Arsenic in soil-plant-human continuum in Asian regions: exposure and risk assessment

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

[1]Division of Soil Science and Agricultural Chemistry, ICAR-Indian Agricultural Research Institute, New Delhi-110 012, India

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

[3]ICAR-Indian Institute of Soil and Water Conservation, RC Koraput, Odisha-763 002, India

[4]School of Science, Engineering and Environment, University of Salford, Salford, Manchester, M50 2EQ, United Kingdom

[5]Department of Emergency Medicine, All India Institute of Medical Sciences, New Delhi-110 029, India

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

[7]Department of General Educational Development, Faculty of Science & Information Technology, Daffodil International University, Ashulia, Savar, Dhaka - 1207, Bangladesh

**Correspondence: debasis.golui@ndsu.edu (D.G.); a.bezbaruah@ndsu.edu (A.B.). Both contributed equally to this review work and the preparation of this manuscript.*

Arsenic in soil-plant-human continuum in Asian regions: exposure and risk assessment

Abstract

Purpose of Review: This review article presents the regional-level health risks due to the consumption of arsenic contaminated rice in the three regions of Asia. Such macro-level review has not been reported so far, while there are micro-level reports for smaller geographic areas. The review also suggests a possible safe limit of bioavailable arsenic in soil for a smaller geographic area based on the solubility-free ion activity model. A discussion on risk assessment analyses for better appraisal of arsenic risks in soil-plant-human system is also included.
Findings: It was found that adults in Asian countries are prone to a high risk of cancer due to the consumption of arsenic contaminated rice. South Asia (SA), South East Asia (SEA), and East Asia (EA) regions exceeded the USEPA-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 found to be 4.526±5.118 for SA, 2.599±0.801 for SEA, and 2.954±2.088 for EA, which is much above the safe limit of HQ of 1.
Summary: This review presents rice consumption related carcinogenic and non-carcinogenic risks to adults. A model was tested to calculate the safe limit of bioavailable arsenic in paddy soils. The methods and findings of this review are expected to be useful for regional level policy making and resource mobilization to alleviate the public health issues related to arsenic and the work can be expanded to arsenic present in drinking water.

Keywords: Arsenic; rice; risk assessment; cancer risk; hazard quotient, FIAM

1. Introduction

Arsenic (As), infamously referred to as the 'king of poison', is a colorless, tasteless and odorless trace element found throughout the environment. It is a carcinogenic metalloid that has been reported to be present in the lithosphere at concentrations as high as 5 mg kg^{-1} [1]. The high levels of arsenic in groundwater can be attributed to geo-biochemical processes that dislodge arsenic from the 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 application of sewage sludge and wastewater [4•]. Additionally, several arsenic-based pesticides were applied to agricultural fields and continued to be used in many countries despite their known harmful effects [5, 6]. Although arsenic pollution of drinking water has been documented in several South Asia 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) set threshold limit of 10 µg As L^{-1} in drinking water. Globally, more than 230 million people are in danger of arsenic toxicity due to drinking water consumption [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 path into the human food chain through the consumption of food crops grown in soils regularly irrigated with arsenic-polluted groundwater [13, 14••]. Rice is the staple food in South-East Asian countries 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 ailments 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 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 [19]. The severity of the impacts of arsenic on human health is governed not only by the length of arsenic exposure but also by the multiple environmental factors. 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]. Apart from this, various neurological disorders and gastrointestinal effects are also reported due to chronic As exposure [23].

Keeping public health issues in view, 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 [24]. In August 2020, the U.S. Food and Drug Administration (FDA) reissued guidelines for arsenic in infant rice cereal limiting it to 100 µg kg^{-1} [25]. Apart from providing good quality drinking water, monitoring of food materials like rice grain is also required to safeguard public health. However, given the heterogeneity in human dietary habits across the world, establishing a generalized limit for arsenic in various food products, including rice, is unwise. But the prescription of the safe limit of plant-available (bioavailable) arsenic in soil is essential for assessing the suitability of arable lands for crop production and 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. In this review article, we have reviewed the (i) distribution of arsenic levels in rice (both at the field level and in market available rice) from Asian regions, (ii) health risks, both non-carcinogenic and carcinogenic, due to rice consumption, and (iii) prediction of arsenic content in rice grain with the employment of modelling approach.

2. Mechanism of arsenic poisoning in humans

Manifestation of arsenic exposure to human 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 [26]. 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, 26]. Non-malignant lung disease, gastroenteritis, portal hypertension, and black foot disease have been reported in people consuming arsenic-contaminated drinking water [27]. The association of arsenic with various human malignancies has made this metalloid a Class-1 human carcinogen [28]. 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) [29], while the severe ones are associated with the lungs (e.g., squamous cell carcinoma of the lungs) [30]. 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 (Figure S1).

Arsenic is metabolized in the human body through redox reactions, of which methylation is essential. Oxidative methylation of arsenic produces methylated trivalent and pentavalent As compounds using S-adenosyl methionine (SAM) [31]. These methylated As compounds are carcinogenic for the skin keratinocytes [32].

The biotransformation of arsenic leads to the generation of reactive oxygen species (ROS) which can damage organs directly by inducing DNA strand breakage [33]. Modifications of gene transcription of WNT/β-catenin and calcium signaling pathways are reported and implicated in the development of many cancers [33]. 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 [34].

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]. Abnormal DNA methylation has been associated with the development of lung and bladder cancers due to the inhibition of the transcription of tumor suppressor genes (like p53, p16INK4A, RASSF1A, and PRSS3) [35]. 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 [36]. 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 [37]. Arsenic also induces angiogenesis by decreasing the miRNA-9 family [38].

3. Arsenic in rice grain of Asia

Rice is the most widely consumed food grain in the world. In Asian countries, where rice is the major staple food, it is cultivated in at least two seasons to cater to the demands [39]. Rice is a very water-demanding crop [40]. 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 high as 83,000 $\mu g\ kg^{-1}$ of arsenic has been found in paddy soils subjected to continuous irrigation in Bangladesh [41]. Increased levels of arsenic in rice grains are reported from paddy fields irrigated with contaminated irrigation water [42, 43]. In this study, we have collected literature-reported rice grain arsenic content data from Asian countries and have evaluated the possible lifetime cancer risk due to the consumption of arsenic contaminated rice.

Materials and methods

The relevant literature published between the years 2000 and 2022 was examined systematically. We used Boolean operators (e.g., “OR” and “AND”) to develop search terms from the keywords (“arsenic”, “rice”, “grain”, “Asia”, “survey”, “farmer filed”, “market”) (Table S1). The research papers were extracted from the ISI Web of Science and Google Scholar. From > 1600 published articles, we excluded the papers based on the conditions provided in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) flowchart. Finally, a total of 89 papers were chosen to find out the risk associated with the consumption of rice grain in these regions (Figure S2). To evaluate the comparison of arsenic content in rice grain from different Asiatic regions, we compiled the data quantitatively set of above individual studies through meta-analysis. The Asia 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 (37 papers from China, Japan, Taiwan, and South Korea) were pooled and analyzed (Table S2). 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) [44··]. Inorganic arsenic data was used to calculate carcinogenic and noncarcinogenic risk following the standard formula. The papers from CA (n=1) and WA (n=5) regions were discarded because they didn't meet the minimum criteria of n > 10 for carrying out further analysis.

Whereas, a total of 60 papers (28 papers from SA covering Bangladesh, India, Iran, Nepal, Pakistan, and Sri Lanka; 9 papers from SEA covering Cambodia, Thailand, and Vietnam; 23 papers from EA covering China, Japan, Taiwan, and South Korea) were selected to find out the relative comparison of total arsenic in rice grain between the different conducted peer-reviewed studies in these regions (Figure S3). 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 centre 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 the diverse studies were combined and averaged. The '*metafor'* package (version 3.8-1) in R-Studio (version 1.3.10932.3.1) was used to perform the data analysis.

Assessment of cancer risk

The 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).

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

where C is iAs (mg kg^{-1}) in rice grain, IR is ingestion rate (0.4 kg day^{-1} or 4×10^5 mg day^{-1} [14••]), ED is exposure duration (30 years for an adult [45]), EF is exposure frequency (365 days year^{-1}), CF is conversion factor (1×10^{-6} kg mg^{-1}), BW is average body weight (70 kg for an adult), and AT is the average time for carcinogen (70×365 days for As) [46]. For the calculation of CDD in children, IR is assumed as 0.2 kg day^{-1} [47•], ED as 6 years, and BW as 20 kg [45].

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

$$\mathrm{CR} = \mathrm{CDD} \times \mathrm{SF} \qquad (2)$$

Where, SF is the slope factor (SF = 1.5 mg kg^{-1} day^{-1} for arsenic). As per the U.S. EPA guidelines [48], 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 [49, 50••], 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) [51].

$$\text{SAMOE}=\text{TDI}/(\text{AF}_{\text{BMR}} \text{ x AF x SF x E}) \quad (3)$$

where, TDI = 3.0 µg kg(bodyweight)$^{-1}$ day^{-1} for arsenic, AF_{BMR} = Non-linear relation in dose range (1/10; BMR - Benchmark response), AF (Assessment factors) = a factor of 10 (conservative assessment), SF (Severity factor) = 100 (for cancer, the most severe category), and E = 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) [49].

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) [52]:

$$HQ = \frac{ADD}{RfD} \qquad (4)$$

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}) which is 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} [53]. The cumulative risk from various non-carcinogens and/or the different ways of exposure (dermal and ingestion) is obtained by summation of 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••, 54].

$$\text{ADD} = \sum_{i=1}^{N} \frac{C_i \times CR_i}{BW} \qquad (5)$$

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 i-th route, CR_i is the consumption rate (kg day^{-1}) of the subscripted ingested material.

In the present review study, exposure to arsenic in humans was considered from rice grain consumption only. Therefore, the average daily dose was computed based on the following assumptions: C = concentration of inorganic arsenic in rice grain in Asian regions, CR = 0.4 kg day^{-1} or 4×10^5 mg day^{-1} [14••], BW = 70 kg for adults [46]. An HQ value less than or equal to 1 is considered safe [52]. However, because other dietary items may potentially be the sources of arsenic getting into the human body, the HQ limit has been adjusted and regarded safe at $HQ \leq 0.5$ [55•].

3.4 Quantitative assessment of rice grain arsenic data

The forest plot for SA shows the list of input studies with their effect sizes (Figure 1). From the random effect model, the overall summary weighted mean value of 218.43 µg kg^{-1}(Confidence Interval: 157.55 to 279.31) of arsenic showed statistically significant ($p < 0.001$). An inconsistency index of 100% indicated significant heterogeneity in the data set which is due to the geographic distribution of paddy-growing areas in the different countries in the SA regions. 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 sites, the contamination might be due to the extensive use of arsenic-contaminated water from shallow tube wells for irrigation of paddy rice [56·], and some areas might have been contaminated by mining and industrial activities [57]. Whereas, the 95% confidence interval crosses the line of no effect in the case of samples from Sri Lanka. Figures 2 and 3 revealed that the overall summary weighted mean for arsenic in rice grain of SEA (118.61, 95% CI:95.79 to 141.43) and EA (128.01, 77.44 to 178.58) is statistically significant ($p < 0.001$). Similarly, significant heterogeneity in data was observed at 99.55% and 99.93% for SEA and EA, respectively.

Carcinogenic risk

The SAMOE value for arsenic toxicity due to rice consumption in SA, SEA, and EA regions showed the risk levels of Class 4 (moderate to high) or Class 3 (low risk) depending on rice arsenic concentration (Figure S4). The mean SAMOE value has been found as 0.282±0.254 for SA, 0.284±0.278 for SEA, and 0.280±0.172 for EA. The carcinogenic risk assessment for adults and children consuming rice in SA, SEA, and EA regions was done. 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 (Figure 4). The average CR value has been found as 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} indicating that the grain produced and sold in these three regions of Asia poses severe cancer risk in adults. Data on cancer risk for the child also exceeded the critical limit of 1×10^{-6} (Figure S5). 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. Several researchers discretely calculated the carcinogenic risk due to the consumption of rice grain mainly in India and Bangladesh [45-47•, 56•, 58, 59]. In the present study, such large-scale regions were considered to calculate the carcinogenic risk, 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 more of a gray area that may require a case-specific judgment as to the acceptability of a particular risk [60]. 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 available. 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 region. 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••, 61]. At the same time, there are also alarmingly high arsenic contents in rice grain from East and South East Asian countries like Cambodia, Indonesia, Thailand, Vietnam, South Korea, North Korea, China, and Japan. This analysis indicates that necessary management options should be adopted 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 came about four to five decades back, effective solution to this burning human health problem remains elusive to date. Researchers have already published several pieces of literature 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 safety. Our analysis has shown that the upper critical limit set by CODEX for arsenic in rice grain is not adequate to protect human 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 As, 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 (Figure S6). 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. As can be seen, 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 as arsenic input to humans may also come 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 to the human body are considered.

5. Appraisal of arsenic menace in 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 is influenced 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••, 62-64]. 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.

There are two types of models (mechanistic and transport model) that can be used to predict arsenic uptake and content in plants. The mechanistic models consider 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 models employed to predict arsenic uptake by plants. The biosorption of arsenic by *Hydrilla verticilata* (a submerged aquatic plant) was reported by Nigam et al. (2013) [65], and they used the Langmuir isotherm and pseudo-second-order kinetic models to represent arsenic adsorption/removal from water indicating 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 amplifies when soil comes into the context as multicomponent reactions need to be considered at the same time. Therefore, solubility speciation models are employed widely 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 arsenic uptake by rice crop based on predicted free ion activity in soil solution [14••, 64]. 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 been used as input parameters to run this model [14••, 64].

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. 7) [66].

$$TF = \frac{[M_{Plant}]}{(M^{n-})} \qquad (6)$$

The (M^{n-}) can be predicted from a pH-dependent Freundlich equation [55]. Arsenic uptake by plant can be calculated by combining Eq. (6) with (M^{n-}) as follows (details in supplementary information, section A1):

$$\log [M_{plant}] = C + \beta_1 pH + \beta_2 \log[M_c] \qquad (7)$$

where C, β1 and β2 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••, 64]. 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, India) [14]. The model parameters were reported as C= –2.30, β1= –0.03, β2= 0.80 (Figure S7). In addition to rice crop, the efficacy of different models such as regression model (linear and multiple), logarithmic model and solubility-FIAM were compared for predicting arsenic content in wheat grains and the risk involved with their human consumption [67•]. The solubility-FIAM model has been found to give a better prediction ($R^2 = 0.97$) of the arsenic content in grains and associated human health risk. For rice, the solubility-FIAM model was validated with the arsenic data set collected from Nadia (West Bengal, India). In future, other important soil parameters like clay content, available Fe, Al, Mn and phosphate content should be incorporated as model parameters to enhance the performance of the model.

Currently, total arsenic in soil (10 to 20 mg kg^{-1}) has been used as a simple index of arsenic hazard globally [68]. However, a poor correlation between total arsenic in soil and plant arsenic was noticed. 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••, 64, •• 69-71•]. Given that people's food habits vary based on geographical local and culture, a common (global) permissible limit of arsenic in rice grain will not have much practical significance. However, prescribing 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 the management of 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 in soil would be 0.43 mg kg^{-1} for rice cultivation if the soil pH and organic carbon 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 S8).

6. 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 such that proper prevention, remediation, and management plan may be adopted.

5.1. Risk mapping

Regional-level arsenic risk mapping across the globe will be needed for successful policy intervention and resource allocation to alleviate the problem and help the population affected so far. 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, carrot) which are part of the human diet also accumulate arsenic [56•, 72-75]. 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) [56•]. Leafy vegetables in Bangladesh were reported to contain arsenic in the range of 130-790 µg kg^{-1} [75] and one report recorded a very range of 0.1-3.99 mg kg^{-1} [72]. The range of arsenic in leafy vegetables (spinach, coriander and peppermint) collected in Pakistan was 0.90–1.20 mg kg^{-1} [73]. Wheat flour samples collected from arsenic exposed Bihar state of India showed considerable amounts of arsenic (mean 49.8 µg kg^{-1}, range 3.59–448 µg kg^{-1}, n = 58) [74]. 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 (e.g., cattle, horse, goat, chicken, duck, fish).

5.2. 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 pin-point 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 will be important. 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) [76]. 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 found to be 15.43% [77]. In the same investigation, chronic lung disease was found in 207 (12.81%) cases while peripheral neuropathy was found in 257 (15.9%) cases. It will be important to use similar data to validate models used for risk assessment for the same population.

5.3. 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 characterisation [48]. 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 level of contaminant, which is then compared to reference values for health impacts and is used in location-specific risks assessment. There are, however, considerable uncertainties in exposure pathways for health risk assessment [78]. 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 [78].

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 aspect impacting the outcomes of a PRA is the choice of probability distributions for input data [79, 80]. 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 from 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 in a number [78, 81-83]. 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} [82]. The deterministic and probabilistic approaches for assessing risks from arsenic from contaminated drinking water have been compared and results showed an overestimation of risks by the deterministic method [83].

6. Conclusions

Arsenic pollution in groundwater-soil-plant continuum is a cause of concern in rice consuming countries as it affects human health. While major pathway of arsenic exposure to human is arsenic contaminated drinking water, consumption of staple foods (particularly rice) grown on the 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 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 Asian region was found to be in the range 7×10^{-4} to 5×10^{-3}, which is much above the acceptable probability level of $1x10^{-6}$, and 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 the arsenic, and assessing the bioavailability of arsenic in soil-plant system for predicting human health risk due to food chain contamination requires elaborate experimentation. Alternatively, this study used a modeling approach involving free-ion activity of arsenic in soil-pore water to estimate arsenic content in rice grain and the safe limit for bioavailable arsenic was found to be 0.43 mg kg^{-1}.

Acknowledgement

Debasis Golui was supported at North Dakota State University by a Fulbright-Nehru Post-Doctoral Research Fellowship from the United States-India Education Foundation (USIEF, New Delhi, Grant#: 2685/FNPDR/2021). Support from the National Science Foundation (grant#: CBET-1707093, PI: Bezbaruah) is acknowledged.

Conflict of interest

The authors declare that they have no conflicts of interest.

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. Applied Geochemistry. 2008;23(4):863-94. 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 research. 2010;44(19):5789-802. doi: 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? Current pollution reports. 2020;6(2):37-42. 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. Journal of preventive medicine and public health. 2014;47(5):253. doi: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. doi: 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. Geoscience frontiers. 2021;12(3):101079. 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. doi: 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. Journal of Trace Elements in Medicine and Biology. 2016;38:33-45. doi: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. Science of The Total Environment. 2021;759:143511.

doi.org/10.1016/j.scitotenv.2020.143511. 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. Regulatory Toxicology and Pharmacology. 2020;110:104539. doi: 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. Environmental Science and Pollution Research. 2014;21(1):609-19. doi: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. doi: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 in plant science. 2004;9(9):415-7. doi:10.1016/j.tplants.2004.07.002.
16. Ahmad A, Bhattacharya P. Arsenic in drinking water: is 10 μg/L a safe limit? Current Pollution Reports. 2019;5(1):1-3. doi:org/10.1007/s40726-019-0102-7.
17. World Health Organization. Exposure to Arsenic: a major public healthconcern. 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. doi: 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. Toxicology and applied pharmacology. 2004;198(3):243-52. doi: 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. American journal of epidemiology. 2011;173(2):183-91. doi: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. Environmental research. 2008;108(1):48-55. doi: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. Environmental health perspectives. 2011;119(3):284-90. doi:10.1289/ehp.1002427.
23. Jomova K, Jenisova Z, Feszterova M, Baros S, Liska J, Hudecova D, et al. Arsenic: toxicity, oxidative stress and human disease. Journal of Applied Toxicology. 2011;31(2):95-107. doi:10.1002/jat.1649.
24. 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.

25. 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.
26. Kuivenhoven M, Mason K. Arsenic toxicity. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2022 PMID:31082169. Available from: https://pubmed.ncbi.nlm.nih.gov/31082169/.
27. 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. doi:org/10.1016/B978- 008043648-7/50016-9.
28. 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/.
29. Yu H-S, Liao W-T, Chai C-Y. Arsenic carcinogenesis in the skin. Journal of biomedical science. 2006;13(5):657-66. doi:org/10.1007/s11373-006-9092-8.
30. Wei S, Zhang H, Tao S. A review of arsenic exposure and lung cancer. Toxicology research. 2019;8(3):319-27. doi:10.1039/c8tx00298c.
31. Ajees AA, Rosen BP. As (III) S-adenosylmethionine methyltransferases and other arsenic binding proteins. Geomicrobiology journal. 2015;32(7):570-6. doi:10.1080/01490451.2014.908983.
32. Cantor K. Drinking water and cancer Cancer Causes Control 8 (3): 292–308. Find this article online. 1997. doi: 10.1023/a:1018444902486.
33. Lantz RC, Hays AM. Role of oxidative stress in arsenic-induced toxicity. Drug metabolism reviews. 2006;38(4):791-804. doi:10.1080/03602530600980108.
34. Medda N, De SK, Maiti S. Different mechanisms of arsenic related signaling in cellular proliferation, apoptosis and neo-plastic transformation. Ecotoxicology and Environmental Safety. 2021;208:111752. doi: org/10.1016/j.ecoenv.2020.111752.
35. Marsit CJ, Karagas MR, Schned A, Kelsey KT. Carcinogen exposure and epigenetic silencing in bladder cancer. Annals of the New York Academy of Sciences. 2006;1076(1):810-21. doi:10.1196/annals.1371.031
36. Zhou X, Sun H, Ellen TP, Chen H, Costa M. Arsenite alters global histone H3 methylation. Carcinogenesis. 2008;29(9):1831-6. doi:10.1093/carcin/bgn063.
37. 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. Toxicological Sciences. 2011;121(1):110-22. doi:10.1093/toxsci/kfr029.
38. 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. Journal of cellular physiology. 2012;227(2):772-83. doi:10.1002/jcp.22789.
39. 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. Journal of Agronomy and Crop Science. 2020;206(4):491-503. doi:org/10.1111/jac.12415.

40. 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. doi:org/10.1007/978-3-030-66530-2_5.
41. 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.
42. 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. doi:org/10.1038/nature02638.
43. 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. Environment international. 2009;35(3):476-9. doi:org/10.1016/j.envint.2008.07.010.
44. ••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. Frontiers in Environmental Science. 2021:547. 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.
45. 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. doi:org/10.1007/s12403-018-0288-8.
46. Adimalla N. Heavy metals contamination in urban surface soils of Medak province, India, and its risk assessment and spatial distribution. Environmental Geochemistry and Health. 2020;42(1):59-75. doi:org/10.1007/s10653-019-00270-1.
47. •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:10.1007/s10653-022-01422-6. This paper described the protocol for carcinogenic risk assessment in an arsenic contaminated area.
48. 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.
49. 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.
50. ••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. 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.

51. 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. doi:org/10.1016/j.scitotenv.2020.138937.
52. IRIS. Integrated risk information system-database, US Environmental Protection Agency. 2003. Available from: https://www.epa.gov/iris.
53. World Health Organization. Trace elements in human nutrition and health. World Health Organization; 1996. Available from: https://apps.who.int/iris/handle/10665/37931.
54. 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.
55. •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. 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.
56. •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. Environmental Geochemistry and Health. 2021;43(8):3027-53. doi: 10.1007/s10653-021-00823-3. This paper described the protocol for non carcinogenic risk assessment in an arsenic contaminated area.
57. 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 international. 2020;35(3):280-95. doi:10.1080/10106049.2018.1516246.
58. Joseph T, Dubey B, McBean EA. Human health risk assessment from arsenic exposures in Bangladesh. Science of the Total Environment. 2015;527:552-60. doi: org/10.1016/j.scitotenv.2015.05.053.
59. 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. Exposure and Health. 2021;13(1):33-50. doi:org/10.1007/s12403-020-00360-x.
60. Rubin ES, Davidson CI. Introduction to Engineering and the Environment. McGraw-Hill New York; 2001.
61. Rahman MA, Kadohashi K, Maki T, Hasegawa H. Transport of DMAA and MMAA into rice (Oryza sativa L.) roots. Environmental and Experimental Botany. 2011;72(1):41-6. doi:org/10.1016/j.envexpbot.2010.02.004.
62. Dias FF, Allen HE, Guimarães JR, Taddei MHT, Nascimento MR, Guilherme LRG. Environmental behavior of arsenic (III) and (V) in soils. Journal of Environmental Monitoring. 2009;11(7):1412-20. doi:org/10.1039/B900545E.
63. 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 Environmental Sciences. 2013;18:26-36. doi:org/10.1016/j.proenv.2013.04.005.
64. 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. Environmental Science and Pollution Research. 2016;23(14):14269-83. doi:10.1007/s11356-016-6556-x.

65. Nigam S, Gopal K, Vankar PS. Biosorption of arsenic in drinking water by submerged plant: Hydrilla verticilata. Environmental Science and Pollution Research. 2013;20(6):4000-8. doi: 10.1007/s11356-012-1342-x.
66. 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
67. •Mandal J, Golui D, Raj A, Ganguly P. Risk assessment of arsenic in wheat and maize grown in organic matter amended soils of Indo-Gangetic plain of Bihar, India. Soil and Sediment Contamination: An International Journal. 2019;28(8):757-72. doi:org/10.1080/15320383.2019.1661353. This paper described the risk assessment protocol of arsenic contaminated soils.
68. Rahaman S, Sinha A, Pati R, Mukhopadhyay D. Arsenic contamination: a potential hazard to the affected areas of West Bengal, India. Environmental geochemistry and health. 2013;35(1):119-32. doi:10.1007/s10653-012-9460-4.
69. 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, and Soil Pollution. 2005;163(1):119-36. doi:org/10.1007/s11270-005-0006-6.
70. 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 Pollution. 2021;232(6):1-11. doi:org/10.1007/s11270-021-05215-y.
71. •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. doi:10.1016/j.chemosphere.2020.128630. This paper described the use of FIAM in predicting the safe limit of arsenic in irrigation water.
72. Das H, Mitra AK, Sengupta P, Hossain A, Islam F, Rabbani G. Arsenic concentrations in rice, vegetables, and fish in Bangladesh: a preliminary study. Environment international. 2004;30(3):383-7. doi: 10.1016/j.envint.2003.09.005.
73. 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 and Chemical Toxicology. 2009;47(1):242-8. doi:10.1016/j.fct.2008.11.009.
74. 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. Science of the Total Environment. 2020;703:134774. doi: 10.1016/j.scitotenv.2019.134774
75. 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. Environmental science & technology. 2006;40(16):4903-8. doi:org/10.1021/es060222i.
76. Mazumder DG, Dasgupta U. Chronic arsenic toxicity: studies in West Bengal, India. The Kaohsiung journal of medical sciences. 2011;27(9):360-70. doi:10.1016/j.kjms.2011.05.003.
77. 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: Official Publication of Indian Association of Preventive & Social Medicine. 2010;35(2):331. doi: 10.4103/0970-0218.66897.

78. 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. Stochastic environmental research and risk assessment. 2021;35(7):1509-28. doi:org/10.1007/s00477-020-01934-6.

79. Hope BK. Distributions selected for use in probabilistic human health risk assessments in Oregon. Human and Ecological Risk Assessment: An International Journal. 1999;5(4):785-808. doi: org/10.1080/10807039.1999.9657740.

80. 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

81. 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, China. Ecotoxicology and environmental safety. 2015;122:198-204. doi:org/10.1016/j.ecoenv.2015.07.018.

82. Saha N, Rahman MS, Ahmed MB, Zhou JL, Ngo HH, Guo W. Industrial metal pollution in water and probabilistic assessment of human health risk. Journal of environmental management. 2017;185:70-8. doi:org/10.1016/j.jenvman.2016.10.023.

83. 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 management & research. 2013;31(12):1245-54. doi:10.1177/0734242X13507305.

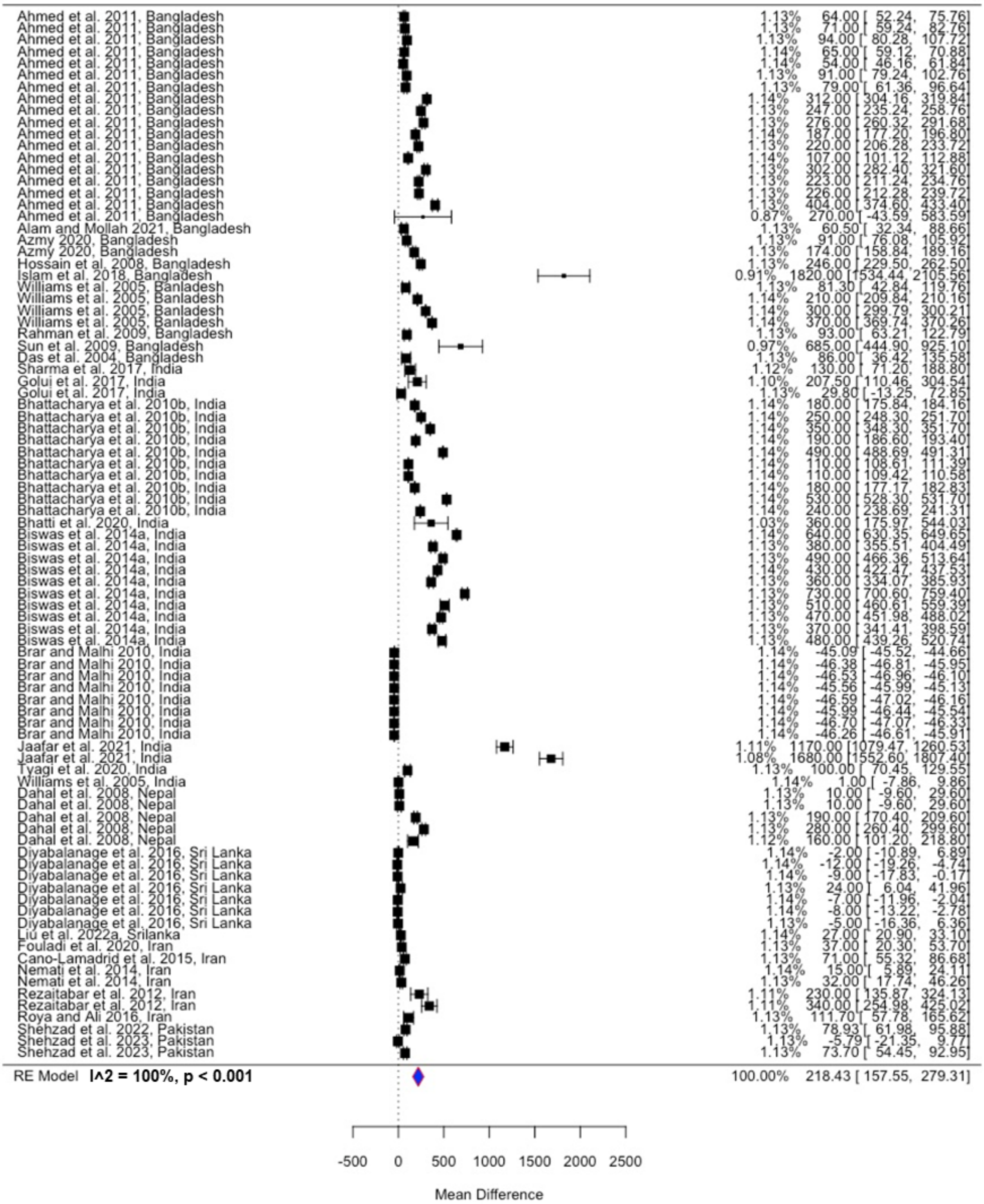

Figure 1. Forest plot showing the weighted mean difference of total arsenic concentration in rice grain between study level and marginal level with their respective confidence intervals and weight in the meta-analysis together with the heterogeneity statistics in South Asia (SA).

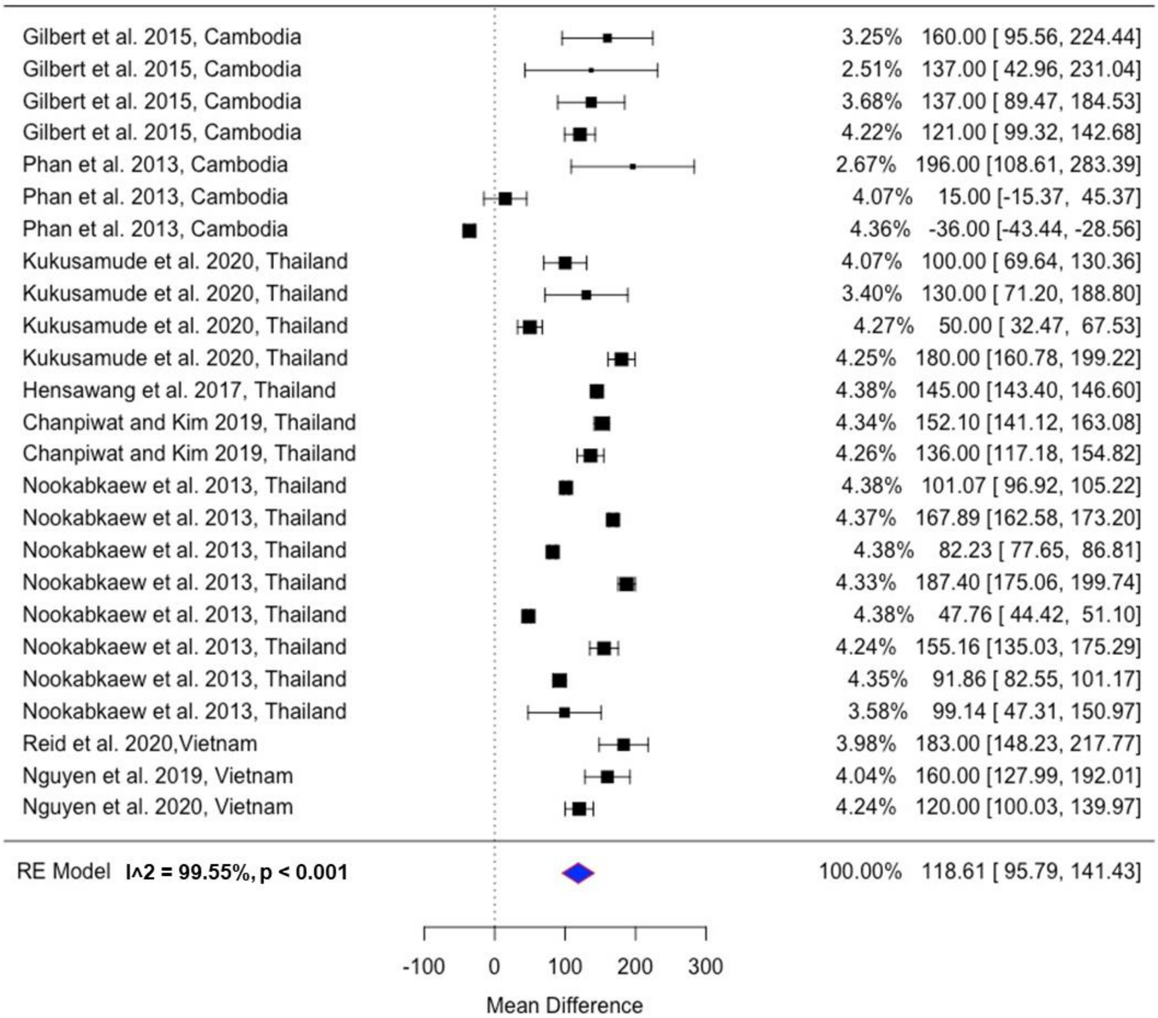
Gilbert et al. 2015, Cambodia 3.25% 160.00 [95.56, 224.44]
Gilbert et al. 2015, Cambodia 2.51% 137.00 [42.96, 231.04]
Gilbert et al. 2015, Cambodia 3.68% 137.00 [89.47, 184.53]
Gilbert et al. 2015, Cambodia 4.22% 121.00 [99.32, 142.68]
Phan et al. 2013, Cambodia 2.67% 196.00 [108.61, 283.39]
Phan et al. 2013, Cambodia 4.07% 15.00 [-15.37, 45.37]
Phan et al. 2013, Cambodia 4.36% -36.00 [-43.44, -28.56]
Kukusamude et al. 2020, Thailand 4.07% 100.00 [69.64, 130.36]
Kukusamude et al. 2020, Thailand 3.40% 130.00 [71.20, 188.80]
Kukusamude et al. 2020, Thailand 4.27% 50.00 [32.47, 67.53]
Kukusamude et al. 2020, Thailand 4.25% 180.00 [160.78, 199.22]
Hensawang et al. 2017, Thailand 4.38% 145.00 [143.40, 146.60]
Chanpiwat and Kim 2019, Thailand 4.34% 152.10 [141.12, 163.08]
Chanpiwat and Kim 2019, Thailand 4.26% 136.00 [117.18, 154.82]
Nookabkaew et al. 2013, Thailand 4.38% 101.07 [96.92, 105.22]
Nookabkaew et al. 2013, Thailand 4.37% 167.89 [162.58, 173.20]
Nookabkaew et al. 2013, Thailand 4.38% 82.23 [77.65, 86.81]
Nookabkaew et al. 2013, Thailand 4.33% 187.40 [175.06, 199.74]
Nookabkaew et al. 2013, Thailand 4.38% 47.76 [44.42, 51.10]
Nookabkaew et al. 2013, Thailand 4.24% 155.16 [135.03, 175.29]
Nookabkaew et al. 2013, Thailand 4.35% 91.86 [82.55, 101.17]
Nookabkaew et al. 2013, Thailand 3.58% 99.14 [47.31, 150.97]
Reid et al. 2020,Vietnam 3.98% 183.00 [148.23, 217.77]
Nguyen et al. 2019, Vietnam 4.04% 160.00 [127.99, 192.01]
Nguyen et al. 2020, Vietnam 4.24% 120.00 [100.03, 139.97]
RE Model I^2 = 99.55%, p < 0.001 100.00% 118.61 [95.79, 141.43]
-100 0 100 200 300
Mean Difference

Figure 2. 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).

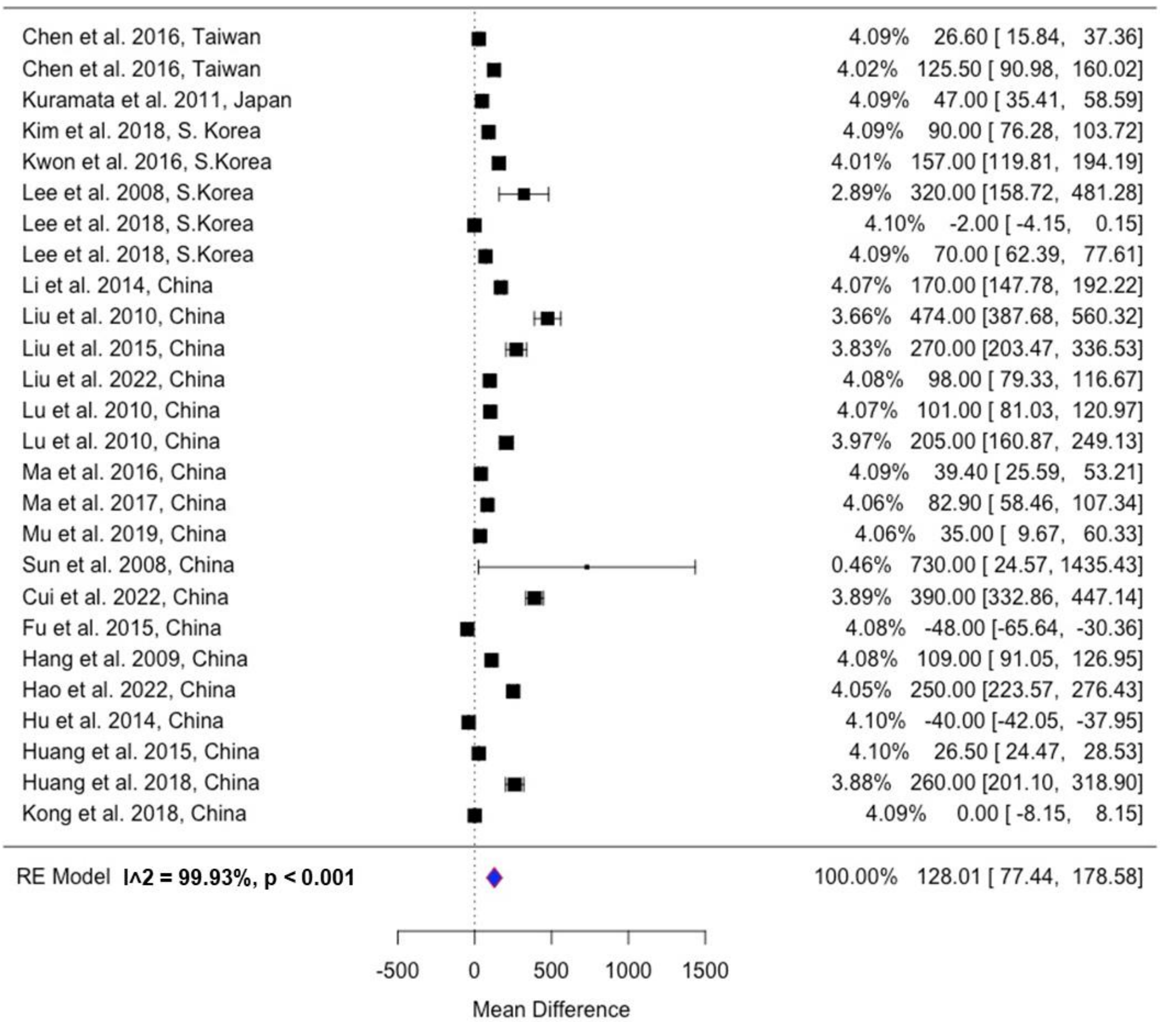

Figure 3. Forest plot showing the weighted mean difference of total arsenic concentration in rice grain between study level and marginal level with their respective confidence intervals and weight in the meta-analysis together with the heterogeneity statistics in East Asia (EA).

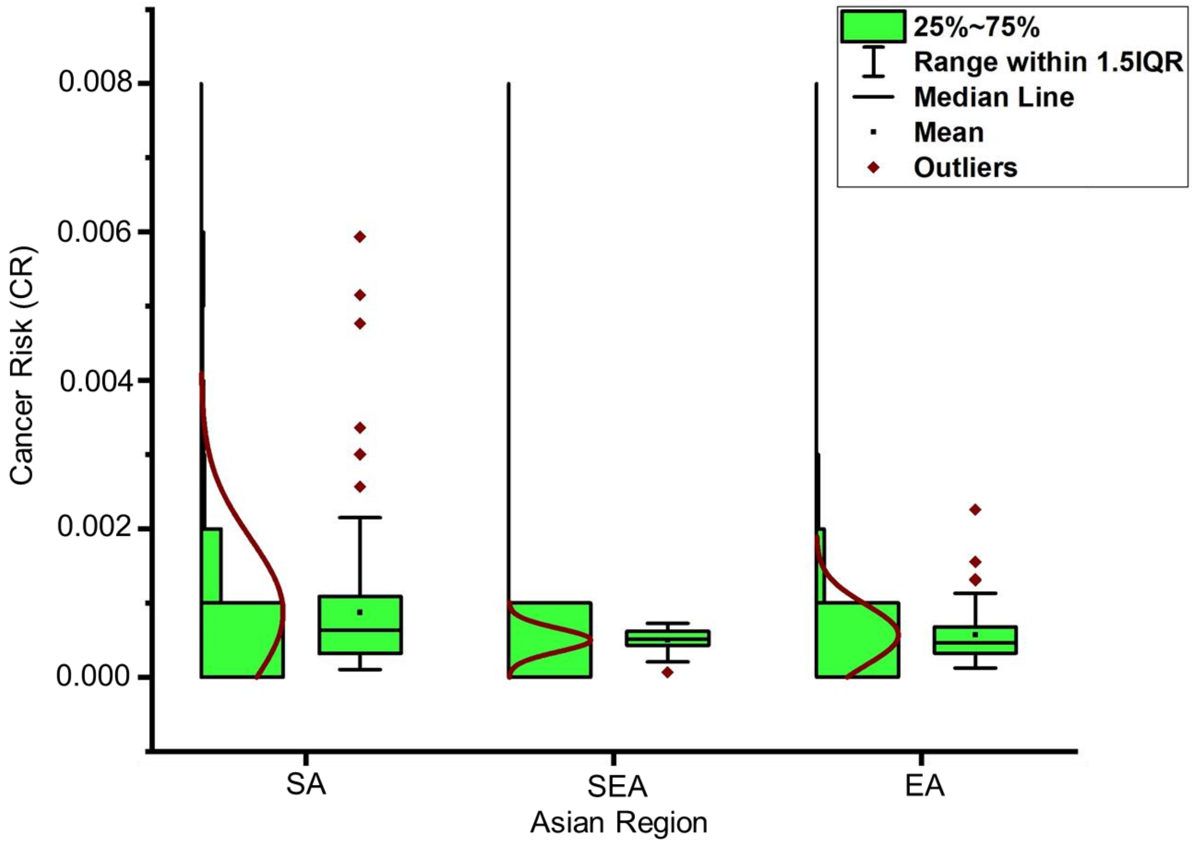

Figure 4. Box plot with data distribution curve showing the comparative distribution of possible carcinogenic risk in adults due to consumption of arsenic contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions. The USEPA suggests a safe limit of 10^{-6} for human health.

Supplementary Information

Arsenic in soil-plant-human continuum in Asian regions: exposure and risk assessment

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

[1]Division of Soil Science and Agricultural Chemistry, ICAR-Indian Agricultural Research Institute, New Delhi-110 012, India

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

[3]ICAR-Indian Institute of Soil and Water Conservation, RC Koraput, Odisha-763 002, India

[4]School of Science, Engineering and Environment, University of Salford, Salford, Manchester, M50 2EQ, United Kingdom

[5]Department of Emergency Medicine, All India Institute of Medical Sciences, New Delhi-110 029, India

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

[7]Department of General Educational Development, Faculty of Science & Information Technology, Daffodil International University, Ashulia, Savar, Dhaka - 1207, Bangladesh

**Correspondence: debasis.golui@ndsu.edu (D.G.); a.bezbaruah@ndsu.edu (A.B.). Both contributed equally to this research and the preparation of this manuscript.*

Section A1: Derivation of solubility free ion activity model (FIAM)

Arsenic content in crop plants can be predicted by the integrated solubility-free ion activity model without actually measuring the free ion activity in soil solution (Hough et al., 2004; Datta and Young, 2005). The free ion activity model (FIAM) suggests that uptake may be controlled by metalloid ion activity in the soil pore water. Transfer factor is expressed as the quotient of metalloid concentration in the plant [M_{plant}] to metalloid ion activity in soil pore water (M^{n-}) as follows:

$$\mathrm{TF} = \log \frac{[\mathrm{M_{Plant}}]}{(\mathrm{M^{n-}})}$$

$$\mathrm{TF} = \log[M_{Plant}] - \log(M^{n-})$$

$$-\log[M_{Plant}] = -\log(M^{n-}) - TF$$

$$p[M_{Plant}] = p(M^{n-}) - TF$$

$$p(M^{n-}) = p[M_{Plant}] + TF \quad \text{.....(1)}$$

Free ion activity of arsenic can be predicted by using the simple pH-dependent Freundlich equation (Jopony and Young, 1994; Datta and Young, 2005) as follows:

$p(M^{n-}) = \{p[M_c] + k_1 + k_2 pH\}/n_F$.....(2)

Where (M^{n-}) is the free metalloid ion (arsenic) activity in soil solution; M_C is the labile pool of metalloid in soil, assumed to be exclusively adsorbed on the humus (mol kg^{-1} carbon); k_1 and k_2 are empirical, metalloid-specific constants; and n_F is the power term from the Freundlich equation. This model predicts the free ion activity of arsenic in soil solution as a function of labile soil extractable metalloid and pH with the simplifying assumption that the whole amount of metalloid is adsorbed on humus. 0.5 *M* $NaHCO_3$ (pH 8.5)-extractable arsenic is used as the estimate of the labile pool. In the case of soil organic carbon, Walkley-Black organic carbon is used. By substituting the value of $p(M^{n-})$ in equation (1), one can write

$$\mathrm{p}[\mathrm{M_{Plant}}] = \frac{\mathrm{p}[\mathrm{M_C}] + \mathrm{k_1} + \mathrm{k_2 pH}}{\mathrm{n_F}} - TF$$

$$\mathrm{p}[\mathrm{M_{Plant}}] = \frac{p[M_c]}{n_F} + \frac{k_1}{n_F} - TF + \frac{k_2 pH}{n_F}$$

$$\mathrm{p}[\mathrm{M_{Plant}}] = C + \beta_1 p[M_C] + \beta_2 pH \text{.......................(3)}$$

Where, $C = \frac{k_1}{n_F} - TF, \beta_1 = \frac{1}{n_F}, \beta_2 = \frac{k_2}{n_F}$

Where, $C, \beta_1,$ *and* β_2 are empirical metalloid and plant-specific coefficients.

Equation (3) is parameterized by non-linear error minimization using the "SOLVER" facilities in Microsoft Excel 2019. The error sum of squares is calculated for numerical rather than logarithmic plant metalloid content data.

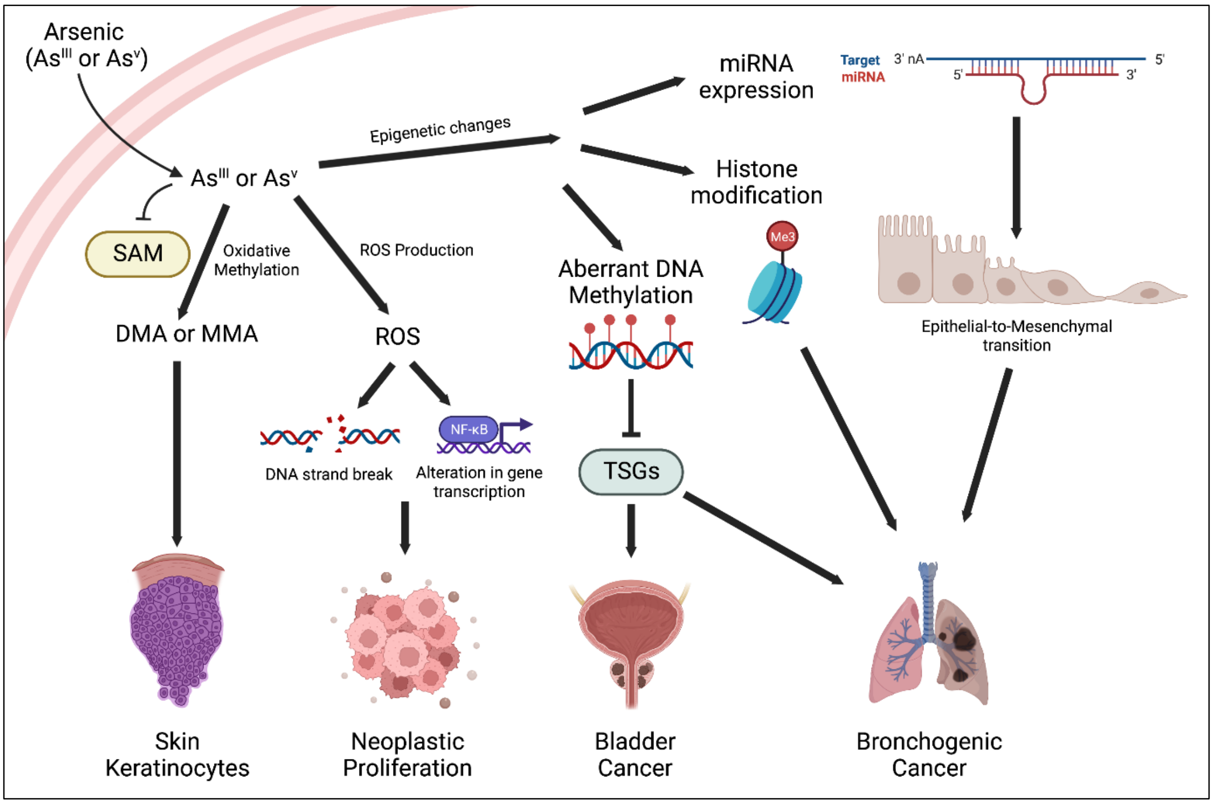

Figure S1. Mechanisms of carcinogenic toxicity of arsenic in humans. Three pathophysiological effects on human body viz. arsenic methylation, oxidative stress, and epigenetic changes are induced by sustained arsenic intake by human body

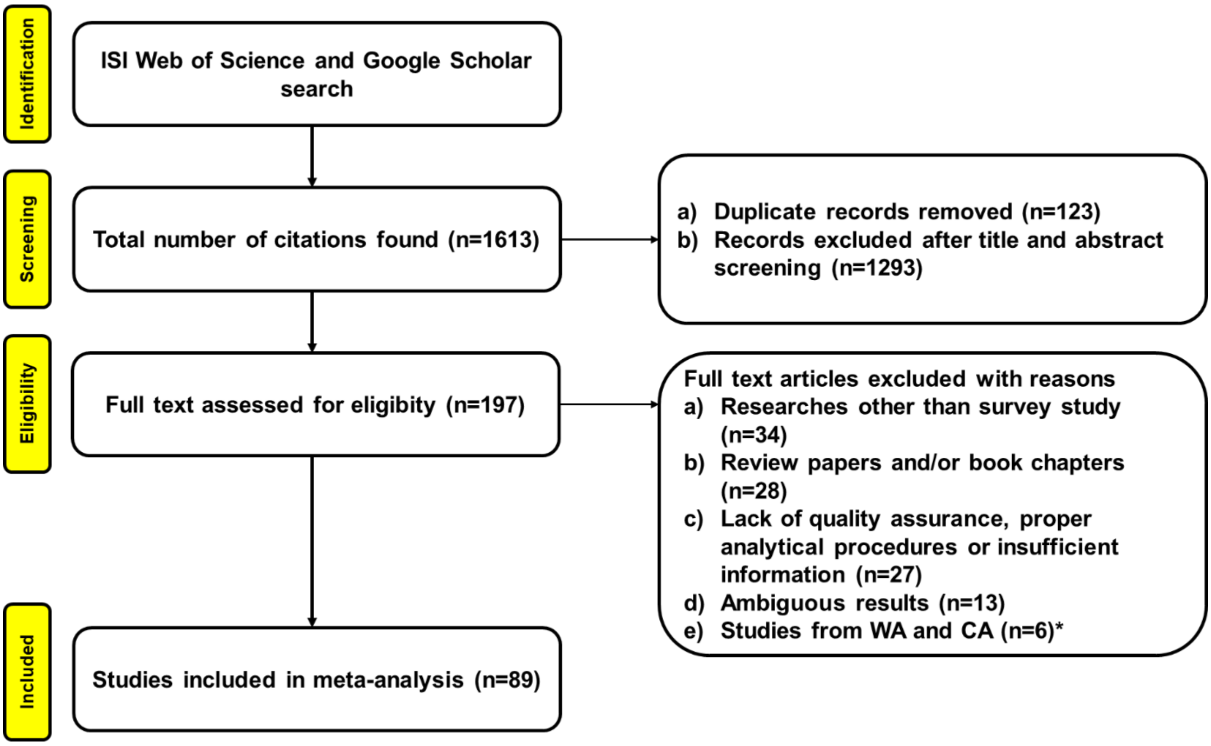

Figure S2. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) diagram for risk assessment

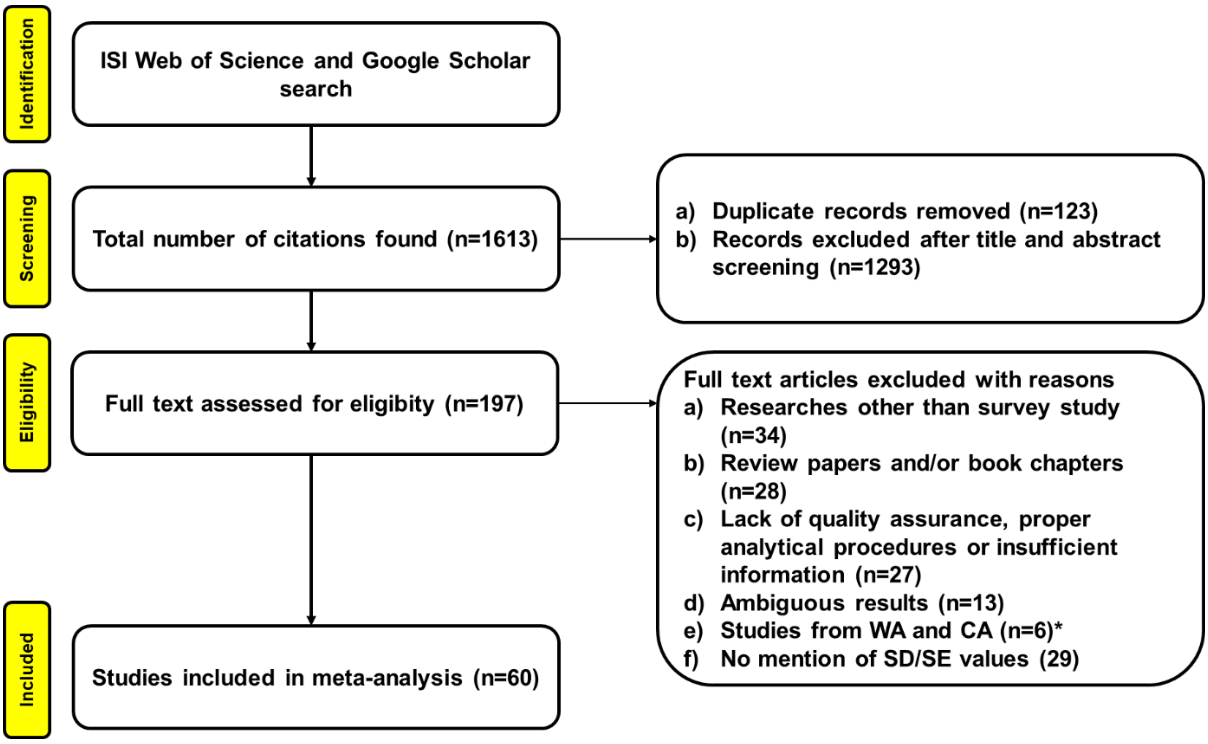

Figure S3. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) for developing forest plot.

*Studies from Western Asia (n=5) and Central Asia (n=1) didn't meet the minimum criteria of n>10 to be considered for further analysis

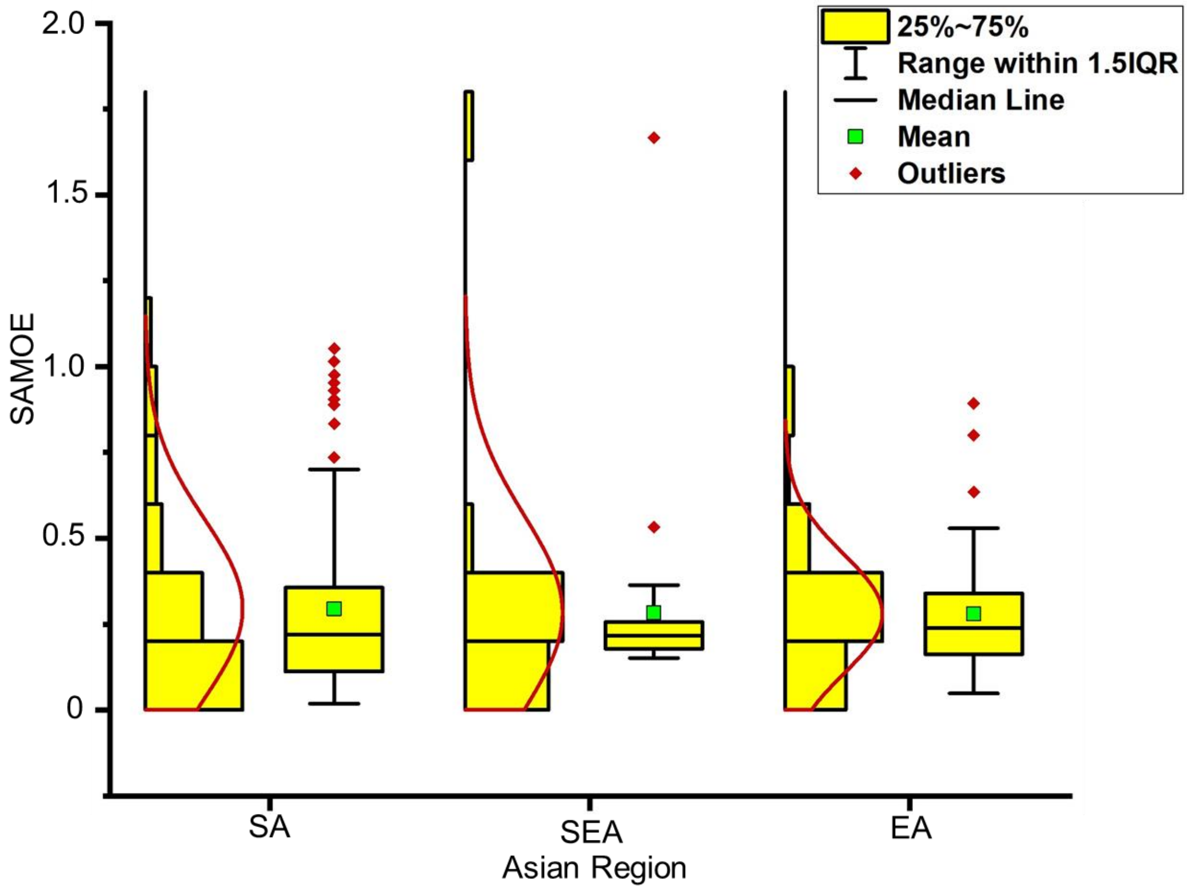

Figure S4. Box plot with data distribution curve showing comparative distribution of SAMOE in adults due to consumption of arsenic contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions.

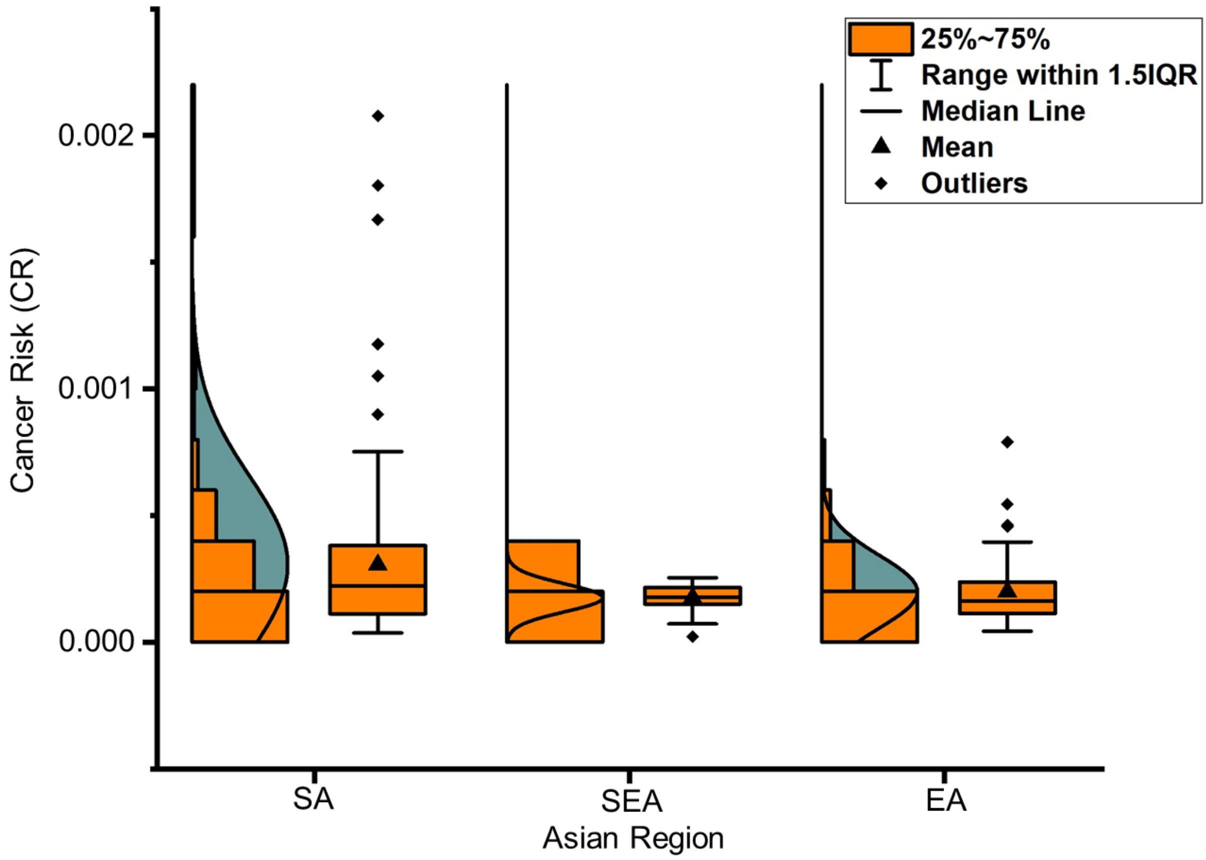

Figure S5. Box plot with data distribution curve showing the comparative distribution of possible carcinogenic risk in children due to consumption of arsenic contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions. The USEPA suggests a safe limit of 10^{-6} for human health.

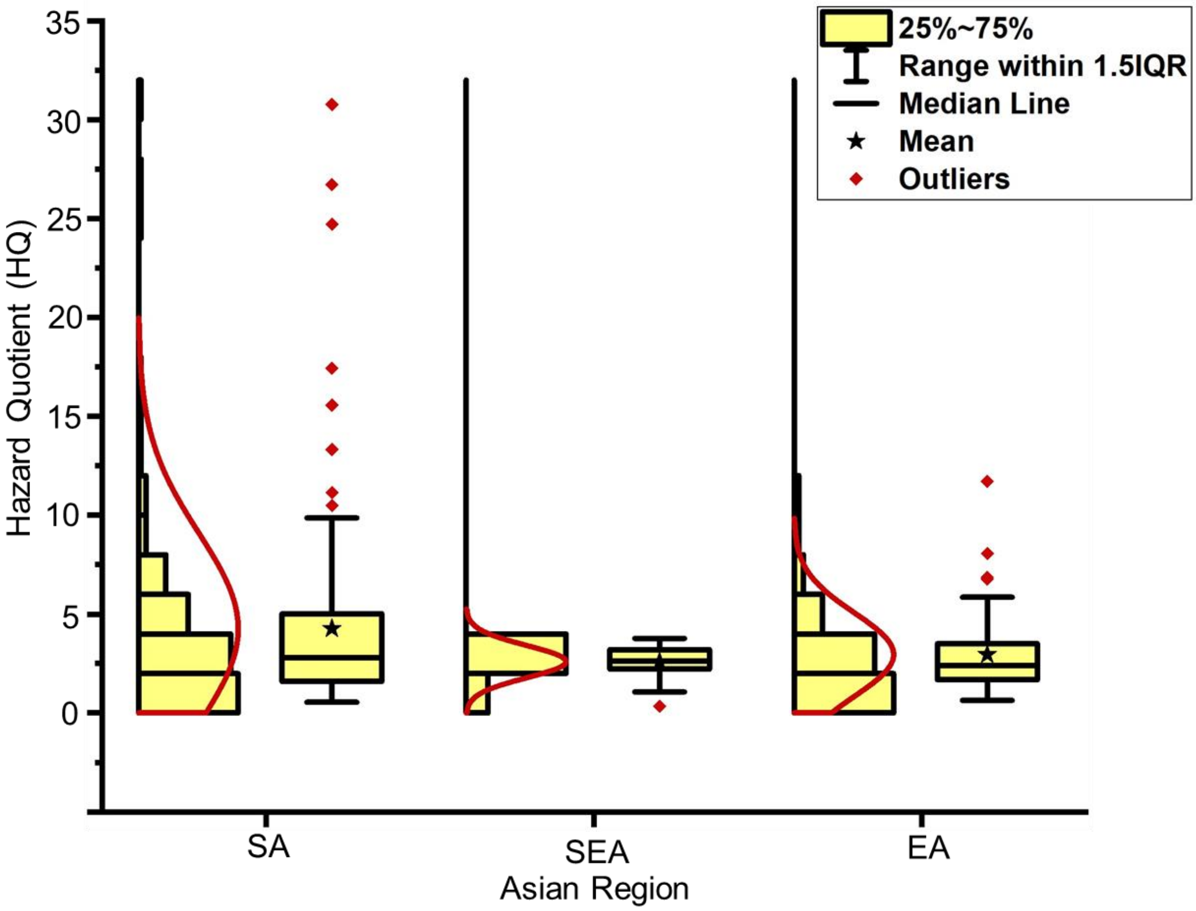

Figure S6. Box plot with data distribution curve showing comparative distribution of possible hazard quotient in adults due to consumption of arsenic contaminated rice grains in South Asia (SA), South East Asia (SEA), and East Asia (EA) regions. The USEPA suggests a safe limit of 1 for human health.

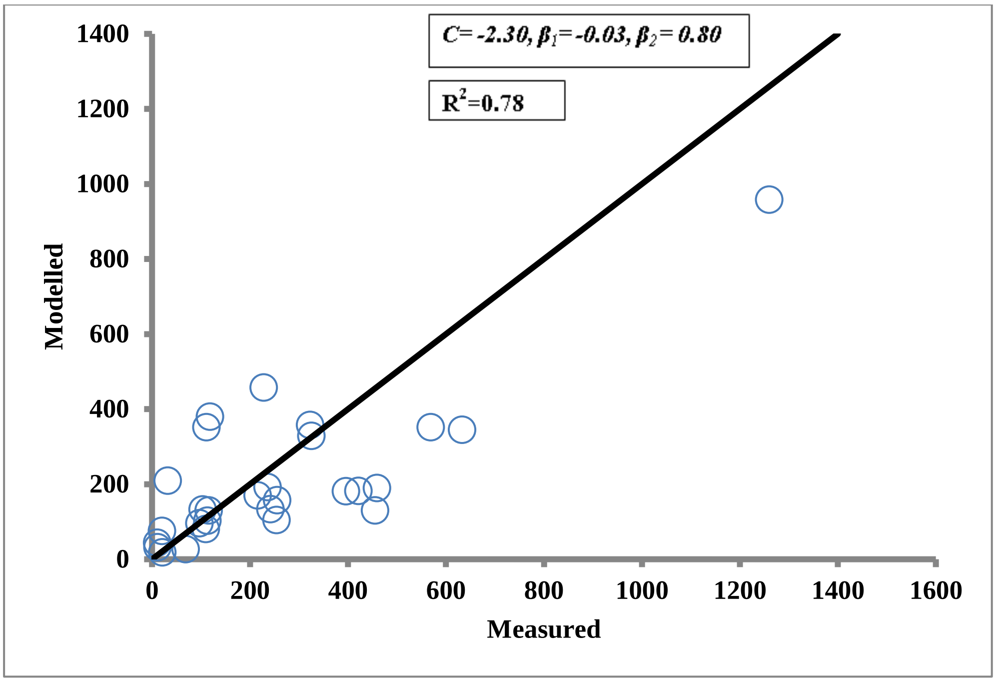

Figure S7. Comparison of observed and predicted arsenic content of rice grain on 1:1 line; arsenic content in rice was predicted by solubility-free ion activity model based on pH Mc(EDTA extractable metal assumed to be adsorbed on Walkley and Black organic carbon (**Source**: Golui et al., 2017)

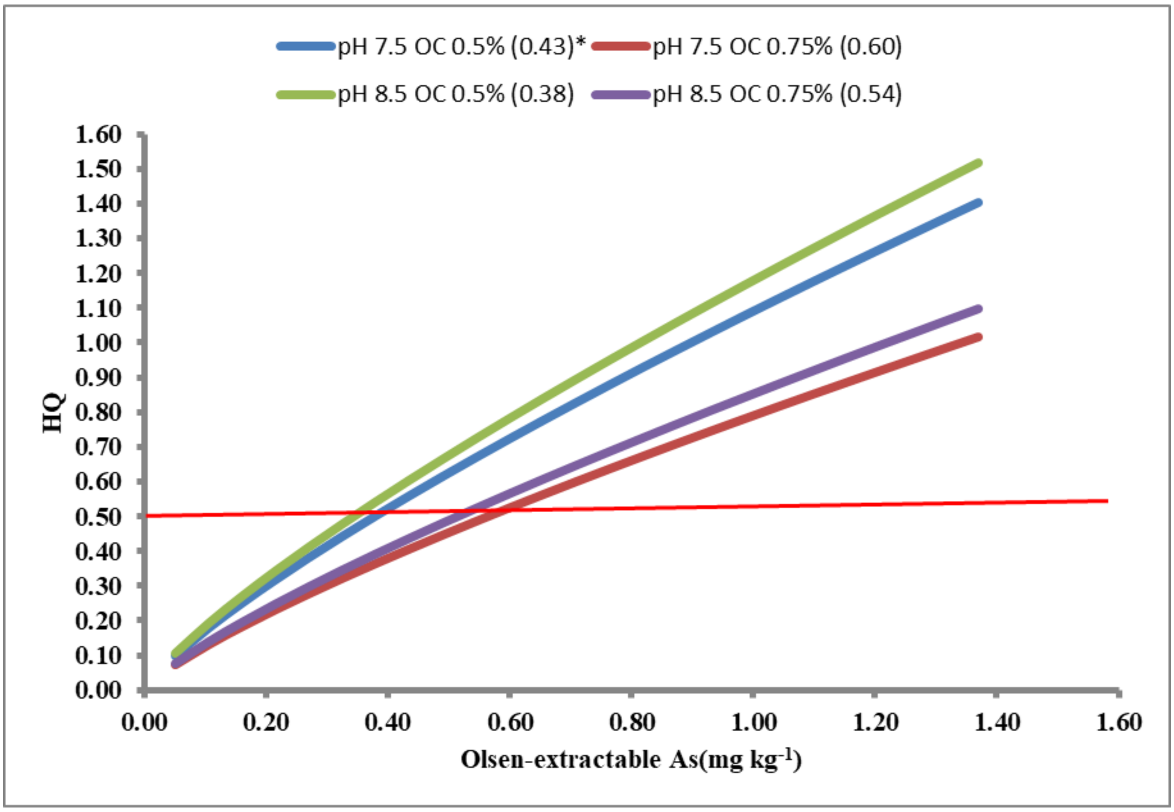

Figure S8. Permissible limit of Olsen-extractable arsenic in soils in relation to pH and organic carbon for intake of arsenic through rice grain by human. * Values in parentheses indicate the toxic limit of extractable arsenic in soil (**Source**: Golui et al., 2017)

Table S1. Key words used to search published literature from the IS Web of Science and Google Scholar

arsenic	rice	grain	United Arab Emirates	
arsenic	rice	grain	Vietnam	
arsenic	rice	grain	Tajikistan	
arsenic	rice	grain	Israel	
arsenic	rice	grain	Turkey	
arsenic	rice	grain	Iran	
arsenic	rice	grain	Bhutan	
arsenic	rice	grain	Laos	
arsenic	rice	grain	Thailand	
arsenic	rice	grain	Lebanon	
arsenic	rice	grain	Kyrgyzstan	
arsenic	rice	grain	Turkmenistan	
arsenic	rice	grain	Singapore	
arsenic	rice	grain	Myanmar	
arsenic	rice	grain	Maldives	
arsenic	rice	grain	South Korea	
arsenic	rice	grain	Oman	
arsenic	rice	grain	State of Palestine	
arsenic	rice	grain	Brunei	
arsenic	rice	grain	Kuwait	
arsenic	rice	grain	Iraq	
arsenic	rice	grain	Georgia	
arsenic	rice	grain	Afghanistan	
arsenic	rice	grain	Saudi Arabia	

arsenic	rice	grain	Uzbekistan	
arsenic	rice	grain	Mongolia	
arsenic	rice	grain	Malaysia	
arsenic	rice	grain	Yemen	
arsenic	rice	grain	Armenia	
arsenic	rice	grain	Nepal	
arsenic	rice	grain	Qatar	
arsenic	rice	grain	Indonesia	
arsenic	rice	grain	North Korea	
arsenic	rice	grain	Pakistan	
arsenic	rice	grain	Sri Lanka	
arsenic	rice	grain	Kazakhstan	
arsenic	rice	grain	Syria	
arsenic	rice	grain	Bahrain	
arsenic	rice	grain	Cambodia	
arsenic	rice	grain	Bangladesh	
arsenic	rice	grain	China	
arsenic	rice	grain	Timor-Leste	
arsenic	rice	grain	Japan	
arsenic	rice	grain	Cyprus	
arsenic	rice	grain	Philippines	
arsenic	rice	grain	Jordan	
arsenic	rice	grain	Azerbaijan	
arsenic	rice	grain	India	
arsenic	rice	grain	Asia	Survey

arsenic	rice	grain	Asia	Farmer field
arsenic	rice	grain	Asia	Market

Table S2. Rice grain inorganic arsenic content (μg kg^{-1}) and the calculated carcinogenic risk (ingestion) (adult and children), SAMOE and hazard quotient values in the Asian region

S. No.	Asian region	Mean total rice grain As (μg kg^{-1})	Mean inorganic As (μg kg^{-1})*	Carcinogenic risk (CR)-Adult	Carcinogenic risk (CR)-Children	SAMOE	Hazard quotient (HQ)	Sources
Field survey								
1.	**South Asia**	114	85.5	0.00031	0.00011	0.35	1.63	Ahmed et al. 2011
		121	90.8	0.00033	0.00012	0.33	1.73	Ahmed et al. 2011
		144	108.0	0.00040	0.00014	0.28	2.06	Ahmed et al. 2011
		115	86.3	0.00032	0.00011	0.35	1.64	Ahmed et al. 2011
		104	78.0	0.00029	0.00010	0.38	1.49	Ahmed et al. 2011
		141	105.8	0.00039	0.00014	0.28	2.01	Ahmed et al. 2011
		129	96.8	0.00036	0.00012	0.31	1.84	Ahmed et al. 2011
		362	271.5	0.00100	0.00035	0.11	5.17	Ahmed et al. 2011
		297	222.8	0.00082	0.00029	0.13	4.24	Ahmed et al. 2011
		326	244.5	0.00090	0.00031	0.12	4.66	Ahmed et al. 2011
		237	177.8	0.00065	0.00023	0.17	3.39	Ahmed et al. 2011

		270	202.5	0.00074	0.00026	0.15	3.86	Ahmed et al. 2011
		157	117.8	0.00043	0.00015	0.25	2.24	Ahmed et al. 2011
		352	264.0	0.00097	0.00034	0.11	5.03	Ahmed et al. 2011
		273	204.8	0.00075	0.00026	0.15	3.90	Ahmed et al. 2011
		276	207.0	0.00076	0.00027	0.14	3.94	Ahmed et al. 2011
		454	340.5	0.00125	0.00044	0.09	6.49	Ahmed et al. 2011
		110.5	82.9	0.00030	0.00011	0.36	1.58	Alam and Mollah 2021
		141	105.8	0.00039	0.00014	0.28	2.01	Azmy 2020
		451	338.3	0.00124	0.00043	0.09	6.44	Bhattacharya et al. 2010a
		334	250.5	0.00092	0.00032	0.12	4.77	Bhattacharya et al. 2010a
		230	172.5	0.00063	0.00022	0.17	3.29	Bhattacharya et al. 2010b
		300	225.0	0.00083	0.00029	0.13	4.29	Bhattacharya et al. 2010b
		400	300.0	0.00110	0.00039	0.10	5.71	Bhattacharya et al. 2010b
		240	180.0	0.00066	0.00023	0.17	3.43	Bhattacharya et al. 2010b
		540	405.0	0.00149	0.00052	0.07	7.71	Bhattacharya et al. 2010b
		160	120.0	0.00044	0.00015	0.25	2.29	Bhattacharya et al. 2010b

		160	120.0	0.00044	0.00015	0.25	2.29	Bhattacharya et al. 2010b
		230	172.5	0.00063	0.00022	0.17	3.29	Bhattacharya et al. 2010b
		580	435.0	0.00160	0.00056	0.07	8.29	Bhattacharya et al. 2010b
		290	217.5	0.00080	0.00028	0.14	4.14	Bhattacharya et al. 2010b
		410	307.5	0.00113	0.00040	0.10	5.86	Bhatti et al. 2020
		690	517.5	0.00190	0.00067	0.06	9.86	Biswas et al. 2014
		430	322.5	0.00118	0.00041	0.09	6.14	Biswas et al. 2014
		540	405.0	0.00149	0.00052	0.07	7.71	Biswas et al. 2014
		480	360.0	0.00132	0.00046	0.08	6.86	Biswas et al. 2014
		410	307.5	0.00113	0.00040	0.10	5.86	Biswas et al. 2014
		780	585.0	0.00215	0.00075	0.05	11.14	Biswas et al. 2014
		560	420.0	0.00154	0.00054	0.07	8.00	Biswas et al. 2014
		520	390.0	0.00143	0.00050	0.08	7.43	Biswas et al. 2014
		420	315.0	0.00116	0.00041	0.10	6.00	Biswas et al. 2014
		530	397.5	0.00146	0.00051	0.08	7.57	Biswas et al. 2014
		4.91	3.68	0.00001	0.000005	0.07	8.14	Singh et al. 2010

		3.62	2.72	0.00001	0.000003	0.05	11.0	Singh et al. 2010
		3.47	2.60	0.00001	0.000003	0.04	11.5	Singh et al. 2010
		4.44	3.33	0.00001	0.000004	0.06	9.00	Singh et al. 2010
		3.41	2.56	0.00001	0.000003	0.04	11.7	Singh et al. 2010
		4.01	3.01	0.00001	0.000004	0.05	9.97	Singh et al. 2010
		3.3	2.48	0.00001	0.000003	0.04	12.1	Singh et al. 2010
		3.74	2.81	0.00001	0.000004	0.05	10.6	Singh et al. 2010
		121	90.8	0.00033	0.00012	0.33	1.73	Cano-Lamadrid et al. 2015
		60	45.0	0.00017	0.00006	0.67	0.86	Dahal et al. 2008
		60	45.0	0.00017	0.00006	0.67	0.86	Dahal et al. 2008
		240	180.0	0.00066	0.00023	0.17	3.43	Dahal et al. 2008
		330	247.5	0.00091	0.00032	0.12	4.71	Dahal et al. 2008
		210	157.5	0.00058	0.00020	0.19	3.00	Dahal et al. 2008
		136	102.0	0.00037	0.00013	0.29	1.94	Das et al. 2004
		48	36.0	0.00013	0.00005	0.83	0.69	Diyabalanage et al. 2016
		38	28.5	0.00010	0.00004	1.05	0.54	Diyabalanage et al. 2016

		41	30.8	0.00011	0.00004	0.98	0.59	Diyabalanage et al. 2016
		74	55.5	0.00020	0.00007	0.54	1.06	Diyabalanage et al. 2016
		43	32.3	0.00012	0.00004	0.93	0.61	Diyabalanage et al. 2016
		42	31.5	0.00012	0.00004	0.95	0.60	Diyabalanage et al. 2016
		45	33.8	0.00012	0.00004	0.89	0.64	Diyabalanage et al. 2016
		183	137.3	0.00050	0.00018	0.22	2.61	Duxbury et al. 2003
		117	87.8	0.00032	0.00011	0.34	1.67	Duxbury et al. 2003
		87	65.3	0.00024	0.00008	0.46	1.24	Fouladi et al. 2020
		296	222.0	0.00082	0.00029	0.14	4.23	Hossain et al. 2008
		150.5	112.9	0.00041	0.00015	0.27	2.15	Islam et al. 2012
		89.1	66.8	0.00025	0.00009	0.45	1.27	Islam et al. 2013
		1870	1402.5	0.00515	0.00180	0.02	26.7	Islam et al. 2018
		1220	915.0	0.00336	0.00118	0.03	17.4	Jaafar et al. 2021
		1730	1297.5	0.00477	0.00167	0.02	24.7	Jaafar et al. 2021
		257.5	193.1	0.00071	0.00025	0.16	3.68	Golui et al. 2017
		2154	1615.5	0.00593	0.00208	0.02	30.7	Karmoker et al. 2020

		58.1	43.6	0.00016	0.00006	0.69	0.83	Kashyap et al. 2019
		932.5	699.4	0.00257	0.00090	0.04	13.3	Khanam et al. 2021
		410	307.5	0.00113	0.00040	0.10	5.86	Norton et al. 2009
		170	127.5	0.00047	0.00016	0.24	2.43	Norton et al. 2009
		273.9	205.4	0.00075	0.00026	0.15	3.91	Patel et al. 2005
		1090	817.5	0.00300	0.00105	0.04	15.5	Ponnugounder and Singh 2020
		143	107.3	0.00039	0.00014	0.28	2.04	Rahman et al. 2009
		153	114.8	0.00042	0.00015	0.26	2.19	Rahman et al. 2011
		390	292.5	0.00107	0.00038	0.10	5.57	Rezaitabar et al. 2012
		57.1	42.8	0.00016	0.00006	0.70	0.82	Sandhi et al. 2017
		103	77.3	0.00028	0.00010	0.39	1.47	Sandhi et al. 2017
		180	135.0	0.00050	0.00017	0.22	2.57	Sharma et al. 2017
		128.93	96.7	0.00036	0.00012	0.31	1.84	Shehzad et al. 2022
		44.21	33.2	0.00012	0.00004	0.90	0.63	Shehzad et al. 2022
		123.7	92.8	0.00034	0.00012	0.32	1.77	Shehzad et al. 2022
		735	551.3	0.00203	0.00071	0.05	10.5	Sun et al. 2009

		260	195.0	0.00072	0.00025	0.15	3.71	Williams et al. 2009
		350	262.5	0.00096	0.00034	0.11	5.00	Williams et al. 2009
		420	315.0	0.00116	0.00041	0.10	6.00	Williams et al. 2009
Market survey								
		320	256.0	0.00094	0.00033	0.12	4.88	Ahmed et al. 2016
		224	179.2	0.00066	0.00023	0.17	3.41	Azmy 2020
		160.3	128.2	0.00047	0.00016	0.23	2.44	Biswas et al. 2019
		252	201.6	0.00074	0.00026	0.15	3.84	Ghoochani et al. 2019
		79.8	63.8	0.00023	0.00008	0.47	1.22	Golui et al. 2017
		77	61.6	0.00023	0.00008	0.49	1.17	Liu et al. 2022a
		65	52.0	0.00019	0.00007	0.58	0.99	Nemati et al. 2014
		82	65.6	0.00024	0.00008	0.46	1.25	Nemati et al. 2014
		280	224.0	0.00082	0.00029	0.13	4.27	Rezaitabar et al. 2012
		161.7	129.4	0.00048	0.00017	0.23	2.46	Roya and Ali 2016
		36.95	29.6	0.00011	0.00004	1.01	0.56	Sarwar et al. 2020
		150	120.0	0.00044	0.00015	0.25	2.29	Tyagi et al. 2020

		51	40.8	0.00015	0.00005	0.74	0.78	Williams et al. 2005
		131.3	105.0	0.00039	0.00014	0.29	2.00	Williams et al. 2005
S. No.	**Asian region**	**Mean total As (μg kg^{-1})**	**Mean inorganic As (μg kg^{-1})**	**Carcinogenic risk (CR)-Adult**	**Carcinogenic risk (CR)-Children**	**SAMOE**	**Hazard quotient (HQ)**	**Sources**
Field survey								
2.	**South East Asia**	212.1	134.0	0.00049	0.00017	0.22	2.55	Chanpiwat and Kim 2019
		196	124.5	0.00046	0.00016	0.24	2.37	Chanpiwat and Kim 2019
		115	86.3	0.00032	0.00011	0.35	1.64	Chu et al. 2021
		256	192.0	0.00071	0.00025	0.16	3.66	Phan et al. 2013
		75	56.3	0.00021	0.00007	0.53	1.07	Phan et al. 2013
		24	18.0	0.00007	0.00002	1.67	0.34	Phan et al. 2013
		160	120.0	0.00044	0.00015	0.25	2.29	Kukusamude et al. 2020
		190	142.5	0.00052	0.00018	0.21	2.71	Kukusamude et al. 2020
		110	82.5	0.00030	0.00011	0.36	1.57	Kukusamude et al. 2020
		240	180.0	0.00066	0.00023	0.17	3.43	Kukusamude et al. 2020

		220	165.0	0.00061	0.00021	0.18	3.14	Nguyen et al. 2019
		180	135.0	0.00050	0.00017	0.22	2.57	Nguyen et al. 2020
		243	182.3	0.00067	0.00023	0.16	3.47	Reid et al. 2020
Market survey								
		220	176.0	0.00065	0.00023	0.17	3.35	Gilbert et al. 2015
		197	157.6	0.00058	0.00020	0.19	3.00	Gilbert et al. 2015
		197	157.6	0.00058	0.00020	0.19	3.00	Gilbert et al. 2015
		181	144.8	0.00053	0.00019	0.21	2.76	Gilbert et al. 2015
		205	164.0	0.00060	0.00021	0.18	3.12	Hensawang et al. 2017
		161.07	128.9	0.00047	0.00017	0.23	2.45	Nookabkaew et al. 2013
		227.89	182.3	0.00067	0.00023	0.16	3.47	Nookabkaew et al. 2013
		142.23	113.8	0.00042	0.00015	0.26	2.17	Nookabkaew et al. 2013
		247.4	197.9	0.00073	0.00025	0.15	3.77	Nookabkaew et al. 2013
		107.76	86.2	0.00032	0.00011	0.35	1.64	Nookabkaew et al. 2013
S. No.	**Asian region**	**Mean total As (µg kg^{-1})**	**Mean inorganic As (µg kg^{-1})**	**Carcinogenic risk (CR)-Adult**	**Carcinogenic risk (CR)-Children**	**SAMOE**	**Hazard quotient (HQ)**	**Sources**

		215.16	172.1	0.00063	0.00022	0.17	3.28	Nookabkaew et al. 2013
		151.86	121.5	0.00045	0.00016	0.25	2.31	Nookabkaew et al. 2013
		159.14	127.3	0.00047	0.00016	0.24	2.42	Nookabkaew et al. 2013
		136.1	108.9	0.00040	0.00014	0.28	2.07	Pedron et al. 2021
		203.61	162.9	0.00060	0.00021	0.18	3.10	Pedron et al. 2021
Field survey								
3.	**East Asia**	200	150.0	0.00055	0.00019	0.20	2.86	Chung et al. 2005
		480	360.0	0.00132	0.00046	0.08	6.86	Cui et al. 2022
		92	69.0	0.00025	0.00009	0.43	1.31	Fu et al. 2011
		199	149.3	0.00055	0.00019	0.20	2.84	Hang et al. 2009
		340	255.0	0.00094	0.00033	0.12	4.86	Hao et al. 2022
		474	355.5	0.00131	0.00046	0.08	6.77	Hsu et al. 2012
		75.6	56.7	0.00021	0.00007	0.53	1.08	Hu et al. 2013
		50	37.5	0.00014	0.00005	0.80	0.71	Hu et al. 2014
		116.5	87.4	0.00032	0.00011	0.34	1.66	Huang et al. 2006
		116.5	87.4	0.00032	0.00011	0.34	1.66	Huang et al. 2015

		350	262.5	0.00096	0.00034	0.11	5.00	Huang et al. 2018
		180	135.0	0.00050	0.00017	0.22	2.57	Kim et al. 2018
		90	67.5	0.00025	0.00009	0.44	1.29	Kong et al. 2018
		146	109.5	0.00040	0.00014	0.27	2.09	Kunhikrishnan et al. 2015
		137	102.8	0.00038	0.00013	0.29	1.96	Kuramata et al. 2011
		247	185.3	0.00068	0.00024	0.16	3.53	Kwon et al. 2016
		410	307.5	0.00113	0.00040	0.10	5.86	Lee et al. 2008
		260	195.0	0.00072	0.00025	0.15	3.71	Li et al. 2014
		245.4	184.1	0.00068	0.00024	0.16	3.51	Li et al. 2015
		148.4	111.3	0.00041	0.00014	0.27	2.12	Li et al. 2015
S. No.	**Asian region**	**Mean total As (μg kg^{-1})**	**Mean inorganic As (μg kg^{-1})**	**Carcinogenic risk (CR)-Adult**	**Carcinogenic risk (CR)-Children**	**SAMOE**	**Hazard quotient (HQ)**	**Sources**
		114.4	85.8	0.00032	0.00011	0.35	1.63	Liang et al. 2010
		119	89.3	0.00033	0.00011	0.34	1.70	Lin et al. 2021
		564	423.0	0.00155	0.00054	0.07	8.06	Liu et al. 2010
		360	270.0	0.00099	0.00035	0.11	5.14	Liu et al. 2015

		188	141.0	0.00052	0.00018	0.21	2.69	Liu et al. 2022b
		191	143.3	0.00053	0.00018	0.21	2.73	Lu et al. 2010
		295	221.3	0.00081	0.00028	0.14	4.21	Lu et al. 2010
		129.4	97.1	0.00036	0.00012	0.31	1.85	Ma et al. 2016
		172.9	129.7	0.00048	0.00017	0.23	2.47	Ma et al. 2017
		125	93.8	0.00034	0.00012	0.32	1.79	Mu et al. 2019
		820	615.0	0.00226	0.00079	0.05	11.7	Sun et al. 2008
		196	147.0	0.00054	0.00019	0.20	2.80	Yao et al. 2020
		63	47.3	0.00017	0.00006	0.63	0.90	Zhu et al. 2008
		215	161.3	0.00059	0.00021	0.19	3.07	Zhu et al. 2008
		303	227.3	0.00083	0.00029	0.13	4.33	Zhu et al. 2008
		190	142.5	0.00052	0.00018	0.21	2.71	Zhu et al. 2008
Market survey								
		116.6	93.3	0.00034	0.00012	0.32	1.78	Chen et al. 2016
		215.5	172.4	0.00063	0.00022	0.17	3.28	Chen et al. 2016
		87	69.6	0.00026	0.00009	0.43	1.33	Chen et al. 2018

		42	33.6	0.00012	0.00004	0.89	0.64	Fu et al. 2015
		88	70.4	0.00026	0.00009	0.43	1.34	Lee et al. 2018
		160	128.0	0.00047	0.00016	0.23	2.44	Lee et al. 2018
		154.91	123.9	0.00046	0.00016	0.24	2.36	Li et al. 2020
		119	95.2	0.00035	0.00012	0.32	1.81	Qian et al. 2010
		121	96.8	0.00036	0.00012	0.31	1.84	Zhu et al. 2008
S. No.	**Asian region**	**Mean total As (μg kg^{-1})**	**Mean inorganic As (μg kg^{-1})**	**Carcinogenic risk (CR)-Adult**	**Carcinogenic risk (CR)-Children**	**SAMOE**	**Hazard quotient (HQ)**	**Sources**
		114	91.2	0.00034	0.00012	0.33	1.74	Zhu et al. 2008
		90	72.0	0.00026	0.00009	0.42	1.37	Zhu et al. 2008
		120	96.0	0.00035	0.00012	0.31	1.83	Zhu et al. 2008

*Inorganic As = 80% of polished rice (market grain samples assumed to be polished rice), and Inorganic As = 75% of husked rice (field grain samples assumed to be husked rice)

Table S3. Clinical features of 182 participants studied in arsenic contaminated areas of Malda district, West Bengal, India (**Source:** Golui et al., 2017)

Characteristics	*Cases*		*Controls*	
	n=80		n=102	
Age	N	%	N	%
12- < 18	1	1.25	2	1.96
18- < 30	11	13.7	27	26.5
30- < 60	46	57.5	53	52.0
> 60	22	27.5	20	19.6
Sex				
Male	56	70.0	43	42.1
Female	24	30.0	59	57.8
Pigmentation				
+	50	62.5	-	-
++	24	30.0	-	-
+++	3	3.75	-	-
Keratosis				
+	30	37.5	-	-
++	10	12.5	-	-
+++	2	2.50	-	-
Cough	11	13.8	1	0.98
Dyspnoea	5	6.25	-	-
Solid Endema Limb	-	-	-	-

Weakness	23	28.8	-	-
Diarrhea	2	2.50	-	-
Limb Pain	11	13.8	-	-
Tinging	8	10.0	-	-
Liver Enlargement	-	-	-	-
Ascites	-	-	-	-
Pitting Limb Swelling	-	-	-	-
Gangrene	-	-	-	-
Conjestion of Eye/Location	-	-	-	-
Cancer	1	1.25	-	-
Bowens Disease	4	5.00	-	-

References

1. Ahmed, M. K., Shaheen, N., Islam, M. S., Habibullah-Al-Mamun, M., Islam, S., Islam, M. M., ... & Bhattacharjee, L. (2016). A comprehensive assessment of arsenic in commonly consumed foodstuffs to evaluate the potential health risk in Bangladesh. *Science of the Total Environment*, *544*, 125-133.

2. Ahmed, Z. U., Panaullah, G. M., Gauch, H., McCouch, S. R., Tyagi, W., Kabir, M. S., & Duxbury, J. M. (2011). Genotype and environment effects on rice (Oryza sativa L.) grain arsenic concentration in Bangladesh. *Plant and Soil*, *338*, 367-382.

3. Alam, M. M., & Mollah, F. H (2021). Accumulation, Distribution and Source Analysis of Arsenic in Rice in Different Growing Areas of Bangladesh. Annals of International Medical and Dental Research, 7(6), 302-308.

4. Azmy, S. (2020). Detection of metals and trace elements in rice in Matlab, Bangladesh: A descriptive study.

5. Bhattacharya, P., Samal, A. C., Majumdar, J., & Santra, S. C. (2010a). Arsenic contamination in rice, wheat, pulses, and vegetables: a study in an arsenic affected area of West Bengal, India. *Water, Air, & Soil Pollution*, *213*, 3-13.

6. Bhattacharya, P., Samal, A. C., Majumdar, J., & Santra, S. C. (2010b). Accumulation of arsenic and its distribution in rice plant (Oryza sativa L.) in Gangetic West Bengal, India. *Paddy and Water Environment*, *8*, 63-70.

7. Bhatti, S. S., Kumar, V., Kumar, A., Kirby, J. K., Gouzos, J., Correll, R., ... & Nagpal, A. K. (2020). Potential carcinogenic and non-carcinogenic health hazards of metal (loid) s in food grains. *Environmental Science and Pollution Research*, *27*, 17032-17042.

8. Biswas, A., Biswas, S., Lavu, R. V. S., Gupta, P. C., & Santra, S. C. (2014). Arsenic-prone rice cultivars: a study in endemic region. *Paddy and water environment*, *12*, 379-386.

9. Biswas, A., Swain, S., Chowdhury, N. R., Joardar, M., Das, A., Mukherjee, M., & Roychowdhury, T. (2019). Arsenic contamination in Kolkata metropolitan city: perspective of transportation of agricultural products from arsenic-endemic areas. *Environmental Science and Pollution Research*, *26*, 22929-22944.

10. Cano-Lamadrid, M., Munera-Picazo, S., Burló, F., Hojjati, M., & Carbonell-Barrachina, Á. A. (2015). Total and inorganic arsenic in Iranian rice. *Journal of Food Science*, *80*(5), T1129-T1135.

11. Chanpiwat, P., & Kim, K. W. (2019). Arsenic health risk assessment related to rice consumption behaviors in adults living in Northern Thailand. *Environmental monitoring and assessment*, *191*, 1-12.

12. Chen, H. L., Lee, C. C., Huang, W. J., Huang, H. T., Wu, Y. C., Hsu, Y. C., & Kao, Y. T. (2016). Arsenic speciation in rice and risk assessment of inorganic arsenic in Taiwan population. *Environmental Science and Pollution Research*, *23*, 4481-4488.

13. Chen, H., Tang, Z., Wang, P., & Zhao, F. J. (2018). Geographical variations of cadmium and arsenic concentrations and arsenic speciation in Chinese rice. *Environmental Pollution*, *238*, 482-490.

14. Chu, D. B., Duong, H. T., Nguyet Luu, M. T., Vu-Thi, H. A., Ly, B. T., & Loi, V. D. (2021). Arsenic and heavy metals in Vietnamese rice: Assessment of human exposure to these elements through rice consumption. *Journal of analytical methods in chemistry*, *2021*.

15. Chung, E., Lee, J. S., Chon, H. T., & Sager, M. (2005). Environmental contamination and bioaccessibility of arsenic and metals around the Dongjeong Au–Ag–Cu mine, Korea. *Geochemistry: Exploration, Environment, Analysis*, *5*(1), 69-74.

16. Cui, H., Wen, J., Yang, L., & Wang, Q. (2022). Spatial distribution of heavy metals in rice grains and human health risk assessment in Hunan Province, China. *Environmental Science and Pollution Research*, *29*(55), 83126-83137.

17. Dahal, B. M., Fuerhacker, M., Mentler, A., Karki, K. B., Shrestha, R. R., & Blum, W. E. H. (2008). Arsenic contamination of soils and agricultural plants through irrigation water in Nepal. *Environmental pollution*, *155*(1), 157-163.

18. Das, H. K., Mitra, A. K., Sengupta, P. K., Hossain, A., Islam, F., & Rabbani, G. H. (2004). Arsenic concentrations in rice, vegetables, and fish in Bangladesh: a preliminary study. *Environment international*, *30*(3), 383-387.

19. Diyabalanage, S., Navarathna, T., Abeysundara, H. T., Rajapakse, S., & Chandrajith, R. (2016). Trace elements in native and improved paddy rice from different climatic regions of Sri Lanka: implications for public health. *SpringerPlus*, *5*, 1-10.

20. Duxbury, J. M., Mayer, A. B., Lauren, J. G., & Hassan, N. (2003). Food chain aspects of arsenic contamination in Bangladesh: effects on quality and productivity of rice. *Journal of Environmental Science and Health, Part A*, *38*(1), 61-69.

21. Hu, Q., Sun, X., Yang, W., Fang, Y., Ma, N., Xin, Z., Fu, J., Liu, X., Liu, M., Mariga, A.M., Zhu, X., Concentrations and health risks of lead, cadmium, arsenic, and mercury in rice and edible mushrooms in China, Food Chemistry (2013), doi: http://dx.doi.org/10.1016/j.foodchem.2013.09.116

22. Fouladi, M., Mohammadi Rouzbahani, M., Attar Roshan, S., & Sabz Alipour, S. (2021). Health risk assessment of potentially toxic elements in common cultivated rice (Oryza sativa) emphasis on environmental pollution. *Toxin Reviews*, *40*(4), 1019-1034.

23. Fu, Q. L., Li, L., Achal, V., Jiao, A. Y., & Liu, Y. (2015). Concentrations of heavy metals and arsenic in market rice grain and their potential health risks to the population of Fuzhou, China. *Human and Ecological Risk Assessment: An International Journal*, *21*(1), 117-128.

24. Fu, Y., Chen, M., Bi, X., He, Y., Ren, L., Xiang, W., ... & Ma, Z. (2011). Occurrence of arsenic in brown rice and its relationship to soil properties from Hainan Island, China. *Environmental pollution*, *159*(7), 1757-1762.

25. Ghoochani, M., Dehghani, M. H., Mehrabi, F., Rahimi Fard, N., Alimohammadi, M., Jahed Khaniki, G., & Nabizadeh Nodehi, R. (2019). 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. *Environmental Science and Pollution Research*, *26*, 24190-24197.

26. Gilbert, P. J., Polya, D. A., & Cooke, D. A. (2015). Arsenic hazard in Cambodian rice from a market-based survey with a case study of Preak Russey village, Kandal Province. *Environmental geochemistry and health*, *37*, 757-766.

27. Golui, D., Mazumder, D. G., Sanyal, S. K., Datta, S. P., Ray, P., Patra, P. K., ... & Bhattacharya, K. (2017). 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*, *144*, 227-235.

28. Hang, X., Wang, H., Zhou, J., Ma, C., Du, C., & Chen, X. (2009). Risk assessment of potentially toxic element pollution in soils and rice (Oryza sativa) in a typical area of the Yangtze River Delta. *Environmental pollution*, *157*(8-9), 2542-2549.

29. Hao, H., Ge, D., Wen, Y., Lv, Y., & Chen, W. (2021). Probabilistic health risk assessment of inorganic arsenic and some heavy metals in rice produced from a typical multi-mining county, China. *Environmental Science and Pollution Research*, 1-14.

30. Hensawang, S., & Chanpiwat, P. (2017). Health impact assessment of arsenic and cadmium intake via rice consumption in Bangkok, Thailand. *Environmental Monitoring and Assessment*, *189*, 1-10.

31. Hossain, M. B., Jahiruddin, M., Panaullah, G. M., Loeppert, R. H., Islam, M. R., & Duxbury, J. M. (2008). Spatial variability of arsenic concentration in soils and plants, and its relationship with iron, manganese and phosphorus. *Environmental Pollution*, *156*(3), 739-744.

32. Hsu, W. M., Hsi, H. C., Huang, Y. T., Liao, C. S., & Hseu, Z. Y. (2012). Partitioning of arsenic in soil–crop systems irrigated using groundwater: a case study of rice paddy soils in southwestern Taiwan. *Chemosphere*, *86*(6), 606-613.

33. Hu, P., Huang, J., Ouyang, Y., Wu, L., Song, J., Wang, S., ... & Christie, P. (2013). Water management affects arsenic and cadmium accumulation in different rice cultivars. *Environmental Geochemistry and Health*, *35*, 767-778.

34. Huang, R. Q., Gao, S. F., Wang, W. L., Staunton, S., & Wang, G. (2006). Soil arsenic availability and the transfer of soil arsenic to crops in suburban areas in Fujian Province, southeast China. *Science of the total environment*, *368*(2-3), 531-541.

35. Huang, Y., Chen, Q., Deng, M., Japenga, J., Li, T., Yang, X., & He, Z. (2018). Heavy metal pollution and health risk assessment of agricultural soils in a typical peri-urban area in southeast China. *Journal of environmental management*, *207*, 159-168.

36. Huang, Y., Wang, M., Mao, X., Qian, Y., Chen, T., & Zhang, Y. (2015). Concentrations of inorganic arsenic in milled rice from China and associated dietary exposure assessment. *Journal of agricultural and food chemistry*, *63*(50), 10838-10845.

37. Islam, M. R., Brammer, H., Mustafizur Rahman, G. K. M., Raab, A., Jahiruddin, M., Solaiman, A. R. M., ... & Norton, G. J. (2012). Arsenic in rice grown in low-arsenic environments in Bangladesh. *Water Quality, Exposure and Health*, *4*, 197-208.

38. Islam, M. S., Proshad, R., Asadul Haque, M., Hoque, M. F., Hossin, M. S., & Islam Sarker, M. N. (2018). Assessment of heavy metals in foods around the industrial areas: Health hazard inference in Bangladesh. *Geocarto international*, *35*(3), 280-295.

39. Jaafar, M., Shrivastava, A., Bose, S. R., Felipe-Sotelo, M., & Ward, N. I. (2021). Transfer of arsenic, manganese and iron from water to soil and rice plants: An evaluation of changes in dietary intake caused by washing and cooking rice with groundwater from the Bengal Delta, India. *Journal of food composition and analysis*, *96*, 103748.

40. Kashyap, R., Ahmad, M., Uniyal, S. K., & Verma, K. S. (2019). Dietary consumption of metal (loid) s-contaminated rice grown in croplands around industrial sectors: A human health risk perspective. *International Journal of Environmental Science and Technology*, *16*, 8505-8516.

41. Khanam, R., Hazra, G. C., Ghosh Bag, A., Kulsum, P. G. P. S., Chatterjee, N., & Shukla, A. K. (2021). Risk assessment of arsenic toxicity through groundwater-soil-rice system in Maldah District, Bengal Delta Basin, India. *Archives of Environmental Contamination and Toxicology*, *81*, 438-448.

42. Kim, D. Y., Kim, J. Y., Kim, K. H., Kim, K. R., Kim, H. S., Kim, J. G., & Kim, W. I. (2018). Arsenic species in husked and polished rice grains grown at the non-contaminated paddy soils in Korea. *Journal of Applied Biological Chemistry*, *61*(4), 391-395.

43. Kong, X., Liu, T., Yu, Z., Chen, Z., Lei, D., Wang, Z., ... & Zhang, S. (2018). Heavy metal bioaccumulation in rice from a high geological background area in Guizhou Province, China. *International journal of environmental research and public health*, *15*(10), 2281.

44. Kormoker, T., Proshad, R., Islam, M. S., Tusher, T. R., Uddin, M., Khadka, S., ... & Sayeed, A. (2020). Presence of toxic metals in rice with human health hazards in Tangail district of Bangladesh. *International journal of environmental health research*, *32*(1), 40-60.

45. Kukusamude, C., Sricharoen, P., Limchoowong, N., & Kongsri, S. (2021). Heavy metals and probabilistic risk assessment via rice consumption in Thailand. *Food Chemistry*, *334*, 127402.

46. Kunhikrishnan, A., Go, W. R., Park, J. H., Kim, K. R., Kim, H. S., Kim, K. H., ... & Cho, N. J. (2015). Heavy metal (loid) levels in paddy soils and brown rice in Korea. *Korean Journal of Soil Science and Fertilizer*, *48*(5), 515-521.

47. Kuramata, M., Abe, T., Matsumoto, S., & Ishikawa, S. (2011). Arsenic accumulation and speciation in Japanese paddy rice cultivars. *Soil science and plant nutrition*, *57*(2), 248-258.

48. Kwon, J. C., Nejad, Z. D., & Jung, M. C. (2017). Arsenic and heavy metals in paddy soil and polished rice contaminated by mining activities in Korea. *Catena*, *148*, 92-100.

49. Lee, J. S., Lee, S. W., Chon, H. T., & Kim, K. W. (2008). Evaluation of human exposure to arsenic due to rice ingestion in the vicinity of abandoned Myungbong Au–Ag mine site, Korea. *Journal of Geochemical Exploration*, *96*(2-3), 231-235.

50. Lee, S. G., Lee, Y. S., Cho, S. Y., Chung, M. S., Cho, M., Kang, Y., ... & Lee, K. W. (2018). Monitoring of arsenic contents in domestic rice and human risk assessment for daily intake of inorganic arsenic in Korea. *Journal of Food Composition and Analysis*, *69*, 25-32.

51. Li, J., Dong, F., Lu, Y., Yan, Q., & Shim, H. (2014). Mechanisms controlling arsenic uptake in rice grown in mining impacted regions in South China. *PloS one*, *9*(9), e108300.

52. Li, L., Feng, H., & Wei, J. (2020). Toxic element (As and Hg) content and health risk assessment of commercially available rice for residents in Beijing based on their dietary consumption. *Environmental Science and Pollution Research*, *27*(12), 13205-13214.

53. Li, X., Xie, K., Yue, B., Gong, Y., Shao, Y., Shang, X., & Wu, Y. (2015). Inorganic arsenic contamination of rice from Chinese major rice-producing areas and exposure assessment in Chinese population. *Science China Chemistry*, *58*, 1898-1905.

54. Liang, F., Li, Y., Zhang, G., Tan, M., Lin, J., Liu, W., ... & Lu, W. (2010). Total and speciated arsenic levels in rice from China. *Food Additives and Contaminants*, *27*(6), 810-816.

55. Lin, J., Sun, D., Zhang, Z., Duan, Z., & Dong, J. (2021). Heavy metals and health risk of rice sampled in Yangtze River Delta, China. *Food Additives & Contaminants: Part B*, *14*(2), 133-140.

56. Liu, C. P., Luo, C. L., Gao, Y., Li, F. B., Lin, L. W., Wu, C. A., & Li, X. D. (2010). Arsenic contamination and potential health risk implications at an abandoned tungsten mine, southern China. *Environmental Pollution*, *158*(3), 820-826.

57. Liu, C., Yu, H. Y., Liu, C., Li, F., Xu, X., & Wang, Q. (2015). Arsenic availability in rice from a mining area: is amorphous iron oxide-bound arsenic a source or sink?. *Environmental Pollution*, *199*, 95-101.

58. Liu, L., Han, J., Xu, X., Xu, Z., Abeysinghe, K. S., Atapattu, A. J., ... & Qiu, G. (2020b). Dietary exposure assessment of cadmium, arsenic, and lead in market rice from Sri Lanka. *Environmental Science and Pollution Research*, *27*, 42704-42712.

59. Liu, Y., Cao, X., Hu, Y., & Cheng, H. (2022). Pollution, Risk and Transfer of Heavy Metals in Soil and Rice: A Case Study in a Typical Industrialized Region in South China. *Sustainability*, *14*(16), 10225.

60. Lu, Y., Dong, F., Deacon, C., Chen, H. J., Raab, A., & Meharg, A. A. (2010). Arsenic accumulation and phosphorus status in two rice (Oryza sativa L.) cultivars surveyed from fields in South China. *Environmental Pollution*, *158*(5), 1536-1541.

61. Ma, L., Wang, L., Jia, Y., & Yang, Z. (2016). Arsenic speciation in locally grown rice grains from Hunan Province, China: Spatial distribution and potential health risk. *Science of the Total Environment*, *557*, 438-444.

62. Ma, L., Wang, L., Jia, Y., & Yang, Z. (2017). Accumulation, translocation and conversion of six arsenic species in rice plants grown near a mine impacted city. *Chemosphere*, *183*, 44-52.

63. Mu, T., Wu, T., Zhou, T., Li, Z., Ouyang, Y., Jiang, J., ... & Wu, L. (2019). Geographical variation in arsenic, cadmium, and lead of soils and rice in the major rice producing regions of China. *Science of the Total Environment*, *677*, 373-381.

64. Nemati, S., Mosaferi, M., Ostadrahimi, A., & Mohammadi, A. (2014). Arsenic intake through consumed rice in Iran: markets role or government responsibility. *Health promotion perspectives*, *4*(2), 180.

65. Nguyen, T. P., Ruppert, H., Pasold, T., & Sauer, B. (2020b). Paddy soil geochemistry, uptake of trace elements by rice grains (Oryza sativa) and resulting health risks in the Mekong River Delta, Vietnam. *Environmental geochemistry and health*, *42*, 2377-2397.

66. Nguyen, T. P., Ruppert, H., Sauer, B., & Pasold, T. (2020a). Harmful and nutrient elements in paddy soils and their transfer into rice grains (Oryza sativa) along two river systems in northern and central Vietnam. *Environmental geochemistry and health*, *42*, 191-207.

67. Nookabkaew, S., Rangkadilok, N., Mahidol, C., Promsuk, G., & Satayavivad, J. (2013). Determination of arsenic species in rice from Thailand and other Asian countries using simple extraction and HPLC-ICP-MS analysis. *Journal of Agricultural and Food Chemistry*, *61*(28), 6991-6998.

68. Norton, G. J., Islam, M. R., Deacon, C. M., Zhao, F. J., Stroud, J. L., McGrath, S. P., ... & Meharg, A. A. (2009). Identification of low inorganic and total grain arsenic rice cultivars from Bangladesh. *Environmental Science & Technology*, *43*(15), 6070-6075.

69. Patel, K. S., Shrivas, K., Brandt, R., Jakubowski, N., Corns, W., & Hoffmann, P. (2005). Arsenic contamination in water, soil, sediment and rice of central India. *Environmental Geochemistry and health*, *27*, 131-145.

70. Pedron, T., Oliveira, G. S. P., Paniz, F. P., de Moura Souza, F., Masuda, H. P., dos Santos, M. C., ... & Batista, B. L. (2021). Determination of chemical elements in rice from Singapore markets: Distribution, estimated intake and differentiation of rice varieties. *Journal of Food Composition and Analysis*, *101*, 103969.

71. Phan, K., Sthiannopkao, S., Heng, S., Phan, S., Huoy, L., Wong, M. H., & Kim, K. W. (2013). Arsenic contamination in the food chain and its risk assessment of populations residing in the Mekong River basin of Cambodia. *Journal of Hazardous Materials*, *262*, 1064-1071.

72. Ponnugounder, T., & Singh, T. N. (2020). Natural occurrence of arsenic in the soil and rice plant system in the Bashkandi Block of Barak Valley, Assam, Northeastern India. *Arabian Journal of Geosciences*, *13*(24), 1296.

73. Qian, Y., Chen, C., Zhang, Q., Li, Y., Chen, Z., & Li, M. (2010). Concentrations of cadmium, lead, mercury and arsenic in Chinese market milled rice and associated population health risk. *Food control*, *21*(12), 1757-1763.

74. Rahman, M. M., Asaduzzaman, M., & Naidu, R. (2011). Arsenic exposure from rice and water sources in the Noakhali district of Bangladesh. *Water Quality, Exposure and Health*, *3*, 1-10.

75. Rahman, M. M., Owens, G., & Naidu, R. (2009). 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. *Environmental Geochemistry and Health*, *31*, 179-187.

76. Reid, M. C., Asta, M. P., Falk, L., Maguffin, S. C., Pham, V. H. C., Le, H. A., ... & Le Vo, P. (2021). Associations between inorganic arsenic in rice and groundwater arsenic in the Mekong Delta. *Chemosphere*, *265*, 129092.

77. Rezaitabar, S., Esmaili-Sari, A., & Bahramifar, N. (2012). 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. *Bulletin of environmental contamination and toxicology*, *88*, 614-616.

78. Roya, A. Q., & Ali, M. S. (2016). Heavy metals in rice samples on the Torbat-Heidarieh market, Iran. *Food Additives & Contaminants: Part B*, *10*(1), 59-63.

79. Sandhi, A., Greger, M., Landberg, T., Jacks, G., & Bhattacharya, P. (2017). Arsenic concentrations in local aromatic and high-yielding hybrid rice cultivars and the potential health risk: a study in an arsenic hotspot. *Environmental Monitoring and Assessment*, *189*, 1-8.

80. Sarwar, T., Khan, S., Yu, X., Amin, S., Khan, M. A., Sarwar, A., ... & Nazneen, S. (2021). Analysis of Arsenic concentration and its speciation in rice of different markets of Pakistan and its associated health risk. *Environmental Technology & Innovation*, *21*, 101252.

81. Sharma, S., Kaur, I., & Nagpal, A. K. (2017). Assessment of arsenic content in soil, rice grains and groundwater and associated health risks in human population from Ropar wetland, India, and its vicinity. *Environmental Science and Pollution Research*, *24*, 18836-18848.

82. Shehzad, M. T., Sabir, M., Zia-ur-Rehman, M., Zia, M. A., & Naidu, R. (2022). Arsenic concentrations in soil, water, and rice grains of rice-growing areas of Punjab, Pakistan: multivariate statistical analysis. *Environmental Monitoring and Assessment*, *194*(5), 346.

83. Sun, G. X., Williams, P. N., Carey, A. M., Zhu, Y. G., Deacon, C., Raab, A., ... & Meharg, A. A. (2008). Inorganic arsenic in rice bran and its products are an order of magnitude higher than in bulk grain. *Environmental science & technology*, *42*(19), 7542-7546.

84. Tyagi, N., Raghuvanshi, R., Upadhyay, M. K., Srivastava, A. K., Suprasanna, P., & Srivastava, S. (2020). 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. *Journal of Food Composition and Analysis*, *93*, 103612.

85. Vicky-Singh, Brar, M. S., Preeti-Sharma, & Malhi, S. S. (2010). Arsenic in water, soil, and rice plants in the Indo-Gangetic plains of northwestern India. *Communications in Soil Science and Plant Analysis*, *41*(11), 1350-1360.

86. Williams, P. N., Islam, S., Islam, R., Jahiruddin, M., Adomako, E., Soliaman, A. R. M., ... & Meharg, A. A. (2009). Arsenic limits trace mineral nutrition (selenium, zinc, and nickel) in Bangladesh rice grain. *Environmental science & technology*, *43*(21), 8430-8436.

87. Williams, P. N., Price, A. H., Raab, A., Hossain, S. A., Feldmann, J., & Meharg, A. A. (2005). Variation in arsenic speciation and concentration in paddy rice related to dietary exposure. *Environmental science & technology*, *39*(15), 5531-5540.

88. Yao, B. M., Chen, P., & Sun, G. X. (2020). Distribution of elements and their correlation in bran, polished rice, and whole grain. *Food science & nutrition*, *8*(2), 982-992.

89. Zhu, Y. G., Sun, G. X., Lei, M., Teng, M., Liu, Y. X., Chen, N. C., ... & Williams, P. N. (2008). High percentage inorganic arsenic content of mining impacted and nonimpacted Chinese rice. *Environmental science & technology*, *42*(13), 5008-5013.