



# Carcinogenic and Non-carcinogenic Health Risk Assessment of Heavy Metals in Ground Drinking Water Wells of Bandar Abbas

Hamidreza Farimani Raad\*, Alireza Pardakhti and Hamidreza Kalarestaghi

School of Environment, College of Engineering, University of Tehran, P.O. Box 14155-6135, Tehran, Iran

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## ABSTRACT

This research evaluates the carcinogenic and non-carcinogenic risks from cadmium, lead, and zinc in Bandar Abbas groundwater sources. The samples from 25 wells were analyzed for cadmium, lead and zinc. Total lifetime cancer risk and non-cancer risk assessment from exposure to these pollutants in drinking water (ingestion, inhalation and skin routes) were conducted for people living in these villages. In these regions most of the drinking water supplied, are from these wells which shows the importance of analyzing the quality of them in order to prevent diseases and cancer risks. The highest risk from cadmium seems to be in village Dehno Paein and also this amount for lead occurs in Tifakan Tal-e Gerdu. The highest hazard index (HI) based on human health risk assessment (HHRA) model for cadmium, lead, and zinc through oral, inhalation and dermal pathways were computed as 0.005, 1.63 and 0.043 which are in Dehno Paein, Tifakan Tal-e Gerdu and Faryab. Results show that lead can lead to more cancer cases in these villages than cadmium. The total expected cancer cases from exposure to cadmium in different routes are lower than lead.

**KEYWORDS:** Risk assessment - Cadmium - Lead - Zinc - Carcinogenic – Groundwater.

## INTRODUCTION

Every natural or man-made material, chemical, physical, or biological agent capable of causing an adverse health result is considered a hazard (Järup, 2003). One of the most important pollutants of groundwater sources which can be considered as hazards, are heavy metals (SUN et al., 2010). Some of these metals are important for the growth and health of human body such as iron and zinc (Adeyemi et al., 2021), but others, such as cadmium, mercury and lead can be harmful because of their level of toxicity to human health. Drinking polluted groundwater can have a long-term health effect on human. Studies show that 20 % of the world's cancer cases and 70 % of the total diseases around the world are due to ingestion of contaminated water (WHO, 2020). From so many different ways, heavy metals can find their way to groundwater sources. Domestic sewage, landfills and atmospheric deposits are some of the main routes of groundwater contamination of heavy metals (Tayebi et al., 2020). Risk assessment is the process of assessing the possibility of an adverse health consequence as a result of exposure to hazards (Bailey et al., 2020). According to US EPA, there are 4 main stages in every risk assessment which are: 1. Hazard Identification, 2. Dose-Response Assessment, 3. Exposure Assessment, 4. Risk Characterization (US EPA, 2020). However, after the last stage which is risk characterization, it is also needed to give some solutions for the obtained results which have

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\* Corresponding Author, Email: hamidreza.fraad@gmail.com

high risks; this process is called risk management. In the first step (i.e. hazard identification) is to identify the pollutants. The second step is to determine the toxicity of the contaminants. The third step (i.e. dose-response assessment) is concerned with assessing the magnitude, extent, and duration of these pollutants' exposure (Sheikhi Alman Abad et al., 2021). In order to achieve cancer risk, HI, and HQ quantitative estimates, the final stage (risk characterization) calculates non-carcinogenic and carcinogenic health risks of heavy metals for children and adults (Rahman et al., 2020, Miranzadeh Mahabadi et al., 2020).

Pollutants' potential to cause harm to humans and ecological systems is discussed in the first stage which is called hazard identification. In the present study, risk assessment of cadmium, lead, and zinc have been performed.

### *Zinc (Zn)*

According to the EPA, no case studies or epidemiological data exists to prove that the oral or inhalation route of zinc is carcinogenic (US EPA, 2020). Some studies have found that zinc is comparatively harmless as compared to many other metal ions with identical chemical properties (Plum et al., 2010). There are 1236 cases of toxicity to zinc compounds in the 2017 Annual Report of the American Association of Poison Control Centers National Poison Data System Annual Report. In a recent paper, it can be found that many of the cases were accidental exposures in children less than five years of age (Gummin et al., 2018). No deaths or significant adverse health events were reported. According to U.S. EPA, zinc is not classifiable as to human carcinogenicity and it is classified in WOE (weight-of-evidence) group D (US EPA, 2020). In the present study, the non-carcinogenic risk assessment of zinc is performed and due to the evidences from U.S. EPA the carcinogenic risk of zinc is neglected.

### *Cadmium (Cd)*

Cadmium is absorbed from the lungs more effectively than from the gastrointestinal tract though it is reported that high doses of cadmium cause gastrointestinal irritation too, which results in vomiting, abdominal pain, and diarrhea. Cadmium has been found to affect the liver, bones, testes, and cardiovascular system to various degrees (US EPA, 2020). According to ATSDR, usually cadmium concentrations in drinking water sources are less than 1 microgram per liter ( $\mu\text{g/L}$ ) or 1 part per billion (ppb) (ATSDR, 2020). It is also found that like many of the other heavy metals, cadmium can be accumulated in organs such as kidney and liver which can cause many disorders in their function like Proteinuria (Hedayatzadeh et al., 2020). It is also proposed that cadmium can be released in waste water from industrial and mining activities (Rahimzadeh et al., 2017). According to U.S. EPA and ATSDR there are some evidences that show inhalation of cadmium can cause respiratory tract cancer, prostate cancer, and lung cancer however there are no clear evidences that show it can be carcinogenic from ingestion and dermal routes. According to U.S. EPA, cadmium is believed to be a probable human carcinogen pollutant and its WOE (weight-of-evidence) is classified as group B1 (US EPA, 2020). In the present study, carcinogenic and non-carcinogenic risks assessment of cadmium are performed.

### *Lead (Pb)*

Lead is a natural element that is available in water and soil. Lead is a soft and malleable metal used for producing lead-acid batteries, bullets and as a radiation shield and it can be used for

constructions (Hedayati et al., 2017). Three main compartments are distributed by lead ingested into the body: blood, soft tissue, and bone. The bone, which comprises about 95 percent of the total body lead burden in adults and about 73 percent in children, is the biggest compartment (The Risk Assessment Information System, 2020). It is found that about 15 percent of ingested lead is absorbed by adults, while almost 50 percent of ingested lead is absorbed by children and pregnant women (Keil et al., 2011). An important problem with lead is its high half-life in bone which is more than 20 years. Lead can cause effects in gastrointestinal tract, hematopoietic system, cardiovascular system, central and peripheral nervous systems, kidneys, immune system, and reproductive system ( US EPA, 2020). In the previous studies, it is found that the inorganic lead form is a general metabolic toxin and blocker of enzymes, and organic forms are much more toxic. According to U.S. EPA WOE (weight-of-evidence) for lead is classified as B2. There are some evidences that shows lead can be carcinogenic (The Risk Assessment Information System, 2020). In this study, carcinogenic and non-carcinogenic risk assessment of lead are conducted.

## MATERIAL AND METHODS

According to the researches performed in Social Determinants of Health Research Center of Hormozgan University of Medical Science, concentrations of cadmium, lead, and zinc in these villages are shown in Table 4. Maximum concentrations of cadmium, lead, and zinc are in Dehno Paein, Tifakan Tal-e Gerdu, and Faryab respectively and the minimum amount are in Chahestan, Shamil (2), and Tazian-Ab Chah Mohamad Abad.

### *Exposure assessment*

Exposure assessments on people living in the villages in Bandar Abbas were performed based on the measured concentrations of cadmium, lead, and zinc in drinking water. The assessment was carried out on all three routes of entry which are oral ingestion, inhalation, and dermal absorption. The main source of contact for inhalation assumed is showering. Table 1 presents the input parameters for the exposure assessment.

**Table 1.** Input parameters and abbreviations for exposure assessment

Input parameters	Units	Values	References
Pollutants Concentration in water	mg/l	See tables	This study
Ingestion rate (IR)	L/day	2.0	USEPA
Absorption efficiency	percent	50%	Lee et al. (Lee et al., 2004)
Water temperature (T)	C	40	Lee et al. (Lee et al., 2004)
Exposure time (ET)	min/day	35 min	Lee et al. (Lee et al., 2004)
Skin surface area (SA)	m <sup>2</sup>	1.8	USEPA
Fraction of skin in contact with water	percent	90 %	Lee et al. (Lee et al., 2004)
Exposure duration (ED)	year	30	Lee et al. (Lee et al., 2004)
Exposure Frequency (EF)	days/year	350 days	Lee et al. (Lee et al., 2004)
Average lifetime (AT)	days	70 × 365	Pardakhti et al.(Pardakhti et al., 2011)
Body Weight (BW)	kg	70	Pardakhti et al.(Pardakhti et al., 2011)

In this study, in order to evaluate the potential cadmium, lead, and zinc risk assessment via oral ingestion, inhalation, and dermal absorption, an exposure assessment was performed based on the measured concentrations in Table 4. The amounts of oral slope factors and inhalation unit risks for all three pollutants studied in this article are shown in Table 2. Chronic daily intakes were calculated using the equations below:

Oral ingestion:

$$CDI_{\text{water-ca-ing}} \left( \frac{\text{mg}}{\text{kg.d}} \right) = \frac{C_{\text{g-water}} \times EF_r \left( \frac{350 \text{ days}}{\text{year}} \right) \times (IFW_{\text{adj}} \left( \frac{1.086 \text{ L-Year}}{\text{Kg-d}} \right))}{AT_r \left( \frac{365 \text{ days}}{\text{year}} \times LT(70 \text{ years}) \right)}$$

Inhalation absorption:

$$CDI_{\text{water-ca-inh}} \left( \frac{\mu\text{g}}{\text{m}^3} \right) = \frac{C_{\text{g-water}} \times \frac{10^3 \mu\text{g}}{\text{mg}} \times EF_r \left( \frac{350 \text{ days}}{\text{year}} \right) \times ED_r(30 \text{ years}) \times ET_{\text{rw}} \left( \frac{24 \text{ hours}}{\text{day}} \right) \times \left( \frac{1 \text{ day}}{24 \text{ hours}} \right) \times K \left( \frac{0.5 \text{ L}}{\text{m}^3} \right)}{AT_r \left( \frac{365 \text{ days}}{\text{year}} \times LT(70 \text{ years}) \right)}$$

Dermal absorption:

$$CDI_{\text{water-ca-der}} \left( \frac{\text{mg}}{\text{kg.d}} \right) = \frac{C_{\text{g-water}} \times EF_r \left( \frac{350 \text{ days}}{\text{year}} \right) \times DFW_{\text{adj}} \left( \frac{6219 \text{ cm}^2 - \text{Year} - \text{hours}}{\text{Kg-day}} \right) \times K_p \left( \frac{\text{cm}}{\text{hr}} \right) \times \left( \frac{1 \text{ L}}{1000 \text{ cm}^3} \right)}{AT_r \left( \frac{365 \text{ days}}{\text{year}} \times LT(70 \text{ years}) \right)}$$

where:

$$DFW_{\text{adj}} \left( \frac{6219 \text{ cm}^2 - \text{Year} - \text{hours}}{\text{Kg-day}} \right) = \frac{ED_c(6 \text{ years}) \times SA_c(6600 \text{ cm}^2) \times ET_c \left( \frac{1 \text{ hours}}{\text{event}} \right) \times EV_c \left( \frac{1 \text{ events}}{\text{day}} \right)}{BW_c(15 \text{ Kg})} + \frac{ED_r - ED_c(24 \text{ years}) \times SA_a(18000 \text{ cm}^2) \times ET_a \left( \frac{0.58 \text{ hours}}{\text{event}} \right) \times EV_a \left( \frac{1 \text{ events}}{\text{day}} \right)}{BW_a(70 \text{ Kg})}$$

$$\text{Cancer Risk} = (CDI_{\text{ingestion}} \times CSF_{\text{oral}}) + (CDI_{\text{inhalation}} \times IUR) + (CDI_{\text{dermal}} \times CSF_{\text{oral}})$$

For non-carcinogenic risk assessment, hazard quotients (HQ) were calculated using equations below and as described in the equations HI values are equal to the sum of the hazard quotients; where  $HQ_{\text{oral}}$  is the hazard quotient from ingestion route;  $HQ_{\text{inhalation}}$  is the hazard quotient from inhalation route; and  $HQ_{\text{dermal}}$  is the hazard quotient through dermal absorption. For  $HI \leq 1$ , based on the references, there are no side effects from the pollutant. In the present study, for evaluating the non-carcinogenic risk assessment of cadmium, lead, and zinc, an exposure assessment was performed based on the concentrations in Table 4. The amounts of reference dose for zinc, cadmium, and lead are shown in Table 3.

$$HQ_{\text{ingestion}} = \frac{CDI}{RfD}$$

$$HQ_{\text{inhalation}} = \frac{CDI}{RfC}$$

$$HQ_{\text{dermal}} = \frac{CDI}{RfD}$$

$$HI = \sum HQ = HQ_{\text{ingestion}} + HQ_{\text{inhalation}} + HQ_{\text{dermal}}$$

**Table 2.** Slope factors and cancer group classifications for cadmium, lead, and zinc

Chemicals	Cancer groups	Carcinogenic Slope factors	
		Oral/dermal (mg/kg day)	Inhalation ( $\mu\text{g}/\text{m}^3$ )
Zinc	D	N.A.	N.A.
Cadmium	B1	N.A.	$1.8 \times 10^{-3}$ (IRIS)
Lead	B2	$8.5 \times 10^{-3}$ (IRIS)	$1.2 \times 10^{-5}$ (IRIS)

B1 probable human carcinogen with limited data;

B2 probable human carcinogen with sufficient animal data;

D Not classified

**Table 3.** Reference Dose of cadmium, zinc, and lead

Chemical	RfD (mg/kg-day)
Zinc	0.3 (IRIS)
Cadmium	$5 \times 10^{-4}$ (IRIS)
Lead	N.A.

## RESULTS AND DISCUSSION

### *Concentration of cadmium, lead, and zinc in different villages*

The information shown in Table 4 shows that for cadmium, the concentrations are much higher in Fin-Lavar, Dehno Paein, and Takht than the other villages. Also, concentration of lead in Tifakan Tal-e Gerdu is very much higher than the others and Faryab has the most concentration of zinc between the villages. The comparison between the concentrations of different pollutants are shown in Figure 1.

**Table 4.** Concentration information of pollutants in groundwater and population of every village

Village	Population	Zinc (mg/L)	Lead (mg/L)	Cadmium (mg/L)
Eisin (Dargir)	1310	0.061	0.009	0.003
Eisin (Patel)	1767	0.009	0.011	0.003
Shahre Fin-Kahtek	195	0.108	0.014	0.005
Fin-Lavar	1209	0.009	0.003	0.012
Fin-Rezvan-Hasan Abad	5066	0.009	0.003	0.004
Fin-Rezvan-Serzeh	939	0.064	0.012	0.004
Tazian-Ghalat Bala	1688	0.02	0.011	0.003
Tazian-Ghalat Paein	5695	0.003	0.011	0.005
Tazian-Ab Chah Mohamad Abad	822	0	0.018	0.002
Kenaro	1616	0.116	0.012	0.004
Chahestan	1693	0.038	0.008	0.001
Ghal-e Ghazi	4239	0.043	0.018	0.007
Sar Khangi	1411	0.032	0.004	0.008
Takht	3000	0.28	0.003	0.011
Dehno Paein	1844	0.005	0.014	0.013
Shamil (1)	727	0.15	0.01	0.01
Shamil (2)	728	0.024	0.002	0.001
Sarkhon	5184	0.051	0.003	0.009
Faryab	1933	0.377	0.003	0.008
Tal-e Gerdu-Forkhurej	458	0.101	0.101	0.001
Gahre (Ghotb Abad)	1881	0.014	0.014	0.006
Tal-e Gerdu	338	0.009	0.009	0.003
Ghotb Abad	522	0.029	0.029	0.003
Geno	367	0.034	0.034	0.002
Tifakan Tal-e Gerdu	147	0.164	0.164	0.003

### Cancer risk analysis

Using the concentration of cadmium and based on assumptions on Table 1, the lifetime cancer risk through inhalation for cadmium and all three different routes for lead were performed and the results are shown in Table 5. The lifetime cancer risk from cadmium is 100% from inhalation. For lead, cancer risk is calculated for all routes including: ingestion, inhalation, and dermal absorption. Based on the calculations, it is obvious that lead can be more cancerous than cadmium in these villages and cancer risk for cadmium has the most amount in Dehno Paein which is  $9.6 \times 10^{-7}$ . Also, the village which has the highest amount of lead cancer risk is Tifakan Tal-e Gerdu which is  $2.08 \times 10^{-7}$ . Higher exposure and larger CSF and IUR values are the reasons for the differences in cancer risk amounts. The lowest risk for cadmium and lead occurs both in Shamil (2).

By using the following equation, total cancer cases due to cadmium and lead were calculated. These results are presented in Table 5. A comparison between cadmium, lead, and zinc is illustrated in Figure 2.

$$\text{Cancer cases} = \text{Total risk} \times \text{Population}$$

**Table 5.** Lifetime cancer risks from cadmium and lead via different routes

Village	Cadmium			lead				Cancer Cases (capita)
	Inhalation Volatile Risk	Total Risk	Cancer Cases (capita)	Ingestion Risk	Inhalation Volatile Risk	Dermal Risk	Total Risk	
Eisin (Dargir)	2.21918E-07	2.21918E-07	0.000291	1.13807E-06	4.43836E-09	2.60687E-09	1.14511E-06	0.0015
Eisin (Patel)	2.21918E-07	2.21918E-07	0.000392	1.39097E-06	5.42466E-09	3.18617E-09	1.39958E-06	0.002473
Shahre Fin-Kahtek	3.69863E-07	3.69863E-07	7.21E-05	1.77033E-06	6.90411E-09	4.05513E-09	1.78129E-06	0.000347
Fin-Lavar	8.87671E-07	8.87671E-07	0.001073	3.79356E-07	1.47945E-09	8.68956E-10	3.81705E-07	0.000461
Fin-Rezvan-Hasan Abad	2.9589E-07	2.9589E-07	0.001499	3.79356E-07	1.47945E-09	8.68956E-10	3.81705E-07	0.001934
Fin-Rezvan-Serzeh	2.9589E-07	2.9589E-07	0.000278	1.51742E-06	5.91781E-09	3.47582E-09	1.52682E-06	0.001434
Tazian-Ghalat Bala	2.21918E-07	2.21918E-07	0.000375	1.39097E-06	5.42466E-09	3.18617E-09	1.39958E-06	0.002362
Tazian-Ghalat Paein	3.69863E-07	3.69863E-07	0.002106	1.39097E-06	5.42466E-09	3.18617E-09	1.39958E-06	0.007971
Tazian-Ab Chah Mohamad Abad	1.47945E-07	1.47945E-07	0.000122	2.27614E-06	8.87671E-09	5.21374E-09	2.29023E-06	0.001883
Kenaro	2.9589E-07	2.9589E-07	0.000478	1.51742E-06	5.91781E-09	3.47582E-09	1.52682E-06	0.002467
Chahestan	7.39726E-08	7.39726E-08	0.000125	1.01162E-06	3.94521E-09	2.31722E-09	1.01788E-06	0.001723
Ghal-e Ghazi	5.17808E-07	5.17808E-07	0.002195	2.27614E-06	8.87671E-09	5.21374E-09	2.29023E-06	0.009708
Sar Khangi	5.91781E-07	5.91781E-07	0.000835	5.05808E-07	1.9726E-09	1.15861E-09	5.08939E-07	0.000718
Takht	8.13699E-07	8.13699E-07	0.002441	3.79356E-07	1.47945E-09	8.68956E-10	3.81705E-07	0.001145
Dehno Paein	9.61644E-07	9.61644E-07	0.001773	1.77033E-06	6.90411E-09	4.05513E-09	1.78129E-06	0.003285
Shamil (1)	7.39726E-07	7.39726E-07	0.000538	1.26452E-06	4.93151E-09	2.89652E-09	1.27235E-06	0.000925
Shamil (2)	7.39726E-08	7.39726E-08	5.39E-05	2.52904E-07	9.86301E-10	5.79304E-10	2.5447E-07	0.000185
Sarkhon	6.65753E-07	6.65753E-07	0.003451	3.79356E-07	1.47945E-09	8.68956E-10	3.81705E-07	0.001979
Faryab	5.91781E-07	5.91781E-07	0.001144	3.79356E-07	1.47945E-09	8.68956E-10	3.81705E-07	0.000738
Tal-e Gerdu-Forkhurej	7.39726E-08	7.39726E-08	3.39E-05	1.27717E-05	4.98082E-08	2.92549E-08	1.28507E-05	0.005886
Gahre (Ghotb Abad)	4.43836E-07	4.43836E-07	0.000835	1.77033E-06	6.90411E-09	4.05513E-09	1.78129E-06	0.003351
Tal-e Gerdu	2.21918E-07	2.21918E-07	7.5E-05	1.13807E-06	4.43836E-09	2.60687E-09	1.14511E-06	0.000387
Ghotb Abad	2.21918E-07	2.21918E-07	0.000116	3.66711E-06	1.43014E-08	8.39991E-09	3.68981E-06	0.001926
Geno	1.47945E-07	1.47945E-07	5.43E-05	4.29937E-06	1.67671E-08	9.84817E-09	4.32599E-06	0.001588
Tifakan Tal-e Gerdu	2.21918E-07	2.21918E-07	3.26E-05	2.07381E-05	8.08767E-08	4.75029E-08	2.08665E-05	0.003067

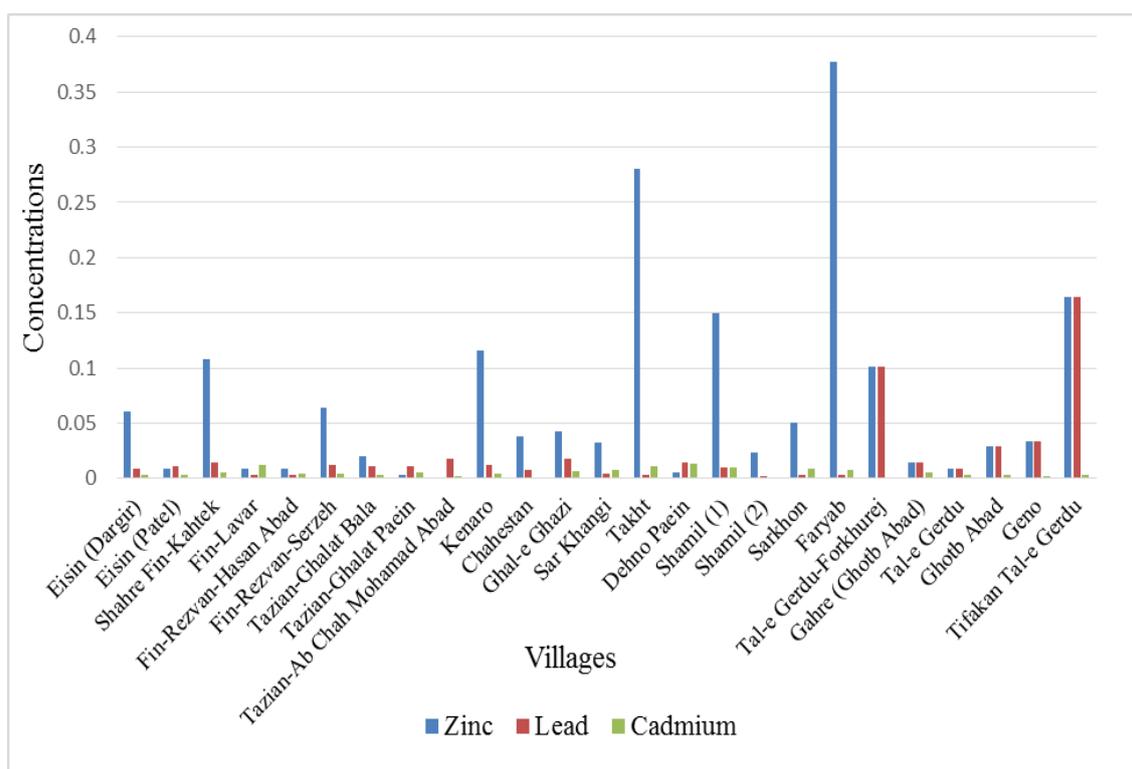


Figure 1. Concentrations of cadmium, lead, and zinc in different villages

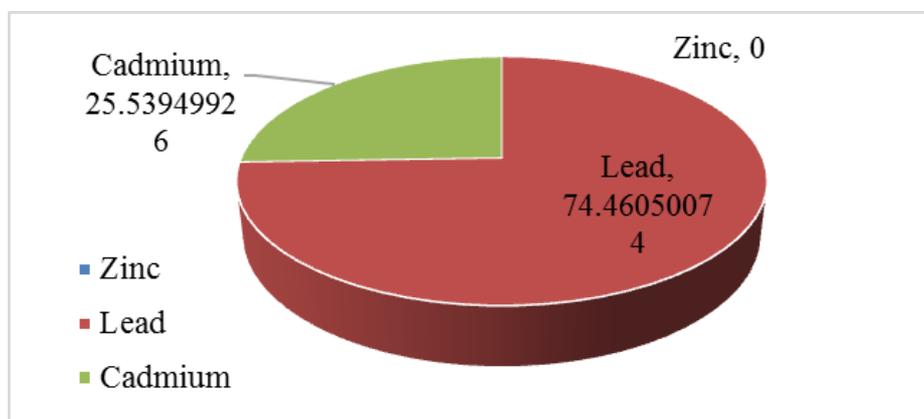


Figure 2. Comparison of total cancer cases between cadmium, lead, and zinc

*Non-cancer risk analysis*

Using the amounts of Rfd in Table 3, hazard quotient (HQ) values for cadmium, lead, and zinc were calculated. Table 6 gives the results of non-carcinogenic risk assessment of these heavy metals for people living in these villages. It can be found from Table 6 that for cadmium and zinc all the HI values calculated are under 1 which shows there are no negative effects of cadmium in all villages and this value for lead is more than 1 in Tifakan Tal-e Gerdu and Tal-e Gerdu-Forkhurej that are 1.63 and 1.003 respectively which can cause some problems for people living in this village.

**Table 6.** Non-carcinogenic risk assessment of cadmium, lead, and zinc

Village	Cadmium HI	Lead HI	Zinc HI
Eisin (Dargir)	0.001193	0.089465	0.007082425
Eisin (Patel)	0.001193	0.109346	0.001044948
Shahre Fin-Kahtek	0.001988	0.139167	0.012539375
Fin-Lavar	0.004771	0.029822	0.001044948
Fin-Rezvan-Hasan Abad	0.00159	0.029822	0.001044948
Fin-Rezvan-Serzeh	0.00159	0.119286	0.007430741
Tazian-Ghalat Bala	0.001193	0.109346	0.002322106
Tazian-Ghalat Paein	0.001988	0.109346	0.000348316
Tazian-Ab Chah Mohamad Abad	0.000795	0.178929	0
Kenaro	0.00159	0.119286	0.013468218
Chahestan	0.000398	0.079524	0.004412002
Ghal-e Ghazi	0.002783	0.178929	0.004992529
Sar Khangir	0.00318	0.039762	0.00371537
Takht	0.004373	0.029822	0.032509491
Dehno Paein	0.005168	0.139167	0.000580527
Shamil (1)	0.003976	0.099405	0.017415799
Shamil (2)	0.000398	0.019881	0.002786528
Sarkhon	0.003578	0.029822	0.005921372
Faryab	0.00318	0.029822	0.043771707
Tal-e Gerdu-Forkhurej	0.000398	1.003993	0.011726638
Gahre (Ghotb Abad)	0.002385	0.139167	0.001625475
Tal-e Gerdu	0.001193	0.089465	0.001044948
Ghotb Abad	0.001193	0.288275	0.003367054
Geno	0.000795	0.337978	0.003947581
Tifakan Tal-e Gerdu	0.001193	1.630246	0.019041273

## CONCLUSION

Groundwater in these villages of Bandar Abbas is the main source of drinking water for people living in these villages. Risk assessment of cadmium, lead, and zinc has been studied in this article. To reduce the risk of heavy metals, researchers must first evaluate the contamination properties, source, and health risk. Results show that lead can produce more cancer cases than cadmium. The results indicate that HI values for most of the villages are lower than 1 except Tifakan Tal-e Gerdu and Tal-e Gerdu-Forkhurej which have exceeded the acceptable limits ( $HI > 1$ ). According to the carcinogenic risk assessment in Table 5, total cancer cases for each village have been showed which shows the importance of considering a good way of treatment for the water extracted from these wells. In general, it can be realized that water sources in villages such as Tifakan Tal-e Gerdu and Dehno Paein are the villages high in cancer risk. These high risk values as a result of high concentration of contaminants can be due to landfills, wastewaters from septic tanks and etc. According to the results in the present study, most of the water sources for the villages are recommended for drinking water except for villages such as Tifakan Tal-e Gerdu, Tal-e Gerdu-Forkhurej and Dehno Paein, which are not recommended for drinking water in spite of their high cadmium and lead concentrations and a reconsideration is needed on their treatment in order to increase their quality.

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## CONFLICT OF INTEREST

The authors declare that there is not any conflict of interests regarding the publication of this manuscript. In addition, the ethical issues, including plagiarism, informed consent, misconduct, data fabrication and/ or falsification, double publication and/or submission, and redundancy has been completely observed by the authors.

## LIFE SCIENCE REPORTING

No life science threat was practiced in this research.

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