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Arsenic in the Soil-Plant-Human Continuum in Regions of Asia: Exposure and Risk Assessment

Debasis Golui[1,2] · Md Basit Raza[1,3] · Arkaprava Roy[1,4] · Jajati Mandal[5] · Ankit Kumar Sahu[6] · Prasenjit Ray[1] · Siba Prasad Datta[7] · Mohammad Mahmudur Rahman[8] · Achintya Bezbaruah[2]

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Abstract

In this review article, a comprehensive meta-analysis based on available literature information has been undertaken to make a relative comparison of total arsenic in rice grain. This involves analyzing the findings of various peer-reviewed studies that examined arsenic-contaminated Asian regions. Also, this article highlights the regional-level human health risks caused by the consumption of arsenic-contaminated rice in the three regions of Asia. Deriving such information at the continental level is of major importance in view of the need for proper monitoring and alleviating serious and continually emerging human health issues in arsenic-contaminated areas. One aim of this paper is to highlight the potential of a viable modeling approach for appraising the danger posed by arsenic in soil-plant-human system. There is an urgent need to fix the safe limit of bioavailable arsenic in soil because total arsenic in soil is not a good index of the arsenic hazard. Our hypothesis is finding out whether the modeling approach can be used in establishing a safe limit of bioavailable arsenic in soils with reference to human health. To achieve the above-mentioned objectives, we have selected reported rice grain arsenic content data from Asian countries following the PRISMA guidelines. Carcinogenic and non-carcinogenic risk was calculated following the US EPA's guidelines. It emerged that adults in Asian countries are prone to a high risk of cancer due to their consumption of arsenic-contaminated rice. South Asia (SA), South East Asia (SEA), and East Asia (EA) exceeded the US EPA-prescribed safe limit for cancer risk with ~ 100 times higher probability of cancer due to rice consumption. The hazard quotient for the ingestion of arsenic containing rice was 4.526 ± 5.118 for SA, 2.599 ± 0.801 for SEA, and 2.954 ± 2.088 for EA. These figures are all above the permissible limit of HQ of 1. The solubility free ion activity model can predict arsenic transfer from soil to rice grain based on easily measurable soil properties and be used to fix the safe limit of bioavailable arsenic in paddy soils. The methods and findings of this review are expected to be useful for regional-level policymaking and mobilizing resources to alleviate public health issues caused by arsenic.

Keywords Arsenic · Rice · Risk assessment · Cancer risk · Hazard quotient, FIAM

Debasis Golui and Achintya Bezbaruah contributed equally to this review work and the preparation of this manuscript.

✉ Debasis Golui
debasis.golui@ndsu.edu

✉ Achintya Bezbaruah
a.bezbaruah@ndsu.edu

1 Division of Soil Science and Agricultural Chemistry, ICAR-Indian Agricultural Research Institute, New Delhi 110012, India

2 Department of Civil, Construction and Environmental Engineering, North Dakota State University, Fargo, ND 58102, USA

3 ICAR-Directorate of Floricultural Research, Pune, Maharashtra 411036, India

4 School of Crop Health Biology Research, ICAR-National Institute of Biotic Stress Management, Raipur, Chhattisgarh 493225, India

5 School of Science, Engineering and Environment, University of Salford, Salford, Manchester M50 2EQ, UK

6 Department of Emergency Medicine, All India Institute of Medical Sciences, New Delhi 110029, India

7 ICAR-Indian Institute of Soil Science, Bhopal, Madhya Pradesh 462038, India

8 Global Centre for Environmental Remediation (GCER), College of Engineering, Science and Environment, The University of Newcastle, Callaghan, NSW 2308, Australia

Introduction

Arsenic (As), infamously referred to as the "king of poison," is a colorless, tasteless, and odorless trace element found throughout the natural environment. It is a carcinogenic metalloid reported to be present in the lithosphere at concentrations as high as 5 mg kg^{-1} [1]. High levels of arsenic in groundwater can be attributed to geo-biochemical processes that dislodge arsenic from arsenic-bearing minerals. The process is further accelerated by the indiscriminate withdrawal of groundwater [2, 3]. Apart from geogenic sources, groundwater may also be contaminated with arsenic through various anthropogenic activities including the disposal of various industrial wastes, mining operations, and dumping of sewage sludge and wastewater [4•]. Several arsenic-based pesticides have been applied to agricultural fields and continued to be used in many countries despite their known harmful effects [5, 6]. Although arsenic contamination of drinking water has been documented in several South Asian countries and the Americas, the severity of contamination in India and Bangladesh is unparalleled [7]. Approximately 85 million people in Bangladesh [8] and 90 million in India [7, 9, 10•] are exposed to arsenic levels higher than the World Health Organization (WHO) threshold limit of 10 µg As L^{-1} in drinking water. Globally, more than 230 million people are in danger of arsenic poisoning due to constant drinking of water [7•].

Human exposure to arsenic-contaminated groundwater, mainly drawn through tube wells, has been identified as a serious public health problem in many countries including Bangladesh [11, 12]. Apart from drinking water, arsenic finds its way into the human food chain through the consumption of food crops grown in soils regularly irrigated with arsenic-polluted groundwater [13, 14••]. It has been estimated that more than 50% of the world's population consumes rice, with global production of rice amounting to approximately 503.27 million tons in 2022–2023. Most importantly, rice is the staple food throughout South East Asia and is the reason behind the rise in arsenic-related health problems in humans due to the regular consumption of rice grains (in addition to drinking water) grown in contaminated soils [15]. Sustained intake of arsenic-contaminated food increases arsenic body burden in humans and may lead to arsenicosis, black foot disease, and diseases of the heart and lungs [14, 16]. Occupational exposure can occur during industrial processes such as mining and production/processing as well as during the use of wood and leather preservatives, pharmaceuticals, glass, alloys, pigments and antifouling paints, poison baits, pesticides, and microelectronic and optical products. Arsenic present in tobacco is known to seriously affect smokers [17].

The traumatic impact of continued ingestion of arsenic on human health has been well documented. The most conspicuous effect of chronic arsenic intake is on the skin. Carcinoma (mainly, intra-epithelial carcinoma or Bowen's disease, squamous cell, and basal cell carcinoma) is the most pernicious effect of arsenic poisoning on human skin [18]. Skin cancers caused by arsenic have a relatively short latency period of roughly 10 years resulting in lethal consequences in a relatively short period of time [19]. The severity of the impacts of arsenic on human health is governed not only by the length of arsenic exposure but also by many environmental factors like sun exposure, fertilizer use, pesticide use, and smoking habit [20]. For instance, people with smoking habits and those exposed to an environment with high fertilizer application are more likely to show early signs of arsenic poisoning [20]. Many studies have reported lung malignancies due to arsenic exposure [21, 22]. Again, poor nutritional status may increase an individual's susceptibility to chronic arsenic toxicity, or alternatively that arsenicosis may contribute to poor nutritional status [23]. For example, participants with poor nutrition were reported from West Bengal, India, as having an overall 1.6-fold increase (for males = 1.5, females = 2.1) in the prevalence of keratoses [24]. Apart from this, various neurological disorders and gastrointestinal effects are reported due to chronic As exposure [25], suggesting that malnutrition may increase the susceptibility to arsenic poisoning [24].

With public health issues in mind, monitoring and assessment of arsenic hazards to humans should be prioritized. The upper critical limit set by WHO (1 mg kg^{-1}) for arsenic in rice grain has now been considered obsolete and unsafe. The new permissible limit which is widely followed is 0.3 mg kg^{-1} for brown rice and 0.2 mg kg^{-1} for polished white rice [26]. In August 2020, the US Food and Drug Administration (FDA) reissued guidelines for arsenic in infant rice cereal limiting it to 100 µg kg^{-1} [27]. Apart from providing good quality drinking water, monitoring of food materials like rice grain is also required to safeguard public health. However, given the wide-ranging human dietary habits throughout the world, establishing a generalized limit for arsenic in various food products, including rice, is unwise. Nonetheless, the prescription of a safe limit of plant-available (bioavailable) arsenic in soil is essential for, firstly, assessing the suitability of arable lands for crop production and, secondly, devising suitable management strategies for remediation of arsenic-contaminated soil. Taking into consideration the ever-increasing food demands, it will be very challenging to exclude the arsenic-polluted land which is otherwise fertile and productive. However, changing the permissible limits to higher values will be detrimental to human and animal health.

Despite the many published studies done to assess the concentration of arsenic in rice grain, no study has yet been done as a systematic review or meta-analysis on arsenic's involvement in cancer risk among people living in Asian countries. We used the existing data on arsenic in rice grain to calculate important parameters like carcinogenic and non-carcinogenic risk. We have also discussed the advantage of the mechanistic model to predict the arsenic transfer from soil to rice crop based on easily measurable soil properties like pH, organic carbon, and extractable arsenic. We have hypothesized that modeled plant arsenic data can serve to fix the safe limit of bioavailable arsenic in soil in relation to human health. The novelty of this review is its use of a protocol for risk assessment of arsenic-contaminated soils and fixing the safe limit of bioavailable arsenic in soil. This protocol certainly helps to better protect the human food chain from arsenic contamination. Under this approach, if one knows extractable arsenic, pH, and organic carbon content of soil, suitability of agricultural land can be easily assessed. Hence, this strategy can easily be adopted for routine risk assessment of contaminated soil. In this review article, we have reviewed the (i) distribution of arsenic levels in rice (both at the field level and in market-sold rice) from Asian regions; (ii) health risks, both non-carcinogenic and carcinogenic, due to rice consumption; and (iii) prediction of the amount of arsenic in rice grain using a modeling approach. In the first section of this review, the mechanism of arsenic poisoning in humans has been discussed to reveal various health implications, which will help to create awareness among people living in arsenic-contaminated regions of the world. The meta-analysis of available literature documents the impact of regional variability on total arsenic content in rice grain. This review article synthesized grain arsenic data to assess carcinogenic and non-carcinogenic risks. Based on such information, risk assessment should be carried out in regions of high importance before cultivating rice crops so that human health is protected. In last section, we have discussed the appraisal of arsenic menace in soil-plant-human continuum and use of modeling approach for routine risk assessment.

Mechanism of Arsenic Poisoning in Humans

Manifestation of humans to arsenic exposure and its effect on their health may be acute or chronic. Acute arsenic toxicity leads to vomiting and diarrhea within hours of ingestion, direct myocardial dysfunction, acute encephalopathy, and severe kidney and lung injury [28]. Low-dose chronic exposure can lead to deleterious effects like malignant and non-malignant skin changes, hypertension, diabetes, peripheral vascular disease, and malignancies of the lung, bladder, and liver [18, 28]. Non-malignant lung disease, gastroenteritis, portal hypertension, and black foot disease have been reported in people consuming arsenic-contaminated drinking water [29]. The association of arsenic with various human malignancies has made this metalloid a class 1 human carcinogen [30]. The most common malignancy associated with arsenic is that of the skin (e.g., squamous cell carcinoma, basal cell carcinoma, Bowen's disease, and Merckel cell carcinoma) [31], while the severe ones are associated with the lungs (e.g., squamous cell carcinoma of the lungs) [32]. Several mechanisms underlying arsenic carcinogenicity have been studied, and three pathophysiologic factors are identified as arsenic methylation, oxidative stress, and epigenetic changes induced by arsenic (Fig. 1).

Arsenic is metabolized in the human body through redox reactions, of which methylation is essential. Oxidative methylation of arsenic produces methylated trivalent and pentavalent arsenic compounds using S-adenosyl methionine (SAM) [33]. These methylated arsenic compounds are carcinogenic to skin keratinocytes [34]. In the above-mentioned methylation process, reactive oxygen species (ROS) are generated. Directly or indirectly, arsenic-induced oxidative stress triggers DNA damage. Both in mouse and human skins, arsenic can induce oxidative damage in cellular DNA and generate 8-hydroxyl 2-deoxy guanosine (8-OHdG) oxidative DNA adducts [35, 36]. Clinical studies in arsenic-induced Bowen's disease (As-BD) indicate that the increased 8-OHdG levels are positively correlated to the lesional arsenic concentration. Suggested here is the involvement of oxidative stress in arsenical skin carcinogenesis [35, 36]. Elevated 8-OHdG has also been found to be implicated in breast cancer [37].

Modifications of gene transcription of WNT/β-catenin and calcium signaling pathways are reported and implicated in the development of many cancers [38]. WNT signaling is a regulatory pathway that orchestrates skin development, homeostasis, and stem cell activation. Aberrant regulation of WNT signaling cascades not only gives rise to tumor initiation, progression, and invasion but also maintains cancer stem cells which contribute to tumor recurrence [39]. In a systematic review and meta-analysis, it was discovered that arsenic causes dysregulation of WNTa and β-catenin levels, leading to neoplastic proliferation [40]. The arsenic-induced ROS has also been shown to dysregulate the epidermal growth factor receptor (EGFR), nuclear factor-κβ (NF-κβ), mitogen-activated protein (MAP) kinase, and matrix-metalloproteinases (MMPs) that help in neoplastic proliferation [41].

The process of arsenic metabolism in the human body utilizes SAM, the cell's methyl group donor, and that leads to the depletion of SAM and resulting epigenetic changes like aberrant DNA methylation, histone modification, and microRNA (miRNA) expression [18]. For tumor suppressor genes, aberrant DNA promoter hypermethylation is greatly associated with transcriptional gene silence [42]. Abnormal DNA methylation has been found to be associated with lung and bladder cancers due to the inhibition

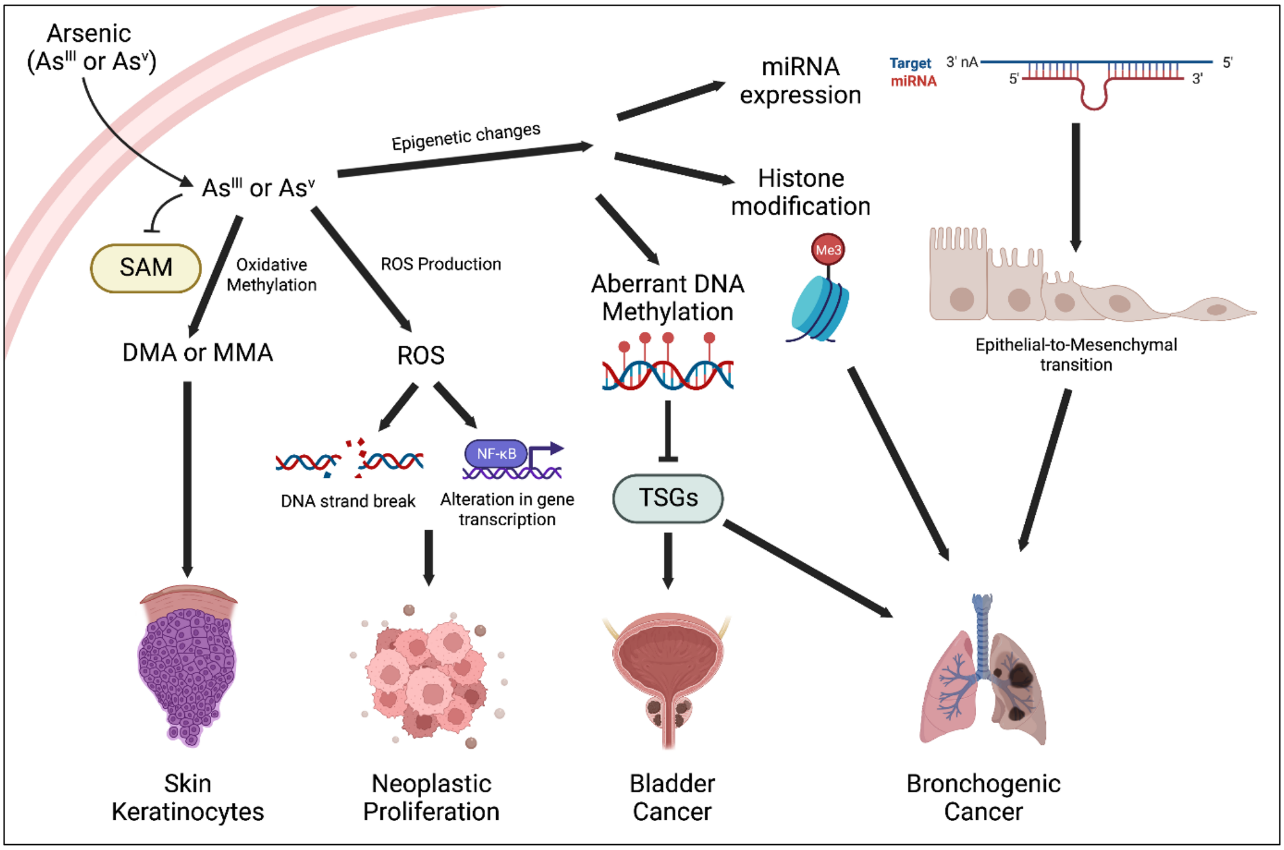

Fig. 1 Mechanisms of carcinogenic toxicity of arsenic in humans. Three pathophysiological effects on human body, viz., arsenic methylation, oxidative stress, and epigenetic changes, are induced by sustained arsenic intake by human body

of the transcription of tumor suppressor genes (like p53, p16INK4A, RASSF1A, and PRSS3) [43]. Through the addition of acetyl groups (via histone acetyltransferases) or the removal of acetyl groups (via histone deacetylases), histone-modifying enzymes catalyze the addition or removal of these modifications to generally induce or maintain an open euchromatic state, or a closed or heterochromatic state, on specific histone residues. Consequently, euchromatin or heterochromatin development is correlated with the transcriptional activity of linked genes [44]. Arsenic metabolites have been shown to modify the methylation of normal histones (like H3K4, H3K9, and H3K27) leading to the malignant transformation of lung tissue [45]. Arsenic compounds were also shown to induce malignant transformation of human nontumorigenic cell lines through changes to histone H3 acetylation, DNA promoter methylation, and decreased expression of the DBC1, FAM83A, ZSCAN12, and C1QTNF6 genes. For each of these under-expressed genes, DNA methylation is inversely correlated with the histone acetylation levels for their respective promoter regions, leading scientists to conclude that changes in histone H3 acetylation occur during arsenic-induced malignant transformation [46].

Small non-coding RNAs called miRNAs control the translation of genes involved in numerous important aspects of cell life by inhibiting the translation of the mRNAs they target [47]. miRNA can interfere with the production of several, and occasionally even hundreds of, target genes because it binds to the 3′-untranslated region of mRNAs through incorrect base pairing. For this reason, miRNA dysregulation is linked to a number of human illnesses and cancer is no exception [48]. Exposure to arsenic has also been shown to induce epithelial-to-mesenchymal transition (malignant transformation) by reducing the miRNA-200 family in bronchial epithelial cells [49]. Arsenic also induces angiogenesis by diminishing the miRNA-9 family [50].

Methodology

In Asian countries, rice is the major staple food, and it is cultivated in at least two seasons to cater for huge demand [51]. Rice is a very water-demanding crop [52]. As a result, there is the excessive withdrawal of groundwater for irrigating the paddy fields during the dry season resulting in elevated levels of arsenic in soils irrigated with arsenic-contaminated groundwater. As much as 83,000 μg kg^{-1} of arsenic has been found in paddy soils subjected to constant irrigation in Bangladesh [53]. Increased levels of arsenic in rice grains are reported from paddy fields irrigated with contaminated irrigation water [54, 55]. In this study, we have collected literature-reported rice grain arsenic content data from Asian countries. The possible lifetime cancer risk due to the consumption of arsenic-contaminated rice was evaluated.

Search Strategy

To find the numerous research articles published on this topic, a systematic search was conducted in the publicly available databases/search engines like ISI Web of Science, Google Scholar, ScienceDirect, Scopus, and PubMed for the years between January 2000 and February 2023. We used Boolean operators (e.g., "OR" and "AND") to develop search terms from the keywords such as "arsenic," "*Oryza sativa*," "rice," "grain," "Asia," "survey," "farmer field," and "market." A full list of keywords is provided in Table S1. The reference lists of articles were checked to find other relevant papers. As shown in Fig. 2, literature search and retrieving articles were done according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [56].

Study Selection

Following a first screening, the potentially eligible articles were downloaded as full texts. Then, the inclusion criteria for article selection were critically assessed. Contradictions between any reported evidence and different researchers' discussion, in the different publications, were addressed and tentatively solved through an open debate and agreement jointly among the authors of this review. Inclusion criteria were full-text availability, published full or abstract text in the English language, detected concentration of arsenic in rice grain, either field or market survey studies, reported

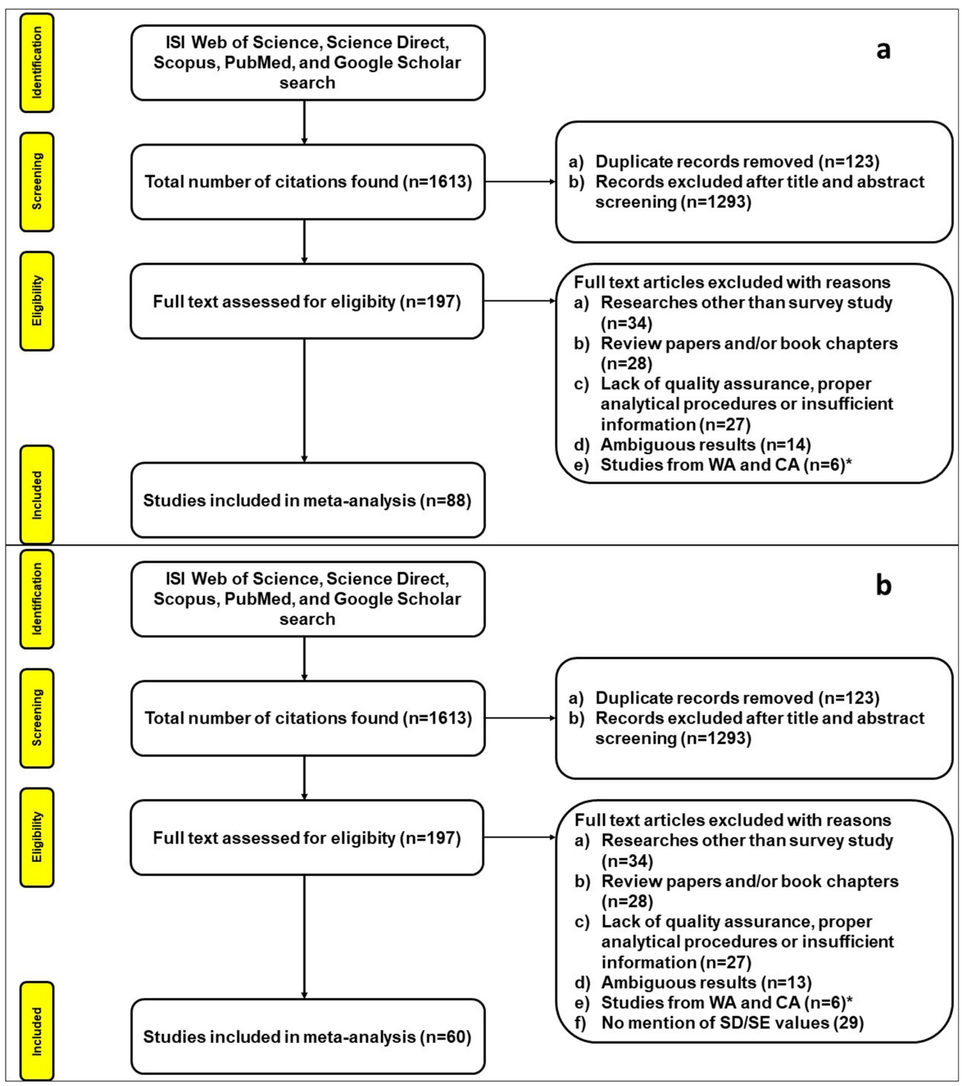

Fig. 2 **a** Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) diagram for risk assessment. **b** Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) for developing forest plot. *Studies from Western Asia ($n = 5$) and Central Asia ($n = 1$) did not meet the minimum criteria of $n > 10$ to be considered for further analysis

standard deviation or standard error, and papers published between 2000 and 2023. Articles that did not meet all of the above criteria above were excluded.

Definition and Data Extraction

The data were extracted and assessed. Data from each study included first author, year of study and year of publication, total sample size, region study, and average or range of concentration of arsenic. Whenever a standard error of mean (SEM) was reported instead of standard deviation (SD) and sample data were available, we calculated SD from [57].

Statistical Analyses and Meta-analysis

To estimate the heterogeneity rate among different studies, an I^2 statistic was applied. The I^2 statistic describes the percentage of variation across studies that is due to heterogeneity rather than chance [58]. When the Q value proved to be significant ($p < 0.05$), this meant that the studies were heterogeneous. As heterogeneity was considered for values > 50%, the random effect model was deployed [59]. Forest plot was created to summarize the information on individual studies in the meta-analysis which also provides a visual indication of the degree of heterogeneities. The lack of difference between the study group and marginal level, commonly known as no effect or zero effect, has been presented by a vertical line in the center of the plot. It was considered that at this point, the mean difference is zero. The subsequent squares depicted the mean difference values for each study, and the size of the squares represents the effect of the estimate and the weight of the studies. Each horizontal segment's succeeding endpoints exhibited 95% confidence intervals (CI) that were symmetrical about the mean. The diamond in the plot represents the point estimate and confidence intervals when all studies were combined and averaged. The *metafor* package (version 3.8–1) in R-Studio (version 1.3.10932.3.1) served to execute the data analysis.

Assessment of Cancer Risk

The inorganic arsenic (iAs) was used to assess the carcinogenic risk for people consuming rice grown in SA, SEA, and EA regions. For this, the chronic daily dose (CDD) was calculated (Eq. 1).

$$\mathrm{CDD} = \frac{\mathrm{C} \times \mathrm{IR} \times \mathrm{ED} \times \mathrm{EF} \times \mathrm{CF}}{\mathrm{BW} \times \mathrm{AT}} \tag{1}$$

where C is the iAs (mg kg^{-1}) in rice grain, IR denotes the ingestion rate (0.4 kg day^{-1} or 4×10^5 mg day^{-1} [14]), ED is the exposure duration (30 years for an adult [60]), EF stands for exposure frequency (365 days year^{-1}), CF is conversion factor (1×10^{-6} kg mg^{-1}), BW represents the average body weight (70 kg for an adult), and AT is the average time for carcinogen (70 × 365 days for As) [61]. For the calculation of CDD in children, IR is assumed to be 0.2 kg day^{-1} [62•], ED is 6 years, and BW is 20 kg [60].

The carcinogenic risk (CR) to an adult human who has consumed arsenic-contaminated rice was calculated based on the CDD value and the slope factor for arsenic (Eq. 2).

$$\mathrm{CR} = \mathrm{CDD} \times \mathrm{SF} \tag{2}$$

where SF is the slope factor (SF = 1.5 mg kg^{-1} day^{-1} for arsenic). As per the US EPA guidelines [63], CR values $< 10^{-6}$ are safe while values $> 10^{-4}$ are harmful to human health.

Risk Thermometer

A risk thermometer is a new holistic protocol on risk characterization [64, 65••], and this gives us a comparison of risks. The risk thermometer for arsenic estimates the severity-adjusted margin of exposure (SAMOE) based on Tolerable Daily Intake (TDI, 3.0 µg kg (body weight)$^{-1}$ day^{-1} for arsenic) and ingestion of arsenic present in food (rice). The human dietary exposure to arsenic through rice consumption can be calculated using the equation (Eq. 3) proposed by Chowdhury et al. (2020) [66].

$$\mathrm{SAMOE} = \mathrm{TDI}/(\mathrm{AF_{BMR}} \times \mathrm{AF} \times \mathrm{SF} \times \mathrm{E}) \tag{3}$$

where TDI is 3.0 µg kg (bodyweight)$^{-1}$ day^{-1} for arsenic, $\mathrm{AF_{BMR}}$ is the non-linear relation in dose range (1/10; BMR-benchmark response), AF (assessment factors) is a factor of 10 (conservative assessment), SF (severity factor) is 100 (for cancer, the most severe category), and E is the exposure factor (iAs concentration in rice). Based on the SAMOE value, the risk classes in the risk thermometer are designated as class 1 (no risk, > 10), class 2 (no to low risk, 1–10), class 3 (low risk, 0.1–1), class 4 (moderate to high risk, 0.01–0.1), and class 5 (high risk, < 0.01) [64].

Assessment of Non-cancer Risk

The hazard quotient (HQ) is the deterministic means for assessing the chronic non-carcinogenic hazard associated with metalloid (Eq. 4) [67]:

$$HQ = \frac{ADD}{Rf\ D} \tag{4}$$

This is a relationship between the average daily dose (ADD; mg kg^{-1} d^{-1}) of arsenic by a population and the toxicological endpoint (reference dose (RfD) mg kg^{-1} d^{-1}). It is in fact an estimate of the limit of daily exposure to the population (including sensitive subpopulations) where there are no deleterious lifetime health effects. For arsenic, the

RfD value is 0.0003 mg arsenic (kg body weight)$^{-1}$ day^{-1} [68]. The cumulative risk from various non-carcinogens and/or the different ways of exposure (dermal and ingestion) are obtained by summing up the HQ values to get a hazard index (HI). If the concentrations of arsenic in the ingested media (soil, water, and food) are known, the ADD via oral intake can be calculated (Eq. 5) [14, 69].

$$ADD = \sum_{i=1}^{N} \frac{Ci \times CRi}{BW} \quad (5)$$

where N is the number of exposure routes to arsenic (e.g., N is 2 if routes of exposure are food and drinking water), C_i is the concentration of inorganic arsenic (mg kg^{-1}) in ith route, and CR_i is the consumption rate (kg day^{-1}) of the subscripted ingested material.

In the present review, exposure to arsenic in humans based solely on rice grain consumption. Therefore, the average daily dose was computed based on the following assumptions: C = concentration of inorganic arsenic in rice grain in regions of Asia, CR = 0.4 kg day^{-1} or 4×10^5 mg day^{-1} [14], and BW = 70 kg for adults [61]. An HQ value less than or equal to 1 is deemed to be safe [67]. However, because other dietary items may potentially be the sources of arsenic entering the human body, the HQ limit has been adjusted and regarded safe at HQ ≤ 0.5 [70•].

Results and Discussion

Study Characteristics

From > 1600 published articles, we excluded papers based on the conditions provided in the PRISMA flowchart (Fig. 2). In total, 88 papers were chosen to establish the risk associated with the consumption of rice grain in the chosen Asian regions. The Asian continent was subdivided into five regions, viz., South Asia (SA), South East Asia (SEA), East Asia (EA), West Asia (WA), and Central Asia (CA). Raw data (1 work common between SA and EA) on grain arsenic content as collected from SA (42 papers from Bangladesh, India, Iran, Nepal, Pakistan, and Sri Lanka), SEA (11 papers from Cambodia, Singapore, Thailand, and Vietnam), and EA (35 papers from China, Japan, Taiwan, and South Korea) were pooled and analyzed. For risk assessment, the total grain arsenic (tAs) content was converted to inorganic arsenic (iAs) by considering iAs to be 75% of tAs in husked rice (farm field grains) and 80% in polished rice (market available grains) [71••]. The papers from CA (n = 1) and WA (n = 5) regions were discarded because they did not meet the minimum criteria of n > 10 for carrying out further analysis. Conversely, a total of 60 papers (28 from SA covering Bangladesh, India, Iran, Nepal, Pakistan, and Sri Lanka; 9 from SEA covering Cambodia, Thailand, and Vietnam; 23 from EA covering China, Japan, Taiwan, and South Korea) were selected to report the relative comparison of total arsenic in rice grain between peer-reviewed studies in these regions. For this purpose, we compiled the data quantitative set of the above individual studies through the meta-analysis method.

Concentration of Arsenic in Rice Grain

A number of studies have been published on the concentration of total arsenic in rice grain grown in a wide range of contexts, including market-based surveys in different parts of Asia (Table 1). Evidence suggests that arsenic content in rice is likely to vary according to the country of origin as well as different production sites. Our studies showed that the maximum concentration of total arsenic was observed in SA countries like Bangladesh (e.g., 780–6050 μg kg^{-1} [72]) and India (e.g., 900–1510 μg kg^{-1} [73]). Conversely, a minimum level of arsenic in raw rice grain was reported in the SEA and EA countries. For example, a study from Thailand which is in the SEA region reported that the level of arsenic in rice samples ranged from 160 to 240 μg kg^{-1} (n = 55) [74]. In the EA region, the minimum level of arsenic in rice grain as reported in China was BDL–100 μg kg^{-1} [75]. In countries like Bangladesh and India, the source of arsenic is geogenic in nature [14]. Large variability in soil arsenic level caused by the excessive uptake of irrigation water during rice cultivation naturally leads to elevated grain arsenic in the rice fields of Bangladesh and India [15]. In contrast, anthropogenic activities like mining, discharge of municipal and industrial wastewater to rivers and soils, and improper use of fertilizer and chemical pesticides may lead to substantial arsenic accumulation in rice grain grown in the SEA and EA regions. Other reasons for the differences in the concentration of arsenic throughout Asia can be due to the various rice species, which bioaccumulate arsenic in their own ways [76]. Our review of the literature showed that the total amount of arsenic in rice grain was mostly reported across the Asian regions. Other arsenic species like inorganic and organic forms are rarely reported due to the lack of a standardized protocol or advanced instruments. One study compared the presence of inorganic arsenic in rice grain among Asian, US, and European countries [77]. They found that 80% of mean inorganic arsenic was detected in rice from Bangladesh and India, whereas relatively lower mean inorganic arsenic content of 64% and 42% was recorded in European and US rice grain, respectively. American rice was found to be enriched with dimethylarsinic acid (DMA) in particular. This signifies the importance of undertaking further risk assessment work on rice grain grown in the Asian regions. The objective of the meta-analysis is to compare the findings of peer-reviewed studies and what they concluded.

The forest plot for SA shows the list of input studies with their effect sizes (Fig. 3). From the random effect model, the

Table 1 Main characteristics of studies included in our review

Country	Total arsenic mean (range) (μg kg^{-1}), *n*	Study type	Other info	Reference
South Asian (SA) region				
Bangladesh	153.8 (104–362), 144	Field trial	*Aman*	[109]
	293.6 (157–454), 173	Field trial	*Boro*	[109]
	320 (140–430), 30	Market survey		[110]
	110.5 (5–805), 100	Field survey		[111]
	141 (18–601), 337	Market survey		[112]
	224 (17–733), 143	Field survey		[112]
	136 (40–270), 10	Field survey		[97]
	183 (108–331), 78	Field survey	*Boro*	[113]
	117 (72–170), 82	Field survey	*Aman*	[113]
	296 (182–436), 56	Field survey		[114]
	89.1 (25–287), 6	Field survey	*Aman*	[115]
	150.5 (31–453), 6	Field survey	*Boro*	[115]
	1870 (720–6050), 56	Field survey		[79]
	2150 (780–6050), 10	Field survey		[72]
	410 (160–740), 72	Field trial		[116]
	170 (70–280), 76	Field trial		[116]
	143 (2–557), 214	Field survey*		[117]
	153 (74–301), 14	Field survey*		[118]
	84.8 (40–130), 9	Field survey		[119]
	735 (410–980), 4	Field survey		[120]
India	451 (190–780), 21	Field survey	*Boro*	[121]
	174 (2–1260), 60	Market and Field survey		[14]
	334 (60–600), 18	Field survey	*Aman*	[121]
	342 (230–540), 63	Field survey	*Boro*	[122]
	284 (160–580), 63	Field survey	*Aman*	[122]
	410 (150–740), 6	Field survey		[123]
	510 (410–690), 240	Field survey	*Boro*	[124]
	562 (420–780), 260	Field survey	*Boro*	[124]
	160.3 (121–197), 9	Market survey		[125]
	58.1 (3–254), 15	Field survey		[126]
	932.5 (630–1090), 4	Field survey		[127]
	273.9 (18–446), 10	Field survey		[128]
	1090 (900–1510), 50	Field survey		[73]
	180 (30–333), 12	Field survey		[129]
	150 (40–450), 44	Market survey		[130]
	51 (30–80), 11	Market survey		[77]
Iran	87 (BDL–210), 60	Field survey		[131]
	65 (30–90), 15	Market survey		[132]
	121 (50.6–222), 15	Field survey		[133]
	101.4 (10–252), 20	Market survey		[134]
	82 (35–130), 17	Market survey		[132]
	280 (BDL–670), 15	Market survey		[135]
	390 (115–800), 20	Field survey		[135]
	161.7 (48–314), 10	Market survey		[136]
Nepal	180 (60–330), 75	Field survey		[137]
Sri Lanka	47.2 (2.48–213), 699	Field survey		[138]
	77 (19–217), 165	Market survey		[139]
Pakistan	98.9 (BDL–225.4), 54	Field survey		[140]
	36.9 (BDL–178.1), 14	Field survey		[141]

Table 1 (continued)

Country	Total arsenic mean (range) (μg kg^{-1}), *n*	Study type	Other info	Reference
South East Asian (SEA) region				
Thailand	204 (< 0.1–412.6), 159	Field survey		[142]
	205 (84–489), 97	Market survey		[143]
	175 (160–240), 55	Field survey		[74]
	176.5 (77.2–343.1), 113	Market survey		[144]
Cambodia	185 (47–771), 131	Field survey		[145]
	118.3 (12–578), 30	Field survey		[146]
	115 (52–328), 70	Field survey		[147]
	243 (63–528), 45	Field survey		[148]
Singapore	136.1 (60.5–361.1), 15	Market survey		[149]
Vietnam	180 (80–556), 78	Field survey		[150]
	220 (110–340), 24	Field survey		[151]
East Asian (EA) region				
China	87 (11–186), 160	Market survey		[152]
	480 (230–930), 34	Field survey		[153]
	92 (5–309), 282	Field survey		[154]
	42 (BDL–100), 16	Market survey		[75]
	199 (BDL–587), 155	Field survey		[155]
	340 (125–1840), 220	Field survey		[156]
	196.9 (33–739), 892	Field survey		[157]
	50 (BDL–310), 92	Field survey		[158]
	116.5 (41–210), 36	Field survey		[159]
	116.5 (BDL–665.2), 1653	Field survey		[160]
	90 (30–192), 32	Field survey		[161]
	260 (170–390)	Field survey		[162]
	154.9 (106.7–246.7), 353	Field survey		[163]
	114.4 (65.3–274.2), 21	Field survey		[164]
	119 (1.35–254), 258	Field survey		[165]
	564 (152–1094), 33	Field survey		[166]
	360 (30–1040), 73	Field survey		[167]
	188 (32–533), 205	Field survey		[168]
	243, (127–431), 29	Field survey		[169]
	129.4 (50.2–253), 43.4	Field survey		[170]
	172.9 (65–277), 27	Field survey		[171]
	125 (20–326), 113	Field survey		[172]
	119 (BDL–490), 712	Field survey		[173]
	820 (460–1180), 2	Field survey		[120]
	196 (54–795), 446	Field survey		[174]
	191.7 (9–624), 195	Field survey		[175]
	111.2 (15–586), 240	Market survey		[175]
Japan	137 (107–166), 10	Field survey		[176]
South Korea	200 (120–280), 3	Field survey		[177]
	180 (60–390), 100	Field survey		[178]
	146 (40–380), 82	Field survey		[179]
	247 (104–774), 40	Field survey		[180]
	410 (240–720), 5	Field survey		[181]
	124, (31–282), 485	Market survey		[182]
Taiwan	474 (290–660), 11	Field survey		[183]

*Household survey—rice grown in own fields

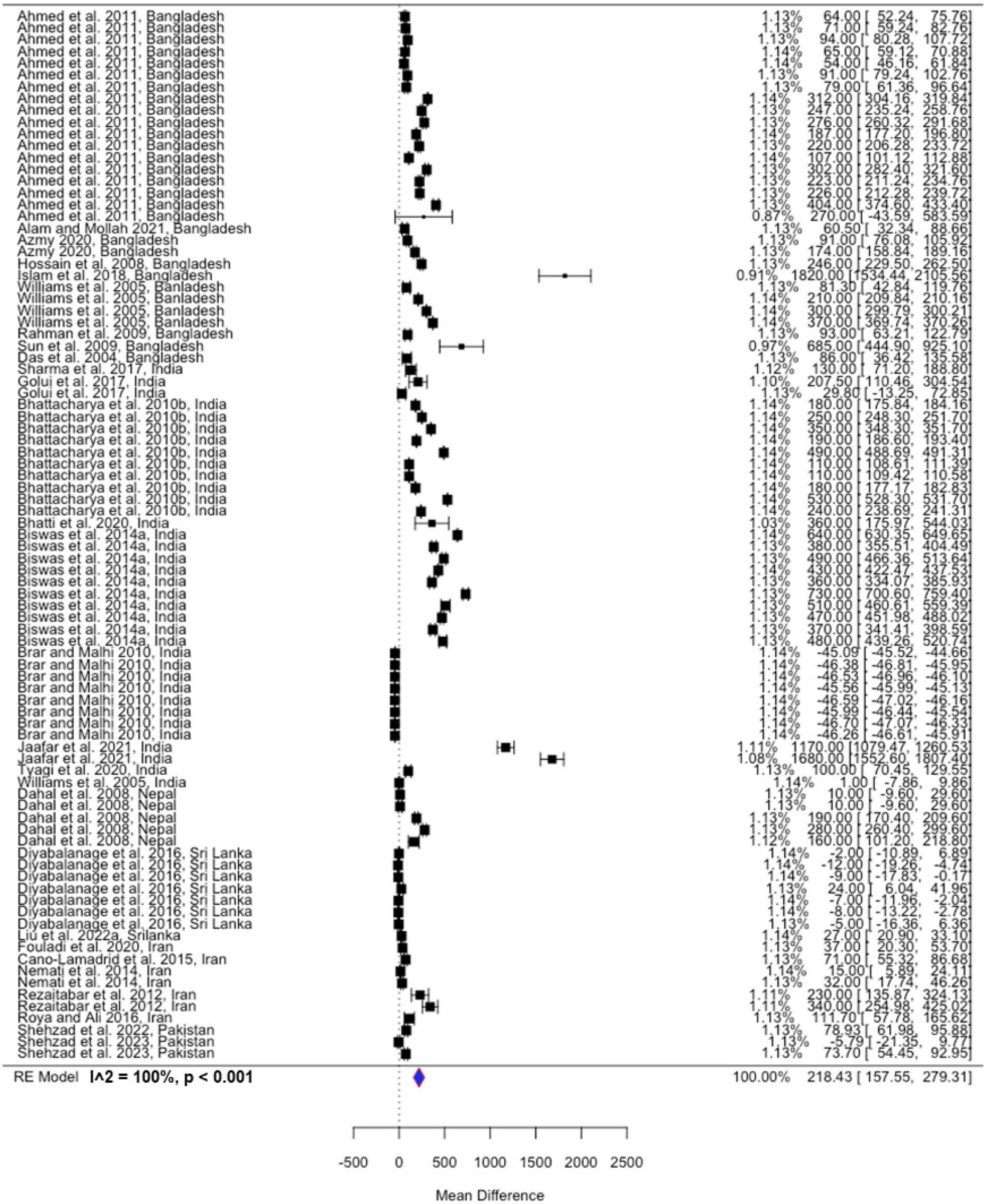

Fig. 3 Forest plot showing the weighted mean difference of total arsenic concentration in rice grain between study level and marginal level with their respective confidence intervals and weight in the meta-analysis together with the heterogeneity statistics in South Asia (SA)

overall summary weighted mean value of 218.43 μg kg^{-1} (95% Confidence Interval: 157.55 to 279.31) of arsenic in rice grain was statistically significant ($p < 0.001$). In fact, it is marginally above the permissible limit of 0.2 mg kg^{-1}[26]. An inconsistency index of 100% indicated significant heterogeneity in the data set which is due to the geographical distribution of paddy-growing areas in the different countries of the SA region. Non-overlapping of the effect sizes with the zero effect line of the majority of rice samples of Bangladesh, India, Nepal, Iran, and Pakistan was observed. At some locations, contamination might be due to the extensive use of arsenic-contaminated water from shallow tube wells for irrigation of paddy rice [78•], and some areas might have been contaminated by mining and industrial activities [79]. In contrast, the 95% confidence interval crosses the line of no effect in the case of samples from Sri Lanka. Figures 4 and 5 reveal that the overall summary weighted mean for arsenic in rice grain of SEA (118.61 μg kg^{-1}, 95% CI: 95.79 to 141.43) and EA (128.01 μg kg^{-1}, 95% CI: 77.44 to 178.58) is statistically significant ($p < 0.001$). It is lower than the permissible limit as prescribed by WHO [26]. Similarly, significant heterogeneity in data was observed at 99.55% and 99.93% for SEA and EA, respectively.

Carcinogenic Risk

A carcinogenic risk assessment for adults and children consuming rice in the SA, SEA, and EA regions was

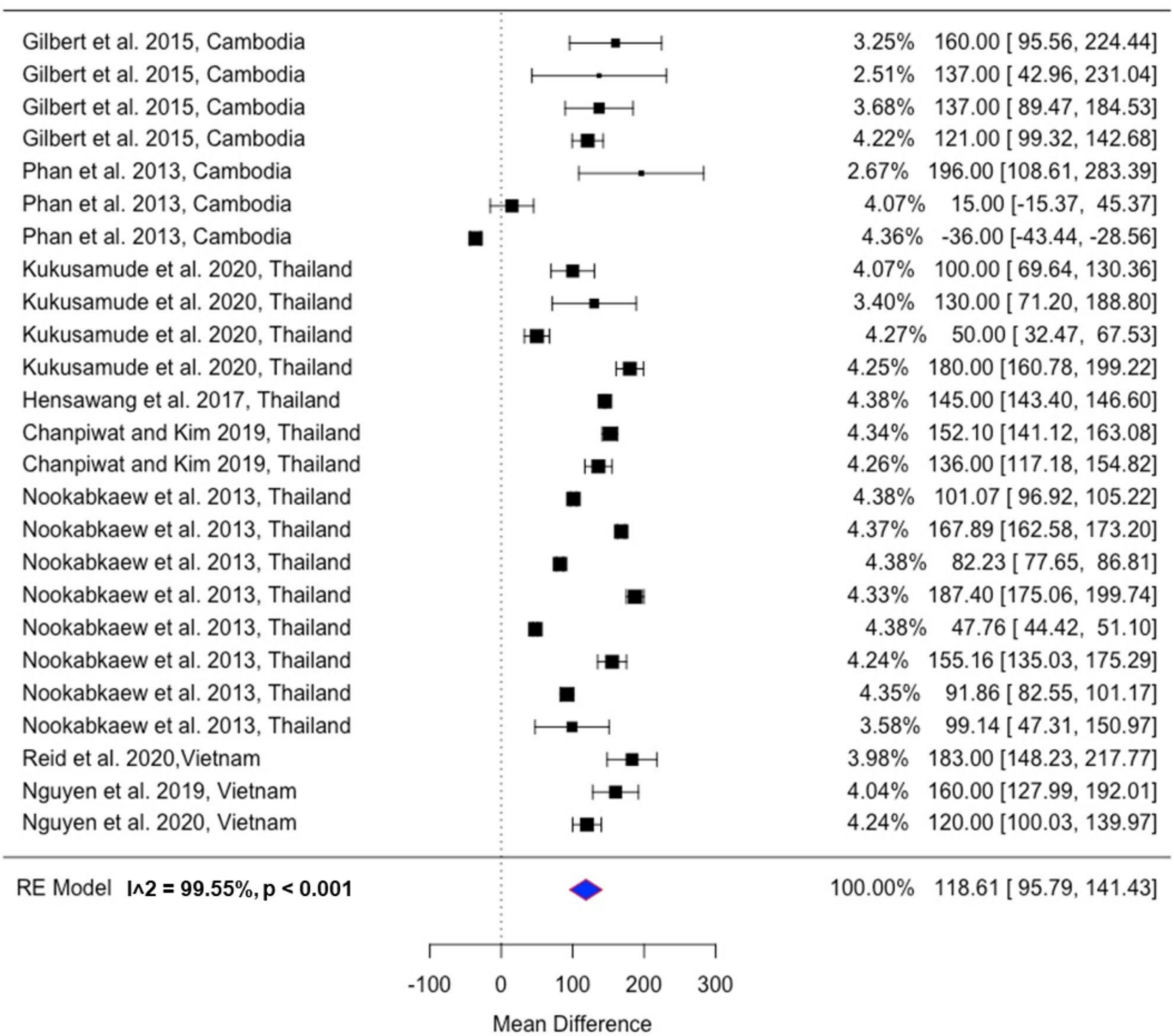

Fig. 4 Forest plot showing the weighted mean difference of total arsenic concentration in rice grain between study level and marginal level with their respective confidence intervals and weight in the meta-analysis together with the heterogeneity statistics in South East Asia (SEA)

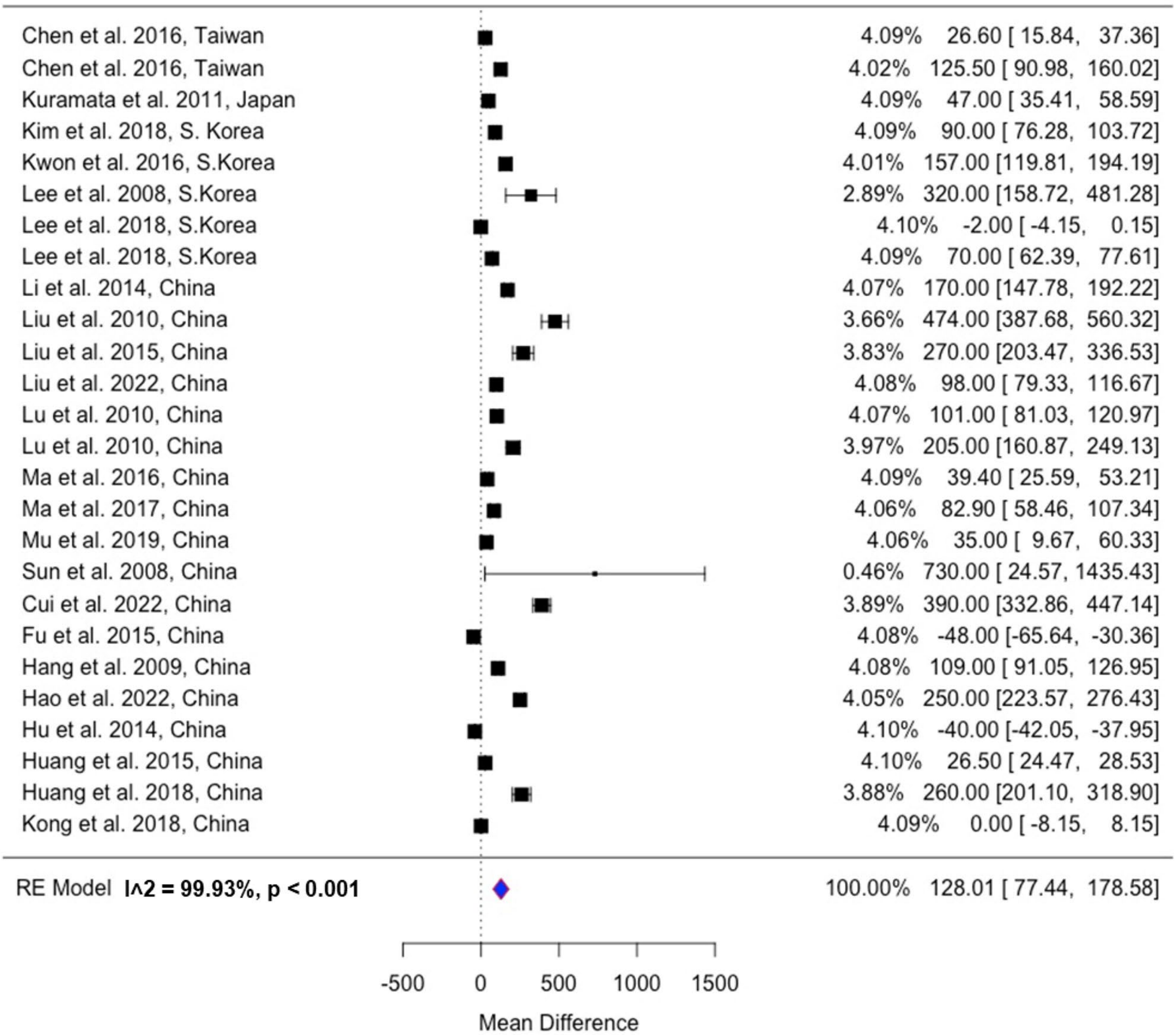

Fig. 5 Forest plot showing the weighted mean difference of total arsenic concentration in rice grain between study level and marginal level with their respective confidence intervals and weight in the meta-analysis together with the heterogeneity statistics in East Asia (EA)

executed (Table S2). Like inorganic arsenic content in rice grain, heterogeneous distribution of the CR value for adults was observed from the box plot with data distribution curve (Fig. 6). The average CR value has been found to be 8×10^{-4} (range: 1×10^{-4} to 5×10^{-3}) for SA, 5×10^{-4} (1×10^{-4} to 7×10^{-4}) for SEA, and 6×10^{-4} (range: 1×10^{-4} to 2×10^{-3}) for EA. These values markedly exceeded the prescribed safe limit of 1×10^{-6} and indicated that the grain produced and sold in these three regions of Asia poses a severe cancer risk to adults. Data on cancer risk for children also exceeded the critical limit of 1×10^{-6} (Fig. 7). The mean CR value in these regions has been observed as 3×10^{-4} (range: 3×10^{-5} to 2×10^{-3}) for SA, 1×10^{-4} (2×10^{-5} to 2×10^{-5}) for SEA, and 1×10^{-4} (range: 4×10^{-5} to 7×10^{-4}) for EA. The SAMOE value for arsenic toxicity due to rice consumption in SA, SEA, and EA showed the risk levels of class 4 (moderate to high) or class 3 (low risk) depending on the rice arsenic concentration (Fig. 8). The mean SAMOE value was 0.282 ± 0.254 for SA, 0.284 ± 0.278 for SEA, and 0.280 ± 0.172 for EA. It is well established that rice is the largest source of inorganic arsenic in the human diet. Estimates showed that about 200 million people have elevated amounts of inorganic arsenic in their water, while half the world consumes rice as a dietary staple [80]. Compared to the countries of Europe and the USA, Bangladesh, India, and China have documented both elevated arsenic levels in rice and populations who eat large amounts of rice.

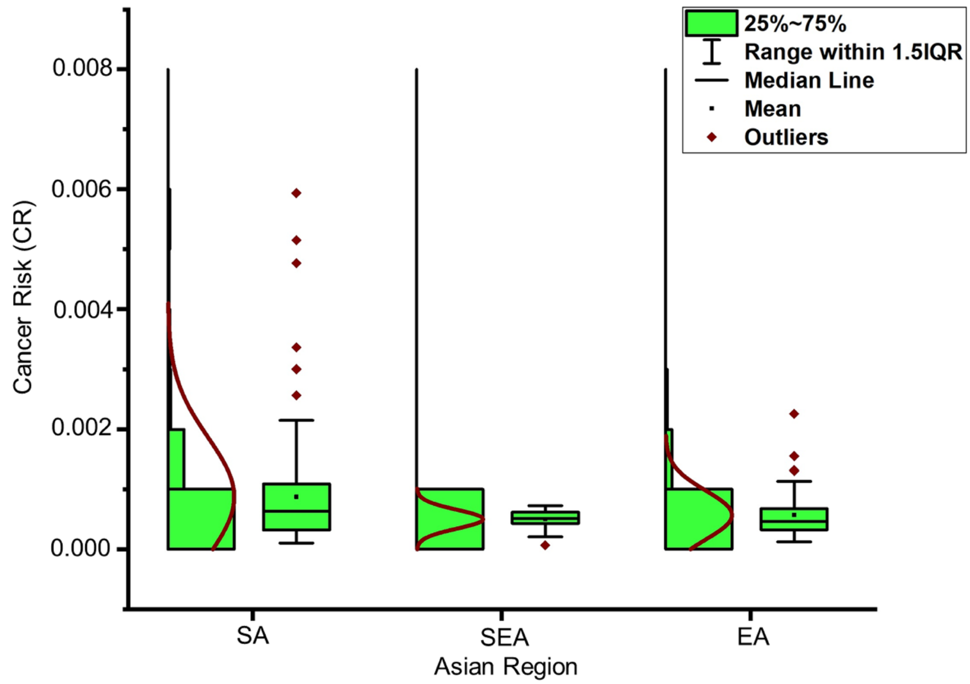

Fig. 6 Box plot with data distribution curve showing the comparative distribution of possible carcinogenic risk in adults due to consumption of arsenic-contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions. The US EPA suggests a safe limit of 10^{-6} for human health

In American rice samples, the median total arsenic was 0.25 mg kg^{-1}, but inorganic arsenic varied only between 0.05 and 0.15 mg kg^{-1}. In Chinese rice, the median total arsenic was lower, 0.14 mg kg^{-1}, but inorganic arsenic showed greater variation, reaching larger levels, between 0.07 and 0.38 mg kg^{-1}. Cancer rates among people were earlier predicted as 1 per 10,000 people in Italy and the USA, 7 per 10,000 in India, 15 per 10,000 in China, and 22 per 10,000 in Bangladesh due to inorganic arsenic being consumed through rice [81]. Several researchers discretely calculated the carcinogenic risk due to the consumption of rice grain mainly in India and Bangladesh [60–62, 78, 82, 83]. In the present study, such large-scale regions were considered to calculate the carcinogenic risk,

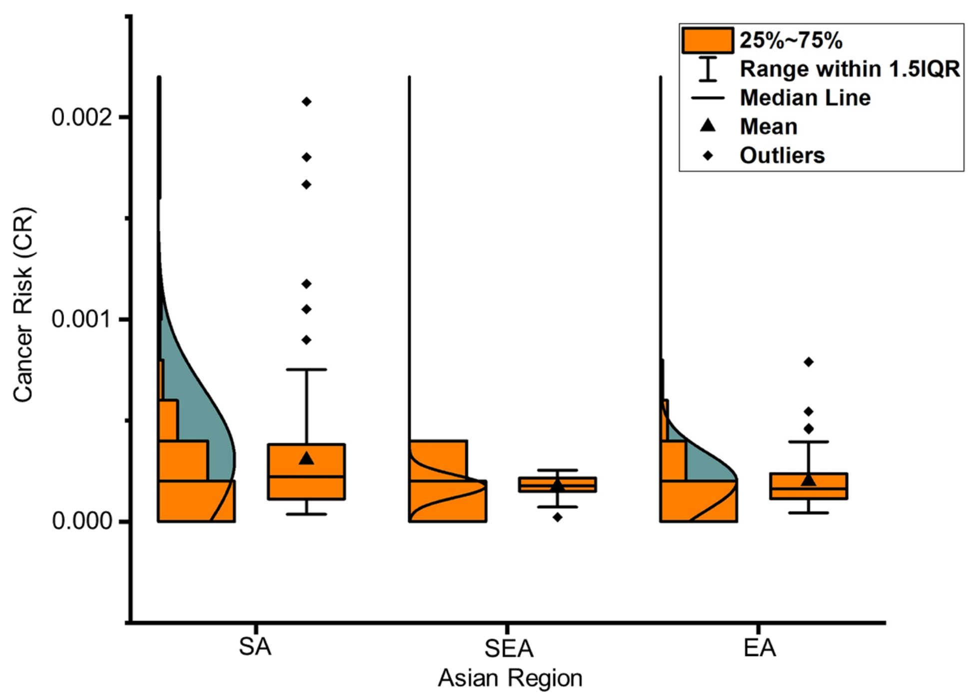

Fig. 7 Box plot with data distribution curve showing the comparative distribution of possible carcinogenic risk in children due to consumption of arsenic-contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions. The US EPA suggests a safe limit of 10^{-6} for human health

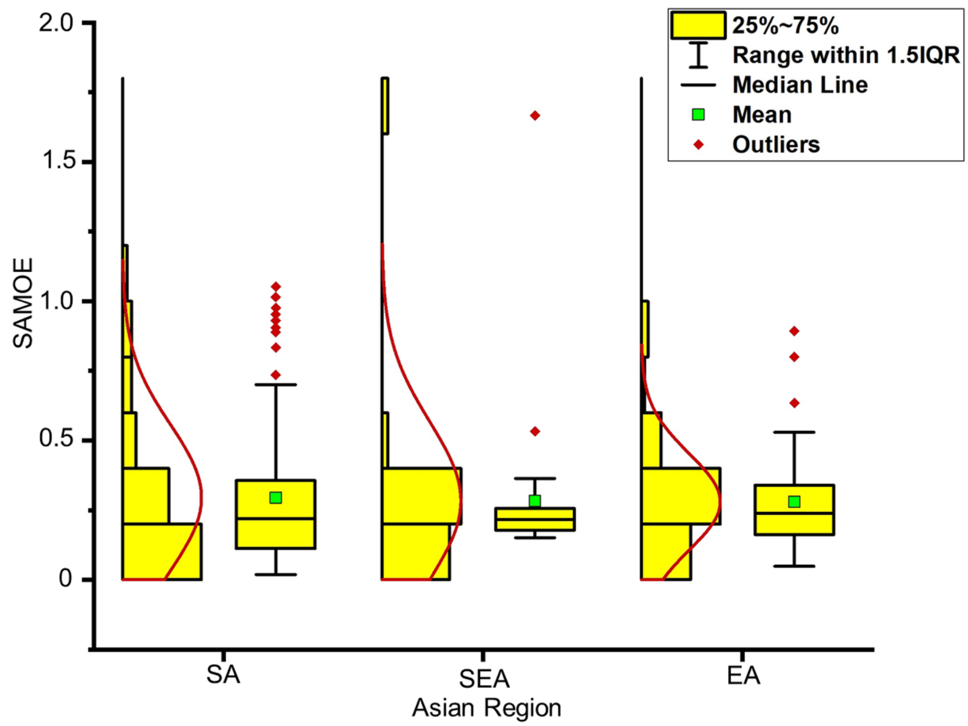

Fig. 8 Box plot with data distribution curve showing comparative distribution of SAMOE in adults due to consumption of arsenic-contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions

which is unique. The CR value between 10^{-6} and 10^{-4} also may be acceptable according to the US EPA criteria, although this range is ambiguous and may require a case-specific judgment regarding the acceptability of a particular risk [84]. To judge the acceptability of this cancer risk, it would have been prudent to compare the risk with background cancer risks in the three regions, but that may not be possible. The average cancer risk in rice grain grown and sold in the South Asian region is the highest followed by South East and East Asian regions. In this review article, rice grain data were analyzed from South Asian countries like Iran, Nepal, Pakistan, Sri Lanka, Bangladesh, and India. The transfer of arsenic in rice grain is well established in Bangladesh and India [14, 85]. At the same time, there are also alarmingly large amounts of arsenic rice grain in East and South East Asian countries like Cambodia, Indonesia, Thailand, Vietnam, South Korea, North Korea, China, and Japan. This analysis indicates that new management options should be implemented in rice-growing soils of these regions to restrict the transfer of arsenic from soil to plant and, thus, to the human body. The assessment of human health using cancer risk as a measure is a better way to convince policymakers, funding agencies, and the general public for necessary actions in these Asian regions. Although the first report of poisoning food materials with arsenic was published four or five decades ago, an effective solution to this burning human health problem remains elusive. Researchers have already published several papers on the management and remediation aspects of arsenic-contaminated soils. The time has come to think about fixing the critical limit of bioavailable arsenic in the soil for the safe cultivation of crops (rice) to ensure human health is safe. Our analysis has shown that the upper critical limit set by CODEX for arsenic in rice grain is not adequate to protect people's health. While comparing the effectiveness of the CODEX limit with that assessed in terms of CR, it is clear that in most of the rice grain samples, the critical value of CR ($> 10^{-6}$) exceeded for arsenic, whereas the CODEX value in those rice grain samples was within the safe limit, i.e., < 0.2 mg kg^{-1}.

Non-carcinogenic Risk

The HQs for human rice consumption in these three regions were calculated (Fig. 9). The HQ was 4.526 ± 5.118 for SA, 2.599 ± 0.801 for SEA, and 2.954 ± 2.088 for the EA region, and they are far above the safe limit of HQ of 1 or 0.5. It is evident that the hazard quotient value for rice grain was highest in the SA region followed by the SEA and EA regions. Assessment of non-carcinogenic risks as computed here is not complete because arsenic input to humans may also originate from other routes like consumption of food materials other than rice and direct ingestion of soil. The cumulative HQ will be far above the critical limit of 1 if other routes of entry of arsenic into the human body are considered.

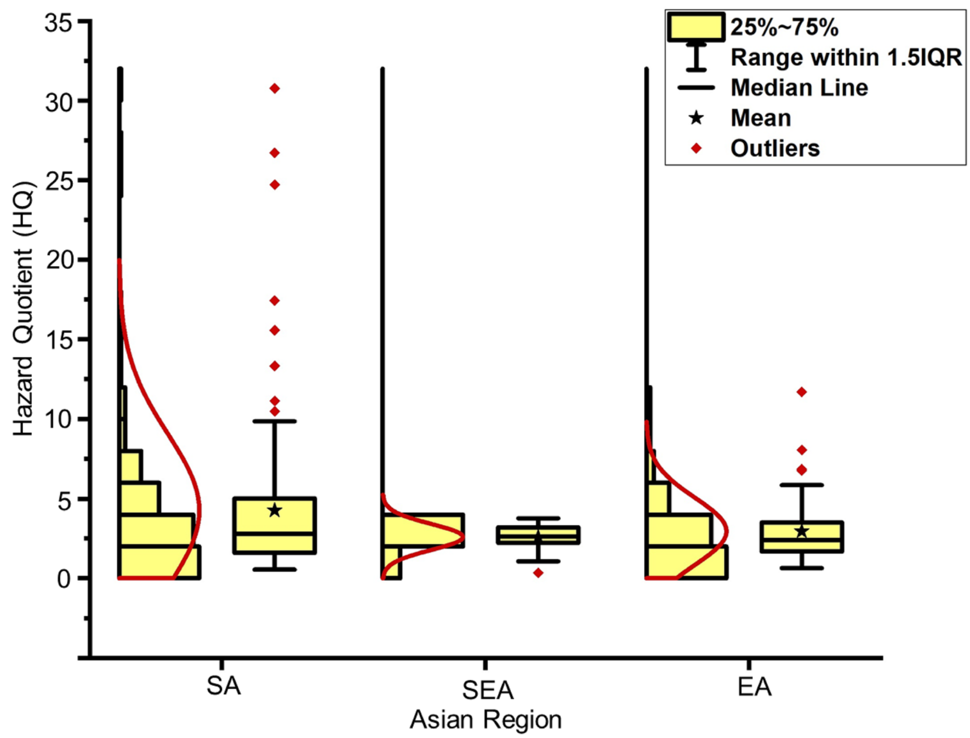

Fig. 9 Box plot with data distribution curve showing comparative distribution of possible hazard quotient in adults due to consumption of arsenic-contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions. The US EPA suggests a safe limit of 1 for human health

Appraisal of Arsenic Menace in the Soil–Plant-Human Continuum

Modeling for Prediction of Arsenic Content in Crop Plants

The phytoavailability of arsenic is governed by several factors including physical, chemical, and biological properties of soil, plant type and variety, and environmental conditions. The mobility and uptake of arsenic from soil to plant are governed by the interactions occurring in the rhizospheric soil environment and the roots. Arsenic transfer from soil to plant is affected by the presence of iron, manganese, aluminum, organic matter, clay, and phosphate in soil and the soil pH [14, 86–88]. Given the complexity of the processes governing arsenic uptake by plants, it is challenging to develop a model which can accurately predict the arsenic uptake and arsenic content in plants. Two types of models (mechanistic and transport models) can be used to predict arsenic uptake and content in plants. The mechanistic model considers the complex interactions taking place between the soil environment and plant root system. The sorption isotherm and sorption kinetic models are the most commonly used mechanistic variants employed to predict arsenic uptake by plants. The biosorption of arsenic by *Hydrilla verticillata* (a submerged aquatic plant) was reported by Nigam et al. (2013) [89], and they used the Langmuir isotherm and pseudo-second-order kinetic models to represent arsenic adsorption/removal from water, indicating the dominance of the chemisorption process and strong bonding of arsenic with the plant biomass. These models are very useful in assessing the performance of various phyto-remediating plants for arsenic removal from water. However, the complexity of modeling increases when soil comes into the context as multicomponent reactions need to be considered at the same time. Therefore, solubility speciation models are widely employed to consider the effect of solid phase interaction with soil solution.

An integrated solubility free ion activity model (FIAM) has been used to predict the uptake of arsenic by rice crop based on predicted free ion activity in soil solution [14, 88]. The model suggests that the uptake of arsenic is controlled by free ion activity in the soil pore water. Soil properties like pH, organic carbon, and extractable arsenic have served as input parameters to run this model [14, 88]. A transfer factor (TF) is defined as the ratio of arsenic concentration in the plant [M_{Plant}] to arsenic ion activity in soil pore water (M^{n-}) (Eq. 6) [90].

$$\mathrm{TF} = \frac{[\mathrm{M}_{\text{Plant}}]}{(\mathrm{M}^{\mathrm{N}-})} \tag{6}$$

The M^{n-} can be predicted from a pH-dependent Freundlich equation [70]. Arsenic uptake by plant can be calculated by combining Eq. 6 with M^{n-} as follows (details in supplementary information, section A1):

$$\log\,[\mathrm{M}_{\text{plant}}] = \mathrm{C} + \beta_1\mathrm{pH} + \beta_2\,\log[\mathrm{M}_c] \tag{7}$$

where C, β_1, and β_2 are coefficients associated with arsenic and plants. Microsoft Excel Solver was used to parameterize

Eq. 7 through non-linear error minimization [14]. For the calculation of the error sum of squares, numerical data on plant metalloid content were used rather than logarithmic data [14, 88]. As high as 78% variation in arsenic content in rice grain could be explained by the solubility-FIAM model for samples collected from the arsenic-affected region in Malda, West Bengal [14]. The model parameters were reported as $C = -2.30$, $\beta_1 = -0.03$, and $\beta_2 = 0.80$ (Figure S1). In another study, solubility-FIAM was also tested in soil subjected to long-term sewage irrigation to predict the transfer of arsenic from soil to rice crop [88]. In this study, as much as 36% variation in arsenic content in rice grain could be explained by the solubility-FIAM model where model parameters were reported as $C = -4.15$, $\beta_1 = 0.28$, and $\beta_2 = 0.68$. Such prediction has been considered very good for routine risk assessment of arsenic-contaminated soil based on important soil chemical properties like pH, extractable arsenic, and organic carbon. Datta and Young (2005) reported that parameterization of solubility, based on actual free ion activity, would improve the predictability of the model [91]. Literature has reported both positive and negative effects of pH on solubility and mobility of arsenic as seen from the model parameter β_1 value. On the other hand, model parameter β_2 is negatively related with the solubility of arsenic in soil. Consequently, mobility of arsenic is generally reduced with an increase in organic matter content in soil through organo-arsenic chelation [92]. In addition to rice crop, the efficacy of different models such as regression model (linear and multiple), logarithmic model, and solubility-FIAM was compared for predicting arsenic content in wheat grains and the risk involved when humans consume them [93]. The solubility-FIAM model has been found to offer a better prediction ($R^2 = 0.97$) of the arsenic content in grains and associated human health risks. The variability in arsenic uptake by wheat grain was explained by multiple regression, linear regression, and logarithmic regression model to the extent of 86%, 76%, and 70%, respectively [93•]. Logarithmic transformation of data reduced the predictability of the regression model by 6%, which indicates that the relationship between extractable arsenic in soil and arsenic content in wheat grain is linear in nature within the observed range of extractable arsenic in experimental soil. Based on these models, it is clear that the arsenic content in wheat grain is mainly affected by Olsen extractable arsenic in soil; inclusion of other soil properties like pH and organic C in multiple regression model enhanced the predictability up to 86%. Apart from the higher prediction coefficient, the solubility free ion activity model had an edge over empirical regression models because the former is not purely empirical. Instead, it is semi-mechanistic in nature, where the assumption had been made that extractable arsenic is adsorbed on oxidizable organic C. For rice, the solubility-FIAM model was validated with the arsenic data set collected from Nadia (West Bengal, India). In the future, other important soil parameters like clay content and available Fe, Al, Mn, and phosphate content should be incorporated as model parameters to enhance the model's performance. Currently, total arsenic in soil (10 to 20 mg kg^{-1}) has been used as a simple index of arsenic hazard globally [94]. However, a poor correlation between total arsenic in soil and plant arsenic was noted. This is because total arsenic in the soil does not consider how its availability is changed by soil properties. For example, arsenic uptake by plants (and, hence, its accumulation in grains) is affected by soil properties like pH, redox potential, organic matter content, and the presence of other ions in the soil pore water [14]. An attempt has been made to prescribe a safe limit of bioavailable arsenic in soil based on (i) solubility of arsenic in soil (controlled by soil chemical properties); (ii) arsenic content in rice grain; and (iii) human health hazard (consumption of food) [14, 88, 91, 95, 96•]. Given that people's food habits vary based on geographical location, environmental circumstances, and culture, a common (global) permissible limit of arsenic in rice grain will not have much practical significance. However, prescribing a safe limit of plant-available arsenic in the soil will be of importance for appraising the suitability of agricultural land for food crop cultivation and managing arsenic-contaminated soil [14]. For fixing the safe limit of bioavailable arsenic in soil at particular pH and organic carbon content, the critical value of HQ is taken as 0.5. Hence, a ready reckoner can be developed to compute the permissible limit of bioavailable arsenic in soils based on pH and organic carbon content. These permissible limits are based on the predicted HQ by solubility-FIAM. In the arsenic-contaminated area of Malda (West Bengal, India), the safe limit of bioavailable arsenic in soil would be 0.43 mg kg^{-1} for rice cultivation if the soil pH and organic carbon levels are 7.5 and 0.50%, respectively. However, the permissible limit of bioavailable arsenic in soil would be 0.54 mg kg^{-1} if soil pH is 8.5 and organic carbon is 0.75% [14] (Figure S2). In another study involving long-term sewage irrigated soils, the permissible limit of bioavailable arsenic would be 0.27 mg kg^{-1} for cultivation of rice crop, assuming that pH and organic carbon content are 6.0 and 0.25%, respectively. In contrast, the critical limit of bioavailable of arsenic would be 3.62 mg kg^{-1}, if pH and organic carbon are 8.0 and 0.5%, respectively [88]. For this reason, the ready reckoner can serve to fix the safe limit of bioavailable arsenic based on model parameters. Safe limit of bioavailable arsenic in soil varied widely with changes in organic matter content, whereas such variation was not seen with pH [14]. The probable reason for no effect of pH might be the initial pH of the study area. Most studies were conducted in areas having a narrow soil pH range, i.e., alkaline soil. This finding strengthens the argument that total arsenic in soil is not a good index of arsenic hazard. Moreover, this emphasizes the importance of fixing a safe limit of bioavailable arsenic in soil.

Future Outlook/Perspectives

Growing rice in the arsenic-contaminated soil is a major route of human arsenic exposure, and that may lead to major public health issues. So, production of rice with arsenic in it is vital for food security. It is imperative to categorize the possible factors affecting bioavailability of arsenic from soil and water in the rice-growing regions in the world. This is critical so that proper prevention, remediation, and management plans can be devised and implemented.

Risk Mapping

Regional-level arsenic risk mapping throughout the world is urgently required for successful policy intervention and resource allocation to alleviate the problem and help the affected population and communities. While there are other contaminants which are ingested with food, arsenic in staple food rice is of major concern. This study specifically discussed the risks due to arsenic present in rice. However, it is now known that other crops (e.g., wheat, red spinach leaf, arum leaf, coriander leaf, potato, radish, beans, brinjal, turnip, cauliflower, and carrot) which are part of the human diet also accumulate arsenic [78, 97–100]. Wheat samples collected from the arsenic-contaminated areas of Nadia district (West Bengal, India) contained 59.2 μg arsenic kg^{-1} (range 3–285 μg kg^{-1}; $n=55$) [78]. Leafy vegetables in Bangladesh were reported to contain arsenic in the 130–790 μg kg^{-1} range [100], and one report recorded a very range of 0.1–3.99 mg kg^{-1} [97]. The range of arsenic in leafy vegetables (spinach, coriander, and peppermint) collected in Pakistan was 0.90–1.20 mg kg^{-1} [98]. Wheat flour samples collected from arsenic-exposed Bihar state of India revealed very large amounts of arsenic (mean 49.8 μg kg^{-1}, range 3.59–448 μg kg^{-1}, $n=58$) [99]. It will be important that the health risks from arsenic in rice and other food items are combined with the risks from arsenic-contaminated drinking water. Such risks should not only be evaluated and mapped for the human population but also for the socio-economically important animals, for instance, cattle, horse, goat, chicken, duck, and fish.

Connecting Risks to Ground Realities

The macro- and micro-level risk calculations should be validated with ground data from affected areas. It may be difficult to pinpoint the occurrences of cancer and other health issues in a particular population to arsenic in food and drinking water alone; nevertheless, documentation of actual cancer and other disease prevalence in arsenic-contaminated areas is vital. For example, 212 (4.35%) cases of skin cancer and 38 (0.78%) cases of internal cancers were detected among 4865 cases of arsenicosis studied in arsenic-affected villages of West Bengal (India) [101]. In another study, 80 (43.96%) cases out of 182 participants showed typical arsenicosis features characterized by pigmentation and keratosis including skin cancer (Table S3) [14]. In a macro-level study, out of 10,469 people examined, the prevalence rate of arsenicosis was in fact 15.43% [102]. In the same investigation, chronic lung disease was detected in 207 (12.81%) cases while peripheral neuropathy was reported in 257 (15.9%) cases. It will be important to use similar data to validate models used for risk assessment for the same population.

Risk Assessment of Arsenic

The assessment of health risk associated with any toxicant entails multiple steps that include (1) identifying the sources and receptors of risks, (2) exposure assessment, (3) toxicity analysis, and (4) risk characterization [63]. The assessment of health risks can be deterministic or probabilistic. It would be prudent to discuss the two methods and evaluate the relative suitability of either of the methods for arsenic risk assessment.

The deterministic method yields a maximum exposure estimate based on the level of contaminant, which is then compared to reference values for health impacts and is used in location-specific risk assessments. There are, however, considerable uncertainties in exposure pathways for health risk assessment [103]. For example, arsenic in the environment can be introduced to the human body via oral ingestion, cutaneous contact, and inhalation, and there are multiple media for exposure including water, foods, air, and soil. Moreover, many site- or chemical-specific characteristics go into calculating arsenic exposure frequency and durations in the sensitive population. The deterministic methods may underestimate or overestimate the threats [103].

The probabilistic risk assessment (PRA) or uncertainty analysis incorporates more of the available data, and thus, probabilistic analyses address the primary limitations of deterministic (point) estimates. The probabilistic approaches deal with uncertainty and variability rationally and scientifically. The single most important aspect influencing the outcomes of a PRA is the choice of probability distributions for input data [104, 105]. The PRA process helps in establishing risk distributions and assessing the impact of each exposure route or input parameter on the total risks. Based on the collective variation of model inputs, probabilistic analysis determines the variation or uncertainty in an output function. Unlike the deterministic "point" approach, the probabilistic approach determines the distribution of essential variables (e.g., chemical concentrations, frequency, and body weight) to indicate their uncertainty. The output function's variability is determined by the variability of the model inputs and is represented as a probability distribution.

Researchers have used both deterministic and probabilistic methods for human health risk prediction due to arsenic present in our food and water [103, 106–108]. The authors advocate the use of the probabilistic method given its inclusiveness of the available data and recognition of the contribution of each parameter to the final output. Saha et al. (2017) reported that deterministically estimated total cancer risk (TCR) via water exceeded the safe limit of 1×10^{-6} for adult and children [85]. However, probabilistically estimated mean TCR values were less than 1×10^{-6} [107]. The deterministic and probabilistic approaches for assessing risks from arsenic from contaminated drinking water have been compared, and results showed an overestimation of risks when deploying the deterministic method [108].

Conclusions

Arsenic contamination in the groundwater-soil-plant continuum is a cause of major concern in rice-consuming countries because it greatly affects human health. While the major pathway of humans' exposure to arsenic is arsenic-contaminated drinking water, consumption of staple foods (particularly rice) grown on arsenic-contaminated soil is often ignored. Arsenic-contaminated groundwater is often used as irrigation water, and arsenic finds its way to the food grains. The relative distribution of total arsenic level in rice grain grown and sold in the South Asian region is the highest followed by South East and East Asian region. The human health risks due to rice consumption in three Asian regions are investigated in this study, and the findings on the potential carcinogenic and non-carcinogenic risks based on literature available data were calculated. The cancer risk in the Asian region was found to be in the range 7×10^{-4} to 5×10^{-3}, which is well above the acceptable probability level of 1×10^{-6}. Meanwhile, the non-carcinogenic risk measured as hazard quotient (HQ) ranged from 0.34 to 30.7 while the acceptable HQ is <1. The authors would like to emphasize that plant uptake depends on bioavailability of arsenic, and assessing its bioavailability in the soil–plant system for predicting human health risk due to food chain contamination requires elaborate experimentation. Also, this study reviewed the usage of a modeling approach involving free ion activity of arsenic in soil pore water, in order to estimate the amount of arsenic in rice grain. In the future, such model prediction will help in routine risk assessments of arsenic-contaminated soils, and protocols can be successfully devised and implemented to fix the safe limit of bioavailable arsenic to grow rice.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40726-023-00279-2.

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Data Availability All data extracted from studies included in this review is available in the electronic supplementary material.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflict of interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Mehmood A, Hayat R, Wasim M, Akhtar MS. Mechanisms of arsenic adsorption in calcareous soils. J Agric Biol Sci. 2009;1(1):59–65. Available from: https://agris.fao.org/agris-search/search.do?recordID=PK2013000993.
2. Mukherjee A, Fryar AE. Deeper groundwater chemistry and geochemical modeling of the arsenic affected western Bengal basin, West Bengal. India Appl Geochem. 2008;23(4):863–94. https://doi.org/10.1016/j.apgeochem.2007.07.011.
3. Chakraborti D, Rahman MM, Das B, Murrill M, Dey S, Mukherjee SC, et al. Status of groundwater arsenic contamination in Bangladesh: a 14-year study report. Water Res. 2010;44(19):5789–802. https://doi.org/10.1016/j.watres.2010.06.051.
4.• Biswas JK, Warke M, Datta R, Sarkar D. Is arsenic in rice a major human health concern. Curr Pollut Rep 2020;6(2):37–42.https://doi.org/10.1007/s40726-020-00148-2. **This review offers the importance of arsenic contamination in rice grain, as well as valuable insights into the impact arsenic exposure on human health**.
5. Chung J-Y, Yu S-D, Hong Y-S. Environmental source of arsenic exposure. J Prev Med Public Health. 2014;47(5):253. https://doi.org/10.3961/jpmph.14.036.
6. Sarkar D, Datta R, Sharma S. Fate and bioavailability of arsenic in organo-arsenical pesticide-applied soils.: part-I: incubation study. Chemosphere. 2005;60(2):188–95.https://doi.org/10.1016/j.chemosphere.2004.11.060.

7.• Shaji E, Santosh M, Sarath K, Prakash P, Deepchand V, Divya B. Arsenic contamination of groundwater: a global synopsis with focus on the Indian Peninsula. Geoscifront. 2021;12(3):101079. https://doi.org/10.1016/j.gsf.2020.08.015. **This review presents an overview of the current scenario of arsenic contamination of groundwater in various countries across the globe with an emphasis on the Indian Peninsula**.
8. Huq ME, Fahad S, Shao Z, Sarven MS, Khan IA, Alam M, et al. Arsenic in a groundwater environment in Bangladesh: occurrence and mobilization. Journal of environmental management. 2020;262:110318. https://doi.org/10.1016/j.jenvman.2020.110318.
9. Chakraborti D, Rahman MM, Chatterjee A, Das D, Das B, Nayak B, et al. Fate of over 480 million inhabitants living in arsenic and fluoride endemic Indian districts: magnitude, health, socio-economic effects and mitigation approaches. J Trace Elem Med Biol. 2016;38:33–45. https://doi.org/10.1016/j.jtemb.2016.05.001.
10.• Mukherjee A, Sarkar S, Chakraborty M, Duttagupta S, Bhattacharya A, Saha D, et al. Occurrence, predictors and hazards of elevated groundwater arsenic across India through field observations and regional-scale AI-based modeling. Sci Total Environ. 2021;759:143511. **This paper estimated the population exposed to groundwater arsenic across the South Asian countries including India.**
11. Smith AH, Lingas EO, Rahman M. Contamination of drinking-water by arsenic in Bangladesh: a public health emergency. Bulletin of the World Health Organization. 2000;78(9):1093–103. Available from: https://apps.who.int/iris/handle/10665/268217.
12. Palma-Lara I, Martínez-Castillo M, Quintana-Pérez J, Arellano-Mendoza M, Tamay-Cach F, Valenzuela-Limón O, et al. Arsenic exposure: a public health problem leading to several cancers. Reg Toxicol Pharmacol. 2020;110:104539. https://doi.org/10.1016/j.yrtph.2019.104539.
13. Biswas A, Deb D, Ghose A, Du Laing G, De Neve J, Santra SC, et al. Dietary arsenic consumption and urine arsenic in an endemic population: response to improvement of drinking water quality in a 2-year consecutive study. Environ Sci Pollut Res. 2014;21(1):609–19. https://doi.org/10.1007/s11356-013-1947-8.
14.•• Golui D, Mazumder DG, Sanyal S, Datta S, Ray P, Patra P, et al. Safe limit of arsenic in soil in relation to dietary exposure of arsenicosis patients from Malda district, West Bengal-a case study. Ecotoxicology and environmental safety. 2017;144:227–35. https://doi.org/10.1016/j.ecoenv.2017.06.027. **This paper described the conceptual framework of fixing the toxic limit of arsenic in soils with respect to soil properties and human health using FIAM**.
15. Meharg AA. Arsenic in rice–understanding a new disaster for South-East Asia. Trends Plant Sci. 2004;9(9):415–7. https://doi.org/10.1016/j.tplants.2004.07.002.
16. Ahmad A, Bhattacharya P. Arsenic in drinking water: is 10 μg/L a safe limit. Curr Pollut Rep. 2019;5(1):1–3. https://doi.org/10.1007/s40726-019-0102-7.
17. World Health Organization. Exposure to arsenic: a major public health concern. Geneva. 2010. Available from: https://www.who.int/publications/i/item/WHO-CED-PHE-EPE-19.4.1.
18. Martinez VD, Vucic EA, Becker-Santos DD, Gil L, Lam WL. Arsenic exposure and the induction of human cancers. Journal of toxicology. 2011;2011. https://doi.org/10.1155/2011/431287.
19. Yoshida T, Yamauchi H, Sun GF. Chronic health effects in people exposed to arsenic via the drinking water: dose–response relationships in review. Toxicol Appl Pharmacol. 2004;198(3):243–52. https://doi.org/10.1016/j.taap.2003.10.022.
20. Melkonian S, Argos M, Pierce BL, Chen Y, Islam T, Ahmed A, et al. A prospective study of the synergistic effects of arsenic exposure and smoking, sun exposure, fertilizer use, and pesticide use on risk of premalignant skin lesions in Bangladeshi men. Am J Epidemiol. 2011;173(2):183–91. https://doi.org/10.1093/aje/kwq357.
21. Celik I, Gallicchio L, Boyd K, Lam TK, Matanoski G, Tao X, et al. Arsenic in drinking water and lung cancer: a systematic review. Environ Res. 2008;108(1):48–55. https://doi.org/10.1016/j.envres.2008.04.001.
22. Gibb H, Haver C, Gaylor D, Ramasamy S, Lee JS, Lobdell D, et al. Utility of recent studies to assess the National Research Council 2001 estimates of cancer risk from ingested arsenic. Environ Health Perspect. 2011;119(3):284–90. https://doi.org/10.1289/ehp.1002427.
23. Milton AH, Hasan Z, Shahidullah S, Sharmin S, Jakariya M, Rahman M, et al. Association between nutritional status and arsenicosis due to chronic arsenic exposure in Bangladesh. Int J Environ Health Res. 2004;14(2):99–108. https://doi.org/10.1080/0960312042000209516.
24. Mazumder DNG, Haque R, Ghosh N, De BK, Santra A, Chakraborty D, et al. Arsenic levels in drinking water and the prevalence of skin lesions in West Bengal. India Int J Epidemiol. 1998;27(5):871–7. https://doi.org/10.1093/ije/27.5.871.
25. Jomova K, Jenisova Z, Feszterova M, Baros S, Liska J, Hudecova D, et al. Arsenic: toxicity, oxidative stress and human disease. J Appl Toxicol. 2011;31(2):95–107. https://doi.org/10.1002/jat.1649.
26. Commission CA. Joint FAO/WHO food standards programme. Report of the 29th session of the codex committee on nutrition and foods for special dietary uses. ALINORM 08/31/26. Draft revised standards for “gluten-free” foods at Step 1 …; 2008. Available from: http://www.ilsijapan.org/English/ILSIJapan/BOOK/Ilsi/ilsi93/No93_p24-31.pdf.
27. Guidance for Industry: action level for inorganic arsenic in rice cereals for infants center for food safety and applied nutrition, U.S. Food and Drug Administration, Docket Number FDA-2016-D-1099; 2020. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-action-level-inorganic-arsenic-rice-cereals-infants.
28. Kuivenhoven M, Mason K. Arsenic toxicity. 2019. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2022 PMID:31082169. Available from: https://pubmed.ncbi.nlm.nih.gov/31082169/.
29. Ma HZ, Xia YJ, Wu KG, Sun TZ, Mumford JL. Human exposure to arsenic and health effects in Bayingnormen, Inner Mongolia. Arsenic Exposure and Health Effects III. Elsevier; 1999. p. 127–31. https://doi.org/10.1016/B978- 008043648–7/50016–9.
30. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Arsenic, metals, fibres and dusts. Lyon (FR): International Agency for Research on Cancer; 2012. (IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, No. 100C.) Arsenic and Arsenic Compounds. Available from: https://www.ncbi.nlm.nih.gov/books/NBK304380/.
31. Yu H-S, Liao W-T, Chai C-Y. Arsenic carcinogenesis in the skin. J Biomed Sci. 2006;13(5):657–66. https://doi.org/10.1007/s11373-006-9092-8.
32. Wei S, Zhang H, Tao S. A review of arsenic exposure and lung cancer. Toxicol Res. 2019;8(3):319–27. https://doi.org/10.1039/c8tx00298c.
33. Ajees AA, Rosen BP. As (III) S-adenosylmethionine methyltransferases and other arsenic binding proteins. Geomicrobiol J. 2015;32(7):570–6. https://doi.org/10.1080/01490451.2014.908983.
34. Cantor K. Drinking water and cancer Cancer Causes Control 8 (3): 292–308. Find this article online. 1997. https://doi.org/10.1023/a1018444902486.
35. Wanibuchi H, Hori T, Meenakshi V, Ichihara T, Yamamoto S, Yano Y, et al. Promotion of rat hepatocarcinogenesis by dimethylarsinic acid: association with elevated ornithine decarboxylase activity and formation of 8-hydroxydeoxyguanosine in the liver. Jpn J Cancer Res. 1997;88(12):1149–54. https://doi.org/10.1111/j.1349-7006.1997.tb00343.x.
36. Matsui M, Nishigori C, Imamura S, Miyachi Y, Toyokuni S, Takada J, et al. The role of oxidative DNA damage in

human arsenic carcinogenesis: detection of 8-hydroxy-2′-deoxyguanosine in arsenic-related Bowen's disease. J Investig Dermatol. 1999;113(1):26–31. https://doi.org/10.1046/j.1523-1747.1999.00630.x.

37. Ruiz-Ramos R, Lopez-Carrillo L, Rios-Perez AD, De Vizcaya-Ruíz A, Cebrian ME. Sodium arsenite induces ROS generation, DNA oxidative damage, HO-1 and c-Myc proteins, NF-κB activation and cell proliferation in human breast cancer MCF-7 cells. Mutation Res/Gen Toxicol Environ Mutagen. 2009;674(1–2):109–15. https://doi.org/10.1016/j.mrgentox.2008.09.021.
38. Lantz RC, Hays AM. Role of oxidative stress in arsenic-induced toxicity. Drug Metab Rev. 2006;38(4):791–804. https://doi.org/10.1080/03602530600980108.
39. Lang CM, Chan CK, Veltri A, Lien W-H. Wnt signaling pathways in keratinocyte carcinomas. Cancers. 2019;11(9):1216. https://doi.org/10.3390/cancers11091216.
40. Li S, Ren Q. Effects of arsenic on wnt/β-catenin signaling pathway: a systematic review and meta-analysis. Chem Res Toxicol. 2020;33(6):1458–67. https://doi.org/10.1021/acs.chemrestox.0c00019.
41. Medda N, De SK, Maiti S. Different mechanisms of arsenic related signaling in cellular proliferation, apoptosis and neo-plastic transformation. Ecotoxicol Environ Saf. 2021;208:111752. https://doi.org/10.1016/j.ecoenv.2020.111752.
42. Weber M, Hellmann I, Stadler MB, Ramos L, Pääbo S, Rebhan M, et al. Distribution, silencing potential and evolutionary impact of promoter DNA methylation in the human genome. Nat Genet. 2007;39(4):457–66. https://doi.org/10.1038/ng1990.
43. Marsit CJ, Karagas MR, Schned A, Kelsey KT. Carcinogen exposure and epigenetic silencing in bladder cancer. Ann N Y Acad Sci. 2006;1076(1):810–21. https://doi.org/10.1196/annals.1371.031.
44. Kouzarides T. Chromatin modifications and their function. Cell. 2007;128(4):693–705. https://doi.org/10.1016/j.cell.2007.02.005.
45. Zhou X, Sun H, Ellen TP, Chen H, Costa M. Arsenite alters global histone H3 methylation. Carcinogenesis. 2008;29(9):1831–6. https://doi.org/10.1093/carcin/bgn063.
46. Jensen TJ, Novak P, Eblin KE, Gandolfi AJ, Futscher BW. Epigenetic remodeling during arsenical-induced malignant transformation. Carcinogenesis. 2008;29(8):1500–8. https://doi.org/10.1093/carcin/bgn102.
47. Filipowicz W, Bhattacharyya SN, Sonenberg N. Mechanisms of post-transcriptional regulation by microRNAs: are the answers in sight? Nat Rev Genet. 2008;9(2):102–14. https://doi.org/10.1038/nrg2290.
48. Calin GA, Croce CM. MicroRNA signatures in human cancers. Nat Rev Cancer. 2006;6(11):857–66. https://doi.org/10.1038/nrc1997.
49. Wang Z, Zhao Y, Smith E, Goodall GJ, Drew PA, Brabletz T, et al. Reversal and prevention of arsenic-induced human bronchial epithelial cell malignant transformation by microRNA-200b. Toxicol Sci. 2011;121(1):110–22. https://doi.org/10.1093/toxsci/kfr029.
50. Cui Y, Han Z, Hu Y, Song G, Hao C, Xia H, et al. MicroRNA-181b and microRNA-9 mediate arsenic-induced angiogenesis via NRP1. J Cell Physiol. 2012;227(2):772–83. https://doi.org/10.1002/jcp.22789.
51. Schneider P, Asch F. Rice production and food security in Asian mega deltas—a review on characteristics, vulnerabilities and agricultural adaptation options to cope with climate change. J Agron Crop Sci. 2020;206(4):491–503. https://doi.org/10.1111/jac.12415.
52. Singh B, Mishra S, Bisht DS, Joshi R. Growing rice with less water: improving productivity by decreasing water demand. Rice improvement. Springer, Cham; 2021. p. 147–70. https://doi.org/10.1007/978-3-030-66530-2_5.
53. Ullah S. Arsenic contamination of groundwater and irrigated soils of Bangladesh. International conference on arsenic pollution of groundwater in Bangladesh: causes, effects and remedies, 1998: Dhaka Community Hospital, Dhaka; 1998.
54. Islam FS, Gault AG, Boothman C, Polya DA, Charnock JM, Chatterjee D, et al. Role of metal-reducing bacteria in arsenic release from Bengal delta sediments. Nature. 2004;430(6995):68–71. https://doi.org/10.1038/nature02638.
55. Adomako EE, Solaiman A, Williams PN, Deacon C, Rahman G, Meharg AA. Enhanced transfer of arsenic to grain for Bangladesh grown rice compared to US and EU. Environ Int. 2009;35(3):476–9. https://doi.org/10.1016/j.envint.2008.07.010.
56. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. International journal of surgery. 2021;88:105906. https://doi.org/10.1136/bmj.n71.
57. Jaykaran J. "Mean±SEM" or "mean (SD)"? 2010. https://doi.org/10.4103/0253-7613.70402
58. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60. https://doi.org/10.1136/bmj.327.7414.557.
59. Kuroki T, Watanabe Y, Teranishi H, Izumiyama S, Amemura-Maekawa J, Kura F. Legionella prevalence and risk of legionellosis in Japanese households. Epidemiol Infect. 2017;145(7):1398–408. https://doi.org/10.1017/S0950268817000036.
60. Adimalla N. Groundwater quality for drinking and irrigation purposes and potential health risks assessment: a case study from semi-arid region of South India. Exposure and health. 2019;11(2):109–23. https://doi.org/10.1007/s12403-018-0288-8.
61. Adimalla N. Heavy metals contamination in urban surface soils of Medak province, India, and its risk assessment and spatial distribution. Environ Geochem Health. 2020;42(1):59–75. https://doi.org/10.1007/s10653-019-00270-1.
62.• Das A, Joardar M, Chowdhury NR, Mridha D, De A, Majumder S, et al. Significance of the prime factors regulating arsenic toxicity and associated health risk: a hypothesis-based investigation in a critically exposed population of West Bengal, India. Environmental Geochemistry and Health. 2022:1–24. doi: https://doi.org/10.1007/s10653-022-01422-6. **This paper described the protocol for carcinogenic risk assessment in an arsenic contaminated area**.
63. Means B. Risk-assessment guidance for superfund. Volume 1. Human health evaluation manual. Part A. Interim report (Final). Environmental Protection Agency, Washington, DC (USA). Office of Solid Waste 1989. Available from: https://www.epa.gov/sites/default/files/2015-09/documents/rags_a.pdf.
64. Sand S, Bjerselius R, Busk L, Eneroth H, Färnstrand JS, Lindqvist R. The risk thermometer–a tool for risk comparison. Swedish National Food Agency. 2015. Available from: 570 https://zenodo.org/record/1220134#.Y5JT8HbMKUk.
65.•• Sengupta S, Bhattacharyya K, Mandal J, Bhattacharya P, Halder S, Pari A. Deficit irrigation and organic amendments can reduce dietary arsenic risk from rice: introducing machine learning-based prediction models from field data. Agriculture, Ecosystems & Environment. 2021;319:107516. https://doi.org/10.1016/j.agee.2021.107516. **This paper described the procedure for calculating risk of dietary exposure to arsenic through rice by severity adjusted margin of exposure (SAMOE) mediated risk thermometer**.
66. Chowdhury NR, Das A, Joardar M, De A, Mridha D, Das R, et al. Flow of arsenic between rice grain and water: Its interaction, accumulation and distribution in different fractions of cooked rice. Science of the Total Environment. 2020;731:138937. https://doi.org/10.1016/j.scitotenv.2020.138937.
67. IRIS. Integrated risk information system-database, US Environmental Protection Agency. 2003. Available from: https://www.epa.gov/iris.
68. World Health Organization. Trace elements in human nutrition and health. World Health Organization; 1996. Available from: https://apps.who.int/iris/handle/10665/37931.

69. United States Environmental Protection Agency. Characterizing risk and hazard. EPA Region 6, Office of Solid Waste, Multimedia Planning and Permitting …; 2005. Available from: https://archive.epa.gov/epawaste/hazard/tsd/td/web/pdf/05hhrap7.pdf.
70.• Golui D, Datta S, Dwivedi B, Meena M, Trivedi V. Prediction of free metal ion activity in contaminated soils using WHAM VII, baker soil test and solubility model. Chemosphere. 2020;243:125408. https://doi.org/10.1016/j.chemosphere.2019.125408. **This paper decribed how solubility and free ion activity model can predict metal or metalloid content in crop plants**.
71.•• Mandal J, Sengupta S, Sarkar S, Mukherjee A, Wood MD, Hutchinson SM, et al. Meta-analysis enables prediction of the maximum permissible arsenic concentration in Asian paddy soil. Front Environ Sci. 2021:547. https://doi.org/10.3389/fenvs.2021.760125. **This paper informed the maximum permissible arsenic concentrations in Asian paddy soil under modelling framework through meta-analysis.**
72. Kormoker T, Proshad R, Islam MS, Tusher TR, Uddin M, Khadka S, et al. Presence of toxic metals in rice with human health hazards in Tangail district of Bangladesh. Int J Environ Health Res. 2022;32(1):40–60. https://doi.org/10.1080/09603123.2020.1724271.
73. Ponnugounder T, Singh TN. Natural occurrence of arsenic in the soil and rice plant system in the Bashkandi block of Barak valley, Assam, Northeastern India. Arab J Geosci. 2020;13(24):1296. https://doi.org/10.1007/s12517-020-06314-6.
74. Kukusamude C, Sricharoen P, Limchoowong N, Kongsri S. Heavy metals and probabilistic risk assessment via rice consumption in Thailand. Food Chem. 2021;334:127402. https://doi.org/10.1016/j.foodchem.2020.127402.
75. Fu Q-L, Li L, Achal V, Jiao A-Y, Liu Y. Concentrations of heavy metals and arsenic in market rice grain and their potential health risks to the population of Fuzhou, China. Hum Ecol Risk Assess Int J. 2015;21(1):117–28. https://doi.org/10.1080/10807039.2014.884398.
76. Clemens S, Ma JF. Toxic heavy metal and metalloid accumulation in crop plants and foods. Annu Rev Plant Biol. 2016;67:489–512. https://doi.org/10.1146/annurev-arplant-043015-112301.
77. Williams P, Price A, Raab A, Hossain S, Feldmann J, Meharg AA. Variation in arsenic speciation and concentration in paddy rice related to dietary exposure. Environ Sci Technol. 2005;39(15):5531–40. https://doi.org/10.1021/es0502324.
78.• Joardar M, Das A, Chowdhury NR, Mridha D, De A, Majumdar KK, et al. Health effect and risk assessment of the populations exposed to different arsenic levels in drinking water and foodstuffs from four villages in arsenic endemic Gaighata block, West Bengal, India. Environ Geochem Health. 2021;43(8):3027–53. https://doi.org/10.1007/s10653-021-00823-3. **This paper described the protocol for non carcinogenic risk assessment in an arsenic contaminated area**.
79. Islam MS, Proshad R, Asadul Haque M, Hoque MF, Hossin MS, Islam Sarker MN. Assessment of heavy metals in foods around the industrial areas: health hazard inference in Bangladesh. Geocarto Int. 2020;35(3):280–95. https://doi.org/10.1080/10106049.2018.1516246.
80. Booth B. Cancer rates attributable to arsenic in rice vary globally. ACS Publications; 2009. https://doi.org/10.1021/es900020m.
81. Meharg AA, Williams PN, Adomako E, Lawgali YY, Deacon C, Villada A, et al. Geographical variation in total and inorganic arsenic content of polished (white) rice. Environ Sci Technol. 2009;43(5):1612–7. https://doi.org/10.1021/es802612a.
82. Joseph T, Dubey B, McBean EA. Human health risk assessment from arsenic exposures in Bangladesh. Sci Total Environ. 2015;527:552–60. https://doi.org/10.1016/j.scitotenv.2015.05.053.
83. Joardar M, Das A, Mridha D, De A, Chowdhury NR, Roychowdhury T. Evaluation of acute and chronic arsenic exposure on school children from exposed and apparently control areas of West Bengal. India Expo Health. 2021;13(1):33–50. https://doi.org/10.1007/s12403-020-00360-x.
84. Rubin ES, Davidson CI. Introduction to Engineering and the Environment. McGraw-Hill New York; 2001.
85. Rahman MA, Kadohashi K, Maki T, Hasegawa H. Transport of DMAA and MMAA into rice (Oryza sativa L.) roots. Environ and Exp Bot. 2011;72(1):41–6. https://doi.org/10.1016/j.envexpbot.2010.02.004.
86. Dias FF, Allen HE, Guimarães JR, Taddei MHT, Nascimento MR, Guilherme LRG. Environmental behavior of arsenic (III) and (V) in soils. J Environ Monit. 2009;11(7):1412–20. https://doi.org/10.1039/B900545E.
87. Feng Q, Zhang Z, Chen Y, Liu L, Zhang Z, Chen C. Adsorption and desorption characteristics of arsenic on soils: kinetics, equilibrium, and effect of Fe (OH) 3 colloid, H2SiO3 colloid and phosphate. Procedia Environ Sci. 2013;18:26–36. https://doi.org/10.1016/j.proenv.2013.04.005.
88. Meena R, Datta S, Golui D, Dwivedi B, Meena M. Long-term impact of sewage irrigation on soil properties and assessing risk in relation to transfer of metals to human food chain. Environ Sci Pollut Res. 2016;23(14):14269–83. https://doi.org/10.1007/s11356-016-6556-x.
89. Nigam S, Gopal K, Vankar PS. Biosorption of arsenic in drinking water by submerged plant: Hydrilla verticilata. Environ Sci Pollut Res. 2013;20(6):4000–8. https://doi.org/10.1007/s11356-012-1342-x.
90. Mirecki N, Agic R, Sunic L, Milenkovic L, Ilic ZS. Transfer factor as indicator of heavy metals content in plants. Fresenius Environmental Bulletin. 2015;24(11c):4212–9. Available from: https://www.researchgate.net/publication/285589331_Transfer_factor_as_indicator_of_heavy_metals_content_in_plants
91. Datta S, Young S. Predicting metal uptake and risk to the human food chain from leaf vegetables grown on soils amended by long-term application of sewage sludge. Water Air Soil Pollut. 2005;163(1):119–36. https://doi.org/10.1007/s11270-005-0006-6.
92. Ghosh K, Das I, Das D, Sanyal S. Evaluation of humic and fulvic acid extracts of compost, oilcake, and soils on complex formation with arsenic. Soil Res. 2012;50(3):239–48. https://doi.org/10.1071/SR12037.
93.• Mandal J, Golui D, Datta SP. Assessing equilibria of organo-arsenic complexes and predicting uptake of arsenic by wheat grain from organic matter amended soils. Chemosphere. 2019;234:419–26. https://doi.org/10.1016/j.chemosphere.2019.06.088. **This paper described the risk assessment protocol of arsenic contaminated soils**.
94. Rahaman S, Sinha A, Pati R, Mukhopadhyay D. Arsenic contamination: a potential hazard to the affected areas of West Bengal, India. Environ Geochem health. 2013;35(1):119–32. https://doi.org/10.1007/s10653-012-9460-4.
95. Raj A, Mandal J, Golui D, Sihi D, Dari B, Kumari PB, et al. Determination of suitable extractant for estimating plant available arsenic in relation to soil properties and predictability by solubility-FIAM. Water Air Soil Pollut. 2021;232(6):1–11. https://doi.org/10.1007/s11270-021-05215-y.
96.• Kumari PB, Singh YK, Mandal J, Shambhavi S, Sadhu SK, Kumar R, et al. Determination of safe limit for arsenic contaminated irrigation water using solubility free ion activity model (FIAM) and Tobit Regression Model. Chemosphere. 2021;270:128630. https://doi.org/10.1016/j.chemosphere.2020.128630. **This paper described the use of FIAM in predicting the safe limit of arsenic in irrigation water**.
97. Das H, Mitra AK, Sengupta P, Hossain A, Islam F, Rabbani G. Arsenic concentrations in rice, vegetables, and fish in Bangladesh: a preliminary study. Environ Int. 2004;30(3):383–7. https://doi.org/10.1016/j.envint.2003.09.005.

98. Arain M, Kazi T, Baig J, Jamali M, Afridi H, Shah A, et al. Determination of arsenic levels in lake water, sediment, and foodstuff from selected area of Sindh, Pakistan: estimation of daily dietary intake. Food Chem Toxicol. 2009;47(1):242–8. https://doi.org/10.1016/j.fct.2008.11.009.
99. Suman S, Sharma PK, Siddique AB, Rahman MA, Kumar R, Rahman MM, et al. Wheat is an emerging exposure route for arsenic in Bihar, India. Sci Total Environ. 2020;703:134774. https://doi.org/10.1016/j.scitotenv.2019.134774
100. Williams PN, Islam M, Adomako E, Raab A, Hossain S, Zhu Y, et al. Increase in rice grain arsenic for regions of Bangladesh irrigating paddies with elevated arsenic in groundwaters. Environ Sci Technol. 2006;40(16):4903–8. https://doi.org/10.1021/es060222i.
101. Mazumder DG, Dasgupta U. Chronic arsenic toxicity: studies in West Bengal, India. Kaohsiung J Med Sci. 2011;27(9):360–70. https://doi.org/10.1016/j.kjms.2011.05.003.
102. Mazumder DNG, Ghosh A, Majumdar KK, Ghosh N, Saha C, Mazumder RNG. Arsenic contamination of ground water and its health impact on population of district of Nadia, West Bengal, India. Indian Journal of Community Medicine. Off Pub Ind Assoc Prev Soc Med. 2010;35(2):331. https://doi.org/10.4103/0970-0218.66897.
103. Sohrabi N, Kalantari N, Amiri V, Saha N, Berndtsson R, Bhattacharya P, et al. A probabilistic-deterministic analysis of human health risk related to the exposure to potentially toxic elements in groundwater of Urmia coastal aquifer (NW of Iran) with a special focus on arsenic speciation and temporal variation. Stoch Env Res Risk Assess. 2021;35(7):1509–28. https://doi.org/10.1007/s00477-020-01934-6.
104. Hope BK. Distributions selected for use in probabilistic human health risk assessments in Oregon. Hum Ecol Risk Assess Int J. 1999;5(4):785–808. https://doi.org/10.1080/10807039.1999.9657740.
105. Firestone M, Fenner-Crisp P, Barry T, Bennett D, Chang S, Callahan M, et al. Guiding principles for Monte Carlo analysis. Washington, DC: US Environmental Protection Agency. 1997. Available from: https://www.epa.gov/risk/guiding-principles-monte-carlo-analysis
106. Jiang Y, Zeng X, Fan X, Chao S, Zhu M, Cao H. Levels of arsenic pollution in daily foodstuffs and soils and its associated human health risk in a town in Jiangsu province. Chin Ecotoxicol Environ Saf. 2015;122:198–204. https://doi.org/10.1016/j.ecoenv.2015.07.018.
107. Saha N, Rahman MS, Ahmed MB, Zhou JL, Ngo HH, Guo W. Industrial metal pollution in water and probabilistic assessment of human health risk. J Environ Manage. 2017;185:70–8. https://doi.org/10.1016/j.jenvman.2016.10.023.
108. Rivera-Velasquez MF, Fallico C, Guerra I, Straface S. A comparison of deterministic and probabilistic approaches for assessing risks from contaminated aquifers: an Italian case study. Waste Manage Res. 2013;31(12):1245–54. https://doi.org/10.1177/0734242X13507305.
109. Ahmed ZU, Panaullah GM, Gauch H, McCouch SR, Tyagi W, Kabir MS, et al. Genotype and environment effects on rice (Oryza sativa L.) grain arsenic concentration in Bangladesh. Plant and Soil. 2011;338:367–82. https://doi.org/10.1007/s11104-010-0551-7.
110. Ahmed MK, Shaheen N, Islam MS, Habibullah-Al-Mamun M, Islam S, Islam MM, et al. A comprehensive assessment of arsenic in commonly consumed foodstuffs to evaluate the potential health risk in Bangladesh. Sci Total Environ. 2016;544:125–33. https://doi.org/10.1016/j.scitotenv.2015.11.133.
111. Alam MM, Mollah FH. Accumulation, distribution and source analysis of arsenic in rice in different growing areas of Bangladesh. Available from: https://aimdrjournal.com/wp-content/uploads/2021/10/42-Mdkariul-Islam4-302-308.pdf
112. Azmy S. Detection of metals and trace elements in rice in Matlab, Bangladesh: a descriptive study. 2020. Available from: http://www.diva-portal.org/smash/get/diva2:1441345/FULLTEXT01.pdf.
113. Duxbury J, Mayer A, Lauren J, Hassan N. Food chain aspects of arsenic contamination in Bangladesh: effects on quality and productivity of rice. J Environ Sci Health, Part A. 2003;38(1):61–9. https://doi.org/10.1081/ese-120016881.
114. Hossain M, Jahiruddin M, Panaullah G, Loeppert R, Islam M, Duxbury J. Spatial variability of arsenic concentration in soils and plants, and its relationship with iron, manganese and phosphorus. Environ Pollut. 2008;156(3):739–44. https://doi.org/10.1016/j.envpol.2008.06.015.
115. Islam M, Brammer H, Mustafizur Rahman G, Raab A, Jahiruddin M, Solaiman A, et al. Arsenic in rice grown in low-arsenic environments in Bangladesh. Water Qual Expo Health. 2012;4:197–208. https://doi.org/10.1007/s12403-012-0079-6.
116. Norton GJ, Islam MR, Deacon CM, Zhao F-J, Stroud JL, McGrath SP, et al. Identification of low inorganic and total grain arsenic rice cultivars from Bangladesh. Environ Sci Technol. 2009;43(15):6070–5. https://doi.org/10.1021/es901121j.
117. Rahman MM, Owens G, Naidu R. Arsenic levels in rice grain and assessment of daily dietary intake of arsenic from rice in arsenic-contaminated regions of Bangladesh—implications to groundwater irrigation. Environ Geochem Health. 2009;31:179–87. https://doi.org/10.1007/s10653-008-9238-x.
118. Rahman MM, Asaduzzaman M, Naidu R. Arsenic exposure from rice and water sources in the Noakhali district of Bangladesh. Water Qual Expo Health. 2011;3:1–10. https://doi.org/10.1007/s12403-010-0034-3.
119. Sandhi A, Greger M, Landberg T, Jacks G, Bhattacharya P. Arsenic concentrations in local aromatic and high-yielding hybrid rice cultivars and the potential health risk: a study in an arsenic hotspot. Environ Monit Assess. 2017;189:1–8. https://doi.org/10.1007/s10661-017-5889-3.
120. Sun G-X, Williams PN, Carey A-M, Zhu Y-G, Deacon C, Raab A, et al. Inorganic arsenic in rice bran and its products are an order of magnitude higher than in bulk grain. Environ Sci Technol. 2008;42(19):7542–6. https://doi.org/10.1021/es801238p.
121. Bhattacharya P, Samal A, Majumdar J, Santra S. Arsenic contamination in rice, wheat, pulses, and vegetables: a study in an arsenic affected area of West Bengal, India. Water Air Soil Pollut. 2010;213:3–13. https://doi.org/10.1007/s11270-010-0361-9.
122. Bhattacharya P, Samal A, Majumdar J, Santra S. Accumulation of arsenic and its distribution in rice plant (Oryza sativa L.) in Gangetic West Bengal, India. Paddy Water Environ. 2010;8:63–70. https://doi.org/10.1007/s10333-009-0180-z.
123. Bhatti SS, Kumar V, Kumar A, Kirby JK, Gouzos J, Correll R, et al. Potential carcinogenic and non-carcinogenic health hazards of metal (loid) s in food grains. Environ Sci Pollut Res. 2020;27:17032–42. https://doi.org/10.1007/s11356-020-08238-w.
124. Biswas A, Biswas S, Lavu RVS, Gupta PC, Santra SC. Arsenic-prone rice cultivars: a study in endemic region. Paddy Water Environ,. 2014;12:379–86. https://doi.org/10.1007/s10333-013-0392-0.
125. Biswas A, Swain S, Chowdhury NR, Joardar M, Das A, Mukherjee M, et al. Arsenic contamination in Kolkata metropolitan city: perspective of transportation of agricultural products from arsenic-endemic areas. Environ Sci Pollut Res. 2019;26:22929–44. https://doi.org/10.1007/s11356-019-05595-z.
126. Kashyap R, Ahmad M, Uniyal S, Verma K. Dietary consumption of metal (loid) s-contaminated rice grown in croplands around industrial sectors: a human health risk perspective. Int J Environ Sci Technol. 2019;16:8505–16. https://doi.org/10.1007/s13762-019-02258-x.
127. Khanam R, Hazra GC, Ghosh Bag A, Kulsum PGPS, Chatterjee N, Shukla AK. Risk assessment of arsenic toxicity through groundwater-soil-rice system in Maldah District, Bengal Delta Basin, India.

Arch Environ Contam Toxicol. 2021;81:438–48. https://doi.org/10.1007/s00244-021-00883-7.
128. Patel K, Shrivas K, Brandt R, Jakubowski N, Corns W, Hoffmann P. Arsenic contamination in water, soil, sediment and rice of Central India. Environ Geochem Health. 2005;27:131–45. https://doi.org/10.1007/s10653-005-0120-9.
129. Sharma S, Kaur I, Nagpal AK. Assessment of arsenic content in soil, rice grains and groundwater and associated health risks in human population from Ropar wetland, India, and its vicinity. Environ Sci Pollut Res. 2017;24:18836–48. https://doi.org/10.1007/s11356-017-9401-y.
130. Tyagi N, Raghuvanshi R, Upadhyay MK, Srivastava AK, Suprasanna P, Srivastava S. Elemental (As, Zn, Fe and Cu) analysis and health risk assessment of rice grains and rice based food products collected from markets from different cities of Gangetic basin, India. J Food Comp Anal. 2020;93:103612. https://doi.org/10.1016/j.jfca.2020.103612.
131. Fouladi M, Mohammadi Rouzbahani M, Attar Roshan S, Sabz AS. Health risk assessment of potentially toxic elements in common cultivated rice (Oryza sativa) emphasis on environmental pollution. Toxin Reviews. 2021;40(4):1019–34. https://doi.org/10.1080/15569543.2020.1818106.
132. Nemati S, Mosaferi M, Ostadrahimi A, Mohammadi A. Arsenic intake through consumed rice in Iran: markets role or government responsibility. Health promotion perspectives. 2014;4(2):180. https://doi.org/10.5681/hpp.2014.024.
133. Cano-Lamadrid M, Munera-Picazo S, Burló F, Hojjati M, Carbonell-Barrachina ÁA. Total and inorganic arsenic in Iranian rice. J Food Sci. 2015;80(5):T1129–35. https://doi.org/10.1111/1750-3841.12849.
134. Ghoochani M, Dehghani MH, Mehrabi F, Rahimi Fard N, Alimohammadi M, Jahed Khaniki G, et al. Determining additional risk of carcinogenicity and non-carcinogenicity of heavy metals (lead and arsenic) in raw and as-consumed samples of imported rice in Tehran. Iran Environ Sci Pollut Res. 2019;26:24190–7. https://doi.org/10.1007/s11356-019-05778-8.
135. Rezaitabar S, Esmaili-Sari A, Bahramifar N. Potential health risk of total arsenic from consumption of farm rice (Oryza sativa) from the Southern Caspian Sea Littoral and from imported rice in Iran. Bull Environ Contam Toxicol. 2012;88:614–6. https://doi.org/10.1007/s00128-012-0537-7.
136. Roya AQ, Ali MS. Heavy metals in rice samples on the Torbat-Heidarieh market. Iran Food Additives & Contaminants: Part B. 2017;10(1):59–63. https://doi.org/10.1080/19393210.2016.1247918.
137. Dahal BM, Fuerhacker M, Mentler A, Karki K, Shrestha R, Blum W. Arsenic contamination of soils and agricultural plants through irrigation water in Nepal. Environ Pollut. 2008;155(1):157–63. https://doi.org/10.1016/j.envpol.2007.10.024.
138. Diyabalanage S, Navarathna T, Abeysundara HT, Rajapakse S, Chandrajith R. Trace elements in native and improved paddy rice from different climatic regions of Sri Lanka: implications for public health. Springerplus. 2016;5:1–10. https://doi.org/10.1186/s40064-016-3547-9.
139. Liu L, Han J, Xu X, Xu Z, Abeysinghe KS, Atapattu AJ, et al. Dietary exposure assessment of cadmium, arsenic, and lead in market rice from Sri Lanka. Environ Sci Pollut Res. 2020;27:42704–12. https://doi.org/10.1007/s11356-020-10209-0.
140. Shehzad MT, Sabir M, Zia-ur-Rehman M, Zia MA, Naidu R. Arsenic concentrations in soil, water, and rice grains of rice-growing areas of Punjab, Pakistan: multivariate statistical analysis. Environ Monit Assess. 2022;194(5):346. https://doi.org/10.1007/s10661-022-10001-2.
141. Sarwar T, Khan S, Yu X, Amin S, Khan MA, Sarwar A, et al. Analysis of arsenic concentration and its speciation in rice of different markets of Pakistan and its associated health risk. Environ Technol Innov. 2021;21:101252. https://doi.org/10.1016/j.eti.2020.101252.
142. Chanpiwat P, Kim K-W. Arsenic health risk assessment related to rice consumption behaviors in adults living in Northern Thailand. Environ Monit Assess. 2019;191:1–12. https://doi.org/10.1007/s10661-019-7836-y.
143. Hensawang S, Chanpiwat P. Health impact assessment of arsenic and cadmium intake via rice consumption in Bangkok. Thai Environ Monitor Assess. 2017;189:1–10. https://doi.org/10.1007/s10661-017-6321-8.
144. Nookabkaew S, Rangkadilok N, Mahidol C, Promsuk G, Satayavivad J. Determination of arsenic species in rice from Thailand and other Asian countries using simple extraction and HPLC-ICP-MS analysis. J Agric Food Chem. 2013;61(28):6991–8. https://doi.org/10.1021/jf4014873.
145. Gilbert PJ, Polya DA, Cooke DA. Arsenic hazard in Cambodian rice from a market-based survey with a case study of Preak Russey village. Kandal Province Environ Geochem Health. 2015;37:757–66. https://doi.org/10.1007/s10653-015-9696-x.
146. Phan K, Sthiannopkao S, Heng S, Phan S, Huoy L, Wong MH, et al. Arsenic contamination in the food chain and its risk assessment of populations residing in the Mekong River basin of Cambodia. J Hazard Mater. 2013;262:1064–71. https://doi.org/10.1016/j.jhazmat.2012.07.005.
147. Chu DB, Duong HT, Nguyet Luu MT, Vu-Thi H-A, Ly B-T, Loi VD. Arsenic and heavy metals in Vietnamese rice: assessment of human exposure to these elements through rice consumption. J Anal Methods Chem. 2021;2021. https://doi.org/10.1155/2021/6661955.
148. Reid MC, Asta MP, Falk L, Maguffin SC, Pham VHC, Le HA, et al. Associations between inorganic arsenic in rice and groundwater arsenic in the Mekong Delta. Chemosphere. 2021;265:129092. https://doi.org/10.1016/j.chemosphere.2020.129092.
149. Pedron T, Oliveira GSP, Paniz FP, de Moura Souza F, Masuda HP, dos Santos MC, et al. Determination of chemical elements in rice from Singapore markets: distribution, estimated intake and differentiation of rice varieties. J Food Compos Anal. 2021;101:103969. https://doi.org/10.1016/j.jfca.2021.103969.
150. Nguyen TP, Ruppert H, Pasold T, Sauer B. Paddy soil geochemistry, uptake of trace elements by rice grains (Oryza sativa) and resulting health risks in the Mekong River Delta. Vietnam Environ Geochem Health. 2020;42:2377–97. https://doi.org/10.1007/s10653-019-00456-7.
151. Nguyen TP, Ruppert H, Sauer B, Pasold T. 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. 2020;42:191–207. https://doi.org/10.1007/s10653-019-00333-3.
152. Chen H, Tang Z, Wang P, Zhao F-J. Geographical variations of cadmium and arsenic concentrations and arsenic speciation in Chinese rice. Environ Pollut. 2018;238:482–90. https://doi.org/10.1016/j.envpol.2018.03.048.
153. Cui H, Wen J, Yang L, Wang Q. Spatial distribution of heavy metals in rice grains and human health risk assessment in Hunan Province. China Environ Sci Pollut Res. 2022;29(55):83126–37. https://doi.org/10.1007/s11356-022-21636-6.
154. Fu Y, Chen M, Bi X, He Y, Ren L, Xiang W, et al. Occurrence of arsenic in brown rice and its relationship to soil properties from Hainan Island. China Environ Pollut. 2011;159(7):1757–62. https://doi.org/10.1016/j.envpol.2011.04.018.
155. Hang X, Wang H, Zhou J, Ma C, Du C, Chen X. Risk assessment of potentially toxic element pollution in soils and rice (Oryza sativa) in a typical area of the Yangtze River Delta. Environ Pollut. 2009;157(8–9):2542–9. https://doi.org/10.1016/j.envpol.2009.03.002.
156. Hao H, Ge D, Wen Y, Lv Y, Chen W. Probabilistic health risk assessment of inorganic arsenic and some heavy metals in rice produced from a typical multi-mining county, China.

Environ Sci Pollut Res. 2021:1–14. https://doi.org/10.1007/s11356-021-16583-7.
157. Li X, Xie K, Yue B, Gong Y, Shao Y, Shang X, et al. Inorganic arsenic contamination of rice from Chinese major rice-producing areas and exposure assessment in Chinese population. SCIENCE CHINA Chem. 2015;58:1898–905. https://doi.org/10.1007/s11426-015-5443-5.
158. Hu P, Huang J, Ouyang Y, Wu L, Song J, Wang S, et al. Water management affects arsenic and cadmium accumulation in different rice cultivars. Environ Geochem Health. 2013;35:767–78. https://doi.org/10.1007/s10653-013-9533-z.
159. Huang R-Q, Gao S-F, Wang W-L, Staunton S, Wang G. Soil arsenic availability and the transfer of soil arsenic to crops in suburban areas in Fujian Province, southeast China. Sci Total Environ. 2006;368(2–3):531–41. https://doi.org/10.1016/j.scitotenv.2006.03.013.
160. Huang Y, Wang M, Mao X, Qian Y, Chen T, Zhang Y. Concentrations of inorganic arsenic in milled rice from China and associated dietary exposure assessment. J Agric Food Chem. 2015;63(50):10838–45. https://doi.org/10.1021/acs.jafc.5b04164.
161. Kong X, Liu T, Yu Z, Chen Z, Lei D, Wang Z, et al. Heavy metal bioaccumulation in rice from a high geological background area in Guizhou Province, China. Int J Environ Res Public Health. 2018;15(10):2281. https://doi.org/10.3390/ijerph15102281.
162. Li J, Dong F, Lu Y, Yan Q, Shim H. Mechanisms controlling arsenic uptake in rice grown in mining impacted regions in South China. PloS one. 2014;9(9):e108300. https://doi.org/10.1371/journal.pone.0108300.
163. Li L, Feng H, Wei J. Toxic element (As and Hg) content and health risk assessment of commercially available rice for residents in Beijing based on their dietary consumption. Environ Sci Pollut Res. 2020;27(12):13205–14. https://doi.org/10.1007/s11356-020-07790-9.
164. Liang F, Li Y, Zhang G, Tan M, Lin J, Liu W, et al. Total and speciated arsenic levels in rice from China. Food Addit Contam. 2010;27(6):810–6. https://doi.org/10.1080/19440041003636661.
165. Lin J, Sun D, Zhang Z, Duan Z, Dong J. Heavy metals and health risk of rice sampled in Yangtze River Delta, China. Food Add Contam: Part B. 2021;14(2):133–40. https://doi.org/10.1080/19393210.2021.1903568.
166. Liu C-p, Luo C-l, Gao Y, Li F-b, Lin L-w, Wu C-a, et al. Arsenic contamination and potential health risk implications at an abandoned tungsten mine, southern China. Environ Pollut. 2010;158(3):820–6. https://doi.org/10.1016/j.envpol.2009.09.029.
167. Liu C, Yu H-Y, Liu C, Li F, Xu X, Wang Q. Arsenic availability in rice from a mining area: is amorphous iron oxide-bound arsenic a source or sink? Environ Pollut. 2015;199:95–101. https://doi.org/10.1016/j.envpol.2015.01.025.
168. Liu Y, Cao X, Hu Y, Cheng H. Pollution, risk and transfer of heavy metals in soil and rice: a case study in a typical industrialized Region in South China. Sustainability. 2022;14(16):10225. https://doi.org/10.3390/su141610225.
169. Lu Y, Dong F, Deacon C, Chen H-j, Raab A, Meharg AA. Arsenic accumulation and phosphorus status in two rice (Oryza sativa L.) cultivars surveyed from fields in South China. Environ Pollut. 2010;158(5):1536–41. https://doi.org/10.1016/j.envpol.2009.12.022.
170. Ma L, Wang L, Jia Y, Yang Z. Arsenic speciation in locally grown rice grains from Hunan Province, China: Spatial distribution and potential health risk. Sci Total Environ. 2016;557:438–44. https://doi.org/10.1016/j.scitotenv.2016.03.051.
171. Ma L, Wang L, Jia Y, Yang Z. Accumulation, translocation and conversion of six arsenic species in rice plants grown near a mine impacted city. Chemosphere. 2017;183:44–52. https://doi.org/10.1016/j.chemosphere.2017.05.089.
172. Mu T, Wu T, Zhou T, Li Z, Ouyang Y, Jiang J, et al. Geographical variation in arsenic, cadmium, and lead of soils and rice in the major rice producing regions of China. Sci Total Environ. 2019;677:373–81. https://doi.org/10.1016/j.scitotenv.2019.04.337.
173. Qian Y, Chen C, Zhang Q, Li Y, Chen Z, Li M. Concentrations of cadmium, lead, mercury and arsenic in Chinese market milled rice and associated population health risk. Food Control. 2010;21(12):1757–63. https://doi.org/10.1016/j.foodcont.2010.08.005.
174. Yao BM, Chen P, Sun GX. Distribution of elements and their correlation in bran, polished rice, and whole grain. Food Sci Nutr. 2020;8(2):982–92. https://doi.org/10.1002/fsn3.1379.
175. Zhu Y-G, Sun G-X, Lei M, Teng M, Liu Y-X, Chen N-C, et al. High percentage inorganic arsenic content of mining impacted and nonimpacted Chinese rice. Environ Sci Technol. 2008;42(13):5008–13. https://doi.org/10.1021/es8001103.
176. Kuramata M, Abe T, Matsumoto S, Ishikawa S. Arsenic accumulation and speciation in Japanese paddy rice cultivars. Soil Sci Plant Nutr. 2011;57(2):248–58. https://doi.org/10.1080/00380768.2011.565479.
177. Chung E, Lee J-S, Chon H-T, Sager M. Environmental contamination and bioaccessibility of arsenic and metals around the Dongjeong Au–Ag–Cu mine, Korea. Geochemistry: Exploration, Environment, Analysis. 2005;5(1):69–74. https://doi.org/10.1144/1467-7873/03-060.
178. Kim JY, Kim KH, Kim KR, Kim HS, Kim JG, Kim WI. Arsenic species in husked and polished rice grains grown at the non-contaminated paddy soils in Korea. J Appl Biol Chem. 2018;61(4):391–5. https://doi.org/10.3839/jabc.2018.055.
179. Kunhikrishnan A, Go W-R, Park J-H, Kim K-R, Kim H-S, Kim K-H, et al. Heavy metal (loid) levels in paddy soils and brown rice in Korea. Korean Soc Soil Sci Fert. 2015;48(5):515–21. https://doi.org/10.7745/KJSSF.2015.48.5.515.
180. Kwon JC, Nejad ZD, Jung MC. Arsenic and heavy metals in paddy soil and polished rice contaminated by mining activities in Korea. CATENA. 2017;148:92–100. https://doi.org/10.1016/j.catena.2016.01.005.
181. Lee J-S, Lee S-W, Chon H-T, Kim K-W. Evaluation of human exposure to arsenic due to rice ingestion in the vicinity of abandoned Myungbong Au–Ag mine site. Korea J Geochem Explor. 2008;96(2–3):231–5. https://doi.org/10.1016/j.gexplo.2007.04.009.
182. Lee SG, Lee YS, Cho S-Y, Chung M-S, Cho M, Kang Y, et al. Monitoring of arsenic contents in domestic rice and human risk assessment for daily intake of inorganic arsenic in Korea. J Food Compos Anal. 2018;69:25–32. https://doi.org/10.1016/j.jfca.2018.02.004.
183. Hsu W-M, Hsi H-C, Huang Y-T, Liao C-S, Hseu Z-Y. Partitioning of arsenic in soil–crop systems irrigated using groundwater: a case study of rice paddy soils in southwestern Taiwan. Chemosphere. 2012;86(6):606–13. https://doi.org/10.1016/j.chemosphere.2011.10.029.