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HEALTH RISK ASSESSMENT OF STOCHASTIC EXPOSURE TO ARSENIC, CADMIUM AND COPPER IN WATER DISTRIBUTION NETWORK. A CASE STUDY OF ROBAT KARIM, TEHRAN, IRAN

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Abstract

An investigation of three heavy metals concentration in water distribution network was carried out. A total of 33 samples were taken from 11 villages and the concentration of heavy metals was measured by ICP-MS. The related health risks via ingestion and dermal pathways were assessed for residents of Robat Karim County, Iran, using hazard quotient (HQ), hazard index (HI), and lifetime cancer risk (CR). Uncertainty analysis for the most susceptible groups (infants and children) were carried out using Monte Carlo Simulation technique. The findings revealed that heavy metals concentrations were below their respective national and international guideline values. The mean As, Cd and Cu concentrations ranged from 0.1-2.6, 1-5 and 0.1-192 μg/L, respectively. Copper showed appreciable variable levels in sampling locations but below the safe limit. The results of the HI values of tested heavy metals through combined pathways were below the safety level (HI < 1) for all groups. Simulation of cancer risk probability distribution for Cd through exposure to drinking water for adults, children and infants were in the range of 4.56 e-4 to 1.25 e-3, 1.15 e-3 to 3.8 e-3 and 1.23 e-3 to 4.04 e-3, respectively. The cancer risks resulting from exposure to Cd were higher than those of arsenic. The carcinogenic risk for three studied groups were in the order of adults > children > infants. Overall, the calculated carcinogenic risk effect for Cd indicated that the ingestion of the drinking water would cause cancer risk due to lifetime consumption.

Key words: health risk assessment, heavy metals, probability analysis, water distribution network

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1. Introduction

Environmental heavy metal contamination, especially its consequent ecological and human risk is one of the global issues that has not gain the appropriate attention from the governments (Masindi and Muedi, 2018). Heavy metals quickly stabilize in the environment due to their broad range and long-lasting characteristic; and their decomposition through biological circulation is difficult. Trace elements almost transfer from multiple (hidden) sources in a long-distance transmission, with severe consequences (BanyYaseen and Al-Naeem, 2018; Huma-Khan et al., 2016). Moreover, the physical and chemical weathering of the rocks or human activities such as disposal of industrial wastes, mining activities and dust storms increase the chance of heavy metal accumulation in the environment which subsequently lead to their high values in groundwater (Faiz et al., 2009; Islam et al., 2020; Rafiee and Jahangiri-Rad,

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2019; Rafiee et al., 2019). Industrial wastes (Rafiee and Jahangiri-Rad, 2019; Rafiee et al., 2019), fertilization (Dong et al., 2001), mining and smelting (Habib et al., 2020; Li et al., 2012; Okegye and Gajere, 2015), and sewage irrigation (Liang et al., 2011b) have been known as possible sources of pollution with heavy metals.

Cadmium, arsenic, lead, and mercury are among ten chemical elements which are considered as important concern of public health according to World Health Organization (WHO, 2010). Among others, the pollution with carcinogenic elements like Cd and As has received particular focus. In comparison with other elements, arsenic and inorganic arsenic compounds (ranked no. 11), as well as cadmium and cadmium compounds (ranked no. 25) are categorized as class 1 carcinogens (amongst 116 species) by International Agency for Research on Cancer (IARC) (Rousseau et al., 2005; Yang et al., 2018). Exposure to these substances for a long time, probably through atmospheric exposure, drinking water consumption, and food ingestion, may increase the carcinogenic risk. Trace carcinogenic elements like As and Cd are easily entered in human body and may cause chronic cumulative effects (Doabi et al., 2018; Malassa et al., 2014; Moldoveanu, 2014).

The respective guideline values of cadmium and arsenic in drinking water are set as 3 and 10 μg/L, according to WHO (WHO, 2011) and 5 and 3 based on Iran national standards organization (INSO, 2010). Cadmium, either carcinogenic or non-carcinogenic, may interfere with the secretion of human estrogen and therefore accumulate in human tissues (WHO, 2004). Small amounts of Cd exist in rocks, coal and petroleum, often combined with zinc (Zn); moreover, it is not vital for human health (Burke et al., 2016). Geological structures are an important source of groundwater contamination with Cd, especially when the water is soft or acidic (Ryan et al., 2000).

Arsenic, on the other hand, is a wide-spread element which may be found everywhere on earth. It is the 20th most copious element in the crust of the earth but is rare in natural water and its detected content has been less than 1.0 μg/L (Ryan et al., 2000). Arsenic is a dangerous cancer-causing substance in the environment (WHO, 2003). High existence of arsenic in groundwater is chiefly governed by natural and anthropogenic activities (Guo et al., 2014).

Copper (Cu), is an essential element for structural component of numerous metalloenzymes in human body (Rafiee and Jahangiri-Rad, 2019). Essential elements pose distinct challenges when establishing regulatory guidelines, because too little or too much intake of them may be dangerous for human health; therefore, their related dose-response curves are almost U-shaped (Stern, 2010). In addition to the presence of high amounts in food stuffs, Cu also exists in drinking water and its level sometimes exceeds suggested guideline of 2 mg/L (WHO, 2003). Copper overloads in the liver of human body as its target (Rousseau et al., 2005; Sadhra et al., 2007; Wiltse and Dellarco, 1996), and is considered in Group D (not classifiable as a carcinogen metal), according to the U.S. EPA (1986) guidelines and IARC (2008) (Rousseau et al., 2005; Wiltse and Dellarco, 1996).

Arsenic and cadmium contamination of groundwater have emerged in many areas (Barati et al., 2010; Mosaferi et al., 2008; Nasrabadi and Maedeh, 2014; Qasemi et al., 2019; Saha et al., 2020). Some parts of Iran are also enriched with cadmium. Ghaderpoori et al. (2018) investigated the cadmium concentration in water distribution system in Khorramabad city, Iran. The mean concentration of cadmium was reported as 0.42 μg/L. The authors concluded high health risks in some sampling points. Mirzabeygi et al. (2017) assessed the heavy metal contamination and health risk of Cd in drinking water of Sistan and Baluchistan, Southeastern Iran. They reported that 36.7% of water samples had concentrations above the WHO guideline.

Robat Karim city, located 27 km south-west of Tehran, with 5 industrial parks and tens of thousands of guilds and production units, considered as one of the important economic points of Tehran province. This city has long been famous for its agricultural products. Groundwater resources play an important role in providing both agricultural and drinking water in this region. In recent years, the groundwater quality in southern parts of Tehran, including our study catchment, has declined due to intense agricultural activities as well as the entry of municipal and industrial discharges into the environment (Ghaderpoori, 2018). In our previous research conducted in rural areas of Robat Karim, the non-carcinogenic health risks of Pb, Hg and NO_3 of drinking water were investigated. The findings revealed significant health hazards of NO_3 for all study groups; while Hg showed health risk in some sampling points for children and infants (Badihi et al., 2021).

To this end, a number of reverse osmosis (RO) devices have been installed in study area primarily aimed at nitrate removal where water quality has been deteriorated sharply. However, these devices are operated privately meaning that not all inhabitants, particularly in rural areas, have easily access to RO-treated water. The present study thus set out to assess human health risks of three heavy metal(oid)s of concern including arsenic, cadmium and copper caused by either ingestion or dermal contact of drinking water in rural water distribution networks of Robat Karim. The results of this investigation can notify the residents and government officials regarding the quality of water (used for both drinking and agricultural purposes) and make them aware of possible exposure health risk due to water consumption.

2. Materials and methods

2.1. Study area

Robat Karim county is located in the southwest of Tehran province (at a longitude of 51.4 and a latitude of 28.35 and 1050 m above sea level) with an area of 275 km^2 (Fig. 1). The mean annual rainfall is less than 200 mm (the highest amount of rainfall occurs in November to March) and the average temperature of 17°C has been recorded (with a maximum temperature of 44°C). Due to the low altitude and the proximity of the county to the desert areas of Qom and Robat Karim salt lake, the area exhibits arid (70%) and semi-arid (30%) climate. This county is located in the south of Alborz Mountains on the sediments of the third and fourth geological periods. In terms of topography, this region has four geological units in the form of alluvial sediments, marl sediments, conglomerates and andesitic texture. The material of these sediments in the slopes of Alborz starts from green tufts and ends in alluvial sedimentsat at the southern part. The constituents of alluvial sediments become finer from the slope to the bottom of the plain. This thinning slows down the movement of groundwater and thus prolongs the contact time of water with soil which results in more salts dissolving in water (Kianifar and Pourkarim, 2011). Agricultural activities and animal raising are the main sources of income for the rural communities.

Groundwater is considered as the main sources for both drinking water and agricultural purposes in this area. In villages, water is supplied by a number of wells that have been dug in or around the area. The water then enters the reservoir, is chlorinated and distributed.

2.2. Sample collection and analysis

A total of 33 potable water samples were taken from 11 rural areas of Robat Karim from distribution network in September 2019 (Fig. 1). Each sample was collected in clean sterilized bottles, stored in a cool box and were instantly transferred to the water and wastewater reference laboratory affiliated to Iran University of Medical Sciences for further analysis. All the samples were acidified with 2 mL nitric acid to prevent adsorption and crystallization of metal elements prior to their analysis. Heavy metals were analyzed by inductively coupled plasma- mass spectrometry (ICP- MS). All samples were analyzed in duplicate, and the average values were reported here.

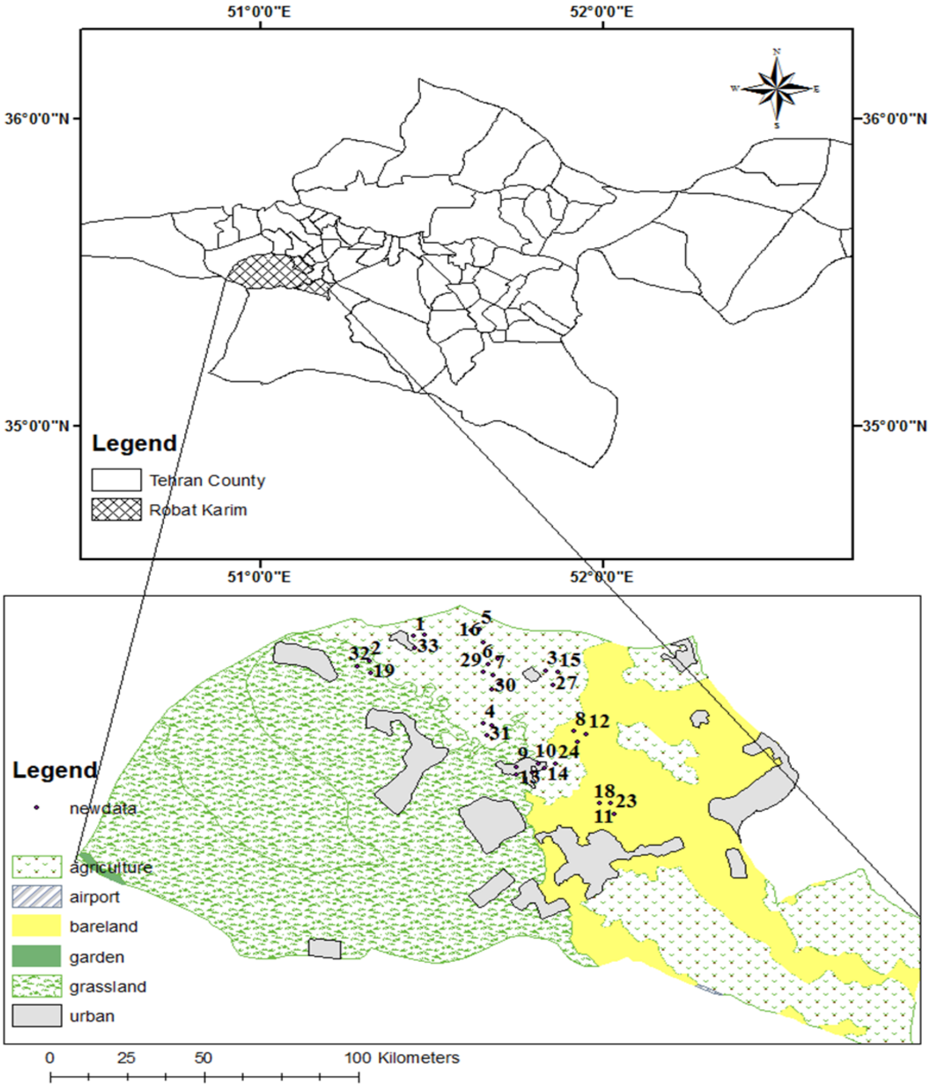


Fig 1. Maps of the study area showing sampling sites and land use-land cover

2.3. Quality control and assurance

In order to verify the precision and accuracy of analytical procedures, appropriate certified reference materials (Multielement standard solution For ICP, 55263, Sigma Aldrich, Germany) were checked under the same conditions as for the samples. The determined results of average recoveries from certified reference material analysis and the obtained limit of detection (LOD) for the tested elements are given in Table 1. The average concentration of each element was used for further analysis because the reproducibility was obtained at 95% confidence level.

Table 1. Limit of detection (LOD) and recovery percentage for the examined elements

Element	***Recovery (%)***	***LOD (µg/L)***
As	97.55	0.09
Cd	105.46	0.11
Cu	102.10	0.10

2.4. Health risk assessment

2.4.1. Average daily dose (ADD)

To estimate average daily dose of the Robat Karim residents to the studied elements through ingestion and dermal contact the Eqs. (1-2) were used (Naveedullah and Hashmi, 2014).

$$ADD_{ingeation} = \frac{C_w \times IR \times EF \times ED}{BW \times AT} \quad (1)$$

$$ADD_{Dermal} = \frac{C_w \times SA \times K_p \times ET \times EF \times ED \times CF}{B_w \times AT} \quad (2)$$

where: $ADD_{ingestion}$ and ADD_{dermal} represents the average daily dose through ingestion and dermal contact of water respectively in µg/kg/day. *Cw* is the heavy metals concentration in water sample in µg/L, *IR* is the water ingestion in L/d (2 L/d for adult, 1.5 L/d for child and 0.8 L/d for infant) (Qasemi et al., 2019), *EF* is the exposure frequency (365 d/y), *ED* shows the exposure duration in years (70, 6 and 2 years for adults, children and infants, respectively), *BW* is the average body weight in kg (70 kg for adult, 20 kg for child and 10 kg for infant) (Qasemi et al., 2019), *AT* is the average time of non-carcinogenic and carcinogenic risk in days; AT = 70 × 365 for carcinogenic and AT = ED ×365 days for non-carcinogenic, *CF* is the unit conversion factor for water in 1L/1000 cm^3, *Kp* is the dermal permeability coefficient in cm/h (0.001 cm/h for Cu, As and Cd) and *SA* is the exposed skin area in cm^2 (18,000 for adults and 6600 for children and infants) (Liang et al., 2011a).

2.4.2. Hazard quotient (HQ) and hazard index (HI)

The non-carcinogenic health risk of elements through water consumption was characterized using the target hazard quotient (*HQ*) which defines as the ratio of average daily dose of a contaminant (*ADD*) to a reference dose level (Eq. 3) (PQRA, 2004).

$$HQ_{ingestion} = \frac{ADD_{ingestion,dermal}}{RfD_{ingestion,dermal}} \quad (3)$$

where, *HQ* (dimensionless) represents the hazard quotient index, and *RfD* (µg/kg/d) is the reference dose of the desired heavy metal.

Hazard index (*HI*) was used to calculate the overall non-carcinogenic risk caused by multi-pathways, which was computed as the sum of the *HQs* from two pathways (Eq. 4) (Means, 1989):

$$HI = \sum_{i=1}^{n} \left(HQ_{ingestion} + HQ_{dermal} \right) \quad (4)$$

The Hazard Index (*HI*) is the sum of *HQ's* for all pathways and similar toxic effects. A *HQ* of < 0.2 for any given pathway is deemed negligible; while an *HI* of < 1.0 is considered acceptable (Federal Contaminated Site Risk Assessment, 2004).

2.4.3. Lifetime carcinogenic risk (LCR)

Carcinogenic risk is generally defined as the excess risk of cancer in a person's lifetime due to the exposure of pollutants. It can be estimated using the Eq. (5) (USEPA, 1989):

$$LCR_{ingestion,dermal} = ADD_{ingestion,dermal} \times CSF \quad (5)$$

where: *LCR* is the probability of an individual developing cancer. *ADD* expressed earlier and *CSF* represents the cancer-causing slope factor in $(mg/kg/d)^{-1}$; which in our study were only available for As, 1.5 $(mg/kg/d)^{-1}$ (Saha et al., 2017; USEPA, 1991) and Cd, 15 $(mg/kg/d)^{-1}$ (CalEPA, 2009).

A risk level of 1.0 E-6 has been considered as the point of excess cancer risk, indicating 1 per 1,000,000 chance of getting cancer via consumption of drinking water containing heavy metals, estimated in µg/L for 70 years. The safe point for carcinogenic risks must be lower than this level (Castorina and Woodruff, 2003). EPA suggested the range of risks borderline as 1.0 e-4 to 1.0 e-6. A risk level of 1.0 e-4 has been considered as the point of excess cancer risk, indicating 1 per 10,000 chance of getting cancer via consumption of drinking water containing toxic metals, the safe point for carcinogenic risks must be lower than this level (USEPA, 2010a).

2.5. Cancer risk probability analysis

Risk assessment calculation is based on the uncertainty that might roots from natural variability in an individual's response, instability in the pollutant concentration, uncertainty in the measurement or estimation of parameters, dearth of accurate knowledge, and data scarcity (Qu et al., 2016). Loss of information and over underestimation in risk calculation can be attributed to ignoring these uncertainties (Qu et al., 2015). Accordingly, there are two approaches to modeling health risk assessment, deterministic and stochastic approaches. Unlike the deterministic approach, the stochastic approach tries to take into account all the uncertainties in both the model input and in the output.

In this regard, researchers have used the stochastic approach to include uncertainties in their studies (Benke and Hamilton, 2008; Djahed et al., 2018). Among all the available models, the Monte Carlo Simulation (MCS) has been widely used in many researches (Kentel and Aral, 2004). Thus, in the present study, the uncertainty analysis was performed by MCS simulation in Microsoft excel with in-built @ Risk software (Palisade Corporation, trial version 7.4). First, the probability distribution of the desired input parameters was determined. After that, through 1000 iterations, the exposure and risk models were simulated.The desired risk ranges (90 % probability) for the three groups of adult, child and infant were determined.

3. Results and discussion

3.1. Heavy metals contamination

The detected concentrations of Cd, As and Cu are shown in Table 2. All three tested parameters displayed high variations in terms of their values, suggesting variable sources and factors influence and contribution to the concentration of these metals in groundwater which subsequently affected their amounts in water distribution network. Generally, concentrations of studied parameters were within the acceptable WHO recommended ranges for potable water and Iran national standards for drinking water. Arsenic concentrations ranged from 1 to 2.6 μg/L with an average value of 0.384 μg/L, illustrating that none of sampling points exceeded the guideline values of 3 and 10 μg/L as set by WHO (2011) and Iran National Standards (2010). Cadmium concentration ranged from 1 to 5 μg/L with the mean value of 1.27 μg/L which shows all the sampling points were within the safe limit of WHO guidelines and INSO for drinking water. A possible reason for As and Cd occurrence in groundwater may be improper management of wastewater in the study area.

The release of Robat Karim’s untreated wastewater into the environment (both soil and waterways) and its related health hazards have been the subject of other research (Karimi et al., 2015; Panahi and Alavi Moghadam 2012). The use of raw wastewater for irrigation of agricultural produces is known as another source of Cd penetration into groundwater in Robat karim, since Hani and Pazira (2011) found high probabilities for exceeding of threshold value for Cd from the north to south which were highly correlated with vegetable cultivation areas.

Cu was the most variable of the studied metals that ranged between ≤ LOD to 192 μg/L with an average value of 24.94 μg/L. These values are lower the maximum acceptable concentration of 2000 μg/L for copper in potable water (INSO, 2010; WHO, 2004). In brief, 78% and 42% of samples recorded levels ≤ LOD for arsenic and copper, respectively. About 69% of samples also contained 1 μg/L of cadmium. Although in the present study the concentrations of arsenic and cadmium were less than the values recommended by international and national organizations, these elements have been detected in higher amounts in many parts of Iran.

The highest arsenic concentration in groundwater samples is found in Rafsanjan plains’ groundwater (Rahnamarad et al., 2020), some areas located in north east of Iran (Alidadi et al., 2019) and Kurdistan and West Azerbaijan provinces (west of Iran) (Keshavarzi et al., 2011). In order to provide a rough comparison with other research conducted in Iran, the relevant papers focusing on the concentration of As, Cd and Cu in drinking water were searched and the results are shown in Table 3.

In our research the average concentration of As were lower than that reported for Hamedan and Ghahavand (Sobhanardakani, 2016) as well as the north west of Iran (Malakootian et al., 2020). In terms of Cd, Sistan and Baluchistan province recorded the highest values of Cd in drinking water as the most of taken samples showed cadmium concentrations above the permissible limit of 5 μg/L recommended by INSO (Mirzabeygi et al., 2017). In our research, most of the sampling points showed the concentration of Cu almost similar to those values reported from different cities of Iran. Moreover, five locations had Cu concentration above 50 μg/L which is in agreement with Sohrabi et al. (2016) findings who reported high amounts of copper in water resources of rural areas of Kermanshah (Sohrabi et al., 2016).

Table 2. Statistical analysis of examined metal(oid)s (n= 33)

Elements	***Min (μg/L)***	***Max (μg/L)***	***Mean (μg/L)***	***Std. Deviation***
As	0.2	2.6	0.38	0.63
Cu	0.1	192	24.94	191.9
Cd	1	5	1.72	1.06

Table 3. Tested heavy metal(oid)s concentration (μg/L) of drinking water samples collected from some cities of Iran

Provincet5		***City***	***Concentration (μg/L)***			***Reference***
			Cu	***Cd***	***As***	
1	Ravazi Khorasan	Neyshbur	8.28±13.125	-	1.07±2.46	Saleh et al. (2019)
		Bar	6.10±0.675		<0.013	
		Chakaneh	5.80±1.482		3.87±2.416	
		Kharv	3.81±1.48		0.52±1.051	
		Darrood	4.61±1.365		2.75±0.17	
		Eshgh Abad	7.96±0.422		2.71±0.052	
		Ghadamgah	5.31±1.58		3.07±0.185	
2	Kermanshah	Kermanshah	195±70	-	-	Sohrabi et al. (2016)
3	Sistan and Baluchistan	Iranshahr	-	4.39±3.49	-	Mirzabeygi et al. (2017)
		Chabahar		4.7±2.9		
		Khash		3.12±3.12		
		Zabol		7.6±3.6		
		Zahedan		4.64±2.6		
		Saravan		3.3±2.54		
		Sarbaz		2.76±3.23		
		Nikshahr		3.04±2.8		
4	Yazd	Abarkouh	11.33±1.69	-	-	Fallahzadeh et al. (2017)
		Ardakan	11.44±2.66			
		Meybod	12.25±1.78			
		Bafgh	12.38±3.8			
		Behabad	12±1.26			
5	Kerman	Kerman	0.59 ± 8	0. 21 ± 6	_	Sarvestani and Aghasi (2019)
6	Northwest of Iran	Urmia	20±10	40±10	50±10	Malakootian et al. (2020)
7	Kurdistan	Dehgolan	-	0.9±0.075	6.8±8.725	Rezaei et al. (2019)
8	Lorestan,	Khorramabad	6.79±9.8	0.43±0.372	-	Mohammadi et al. (2019)
9	Hamadan	Ghahavand	9.25±5.37	-	9.03±3.90	Sobhanardakani (2016)

Naturally, concentrations of up to about 50 ppm of copper are found in the earth's crust mainly as sulphide ores (chalcopyrite and chalcocite) and less commonly in its metallic form (Ferrante et al., 2013). The primary anthropogenic source of copper in most water distribution network is through corrosion of copper pipes especially when the water becomes acidic (Becking et al., 2007). There is no copper piping system in the area, hence, the likely source of the Cu could be from the mining, farming, manufacturing operations, and municipal or industrial wastewater releases into the environment (Becking et al., 2007). In brief, the average concentration of investigated heavy metals in this study were far below the permissible limits to guarantee safe consumption of drinking water.

3.2. Health risk assessment

Health risk assessment is a process by which the adverse effects of a factor on individuals can be investigated over a period of time (Karim and Qureshi, 2014). The final results of the risk assessment are quantified and expressed as carcinogenic and non-carcinogenic risk assessments in the study population (Bade et al., 2013). One major route of heavy metal exposure⁄accumulation to humans is via drinking water. This is especially the case in areas located within industrial parks and agricultural lands where the groundwater or soil might be contaminated by sewage discharge or atmospheric deposition. The effect of water pollutants on the human body is possible through three main routes; direct drinking water, inhaling evaporated water and dermal adsorption of contaminant through the skin (Schwarz et al., 2014). In the current research, non-carcinogenic and carcinogenic health risks posed by oral ingestion and dermal adsorption of groundwater containing arsenic, cadmium and copper were assessed.

3.3. Average daily dose (ADD) evaluation

The entry of heavy metals into the body is considered a health problem and therefore it is important to calculate their potential health risk. Due to the fact that there is no information about the possible health risk of arsenic, cadmium and copper in this area, first average daily dose was calculated based on Eqs. (1) and (2) through ingestion of drinking water and skin adsorption in three groups (adults, children and infants) and the results are displayed in Fig. 2.

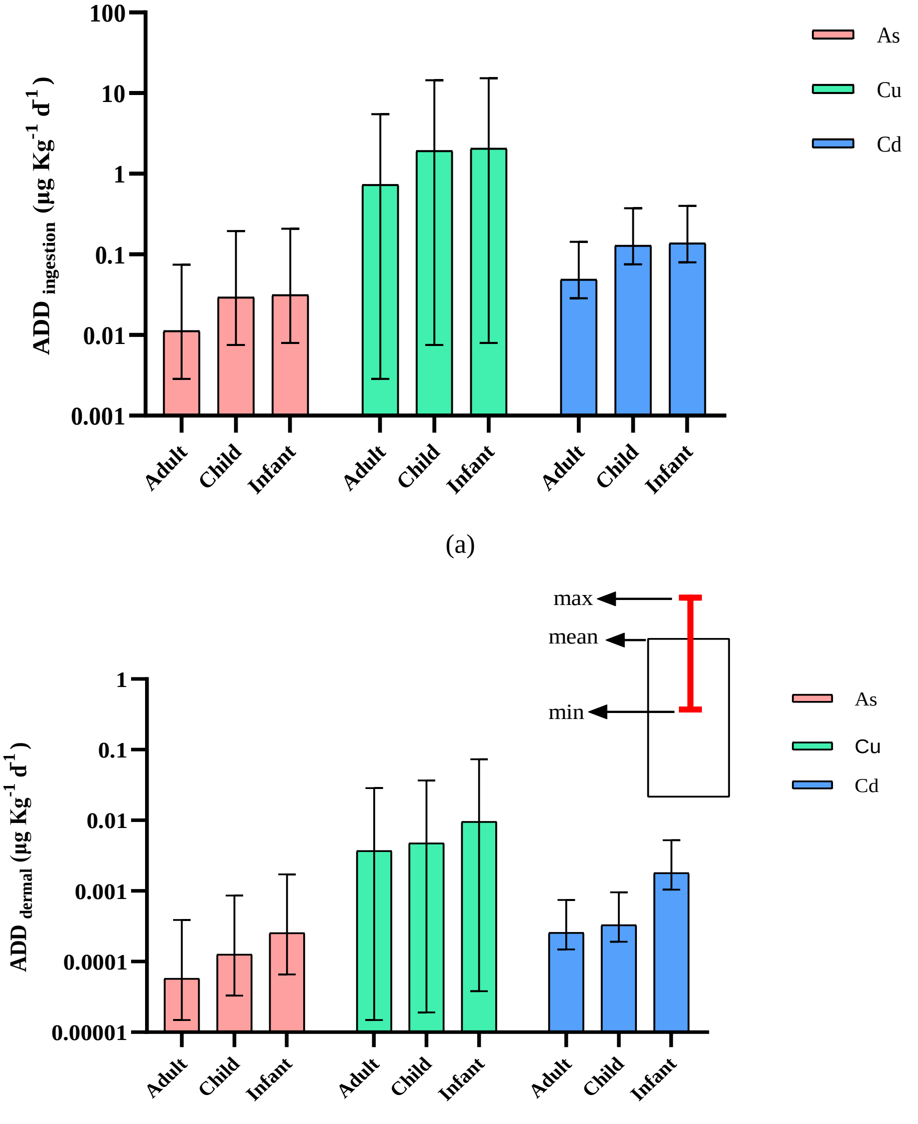
As depicted, water ingestion exhibited higher contribution in ADD_{total} (μg/kg/d) as compared with dermal adsorption. The daily intakes of Cu through both ingestion and dermal adsorption most contributed to ADD_{total} in all three groups. In general, $ADD_{ingestion}$ values were almost one orders of magnitude higher than ADD_{dermal} for As and Cd. However, in the case of Cu this value was about two orders of magnitude, exhibiting water ingestion as the main route for this heavy metals exposure. These results are consistent with those of other studies and suggest the ingestion as the main path of arsenic, cadmium and copper exposure (Chonokhuu et al., 2019; Jiang et al., 2019).

In addition, the mean value of $ADD_{ingestion}$ showed that children and infants are approximately 2.6 and 2.8 times more exposed to heavy metals than adults; while, these values were almost 1.5-2 times for children and 2.5 times for infants through dermal adsorption. In accordance with the present results, previous studies have demonstrated that children and infants are at higher risk than adults in terms of heavy metals intake and their associated adverse health effects (Adewoyin et al., 2019; Eticha et al., 2018).

3.4. Non-carcinogenic risk assessment

HQ and *HI* values of investigated heavy metals in drinking water for each study group are given in Table 4. As shown the $HQ_{ingestion}$ values of Cd exceeded the threshold level of 0.2 for children and infants illustrating these groups are more exposed to the risk via ingestion. However, in the case of dermal pathway, HQ_{dermal} values for all three metals were all below the threshold level of 0.2 suggesting no health risk for tested population. The calculated HI values through ingestion and dermal exposure did not exceed the safe limit of 1 for all groups. This explains that the daily intake level of examined As, Cu and Cd were lower than the level of concern ($HQ < 1$); therefore, the non-carcinogenic risk from heavy metals through ingestion and dermal contact of drinking water can be ignored for adults, children and infants. Cd exhibited higher values of HQ_{dermal} in comparison with Cu and As showing its health importance from dermal adsorption.

This was consistent with the previous studies that reported higher dermal adsorption of cadmium than some other heavy metals (Muhammad et al., 2011; Opoku et al., 2020). In an attempt at a rough comparison, health risk evaluation was compared to other studies in Iran.



(a)

(b)

Fig 2. Estimated average daily dose (*ADD*) of heavy metals for drinking water through: (a) ingestion and (b) dermal contact by adult, child and infant

Table 4. Reference Dose (RfD), Hazard Quotient (HQ) and Hazard Index (HI) for surveyed elements in water distribution network

Element	***RfD ingestion***	***HQ ingestion (±SD)***			***RfD dermal***	***HQ dermal***			***HI=ΣHQs***		
		Adult	***Child***	***Infant***		***Adult***	***Child***	***Infant***	***Adult***	***Child***	***Infant***
AS	$3e^{-4}$	0.036±0.06	0.096±0.16	0.102±0.17	$28e^{-4}$	$2.04e^{-5}$	$4.53e^{-5}$	$9.07e^{-5}$	0.037±0.06	0.096±0.16	0.102±0.17
Cu	$4e^{-2}$	0.017±0.04	0.046±0.10	0.049±0.11	$12e^{-3}$	$3e^{-4}$	$3.9e^{-4}$	$7.9e^{-4}$	0.018±0.04	0.047±0.10	0.050±0.11
Cd	$5e^{-4}$	0.100±0.061	0.250±0.16	0.280±0.17	$25e^{-6}$	0.010	0.013	0.026	0.109±0.07	0.273±0.17	0.302±0.21

In a research conducted by Malakootian et al. (2020) in northwest of Iran, *HQ* values indicated a reasonable high non- carcinogenic risk for arsenic, cadmium and nitrate. Fakhri et al. (2015) examined the human health risks of some heavy metals for male and female adults, children, and infants in samples of tap water from eight regions of Jask town, Iran. The *HQ* of cadmium was less than 1, suggested no related critical risk of Cd due to water consumption (Fakhri et al., 2015). Alidadi et al. (2019) conducted heavy metals water screening work in northeast Iran. The results of the *HQ* values of arsenic and heavy metals for combined pathways were below the safety level ($HQ < 1$) for adults, while the *HI* for children were higher than the safety limit in some locations. The findings suggested the probability of non-carcinogenic risk for the children and adults to the elements via ingestion and dermal routes.

3.5. Carcinogenic risk

Arsenic and cadmium are classified as the carcinogenic elements via either ingestion or inhalation. The cancer risk is defined by USEPA as *"the incremental probability of an individual to develop cancer over a lifetime as a result of exposure to a potential carcinogen"* (USEPA, 2012). The range of 1 e^{-6} (1 in 1,000,000) to 1 e^{-4} (1 in 10,000) were considered as the safe limit of carcinogenic risks (USEPA 2014). 1 e^{-6} is thought to be safe when the human is exposed with only one element; while for multi-element exposure the safe limit is 1.0 e^{-4} (USEPA, 2010b). In the current study, the carcinogenic risks were estimated for arsenic and cadmium, because the CSF was not determined for copper.

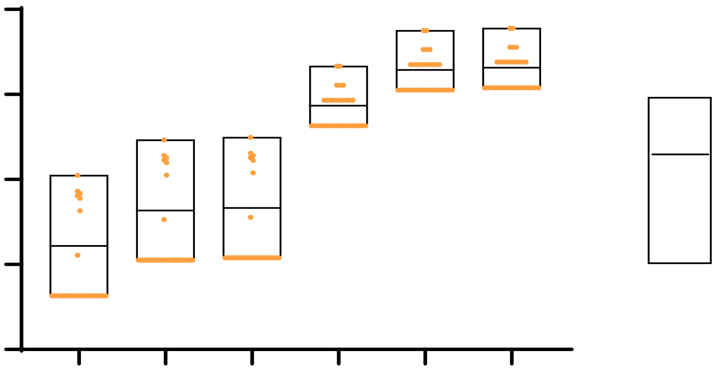
Fig. 3 depicts the results of carcinogenic risks for As and Cd due to the ingestion and dermal contact. Based on calculated data, the chance of developing cancer risk due to arsenic ingestion ranged from 4.28 e^{-6} to $1.1e^{-4}$, $1.12e^{-5}$ to $2.9e^{-4}$ and $1.2e^{-5}$ to $3.12e^{-4}$ for adults, children and infants, respectively. In fact, one sampling point for adults and 6 sampling points for children and infant groups represented far higher values than 1.0 e^{-4} suggesting potential serious health consequences and carcinogenic risks (roughly 3-4 persons in 10,000) through water consumption during life span for local population as compared with other sampling points. In general, EPA considers excess cancer risks that are below 1 chance in 1,000,000 (1.0 e^{-6}) unlikely to pose significant health risks.

To be more precise, based on *CR* values, the risk of developing cancer due to lifetime exposure to As in water exist for all exposed population with the infants as the most susceptible group. The spatial trend of the calculated carcinogenic risk of arsenic for the three studied groups is shown in Fig. 4. As shown 6 sampling points (1 to 6) registered the highest values of carcinogenic health hazards with regard to arsenic consumption from drinking water for children and infants. The sample taken from point 5 contained higher amounts of arsenic and therefore showed elevated carcinogenicity for all groups.

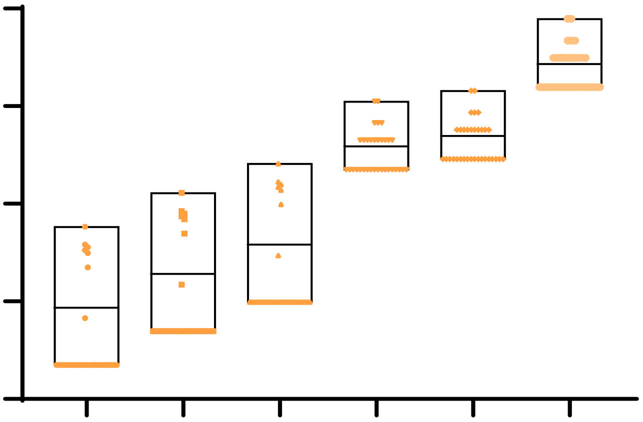
As seen in Fig. 3a, the carcinogenic risk assessment of Cd for all three groups were higher the critical safe limit of 1.0 e^{-6} set by USEPA (2010), revealing risk of cancers among all people through ingestion of drinking water. In fact all sampling points exhibited possible cancer risks for adults, children and infants. The levels of risks associated with resident adults in the study area were lower compared to those of resident infants and children investigated, which may be due to the lower weight of children and infants compared to adults. The *CR* spatial distribution of cadmium through water ingestion for two groups with the higher carcinogenic risks (infants and children) are depicted in Figs. 5 (a, b). The carcinogenic risk which is related to cadmium contained water ingestion can be observed in all sampling points. Three villages, where nine sampling points were taken from, recorded worse condition and had a higher risk of carcinogenesis for children and infants.

Estimated average CR_{dermal} (Fig. 3b) values for arsenic obtained 8.6 e^{-8}, 1.9 e^{-7}, 3.8 e^{-7} for adults, children and infants, respectively. Thus, it can be inferred that the dermal contact of water would not cause cancer risk for lifetime exposure to As. Accordingly, the average CR_{dermal} values for Cd were calculated 3.86 e^{-6}, 4.95 e^{-6} and 2.7 e^{-5} respectively, which are beyond the safety level of 1.0 e^{-6} indicating that consumption of water would result in an excess of cancer risks due to dermal adsorption.

However, these values are not surpassing the unacceptable critical risk of 1.0 e^{-4} which is sufficiently large, poses health hazards, and need some sort of intervention and remediation (USEPA, 2012). Since based on Eq. (5) the carcinogenic risk related to cadmium through water ingestion was higher than the critical safe limit in all groups, the Monte Carlo Simulation was used to more accurately investigate and determine the risk range (Figs. 6 (a-c)).



(a)



(b)

Fig 3. Estimated carcinogenic risk (CR) through (a) ingestion and (b) dermal contact for adult, child and infant

Prior to assessing the risk range by Monte Carlo Simulation, the distribution of data was investigated by different models provided in @ Risk software (Palisade Corporation, trial version 7.4). The results showed that cadmium distribution for adult, child and infant were followed by the Perth, Pareto and Pareto model with 99.8% and 99.6 % and 97.4 % similarity, respectively.

According to Ma et al. (2016) the cancer risk is acceptable when its probability lies in the range of 1.0 E-6 to 1.0 E-4. Based on Figs. 6 (a-c) the MCS depicted that, 90 percent of iteration for calculation of Cd cancer risk probability ranged from 4.56 E-4 to 1.25 E-3, 1.15 E-3 to 3.8 E-3 and 1.23 E-3 to 4.04 E-3 for adults, child and infants, respectively. Likewise, it is notable that the 90 percentile calculated CR values for this element were over 1.0 E-4. Thus, it can be concluded that the water ingestion would cause cancer risk for lifetime consumption. Malakootian et al. (2020) stated excess lifetime cancer risk (ELCR) of arsenic due to the groundwater use in the study area (northwest of Iran).

In the study by Mirzabeygi et al. (2017) the calculated ELCR value of chromium and cadmium in drinking water of Sistan and Baluchistan, southeastern Iran was more than acceptable risk levels.

4. Conclusions

In this study, a total of 33 samples of drinking water were collected from water distribution network of Robat Karim. Arsenic, cadmium and copper concentrations were assessed by comparing with drinking water quality guidelines (WHO) and national standards. The non-carcinogenic and carcinogenic health risks of these metals through ingestion and dermal adsorption have been assessed. The uncertainties of cadmium risk assessment have also been evaluated.

The following conclusions can be summarized:

1. The arsenic, cadmium and copper concentrations in potable water samples ranged from 0.1-2.6, 1.0-5.0 and 0.1 to 192.0 µg/L, with the averages of 0.38, 1.72 and 24.92 µg/L, respectively.

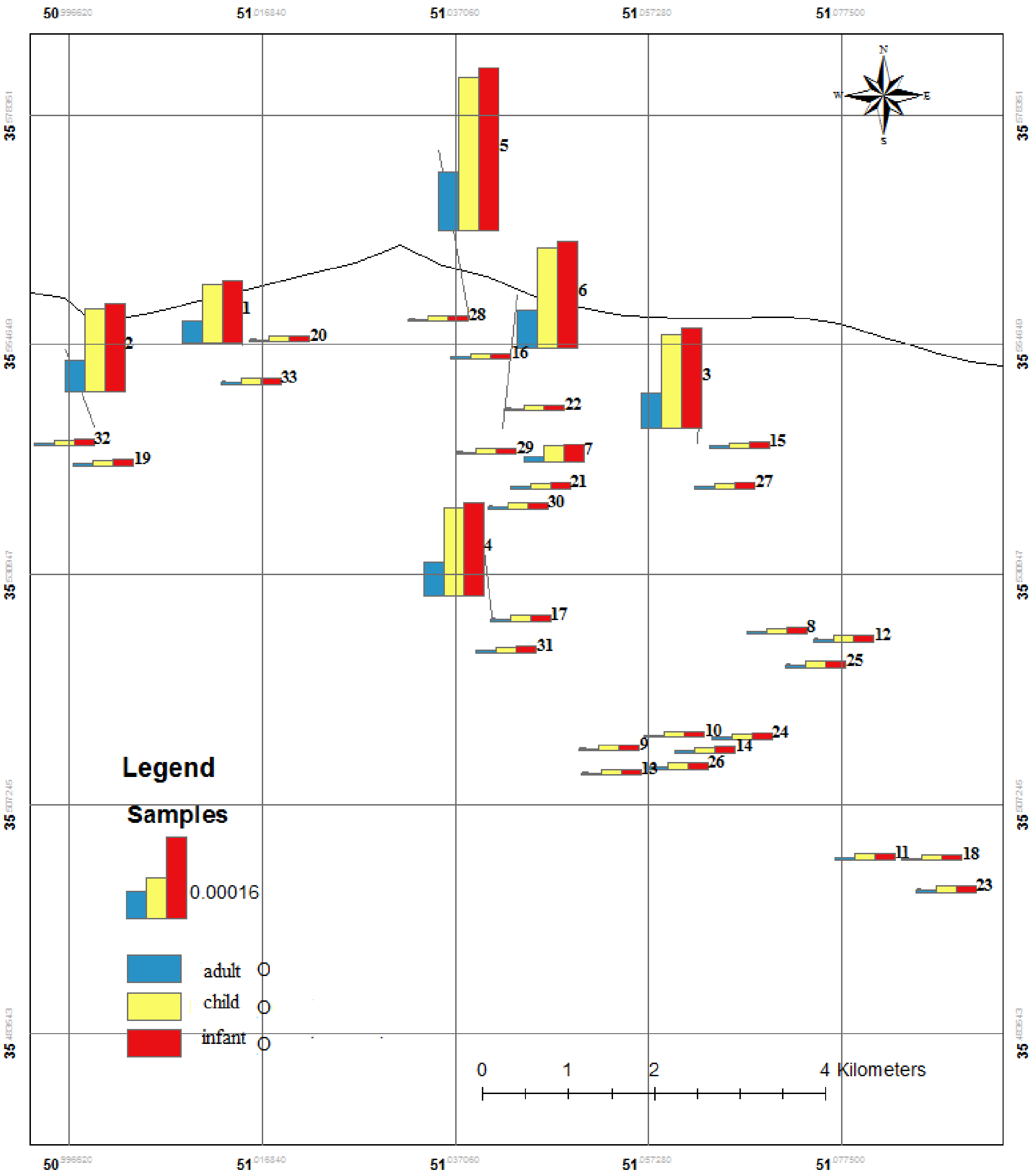


Fig 4. Calculated *CR* $_{ingestion}$ of arsenic in each sampling location adult and child and infant

Heavy metals concentrations in all of drinking water samples were below the national standards and international guidelines.

2. With regard to the non-carcinogenic risk, the HQ and HI values never exceeded the level of concern for adult, children and infants. Nonetheless, the maximum arsenic carcinogenic risks via ingestion for adults, children and infants obtained 1.1 e^{-4}, 2.9 e^{-4} and 3.1 e^{-4}, respectively, which were obviously higher than the critical risk of 1.0 e^{-4}. Likewise, the lifetime carcinogenic risk of cadmium through ingestion was higher than the critical risk set by US EPA, indicating that there was carcinogenic risk to adults, children, and infants through water consumption.

3. In case of Cd, the cancer risk probability through the MCS showed that 90th percentile of *CR* was over 1.0 e^{-4}, demonstrating that the ingestion of cadmium from drinking water would cause cancer risk for lifetime consumption.

4. In the present study, there observed uncertainties that may affect the results of the calculated risk. For instance, (i) body weight and water consumption in study groups were extracted from the previous study conducted in one of the cities of Iran and was not related to the residents of Robat Karim, (ii) the cancer slope factor (CSF) value were obtained from US EPA guideline which may not be generalizable to the study population, (iii) the

calculated non-carcinogenic risk was related only to the presence of three heavy metals, of which only two (As and Cd) were the basis for the calculation of carcinogenic risk assessment; while groundwater in agricultural areas is likely to contain other contaminants that affect the estimated risk values, (iv) given the high risk of nitrate in this area, which was reported in our previous study, reverse osmosis (RO) devices have been installed in 3 villages with the primary aim of nitrate reduction.

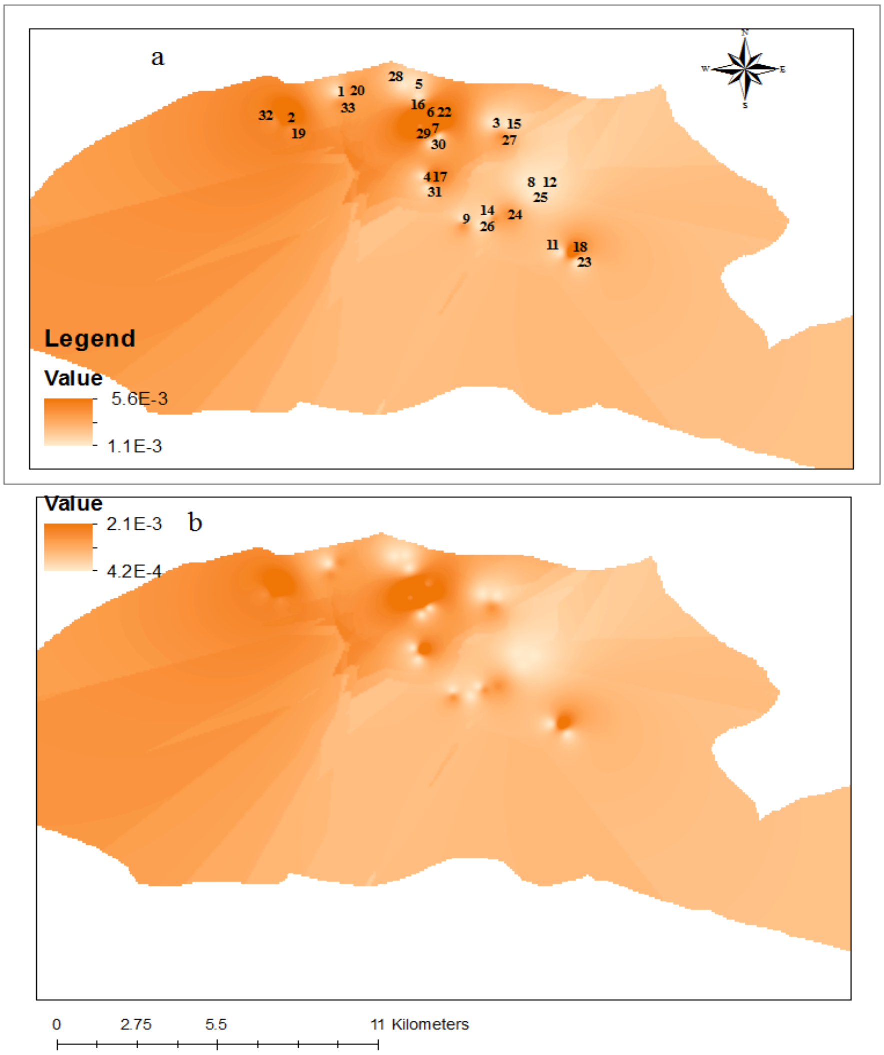
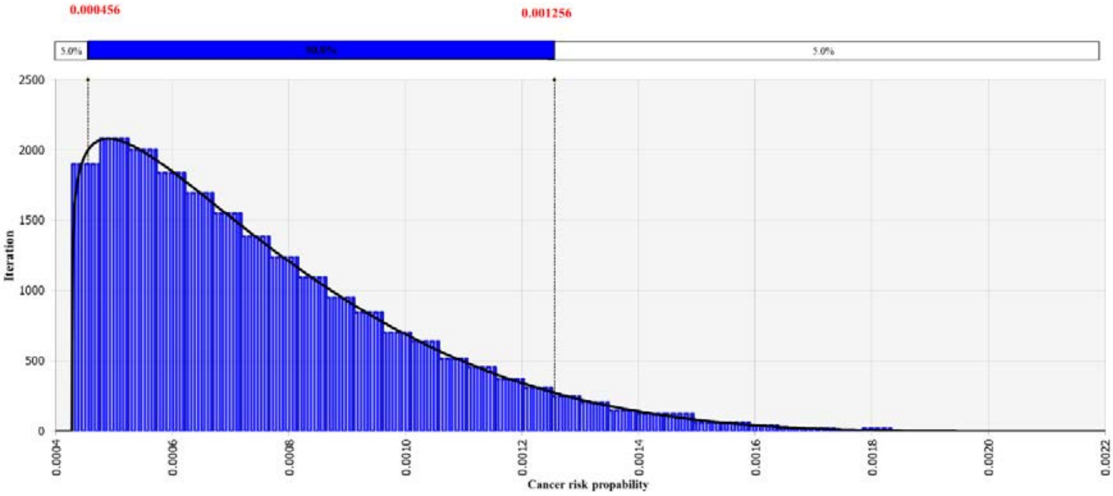
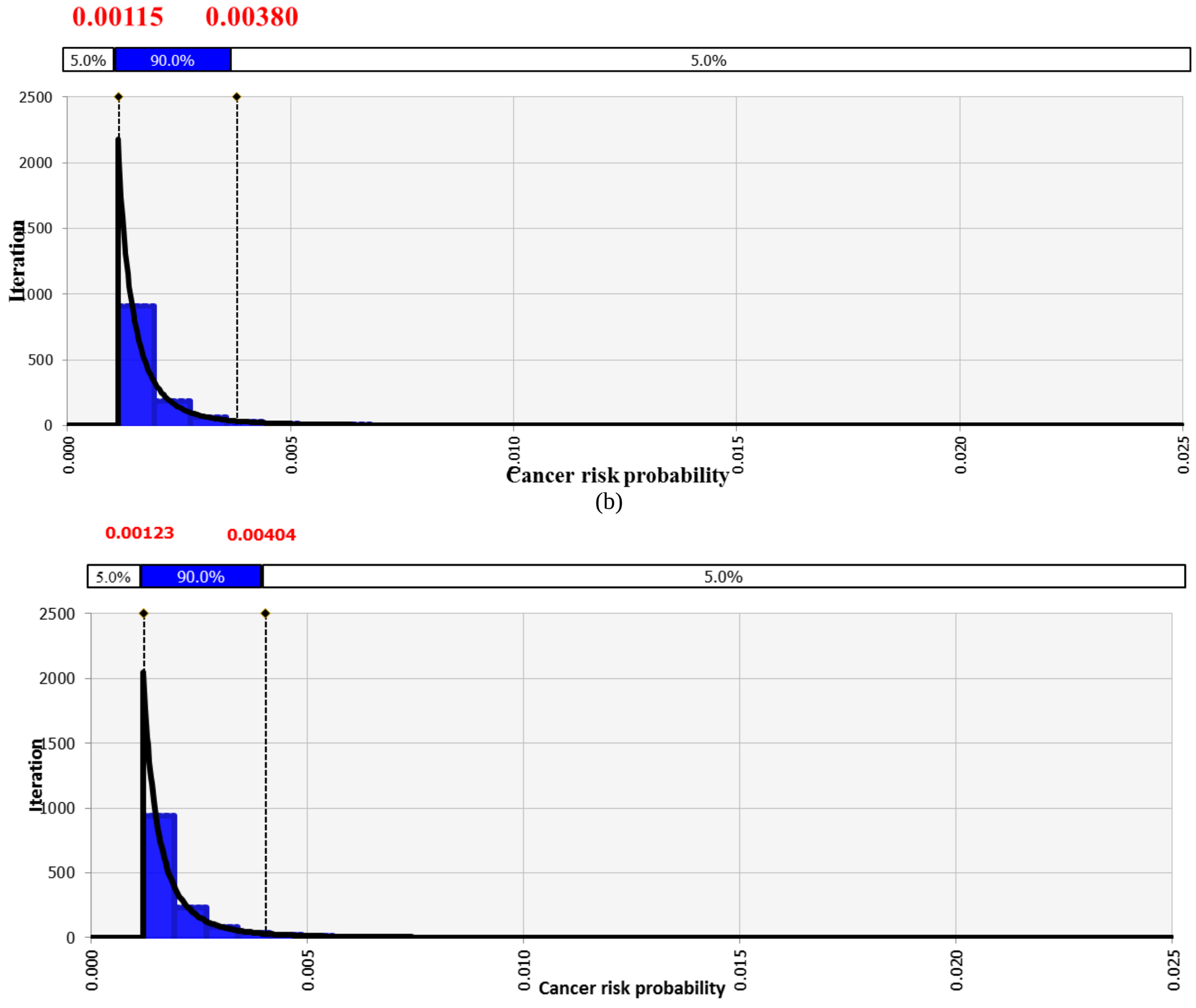


Fig 5. Spatial distribution of CR $_{\text{ingestion}}$ attributed to cadmium for (a) infant and (b) child. Higher values were located in central and west of study area



(a)



(b)

(c)

Fig. 6. Simulation of cancer risk probability distribution of Cd (ingestion) for (a) adults (b) children) and (c) infants through 1000 iterations

Water is introduced from distribution network to these devices and some residents buy the RO-treated water for potable use. Based on our previous report, nitrate concentration in the output of these devices and consequently its related risk substantially decreased. Thus, it is reasonable to determine the heavy metals concentrations in the output of these newly installed devices. This also may justify the necessity of RO devices application that had been installed in some villages for heavy metals reduction.

5. The outcomes of the study demand regular monitoring of drinking water, the use of advanced technologies (RO) to purify water or otherwise alternative recourses should be proposed.

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