > 1×10^{-4}) associated with rice consumption, highlighting potential health concerns in the Southeast Asian region. Additionally, six studies with unspecified risks. In Vietnam, Bangladesh, India, and Cambodia, arsenic contamination in groundwater has been associated with arsenicosis and elevated cancer risks. Although a positive correlation between low-level arsenic exposure (below 50 μg/L) and cognitive decline has been observed in the Asian countries, this link remains underexplored in Southeast Asia. Further research is needed to investigate arsenic exposure during critical developmental periods and its impact on neurobehavioral outcomes in vulnerable populations.

1. Introduction

Arsenic (As), a naturally occurring metalloid has become a widespread environmental contaminant due to excessive anthropogenic activities in the last century such as mining, various industrial activities and agricultural practices (Briffa et al., 2020). In the environment, arsenic exists in two primary forms: organic arsenic and inorganic arsenic. These can be further classified based on their oxidation states such as arsenite [As(III)], arsenate [As(V)], elemental arsenic [As(0)], and arsine [As (0)] (Ghosh et al., 2022). Within living organisms, inorganic As(III) and As(V) undergo a series of reduction and oxidative-methylation reactions, yielding monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) (Davydiuk et al., 2023). Arsenobetaine, arsenocholine, and arsenosugar are the primary methylated arsenic forms found in marine food chains (Ghosh et al., 2022). The toxicity, mobility, and solubility of arsenic vary among species. In its inorganic form, arsenic is highly toxic: As (III) > As(V) compared to its less toxic organic form (Ganie et al., 2024; Mawia et al., 2021). Besides occupational exposure, the abilities of arsenic to bioaccumulate and biomagnify have caused extensive distribution in the food webs and water bodies (Ghosh et al., 2022). The widespread contamination of the environment, food and water led to massive increases in human exposure to arsenic (Fatoki and Badmus, 2022). The contamination of various staple foods and drinking water by this toxic heavy metal poses a pervasive threat to the human population (Naujokas et al., 2013; Podgorski and Berg, 2020).

Affecting millions of people worldwide, chronic, low level arsenic exposure can lead to skin disorders (Karagas et al., 2015; Naujokas et al., 2013), cancer (Issanov et al., 2024), cardiovascular disease (Yu et al., 2023), diabetes (Li et al., 2023), impaired immune function (Giles and

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Mann, 2022) increased infant mortality, lower birth weight, and larger head circumference (Mullin et al., 2019; Muse et al., 2020). However, existing studies often overlook the risks to children and its effect on central nervous system (CNS). This is concerning as arsenic is a known neurotoxicant, with the CNS being particularly susceptible during early development (Grandjean and Landrigan, 2006). Prenatal exposure can induce oxidative stress, leading to improper brain development and impaired neurobehavior (Farzan et al., 2013; Htway et al., 2019). In Bangladesh, early childhood and prenatal exposure to low-level arsenic (50 μg/L) detected in urine was modestly associated with reduced cognitive in 5-year-old children (Vahter et al., 2020). A previous review highlighted that a 50 % increase in arsenic levels in drinking water (51–117 μg/L) or urine (94–118 μg/L) corresponded to a 0.5-point IQ decrease in children aged 5–15 years (Rodríguez-Barranco et al., 2013), underscoring the detrimental impact of low-level arsenic exposure during critical developmental period (Signes-Pastor et al., 2022). This aligns with earlier findings showing that arsenic levels in hair correlate with autism spectrum disorder (ASD) symptom severity in Italian children (Fiore et al., 2020) and increased risk of depression, anxiety and attention problems (Renzetti et al., 2021). However, there is no clear association has been published so far in relation to As exposure and cognitive impairment as one of ASD traits.

About 85–90 % of the population in Southeast Asia and Asia is at risk of arsenic poisoning due to contaminated drinking water, rice, food preparation, and crop irrigation (Podgorski and Berg, 2020; Su et al., 2022). Risk Assessment Report by the United States Food and Drug Administration (FDA) highlighted that rice, contains the highest levels of inorganic arsenic and widely consumed globally, making it a significant contributor to dietary exposure (U.S. Food and Drug Administration, 2016). In 2023, India, Bangladesh, China, and Indonesia, the top global rice producers, collectively produced 523.9 million tonnes of rice, despite these areas being highly to moderately polluted with arsenic (FAO, 2023). The growing prevalence of ASD among Southeast Asian children (Shrestha et al., 2024) and the substantial economic burden of mental disorders globally further highlight the urgency of assessing rice's role in arsenic exposure. Mental disorders (ASD, ADHD) affect nearly 1 billion people globally, costing the economy $1 trillion annually in lost productivity, with projections of $6 trillion by 2030 (Bloom et al., 2011; The Lancet Global Health, 2020). Recent global burden study estimates global losses at $5 trillion, with regional losses in Southeast Asia and Asia accounting for up to 5 % of gross domestic product (Arias et al., 2022). This economic burden highlights the need for cost-effectiveness of prevention and treatment strategies. Despite extensive studies on arsenic levels in rice and water in Southeast Asia and Asia, there is a critical gap in research on the impact of chronic, low-level arsenic exposure on cognitive function. Additionally, there is no clear association between arsenic exposure and neurobehavioral dysfunction. Existing studies often overlook the apparent arsenic abnormalities at low level and the risk to vulnerable populations such as pregnant women and developing children. Evidence from the 1955 mass arsenic poisoning in Japan reveals that adults exposed to arsenic during infancy exhibited neuropsychological dysfunctions in later life, highlighting the risk of arsenic exposure during critical developmental periods results in permanent cognitive impairment (Yorifuji et al., 2016). Thus, to address this growing concern, this review explores the current arsenic contamination in rice, as a staple food and water sources across Southeast Asia (Malaysia, Thailand, Cambodia, Indonesia, Vietnam, Myanmar, Singapore), comparing it with Bangladesh, India, and China—three of the world's largest rice producers and consumers including South Korea, focusing on its potential impact on cognitive function related to ASD traits.

2. Methodology

2.1. Search process

The literature search was conducted for published reports, research articles and case studies. The data was obtained electronically from the database available (Science Direct, PubMed, Springer, Royal Society of Chemistry, and Tailor and Francis) from the year 2000–2024 and restricted to English-language. Different combinations of keywords in relation to the review topic were used: southeast Asia, Asia, Malaysia, Thailand, Cambodia, Indonesia, Vietnam, Myanmar, Singapore, Bangladesh, India, and China, South Korea, Japan, arsenic, heavy metal, trace metal, pregnant women, children, infant, neurodevelopmental disorders, autism, ADHD, maternal blood, cord blood, cognitive, IQ, intelligence, maternal, hair, urine, cord blood, blood, prenatal, postnatal, rice, rice products, infant foods, and drinking water. Fig. 1 summarize the selection process.

2.2. Selection process

The information thus attained from the selected articles with following inclusion criteria: a) full-text, b) English language, c) study design (cross-sectional studies, cohort studies, case control studies, biomonitoring studies), d) duration exposure (>6 months, continuous exposure through oral and dermal route >100 subjects and for discrete effects >5). Long-term arsenic exposure (>6 months) was selected to establish reliable dose-response relationships for chronic health outcomes, particularly since previous risk assessments showed effects like skin lesions, cancer, and IQ deficit occurring at low to high arsenic concentrations over extended exposure periods (Jha et al., 2023; Shaibur et al., 2024; Yorifuji et al., 2016). To ensure reliable assessment of arsenic exposure effects, a minimum sample size of 100 subjects was required for continuous arsenic adverse effects, while discrete effects need at least 5 cases, allowing robust epidemiological analysis at both individual and group levels (Memon et al., 2020; Verma and Verma, 2020), e) arsenic concentrations (>10 μg/L in drinking water, >0.2 mg/kg in rice or corresponding exposure level for arsenic biomarkers—hair, urine, blood), f) population (Asia, Southeast Asia, children, infants, adult, pregnant women) and g) findings (any long-term adverse outcomes—cognitive impairment).

This review excluded articles discussing co-exposure with other pollutants, data from in vitro and in vivo research studies, data from studies where exposure is not from the oral and dermal route, articles on exposure from oral consumption of soils by children, although this is an acknowledged route of oral exposure for children. After exclusion, a comprehensive analysis of 170 full-text articles, strategically selected to cover four critical areas: arsenic levels in rice across Southeast Asia and Asia, arsenic contamination in various drinking water sources throughout Southeast Asia and Asia, epidemiological studies examining arsenic's cognitive impacts on infants, children, and adults in Southeast Asia, and a comparative analysis with similar studies from other Asian regions and global contexts. This systematic approach ensured a thorough examination of arsenic contamination in key dietary sources and its cognitive effects, providing a robust foundation for understanding the issue in Southeast Asia within a broader geographical context. By integrating data on contamination levels in staple food and water sources with epidemiological findings, the study offers a holistic view of the arsenic-cognition relationship in the region. Epidemiological studies from Laos and Brunei were excluded from this review due to limited arsenic exposure data, lack of systematic surveillance programs, and absence of comprehensive population-based studies that meet the quality assessment criteria for exposure metrics and health outcomes.

2.3. Analysis

VOSviewer version 1.6.20 was used to map the keyword occurrence

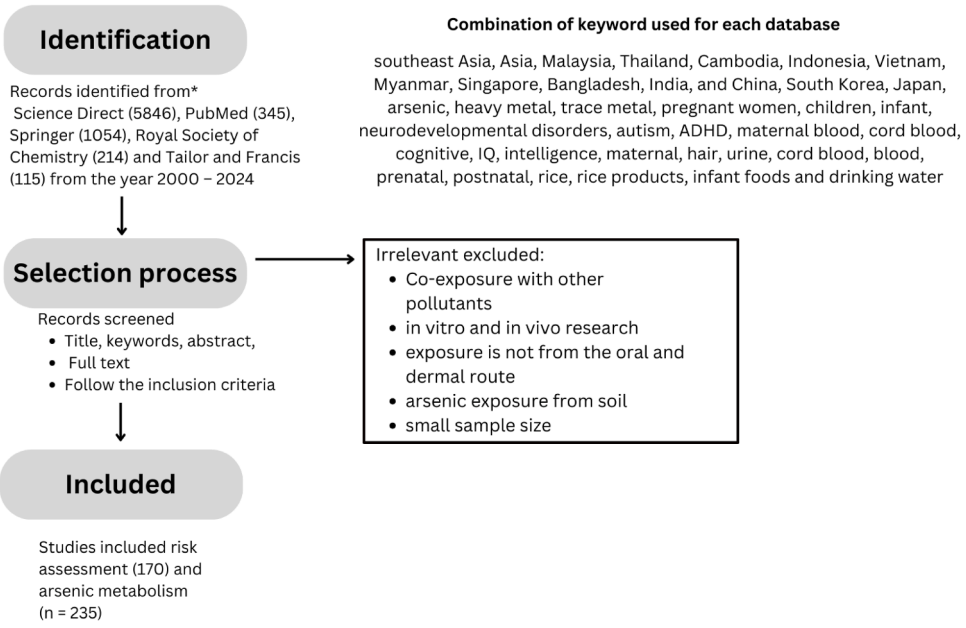

Fig. 1. Illustration of the literature selection process.

between selected articles and progression of research by year. Fig. 2A indicates that keywords such as `arsenic,' `toxicity,' `human,' `risk assessment,' `rice,' and `groundwater' were well-established in the literature. The bigger size of the circle indicates high occurrence of studies. However, the distant location of the keyword `cognitive' suggests a lack of studies focused on the cognitive effects of arsenic exposure. The number of studies reached its peak between 2016 and 2018 as indicated by the green color in the center (Fig. 2B). The number of studies from each country in the heatmap were categorized based on scales for non-carcinogenic and carcinogenic risk assessment: a) HQ/H1 < 0.1 - Cancer risk very low, risk level 1, chronic risk can be negligible, cancer occurrence <1 per 1,000,000 (10^{-6}), b) HQ/H1 ≥ 0.1 to <1 - Cancer risk low, risk level 2, chronic risk low, cancer occurrence >1 per 1,000,000 (10^{-6}) to <1 per 100,000 (10^{-5}), c) HQ/H1 ≥ 1 to < 4 - Cancer risk medium, risk level 3, chronic risk medium, cancer occurrence > 1 per 100,000 (10^{-5}) to <1 per 10,000 (10^{-4}), and d) HQ/H1 ≥ 4 - Cancer risk high, risk level 4–5, chronic risk high, cancer occurrence >1 per 10,000 (10^{-4}) to <1 per 1000 (10^{-4}) (Shaibur et al., 2024).

3. Results and discussion

3.1. Regulating bodies and arsenic standards

The toxic effects of arsenic depend on the exposure dose or concentration, types of arsenic (arsenite [As(III)], arsenate [As(V)], elemental arsenic [As(0)] and arsine [As (0)]), duration of exposure (acute, sub-chronic or chronic), frequency of exposure (single or multiple times) and route of exposure (oral, dermal, or inhalation). Different countries may have varying regulatory bodies and arsenic standards due to differences in demographic factors. At the international level, U.S. government standards for arsenic include regulations for airborne arsenic levels in workplaces, arsenic in animals and plants used as food, and arsenic in drinking water. The Occupational Safety and Health Administration (OSHA) standard sets the maximum permissible level for airborne arsenic exposure in the workplace at 10 μg/m^3 over an 8-hour workday (ATSDR, 2007). In contrast, the National Institute for Occupational Safety and Health (NIOSH) recommends a limit of 2 μg/m^3 of arsenic in air for no more than a 15-minute period, due to the classification of arsenic, a potential human carcinogen (ATSDR, 2007). The U. S. Environmental Protection Agency (EPA) classifies arsenic as a hazardous air pollutant under the Clean Air Act. It is largely emitted through industrial activities such as primary copper smelters, arsenic plants, and glass manufacturing plants. While no specific ambient air pollution limit exists for arsenic, both the EPA and the World Health Organization (WHO) have established a drinking water limit of 10 μg/L arsenic, a standard adopted by across countries over the past two decades including Southeast Asia and Asia, though data availability varies (Podgorski and Berg, 2020). WHO designates 10 μg/L of arsenic in drinking water as provisional, recommending levels be kept `as low as reasonably possible'due to challenges in water treatment and analysis (Ramsay et al., 2021). This follows the precautionary principle, given uncertainties about arsenic mode of action and debates on the dose-response curve at low concentrations. However, in India, 50 μg/L is permissible when alternative sources are unavailable, while it remains the maximum contaminant level (MCL) in Bangladesh and rural China (Zheng, 2020). This disparity is concerning, as emerging evidence suggests even 10 μg/L may not be sufficiently protective, particularly during vulnerable early life stages.

Council Regulation (EEC) No 315/93 implement that food containing contaminants at levels harmful to public health must not be placed on the market, and that contaminant levels should be kept as low as reasonably achievable (Arcella et al., 2021; EFSA et al., 2024). If needed, the European Commission may set maximum levels for specific contaminants, which are detailed in Annex I of Commission Regulation (EU) 2023/915 (Arcella et al., 2021; EFSA et al., 2024). Notably, the authorities recommend a much lower limit of 100 ng/g of inorganic arsenic for infant and young children's food (U.S. Food and Drug Administration, 2016). To minimize health risks like cancer and skin lesions, regulatory bodies have tightened limits on daily inorganic arsenic intake. The European Food Safety Authority (EFSA) Panel on Contaminants in the Food Chain (CONTAM) Panel recently lowered the recommended level to 0.06 μg/kg body weight per day, encompassing broader health concerns such as bladder cancer, lung cancer, ischemic heart, skin lesions disease, chronic kidney disease, respiratory disease, spontaneous stillbirth, abortion, infant mortality, and neurodevelopmental effects (Arcella et al., 2021; EFSA et al., 2024). This stricter limit replaces the previous range of 0.3 to 8 μg/kg (Arcella et al., 2021; EFSA, 2009). The Codex Alimentarius Commission (Codex) under Joint FAO/WHO Food Standards Programme has established different maximum levels for inorganic arsenic in rice is 0.2 mg/kg (Arcella et al., 2021). EFSA also

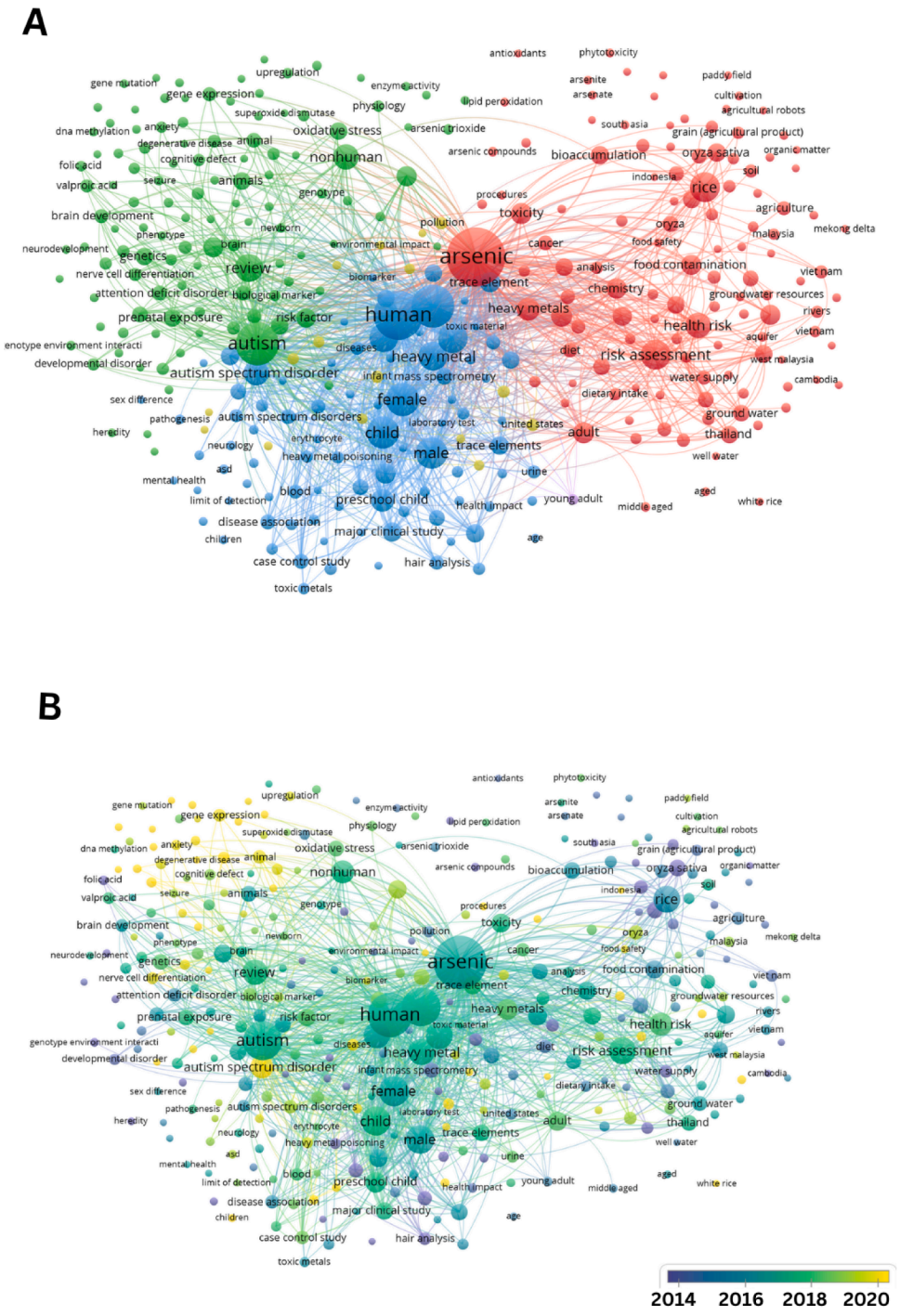

Fig. 2. Keyword co-occurrence map. A) Frequently studied keywords, such as `arsenic,' `toxicity,' `human,' `risk assessment,' `rice,' and `groundwater,' are represented by larger circles, indicating higher occurrence rates in the literature. In contrast, the distant position of the keyword `cognitive' suggests a gap in studies examining the cognitive effects of arsenic exposure. B) The number of studies reached its peak between 2016 and 2018 as indicated by the green color.

highlighted that arsenic in non-alcoholic rice-based drinks and fruit juices (including fruit nectars) were capped at 0.030 mg/kg and 0.020 mg/kg of inorganic arsenic, respectively (EFSA et al., 2024). Meanwhile, the maximum levels of total arsenic in cereals and cereal-based products, including rice and its derivatives (non-parboiled milled rice, parboiled rice, rice flour, rice snacks, and rice-based infant food), limits range from 0.10 mg/kg to 0.30 mg/kg (EFSA et al., 2024). Infant formulae and baby food have a maximum inorganic arsenic limit of 0.020 mg/kg when in powder form and 0.010 mg/kg in liquid form EFSA et al. (2024). The Food and Agriculture Organization (FAO) and other regulatory agencies set maximum permissible limits for As in rice. While this regulation is well-established in Europe and United States countries, there is a lack of regulation in Southeast Asia and Asia (EFSA, 2009; U.S. Food and Drug Administration, 2016). This lack of regulation is especially concerning considering rice and rice-based products are major contributors to arsenic exposure (Lynch et al., 2015). At global level, most of the countries including Southeast Asia and Asia countries adopt the FAO/WHO limits for arsenic 0.2 mg/kg in food and 10 μg/L drinking water. Beside following the FAO/WHO global standard limit, Malaysia also implements the maximum level 1.0 mg/kg of inorganic arsenic in food products following the Malaysian Food Regulations 1985 to account for demographic and environmental differences.

3.2. Route of exposure to arsenic

Arsenic (As) is ubiquitously found in the environment through natural sources such as volcanic activities, atmospheric dry and wet depositions as well as geothermal activities that deposit arsenic in water, atmosphere, sediment, soils, and rocks from runoff and leaching (Hama et al., 2023; Zhao et al., 2020, 2021; Zhou et al., 2022). Another source of arsenic enters into the environment largely through anthrophonic sources such as mining, industrial emission, smelting of metals (copper, lead), combustion of fossil fuels, livestock feed additives, wood preservatives, and pesticides applications (Chételat et al., 2023; Shi et al., 2023; Smedley and Kinniburgh, 2002). Improper sewage disposal contributes to the introduction of arsenic to soil and ground water (Fatoki and Badmus, 2022). In the air, arsines and arsenic oxides gradually precipitate on the soil. These substances then make their way into the groundwater through water surface runoff and rain (Patel et al., 2023). In groundwater, arsenic is released from rock weathering and through the application of fertilizers, pesticides, and irrigation of arsenicenriched soil (Patel et al., 2023). Arsenic in natural water is commonly found in the form of arsenite [(As(III)] and arsenate [As(V)], either dissolved or in particulate form. In well-oxygenated water and sediment, arsenic is present in the arsenate form As(V) (Qaiser et al., 2023). Both As(III) and As(V) will then undergoes oxidation, reduction, methylation, demethylation. Microorganisms like bacteria, yeast, and bacteria fungi are capable of methylating inorganic arsenic [As(III), As(V)], converting it to organic arsenic compounds such as dimethylarsinic acid (DMA), monomethylarsonic acid (MMA), and other derivatives (Fatoki and Badmus, 2022). In mammals, As(III) is reduced into As(V) and further metabolized (oxidatively biomethylated) to form arsenic byproducts (DMA and MMA), which are typically excreted from the body through urine (Roy et al., 2020).

Fig. 3 summarize the general route of arsenic exposure. In addition to occupational exposure, the primary route for arsenic entering the human body is through drinking groundwater, particularly when levels exceed 10 μg/L (WHO, 2017). Other significant exposure pathways include consuming food and beverages made from contaminated water (Xue et al., 2020). A global assessment of arsenic risk shows that between 94 million and 220 million people worldwide, with 85 % to 90 % of them in Southeast Asia and Asia, are potentially exposed to harmful levels of arsenic in their household water supply (Podgorski and Berg, 2020). Soil and water enriched with arsenic, excessive use of pesticides, and improper waste disposal from agricultural and industrial activities contribute to the contamination of the food web. Consuming inorganic arsenic through rice can significantly contribute to overall exposure, with rice having the highest capacity to absorb arsenic compared to other cereals (Khan et al., 2022; Mridha et al., 2022). Processed foods are another source of inorganic arsenic exposure for the general population, while water, rice, and dairy products are particularly significant contributors to inorganic arsenic exposure in child-bearing women, infants, and toddlers (Khan et al., 2022). This is especially concerning in Asia and Southeast Asia, where rice is a staple food. Seafood including fish, shellfish, crustacean, another important source of inorganic arsenic, typically contains organic arsenic forms such as arsenobetaine, while beverages like apple juice contain arsenocholine (Luvonga et al., 2020; EFSA et al., 2024). Collectively, the combined exposure arsenic from drinking water, groundwater, and consumption of arsenic contaminated food significantly contributes to the development of diseases, including cancer, developmental disorders and many others.

3.3. Arsenic exposure through consumption of rice and rice-based products

Thirty-one studies from Southeast Asia and Asia including Malaysia, Indonesia, Vietnam, Thailand, Cambodia, Philippines, Singapore, Myanmar, Bangladesh, India, China, South Korea, and Japan were selected examined arsenic levels in rice (Table 1). Laos and Brunei were

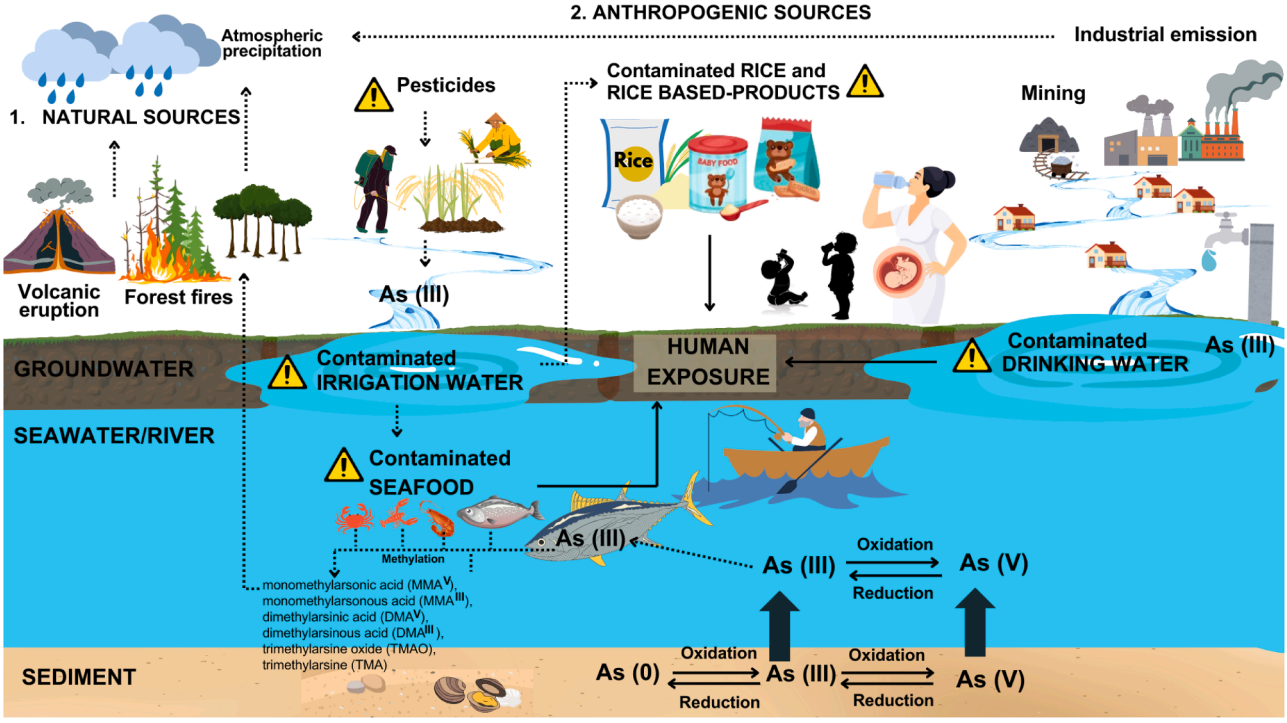

Fig. 3. Source of arsenic exposure can be divided into natural and anthropogenic sources. Route of arsenic exposure to human mainly through consumption of contaminated water sources, seafood, as well as ingestion of rice and rice-based products contaminated with arsenic due to polluted irrigation water and drinking water. Arsenic metabolized into different form as it transferred from water, atmosphere, sediment, soils, and rocks from runoff and leaching until it reaches living organism. Once in the cell, arsenic will further metabolize (oxidatively biomethylated) to form arsenic byproducts (DMA and MMA), which are typically excreted from the body through urine.

Table 1
Epidemiological studies on arsenic contamination and risk assessment to indicate potential risk of non-cancer (hazard quotient/hazard index, HQ/HI > 1) and cancer (cancer risk, CR > 1×10^{-4}) in Southeast Asian and Asian staple rice.

Country	Arsenic (mg/kg)	Status (<0.2 mg/kg)	Noncarcinogenic risk (HQ)	Carcinogenic risk (CR)	Reference
Malaysia	0.015	Below (<0.2 mg/kg)	adult HQ >1 children HQ< 1	High CR > 1×10^{-4}	Omar et al., 2015
	0.077–0.094	Below (<0.2 mg/kg)	High HQ > 1 children (18) and adult (27)	High CR >1×10^{-4}	Praveena and Omar, 2017
	0.189–0.541	Below (<0.2 mg/kg)	Low HQ <1 children and adult	High CR >1×10^{-4}	Zulkafflee et al., 2019
	0.35	Above (>0.2 mg/kg)	HQ >1 children and adult	High CR >1×10^{-4}	Navaretnam et al., 2023
Indonesia	0.13–3.71	Above (>0.2 mg/kg)	Not specified	Not specified	Ginting et al., 2018
	0.154	Above (>0.2 mg/kg)	HQ >1 children and adult	High CR >1×10^{-4}	Laela et al., 2023
Vietnam	0.001 -0.15	Below (<0.2 mg/kg)	Not specified	Not specified	Nguyen et al., 2020; Nguyen et al., 2021
	0.17	Below (<0.2 mg/kg)	HQ < 1 children and adult	High CR >1×10^{-4}	Le et al., 2023
Thailand	0.205	Certain rice above (>0.2 mg/kg)	HQ > 1 children and adult	CR (negligible in all groups.) < 1×10^{-4}	Hensawang and Chanpiwat, 2017
	0.2–0.35	Above (>0.2 mg/kg)	HQ < 1 children and adult	High CR >1×10^{-4}	Hensawang and Chanpiwat, 2018
	0.032–0.137	Below (<0.2 mg/kg)	HQ >1 children and adult	High CR >1×10^{-4} ($2–6 \times 10^{-4}$)	Chanpiwat et al., 2019
Cambodia	0.1–0.185	Below (<0.2 mg/kg)	Not specified	Not specified	Gilbert et al., 2015; Seyfferth et al., 2014
	0.029–0.598	Above (>0.2 mg/kg)	Not specified	Not specified	Murphy et al., 2018; Phan et al., 2013
Philippines	8–27	Below maximum contaminant level (MCL) <150 μg/L	Not specified	Not specified	Saong and Marbella, 2024
Singapore	0.134 -0.209	Above (>0.2 mg/kg)	Not specified	Not specified	Pedron et al., 2021
Myanmar	0.16	Below (<0.2 mg/kg)	HQ<1 children and adult	High CR >1×10^{-4} for children and adult (17×10^{-4})	Soe et al., 2023
South Korea	0.060 -0.114	Below (<0.2 mg/kg)	Not specified	Not specified	Lee et al., 2018
	Adult	Adult below (<0.2 mg/kg)			
	0.065–0.109	Infant above the maximum level (100 μg/kg) set by EU for the infant foods	Not specified	Not specified	Jung et al., 2018
	Infant 0.004–0.070				
Japan	0.101	Above (>0.2 mg/kg)	HQ > 1 children and adult	MOE for lung cancer <100 (5.81)	Takamoto et al., 2020
China	0.132–2.05	Below (<0.2 mg/kg)	HQ > 1 children and adult	MOE < 100 (significant carcinogenic risk)	Liu et al., 2023
	0.007–0.82	Below (<0.2 mg/kg)	HQ > 1 children (2.9) and adult (1.8)	High LCR > 1×10^{-4} for children and adult (3×10^{-4})	Xiao et al., 2024
Bangladesh	0.334–0.451	Below (<0.2 mg/kg)	HQ > 1 Adults (3.04–3.89) Children (3.38–4.32)	High LCR > 1×10^{-4} children (0.0043–0.0211) adult (0.0039×10^{-4} –0.019)	Baruah et al., 2021
	0.26–1.23	Above (>0.2 mg/kg)	HQ > 1 for both children and adult (1.354–3.815)	LCR > 1×10^{-4} for both children and adult (>10^{-6}) 6.53×10^{-3}	Rahman et al., 2023; Rokonuzzaman et al., 2022a, 2022b
	0.04–0.35	Above (>0.2 mg/kg)	HQ > 1 for both children and adult	LCR > 1×10^{-4} for both children and adult (>10^{-6})	Shaheen et al., 2024
India	0.29–0.95	Above (>0.2 mg/kg)	HQ > 1 for both children and adult (14)	Not specified	Upadhyay et al., 2019
	0.41	Above (>0.2 mg/kg)	HQ > 1 for both children and adult (3.49–15.94)	High LCR > 1×10^{-4}	Bhatti et al., 2020
	0.209 and 0.180	Above (>0.2 mg/kg)	Not specified	Not specified	Majumder et al., 2023

excluded due to limited data availability. Rice accumulates predominantly inorganic arsenic, a highly toxic form than the organic arsenic species (Coelho et al., 2020; Wang et al., 2021a, 2021b). Studies in Malaysia found that arsenic concentrations in various commercial rice types (basmati, glutinous, brown, local white, and fragrant) ranging from 0.015 to 0.541 mg/kg were within the safe limits set by FAO/WHO (0.35 mg/kg) (Navaretnam et al., 2023; Omar et al., 2015; Praveena and Omar, 2017; Zulkafflee et al., 2019). While another Malaysian study (Sibuar et al., 2022) suggests arsenic levels in rice was below the provisional tolerable daily intake (PTDI) established by Joint FAO/WHO Expert Committee on Food Additives (JECFA), highlighting the low risk from rice consumption. In Thailand, arsenic levels in brown jasmine and white rice were about 1.5 times higher than the Codex Committee on Food Additives and Contaminants Standard 1993–1995 for inorganic arsenic in polished (0.2 mg/kg) and husked rice (0.35 mg/kg) (Hensawang and Chanpiwat, 2017; Nookabkaew et al., 2013). In the subsequent year, the arsenic levels in husked rice compared to polished rice (3.2–7.2 μg/L) were detected to be 1.5 to 3.8 times greater, but still

below the Codex standard (Hensawang and Chanpiwat, 2018). Contaminated irrigation water may have increased arsenic levels in rice, as seen in Thailand (0.619 mg/kg) and Vietnam (0.1–0.2 μg/kg), with rice roots readily absorbing arsenic, and cooking with arsenic contaminated water could further elevate exposure risks (Menon et al., 2024; Nguyen et al., 2021; Weber et al., 2021). Based on Table 1, most studies in Southeast Asia found arsenic levels in rice below the permissible limit (<0.2 mg/kg), unlike in Bangladesh and India, where levels often exceed this threshold (>0.2 mg/kg).This highlighted that rice consumption remains a possible pathway for exposure to this toxic metalloid, potentially leading to noncarcinogenic and carcinogenic health issues.

Noncarcinogenic risk for individuals consuming arsenic contaminated rice were accessed using the target hazard quotient (THQ). A THQ values greater than 1 (THQ >1) indicates a significant noncarcinogenic risk, while a value less than 1 (THQ <1) suggests no such risk (Demissie et al., 2024). Noncarcinogenic risks include neurotoxicity, developmental effects, cardiovascular disease, development of hard patches of skin on the soles of the feet and palm of the hands (Lee et al., 2006). Meanwhile, carcinogenic risk is assessed using the incremental lifetime cancer risk (ILCR) or total cancer risk (CR_{total}), which estimates the probability of developing cancer from a lifetime exposure to a carcinogen (Demissie et al., 2024). An ILCR or $CR_{total} < 10^{-6}$ suggests a negligible risk, 10^{-6} to 10^{-4} indicates a moderate risk, and $> 10^{-4}$ signals a serious health hazard to human (US EPA, 2001). In China, carcinogenic risk is assessed using the margin of exposure (MOE), where MOE $\geq$ 100 indicates no significant risk, and MOE $\leq$ 100 signals an unacceptable risk (Liu et al., 2023). The margin of exposure (MOE) approach was used for comparative risk assessment, where a toxicological threshold with the exposure above 10,000 indicate as low priority for risk management action (Lachenmeier et al., 2012). This suggests an increased cancer risk from long-term rice consumption for both adults and children.

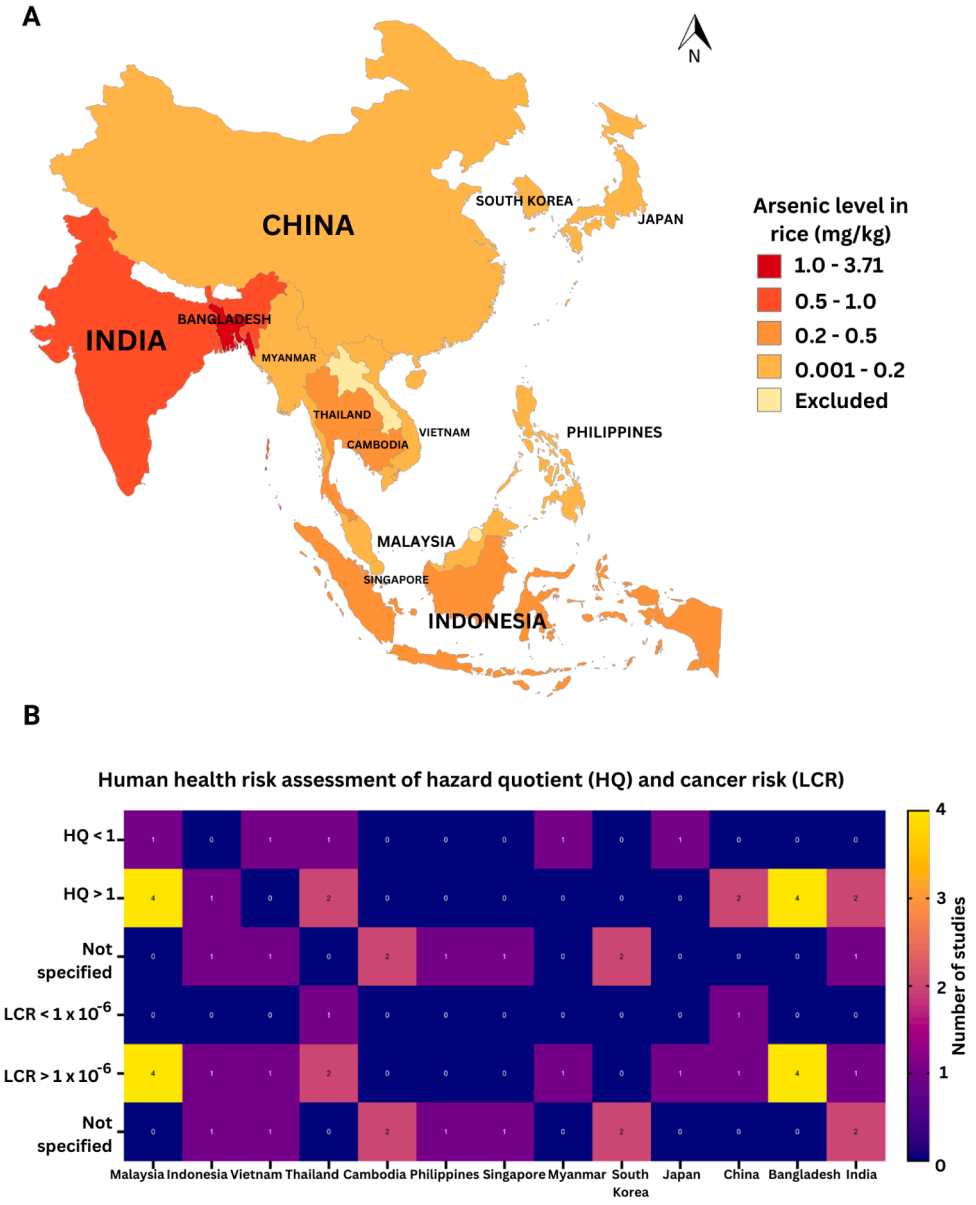

Fig. 4. Arsenic contamination in rice. A) Geographic distribution of arsenic-contaminated rice. B) Studies from Thailand, China, and Indonesia report high noncarcinogenic risk (HQ > 1), while nine studies from Indonesia, Vietnam, Cambodia, the Philippines, Singapore, South Korea, and India lack HQ and LCR values. Five studies found low noncarcinogenic risk (HQ < 1), whereas sixteen studies indicated elevated cancer risk (LCR > 1×10^{-6}) across various countries, suggesting increased noncarcinogenic and cancer risks from long-term rice consumption in these regions. `Not specified' indicates studies measuring arsenic without risk assessment.

Fig. 4 showed an overview of distribution of rice contaminated with As from Southeast Asia and Asia together with its hazard quotient (HQ) and lifetime cancer risk (LCR) risk value. Despite lower arsenic levels in Malaysian rice compared to highly polluted areas like Bangladesh and India, Malaysia could face similar risks for developing noncarcinogenic and carcinogenic effects. Two studies from Thailand and China, and one from Indonesia, reported HQ values over 1 indicating high risk of noncarcinogenic issues. Nine studies, including those from Indonesia, Vietnam, Cambodia, the Philippines, Singapore, South Korea, and India, did not specify both HQ and LCR. Five studies indicated low noncarcinogenic risk (HQ <1). Sixteen studies found a high risk of cancer (LCR > 1×10^{-6}), with four each from Bangladesh and Malaysia, two from Thailand, and one each from Indonesia, Vietnam, Myanmar, Japan, China, and India. In Malaysia, despite arsenic levels in rice being below the permissible limit and varying HQ values (either below or above 1), LCR values exceed the acceptable threshold (LCR > 1×10^{-4}) (Navaretnam et al., 2023; Omar et al., 2015; Praveena and Omar, 2017; Zulkafflee et al., 2019) (Table 1). This suggests an increased noncarcinogenic and cancer risk from long-term rice consumption for both adults and children. Similar findings were reported in rice from Vietnam, Thailand, and Myanmar, with 2 to 6 in 10,000 residents potentially developing cancer over a 75-year lifetime due to daily rice consumption (Chanpiwat et al., 2019; Le et al., 2023; Soe et al., 2023). In contrast, rice from Bangladesh, India, Indonesia, and China shows higher As levels (>0.2 mg/kg), HQ values above 1, and LCR values over 1×10^{-4}, posing significant noncarcinogenic and carcinogenic risks (Baruah et al., 2021; Laela et al., 2023; Majumder et al., 2023; Rahman et al., 2023; Rokonuzzaman et al., 2022a; Upadhyay et al., 2019; Xiao et al., 2024). This indicates a significant noncarcinogenic and carcinogenic risk, with 2.8 % of people at considerable risk and 1.6 per 1000 at threshold risk from rice consumption (Rokonuzzaman et al., 2022a). Hence, increased susceptibility of both children and adults to noncarcinogenic and carcinogenic effects from rice consumption. However, data from Southeast Asia are lacking, with 10 studies only reporting arsenic levels in rice without risk assessments (Gilbert et al., 2015; Jung et al., 2018; Lee et al., 2018; Murphy et al., 2018; Nguyen et al., 2020; Nguyen et al., 2021; Pedron et al., 2021; Phan et al., 2011; Saong and Marbella, 2024; Seyfferth et al., 2014).

Children have higher dietary inorganic arsenic exposure but are underrepresented in most adult-focused epidemiological studies. This lack of data creates uncertainty for potentially more susceptible individuals with higher genetic risk. In 2021, EFSA report had highlighted rice, rice-based products, grains (excluding rice), and drinking water as the primary sources of inorganic arsenic exposure across various age groups. In younger population (< 3 years old), dietary inorganic arsenic intake is particularly influenced by specific foods like cereals, cookies, rusks, and rice-based snacks (crackers, cakes). Since rice is a staple food, approximately 90 % of pregnant women consume rice or rice products, potentially increasing their daily inorganic arsenic exposure by 5.2 to 7.8 μg per serving (U.S. Food and Drug Administration 2016). This raises concerns about fetal health, as studies suggest early exposure to inorganic arsenic might have neurotoxic effects (Mochizuki, 2019; Signes-Pastor et al., 2017). However, the long-term consequences and reversibility of these effects remain unclear. A significant knowledge gap exists regarding the quantitative impact of maternal inorganic arsenic intake (*in utero*, infancy, and early childhood) on non-cancerous health outcomes in Western populations (Cubadda et al., 2017).

Research on arsenic in rice-based products particularly in Southeast Asian infant foods is scarce where rice consumption is even higher. In Thailand, high level of arsenic was detected mostly in brown jasmine rice and white jasmine rice. The highest total arsenic concentrations in brown jasmine rice and white jasmine rice were approximately 50 % (1.5 times) greater than the Codex Committee on Food Additives and Contaminants Standard 1993–1995 for maximum permissible inorganic arsenic in polished rice (0.2 mg/kg) and husked rice (0.35 mg/kg) (Hensawang and Chanpiwat, 2017; Nookabkaew et al., 2013). A risk assessment study in Thailand found significantly higher bioaccessible As concentrations in husked rice compared to polished rice (3.2–7.2 μg/L of As, 1.5 to 3.8 times greater) (Hensawang and Chanpiwat, 2018). However, these concentrations remained below the Codex standard for total arsenic in rice. Despite this, the study estimated a potential risk of both carcinogenic and non-carcinogenic effects for 3 children and 6 adults per 10,000 individual consuming either type of rice. A stricter guideline was implemented for inorganic arsenic, the more toxic form, setting limits of 200 ng/g for white rice and 300 ng/g for brown rice (U.S. Food and Drug Administration, 2016). Notably, the authorities recommend a much lower limit of 100 ng/g of inorganic arsenic for infant and young children's food (U.S. Food and Drug Administration, 2016). For instance, the maximum levels of total arsenic in cereals and cereal-based products, including rice and its derivatives (non-parboiled milled rice, parboiled rice, rice flour, rice snacks, and rice-based infant food), limits range from 0.10 mg/kg to 0.30 mg/kg (EFSA et al., 2024). Infant formulae and baby food have a maximum inorganic arsenic limit of 0.020 mg/kg when in powder form and 0.010 mg/kg in liquid form (EFSA et al., 2024). This highlights the critical need to consider both total arsenic and inorganic arsenic levels when assessing potential health risks, particularly neurodevelopmental effects in infants, providing insight for development of strategies to minimize its toxic impact.

3.4. Arsenic uptake and transport in rice

In rice plants, the uptake of rice involves a different complex mechanism depending on the arsenic species. The are two form of arsenic species such as arsenate (AsV) and arsenite (AsIII) which primarily found in the soil (Mawia et al., 2021). Arsenate has analogous structure to phosphate, leading to its uptake by the plant through the same transporters involved in phosphate uptake, such as phosphate transporters and high-affinity phosphate transporters (Zvobgo et al., 2018). In paddy soils, available phosphorus can compete with arsenate (AsV) uptake in rice plants, as both phosphorus and arsenate use similar transport pathways. This competition can reduce arsenate absorption when phosphorus levels are sufficient (Mlangeni, 2023). Arsenate acts as a phosphate analog, interfering with phosphorylation-dependent metabolic pathways and compromising ATP synthesis through competitive substitution of phosphate groups. Conversely, arsenite exhibits high affinity for protein sulfhydryl groups, forming stable complexes with enzymes and cofactors that result in structural modifications and subsequent loss of catalytic activity. These complementary mechanisms of metabolic disruption culminate in the generation of various reactive oxygen species (ROS), including nitric oxide, superoxide, and hydroxyl radicals. Arsenite (AsIII), which is neutral, is absorbed through aquaporins—specialized water channels that facilitate the entry of small molecules like arsenite into the plant (Zhao et al., 2009). Therefore, controlling phosphorus levels and soil water conditions can help manage arsenic uptake in rice, as these factors influence whether arsenic is present as AsV or AsIII and, consequently, its uptake pathway. Meanwhile, AsIII is a neutral compound and is taken up by rice plants through aquaporins, which are specialized water channels that allow the passage of small molecules like arsenic.

Once inside the rice plant cell, the metabolism of arsenic begin with AsV is either reduced to AsIII by arsenate reductases (Shi et al., 2016; Xu et al., 2017) or loaded to xylem vessels by the phosphate transporters (Mendoza-Cózatl et al., 2011; Wu et al., 2011). AsV is reduced to AsIII through two primary mechanisms. In a non-enzymatic pathway, AsV reduction is slow, relying on the oxidation of two reduced glutathione (GSH) molecules, which are recycled by GSH reductase (Mawia et al., 2021). In contrast, enzymatic pathways utilize arsenate reductase enzymes, such as High Arsenic Content 1 (*HAC1)*, which rapidly reduces AsV to AsIII and facilitates AsIII efflux back to the soil, limiting arsenic transport to the shoot (Mawia et al., 2021). Loss of *HAC1* function decreases AsIII efflux, raising AsIII translocation to shoots (Shi et al.,

2016). In rice, homologs like *OsHAC1;1, OsHAC1;2,* and *OsHAC4* have been identified with similar roles (Shi et al., 2016; Xu et al., 2017). Overexpression of these genes increases arsenite efflux from root to the soil and reduces arsenic accumulation in rice, while knockouts lead to higher arsenic accumulation in rice.

Rice plant respond to elevated AsIII levels since not all is effluxed out of the cell by metabolizing it into complexes with sulfhydryl-rich compounds. Arsenic exposure increases plant cellular glutathione (GSH), a precursor for phytochelatin (PC) biosynthesis and a limiting factor for high phytochelatin synthase (PCS) activity, which plays a key role in arsenic tolerance (Guo et al., 2008). Phytochelatin synthase catalyzes PC synthesis from glutathione forming arsenic-PC complexes that are sequestered into vacuoles via ABCC1/ABCC2 transporters (Kumar and Trivedi, 2018). In rice, *OsPCS1* and *OsPCS2* genes are responsible for PC biosynthesis (Yamazaki et al., 2018). Glutathione S-transferases (GSTs) also utilize GSH to form AsIII-GSH complexes, further aiding in arsenic detoxification. AsIII-GSH and AsIII-PC complexes are transported by vacuolar transporters to vacuoles for detoxification. Under arsenic exposure, *OsCLT1* mutants show reduced phytochelatin synthase levels and lower arsenic accumulation in roots but similar or higher levels in shoots compared to wild-type (Mawia et al., 2021).

Arsenic accumulation depends on the rice genotype, soil type, arsenic concentration in the soil, age and the physiological state of the rice plant (Niazi et al., 2022). Rice plants display varying patterns of arsenic accumulation, showing the order as grain < husk < leaf < straw (stem) < root (Islam et al., 2017), while others report it as grain < husk < stem < leaf < root, highlighting that rice roots and leaves accumulate higher arsenic level than stems and grains (Yao et al., 2021). In line with these findings, a similar trend was previously reported, with arsenic concentrations being higher in roots followed by shoots and leaves (Rokonuzzaman et al., 2022a, 2022b). Research has established a positive correlation between irrigation water arsenic and grain arsenic content, soil-available arsenic and root/grain arsenic content, and straw arsenic and grain arsenic across different rice varieties (Bhattacharya et al., 2010; Islam et al., 2016; Rokonuzzaman et al., 2022a, 2022b). Research indicates that rice bran, the outermost layer of the grain, can accumulate 7–20 times more arsenic than the endosperm, the starchy core typically consumed as polished rice (Pedron et al., 2019; Yao et al., 2020).

The physicochemical properties of arsenic in rice are influenced by soil pH, present of phosphorus and silicon in the soil and different water treatments regimes which generate impact on As accumulation in rice grains. Soil pH significantly influences arsenic mobility and bioavailability in soils, with increased arsenic solubility generally observed at low pH (<5.5), though there is some debate about the relationship between pH and arsenic accumulation at higher pH levels. In rice grain specifically, arsenic uptake tends to be higher in acidic soil conditions (pH < 5.5) due to increased arsenic solubility and mobility in the soil solution, which allows greater absorption by the rice plant and subsequent translocation to the grain (Signes-Pastor et al., 2007; Zhao and Wang, 2020). This relationship is particularly important for rice safety since it's a major dietary source of arsenic exposure in many populations. Phosphate in soil significantly influences arsenic uptake in rice cultivars, with studies showing that rice plants with poor internal phosphate status exhibit increased sensitivity to arsenate uptake (Wang and Duan, 2009). Consequently, soil management strategies incorporating higher phosphate concentrations have emerged as an effective approach to reduce arsenic accumulation in rice grain (Lu et al., 2010). Silicon existence in soil also plays a vital role in reducing arsenic mobility and uptake in rice (Zhang et al., 2020). Spraying silicon through foliar application effectively reduces inorganic arsenic accumulation in rice grain by increasing silicon concentrations in shoots and roots, which subsequently downregulates silicon transporters (*Lsi1, Lsi2* in roots and *Lsi6* in blade and sheath), ultimately decreasing arsenic uptake and transport. This foliar approach presents an efficient alternative for minimizing grain arsenic content in contaminated soils (Zhang et al., 2020). Bioavailability of arsenic in soil and rice plant largely influenced by overexploitation of groundwater contaminated with arsenic Irrigation of rice fields with arsenic-contaminated groundwater and tubewells, particularly in China and India, has significantly increased arsenic bioavailability for rice plant uptake, with soil concentrations reaching up to 83 mg/kg. Arsenic levels of 19 μg/kg exceeding the permissible level were found in Bihar's rice grains irrigated from shallow aquifer (Kumar et al., 2016). Farmers prefer upland rice cultivation due to naturally low water stagnancy, creating semi-aerobic conditions that reduce arsenic contamination, though runoff can transfer arsenic to lowland fields. In Vietnam, it has been previously reported that alternating wetting-drying and upland rice cultivation has lower arsenic accumulation than the low land flooded rice cultivation (Hu et al., 2015;Tran et al., 2020) In contrast, rice grain grown in continuous flooded condition was reported the highest arsenic accumulation compared to rice grain grown wetting-drying condition (Harine et al., 2021). These findings highlighted that water management could be considered a key player for arsenic uptake in rice. Therefore, arsenic accumulation in paddy soil and its transfer to rice varies based on soil type, background arsenic levels, irrigation water concentration, depth, distance from water source, and monsoon flood duration (Sarwar et al., 2021; Khan et al., 2010; Hossain et al., 2009).

3.5. Arsenic exposure through water consumption

It's alarming to note that a global risk assessment indicates that 85 % to 95 % of South Asians could potentially be exposed to high and low levels of arsenic in groundwater from their domestic water supply (Grandjean and Landrigan, 2006; Podgorski and Berg, 2020). Fig. 5A showed the distribution of arsenic contamination in Southeast Asia and Asia. Philippines, Japan, Brunei, Laos and Singapore were excluded due to limited data access and do not meet the inclusion criteria. Arsenic concentrations vary widely, ranging from below the World Health Organization (WHO) guideline of 10 μg/L in some areas to alarmingly high levels exceeding 1000 μg/L in others (Table 2). Countries such as Bangladesh, India, Cambodia, and Vietnam consistently show high arsenic levels in groundwater, often surpassing 100 μg/L. Malaysia, Thailand, Indonesia and Myanmar demonstrate variable levels, with some regions below the WHO guideline and others significantly above. China and South Korea generally show lower levels. The non-cancer risk, represented by Hazard Quotient (HQ) or Hazard Index (HI), is frequently reported as greater than 1 across most countries, indicating potential noncarcinogenic health effects. Cancer risk, expressed as Lifetime Cancer Risk (LCR), is predominantly high, with many studies reporting values exceeding the acceptable risk threshold of 1×10^{-4} or 1×10^{-6}. Vietnam reports the highest number of studies indicating significant noncarcinogenic (HQ > 1) and carcinogenic risks (LCR > 1×10^{-6}), followed by Bangladesh, India, China, Thailand, and Cambodia (Fig. 5B). Three studies from Malaysia, and one each from Indonesia, Thailand, Cambodia, South Korea, and Myanmar did not specify either risk (Table 2). Notably, countries like Bangladesh, India, and parts of Vietnam and Cambodia not only exhibit high cancer risks but also report cases of arsenicosis. While some countries like South Korea and parts of Malaysia show lower arsenic levels, the overall trend suggests a significant public health concern related to arsenic exposure through drinking water in many parts of Southeast Asia and Asia.

Malaysia's Langat River has seen a significant increase in arsenic concentration (0.98–21.94 μg/L) due to extensive pesticide use on oil palm plantations and landscape changes (Ahmed et al., 2021). In Thailand, arsenic contamination is primarily attributed to tin mining activities and urbanization, with oral intake posing a greater risk than dermal contact (Nilkarnjanakul et al., 2023; Vitayavirasak et al., 2005; Wongsasuluk et al., 2018). Groundwater consistently emerges as the most contaminated source, though surface water, tap water, and even some bottled water show concerning levels in certain areas (Table 2). Despite documented arsenic existence in water sources as the main

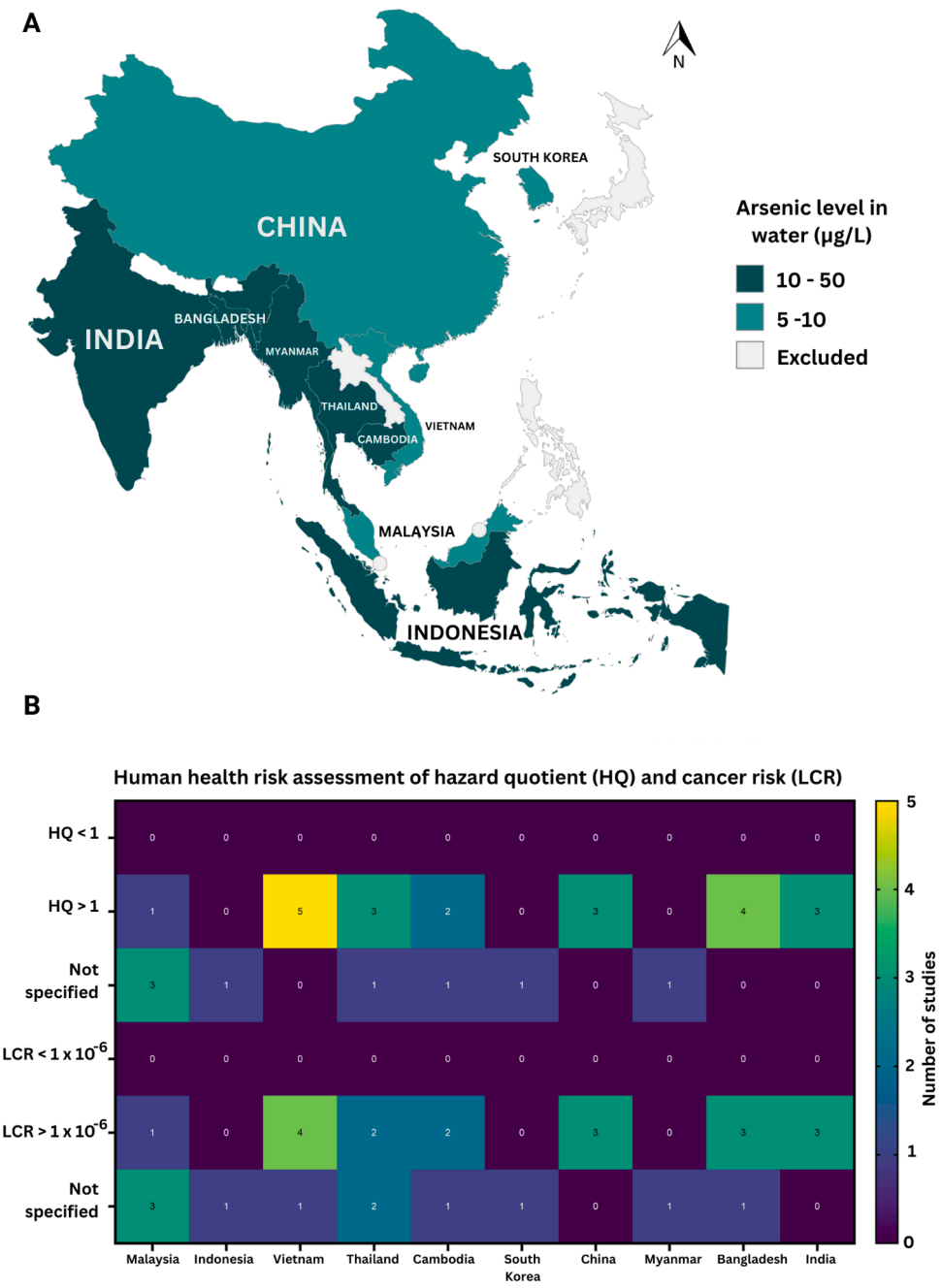

Fig. 5. Distribution of arsenic-contaminated water in Southeast Asia and other Asian countries, highlighting noncarcinogenic and carcinogenic risks. A) Arsenic levels in water sources frequently exceed the permissible limit (10 µg/L) across Southeast Asia and Asia. B) Studies reporting significant noncarcinogenic (HQ $>$ 1) and carcinogenic (LCR $>$ 1 $\times$ 10^{-6}) risks due to arsenic in water show Vietnam with the highest number, followed by Bangladesh, India, China, Thailand, and Cambodia. Bangladesh, India, and parts of Vietnam and Cambodia also report cases of arsenicosis. Lower arsenic levels are noted in South Korea and parts of Malaysia, but a broad public health concern remains. 'Not specified' denotes studies measuring arsenic levels without a risk assessment.

contributor to exposure, research on its impact on cognition and potential neurodevelopmental disorders is scarce in Southeast Asia, with most existing studies focusing on adults and neglecting potential risks to children. This data underscores the critical nature of arsenic contamination as both an environmental and public health crisis across much of Southeast Asia and Asia, highlighting the urgent need for effective water treatment, management strategies, and further research to mitigate these risks, especially for vulnerable populations like children.

3.6. Toxicity effect of arsenic

Chronic arsenic exposure at elevated level through contaminated water or food sources like rice, a staple food in Southeast Asia, can lead to arsenicosis, a disease characterized by hyperpigmentation, depigmentation, skin lesions, and keratosis (Karagas et al., 2015; Naujokas et al., 2013). This raises particular concern for children in the region, as early life development appears to be especially vulnerable to arsenic exposure even at low concentration which can cross the placental barrier, potentially increasing risks of kidney failure, skin cancer, and neurological impairments later in life (Karagas et al., 2015; Naujokas et al., 2013). Studies have shown an association between prenatal arsenic exposure and a range of adverse health outcomes in infants, including increased infant mortality, miscarriage risk, lower birth weight, larger head circumference, longer labor duration, and

Table 2
Epidemiological studies on arsenic concentration and non-cancer risk (hazard quotient/hazard index, HQ/HI >1)/carcinogenic risk (1×10^{-4}) in Southeast and Asia water sources.

Country	Arsenic (μg/L)	Status	Noncancer risk (HQ/HI)	Cancer risk (CR)	Reference
Malaysia	0.16–168	Below < 10 μg/L	Not specified	Not specified	Azrina et al., 2011; DOE, 2020; Kusin et al., 2017
	Drinking water (1.68) Mineral water (13.51)	Bottled drinking water below < 10 μg/L Mineral water above > 10 μg/L	Not specified	Not specified	Azlan et al., 2012
	4–56	Above > 10 μg/L	HI (14) > 1 high	CR > 1×10^{-4} (1.82×10^{-3})	Koki et al., 2018
	22.3	Above > 10 μg/L	Not specified	Not specified	Ramly et al., 2023
Thailand	0.68–8.79	Lake water above > 50 and 10 μg/L	Not specified	Not specified	Tupwongse et al., 2007
	Shallow groundwater (1.584 ± 0.03) Tap water (2.185 ± 0.033)	Below < 10 μg/L and cera	HQ > 1 (0–8.65) HI (1.53) > 1 (0.00–25.86)	High Carcinogenic, $>1 \times 10^{-6}$ (8.07E−07)	Wongsasuluk et al., 2018
	75.93 mg/L <0.300–183.00	Surface water Above > 10 μg/L Groundwater above > 10 μg/L	HQ > 1 HQ >1 4.33×10^{-2} to 17.6 (oral exposure) 2.55×10^{-4}–1.04×10^{-1} (dermal contact)	Not specified Carcinogenic, High $CR_{adult} > 1 \times 10^{-6}$) Not carcinogenic $CR_{children} < 1 \times 10^{-6}$)	Kladsomboon et al., 2020 Nilkarnjanakul et al., 2023
Indonesia	Hot spring (166.73) Rivers (0.80)	hot spring and river water above > 50 and 10 μg/L	Not specified	Not specified	Irnawati et al., 2021
Vietnam	48–325	Groundwater and drinking water above > 10 μg/L	High HQ > 1	Carcinogenic High CR > 1×10^{-4} *arsenicosis	Nguyen et al., 2009
	12.8–884 (614.7, 160.1)	Groundwater above > 10 μg/L	HQ >1 (1–10)	Carcinogenic High CR > 1×10^{-4} (4×10^{-4})	Pham et al., 2017
	Drinking water (4–15) River (3.2)	Tap water below <10 μg/L	HQ > 1 (0–2)	High CR > $1 \times 10^{--4}$ (0–25)	Tran and Nguyen, 2018
	0.2–131.15	Ground water below >10 μg/L	HI > 1 adults (1.83–7.4) children (2.6–10.5)	High CR > 1×10^{-4} Carcinogenic for adults (1×10^{-4}–4.96×10^{-4})	Nguyen et al., 2019
	3.93	Reservoirs, rivers, and narrow waterways <10 μg/L	HI > 1 children (1.2–1.48) adults HI < 1	Not specified	Le and Nguyen, 2024
Cambodia	5–1543	Well water above > 10 μg/L and 50 μg/L	HQ > 1 (15.12)	High CR > 1×10^{-4} *arsenicosis	Sthiannopkao et al., 2010
	1–20	Tap water above > 10 μg/L	HQ > 1	Medium CR > 1×10^{-4} (3×10^{-4})	Kelly et al., 2018
	65–959	Well water above > 10 μg/L	Not specified	Not specified	Murphy et al., 2018
Myanmar	0.02–198 (2.2 μg/L)	Drinking water above > 10 μg/L	Not specified	Not specified	Mar Wai et al., 2019
	20	Well water above > 10 μg/L	Not specified	Not specified	Bacquart et al., 2015
	>50	Groundwater above > 10 μg/L	Not specified	Not specified	Pincetti-Zúniga et al., 2020
South Korea	5.83	Tap water below < 50 μg/L MOE, 2020; US EPA, 2021)	Not specified	Not specified	Park and Choi, 2021
China	0.7–26 (mean 2.19)	Groundwater above > 5 μg/L	HQ > 1	High CR > 1×10^{-6} adult and children	Zhu et al., 2023
	29.98	Tap water above > 10 μg/L	HQ > 1 (7.25)	Low CR > 1×10^{-4} (1.03E−4–1.21E−3)	Chen et al., 2023
	8.6	Groundwater below <10 μg/L	HQ > 1 infants (2.69) children (1.66) females (1.43) males (1.02)	High CR > 1×10^{-4} infants, (8.6E−06) children, (6.4E−0) females, (2.8E−04) males (2.0E−04)	Wang et al., 2024
Bangladesh	0.10–100	Groundwater above > 10 μg/L	HQ > 1 children (0.0277–6.033) adults (0.0092–2.011)	Not specified	Islam et al., 2023
	20.22–292	Ground water above > 10 μg/L	HQ > 1	Carcinogenic High CR >10^{-6}	Rahman et al., 2023
	191	Groundwater above > 10 μg/L	HQ >1 children (6–65) adult (2.92–44.89)	Carcinogenic High CR > 1×10^{-4} children (1.94 × 10–3) adults (9.20× 10–4)	Shaibur et al., 2024
	20.22	Ground water above > 10 μg/L	HQ > 1	Carcinogenic High CR >10–6	Habib et al., 2024

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Table 2 (*continued*)

Country	Arsenic (μg/L)	Status	Noncancer risk (HQ/HI)	Cancer risk (CR)	Reference
India	86–513	Groundwater above > 10 μg/L	HQ > 1	Carcinogenic High CR > 1×10^{-6}	Mishra et al., 2022
	> 10–912	Ground water above > 10 μg/L	HQ >1	Carcinogenic High CR > 0.000001 100 % children, females, and males exhibit arsenicosis	Jha et al., 2023
	>10	Ground water above > 10 μg/L (WHO, 2017)	HQ > 1	Carcinogenic High CR > 1×10^{-6}	Soni et al., 2024

Abbreviations: Noncarcinogenic risk: HQ, hazard quotient; HI, hazard index; Carcinogenic risk: CR, Cancer risk

neurological dysfunction in children (Mullin et al., 2019; Muse et al., 2020). This is consistent with the epidemiological data obtained previously, showing hair arsenic burden associated with the symptom severity in Italian children with Autism Spectrum Disorder (ASD), including social deficits, communication impairments, and repetitive behaviors (Fiore et al., 2020). In a study for a cohort of Italian schoolchildren (6 to 11 years old) living in the heavily polluted area, urinary arsenic was found to significantly impact depression, anxiety, attention problems and rule-breaking behavior, with a notable association with ASD (Renzetti et al., 2021). In Bangladesh, childhood and early prenatal exposure to low level (50 μg/L) detected in urine were modestly associated with the cognitive capabilities of 5 years old school children (Vahter et al., 2020). Moreover, a previous review highlighted that a 50 % increase in As level drinking water (51–117 μg/L) or urine (118–94 μg/) resulted in 0.5 decrement of IQ among 5–15 years old children (Rodríguez-Barranco et al., 2013). This finding emphasizes the detrimental impact of low-level arsenic exposure during critical developmental windows on children's cognitive abilities (Signes-Pastor et al., 2022). Although numerous studies in Southeast Asia have examined arsenic levels in food, water, and human samples, there is a critical lack of research on how chronic, low-level arsenic exposure might affect cognitive function in this region. Supporting this concern, the rising prevalence of 0.6 % ASD among Southeast Asian children, mirroring the global trend of increasing ASD prevalence (Shrestha et al., 2024).

3.7. Pre- and postnatal arsenic exposure and cognition

Only outcomes related to arsenic exposure and cognition were selected for this section. Studies have shown an association between prenatal arsenic exposure and a range of adverse health outcomes in infants, including increased infant mortality, miscarriage risk, lower birth weight, larger head circumference, longer labor duration, and neurological dysfunction in children (Mullin et al., 2019; Muse et al., 2020). Eight studies reviewed by EFSA CONTAM Panel provide substantial evidence on the effects of childhood exposure to arsenic (EFSA et al., 2024), as well as exposure level in areas contaminated with high levels of arsenic in drinking water (Calderón et al., 2001; Rosado et al., 2007; Tofail et al., 2009; Tseng et al., 2006; Von Ehrenstein et al., 2007; Wang et al., 2007; Wasserman et al., 2004, 2007). Since then, further longitudinal studies are crucial to assess the most sensitive windows of exposure, dose-response relationships and the specific types of effects. Emerging studies investigating the association between arsenic exposure and cognitive function have been published. However, most of these studies are cross-sectional, involve relatively small sample sizes, and utilize a range of cognitive, behavioral, or motor/sensory function tests on children aged 5–11 years. At global level, further research has also explored the association between arsenic exposure and neurodevelopmental outcomes, such as autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD).

Supporting these concerns, extensive global research shows arsenic's impact on cognitive function (Table 3). A significant positive correlation was reported between hair arsenic burden and symptom severity in Italian children with ASD, including social deficits, communication impairments, and repetitive behaviors (Fiore et al., 2020). Furthermore, elevated urinary arsenic level was previously reported associated with ADHD among school children living in an area with high industrial and mining activities in Southwestern Spain (Rodríguez-Barranco et al., 2016). Rodríguez-Barranco et al., (2013) reviewed that a 50 % increase in arsenic level drinking water (51–117 μg/L) or urine (118- 194 μg/) resulted in 0.5 decrement of IQ among 5–15 years old children. In a study for a cohort of Italian schoolchildren (6 to 11 years old) living in the heavily polluted area, urinary arsenic was found to significantly impact depression, anxiety, attention problems and rule-breaking behavior, with a notable association with ASD (Renzetti et al., 2021). Childhood arsenic exposure has been linked to increased risks of anxiety and depression in girls (Dai et al., 2023), reduced attention and cognitive function, and a higher risk of ADHD (Rodríguez-Barranco et al., 2016). In Bangladesh, childhood and early prenatal exposure to low level (50 μg/L) detected in urine were modestly associated with the cognitive capabilities of 5 years old school children (Vahter et al., 2020). This finding underscores that low-level arsenic exposure during critical periods of growth and development can adversely affect children's cognitive abilities (Signes-Pastor et al., 2022). This is consistent with the previous finding showing a greater reduction in urinary arsenic and creatine concentration (100μg/g) correlates with a 0.91point improvement in working memory, but not with Full Scale IQ (Wasserman et al., 2016). Adults who suffered arsenic poisoning during infancy showed neuropsychological dysfunctions, even without recognized disabilities, as seen in the 1955 mass arsenic poisoning in Japan, indicating that developmental neurotoxicity from arsenic likely causes permanent cognitive impairment (Yorifuji et al., 2016). In China, adults exposed to arsenic in hair (0.21 mg/kg) or drinking water (>100 μg/L) showed reduced MMSE scores and cognitive impairment, with arsenicosis affecting 49.2 % of the exposed population (Liu et al., 2017; Wang et al., 2021a, 2021b).

Urinary arsenic concentrations, reflecting exposure from water and food, were linked to small decreases in intellectual function in 5–15 years old children in West Bengal, India, but no associations were found with long-term water arsenic levels during pregnancy (110 μg/L) or childhood (147 μg/L) (Von Ehrenstein et al., 2007). In a study from Pabna and Sirajdikhan, Bangladesh, no association was found between arsenic exposure from pregnancy to 20–40 months and children's language or motor skills. However, higher water arsenic levels in Pabna (25.7 μg/L) were linked to lower cognitive scores, especially with first trimester exposure (Rodrigues et al., 2016). In a mother-child cohort study in Spanish children (4–5 years old), monomethylarsonic acid (MMA) was inversely associated with general, verbal, memory, quantitative, working memory and executive function scales (Soler-Blasco et al., 2022).

Despite extensive research on arsenic levels in environmental matrices (food, water) as well as human samples (blood, urine, hair), a clear information on the association between prenatal arsenic exposure and neurodevelopmental disorders (NDDs) such as ASD or ADHD remains scarce. This knowledge gap is particularly concerning in Southeast Asia. Cambodia is the sole Southeast Asia country to have investigated the effects of arsenic on cognitive function through neurobehavioral testing, highlighting a critical need for further research. Cambodian children with high arsenic levels in their hair had a

Table 3
Cross-country epidemiological studies on arsenic exposure and cognitive outcome using different cognitive scales.

Country	Cognitive scale	Arsenic (As) concentration	Population size, Age	Findings	Reference
Bangladesh	WISC-III	Well-water As <5.5 μg/L & Well-water As >50 μg/L	Children (9–10 years)	↓total IQ ↓ Performance and Full-Scale IQ with As > 50 μg/L	Wasserman et al., 2004
Bangladesh	WPPSI	Urinary As: 100 μg/l	Children (5 years)	↓total IQ (females) 1–3 point decrement in VIQ and FSIQ	Hamadani et al., 2011
Bangladesh	BSID-III	Water As (20–40 months): 25.7 μg/L Water As (1st trimester pregnancy) : 26.5 μg/L	525 20–40 months	↓total IQ Increased water As was associated with decreased cognitive scores in Pabna. No associations (receptive and expressive language or gross motor domains, Full developmental score, Verbal Comprehension, Perceptual reasoning, Working memory, and Processing speed)	Rodrigues et al., 2016
Bangladesh	WISC-IV—Full Scale scores, and Verbal Comprehension, Perceptual Reasoning, Working Memory and Processing Speed Indices	Well water As: 37.57 μg/L Urinary As: 157.79 μg/gCr Blood As: 4.84 μg/L	726 14–16 years	↓IQ (Prenatal exposure linked to deficits in intelligence) Blood As was significantly negatively associated with all WISC-IV scores except for Perceptual Reasoning.	Wasserman et al., 2018
Bangladesh	WISC-IV	Urinary As at 10 years - 58 μg/L (7.3–940 μg/L)	1523 Children (5 & 10 years)	↓ Full developmental scores (Verbal comprehension and Perceptual reasoning)	Vahter et al., 2020
Bangladesh	CANTAB	Blood As: 3.52 μg/L	572 adolescents (14–16 years)	↓working memory	Saxena et al., 2022
India	WISC (no edition provided), Raven Coloured, Progressive Matrices test, Total Sentence Recall test, Purdue pegboard test	>50 μg/L	Children (5–15 years)	Intelligence (↓total IQ) Verbal (↓vocabulary, language) visual perception (↓picture completion, object assembly)	Von Ehrenstein et al., 2007
China	MMSE, Chinese version	Drinking water As: 4–183 μg/L)	Adults > 40 years old	↓total IQ (As >100 μg/L in drinking water was positively correlated with reduction in MMSE score and cognitive impairment)	Liu et al., 2017
China	MMSE, Chinese version	Hair As (0.21 mg/kg)	1556 adults	↓total IQ (Reduce MMSE score) Arsenicosis, $N = 766$ (49.2 %)	Wang et al., 2021a, 2021b
China	CBCL	Urinary As: Maternal (22.22 μg/L) 6-year-old (33.86 μg/L)	389 mother-child pairs Children (6 years)	Childhood As exposure: ↑ Anxious and Depressed Problems in Girls	Dai et al., 2023
Cambodia	Digit symbol, digit span, Santa Ana manual dexterity, Benton visual retention, pursuit aiming, trail making and simple reaction time	Groundwater As: 50–500 μg/L	157 Children (12 and 16 years)	Significant differences in neurobehavioral test scores among the 3 sites, except for digit span (backward) test. Children with high hair As (>0.93 μg/g) levels experienced 1.57–4.67 times greater risk of having lower neurobehavioral test scores compared to those with low hair As level	Vibol et al., 2015
Japan	WAIS-III - Vocabulary and Block Design (WRAML2) - Design memory subtest Grooved pegboard test (measure complex visual-motor coordination) Finger tapping test (measures maximum oscillation rate of the index finger, as an indicator of psychomotor disruption)	Contaminated milk powder (1955 mass As poisoning)	50 Adults (exposed as infants)	Cognitive impairment ↓ all scores except for Finger tapping Developmental neurotoxicity due to As likely results in permanent changes in brain functions.	Yorifuji et al., 2016
Mexico	WISC-RM	>50 μg/L	Children	↓verbal IQ ↓total IQ	Calderón et al., 2001
Mexico	Visual-Spatial Abilities (Figure Design), Peabody Picture Vocabulary Test, WISC-RM (Digit Span subscale, Visual Search, and Letter Sequencing Tests)	Urinary As: 58.1 μg/L) > 50 μg/L	Children (6–7 years)	Intelligence (↓total IQ) Verbal (↓figure design, vocabulary, letter sequencing)	Rosado et al., 2007
Mexico	MMSE, EXIT25, RBANS, TMTA and TMTB, COWAT	Long term As water: 3.06–7.39 μg/L Current As water: 6.33 μg/L	434 Adults (>40 years)	↓ Poorer scores in language, visuospatial skills, executive functioning, global cognition, processing speed, and immediate memory.	O'Bryant et al., 2011
Mexico	Conners Behavior Rating Scales (Oppositional Behavior, Cognitive Problems, Hyperactivity and ADHD Index), PPVT-R, Spanish version	Urinary As (55.2 μg/L), MMA (6.7 μg/L), DMA (39.3 μg/L)	526 Children (6–7 years)	↑ Risk for ADHD, Association with Cognitive Deficits Higher urinary DMA was associated with higher ratings on the Oppositional, Cognitive Problems and ADHD Index	Roy et al., 2011
United States	BSID (no edition provided) (1–3 years) WPPSI (5 years) WISC (8 years)	Maternal urinary As : 3.63 (2.40–5.86) μg/L) Children urinary As: 3.61–3.74 μg/L	260 children urine (1–3, 5 years)	Modest, non-statistically significant decrease ↓ Full developmental and Full scale IQ	Signes-Pastor et al., 2022
Spain	MSCA	7.78 μg/g creatinine	807 mother–child	Association with MMA: Inversely associated (general verbal,	Soler-Blasco et al., 2022

(*continued on next page*)

Table 3 (*continued*)

Country	Cognitive scale	Arsenic (As) concentration	Population size, Age	Findings	Reference
			pairs Children (4–5 years)	quantitative, memory, executive function and working memory scales) Children whose mothers had lower nutrient levels obtained lower scores on cognitive tests.	
Spain	BARS (assess attention)	Urinary As: 0.70 μg/L	261 Children (6–9 years)	↑risk for ADHD ↓ attention /cognitive function,	Rodríguez-Barranco et al., 2016
Italy	CBCL (Aggressive Behavior, Anxious/ Depressed, Attention Problems, Rule-Breaking Behavior, Somatic Complaints, Social Problems, Thought Problems, Withdrawn/ Depressed) Social Responsiveness Scale (measure autistic traits) DSM scales (Affective Problems, Anxiety Problems, Somatic Problems, ADHD Problems, Oppositional Defiant Problems, Conduct Problems).	Urinary As: 8.3 ng/mL	299 Children (6–11 years)	↑risk for anxiety and depression, somatic problems, attention problems and rule breaking behavior.	Renzetti et al., 2021

Abbreviations: WISC-RM, Wechsler Intelligence Scale for Children Revised Version for México; WISC-III, Wechsler Intelligence Scale for Children Third edition; WISC-IV, Wechsler Intelligence Scale for Children Fourth edition; BSID-III, Bayley Scales of Infant and Toddler Development Third Edition; WPPSI, Wechsler Preschool and Primary Scale of Intelligence; WAIS-III, Wechsler Adults Intelligent Scale III; WRAML2, Design memory subtest from Wide Range Assessment of Memory and Learning 2; MSCA, McCarthy Scales of Children's Abilities; CANTAB, Cambridge Neuropsychological Test Automated Battery; MMSE, Mini-Mental State Examination; EXIT25, Exit Interview; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; TMTA and TMTB, Trails Making Test; COWAT, Controlled Oral Word Association Test; BARS, Behavioral Assessment and Research System; CBCL, Child Behavior Checklist; DSM, Diagnostic and Statistical Manual of Mental Disorders; PPVT-R, Peabody Picture Vocabulary Test-Revised, Spanish version.

1.57–4.67 times greater possibility of attaining poorer neurobehavioral test scores (Vibol et al., 2015). Research in Southeast Asia has highlighted that maternal blood arsenic concentration correlate with fetal arsenic exposure. Arsenic level in Malaysian maternal and cord blood (0.82 ± 1.1 μg/dL) was found equivalent. This emphasizes the maternal-to-fetal transfer and could have attributable risks of chronic toxicity (Sakai et al., 2017). In comparison to Thai (5.79 ± 0.5 μg/g) and Vietnamese (2.46 μg/L) newborns, maternal and cord blood arsenic concentration in Malaysian newborn is significantly higher (Navasumrit et al., 2019; Sakai et al., 2017). In fact, Malaysian cord blood arsenic levels are four times higher than those reported in Japan (Tohuku) and the United States (Iwai-Shimada et al., 2019; Tsuji et al., 2015). Prenatal exposure to medium and high concentration of arsenic were reported associated with an increase of developmental delays in communication, gross motor skills, fine motor skills, problem solving, and personal-social skills in 6-month-old infants (Liang et al., 2020). This scenario highlights that arsenic can cross the placenta, increasing the risk of ASD (Long et al., 2019).

Arsenic has also been detected in hair and urine samples for risk assessment purposes. For instance, elevated arsenic level in hair samples of Malaysian teenagers and adults, reported above 1 μg/g had arsenicosis due to smoking habits (Ramly et al., 2023), living in industrial area (Aldroobi et al., 2013), and high consumption of fish contaminated with arsenic (Mohammad Sham et al., 2022). A risk assessment study from Indonesia revealed that the highest arsenic exposure from fish and processed fishery products was in toddlers (0–4 years) and the lowest in the age group of 19–55 years (Dwiyitno et al., 2024). In Vietnam and Cambodia hair samples (0.088–2.77 μg/g) showed elevated arsenic level primarily due to consumption of groundwater contaminated with arsenic (<0.10–330 μg/L), exceeding the WHO drinking water guideline of 10 μg/L (Agusa et al., 2006; Hashim et al., 2013; Nguyen et al., 2009; Phan et al., 2011). In Thailand, Nilkarnjanakul et al., (2023) observed the excretion of arsenic in the urine tends to increase as the arsenic content in the groundwater increases, suggesting a potential route of exposure via drinking water. Additionally, a study from Thailand found that arsenic level detected in hair samples (1.05–2.24 mg/kg) of school children correlated with the distance from a secured landfill (Rujiralai et al., 2018).

3.8. Arsenic and autism spectrum disorder

This current review selected ten studies linking arsenic to ASD. In a study involving Arabic children (ages 3–9) that were diagnosed with autism spectrum disorder (ASD) have shown that these children to have higher levels of arsenic in their hair as compared to healthy children in the control group (Blaurock-Busch et al., 2011). In Poland, a case-control study has shown that children aged 2 to 8 years that were diagnosed with ASD have higher arsenic content in their hair compared to controls (Fiłon et al., 2020). Similar findings have been reported in the USA and China, where higher arsenic hair content was observed in children aged 3 to 7 years and under 6 years, respectively (Obrenovich et al., 2011; Zhai et al., 2019). However, these findings differ from those in Russia and Italy. In Russia, control studies of children aged 2 to 9 years and in Italy, studies of children aged 8 to 9 years, found no significant difference in hair arsenic levels between children diagnosed with ASD and controls (De Palma et al., 2012; Skalny et al., 2017a, 2017b). Additionally, a study in the US reported significantly lower arsenic levels in the hair of children with ASD compared to controls (Kern et al., 2007). A metallomics study found that the maximum arsenic levels in the hair of 1967 Japanese children with ASD were 33.5 times higher than the reference level (Yasuda et al., 2013). Moreover, a previous study also reported a significant positive correlation between arsenic levels in hair and the severity of ASD symptoms, particularly social communication deficits and repetitive behaviors (Fiore et al., 2020). This review noted that studies using hair arsenic as an exposure metric showed relatively high levels, while those showing no association with ASD typically had hair arsenic levels below 0.1 μg/g. Despite extensive research on arsenic levels in water and rice in Malaysia, Thailand, Indonesia, Cambodia, and Vietnam (refer to Tables 1 and 2), there are almost no studies examining the association between arsenic levels in human samples (hair, toenail, urine) and ASD severity. The few available studies focused on other heavy metals and were excluded for not meeting inclusion criteria. Overall, the evidence is insufficient to establish a link between low arsenic exposure and ASD in Southeast Asia. Restricting our review to English reports might exclude relevant studies in other languages. However, evidence suggests this issue is minimal and unlikely to overestimate the associations investigated

(Dechartres et al., 2018).

3.9. Metabolism of neurotoxicity, hepatotoxicity and nephrotoxicity

3.9.1. Arsenic and oxidative stress

Arsenic exposure induces oxidative stress via production of excessive reactive oxygen species (ROS), disruptions in signaling pathways like Extracellular signal-regulated kinase (ERK), nuclear factor E2-related factor 2/antioxidant response element (Nrf2-ARE), and Mitogen-activated protein kinases (MAPK), and altered gene expression (Hu et al., 2020; Rahaman et al., 2021; Sun et al., 2022). Arsenic exposure also affects SH-protein structure and function, leading to mitochondrial dysfunction, impaired antioxidant defences, and altered hormone secretion (kaur et al., 2024). Arsenic increases ROS production by suppressing cellular antioxidants such as superoxide dismutase (SOD), reduced glutathione (GSH), and catalase (CAT) (Jomova et al., 2023). Elevated ROS levels inhibit survival proteins like the mammalian target of rapamycin (mTOR), protein kinase B (Akt), nuclear factor erythroid 2-related factor 2 (Nrf2), and Extracellular signal-regulated kinase 1 (ERK1), promoting DNA damage (Rahaman et al., 2020). Excess ROS also activates autophagy-related proteins autophagy activating kinase 1 (ULK1) and microtubule-associated protein 1A/1B-light chain 3 (LC3) protein a, ultimately leading to apoptotic cell death (Rahaman et al., 2020). Arsenic-induced toxicity primarily results from excessive ROS generation, leading to DNA damage, cell membrane disruption, mitochondrial membrane potential loss, upregulation of pro-apoptotic proteins (Bax, p53, caspase-3, LC3), and downregulation of survival proteins (Bcl-2, Akt, mTOR).These alterations contribute to carcinogenicity and genotoxicity by promoting oxidative DNA damage, disrupted DNA methylation, altered cell proliferation, and tumor progression. ROS interacts with DNA components, causing base lesions, strand breaks, and mutations, which in turn affect DNA repair, gene regulation, and genetic stability (Poetsch, 2020).

3.9.2. Arsenic induced neurotoxicity

Neuronal damage resulting from arsenic exposure is well establish in scientific literature. In particular, both epidemiological and experimental studies have demonstrated that arsenic exposure significantly increases risk for various neurological disorders (Yang et al., 2024; Zhou et al., 2020; Zhou et al., 2024). Manifestation of these neurological disorders primarily triggered by excessive production of ROS, DNA damage and a chromosomal aberration (Pugsley et al., 2022). Arsenic has been shown to cross the blood-brain barrier (BBB) and accumulate in the brain (striatum and hippocampus), leading to various neurological and behavioural disorders (Tolins et al., 2014). Epidemiological studies have indicated an association between high-level oral exposures to inorganic arsenic and sensitive endpoints for peripheral and central neurotoxicity. Peripheral neuropathy is observed at both acute and chronic high arsenic exposures, with clinical features including numbness and paresthesias in the hands and soles of the feet. Symmetrical peripheral neuropathy is often one of the earliest symptoms of arsenic poisoning. Pre-menopausal women in eastern India who drank water with arsenic levels of 11–50 μg/L were previously reported had a higher risk of peripheral nervous system symptoms, such as a burning sensation in extremities, tingling, numbness, reduced taste, and diminished sense of smell, compared to those drinking water with arsenic levels below 10 μg/L (Mukherjee et al., 2014). Adult and children in Myanmar consuming water with arsenic concentrations above 10 μg/L also showed similar risk of peripheral neuropathy (Mochizuki, 2019). Low chronic arsenic exposure has also been reported a higher prevalence of depression and other neurobehavioral symptoms among the same eastern Indian pre-menopausal women (Mukherjee et al., 2014). Additionally, studies in various countries (see Section 3.7) have reported cognitive impairment associated with higher arsenic concentrations in drinking water.

The effects of arsenic-induced neurotoxicity include the alteration of neurotransmitter concentrations, reduced synaptic plasticity, signaling, neurogenesis, altered sensory function and peripheral nerve neuropathy serotonin (Alao et al., 2021; Li et al., 2020). Arsenic can induce neurotoxic effects by altering levels of key neurotransmitters, including dopamine, norepinephrine, and serotonin (Alao et al., 2021; Li et al., 2020). It can also disrupt levels of glutamate, GABA, and other biogenic amines (Singh et al., 2016). These changes reduce acetylcholinesterase activity, leading to impairments in learning and memory in both humans and rodents (Tyler and Allan, 2014). Neurotoxic effects of arsenic also mediated through reduced glutamate levels and mGluR5 expression in the hippocampus (Jiang et al., 2014). In mice, arsenic exposure caused reductions in glutamatergic, GABAergic, dopaminergic, and serotonergic neurotransmitter levels, and structural abnormalities. In response, amino acid and fatty acid compounds were predominantly upregulated in hippocampal and cortical tissues. Specifically, homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC) compounds increased in the hippocampus, while purine ribose-related compounds were upregulated in the cortex (Huang et al., 2024). This alteration mainly associated with disruptions in glutathione metabolism, arginine and proline metabolism, and alanine, aspartate, and glutamate metabolism (Huang et al., 2024). Another potential mechanism underlying arsenic-induced neurobehavioral dysfunction may involve the transcriptional regulation of ectonucleotidases. The uncoupling of oxidative phosphorylation is associated with the formation of arsenate-ADP complexes (Baldissarelli et al., 2012). Normally, ATP is generated in mitochondria from ADP to provide cellular energy; however, the formation of ADP-arsenate complexes can occur more rapidly than ATP synthesis, disrupting ATP production. This process leads to a significant reduction in the mRNA expression of NTPDase family members (entpd2_mg, entpd2_mq) and Ecto-5′-nucleotidase, ultimately decreasing ATP, ADP, and AMP hydrolysis (Thakur et al., 2021). Arsenic may also affect the cholinergic system by interacting with thiol (-SH) groups that are crucial for choline uptake and with the disulfide group of acetylcholinesterase (Bartos et al., 2024; Thakur et al., 2021). Developmental neurotoxic effect of inorganic arsenic in rodent offspring showed marked changes in antioxidant status within the prefrontal cortex, with increased activities of acetylcholinesterase and glutamate pyruvate transaminase, alongside decreased glutamate oxaloacetate transaminase activity (Bartos et al., 2024). A notable downregulation in the mRNA expression of the α1 GABAA receptor was also observed in this brain region. These findings suggest that inorganic arsenic exposure during early development disrupts brain oxidative stress markers, alters cholinergic and glutamatergic enzyme activities, and reduces GABA receptor levels in the prefrontal cortex (Bartos et al., 2024). Chronic dietary exposure to arsenic in zebrafish leads to arsenic accumulation, increased dopamine levels, oxidative stress (marked by thiol redox reduction, lipid peroxidation, and upregulation of antioxidant genes), and disrupts the dopaminergic system by altering genes related to dopamine receptors, thyroxine hydroxylase, and monoamine oxidase (Rachamalla et al., 2023). This exposure also downregulates genes crucial for learning and memory, such as brain-derived neurotrophic factor BDNF and ectonucleotidases, indicating potential impairment in cognitive performance (Rachamalla et al., 2023). Arsenic induced neurotoxicity also involved mitochondrial dysfunction (Prakash et al., 2016). Integrative proteomic and metabolomic analysis of the cortex in rats exposed to arsenic-contaminated drinking water revealed that arsenic impairs cognitive function, promotes excessive generation of amyloid-β (Aβ) peptides, and disrupts mitochondrial redox balance (Du et al., 2022). Additionally, the enhancement of glycolysis and the tricarboxylic acid (TCA) cycle, driven by increased levels of heterogeneous nuclear ribonucleoprotein L (hnRNP L), serves as a low-dose protective mechanism against arsenic-induced ATP deficiency and oxidative stress (Du et al., 2022).

3.9.3. Arsenic induced hepatoxicity

The liver, as the primary site for xenobiotic detoxification, is a major

target for many toxic substances due to its abundance of metabolizing enzymes within hepatocytes (Gu and Manautou, 2012). Epidemiological and animal studies confirm arsenic's damaging effects on the liver, though its mechanisms remain multifaceted. For instance, a study in mice exposed to 10 mg/L sodium arsenite in drinking water for 30 days showed disorganized liver tissue, lax cytoplasm, inflammatory cell infiltration, and elevated plasma aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, indicating early markers of hepatotoxicity (Wang et al., 2023). This study also reported that five metabolic pathways, including phenylalanine, tyrosine, tryptophan biosynthesis, and nicotinate and nicotinamide metabolism, were implicated in arsenic-induced hepatotoxicity, primarily affecting lipid metabolism, apoptosis, and DNA damage (Wang et al., 2023). Network pharmacology indicated that arsenic hepatotoxicity may involve targets such as Hsp90aa1, Akt2, Egfr, and Tnf, influencing PI3K-Akt, HIF-1, MAPK, and TNF signaling pathways. Combined metabolomics and network pharmacology identified eight key targets linked to arsenic-induced hepatotoxicity: MAOA, DNMT1, MAOB, PARP1, EPHX2, ANPEP, ADA and XDH (Wang et al., 2023). Other studies in mice suggest that arsenic-induced autophagy in the liver involves changes in PI3K, mTOR, Beclin-1, ATG5, LC3, and P62 expression, while apoptosis is linked to altered levels of proapoptotic P53, Bax, Bcl-2, Caspase-3, Caspase-9, Cleaved-Caspase-3, and Cytc (Zhong et al., 2022).

Recent studies in mice have shown that a diet containing 30 mg/kg arsenic for 60 days induces oxidative stress, disrupts liver metabolic pathways, and triggers ferroptotic cell death (Shao et al., 2024). This oxidative stress is associated with a reduction in the antioxidant metabolite glutathione (GSH) in the liver. GSH, a crucial intracellular antioxidant, scavenges free radicals and protects cells from oxidative damage, serving as a vital detoxification mechanism in liver cells. The increase in spermidine levels following arsenic exposure suggests a disturbance in arginine and proline metabolism (Shao et al., 2024), indicating elevated oxidative stress in the livers. Also, the arsenic exposed group exhibited significant increases in pro-inflammatory polyunsaturated fatty acids (PUFAs), including arachidonic acid and linoleic acid (Alba et al., 2023). Notably, arachidonic acid can generate prostaglandins and leukotrienes that promote inflammation, potentially contributing to liver disease like cirrhosis and fibrosis (Alvarez and Lorenzetti, 2021). Substantial evidence indicates that arsenic-induced hepatoxicity is linked to oxidative stress, inflammation, mitochondrial dysfunction, and apoptosis (Banerjee et al., 2017; Lv et al., 2024). Dysregulation of AKT2/NF-κB and mTOR-mediated have been highlighted involved in arsenic-induced hepatoxicity (Yang et al., 2021; Zhang et al., 2021).

3.9.4. Arsenic induced nephrotoxicity

Hepatocytes are the primary site of arsenic metabolism, while renal cells play a crucial role in its excretion. Additionally, arsenate (AsV) is reduced to arsenite (AsIII) in the kidneys (González-Martínez et al., 2024). During arsenic elimination through the renal system, arsenic accumulates in the kidneys, which can cause cytotoxicity (Chen et al., 2024). Arsenic toxicity can cause hypourea, high levels of blood urea nitrogen, serum creatinine, and proteinuria followed by acute tubular necrosis (renal injury) (Sasaki et al., 2007). Moreover, a positive association between arsenic exposure in drinking water (>100 μg/L) and the incidence of albuminuria and proteinuria has been reported in population living in Bangladesh, China, Taiwan, Chile, and Sri Lanka (Zheng et al., 2014). Arsenic accumulation in kidneys can cause dysfunction of proximal tubules and kidney fibrosis and may reduce the glomerular filtration rate as the key features of arsenic nephrotoxicity (Cheng et al., 2018). Metabolomic analysis of mice kidney revealed that arsenic exposure inhibited linoleic acid and glycerophospholipid metabolism, suggesting that arsenic may suppress kidney antioxidant and anti-inflammatory activities, potentially leading to renal injury (He et al., 2024). This aligns with findings in metabolomic analysis in zebrafish larvae, where linoleic acid was found to be dysregulated following arsenic exposure, although kidney examination was not conducted (Abu Bakar et al., 2022). Inhibition of linoleic acid metabolism after arsenic exposure suggests that arsenic may impair kidney antioxidant and anti-inflammatory activity, potentially leading to renal injury (He et al., 2024). The study in mice found that arsenic trioxide significantly increased NF-κB expression in kidney tissue, activating inflammatory mediators such as TNF-α, IL-6, and IL-8 (Jin et al., 2020). High-dose arsenic significantly induced autophagy, evidenced by lysosome acidification, autophagosome formation, elevated LC3-II/I, Lamp2, and Beclin1 expression, alongside PI3K/AKT/mTOR pathway downregulation (Das et al., 2023).

4. Conclusion

In conclusion, arsenic contamination in rice and drinking water across Southeast Asia poses a serious, yet often overlooked, threat to public health, especially for children. Although countries like Malaysia, Myanmar, and Thailand generally report lower arsenic levels, the potential risk associated with prolonged low-level exposure, including both carcinogenic and non-carcinogenic effects remains concerning. Most epidemiological and biomonitoring studies have focused on moderate to high arsenic levels, often overlooking the impact of low-level exposure. The potential link between low-level arsenic exposure and cognitive impairment, particularly during critical developmental stages, remains underexplored. Future biomonitoring research should integrate multi-omics approaches to identify metabolites potentially affected by arsenic's neurotoxic effects. Comprehensive risk assessments must also consider neurodevelopmental impacts and control for confounding factors such as co-exposure to other pollutants, nutritional status, and socioeconomic condition to better understand arsenic's influence on cognitive and neurodevelopmental health in vulnerable populations.

CRediT authorship contribution statement

Noraini Abu Bakar: Writing – review & editing, Writing – original draft, Visualization, Investigation, Funding acquisition, Conceptualization. **Wan Norhamidah Wan Ibrahim:** Validation, Supervision. **Siti Munirah Mohd Faudzi:** Validation, Supervision.

Declaration of competing interest

The authors declare that they have no known competing personal relationships or financial interests that could have appeared to influence the work reported in this paper.

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Data availability

Data presented within the reported article.

References

Abu Bakar, N., Wan Ibrahim, W.N., Che Abdullah, C.A., Ramlan, N.F., Shaari, K., Shohaimi, S., Mediani, A., Nasruddin, N.S., Kim, C.-H., Mohd Faudzi, S.M., 2022. Embryonic arsenic exposure triggers long-term behavioral impairment with metabolite alterations in zebrafish. Toxics 10 (9), 493. https://doi.org/10.3390/toxics10090493.

Agusa, T., Kunito, T., Fujihara, J., Kubota, R., Minh, T.B., Kim Trang, P.T., Iwata, H., Subramanian, A., Viet, P.H., Tanabe, S., 2006. Contamination by arsenic and other trace elements in tube-well water and its risk assessment to humans in Hanoi, Vietnam. *Environ. Pollut.* (Barking, Essex: 1987) 139 (1), 95–106. https://doi.org/10.1016/j.envpol.2005.04.033.

Ahmed, M.F., Mokhtar, M.Bin, Alam, L, 2021. Carcinogenic and non-carcinogenic health risk of arsenic ingestion via drinking water in Langat River Basin, Malaysia. Environ. Geochem. Health 43 (2), 897–914. https://doi.org/10.1007/s10653-020-00571-w.

Alao, M.E., Perin, J., Brooks, W.A., Hossain, L., Goswami, D., Zaman, K., Yunus, M., Khan, M.A., Jahan, Y., Ahmed, D., Slavkovich, V., Graziano, J., Prosperi, C., Higdon, M., Deloria-Knoll, M., O'Brien, K.L., George, C.M., 2021. Urinary arsenic is associated with wasting and underweight status in young children in rural Bangladesh. Environ. Res. 195, 110025. https://doi.org/10.1016/J.ENVRES.2020.110025.

Alba, M.M., Ebright, B., Hua, B., Slarve, I., Zhou, Y., Jia, Y., Louie, S.G., Stiles, B.L., 2023. Eicosanoids and other oxylipins in liver injury, inflammation and liver cancer development. Front. Physiol. 14, 1098467. https://doi.org/10.3389/fphys.2023.1098467.

Aldroobi, K.S.A., Shukri, A., Bauk, S., Munem, E.M.A., Abuarra, A.M.A., 2013. Determination of arsenic and mercury level in scalp hair from a selected population in Penang, Malaysia using XRF technique. Radiat. Phys. Chemi. 91, 9–14. https://doi.org/10.1016/j.radphyschem.2013.06.004.

de Luján Alvarez, M., Lorenzetti, F., 2021. Role of eicosanoids in liver repair, regeneration and cancer. Biochem. Pharmacol. 192, 114732. https://doi.org/10.1016/J.BCP.2021.114732.

Arcella, D., Cascio, C., Gómez Ruiz, J.Á., 2021. Chronic dietary exposure to inorganic arsenic. EFSA J. 19 (1), 6380. https://doi.org/10.2903/j.efsa.2021.6380.

Arias, D., Saxena, S., Verguet, S., 2022. Quantifying the global burden of mental disorders and their economic value. EClinicalMedicine 54, 101675. https://doi.org/10.1016/j.eclinm.2022.101675.

ATSDR, 2007. Toxicological profile for arsenic. In: U.S Public Health Service, Agency for Toxic Substances and Disease Registry (Issue August). Atlanta, Georgia. www.atsdr.cdc.gov/csem/arsenic/standards.html.

Azlan, A., Khoo, H.E., Idris, M.A., Ismail, A., Razman, M.R., 2012. Evaluation of minerals content of drinking water in Malaysia. Sci. World J. 2012, 403574. https://doi.org/10.1100/2012/403574.

Azrina, A., Khoo, H.E., Idris, M.A., Amin, I., Razman, M.R., 2011. Major inorganic elements in tap water samples in Peninsular Malaysia. Malays. J. Nutr. 17 (2), 271–276. https://pubmed.ncbi.nlm.nih.gov/22303580/.

Bacquart, T., Frisbie, S., Mitchell, E., Grigg, L., Cole, C., Small, C., Sarkar, B., 2015. Multiple inorganic toxic substances contaminating the groundwater of Myingyan Township, Myanmar: arsenic, manganese, fluoride, iron, and uranium. Sci. Total Environ. 517, 232–245. https://doi.org/10.1016/j.scitotenv.2015.02.038.

Baldissarelli, L.A., Capiotti, K.M., Bogo, M.R., Ghisleni, G., Bonan, C.D., 2012. Arsenic alters behavioral parameters and brain ectonucleotidases activities in zebrafish (Danio rerio). Comp. Biochem. Physiol. Part C 155 (4), 566–572. https://doi.org/10.1016/J.CBPC.2012.01.006.

Banerjee, S., Mahanty, A., Mohanty, S., Mazumder, D.G., Cash, P., Mohanty, B.P., 2017. Identification of potential biomarkers of hepatotoxicity by plasma proteome analysis of arsenic-exposed carp Labeo rohita. J. Hazard. Mater. 336, 71–80. https://doi.org/10.1016/J.JHAZMAT.2017.04.054.

Bartos, M., Gallegos, C.E., Mónaco, N., Lencinas, I., Dominguez, S., Bras, C., del Carmen Esandi, M., Bouzat, C., Gumilar, F., 2024. Developmental exposure to arsenic reduces anxiety levels and leads to a depressive-like behavior in female offspring rats: molecular changes in the prefrontal cortex. Neurotoxicology 104, 85–94. https://doi.org/10.1016/J.NEURO.2024.07.013.

Baruah, S.G., Ahmed, I., Das, B., Ingtipi, B., Boruah, H., Gupta, S.K., Nema, A.K., Chabukdhara, M., 2021. Heavy metal(loid)s contamination and health risk assessment of soil-rice system in rural and peri-urban areas of lower brahmaputra valley, northeast India. Chemosphere 266, 129150. https://doi.org/10.1016/j.chemosphere.2020.129150.

Bhattacharya, P., Samal, A.C., Majumdar, J., Santra, S.C., 2010. Arsenic contamination in rice, wheat, pulses, and vegetables: a study in an arsenic affected area of West Bengal, India. Water, Air, Soil Pollut. 213, 3–13. https://doi.org/10.1007/s11270-010-0361-9.

Bhatti, S.S., Kumar, V., Kumar, A., Kirby, J.K., Gouzos, J., Correll, R., Singh, J., Sambyal, V., Nagpal, A.K., 2020. Potential carcinogenic and non-carcinogenic health hazards of metal(loid)s in food grains. Environ. Sci. Pollut. Res. 27 (14), 17032–17042. https://doi.org/10.1007/s11356-020-08238-w.

Blaurock-Busch, E., Amin, O.R., Rabah, T., 2011. Heavy metals and trace elements in hair and urine of a sample of Arab children with autistic spectrum disorder. Maedica (Bucur) 6 (4), 247–257. https://pubmed.ncbi.nlm.nih.gov/22879836/.

Bloom, D.E., Cafiero, E.T., Jané-Llopis, E., Abrahams-Gessel, S., Bloom, L.R., Fathima, S., Feigl, A.B., Gaziano, T., Mowafi, M., Pandya, A., Prettner, K., Rosenberg, L., Seligman, B., Stein, A.Z., & Weinstein, C. (2011). *The Global Economic Burden of Non-communicable Diseases*. https://www3.weforum.org/docs/WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf.

Briffa, J., Sinagra, E., Blundell, R., 2020. Heavy metal pollution in the environment and their toxicological effects on humans. Heliyon 6 (9), e04691. https://doi.org/10.1016/j.heliyon.2020.e04691.

Calderón, J., Navarro, M.E., Jimenez-Capdeville, M.E., Santos-Diaz, M.A., Golden, A., Rodriguez-Leyva, I., Borja-Aburto, V., Díaz-Barriga, F., 2001. Exposure to arsenic and lead and neuropsychological development in Mexican children. Environ. Res. 85 (2), 69–76. https://doi.org/10.1006/enrs.2000.4106.

Chanpiwat, P., Hensawang, S., Suwatvitayakorn, P., Ponsin, M., 2019. Risk assessment of bioaccessible arsenic and cadmium exposure through rice consumption in local residents of the Mae Tao Sub-district, Northwestern Thailand. Environ. Geochem. Health 41 (1), 343–356. https://doi.org/10.1007/s10653-018-0098-8.

Chen, X., Liu, S., Luo, Y., 2023. Spatiotemporal distribution and probabilistic health risk assessment of arsenic in drinking water and wheat in Northwest China. Ecotoxicol. Environ. Saf. 256, 114880. https://doi.org/10.1016/j.ecoenv.2023.114880.

Chen, X., Yan, X., Tang, X., Wang, Y., Zhang, X., Cao, X., Ran, X., Ma, G., Hu, T., Qureshi, A., Luo, P., Shen, L., 2024. Study on the mechanism of arsenic-induced renal injury based on SWATH proteomics technology. J. Trace Elem. Med. Biol. 83, 127390. https://doi.org/10.1016/J.JTEMB.2024.127390.

Cheng, Y.Y., Chang, Y.T., Cheng, H.L., Shen, K.H., Sung, J.M., Guo, H.R., 2018. Associations between arsenic in drinking water and occurrence of end-stage renal disease with modifications by comorbidities: a nationwide population-based study in Taiwan. Sci. Total Environ. 626, 581–591. https://doi.org/10.1016/J.SCITOTENV.2018.01.043.

Chételat, J., Palmer, M.J., Paudyn, K., Jamieson, H., Amyot, M., Harris, R., Hesslein, R., Pelletier, N., Peraza, I., 2023. Remobilization of legacy arsenic from sediment in a large subarctic waterbody impacted by gold mining. J. Hazard. Mater. 452, 131230. https://doi.org/10.1016/j.jhazmat.2023.131230.

Coelho, D.G., Marinato, C.S., de Matos, L.P., de Andrade, H.M., da Silva, V.M., Santos-Neves, P.H., Araújo, S.C., Oliveira, J.A., 2020. Is arsenite more toxic than arsenate in plants? Ecotoxicology 29 (2), 196–202. https://doi.org/10.1007/s10646-019-02152-9.

Cubadda, F., Jackson, B.P., Cottingham, K.L., Van Horne, Y.O., Kurzius-Spencer, M., 2017. Human exposure to dietary inorganic arsenic and other arsenic species: state of knowledge, gaps and uncertainties. Sci. Total Environ. 579, 1228–1239. https://doi.org/10.1016/j.scitotenv.2016.11.108.

Dai, Y., Lu, H., Zhang, J., Ding, J., Wang, Z., Zhang, B., Qi, X., Chang, X., Wu, C., Zhou, Z., 2023. Sex-specific associations of maternal and childhood urinary arsenic levels with emotional problems among 6-year-age children: evidence from a longitudinal cohort study in China. Ecotoxicol. Environ. Saf. 267, 115658. https://doi.org/10.1016/j.ecoenv.2023.115658.

Das, A., Chowdhury, O., Gupta, P., Das, N., Mitra, A., Ghosh, S., Ghosh, S., Sarkar, S., Bandyopadhyay, D., Chattopadhyay, S., 2023. Arsenic-induced differential inflammatory responses in mouse thymus involves NF-κB/STAT-3 disruption, Treg bias and autophagy activation. Life Sci. 314, 121290. https://doi.org/10.1016/J.LFS.2022.121290.

Davydiuk, T., Tao, J., Lu, X., Le, X.C., 2023. Effects of dietary intake of arsenosugars and other organic arsenic species on studies of arsenic methylation efficiency in humans. Environ. Health 1 (4), 236–248. https://doi.org/10.1021/envhealth.3c00090.

De Palma, G., Catalani, S., Franco, A., Brighenti, M., Apostoli, P., 2012. Lack of correlation between metallic elements analyzed in hair by ICP-MS and autism. J. Autism. Dev. Disord. 42 (3), 342–353. https://doi.org/10.1007/s10803-011-1245-6.

Dechartres, A., Atal, I., Riveros, C., Meerpohl, J., Philippe, R., 2018. Association between publication characteristics and treatment effect estimates a meta-epidemiologic study. Ann. Intern. Med. 169 (6), 385–393. https://doi.org/10.7326/M18-1517.

Demissie, S., Mekonen, S., Awoke, T., Teshome, B., Mengistie, B., 2024. Examining carcinogenic and noncarcinogenic health risks related to arsenic exposure in Ethiopia: a longitudinal study. Toxicol. Rep. 12, 100–110. https://doi.org/10.1016/j.toxrep.2024.01.001.

DOE Department of Environment, Malaysia, 2020. Environmental Quality Report https://enviro2.doe.gov.my/ekmc/wp-content/uploads/2021/09/EQR-2020-1.pdf.

Du, X., Luo, L., Huang, Q., Zhang, J., 2022. Cortex metabolome and proteome analysis reveals chronic arsenic exposure via drinking water induces developmental neurotoxicity through hnRNP L mediated mitochondrial dysfunction in male rats. Sci. Total Environ. 820, 153325. https://doi.org/10.1016/j.scitotenv.2022.153325.

Dwiyitno, D., Andarwulan, N., Lioe, H.N., Imanningsih, N., Giriwono, P.E., Presiana, D., Adriany, R., Nikastri, E., Pusparini, N., Audia, I., Amaliya, N.N., Takhwifa, F., 2024. Estimated inorganic arsenic from total arsenic in fishery products and its health risk to the Indonesian population. Emerg. Contam. 10 (4), 100340. https://doi.org/10.1016/J.EMCON.2024.100340.

EFSA, 2009. Scientific report on the effects of farming systems on dairy cow welfare and disease. EFSA J 7 (7), 1143r. https://doi.org/10.2903/j.efsa.2009.1143r.

EFSA Panel on Contaminants in the Food Chain (CONTAM), Schrenk, D., Bignami, M., Bodin, L., Chipman, J.K., Del Mazo, J., Grasl-Kraupp, B., Hogstrand, C., Hoogenboom, L.R., Leblanc, J.C., Nebbia, C.S., Nielsen, E., Ntzani, E., Petersen, A., Sand, S., Vleminckx, C., Wallace, H., Barregård, L., Benford, D., Broberg, K., Schwerdtle, T., 2024. Update of the risk assessment of inorganic arsenic in food. EFSA journal. European Food Safety Authority 22 (1), e8488. doi:10.2903/j.efsa.2024.8488.

FAO, 2023. Food Outlook – Biannual report on global food markets. Food Outlook, November 2023 104. https://doi.org/10.4060/cc8589en.

Farzan, S.F., Karagas, M.R., Chen, Y., 2013. In utero and early life arsenic exposure in relation to long-term health and disease. Toxicol. Appl. Pharmacol. 272 (2), 384–390. https://doi.org/10.1016/j.taap.2013.06.030.

Fatoki, J.O., Badmus, J.A., 2022. Arsenic as an environmental and human health antagonist: a review of its toxicity and disease initiation. J. Hazard. Mater. Adv. 5, 100052. https://doi.org/10.1016/j.hazadv.2022.100052.

Fiłon, J., Ustymowicz-Farbiszewska, J., Krajewska-Kułak, E., 2020. Analysis of lead, arsenic and calcium content in the hair of children with autism spectrum disorder. BMC Public Health 20 (1), 383. https://doi.org/10.1186/s12889-020-08496-w.

Fiore, M., Barone, R., Copat, C., Grasso, A., Cristaldi, A., Rizzo, R., Ferrante, M., 2020. Metal and essential element levels in hair and association with autism severity. J. Trace Elem. Med. Biol. 57, 126409. https://doi.org/10.1016/j.jtemb.2019.126409.

Ganie, S.Y., Javaid, D., Hajam, Y.A., Reshi, M.S., 2024. Arsenic toxicity: sources, pathophysiology and mechanism. Toxicol. Res. 13 (1), tfad111. https://doi.org/10.1093/toxres/tfad111.

Ghosh, D., Ghosh, A., Bhadury, P., 2022. Arsenic through aquatic trophic levels: effects, transformations and biomagnification—A concise review. Geosci. Lett. 9 (1), 20. https://doi.org/10.1186/s40562-022-00225-y.

Gilbert, P.J., Polya, D.A., Cooke, D.A., 2015. Arsenic hazard in Cambodian rice from a market-based survey with a case study of Preak Russey village, Kandal Province. Environ. Geochem. Health 37 (4), 757–766. https://doi.org/10.1007/s10653-015-9696-x.

Giles, B.H., Mann, K.K., 2022. Arsenic as an immunotoxicant. Toxicology and applied pharmacology 454, 116248. https://doi.org/10.1016/j.taap.2022.116248.

Ginting, E.E., Silalahi, J., Putra, E.D., 2018. Analysis of arsenic in rice in Medan, North Sumatera Indonesia by atomic absorption spectrophotometer. Orient. J. Chem. 34 (5), 2651–2655. https://doi.org/10.13005/ojc/340557.

González-Martínez, F., Johnson-Restrepo, B., Quiñones, L.A., 2024. Arsenic inorganic exposure, metabolism, genetic biomarkers and its impact on human health: a mini-review. Toxicol. Lett. 398, 105–117. https://doi.org/10.1016/J.TOXLET.2024.06.008.

Grandjean, P., Landrigan, P.J., 2006. Developmental neurotoxicity of industrial chemicals. Lancet 368 (9553), 2167–2178. https://doi.org/10.1016/S0140-6736(06)69665-7.

Gu, X., Manautou, J.E., 2012. Molecular mechanisms underlying chemical liver injury. Expert. Rev. Mol. Med. 14, e4. https://doi.org/10.1017/S1462399411002110.

Guo, J., Dai, X., Xu, W., Ma, M., 2008. Overexpressing GSH1 and AsPCS1 simultaneously increases the tolerance and accumulation of cadmium and arsenic in *Arabidopsis thaliana*. Chemosphere 72 (7), 1020–1026. https://doi.org/10.1016/j.chemosphere.2008.04.018.

Habib, M.A., Reza, A.H.M.S., Hasan, M.I., Ahsan, M.A., Moniruzzaman, M., Hasan, A.B., Shofi, S.I., Hridoy, K.M., 2024. Evaluating arsenic contamination in northwestern Bangladesh: a GIS-Based assessment of groundwater vulnerability and human health impacts. Heliyon 10 (6), e27917. https://doi.org/10.1016/j.heliyon.2024.e27917.

Hama, T., Ito, H., Kawagoshi, Y., Nakamura, K., Kubota, T., 2023. Natural attenuation and remobilization of arsenic in a small river contaminated by the volcanic eruption of Mount Iou in southern Kyushu Island, Japan. J. Hazard. Mater. 455, 131576. https://doi.org/10.1016/j.jhazmat.2023.131576.

Hamadani, J.D., Tofail, F., Nermell, B., Gardner, R., Shiraji, S., Bottai, M., Arifeen, S.E., Huda, S.N., Vahter, M., 2011. Critical windows of exposure for arsenic-associated impairment of cognitive function in pre-school girls and boys: a population-based cohort study. Int. J. Epidemiol. 40 (6), 1593–1604. https://doi.org/10.1093/ije/dyr176.

Harine, I.J., Islam, M.R., Hossain, M., Afroz, H., Jahan, R., Siddique, A.B., Uddin, S., Hossain, M.A., Alamri, S., Siddiqui, M.H., Henry, R.J., 2021. Arsenic accumulation in rice grain as influenced by water management: Human health risk assessment. Agronomy 11 (9), 1741. https://doi.org/10.3390/agronomy11091741.

Hashim, J.H., Radzi, R.S.M., Aljunid, S.M., Nur, A.M., Ismail, A., Baguma, D., Sthiannopkao, S., Phan, K., Wong, M.H., Sao, V., Yasin, M.S.M., 2013. Hair arsenic levels and prevalence of arsenicosis in three Cambodian provinces. Sci. Total Environ. 463-464, 1210–1216. https://doi.org/10.1016/j.scitotenv.2013.04.084.

He, T., Xiong, L., Lin, K., Yi, J., Duan, C., Zhang, J., 2024. Functional metabolomics reveals arsenic-induced inhibition of linoleic acid metabolism in mice kidney in drinking water. Environ. Pollut. 349, 123949. https://doi.org/10.1016/J.ENVPOL.2024.123949.

Hensawang, S., Chanpiwat, P., 2017. Health impact assessment of arsenic and cadmium intake via rice consumption in Bangkok, Thailand. Environ. Monit. Assess. 189 (11), 599. https://doi.org/10.1007/s10661-017-6321-8.

Hensawang, S., Chanpiwat, P., 2018. Analysis and probabilistic risk assessment of bioaccessible arsenic in polished and husked jasmine rice sold in Bangkok. Chemosphere 207, 637–648. https://doi.org/10.1016/j.chemosphere.2018.05.125.

Hossain, M.B., Jahiruddin, M., Loeppert, R.H., Panaullah, G.M., Islam, M.R., Duxbury, J. M., 2009. The effects of iron plaque and phosphorus on yield and arsenic accumulation in rice. Plant Soil 317, 167–176. https://doi.org/10.1007/s11104-008-9798-7.

Htway, S.M., Sein, M.T., Nohara, K., Win-Shwe, T.T., 2019. Effects of developmental arsenic exposure on the social behavior and related gene expression in C_3H adult male mice. Int. J. Environ. Res. Public Health 16 (2), 174. https://doi.org/10.3390/ijerph16020174.

Hu, Y., Li, J., Lou, B., Wu, R., Wang, G., Lu, C., Wang, H., Pi, J., Xu, Y., 2020. The role of reactive oxygen species in arsenic toxicity. Biomolecules 10 (2), 240. https://doi.org/10.3390/biom10020240.

Hu, P., Ouyang, Y., Wu, L., Shen, L., Luo, Y., Christie, P., 2015. Effects of water management on arsenic and cadmium speciation and accumulation in an upland rice cultivar. J. Environ. Sci. (China) 27, 225–231. https://doi.org/10.1016/j.jes.2014.05.048.

Huang, Z., Guo, L., Huang, J., Chen, X., Sun, J., Ye, Y., Sheng, L., Zhang, Y., Zhou, J., Ji, J., Sun, X., 2024. Neurotoxicity and brain metabolic dysfunction induced by long-term food-derived arsenic exposure. Food Biosci. 59, 103804. https://doi.org/10.1016/j.fbio.2024.103804.

Irnawati, I., Idroes, R., Zulfiani, U., Akmal, M., Suhartono, E., Idroes, G.M., Muslem, M., Lala, A., Yusuf, M., Saiful, S., Suhud, K., Safitri, E., Jalil, Z., 2021. Assessment of arsenic levels in water, sediment, and human hair around ie seu'um geothermal manifestation area, aceh, indonesia. Water (Switzerland) 13 (17), 2343. https://doi.org/10.3390/w13172343.

Islam, M.N., Haque, M.I., Hossain, M.A., 2023. Spatial pattern of arsenic concentration and associated noncarcinogenic health risk assessment: a case study on Gangni Union of Chuadanga district of Bangladesh. Environ. Syst. Res. 12 (1), 29. https://doi.org/10.1186/s40068-023-00313-8.

Islam, S., Rahman, M.M., Islam, M.R., Naidu, R., 2016. Arsenic accumulation in rice: consequences of rice genotypes and management practices to reduce human health risk. Environ. Int. 96, 139–155. https://doi.org/10.1016/j.envint.2016.09.006.

Islam, S., Rahman, M.M., Islam, M.R., Naidu, R., 2017. Effect of irrigation and genotypes towards reduction in arsenic load in rice. Sci. Total Environ. 609, 311–318. https://doi.org/10.1016/j.scitotenv.2017.07.111.

Issanov, A., Adewusi, B., Saint-Jacques, N., Dummer, T.J.B., 2024. Arsenic in drinking water and lung cancer: a systematic review of 35 years of evidence. Toxicol. Appl. Pharmacol. 483, 116808. https://doi.org/10.1016/j.taap.2024.116808.

Iwai-Shimada, M., Kameo, S., Nakai, K., Yaginuma-Sakurai, K., Tatsuta, N., Kurokawa, N., Nakayama, S.F., Satoh, H., 2019. Exposure profile of mercury, lead, cadmium, arsenic, antimony, copper, selenium and zinc in maternal blood, cord blood and placenta: the Tohoku study of child development in Japan. Environ. Health Prev. Med. 24 (1), 35. https://doi.org/10.1186/s12199-019-0783-y.

Jha, M., Kumar, S., Singh, T.B.N., Srivastava, S.K., Azad, G.K., Yasmin, S., 2023. Potential health risk assessment through the consumption of arsenic-contaminated groundwater in parts of the middle Gangetic plain. Bull. Natl. Res. Cent. 47 (1), 77. https://doi.org/10.1186/s42269-023-01054-5.

Jiang, S., Su, J., Yao, S., Zhang, Y., Cao, F., Wang, F., Wang, H., Li, J., Xi, S., 2014. Fluoride and arsenic exposure impairs learning and memory and decreases mGluR5 expression in the hippocampus and cortex in rats. PLoS One 9 (4), e96041. https://doi.org/10.1371/journal.pone.0096041.

Jin, W., Xue, Y., Xue, Y., Han, X., Song, Q., Zhang, J., Li, Z., Cheng, J., Guan, S., Sun, S., Chu, L., 2020. Tannic acid ameliorates arsenic trioxide-induced nephrotoxicity, contribution of NF-κB and Nrf2 pathways. Biomed. Pharmacother. 126, 110047. https://doi.org/10.1016/J.BIOPHA.2020.110047.

Jomova, K., Raptova, R., Alomar, S.Y., Alwasel, S.H., Nepovimova, E., Kuca, K., Valko, M., 2023. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. Arch. Toxicol. 97 (10), 2499–2574. https://doi.org/10.1007/s00204-023-03562-9.

Jung, M.Y., Kang, J.H., Jung, H.J., Ma, S.Y., 2018. Inorganic arsenic contents in ready-to-eat rice products and various Korean rice determined by a highly sensitive gas chromatography-tandem mass spectrometry. Food Chem. 240, 1179–1183. https://doi.org/10.1016/j.foodchem.2017.08.053.

Karagas, M.R., Gossai, A., Pierce, B., Ahsan, H., 2015. Drinking water arsenic contamination, skin lesions, and malignancies: a systematic review of the global evidence. Curr. Environ. Health Rep. 2 (1), 52–68. https://doi.org/10.1007/s40572-014-0040-x.

kaur, R., Garkal, A., Sarode, L., Bangar, P., Mehta, T., Singh, D.P., Rawal, R., 2024. Understanding arsenic toxicity: implications for environmental exposure and human health. J. Hazard. Mater. Lett. 5, 100090. https://doi.org/10.1016/J.HAZL.2023.100090.

Kelly, B.C., Myo, A.N., Pi, N., Bayen, S., Leakhena, P.C., Chou, M., Tan, B.H., 2018. Human exposure to trace elements in central Cambodia: influence of seasonal hydrology and food-chain bioaccumulation behaviour. Ecotoxicol. Environ. Saf. 162, 112–120. https://doi.org/10.1016/j.ecoenv.2018.06.071.

Kern, J.K., Grannemann, B.D., Trivedi, M.H., Adams, J.B., 2007. Sulfhydryl-reactive metals in autism. J. Toxicol. Environ. Health Part A 70 (8), 715–721. https://doi.org/10.1080/15287390601188060.

Khan, M.I., Ahmad, M.F., Ahmad, I., Ashfaq, F., Wahab, S., Alsayegh, A.A., Kumar, S., Hakeem, K.R., 2022. Arsenic exposure through dietary intake and associated health hazards in the Middle East. Nutrients 14 (10), 2136. https://doi.org/10.3390/nu14102136.

Khan, M.A., Islam, M.R., Panaullah, G.M., Duxbury, J.M., Jahiruddin, M., Loeppert, R.H., 2010. Accumulation of arsenic in soil and rice under wetland condition in Bangladesh. Plant Soil 333, 263–274. https://doi.org/10.1007/s11104-010-0340-3.

Kladsomboon, S., Jaiyen, C., Choprathumma, C., Tusai, T., Apilux, A., 2020. Heavy metals contamination in soil, surface water, crops, and resident blood in Uthai District, Phra Nakhon Si Ayutthaya, Thailand. Environ. Geochem. Health 42 (2), 545–561. https://doi.org/10.1007/s10653-019-00388-2.

Koki, I.B., Low, K.H., Juahir, H., Abdul Zali, M., Azid, A., Zain, S.M., 2018. Consumption of water from ex-mining ponds in Klang Valley and Melaka, Malaysia: a health risk study. Chemosphere 195, 641–652. https://doi.org/10.1016/J.CHEMOSPHERE.2017.12.112.

Kumar, M., Rahman, M.M., Ramanathan, A.L., Naidu, R., 2016. Arsenic and other elements in drinking water and dietary components from the middle Gangetic plain of Bihar, India: health risk index. Sci. Total Environ. 539, 125–134. https://doi.org/10.1016/J.SCITOTENV.2015.08.039.

Kumar, S., Trivedi, P.K., 2018. Glutathione S-transferases: role in combating abiotic stresses including arsenic detoxification in plants. Front. Plant Sci. 9, 751. https://doi.org/10.3389/fpls.2018.00751.

Kusin, F.M., Rahman, M.S.A., Madzin, Z., Jusop, S., Mohamat-Yusuff, F., Ariffin, M., Mohd, Syakirin Md, Z., 2017. The occurrence and potential ecological risk assessment of bauxite mine-impacted water and sediments in Kuantan, Pahang, Malaysia. Environ. Sci. Pollut. Res. 24 (2), 1306–1321. https://doi.org/10.1007/s11356-016-7814-7.

Lachenmeier, D.W., Przybylski, M.C., Rehm, J., 2012. Comparative risk assessment of carcinogens in alcoholic beverages using the margin of exposure approach. Int. J. Cancer 131 (6), E995–E1003. https://doi.org/10.1002/ijc.27553.

Laela, N., Pasma, S.A., Santoso, M., 2023. Arsenic levels in soil and rice and health risk assessment via rice consumption in industrial areas of East Java, Indonesia. Environ. Nat. Resour. J. 21 (4), 370–380. https://doi.org/10.32526/ennrj/21/20230049.

Le, T.T., Kim, K.W., Nguyen, D.Q., Ngo, H.T.T., 2023. Trace element contamination in rice and its potential health risks to consumers in North–Central Vietnam. Environ. Geochem. Health 45 (6), 3361–3375. https://doi.org/10.1007/s10653-022-01415-5.

Le, T.V., Nguyen, B.T., 2024. Heavy metal pollution in surface water bodies in provincial Khanh Hoa, Vietnam: pollution and human health risk assessment, source quantification, and implications for sustainable management and development.

Environ. Pollut. (Barking, Essex: 1987) 343, 123216. https://doi.org/10.1016/j.envpol.2023.123216.
Lee, S.G., Kim, D.H., Lee, Y.S., Cho, S.Y., Chung, M.S., Cho, M.J., Kang, Y.W., Kim, H.J., Kim, D.S., Lee, K.W., 2018. Monitoring of arsenic contents in domestic rice and human risk assessment for daily intake of inorganic arsenic in Korea. J. Food Compos. Anal. 69, 25–32. https://doi.org/10.1016/j.jfca.2018.02.004.
Lee, S.W., Lee, B.T., Kim, J.Y., Kim, K.W., Lee, J.S., 2006. Human risk assessment for heavy metals and as contamination in the abandoned metal mine areas, Korea. Environ. Monit. Assess. 119 (1-3), 233–244. https://doi.org/10.1007/s10661-005-9024-5.
Li, Z., Li, X., Qian, Y., Guo, C., Wang, Z., Wei, Y., 2020. The sustaining effects of e-waste-related metal exposure on hypothalamus-pituitary-adrenal axis reactivity and oxidative stress. Sci. Total Environ. 739, 139964. https://doi.org/10.1016/J.SCITOTENV.2020.139964.
Li, W., Li, Z., Yan, Y., Zhang, J., Zhou, Q., Wang, R., He, M., 2023. Association of urinary arsenic metabolism with type 2 diabetes and glucose homeostasis: Cross-sectional and longitudinal associations. Environ. Res. 239 (Pt 2), 117410. https://doi.org/10.1016/j.envres.2023.117410.
Liang, C., Wu, X., Huang, K., Yan, S., Li, Z., Xia, X., Pan, W., Sheng, J., Tao, R., Tao, Y., Xiang, H., Hao, J., Wang, Q., Tong, S., Tao, F., 2020. Domain- and sex-specific effects of prenatal exposure to low levels of arsenic on children's development at 6 months of age: findings from the Ma'anshan birth cohort study in China. Environ. Int. 135, 105112. https://doi.org/10.1016/j.envint.2019.105112.
Liu, J., Gao, Y., Liu, H., Sun, J., Liu, Y., Wu, J., Li, D., Sun, D., 2017. Assessment of relationship on excess arsenic intake from drinking water and cognitive impairment in adults and elders in arsenicosis areas. Int. J. Hyg. Environ. Health 220 (2 Pt B), 424–430. https://doi.org/10.1016/j.ijheh.2016.12.004.
Liu, Y., Huang, Y., Li, L., Xiong, Y., Wang, X., Tong, L., Wang, F., Fan, B., Gong, J., 2023. Arsenic source analysis of rice from different growing environments and health risk assessment in Hunan Province, China. J. Food Compos. Anal. 123, 105637. https://doi.org/10.1016/j.jfca.2023.105637.
Long, M., Ghisari, M., Kjeldsen, L., Wielsøe, M., Nørgaard-Pedersen, B., Mortensen, E.L., Abdallah, M.W., Bonefeld-Jørgensen, E.C., 2019. Autism spectrum disorders, endocrine disrupting compounds, and heavy metals in amniotic fluid: a case-control study. Mol. Autism. 10 (1). https://doi.org/10.1186/s13229-018-0253-1.
Lu, Y., Dong, F., Deacon, C., Chen, H.J., Raab, A., Meharg, A.A., 2010. Arsenic accumulation and phosphorus status in two rice (Oryza sativa L.) cultivars surveyed from fields in South China. Environ. Pollut. 158 (5), 1536–1541. https://doi.org/10.1016/j.envpol.2009.12.022.
Luvonga, C., Rimmer, C.A., Yu, L.L., Lee, S.B., 2020. Organoarsenicals in seafood: occurrence, dietary exposure, toxicity, and risk assessment considerations—A review. J. Agric. Food Chem. 68 (4), 943–960. https://doi.org/10.1021/acs.jafc.9b07532.
Lv, Y., Wang, H., Zheng, D., Shi, M., Bi, D., Hu, Q., Zhi, H., Lou, D., Li, J., Wei, S., Hu, Y., 2024. Environmental arsenic pollution induced liver oxidative stress injury by regulating miR-155 through inhibition of AUF1. Sci. Total Environ. 922, 171237. https://doi.org/10.1016/J.SCITOTENV.2024.171237.
Lynch, C.J., Kimball, S.R., Xu, Y., Salzberg, A.C., Kawasawa, Y.I., 2015. Global deletion of BCATm increases expression of skeletal muscle genes associated with protein turnover. Physiol. Genom.. 47 (11), 569–580. https://doi.org/10.1152/physiolgenomics.00055.2015.
Majumder, S., Joardar, M., Das, A., De, A., Mridha, D., Ghosh, S., Lama, U., Dey, A., Chowdhury, N.R., Majumdar, A., Roychowdhury, T., 2023. Arsenic toxicity, biomarkers of exposure and risk assessment among different aged young population from endemic areas of West Bengal, India. Groundw. Sustain. Dev. 23, 101022. https://doi.org/10.1016/j.gsd.2023.101022.
Mar Wai, K., Umezaki, M., Mar, O., Umemura, M., Watanabe, C, 2019. Arsenic exposure through drinking water and oxidative stress status: a cross-sectional study in the Ayeyarwady region, Myanmar. J. Trace Elem. Med. Biol. 54, 103–109. https://doi.org/10.1016/j.jtemb.2019.04.009.
Mawia, A.M., Hui, S., Zhou, L., Li, H., Tabassum, J., Lai, C., Wang, J., Shao, G., Wei, X., Tang, S., Luo, J., Hu, S., Hu, P., 2021. Inorganic arsenic toxicity and alleviation strategies in rice. J. Hazard. Mater. 408, 124751. https://doi.org/10.1016/j.jhazmat.2020.124751.
Memon, M.A., Ting, H., Cheah, J.H., Thurasamy, R., Chuah, F., Cham, T.H., 2020. Sample size for survey research: review and recommendations. J. Appl. Struct. Equ. Model. 4 (2), i–xx. https://doi.org/10.47263/jasem.4(2)01.
Mendoza-Cózatl, D.G., Jobe, T.O., Hauser, F., Schroeder, J.I., 2011. Long-distance transport, vacuolar sequestration, tolerance, and transcriptional responses induced by cadmium and arsenic. Curr. Opin. Plant Biol. 14 (5), 554–562. https://doi.org/10.1016/j.pbi.2011.07.004.
Menon, M., Nicholls, A., Smalley, A., Rhodes, E., 2024. A comparison of the effects of two cooking methods on arsenic species and nutrient elements in rice. Sci. Total Environ. 914, 169653. https://doi.org/10.1016/j.scitotenv.2023.169653.
Mishra, D., Sen, K., Mondal, A., Kundu, S., Mondal, N.K., 2022. Geochemical appraisal of groundwater arsenic contamination and human health risk assessment in the Gangetic Basin in Murshidabad District of West Bengal, India. Environ. Earth. Sci. 81 (5), 157. https://doi.org/10.1007/s12665-022-10273-4.
Mlangeni, A.T., 2023. Methylation of arsenic in rice: mechanisms, factors, and mitigation strategies. Toxicol. Rep. 11, 295–306. https://doi.org/10.1016/j.toxrep.2023.09.018.
Mochizuki, H., 2019. Arsenic neurotoxicity in humans. Int. J. Mol. Sci. 20 (14), 3418. https://doi.org/10.3390/ijms20143418.
MOE, 2020. Enforcement Decree of the Framework Act on Environmental Policy Korean Ministy of Environment. Sejong, Korea.
Mohammad Sham, N., Anual, Z.F., Shaharudin, R, 2022. GIS based interpolation method to urinary metal concentrations in Malaysia. Food Chem. Toxicol. 163, 112949. https://doi.org/10.1016/j.fct.2022.112949.
Mridha, D., Gorain, P.C., Joardar, M., Das, A., Majumder, S., De, A., Chowdhury, N.R., Lama, U., Pal, R., Roychowdhury, T., 2022. Rice grain arsenic and nutritional content during post harvesting to cooking: a review on arsenic bioavailability and bioaccessibility in humans. Food Res. Int. 154, 111042. https://doi.org/10.1016/j.foodres.2022.111042.
Mukherjee, B., Bindhani, B., Saha, H., Sinha, D., Ray, M.R., 2014. Platelet hyperactivity, neurobehavioral symptoms and depression among Indian women chronically exposed to low level of arsenic. Neurotoxicology 45, 159–167. https://doi.org/10.1016/j.neuro.2014.10.011.
Mullin, A.M., Amarasiriwardena, C., Cantoral-Preciado, A., Claus Henn, B., Leon Hsu, H. H., Sanders, A.P., Svensson, K., Tamayo-Ortiz, M., Téllez-Rojo, M.M., Wright, R.O., Burris, H.H., 2019. Maternal blood arsenic levels and associations with birth weight-for-gestational age. Environ. Res. 177, 108603. https://doi.org/10.1016/j.envres.2019.108603.
Murphy, T., Phan, K., Yumvihoze, E., Irvine, K., Wilson, K., Lean, D., Ty, B., Poulain, A., Laird, B., Chan, L.H.M, 2018. Groundwater irrigation and arsenic speciation in rice in Cambodia. J. Health Pollut. 8 (19), 180911. https://doi.org/10.5696/2156-9614-8.19.180911.
Muse, M.E., Li, Z., Baker, E.R., Cottingham, K.L., Korrick, S.A., Karagas, M.R., Gilbert-Diamond, D., 2020. Relation between in utero arsenic exposure and growth during the first year of life in a New Hampshire pregnancy cohort. Environ. Res. 180, 108604. https://doi.org/10.1016/j.envres.2019.108604.
Naujokas, M.F., Anderson, B., Ahsan, H., Vasken Aposhian, H., Graziano, J.H., Thompson, C., Suk, W.A., 2013. The broad scope of health effects from chronic arsenic exposure: update on a worldwide public health problem. Environ. Health Perspect. 121 (3), 295–302. https://doi.org/10.1289/ehp.1205875.
Navaretnam, R., Hassan, H.N., Isa, N.M., Aris, A.Z., Looi, L.J., 2023. Metal(loid) analysis of commercial rice from Malaysia using ICP-MS: potential health risk evaluation. Environ. Sci. Pollut. Res. 30 (37), 87695–87720. https://doi.org/10.1007/s11356-023-28459-z.
Navasumrit, P., Chaisatra, K., Promvijit, J., Parnlob, V., Waraprasit, S., Chompoobut, C., Binh, T.T., Hai, D.N., Bao, N.D., Hai, N.K., Kim, K.W., Samson, L.D., Graziano, J.H., Mahidol, C., Ruchirawat, M., 2019. Exposure to arsenic in utero is associated with various types of DNA damage and micronuclei in newborns: a birth cohort study. Environ. Health 18 (1), 51. https://doi.org/10.1186/s12940-019-0481-7.
Nguyen, K.T., Nguyen, H.M., Truong, C.K., Ahmed, M.B., Huang, Y., Zhou, J.L., 2019. Chemical and microbiological risk assessment of urban river water quality in Vietnam. Environ. Geochem. Health 41 (6), 2559–2575. https://doi.org/10.1007/s10653-019-00302-w.
Nguyen, T.P., Ruppert, H., Sauer, B., Pasold, T., 2020. Harmful and nutrient elements in paddy soils and their transfer into rice grains (Oryza sativa) along two river systems in northern and central Vietnam. Environ. Geochem. Health 42 (1), 191–207. https://doi.org/10.1007/s10653-019-00333-3.
Nguyen, T.Q., Tran-Lam, T.T., Nguyen, H.Q., Dao, Y.H., Le, G.T., 2021. Assessment of organic and inorganic arsenic species in Sengcu rice from terraced paddies and commercial rice from lowland paddies in Vietnam. J. Cereal. Sci. 102, 103346. https://doi.org/10.1016/J.JCS.2021.103346.
Nguyen, V.A., Bang, S., Viet, P.H., Kim, K.W., 2009. Contamination of groundwater and risk assessment for arsenic exposure in Ha Nam province, Vietnam. Environ. Int. 35 (3), 466–472. https://doi.org/10.1016/j.envint.2008.07.014.
Niazi, N.K., Hussain, M.M., Bibi, I., Natasha, Shahid, M., Ali, F., Iqbal, J., Shaheen, S.M., Abdelrahman, H., Akhtar, W., Wang, H., Rinklebe, J, 2022. The significance of eighteen rice genotypes on arsenic accumulation, physiological response and potential health risk. Sci. Total Environ. 832 (1), 155004. https://doi.org/10.1016/j.scitotenv.2022.155004.
Nilkarnjanakul, W., Watchalayann, P., Chotpantarat, S., 2023a. Urinary arsenic and health risk of the residents association in contaminated-groundwater area of the urbanized coastal aquifer, Thailand. Chemosphere 313, 137313. https://doi.org/10.1016/j.chemosphere.2022.137313.
Nookabkaew, S., Rangkadilok, N., Akib, C.A., Tuntiwigit, N., Saehun, J., Satayavivad, J., 2013. Evaluation of trace elements in selected foods and dietary intake by young children in Thailand. Food Addit. Contam. Part B, Surveill. 6 (1), 55–67. https://doi.org/10.1080/19393210.2012.724089.
Obrenovich, M.E., Shamberger, R.J., Lonsdale, D., 2011. Altered heavy metals and transketolase found in autistic spectrum disorder. Biol. Trace Elem. Res. 144 (1–3), 475–486. https://doi.org/10.1007/s12011-011-9146-2.
O'Bryant, S.E., Edwards, M., Menon, C.V., Gong, G., Barber, R, 2011. Long-term low-level arsenic exposure is associated with poorer neuropsychological functioning: a project FRONTIER study. Int. J. Environ. Res. Public Health 8 (3), 861–874. https://doi.org/10.3390/ijerph8030861.
Omar, N.A., Praveena, S.M., Aris, A.Z., Hashim, Z., 2015. Health risk assessment using in vitro digestion model in assessing bioavailability of heavy metal in rice: a preliminary study. Food Chem. 188, 46–50. https://doi.org/10.1016/j.foodchem.2015.04.087.
Park, M.K., Choi, S.D., 2021. Monitoring and risk assessment of arsenic species and metals in the Taehwa River in Ulsan, the largest industrial city in South Korea. Mar. Pollut. Bull. 172, 112862. https://doi.org/10.1016/j.marpolbul.2021.112862.
Patel, K.S., Pandey, P.K., Martín-Ramos, P., Corns, W.T., Varol, S., Bhattacharya, P., Zhu, Y., 2023. A review on arsenic in the environment: contamination, mobility, sources, and exposure. RSC Adv. 13 (13), 8803–8821. https://doi.org/10.1039/d3ra00789h.
Pedron, T., Paulino Oliveira, G.S., Paniz, F.P., de Moura Souza, F., Masuda, H.P., dos Santos, M.C., Rocha, B.A., Pereira, R.M., Batista, B.L., 2021. Determination of

chemical elements in rice from Singapore markets: distribution, estimated intake and differentiation of rice varieties. J. Food Compos. Anal. 101, 103969. https://doi.org/10.1016/j.jfca.2021.103969.
Pedron, T., Segura, F.R., Paniz, F.P., de Moura Souza, F., dos Santos, M.C., de Magalhães Júnior, A.M., Batista, B.L., 2019. Mitigation of arsenic in rice grains by polishing and washing: evidencing the benefit and the cost. J. Cereal. Sci. 87, 52–58. https://doi.org/10.1016/j.jcs.2019.03.003.
Pham, L.H., Nguyen, H.T., Van Tran, C., Nguyen, H.M., Nguyen, T.H., Tu, M.B., 2017. Arsenic and other trace elements in groundwater and human urine in Ha Nam province, the Northern Vietnam: contamination characteristics and risk assessment. Environ. Geochem. Health 39 (3), 517–529. https://doi.org/10.1007/s10653-016-9831-3.
Phan, K., Sthiannopkao, S., Heng, S., Phan, S., Huoy, L., Wong, M.H., Kim, K.W., 2013. Arsenic contamination in the food chain and its risk assessment of populations residing in the Mekong River basin of Cambodia. J. Hazard. Mater. 262, 1064–1071. https://doi.org/10.1016/j.jhazmat.2012.07.005.
Phan, K., Sthiannopkao, S., Kim, K.W., 2011. Surveillance on chronic arsenic exposure in the Mekong River basin of Cambodia using different biomarkers. Int. J. Hyg. Environ. Health 215 (1), 51–58. https://doi.org/10.1016/j.ijheh.2011.07.002.
Pincetti-Zúniga, G.P., Richards, L.A., Tun, Y.M., Aung, H.P., Swar, A.K., Reh, U.P., Khaing, T., Hlaing, M.M., Myint, T.A., Nwe, M.L., Polya, D.A., 2020. Major and trace (including arsenic) groundwater chemistry in central and southern Myanmar. Appl. Geochem. 115, 104535. https://doi.org/10.1016/j.apgeochem.2020.104535.
Podgorski, J., Berg, M., 2020. Global threat of arsenic in groundwater. Science 368 (6493), 845–850. https://doi.org/10.1126/science.aba1510.
Poetsch, A.R., 2020. The genomics of oxidative DNA damage, repair, and resulting mutagenesis. Comput. Struct. Biotechnol. J. 18, 207–219. https://doi.org/10.1016/J.CSBJ.2019.12.013.
Prakash, C., Soni, M., Kumar, V., 2016. Mitochondrial oxidative stress and dysfunction in arsenic neurotoxicity: a review. J. Appl. Toxicol. 36 (2), 179–188. https://doi.org/10.1002/jat.3256.
Praveena, S.M., Omar, N.A., 2017. Heavy metal exposure from cooked rice grain ingestion and its potential health risks to humans from total and bioavailable forms analysis. Food Chem. 235, 203–211. https://doi.org/10.1016/j.foodchem.2017.05.049.
Pugsley, K., Scherer, S.W., Bellgrove, M.A., Hawi, Z., 2022. Environmental exposures associated with elevated risk for autism spectrum disorder may augment the burden of deleterious de novo mutations among probands. Mol. Psychiatry 27 (1), 710–730. https://doi.org/10.1038/s41380-021-01142-w.
Qaiser, F.U.R., Zhang, F., Pant, R.R., Zeng, C., Khan, N.G., Wang, G., 2023. Characterization and health risk assessment of arsenic in natural waters of the Indus River Basin, Pakistan. Sci. Total Environ. 857 (Part 2), 159408. https://doi.org/10.1016/j.scitotenv.2022.159408.
Rachamalla, M., Salahinejad, A., Khan, M., Datusalia, A.K., Niyogi, S., 2023. Chronic dietary exposure to arsenic at environmentally relevant concentrations impairs cognitive performance in adult zebrafish (Danio rerio) via oxidative stress and dopaminergic dysfunction. Sci. Total Environ. 886, 163771. https://doi.org/10.1016/j.scitotenv.2023.163771.
Rahaman, M.S., Akter, M., Rahman, M.M., Sikder, M.T., Hosokawa, T., Saito, T., Kurasaki, M., 2020. Investigating the protective actions of D-pinitol against arsenic-induced toxicity in PC12 cells and the underlying mechanism. Environ. Toxicol. Pharmacol. 74, 103302. https://doi.org/10.1016/j.etap.2019.103302.
Rahaman, M.S., Rahman, M.M., Mise, N., Sikder, M.T., Ichihara, G., Uddin, M.K., Kurasaki, M., Ichihara, S., 2021. Environmental arsenic exposure and its contribution to human diseases, toxicity mechanism and management. Environ. Pollut. 289, 117940. https://doi.org/10.1016/j.envpol.2021.117940.
Rahman, M.S., Reza, A.H.M.S., Siddique, M.A.B., Akbor, M.A., Hasan, M., 2023. Accumulation of arsenic and other metals in soil and human consumable foods of Meherpur district, southwestern Bangladesh, and associated health risk assessment. Environ. Sci. Eur. 35 (1), 47. https://doi.org/10.1186/s12302-023-00751-2.
Ramly, N., Ahmad Mahir, H.M., Wan Azmi, W.N.F., Hashim, Z., Hashim, J.H., Shaharudin, R., 2023. Arsenic in drinking water, hair, and prevalence of arsenicosis in Perak, Malaysia. Front. Public Health 11, 998511. https://doi.org/10.3389/fpubh.2023.998511.
Ramsay, L., Petersen, M.M., Hansen, B., Schullehner, J., Van Der Wens, P., Voutchkova, D., Kristiansen, S.M., 2021. Drinking water criteria for arsenic in high-income, low-dose countries: the effect of legislation on public health. Environ. Sci. Technol. 55 (6), 3483–3493. https://doi.org/10.1021/acs.est.0c03974.
Renzetti, S., Cagna, G., Calza, S., Conversano, M., Fedrighi, C., Forte, G., Giorgino, A., Guazzetti, S., Majorani, C., Oppini, M., Peli, M., Petrucci, F., Pino, A., Placidi, D., Senofonte, O., Zoni, S., Alimonti, A., Lucchini, R.G., 2021. The effects of the exposure to neurotoxic elements on Italian schoolchildren behavior. Sci. Rep. 11 (1), 9898. https://doi.org/10.1038/s41598-021-88969-z.
Rodrigues, E.G., Bellinger, D.C., Valeri, L., Hasan, M.O.S.I., Quamruzzaman, Q., Golam, M., Kile, M.L., Christiani, D.C., Wright, R.O., Mazumdar, M., 2016. Neurodevelopmental outcomes among 2- to 3-year-old children in Bangladesh with elevated blood lead and exposure to arsenic and manganese in drinking water. Environ. Health 15 (1), 44. https://doi.org/10.1186/s12940-016-0127-y.
Rodríguez-Barranco, M., Gil, F., Hernández, A.F., Alguacil, J., Lorca, A., Mendoza, R., Gómez, I., Molina-Villalba, I., González-Alzaga, B., Aguilar-Garduño, C., Rohlman, D.S., Lacasaña, M., 2016. Postnatal arsenic exposure and attention impairment in school children. Cortex 74, 370–382. https://doi.org/10.1016/j.cortex.2014.12.018.
Rodríguez-Barranco, M., Lacasaña, M., Aguilar-Garduño, C., Alguacil, J., Gil, F., González-Alzaga, B., Rojas-García, A., 2013. Association of arsenic, cadmium and manganese exposure with neurodevelopment and behavioural disorders in children: a systematic review and meta-analysis. Sci. Total Environ. 454–455, 562–577. https://doi.org/10.1016/j.scitotenv.2013.03.047.
Rokonuzzaman, M.D., Li, W.C., Wu, C., Ye, Z.H., 2022a. Human health impact due to arsenic contaminated rice and vegetables consumption in naturally arsenic endemic regions. Environ. Pollut. 308, 119712. https://doi.org/10.1016/j.envpol.2022.119712.
Rokonuzzaman, M., Li, W.C., Man, Y.B., Tsang, Y.F., Ye, Z., 2022b. Arsenic accumulation in rice: sources, human health impact and probable mitigation approaches. Rice Sci. 29 (4), 309–327. https://doi.org/10.1016/j.rsci.2022.02.002.
Rosado, J.L., Ronquillo, D., Kordas, K., Rojas, O., Alatorre, J., Lopez, P., Garcia-Vargas, G., del Carmen Caamaño, M., Cebrián, M.E., Stoltzfus, R.J., 2007. Arsenic exposure and cognitive performance in Mexican Schoolchildren. Environ. Health Perspect. 115 (9), 1371–1375. https://doi.org/10.1289/ehp.9961.
Roy, A., Kordas, K., Lopez, P., Rosado, J.L., Cebrian, M.E., Vargas, G.G., Ronquillo, D., Stoltzfus, R.J., 2011. Association between arsenic exposure and behavior among first-graders from Torreón, Mexico. Environ. Res. 111 (5), 670–676. https://doi.org/10.1016/j.envres.2011.03.003.
Roy, N.K., Murphy, A., Costa, M., 2020. Arsenic methyltransferase and methylation of inorganic arsenic. Biomolecules 10 (9), 1351. https://doi.org/10.3390/biom10091351.
Rujiralai, T., Juansai, N., Cheewasedtham, W., 2018. Arsenic determination in soils and hair from schools in past mining activity areas in Ron Phibun district, Nakhon Si Thammarat province, Thailand and relationship between soil and hair arsenic. Chem. Pap. 72 (2). https://doi.org/10.1007/s11696-017-0287-4.
Sakai, N., Alsaad, Z., Thuong, N.T., Shiota, K., Yoneda, M., Ali Mohd, M., 2017. Source profiling of arsenic and heavy metals in the Selangor River basin and their maternal and cord blood levels in Selangor State, Malaysia. Chemosphere 184, 857–865. https://doi.org/10.1016/j.chemosphere.2017.06.070.
Saong, M., Marbella, I.M., 2024. Analysis of arsenic in rice and domestic water supply in Baguio City, Philippines. Int. J. Sci., Technol., Eng. Math. 4 (2), 1–22. https://doi.org/10.53378/353061.
Sarwar, T., Khan, S., Muhammad, S., Amin, S., 2021. Arsenic speciation, mechanisms, and factors affecting rice uptake and potential human health risk: A systematic review. Environ. Technol. Innovation 22, 101392. https://doi.org/10.1016/j.eti.2021.101392.
Sasaki, A., Oshima, Y., Fujimura, A., 2007. An approach to elucidate potential mechanism of renal toxicity of arsenic trioxide. Exp. Hematol. 35 (2), 252–262. https://doi.org/10.1016/J.EXPHEM.2006.10.004.
Saxena, R., Gamble, M., Wasserman, G.A., Liu, X., Parvez, F., Navas-Acien, A., Islam, T., Factor-Litvak, P., Uddin, M.N., Kioumourtzoglou, M.A., Gibson, E.A., Shahriar, H., Slavkovich, V., Ilievski, V., LoIacono, N., Balac, O., Graziano, J.H., 2022. Mixed metals exposure and cognitive function in Bangladeshi adolescents. Ecotoxicol. Environ. Saf. 232, 113229. https://doi.org/10.1016/j.ecoenv.2022.113229.
Seyfferth, A.L., McCurdy, S., Schaefer, M.V., Fendorf, S., 2014. Arsenic concentrations in paddy soil and rice and health implications for major rice-growing regions of Cambodia. Environ. Sci. Technol. 48 (9), 4699–4706. https://doi.org/10.1021/es405016t.
Shaheen, N., Hasan, T., Sultana, M., Akhter, K.T., Khan, I.N., Irfan, N.M., Ahmed, M.K., 2024. Carcinogenic and non-carcinogenic health hazards of potentially toxic elements in commonly consumed rice cultivars in Dhaka city, Bangladesh. PLoS One 19 (5), e0303305. https://doi.org/10.1371/journal.pone.0303305.
Shaibur, M.R., Howlader, M., Ahmmed, I., Sarwar, S., Hussam, A., 2024. Water quality index and health risk assessment for heavy metals in groundwater of Kashiani and Kotalipara upazila, Gopalganj, Bangladesh. Appl. Water Sci. 14 (5), 106. https://doi.org/10.1007/s13201-024-02169-4.
Shao, J., Lai, C., Zheng, Q., Luo, Y., Li, C., Zhang, B., Sun, Y., Liu, S., Shi, Y., Li, J., Zhao, Z., Guo, L., 2024. Effects of dietary arsenic exposure on liver metabolism in mice. Ecotoxicol. Environ. Saf. 274, 116147. https://doi.org/10.1016/J.ECOENV.2024.116147.
Shi, S., Wang, T., Chen, Z., Tang, Z., Wu, Z., Salt, D.E., Chao, D.Y., Zhao, F.J., 2016. OsHAC1;1 and OsHAC1;2 function as arsenate reductases and regulate arsenic accumulation. Plant Physiol. 172 (3), 1708–1719. https://doi.org/10.1104/pp.16.01332.
Shi, T., Xu, B., He, J., Liu, X., Zuo, Z., 2023. Arsenic release pathway and the interaction principle among major species in vacuum sulfide reduction roasting of copper smelting flue dust. Environ. Pollut. 330, 121809. https://doi.org/10.1016/j.envpol.2023.121809.
Shrestha, M., Basukala, S., Thapa, N., Shrestha, O., Basnet, M., Shrestha, K., Regmi, S., Chhetri, S.T., Kunwor, B., 2024. Prevalence of autism spectrum disorder among children in Southeast Asia from 2002 to 2022: an updated systematic review and meta-analysis. Health Sci. Rep. 7 (4), e2005. https://doi.org/10.1002/hsr2.2005.
Sibuar, A.A., Zulkafflee, N.S., Selamat, J., Ismail, M.R., Lee, S.Y., Razis, A.F.A., 2022. Quantitative analysis and human health risk assessment of heavy metals in paddy plants collected from Perak, Malaysia. Int. J. Environ. Res. Public Health 19 (2), 731. https://doi.org/10.3390/ijerph19020731.
Signes-Pastor, A., Burló, F., Mitra, K., Carbonell-Barrachina, A.A., 2007. Arsenic biogeochemistry as affected by phosphorus fertilizer addition, redox potential and pH in a west Bengal (India) soil. Geoderma 137 (3–4), 504–510. https://doi.org/10.1016/j.geoderma.2006.10.012.
Signes-Pastor, A.J., Carey, M., Meharg, A.A., 2017. Inorganic arsenic removal in rice bran by percolating cooking water. Food Chem. 234, 76–80. https://doi.org/10.1016/j.foodchem.2017.04.140.
Signes-Pastor, A.J., Romano, M.E., Jackson, B., Braun, J.M., Yolton, K., Chen, A., Lanphear, B., Karagas, M.R., 2022. Associations of maternal urinary arsenic concentrations during pregnancy with childhood cognitive abilities: the HOME

study. Int. J. Hyg. Environ. Health 245, 114009. https://doi.org/10.1016/j.ijheh.2022.114009.
Singh, V., Gera, R., Kushwaha, R., Sharma, A.K., Patnaik, S., Ghosh, D., 2016. Hijacking microglial glutathione by inorganic arsenic impels bystander death of immature neurons through extracellular cystine/glutamate imbalance. Sci. Rep. 6 (1), 30601. https://doi.org/10.1038/srep30601.
Skalny, A.V., Simashkova, N.V., Klyushnik, T.P., Grabeklis, A.R., Bjørklund, G., Skalnaya, M.G., Nikonorov, A.A., Tinkov, A.A., 2017a. Hair toxic and essential trace elements in children with autism spectrum disorder. Metab. Brain Dis. 32 (1), 195–202. https://doi.org/10.1007/s11011-016-9899-6.
Skalny, A.V., Simashkova, N.V., Klyushnik, T.P., Grabeklis, A.R., Radysh, I.V., Skalnaya, M.G., Tinkov, A.A., 2017b. Analysis of hair trace elements in children with autism spectrum disorders and communication disorders. Biol. Trace Elem. Res. 177 (2), 215–223. https://doi.org/10.1007/s12011-016-0878-x.
Smedley, P.L., Kinniburgh, D.G., 2002. A review of the source, behaviour and distribution of arsenic in natural waters. Appl. Geochem. 17 (5), 517–568. https://doi.org/10.1016/S0883-2927(02)00018-5.
Soe, A.M.M., Mu, A.A., Toyoda, K., 2023. Arsenic and heavy metal contents in white rice samples from rainfed paddy fields in Yangon division, Myanmar—Natural background levels? PLoS One 18 (3), e0283420. https://doi.org/10.1371/journal.pone.0283420.
Soler-Blasco, R., Murcia, M., Lozano, M., Sarzo, B., Esplugues, A., Riutort-Mayol, G., Vioque, J., Lertxundi, N., Santa Marina, L., Lertxundi, A., Irizar, A., Braeuer, S., Ballester, F., Llop, S., 2022. Prenatal arsenic exposure, arsenic methylation efficiency, and neuropsychological development among preschool children in a Spanish birth cohort. Environ. Res. 207, 112208. https://doi.org/10.1016/j.envres.2021.112208.
Soni, D.K., Mishra, P.K., Pandey, P., 2024. Potential health risks assessment associated with arsenic-contaminated groundwater in the eastern district of Uttar Pradesh, India: a case study. Environ. Sustain. 7 (1), 61–75. https://doi.org/10.1007/s42398-024-00303-1.
Sthiannopkao, S., Kim, K.W., Cho, K.H., Wantala, K., Sotham, S., Sokuntheara, C., Kim, J. H., 2010. Arsenic levels in human hair, Kandal Province, Cambodia: the influences of groundwater arsenic, consumption period, age and gender. Appl. Geochem. 25 (1), 81–90. https://doi.org/10.1016/j.apgeochem.2009.10.003.
Su, Z., Wei, M.N., Jia, X.H., Fan, Y.G., Zhao, F.H., Zhou, Q.H., Taylor, P.R., Qiao, Y.L., 2022. Arsenic, tobacco use, and lung cancer: an occupational cohort with 27 follow-up years. Environ. Res. 206, 112611. https://doi.org/10.1016/J.ENVRES.2021.112611.
Sun, H.J., Ding, S., Guan, D.X., Ma, L.Q., 2022. Nrf2/Keap1 pathway in countering arsenic-induced oxidative stress in mice after chronic exposure at environmentally-relevant concentrations. Chemosphere 303, 135256. https://doi.org/10.1016/j.chemosphere.2022.135256.
Takamoto, A., Ishibashi, H., Fukushima, S., Tomoyori, H., Arizono, K., 2020. Analysis and health risk assessment of cadmium and arsenic in Japanese, Vietnamese, and Indonesian rice. J. Food Hyg. Soc. Jpn. 61 (5), 192–199. https://doi.org/10.3358/SHOKUEISHI.61.192.
Thakur, M., Rachamalla, M., Niyogi, S., Datusalia, A.K., Flora, S.J.S., 2021. Molecular mechanism of arsenic-induced neurotoxicity including neuronal dysfunctions. Int. J. Mol. Sci. 22 (18), 10077. https://doi.org/10.3390/ijms221810077.
The Lancet Global Health, 2020. Mental health matters. Lancet Glob. Health 8 (11), e1352. https://doi.org/10.1016/S2214-109X(20)30432-0.
Tofail, F., Vahter, M., Hamadani, J.D., Nermell, B., Huda, S.N., Yunus, M., Rahman, M., Grantham-McGregor, S.M., 2009. *Effect of arsenic exposure during pregnancy on infant development at 7 months in rural matlab*, Bangladesh. Environ. Health Perspect. 117 (2), 288–293. https://doi.org/10.1289/ehp.11670.
Tolins, M., Ruchirawat, M., Landrigan, P., 2014. The developmental neurotoxicity of arsenic: cognitive and behavioral consequences of early life exposure. Ann. Glob. Health 80 (4), 303–314. https://doi.org/10.1016/j.aogh.2014.09.005.
Tran, C.T., Le, T.T., Duong, L.T., Dultz, S., Nguyen, M.N., 2020. A comparative study of arsenic in rice in lowland and terraced paddies in the Red River Basin, Vietnam. Land Degrad. Dev. 31 (17), 2635–2647. https://doi.org/10.1002/ldr.3638.
Tran, T.H.M., Nguyen, K.G., 2018. Metal and metalloid concentrations in soil, surface water, and vegetables and the potential ecological and human health risks in the northeastern area of Hanoi, Vietnam. Environ. Monit. Assess. 190 (11), 624. https://doi.org/10.1007/s10661-018-6994-7.
Tseng, H.P., Wang, Y.H., Wu, M.M., The, H.W., Chiou, H.Y., Chen, C.J., 2006. Association between chronic exposure to arsenic and slow nerve conduction velocity among adolescents in Taiwan. J. Health, Popul. Nutr. 24 (2), 182–189. https://pubmed.ncbi.nlm.nih.gov/17195559/.
Tsuji, J.S., Garry, M.R., Perez, V., Chang, E.T., 2015. Low-level arsenic exposure and developmental neurotoxicity in children: a systematic review and risk assessment. Toxicology 337, 91–107. https://doi.org/10.1016/j.tox.2015.09.002.
Tupwongse, V., Parkpian, P., Watcharasit, P., Satayavivad, J., 2007. Determination of levels of Mn, As, and other metals in water, sediment, and biota from Phayao Lake, Northern Thailand, and assessment of dietary exposure. J. Environ. Sci. Health - Part A 42 (8), 1029–1041. https://doi.org/10.1080/10934520701418458.
Tyler, C.R., Allan, A.M., 2014. The effects of arsenic exposure on neurological and cognitive dysfunction in human and rodent studies: a review. Curr. Environ. Health Rep. 1, 132–147. https://doi.org/10.1007/s40572-014-0012-1.
Upadhyay, M.K., Majumdar, A., Barla, A., Bose, S., Srivastava, S., 2019. An assessment of arsenic hazard in groundwater–soil–rice system in two villages of Nadia district, West Bengal, India. Environ. Geochem. Health 41 (6), 2381–2395. https://doi.org/10.1007/s10653-019-00289-4.
U.S. Food and Drug Administration. (2016). *Arsenic in Rice and Rice Products Risk Assessment Report.* http://www.fda.gov/Food/FoodScienceResearch/RiskSafetyAssessment/default.htm.
US EPA, 2021. National Recommended Water Quality Criteria - Aquatic Life Criteria Table. United States Environmental Protection Agency. https://www.epa.gov/wqc/national-recommended-water-quality-criteria-aquatic-life-criteria-table#table.
The United States Environmental Protection Agency (US EPA), 2001. Risk Assessment Guidance for Superfund: Process for Conducting Probabilistic Risk Assessment (Part A) 3, EPA 540-R-02–002. https://www.epa.gov/sites/default/files/2015-09/documents/rags3adt_complete.pdf.
Vahter, M., Skröder, H., Rahman, S.M., Levi, M., Derakhshani Hamadani, J., Kippler, M., 2020. Prenatal and childhood arsenic exposure through drinking water and food and cognitive abilities at 10 years of age: a prospective cohort study. Environ. Int. 139, 105723. https://doi.org/10.1016/j.envint.2020.105723.
Verma, J.P., Verma, P., 2020. Determining sample size and power in research studies. Determining Sample Size and Power in Research Studies. https://doi.org/10.1007/978-981-15-5204-5.
Vibol, S., Hashim, J.H., Sarmani, S., 2015. Neurobehavioral effects of arsenic exposure among secondary school children in the Kandal Province, Cambodia. Environ. Res. 137, 329–337. https://doi.org/10.1016/j.envres.2014.12.001.
Vitayavirasak, B., Rakwong, K., Chatchawej, W., 2005. Environmental arsenic exposure of schoolchildren in a former tin mining and smelting community of southern Thailand. Environ. Sci. 12 (4), 195–205. https://pubmed.ncbi.nlm.nih.gov/16184078/.
Von Ehrenstein, O.S., Poddar, S., Yuan, Y., Mazumder, D.G., Eskenazi, B., Basu, A., Hira-Smith, M., Ghosh, N., Lahiri, S., Haque, R., Ghosh, A., Kalman, D., Das, S., Smith, A. H., 2007. Children's intellectual function in relation to arsenic exposure. Epidemiology 18 (1), 44–51. https://doi.org/10.1097/01.ede.0000248900.65613.a9.
Wang, H., Cui, S., Ma, L., Wang, Z., Wang, H., 2021a. Variations of arsenic forms and the role of arsenate reductase in three hydrophytes exposed to different arsenic species. Ecotoxicol. Environ. Saf. 221, 112415. https://doi.org/10.1016/J.ECOENV.2021.112415.
Wang, S., Chen, J., Zhang, S., Bai, Y., Zhang, X., Jiang, W., Yang, S., 2024. Shallow groundwater quality and health risk assessment of fluoride and arsenic in Northwestern Jiangsu Province, China. Appl. Water Sci. 14 (6), 119. https://doi.org/10.1007/s13201-024-02174-7.
Wang, S.X., Wang, Z.H., Cheng, X.T., Li, J., Sang, Z.P., Zhang, X.D., Han, L.L., Qiao, X.Y., Wu, Z.M., Wang, Z.Q., 2007. *Arsenic and fluoride expose in drinking water: children's IQ and growth in Shanyin Country*, Shanxi Province, China. Environ. Health Perspect. 115 (4), 643–647. https://doi.org/10.1289/ehp.9270.
Wang, L., Duan, G., 2009. Effect of external and internal phosphate status on arsenic toxicity and accumulation in rice seedlings. Journal of environmental sciences (China) 21 (3), 346–351. https://doi.org/10.1016/s1001-0742(08)62275-5.
Wang, X., Huang, X., Zhou, L., Chen, J., Zhang, X., Xu, K., Huang, Z., He, M., Shen, M., chen, X., Tang, B., Shen, L., Zhou, Y., 2021b. Association of arsenic exposure and cognitive impairment: a population-based cross-sectional study in China. Neurotoxicology 82, 100–107. https://doi.org/10.1016/j.neuro.2020.11.009.
Wang, Y., Cheng, W., Wang, X., He, T., Liu, J., Chen, S., Zhang, J., 2023. Integrated metabolomics and network pharmacology revealing the mechanism of arsenic-induced hepatotoxicity in mice. Food Chem. Toxicol. 178, 113913. https://doi.org/10.1016/J.FCT.2023.113913.
Wasserman, G.A., Liu, X., Parvez, F., Ahsan, H., Factor-Litvak, P., Kline, J., van Geen, A., Slavkovich, V., Lolacono, N.J., Levy, D., Cheng, Z., Graziano, J.H., 2007. *Water arsenic exposure and intellectual function in 6-year-old children in Araihazar*, Bangladesh. Environ. Health Perspect. 115 (2), 285–289. https://doi.org/10.1289/ehp.9501.
Wasserman, G.A., Liu, X., Parvez, F., Ahsan, H., Factor-Litvak, P., van Geen, A., Slavkovich, V., Lolacono, N.J., Cheng, Z., Hussain, I., Momotaj, H., Graziano, J.H., 2004. *Water arsenic exposure and children's intellectual function in Araihazar*, Bangladesh. Environ. Health Perspect. 112 (13), 1329–1333. https://doi.org/10.1289/ehp.6964.
Wasserman, G.A., Liu, X., Parvez, F., Chen, Y., Factor-Litvak, P., LoIacono, N.J., Levy, D., Shahriar, H., Uddin, M.N., Islam, T., Lomax, A., Saxena, R., Gibson, E.A., Kioumourtzoglou, M.A., Balac, O., Sanchez, T., Kline, J.K., Santiago, D., Ellis, T., van Geen, A., Graziano, J.H., 2018. A cross-sectional study of water arsenic exposure and intellectual function in adolescence in Araihazar, Bangladesh. Environ. Int. 118, 304–313. doi:10.1016/j.envint.2018.05.037.
Wasserman, G.A., Liu, X., Parvez, F., Factor-Litvak, P., Kline, J., Siddique, A.B., Shahriar, H., Uddin, M.N., Van Geen, A., Mey, J.L., Balac, O., Graziano, J.H., 2016. Child intelligence and reductions in water arsenic and manganese: a two-year follow-up study in Bangladesh. Environ. Health Perspect. 124 (7), 1114–1120. https://doi.org/10.1289/ehp.1509974.
Weber, A.M., Baxter, B.A., McClung, A., Lamb, M.M., Becker-Dreps, S., Vilchez, S., Koita, O., Wieringa, F., Ryan, E.P., 2021. Arsenic speciation in rice bran: agronomic practices, postharvest fermentation, and human health risk assessment across the lifespan. Environ. Pollut. 290, 117962. https://doi.org/10.1016/J.ENVPOL.2021.117962.
WHO, 2017. Guidelines for drinking water, quality. 4th edition with 1st addendum Geneva. 38(4), 104-108 World Health Organization https://iris.who.int/rest/bitstreams/907844/retrieve.
Wongsasuluk, P., Chotpantarat, S., Siriwong, W., Robson, M., 2018. Using urine as a biomarker in human exposure risk associated with arsenic and other heavy metals contaminating drinking groundwater in intensively agricultural areas of Thailand. Environ. Geochem. Health 40 (1), 323–348. https://doi.org/10.1007/s10653-017-9910-0.

Wu, Z., Ren, H., McGrath, S.P., Wu, P., Zhao, F.J., 2011. Investigating the contribution of the phosphate transport pathway to arsenic accumulation in rice. Plant Physiol. 157 (1), 498–508. https://doi.org/10.1104/pp.111.178921.

Xiao, W., Yang, Y., Tang, N., Huang, X., Zhang, Q., Zhao, S., Chen, D., Guo, B., Zhao, Z., Jiang, Y., Ye, X., 2024. Innovative accumulative risk assessment of co-exposure to Cd, As, and Pb in contaminated rice based on their in vivo bioavailability and in vitro bioaccessibility. Sci. Total Environ. 912, 168922. https://doi.org/10.1016/j.scitotenv.2023.168922.

Xu, J., Shi, S., Wang, L., Tang, Z., Lv, T., Zhu, X., Ding, X., Wang, Y., Zhao, F.J., Wu, Z., 2017. OsHAC4 is critical for arsenate tolerance and regulates arsenic accumulation in rice. New Phytol. 215 (3), 1090–1101. https://doi.org/10.1111/nph.14572.

Xue, L., Zhao, Z., Zhang, Y., Liao, J., Wu, M., Wang, M., Sun, J., Gong, H., Guo, M., Li, S., Zheng, Y., 2020. Dietary exposure to arsenic and human health risks in western Tibet. Sci. Total Environ. 731, 138840. https://doi.org/10.1016/j.scitotenv.2020.138840.

Yamazaki, S., Ueda, Y., Mukai, A., Ochiai, K., Matoh, T., 2018. Rice phytochelatin synthases OsPCS1 and OsPCS2 make different contributions to cadmium and arsenic tolerance. Plant Direct 2 (1), e00034. https://doi.org/10.1002/pld3.34.

Yang, X., Chu, F., Jiao, Z., Yu, H., Yang, W., Li, Y., Lu, C., Ma, H., Wang, S., Liu, Z., Qin, S., Sun, H., 2024. Ellagic acid ameliorates arsenic-induced neuronal ferroptosis and cognitive impairment via Nrf2/GPX4 signaling pathway. Ecotoxicol. Environ. Saf. 283, 116833. https://doi.org/10.1016/J.ECOENV.2024.116833.

Yang, Y., Wang, Q., Wang, W., Wei, S., Zeng, Q., Zhang, A., 2021. Semaphorin 4A antibody alleviates arsenic-induced hepatotoxicity in mice via inhibition of AKT2/NF-κB inflammatory signaling. Toxicol. Appl. Pharmacol. 410, 115364. https://doi.org/10.1016/J.TAAP.2020.115364.

Yao, B.M., Chen, P., Sun, G.X., 2020. Distribution of elements and their correlation in bran, polished rice, and whole grain. Food Sci. Nutr. 8 (2), 982–992. https://doi.org/10.1002/fsn3.1379.

Yao, B.M., Chen, P., Zhang, H.M., Sun, G.X., 2021. A predictive model for arsenic accumulation in rice grains based on bioavailable arsenic and soil characteristics. J. Hazard. Mater. 412, 125131. https://doi.org/10.1016/j.jhazmat.2021.125131.

Yasuda, H., Kobayashi, M., Yasuda, Y., Tsutsui, T., 2013. Estimation of autistic children by metallomics analysis. Sci. Rep. 3, 1199. https://doi.org/10.1038/srep01199.

Yorifuji, T., Kato, T., Ohta, H., Bellinger, D.C., Matsuoka, K., Grandjean, P., 2016. Neurological and neuropsychological functions in adults with a history of developmental arsenic poisoning from contaminated milk powder. Neurotoxicol. Teratol. 53, 75–80. https://doi.org/10.1016/j.ntt.2015.12.001.

Yu, Q., Wang, W., Wu, Z., Sun, B., Zhang, A., 2023. Association between exposure to arsenic and the risk of cardiovascular disease: Potential role of vascular endothelial injury. Environ. Toxicol. Pharmacol. 104303. https://doi.org/10.1016/j.etap.2023.104303.

Zhai, Q., Cen, S., Jiang, J., Zhao, J., Zhang, H., Chen, W., 2019. Disturbance of trace element and gut microbiota profiles as indicators of autism spectrum disorder: a pilot study of Chinese children. Environ. Res. 171, 501–509. https://doi.org/10.1016/j.envres.2019.01.060.

Zhang, M., Xue, Y., Zheng, B., Li, L., Chu, X., Zhao, Y., Wu, Y., Zhang, J., Han, X., Wu, Z., Chu, L., 2021. Liquiritigenin protects against arsenic trioxide-induced liver injury by inhibiting oxidative stress and enhancing mTOR-mediated autophagy. Biomed. Pharmacother. 143, 112167. https://doi.org/10.1016/J.BIOPHA.2021.112167.

Zhang, S., Geng, L., Fan, L., Zhang, M., Zhao, Q., Xue, P., Liu, W., 2020. Spraying silicon to decrease inorganic arsenic accumulation in rice grain from arsenic-contaminated paddy soil. Sci. Total Environ. 704, 135239. https://doi.org/10.1016/J.SCITOTENV.2019.135239.

Zhao, F.J., Ma, J.F., Meharg, A.A., McGrath, S.P., 2009. Arsenic uptake and metabolism in plants. New Phytol. 181 (4), 777–794. https://doi.org/10.1111/j.1469-8137.2008.02716.x.

Zhao, F.J., Wang, P., 2020. Arsenic and cadmium accumulation in rice and mitigation strategies. Plant Soil. 446 (1–2), 1–21. https://doi.org/10.1007/s11104-019-04374-6.

Zhao, Z., Li, S., Xue, L., Liao, J., Zhao, J., Wu, M., Wang, M., Sun, J., Zheng, Y., Yang, Q., 2020. Effects of dam construction on arsenic mobility and transport in two large rivers in Tibet, China. Sci. Total Environ. 741, 140406. https://doi.org/10.1016/j.scitotenv.2020.140406.

Zhao, Z., Li, S., Xue, L., Liao, J., Zhao, J., Wu, M., Wang, M., Yang, Q., Sun, J., Zheng, Y., 2021. Abundance and mobility of metal(loid)s in reservoir sediments of Singe Tsangpo and Yarlung Tsangpo in Tibet, China: implications for ecological risk. Environ. Geochem. Health 43 (8), 3213–3228. https://doi.org/10.1007/s10653-021-00810-8.

Zheng, L., Kuo, C.C., Fadrowski, J., Agnew, J., Weaver, V.M., Navas-Acien, A., 2014. Arsenic and chronic kidney disease: a systematic review. Curr. Environ. Health Rep. 1 (3), 192–207. https://doi.org/10.1007/s40572-014-0024-x.

Zheng, Y., 2020. Global solutions to a silent poison. Science 368 (6493), 818–819. https://doi.org/10.1126/science.abb9746.

Zhong, G., Rao, G., Tang, L., Wu, S., Tang, Z., Huang, R., Ruan, Z., Hu, L., 2022. Combined effect of arsenic and polystyrene-nanoplastics at environmentally relevant concentrations in mice liver: activation of apoptosis, pyroptosis and excessive autophagy. Chemosphere 300, 134566. https://doi.org/10.1016/J.CHEMOSPHERE.2022.134566.

Zhou, H., Lin, Y., Zhao, W., Teng, Y., Cui, Y., Wang, T., Li, C., Jiang, Y.hui, Zhang, J, (Jim), Wang, Y., 2020. The role of Hipk2-p53 pathways in arsenic-induced autistic behaviors: a translational study from rats to humans. Environ. Pollut. 267, 115568. https://doi.org/10.1016/J.ENVPOL.2020.115568.

Zhou, L., Li, R., Wang, F., Zhou, R., Xia, Y., Jiang, X., Cheng, S., Wang, F., Li, D., Zhang, J., Mao, L., Cai, X., Zhang, H., Qiu, J., Tian, X., Zou, Z., Chen, C., 2024. N6-methyladenosine demethylase FTO regulates neuronal oxidative stress via YTHDC1-ATF3 axis in arsenic-induced cognitive dysfunction. J. Hazard. Mater. 480, 135736. https://doi.org/10.1016/J.JHAZMAT.2024.135736.

Zhou, L., Xu, Z., Zhou, J., Fan, P., 2022. Natural arsenic source, migration, and flux in a catchment on the Southern Tibetan Plateau. Sci. Total Environ. 838 (Pt 2), 155898. https://doi.org/10.1016/j.scitotenv.2022.155898.

Zhu, Y., Yang, Q., Wang, H., Yang, J., Zhang, X., Li, Z., Martín, J.D., 2023. A hydrochemical and isotopic approach for source identification and health risk assessment of groundwater arsenic pollution in the central Yinchuan basin. Environ. Res. 231 (Pt 2), 116153. https://doi.org/10.1016/j.envres.2023.116153.

Zulkafflee, N.S., Redzuan, N.A.M., Hanafi, Z., Selamat, J., Ismail, M.R., Praveena, S.M., Razis, A.F.A, 2019. Heavy metal in paddy soil and its bioavailability in rice using in vitro digestion model for health risk assessment. Int. J. Environ. Res. Public Health 16 (23), 4769. https://doi.org/10.3390/ijerph16234769.

Zvobgo, G., LwalabaWaLwalaba, J., Sagonda, T., Mutemachani Mapodzeke, J., Muhammad, N., Haider Shamsi, I., Zhang, G., 2018. Phosphate alleviates arsenate toxicity by altering expression of phosphate transporters in the tolerant barley genotypes. Ecotoxicol. Environ. Saf. 147, 295–306. https://doi.org/10.1016/j.ecoenv.2017.09.043.