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Fluoride in Iranian Drinking Water Resources: a Systematic Review, Meta-analysis and Non-carcinogenic Risk Assessment

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Abstract

A systematic review, meta-analysis, and non-carcinogenic risk considering fluoride content of drinking water resources of 31 provinces of Iran among some international databases such as Science Direct, Scopus, PubMed, and national databases including SID and Irandoc (2011 to July 2017) were conducted. In this context, 10 articles (40 studies) with 1706 samples were included in meta-analyses and risk assessment studies. The pooled concentration of fluoride in the cold, mild, and warm weather provinces were calculated as 0.39 mg/L (95% CI 0.32–0.48 mg/L), 0.52 (95% CI 0.43–0.61 mg/L), and 0.75 (95% CI 0.56–0.94 mg/L), respectively. The pooled concentration of fluoride in Iranian drinking water resources was 0.51 (95% CI 0.45–0.57 mg/L). The minimum and maximum concentrations of fluoride content were related to Kermanshah (0.19 mg/L) and Kerman (1.13 mg/L) provinces, respectively. The HQ of fluoride in the children and adults were 0.462 and 0.077, respectively as children are more vulnerable than adults. The HQ for children and adults was lower than 1 value. Therefore, there is no considerable non-carcinogenic risk for consumers due to drinking water in Iran. Although the non-carcinogenic of fluoride in drinking water was not significant, fluoride entry from other sources, such as food or inhalation, could endanger the health of the residents of Kerman and Bushehr provinces.

Keywords Fluoride · Drinking water · Meta-analysis · Risk assessment · Iran · Systematic review · Resources · Hazard quotient

Introduction

Today, pollution of water sources with chemical contaminants such as heavy metals, nitrate, and fluoride and radioactive materials is one of most important raised concerns [1–5]. The concentration of fluoride in different forms such as fluorspar, mica, cryolite, and fluorapatite is highly notable in the environment [6, 7]. Fluoride could enter the human body through the ingestion of food, drinking water, inhalation, and dermal contact [8]. However, drinking water is the most important exposure pathway of fluoride, as about 75% of fluoride intake [9]. The previous investigations showed that

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fluoride content of drinking water, at low concentrations, can pose beneficial impacts on the growth of teeth and bones, as well as preventing dental fluorosis [10]. However, some harmful effects on human health due to chronic exposure to fluoride via drinking water such as skeletal fluorosis and cancer [11, 12] as well as increasing of blood pressure [13, 14], damage to the kidney, testis, lung, and soft tissues such as liver in addition to some neurotoxicological effects were reported [15, 16].

Dental fluorosis with high prevalence in some countries [17, 18], can decrease the quality of life through incurring treatment costs, impeding nutrition, and inflicting pains [19]. Several studies in different countries such as India [20, 21], Iran [22], China [23], Turkey [24], South Africa [25], Japan [26], India [27], Mexico [28], and the USA [11] demonstrated that exposure to drinking water with high concentrations of fluoride can be considered as a notable risk for human health. In this regard, approximately, 200 million people among 25 countries are suffering from severe fluorosis [29], mostly from low and middle-income countries [30]. In another study, it is estimated that about 70 million people may have fluorosis in Africa, India, Eastern Mediterranean, and China [31].

On the other hand, the probabilistic risk assessment (PRA) like Monte Carlo simulation (MCS) has often been used for health risk assessment to perform a more realistic health risk assessment of chemical contaminants [32]. The PRA successfully was used to estimate the potential adverse health risks of pollutants in water resources and other environments [33–36].

In many provinces of Iran, groundwater is the most important water resource for drinking water, agriculture, and industry activities [37]. Although many studies have been conducted on drinking water resources content of fluoride in Iran, no study was perform with the aid of meta-analysis to determine health risk assessment of fluoride in Iranian drinking water. Therefore, the current study is the first investigation regarding fluoride concentrations in drinking water resources based on three weather category including cold, mild, and warm weather provinces by a meta-analysis approach. Also, the non-carcinogenic risks due to exposure to fluoride in drinking water for consumers (adults and children) were assessed.

Materials and Methods

Literature Search

The International databases such as Science Direct, Scopus, PubMed, and national database including Scientific Information Database (SID) were screened by two investigators separately, to obtain all studies published about fluoride in drinking water of Iran.

The used following keywords were ((TITLE-ABS-KEY (*fluoride*) AND TITLE-ABS-KEY (f-) AND TITLE-ABS-KEY (fluorosis))) AND ((TITLE-ABS-KEY (drinking AND water) AND TITLE-ABS-KEY (water) AND TITLE-ABS-KEY (tap AND water))) OR (TITLE-ABS-KEY (Iran)). Furthermore, references of screened papers were checked to obtain additional citations which not retrieved in the databases. The PRISMA guideline was used for screening of the literature (Fig. 1) [38].

Inclusion and Exclusion Criteria

In the initial research, after removing repetition papers by using EndNote X8.2.0 Build 11343 software (Thomson Reuters, New York, NY), based on the title assessment, some papers were excluded. Then, abstract of remained articles was carefully checked, and some irrelevant papers were excluded. Full texts of remained papers were downloaded. The full-text papers were checked to examine the final inclusion criteria. Then, the selected papers were assessed carefully. Original research; cross-sectional studies that measure fluoride content in drinking water of Iran; published in full text or abstract; published between 2011 to July 2017; Moreover, based on the previously published meta-analysis studies [39], to avoid any mistake in the translation process and for the clarity of the reports, manuscripts published only in the "English" were included. The articles were excluded while they did not meet the proposed criterion.

Data Extraction and Definitions

The following variables were extracted from studies: province of study, year of study, type of water resources, sample size, the method of detection, and weather condition. Three investigators extracted data from the included studies separately. Inconsistencies between the investigators were discussed to reach consensus.

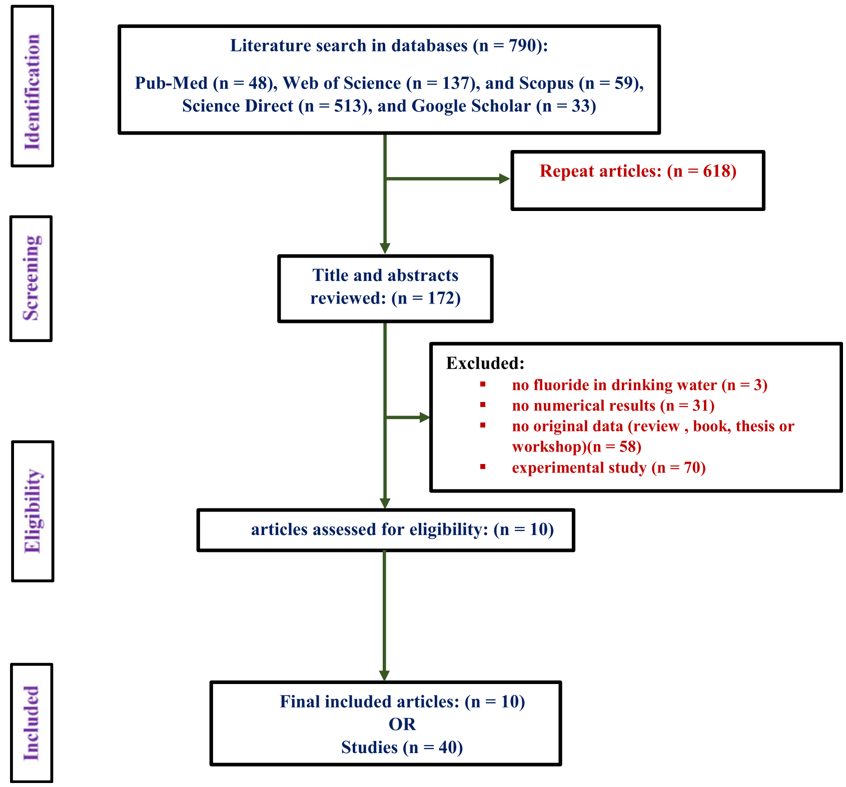
Meta-analysis and Statistical Analysis

The 95% confidence interval (CI) was calculated for all evaluated studies regarding fluoride levels in drinking water. Meta-analysis was performed based on the mean and standard error (SE) of the concentration of fluoride in water resources. Since the heterogeneity was > 50%, the random effect model (REM) was used to evaluate pooled regarding fluoride concentration in drinking water in the cold, mild, and warm weather subgroups [40]. Meta-analysis of data was carried out using STATA (version 9.2, STATA Corporation, College Park, Texas, USA).

Non-carcinogenic Risk Assessment

Risk assessment is a method used to evaluate the potential hazards of chemical contaminants for a period on the health

Fig. 1 Flow chart selection process showing inclusion and exclusion of studies identified



of humans [41]. In this study, the target population was categorized as children and adults.

According to ingestion and dermal exposure pathways, the dose of fluoride in drinking water was estimated using Eqs. 1 and 2 [42, 43].

$$EDI_{ing} = \frac{Cw \times IRw \times EF \times ED}{BW \times AT} \quad (1)$$

$$EDI_{derm} = \frac{Cw \times SA \times Kp \times F \times ETs \times EF \times ED \times 10{-}3}{BW \times AT} \quad (2)$$

where input parameters of the non-carcinogenic risk assessment are shown in Table 1.

In the current study, HQ was used to estimate the non-carcinogenic risk of fluoride (Eq. 3) [41, 43]:

Table 1 Input parameters of the non-carcinogenic risk assessment

Parameters	Units	Value	Reference
Ingestion rate (IRw)	l/day	Children 0.89 Adults 2.1	[44]
Exposure frequency (EF)	Day/year	365	[45]
Exposure duration (ED)	Year	6	[45]
Averaging time (AT)	Days	Children 2190 Adults 9125	[46]
Dermal permeability constant (Kp)	cm/h	0.001	[46]
Fraction of skin in contact with water (F)	Unitless	0.4–0.9	[47]
Body weight (BW)	Kg	Children 16.68 Adults 57.03	[48]
Skin surface area (SA)	cm^2	Children 7422 Adults 18182	[48]
Exposure time in the shower (ETs)	h/day	0.13	[47]
Oral reference dose (RfDo)	mg/kg/day	0.06	[49]
Fraction of fluoride absorbed in gastrointestinal tract (ABSgi)	Unitless	1	[46]

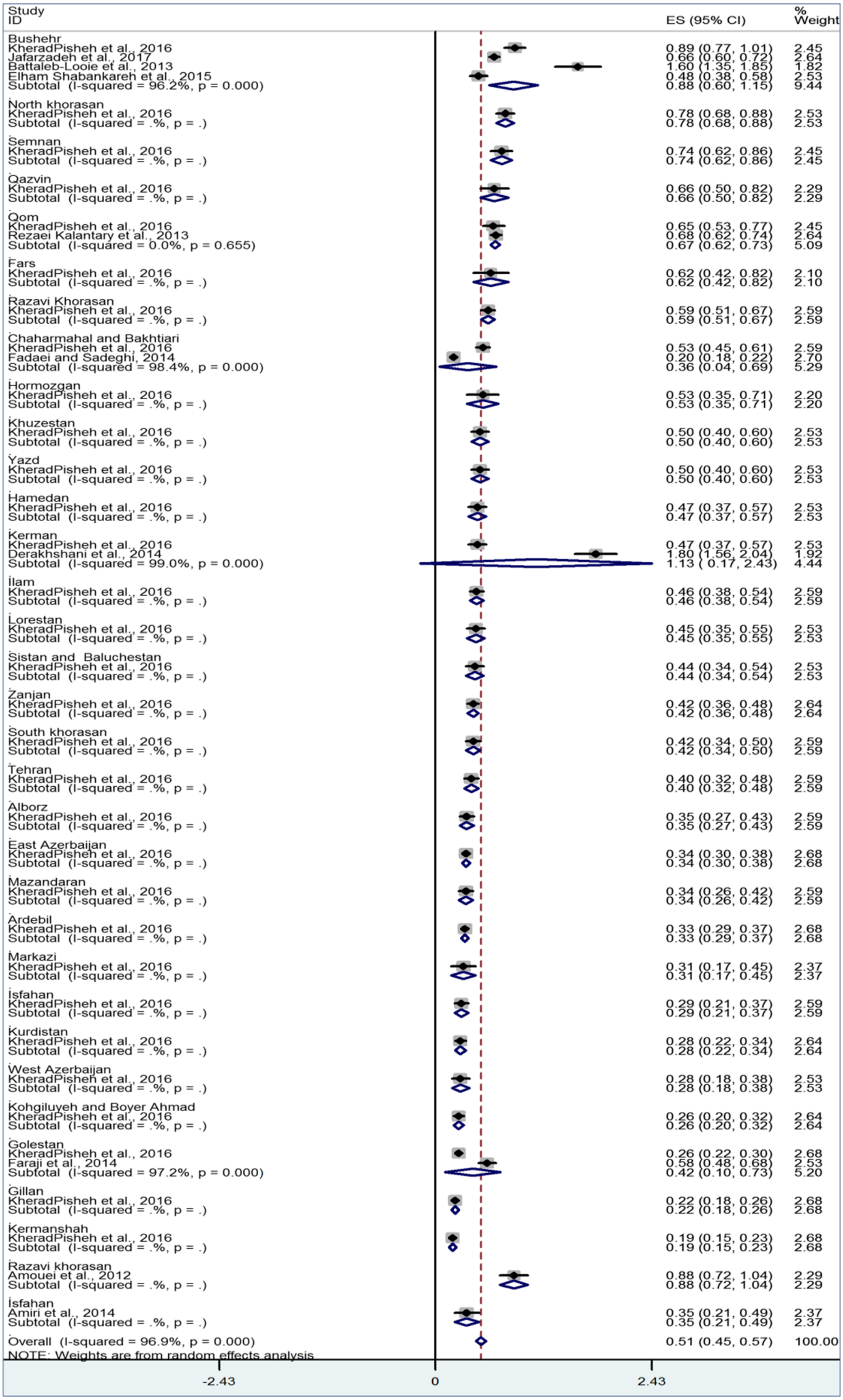


Fig. 2 Forest plot concentration of fluoride in drinking water based on province in Iran. ES effect size

Table 2 The main characteristics included in our study

Province	Year study	Year publish	Water resources	Average	SD	Min	Max	Samples	Method	Ref
Bushehr	2014	2016	Tap water	0.89	0.31	0.05	3.52	30	SPADNS	[52]
Khorasan-north	2014	2016	Tap water	0.78	0.29	0.04	1.52	30	SPADNS	
Semnan	2014	2016	Tap water	0.74	0.32	0.13	1.49	30	SPADNS	
Qazvin	2014	2016	Tap water	0.66	0.45	0.18	1.8	30	SPADNS	
Qom	2014	2016	Tap water	0.65	0.32	0.1	1.5	30	SPADNS	
Fars	2014	2016	Tap water	0.62	0.57	0.01	3.72	30	SPADNS	
Razavi Khorasan-	2014	2016	Tap water	0.59	0.23	0.03	1.5	30	SPADNS	
Chaharmahal and Bakhtiari	2014	2016	Tap water	0.53	0.22	0.033	1.23	30	SPADNS	
Hormozgan	2014	2016	Tap water	0.53	0.49	0.01	3	30	SPADNS	
Khuzestan/Shush	2014	2016	Tap water	0.50	0.25	< 0.02	2.38	30	SPADNS	
Yazd	2014	2016	Tap water	0.50	0.27	< 0.02	1.39	30	SPADNS	
Hamedan	2014	2016	Tap water	0.47	0.26	0.06	1.23	30	SPADNS	
Kerman	2014	2016	Tap water	0.47	0.25	0.02	1.74	30	SPADNS	
Ilam	2014	2016	Tap water	0.46	0.23	0.16	1.18	30	SPADNS	
Lorestan	2014	2016	Tap water	0.45	0.27	< 0.02	1.2	30	SPADNS	
Sistan Baluchestan	2014	2016	Tap water	0.44	0.25	< 0.02	1.15	30	SPADNS	
Zanjan	2014	2016	Tap water	0.42	0.19	0.14	1.56	30	SPADNS	
Khorasan-south	2014	2016	Tap water	0.42	0.21	0.1	1.1	30	SPADNS	
Tehran	2014	2016	Tap water	0.40	0.2	0.02	1.58	30	SPADNS	
Alborz	2014	2016	Tap water	0.35	0.23	0.029	1.548	30	SPADNS	
East Azerbaijan	2014	2016	Tap water	0.34	0.12	0.19	0.847	30	SPADNS	
Mazandaran	2014	2016	Tap water	0.34	0.21	< 0.02	1.16	30	SPADNS	
Ardebil	2014	2016	Tap water	0.33	0.11	0.12	0.58	30	SPADNS	
Markazi	2014	2016	Tap water	0.31	0.4	0.01	1.52	30	SPADNS	
Isfahan	2014	2016	Tap water	0.29	0.23	< 0.02	1.5	30	SPADNS	
Kurdistan	2014	2016	Tap water	0.28	0.16	< 0.02	0.8	30	SPADNS	
West Azerbaijan	2014	2016	Tap water	0.28	0.29	< 0.02	2.2	30	SPADNS	
Kohgiluyeh and Boyer Ahmad	2014	2016	Tap water	0.26	0.17	0.01	0.81	30	SPADNS	
Golestan	2014	2016	Tap water	0.26	0.11	0.09	0.72	30	SPADNS	
Gillan	2014	2016	Tap water	0.22	0.13	< 0.02	0.82	30	SPADNS	
Kermanshah	2014	2016	Tap water	0.19	0.11	0.01	0.86	30	SPADNS	
Bushehr	2009–2012	2017	Tap water	0.66	0.43	< 0.02	6	228	SPADNS	[53]
Bushehr	2010	2013	Well/spring	1.60	0.65	0.5	3	27	SPADNS	[9]
Bushehr	2012–2013	2015	Tap water	0.48	0.34	0.42	0.59	50	AB-S-DR2000	[54]
Qom	2011–2012	2013	Well	0.68	0.25	0.42	1.15	100	SPADNS	[55]
Razavi Khorasan	2009–2010	2012	Tap water	0.88	0.62	0.11	3.06	62	SPADNS	[56]
Chaharmahal and Bakhtiari	2013	2014	Tap water	0.20	0.1	0.19	0.28	230	SPADNS	[57]
Kerman/Zarand	2012–2013	2014	Tap water	1.80	0.86	0.33	3.5		NM[1]	[58]
Isfahan	2009–2010	2014	Well	0.35	0.54	0.05	2.54	59	NM	[59]
Golestan	2012	2014	Well	0.58	0.22	0.3	0.8	20	SPADNS	[60]

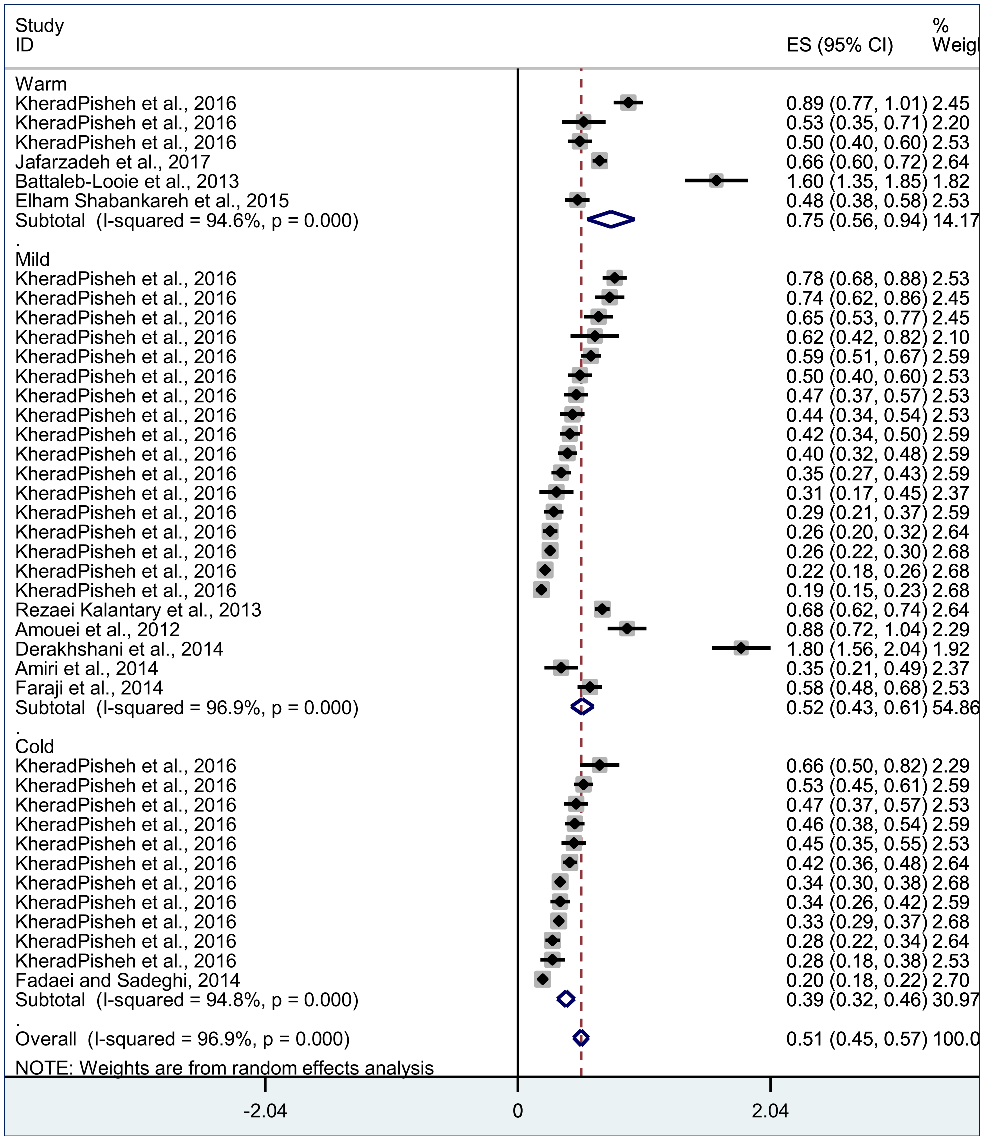
[1] Not mentioned

$$HQ = \frac{EDI}{RfD} \quad (3)$$

RfD (mg/kg/day) is the oral reference dose of fluoride. Based on a database of the United States Environmental Protection Agency (USEPA), RfD for fluoride is 0.06 mg/kg/day [49]. When HQ ≤ 1, the population exposed are in the safe range of risk of non-carcinogenic, while HQ > 1 showed considerable non-carcinogenic health risk.

RfD_{derm} (dermal toxicological of fluoride exposure) is calculated using Eq. (4) which was recommended by the USEPA [50]:

Fig. 3 Forest plot concentration of fluoride in drinking water based on cold, mild, and warm weather condition in Iran. ES effect size



$$\mathrm{RfD_{derm}} = \mathrm{RfD_O} \times \mathrm{ABSgi} \tag{4}$$

where $\mathrm{RfD_{derm}}$ is reference dose due to dermal contact, RfDo is reference dose due to oral intake (mg/kg/day), and ABSgi is a factor of the gastrointestinal absorption.

In the current study, non-carcinogenic risk assessment for drinking water resources content of fluoride was performed using Monte Carlo Simulation (MCS) model (Crystal Ball v 7.2 software, Oracle, Decisioneering, Denver, USA) [51]. The MCS model was run for 10,000 iterations.

The geostatistical distribution HQ for children and adults was conducted using ArcGIS mapping software (ESRI, Redlands, CA). The comparison of HQ between children and adults was carried out using independent sample t test statistical through IBM SPSS Statistics 23.0 software (IBM Corporation, Armonk, NY). The significance level was adjusted as p value < 0.05.

Results and Discussion

Study Characteristics

Among 790 articles collected, 618 were excluded in the primary assessment. Based on titles and abstracts, 172 articles were identified as suitable. All 172 articles were considered separately by three investigators. One hundred and sixty-two articles were excluded, due to (1) no fluoride in drinking water; (2) no numerical results;(3) no original data; and (4) experimental study (Fig. 1). Finally, 10 articles (40 studies) that

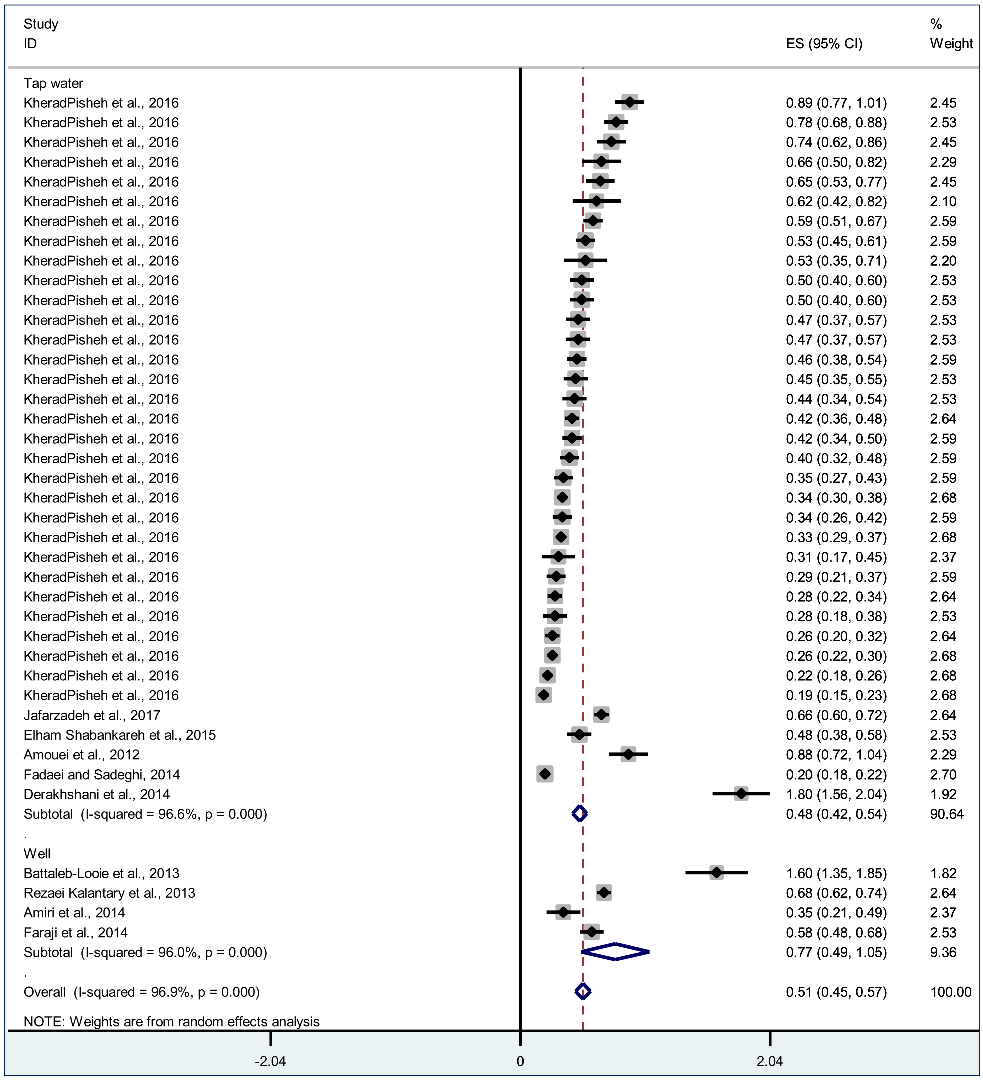


Fig. 4 Forest plot concentration of fluoride in drinking water based on type of water resources. ES effect size

published between 2011 and 2017 were included in meta-analysis and risk health assessment studies.

Results of Meta-analysis

The pooled level of fluoride in drinking water of Iran was 0.51 mg/L (0.45–0.57 mg/L) (Fig. 2). According to Guissouma et al. (2017), the concentration of fluoride in tap drinking water of 24 provinces of Tunisia was measured in the range 0 to 2.4 mg/L that was lower than Iran (< 0.02 to 6 mg/L) (Table 2) [61]. Also, the fluoride content in tap drinking water of 29 provinces of China was determined as 0.1 to 2.24 mg/L as lower of our result [62]. The fluoride level in the deep and shallow well water of Chiang Mai city, Thailand, was reported as 2.21 ± 3.17 and 0.65 ± 0.76 mg/L, respectively, which was higher than Iran (0.51 mg/L) [63]. Similarly, the concentration of fluoride in drinking water (groundwater) of Ethiopian Rift Valley was 6.4 ± 4.2 mg/L [64]. The range of fluoride concentration in drinking water resources of many states of India including Assam (1.6 to 29 mg/L) [27, 65], Chhattisgarh (10 mg/L<) [66, 67], and Jharkhand (0.5 to 14.32 mg/L) [68] was higher than Iran but Manipur state in India (0.7 to 0.84 mg/L) was similar to Iran [69].

According to REM, the concentration of fluoride in the provinces with cold, mild, and warm weathers were 0.39 mg/L (95% CI 0.32–0.48 mg/L), 0.52 mg/L (95% CI 0.43–0.61 mg/L), and 0.75 mg/L (95% CI 0.58–0.94 mg/L), respectively (Fig. 3). The lowest and highest concentration of fluoride in drinking water in the cold weather provinces were noted in Kermanshah province as 0.19 mg/L (95% CI 0.15–0.23 mg/L) and North Khorasan province as 0.78 mg/L (95% CI 0.68–0.89 mg/L), respectively. The lowest and highest concentration of fluoride in drinking water for the mild weather provinces was Isfahan province (0.29 mg/L (95% CI 0.21–0.37 mg/L)) and Kerman (1.80 mg/L (95% CI 1.56–2.04 mg/L)), respectively (Fig. 3). Also, the lowest and highest concentration of fluoride in drinking water for the warm weather provinces was 0.50 mg/L (95% CI 0.40–0.60 mg/L) and

Table 3 EDI and HQ induced to fluoride exposure in drinking water of Iran

	Children						Adults					
	EDI ing	HQ ing	EDI derm	HQ derm	Total EDI (mg/kg/day)	Total HQ	EDI ing	HQ ing	EDI derm	HQ derm	Total EDI (mg/kg/day)	Total HQ
Alborz	0.019	0.313	0.00001	0.00024	0.0190	0.313	0.003	0.052	0.000002	0.00004	0.0030	0.052
Ardebil	0.018	0.292	0.00001	0.00022	0.0180	0.292	0.003	0.048	0.000002	0.00004	0.0030	0.048
Bushehr	0.047	0.781	0.00004	0.00059	0.0470	0.782	0.008	0.129	0.000006	0.00010	0.0080	0.129
Chaharmahal and Bakhtiari	0.019	0.324	0.00001	0.00025	0.0190	0.324	0.003	0.054	0.000003	0.00004	0.0030	0.054
East Azerbaijan	0.018	0.305	0.00001	0.00023	0.0180	0.305	0.003	0.051	0.000002	0.00004	0.0030	0.051
Fars	0.033	0.549	0.00002	0.00042	0.0330	0.549	0.005	0.091	0.000004	0.00007	0.0050	0.091
Gillan	0.012	0.195	0.00001	0.00015	0.0120	0.195	0.002	0.032	0.000002	0.00003	0.00280	0.032
Golestan	0.022	0.373	0.00002	0.00028	0.0221	0.374	0.004	0.062	0.000003	0.00005	0.0040	0.062
Hamedan	0.025	0.42	0.00002	0.00032	0.0250	0.420	0.004	0.07	0.000003	0.00005	0.0040	0.070
Hormozgan	0.028	0.471	0.00002	0.00036	0.0281	0.472	0.005	0.078	0.000004	0.00006	0.0050	0.078
Ilam	0.025	0.409	0.00002	0.00031	0.0251	0.409	0.004	0.068	0.000003	0.00005	0.0040	0.068
Isfahan	0.017	0.285	0.00001	0.00022	0.0171	0.285	0.003	0.047	0.000002	0.00004	0.0030	0.047
Kerman	0.058	0.963	0.00004	0.00073	0.0581	0.964	0.01	0.159	0.000008	0.00013	0.0100	0.160
Kermanshah	0.01	0.172	0.00001	0.00013	0.0101	0.172	0.002	0.028	0.000001	0.00002	0.0021	0.028
Khuzestan	0.027	0.448	0.00002	0.00034	0.0271	0.449	0.004	0.074	0.000004	0.00006	0.0040	0.074
Kohgiluyeh and Boyer Ahmad	0.014	0.235	0.00001	0.00018	0.0141	0.235	0.002	0.039	0.000002	0.00003	0.0026	0.039
Kurdistan	0.015	0.251	0.00001	0.00019	0.0151	0.251	0.002	0.042	0.000002	0.00003	0.0028	0.042
Lorestan	0.024	0.397	0.00002	0.0003	0.0241	0.397	0.004	0.066	0.000003	0.00005	0.0040	0.066
Markazi	0.017	0.276	0.00001	0.00021	0.0171	0.276	0.003	0.046	0.000002	0.00004	0.0030	0.046
Mazandaran	0.018	0.298	0.00001	0.00023	0.0181	0.298	0.003	0.049	0.000002	0.00004	0.0030	0.049
North-Khorasan	0.042	0.696	0.00003	0.00053	0.0421	0.697	0.007	0.115	0.000005	0.00009	0.0070	0.115
Qazvin	0.035	0.589	0.00003	0.00045	0.0351	0.589	0.006	0.098	0.000005	0.00008	0.0060	0.098
Qom	0.035	0.591	0.00003	0.00045	0.0351	0.591	0.006	0.098	0.000005	0.00008	0.0060	0.098
Razavi Khorasan	0.031	0.525	0.00002	0.0004	0.0321	0.525	0.005	0.087	0.000004	0.00007	0.0050	0.087
Razavi Khorasan	0.047	0.783	0.00004	0.00059	0.0470	0.783	0.008	0.13	0.000006	0.00010	0.0080	0.130
Semnan	0.04	0.66	0.00003	0.0005	0.0401	0.660	0.007	0.109	0.000005	0.00009	0.0070	0.109
Sistan Baluchestan	0.023	0.39	0.00002	0.0003	0.0231	0.391	0.004	0.065	0.000003	0.00005	0.0040	0.065
South-Khorasan	0.022	0.373	0.00002	0.00028	0.0220	0.373	0.004	0.062	0.000003	0.00005	0.0040	0.062
Tehran	0.021	0.355	0.00002	0.00027	0.0210	0.355	0.004	0.059	0.000003	0.00005	0.0040	0.059
West Azerbaijan	0.015	0.25	0.00001	0.00019	0.0150	0.250	0.002	0.041	0.000002	0.00003	0.0020	0.041
Yazd	0.027	0.445	0.00002	0.00034	0.0270	0.445	0.004	0.074	0.000003	0.00006	0.0040	0.074
Zanjan	0.022	0.374	0.00002	0.00028	0.0220	0.374	0.004	0.062	0.000003	0.00005	0.0040	0.062
Mean	0.028	0.462	0.00002	0.00035	0.0280	0.462	0.005	0.077	0.000004	0.00006	0.0050	0.077

0.88 mg/L (95% CI 0.60–1.15 mg/L) in the Khuzestan and Bushehr provinces, respectively (Fig. 3).

Significant differences in the concentration of fluoride between the cold and mild weather provinces (p value = 0.022) and warm weather provinces (p value = 0.007) were noted. However, no significant difference in the concentration of fluoride in the mild weather with warm weather provinces (p value = 0.314) was observed. The rank order of provinces according to the concentration of fluoride was warm weather > mild weather > cold weather provinces. The meta-analysis of data based on the type of water resources indicated that concentration of fluoride in tap drinking water [0.48 mg/L (95% CI 0.42–0.54 mg/L)] and well water [0.51 mg/L (95% CI 0.45–0.1.05 mg/L)] was equal almost (Fig. 4).

The standard limits of fluoride in drinking water in each province should be determined based on the level of water ingestion, the weather conditions, average annual temperature, and fluoride intake through other sources (food, tooth protectors, and air) [70, 71]. The range of national standard limit for fluoride in drinking water in the cold (12–14.6 °C), mild (17.7–21.5 °C), and warm (26.3–32.5 °C) weather provinces is 1–2.2 mg/L, 0.7–1.6 mg/L, and 0.6–1.4 mg/L,

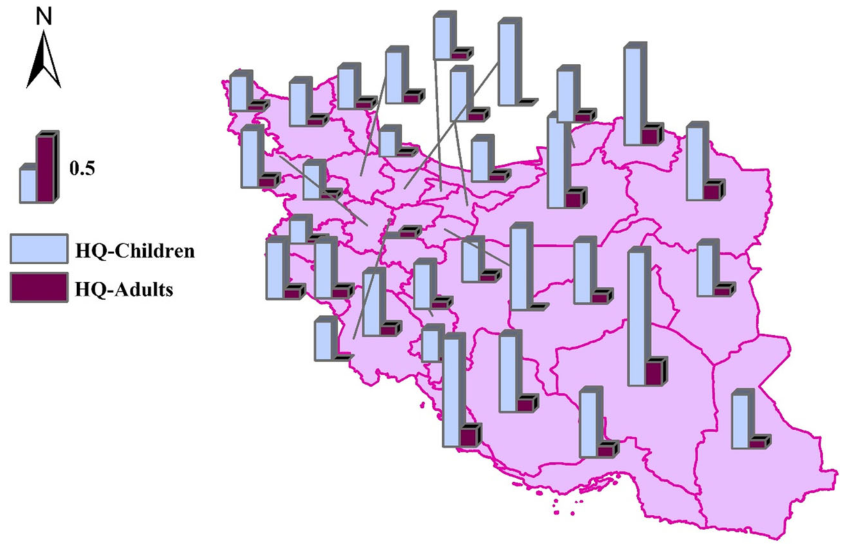


Fig. 5 Distribution of HQ among children and adults induced to fluoride in drinking water exposure from 31 provinces in Iran using geographic information system (GIS)

respectively [71]. The mean concentration of fluoride in drinking water for cold weather provinces (20/20, 100%) was lower than range proposed by the national standard limit. Except for Semnan, Kerman, and Khorasan Razavi provinces, the mean concentration of fluoride in drinking water for mild weather provinces (11/14, 78%) was higher than standard limit. Also, except Bushehr province, mean concentration of fluoride in drinking water for other warm weather provinces (2/6, 33%) was lower than the range of standard limit (Fig. 3). In similar studies, the mean concentration of fluoride in the Kerman [58] and Bushehr [9] provinces was a higher than recommended levels by World Health Organization (WHO) (1.5 mg/L) [72]. Overall, unlike warm weather provinces, the mean concentration of fluoride in cold and mild weather provinces subgroups (Fig. 3) was lower than standard range.

The lowest fluoride concentration in drinking water was related to Kermanshah and Gillan provinces, and the highest was associated with Kerman and Bushehr provinces (Fig. 3). Although in the many investigated provinces of Iran, levels of fluoride in drinking water were lower than range guideline, the adverse health effects due to a shortage of fluoride should also be taken into account. Also, the higher concentration of fluoride than guidelines or standard limits can induce adverse health effects including renal damages change of human chromosome structure, mental disability, and osteomalacia [72, 73].

According to previous studies, the exposure to drinking water content of high concentration of fluoride can increase the fluorosis prevalence [74, 75]. According to outcomes from Fluoride Scientific Association (FSA), a higher concentration than 0.7 mg/L can pose some adverse health effects such as fluorosis [76]. The incorporation of fluoride into drinking could increase the prevalence of specific diseases besides further economic costs [77]. In contrast with the low levels of fluoride in water resources of Iran, the high fluorosis prevalence was reported in different provinces of Iran [78]. Other resources of fluoride such as toothpaste, food products, and tea may contribute to the high prevalence of fluorosis in Iran. The observed low level of the fluoride in Iranian drinking water may be attributed to the shift in the water resource from groundwater to surface water resources [79], use physical or chemical defluoridation projects [80], or promotion of the operation of water treatment plants [81].

However, Iran can be considered as one of the 20 countries with high concentrations of fluoride in the soil and aquatic environments [82]. In this context, the high levels of fluoride in soil and water resources of Iran were reported by several investigations [9, 55, 58, 83]. Groundwater resources are mainly used for drinking water in the rural provinces of Iran which their quality depends on the geological structure [84, 85]. Also, recent studies have indicated that the mean levels of fluoride in drinking water in rural provinces is more than urban [86–88]. Therefore, well-developed plans should be approached to control and adjust the concentration of fluoride in drinking water resources in rural provinces [19]. Moreover, defluoridation and other recommended processes can be applied to remove or adjust fluoride in drinking water.

Non-carcinogenic Risk Assessment of Fluoride

Minimum and maximum total EDI for children was related to Kermanshah (0.01 mg/kg/day) and Kerman (0.058 mg/kg/day) provinces, and for adults was Kermanshah (0.0021 mg/kg/day) and Kerman (0.01 mg/kg/day) provinces, respectively (Table 3). Except for children in the Kerman province, EDI in the others investigated provinces of Iran was lower than Integrated Risk Information System (IRIS) standard limit (0.05 mg/kg/day) [49]. EDI in the children was significantly higher than adults (p value < 0.05). EDI from ingestion pathway was almost 1900 times more than a dermal pathway.

Minimum and maximum HQ for children was related to Kermanshah (0.172) and Kerman (0.964) provinces and for adults, Kermanshah (0.028) and Kerman (0.160) provinces, respectively (Table 3, Fig. 5). According to the previous investigation, the residents Zarand and Kouhbanan cities in the Kerman province suffer from moderate and severe fluorosis [89].

Overall, total HQ in the children and adults was 0.462 and 0.077, respectively (Table 3). The HQ in the children was 6 times higher than adults (p value < 0.05). Among the children and adults, children were at the highest HQ since they have the lowest BW. The HQ for children and adults was lower than 1 value. Therefore non-carcinogenic risk does not threaten drinking water residents' in Iran. However, there are non-carcinogenic risks due to drinking water content of fluoride in Kerman and Bushehr provinces because the HQ of fluoride were higher than other provinces (Fig. 5).

Limitations of Study

However, MCS was performed to decrease the limitations of the estimated risk; other limitations remained during health risk assessment of fluoride, especially regarding the sensitivity of used methods for analyses among the studies investigated. In this study, it is assumed that the fluoride in drinking water was relatively stable in various types of water samples including groundwater, surface water, and springs which may cause further limitations in the conducted risk assessment. Furthermore, amount of drinking water ingested can be different due to the effect of the weather conditions. Drinking water ingestion in warm weather regions is much higher from an area with cold weather regions. Consequently, fluoride intake in warm weather regions is higher than cold or mild weather regions [90]. In the current study, the health risk of drinking water content of fluoride via inhalation pathway was not estimated due to the limited data.

Conclusion

In this study, the levels of fluoride in drinking water resources in Iran was assessed using meta-analyzed approach and health risk was estimated via MCS method. A review of recent studies in Iran indicated that except in some provinces of southern Iran such as Kerman and Bushehr provinces, the levels of fluoride in drinking water was lower than national standard in many other provinces of Iran. Meta-analysis of data obtained in three weather provinces of Iran as subgroups indicated that the levels of fluoride in warm provinces of Iran was higher than other provinces; therefore, in these provinces, defluoridation processes of drinking water should be approached. The minimum and maximum HQ for children and adults were in the Kermanshah and Kerman provinces. Furthermore, children are at higher non-carcinogenic risks induced by fluoride in drinking water. Since HQ < 1 value, the health risk analysis indicated that the non-carcinogenic risk of fluoride in drinking water resources of Iran was acceptable. However, in some provinces of Iran, such as Kerman and Bushehr provinces, defluoridation projects should conduct to decrease the concentration of fluoride in the drinking water.

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Compliance with Ethical Standards

Competing Interests The authors declare that they have no conflict of interest.

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