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Investigating the relationship between water fluoride level and anthropometric parameters and blood pressure in adults of Zarand and Sarbisheh cities

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Research Article

Keywords: Fluoride, Drinking water, Body mass index, Blood pressure, Obesity

Posted Date: March 8th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-8917264/v1

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Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Environmental Geochemistry and Health on May 20th, 2026. See the published version at https://doi.org/10.1007/s10653-026-03229-1.

Abstract

Drinking water is the main source of fluoride, which prevents dental caries at recommended levels, while high intake has been linked to adverse outcomes, including noncommunicable diseases. This cross-sectional study was conducted in 2023 on 600 adults aged 18–75 years residing in urban and rural areas of Zarand and Sarbisheh, Iran. Demographic characteristics and determinants of fluoride exposure were collected using a structured questionnaire. Anthropometric measurements, including body mass index (BMI) and waist circumference (WC), as well as blood pressure parameters, including systolic blood pressure (BP) and diastolic blood pressure (DBP), were measured through physical examinations. Drinking water samples were obtained from 43 villages and 4 cities. Simple linear regression and generalized linear model–based tree (GLM-tree) analyses were applied to assess the associations while accounting for potential confounding and moderating factors. The mean age of participants was 40.27 ± 14.54 years, and 68.8% were female. The mean fluoride was 1.06 ± 0.45 mg/L in Zarand and 0.51 ± 0.18 mg/L in Sarbisheh. After adjustment for confounding variables, fluoride exposure at low to moderate levels (0.5–1.5 mg/L) was positively associated with BMI and negatively associated with DBP ($P < 0.05$). In contrast, high fluoride exposure (> 1.5 mg/L) showed a positive association with WC ($P < 0.001$). GLM-tree analysis showed that health, lifestyle, and water composition factors moderated the associations between fluoride exposure and anthropometric and blood pressure measures. Overall, the results suggest a possible association between drinking water fluoride levels within recommended standards and anthropometric indicators.

1. Introduction

Today, obesity is one of the most important health issues in the world, and due to its direct relationship with chronic diseases such as type 2 diabetes, high blood pressure, and cardiovascular diseases, it has attracted a lot of attention (1). High blood pressure, as one of the main causes of cardiovascular diseases and stroke, is the cause of death of more than 7.5 million people worldwide every year (2). This disease is related to heredity, diet, obesity, and exposure to environmental factors. Meanwhile, the quality of drinking water, especially the amount of fluoride in it, has been considered as one of the factors affecting health (3, 4).

Fluoride is one of the essential micronutrients for the health of animals and humans, which in small amounts plays an important role in protecting teeth and preventing caries (5, 6). However, exposure to high concentrations of fluoride can have adverse health effects. These effects include disruption of skeletal structure, increased risk of uterine and bladder cancers (7), genetic mutations, and birth defects. Fluoride can also affect growth and development and lead to changes in the weight and height of babies. The negative effects of this element on fertility, kidney and liver function, and the nervous and cardiovascular systems have also been reported (8, 9). Studies have shown that long-term fluoride exposure can be associated with increased blood pressure and the risk of cardiovascular diseases (10–12). This element also affects body weight and anthropometric parameters by disrupting lipid metabolism and increasing adipogenesis (13, 14).

Fluoride is one of the anions that can endanger human health in concentrations lower or higher than the standard. This issue has become one of the main challenges, especially in many parts of the world (15). Fluoride can enter the environment from natural and artificial sources. Natural sources include the dissolution of fluoride-bearing rocks and mineral soils, while man-made sources include industrial activities such as aluminum extraction, mining, ceramic production, bricks, and animal manure (16). Other sources of human exposure to high levels of fluoride include: the consumption of drinking water, tea, foods containing fluoride, supplements, and industrial pollution (15). This element is widely found in water, air, and soil and enters the human body through drinking water, breathing, or skin contact (17). However, drinking water is recognized as the main source of fluoride exposure (16, 18). The amount of fluoride in water sources usually depends on the type of rock and soil through which the water passes (19). Factors such as pH, alkalinity, and water hardness greatly affect the fluoride dissolution process (17, 18). In addition, increasing consumption of groundwater resources and mismanagement can reduce the quality and quantity of these resources and increase fluoride concentration (19). In areas with minerals containing high fluoride, the probability of high concentrations of this anion accumulating in drinking water is higher (20, 21). One of the basic factors in ensuring the health and growth of communities is access to high-quality drinking water. Continuous monitoring and supervision of drinking water quality is essential, especially in areas exposed to pollutants such as fluoride (21). In addition, investigating the relationship between water quality characteristics and the incidence of chronic and non-communicable diseases, such as obesity and cardiovascular diseases, can help improve drinking water standards and water resources management.

In general, it is always recommended to use models that handle more complexity and detail of the data (22). Simple linear regression results are presented with the assumption that there is a linear relationship between the variables and are not capable of nonlinear relationships. In this study, a GLMtree model was used to better examine the relationships. A GLMtree is a decision tree with GLM at its leaves (regardless of whether they are linear or nonlinear) (23). Therefore, the study aimed to investigate the relationship between drinking water fluoride at low, medium, and high levels with anthropometric indicators and blood pressure in adults.

2. Materials and methods

2.1. Study areas

Sarbisheh city, with an approximate area of 8,199 km², is one of the border cities of South Khorasan Province, located in eastern Iran. It lies about 65 km from Birjand, the capital of South Khorasan Province, and is situated between 59°32' and 59°58' east longitude and 32°15' to 32°51' north latitude. Sarbisheh has a moderate and dry climate, which shifts to a moderate and semi-arid climate in its highlands. Annual precipitation in the region ranges from 95 mm in dry years to 375 mm in wet years. The average annual temperature is 12.2°C, and the average annual precipitation is approximately 206 mm (24). In terms of drinking water supply, Sarbisheh relies entirely on underground water resources, which are accessed through wells, canals, and springs (25).

Zarand County, located in Kerman Province in southeastern Iran, spans approximately 11,521 Km^2. Geographically, it is situated between 56°34' E longitude and 30°49' N latitude, with an average elevation of 1,660 m above sea level (26, 27). The region is characterized by a semi-arid climate. Zarand experiences hot summers and relatively cool winters, with an average summer temperature of 37.8°C and a winter temperature of approximately 13°C. The annual rainfall in the area averages about 140 mm, highlighting its dry climate with limited precipitation. The county's drinking water primarily comes from underground sources, including wells, qanats, and springs. The region's proximity to coal mines significantly affects both the quality and quantity of its water resources (28).

2.2. Study population

The present study was conducted cross-sectionally in 2023 in Zarand and Sarbisheh cities. The study population consisted of 600 adults between the ages of 18 and 75 from these two cities. Random sampling was done from different regions of the cities so that 296 people from Zarand city and 304 people from Sarbisheh city were randomly selected from among the people referring to health centers. The criteria for entering the study included living in Sarbisheh and Zarand cities and being between 18 and 75 years old. Exclusion criteria included drug use in the last six months and non-cooperation in the implementation of the plan (8).

2.3. Questionnaire

A structured questionnaire was used to collect information. The questionnaire includes factors such as demographic information, physical activity, lifestyle, exposure to fluoride (foods containing fluoride, tea, toothpaste, and mouthwash), drinking water supply (distribution network, use of household water purifier), amount of water consumption in the day, and the history of chronic disease and drug use. Before completing the questionnaire, all participants signed the informed consent form and were informed about the details of the study (8). The collected information was kept strictly confidential and used only for scientific purposes.

2.4. Physical examinations

Physical examinations, including measurement of height, weight, waist circumference (WC), and blood pressure, were taken from the subjects. Physical examinations, including measurement of height, weight, waist circumference, systolic blood pressure (SBP), and diastolic blood pressure (DBP), were taken from the subjects. The height of the subjects was measured in a standing position using a meter. In this position, three parts of the body (back, buttocks, and heels) must be completely tangential to the wall for an accurate measurement. Subjects' weight was measured using a digital scale with high accuracy while subjects were wearing the least possible clothes and without shoes. WC was measured using a tape measure from the hollowest part of the waist (between the chest and pelvis). Body mass index (BMI) was calculated based on the formula of weight (Kg) divided by height to the power of two (m). Blood pressure was measured in a sitting position and after at least 5 minutes of rest, with a digital sphygmomanometer from the right hand (29).

2.5. Water fluoride

The information about the amount of fluoride in water in 2023 in Zarand City was obtained from the data measured by the health center of Zarand City, and for Sarbisheh City, from the water and wastewater company of this city. Information on drinking water sampling at 51 points within the water distribution networks of Zarand (22 villages and one city) and Sarbisheh (25 villages and three cities) was collected. Water fluoride levels in the studied areas were categorized into three groups: low (< 0.5 mg/L), moderate (0.5–1.5 mg/L), and high (> 1.5 mg/L) (9). In addition, several chemical parameters of water, including EC (µmhos/cm), TDS (mg/L), SO_4^{2-} (mg/L), NO_3^- (mg/L), total hardness (mg/L as $CaCO_3$), HCO_3^- (mg/L), and Cl^- (mg/L), were measured. Their average values at the sampling points were compared with the limits set by the Iran National Standards Organization (INSO, 6th Revision, 2025; Standard No. 1053) and the World Health Organization (WHO, 2022) guidelines.

2.6. Statistical analysis

Data analysis was performed using R software (version 4.3.3). The data were analyzed in two descriptive and analytical categories. For statistical analysis, independent t-tests, correlation, and linear regression were used, considering the significance level of 5%. Finally, the regression tree was used to examine the relationship between water fluoride and anthropometric parameters and blood pressure, in terms of demographic variables. A GLMtree is a decision tree with GLM at its leaves (regardless of whether they are linear or nonlinear). A particular

stochastic expectation maximization algorithm is used to draw a few good trees, which are then assessed via the user's criterion of choice among BIC / AIC / test set Gini (23). For the regression tree model, the “partykit” package (version 1.2–20) and the “glmtree” command were used.

3. Results

Table 1 shows the average concentrations of selected chemical parameters in drinking water samples from Zarand and Sarbisheh, compared to the limits established by the Iran National Standards Organization (INSO, 6th Revision, 2025; Standard No. 1053) and the World Health Organization (WHO, 2022) guidelines. In Zarand city, the mean ± SD concentrations were as follows: TDS 1131.28 ± 377.93 mg/L, SO_4^{2-} 428.04 ± 107.56 mg/L, total hardness as $CaCO_3$, 686.09 ± 262.08 mg/L, and Cl^- 308.31 ± 187.79 mg/L, all of which exceeded the maximum allowable limits set by both INSO and WHO. In Sarbisheh city, the average concentrations of TDS 1101.25 ± 325.17 mg/L, SO_4^{2-} 310.71 ± 111.38 mg/L, and Cl^- 273.80 ± 113.05 mg/L also surpassed the corresponding standard limits. Additionally, the average total hardness in Sarbisheh, 274.38 mg/L as $CaCO_3$, was above the WHO’s recommended limit but remained within the INSO standard.

Table 1
The average concentration of water chemical parameters in the cities of Zarand and Sarbisheh.

Variables	Zarand (n = 23)			Sarbisheh (n = 28)			Standards	
	Min	Max	Mean ± SD	Min	Max	Mean ± SD	Iranian (2025)	WHO (2022)
EC (µmhos/cm)	971	4120	2264.96 ± 753.48	715	3400	1972.57 ± 557.18	-	-
NO_3^- (mg/L)	1.20	6.20	1.42 ± 2.83	1.70	44.40	22.36 ± 9.73	50	50
Fluoride (mg/L)	0.40	2.39	1.06 ± 0.45	0.26	1.24	0.51 ± 0.18	1.5	1.5
HCO_3^- (mg/L)	110	350	180.00 ± 54.41	44	488	148.71 ± 102.89	-	-

The average water fluoride concentration in Zarand city is 1.06 mg/L, which is significantly higher than the average level in Sarbisheh city at 0.51 mg/L ($p < 0.001$). Furthermore, the data indicate that the average fluoride levels in both cities comply with the guidelines set by the Iran National Standards Organization (INSO, 6th Revision, 2025; Standard No. 1053) and the World Health Organization (WHO, 2022), which establish a maximum allowable limit of 1.5 mg/L. Although the fluoride concentration in Zarand is higher than in Sarbisheh, it is still 0.44 mg/L lower than the INSO and WHO standards ($p < 0.001$). The average fluoride concentration in Sarbisheh is lower than the INSO and WHO limits by a difference of 0.99 mg/L ($p < 0.001$) **(**Fig. 1**).**

The results (Table 2) showed that the average age of the study population was 40.27 ± 14.54 years. The results showed that 68.8% of the participants were female, and 30.1% of the population had a university education. 54.2% of the participants were unemployed, 50.8% had a low income, and 85% were not smokers. 38.7% of the participants reported engaging in physical activity less than 3 days a week. The results of the averages related to the physical characteristics of the participants showed that WC was 83.32 ± 19.31 cm, BMI was 24.92 ± 13.89, SBP was 110.86 ± 13.89 mmHg, and DBP was 71.50 ± 10.17 mmHg.

Table 2. Participant characteristics by water fluoride levels					
Variables	**Fluoride (Level)**				**p-value**
	Total	**Low**	**Moderate**	**High**	
N (%)					
Sex					
Female	413 (68.8)	139 (33.7)	235 (56.9)	39 (9.4)	**0.002**
Male	187 (31.2)	89 (47.6)	90 (48.1)	8 (4.3)	
Education					
Academic	420 (70.0)	166 (39.5)	213 (50.7)	41 (9.8)	**0.005**
Non-academic	180 (30.0)	62 (34.4)	112 (62.2)	6 (3.3)	
Job					
Yes	275 (45.8)	120 (43.6)	145 (52.7)	10 (3.6)	**< 0.001**
No	325 (54.2)	108 (33.2)	180 (55.4)	37 (11.4)	
Income[a]					
Low	305 (50.8)	120 (39.3)	166 (54.4)	19 (6.2)	0.258
Moderate	248 (41.3)	92 (37.0)	130 (52.4)	26 (10.5)	
High	47 (7.8)	16 (34.0)	29 (61.7)	2 (4.3)	
Smoking					
Yes	90 (15.0)	21 (23.3)	60 (66.7)	9 (10.0)	**0.008**
No	510 (85.0)	207 (40.6)	256 (52.0)	38 (7.5)	
Body activity (day)					
None	105 (17.5)	37 (35.2)	61 (58.1)	7 (6.7)	0.147
< 3	232 (38.7)	76 (32.8)	133 (57.3)	23 (9.9)	
3–7	161 (26.8)	75 (46.6)	77 (47.8)	9 (5.6)	
Every day	102 (17.0)	40 (39.2)	54 (52.9)	8 (7.8)	
	Mean ± SD				
Age (year)	40.27 ± 14.54	40.53 ± 14.20	39.67 ± 15.01	43.21 ± 12.71	0.280
WC (cm)	83.32 ± 19.31	81.25 ± 18.09	83.66 ± 20.53	91.00 ± 13.72	**0.006***
BMI	24.92 ± 13.89	24.36 ± 4.63	25.19 ± 4.99	25.75 ± 5.14	0.068
SBP (mmHg)	110.86 ± 13.89	110.86 ± 12.95	110.63 ± 13.89	112.39 ± 17.99	0.719
DBP (mmHg)	71.50 ± 10.17	70.88 ± 9.21	71.74 ± 10.70	72.85 ± 10.78	0.398
a. Low: ≤192$, Moderate: 192–384, and High: ≥384					b.

In Table 3, the prevalence of chronic diseases among the participants is shown based on water fluoride levels (low, moderate, and high). The results indicated that 4.3% had a history of cardiovascular diseases, and 14.5% were on antihypertensive medications. Additionally, 38.7% engaged in physical activity fewer than three days per week. The results show that 17.2% of participants had a history of high blood pressure, 31.9% of people living in areas with high average water fluoride concentrations (0.5 to 1.5 mg/L) had a history of hypertension, while this percentage was about 15–16% in areas with low or moderate average water fluoride concentrations (p-value = 0.019).

Table 3
Chronic disease status of the participants based on water fluoride concentration

Diseases	Fluoride (Level)				p-value
	Total	Low	Moderate	High	
	N (%)				
Hypertension					
Yes	103(17.2)	35(15.4)	53(16.3)	15(**31.9**)	**0.019**
No	497(82.8)	193(84.6)	272(83.7)	32(68.1)	
Cardiovascular					
Yes	26(4.3)	9(3.9)	13(4.0)	4(8.5)	0.342
No	574(95.7)	219(96.1)	312(96.0)	43(91.5)	
Diabetes					
Yes	40(6.7)	18(7.0)	21(6.5)	3(6.4)	0.964
No	560(93.3)	212(93.0)	304(93.5)	44(93.6)	
Kidney					
Yes	26(4.3)	14(6.1)	11(3.4)	1(2.1)	0.217
No	574(95.7)	214(93.9)	314(96.6)	45(97.9)	

Figure 2 shows the characteristics of the parameters influencing fluoride exposure among the participants. The results of the study examined the prevalence of dietary, behavioral, and environmental factors associated with fluoride exposure among study participants, indicating that individuals were exposed to varying levels of potential fluoride sources. Among food sources, fish, spinach, and soy consumption were relatively common, with 49% of participants reporting monthly fish consumption and 40.2% monthly soy consumption. For spinach, 47.7% reported no consumption. In terms of daily habits, more than half of the participants (91.2%) did not use mouthwash, and almost half (56.7%) brushed their teeth daily. In terms of water consumption, 38% of participants drank between 3 and 5 glasses of water per day. Also, in terms of daily tea consumption, only 8% of the study population did not drink tea, and the rest of the people drank at least one cup of tea per day. Regarding the type of water consumed, 58.7% of people used a home water purifier, and only 41.3% used tap water only. Also, the use of nutritional supplements was significant, with only 12.7% of participants taking zinc supplements and 16.7% taking calcium supplements.

Table 4 shows the relationship between anthropometric indices and blood pressure and water fluoride levels, categorized as low/moderate and high, analyzed using three models: Crude, adjusted model 1, and model 2. In model 1, the adjusted parameters include age, gender, educational level, exposure to cigarette smoke, and physical activity. In model 2, the adjusted parameters include fluoride levels, history of hypertension, cardiovascular disease, diabetes, and kidney problems. The results showed that the fluoride concentration in the water of Sarbisheh city did not exceed the upper limit in any of the sampled areas. The results showed that in participants consuming water with low/moderate fluoride concentrations (0.5-1.5 mg/L), for each one-unit increase in water fluoride, BMI increased by 0.83 units in the crude model, 0.89 units in Model 1, and 0.81 units in Model 2, all with statistical significance (p-value<0.05). The results showed that in participants who consume water with high fluoride content (>1.5 mg/L), for each one-unit increase in water fluoride, WC increased by 9.74 units in the crude model, 9.61 units in model 1, and 8.22 units in model 2, all with statistical significance (p-value<0.001). The results showed no significant relationship between diastolic DBP and SBP in the investigated models with water fluoride. However, in Sarbisheh, among individuals who consume water with low/moderate fluoride content (0.5-1.5 mg/L), for each one-unit increase in water fluoride, DBP decreased by 4.88 units (p-value = 0.044).

Table 4. Relationship between anthropometric indices, blood pressure, and fluoride levels in crude and adjusted models

Models	Floraide (mg/L)	BMI		WC (cm)		SBP (mmHg)		DBP (mmHg)	
		β(SE)	p-value*	β(SE)	p-value*	β(SE)	p-value*	β(SE)	p-value*
Crude	High	1.39(0.78)	0.074	9.74(3.06)	0.001*	1.53(2.22)	0.491	1.96(1.62)	0.227
	Low/ Moderate	0.83(0.41)	0.048*	2.41(1.65)	0.145	-0.23(1.19)	0.846	0.86(0.88)	0.329
Model 1	High	1.17(0.77)	0.129	9.61(3.03)	0.002*	1.89(2.14)	0.378	2.04(1.63)	0.211
	Low/ Moderate	0.89(0.41)	0.034*	3.00(1.63)	0.067	0.49(1.16)	0.670	1.02(0.88)	0.250
Model 2	High	1.09(0.77)	0.158	8.22(3.04)	0.007*	-1.21(1.99)	0.544	0.87(1.56)	0.574
	Low/ Moderate	0.81(0.40)	0.049*	2.27(1.63)	0.163	-0.34(1.06)	0.751	0.89(0.83)	0.284
Zarand	High	-1.00(1.23)	0.418	0.24(4.79)	0.960	2.93(3.71)	0.429	-3.71(2.81)	0.187
	Low/ Moderate	-1.12(1.06)	0.287	-5.89(4.11)	0.152	0.23(3.18)	0.941	-4.88(2.42)	0.044*
Sarbishe	High	-	-	-	-	-	-	-	-
	Low/ Moderate	-0.04(0.60)	0.949	0.30(2.42)	0.900	2.09(1.65)	0.205	1.63(1.13)	0.149

*Simple linear regression: Dependent variables: BMI: Body mass index, WC: Waist circumference, SBP: Systolic blood pressure, and DBP: Diastolic blood pressure

[a]Independent variable: fluoride level (reference: low fluoride)

[b]Independent variables in Model 1: fluoride, adjusted for age, gender, education, smoking, and body activity

[c]Independent variables in Model 2: fluoride, along with a history of hypertension, cardiovascular disease, diabetes, and kidney problems

In Fig. 3, all models of water fluoride association and anthropometric parameters, blood pressure were fitted by adjusting for demographic factors, and only the results of the models that were significant are reported. The association between water fluoride and BMI was significant only in participants without diabetes ($\beta_{\text{Fluoride}} = 0.95, \text{p} = 0.017$), but not in diabetic participants. The association between water fluoride and diabetes was also significant only in participants with low income ($\beta_{\text{Fluoride}} = 1.72, \text{p} = 0.004$). The association between water fluoride and waist circumference was significant in participants who consumed calcium ($\beta_{\text{Fluoride}} = 12.34, \text{p} = 0.001$) and participants who did not consume it ($\beta_{\text{Fluoride}} = 3.78, \text{p} = 0.026$), but the intensity of the association was greater in participants who did not consume calcium. In participants over 46 years of age, DBP was also high with high water fluoride ($\beta_{\text{Fluoride}} = 5.83, \text{p} < 0.001$).

4. Discussion

The present study investigated the relationship between water fluoride levels (low, moderate, high), anthropometric indicators, and blood pressure in the adult population. The average fluoride concentrations in the water of Zarand and Sarbisheh cities were 1.06 mg/L and 0.51 mg/L, respectively. Both values are within the maximum allowable limits set by the Iranian National Standards Organization (INSO, 6th Revision, 2025; Standard No. 1053) and align with the World Health Organization (WHO, 2022) guideline of 1.5 mg/L. The primary water source analyzed in this study was groundwater, which typically contains higher fluoride levels than other sources. This is particularly evident in regions with coal mines or where rock weathering contributes to increased fluoride concentrations in the water (30). One of the primary reasons for the elevated fluoride levels in Zarand's water is the presence of coal mines in the area. When water flows through these regions, it interacts with geological formations, leading to increased fluoride concentrations. The weathering of clay, sand, and silt rocks found in coal, lime, scheelite, and dolomite layers facilitates the chemical process where hydroxide ions are replaced with fluoride ions, contributing to the higher fluoride content in the water (31). Therefore, it can be said that due to the high initial fluoride level in Zarand city's water (32), as well as the high hardness of the city's water (33), and sometimes some factors such as late replacement of home water purifier filters, despite the use of home water purifiers in 58.7% of the participants in this study, the fluoride level was still higher than the permissible limit.

Fluoride intake is not solely derived from drinking water but also occurs through other sources such as tea consumption, certain foods (e.g., fish, vegetables like cabbage and spinach, and peanuts), as well as the use of fluoride-containing products like toothpaste and mouthwash (13, 15). In this study, data on exposure to other fluoride-containing sources were collected from participants using a questionnaire. The findings

revealed that most participants brushed their teeth daily and included tea, soybeans, and fish in their diets, all of which could contribute to increased fluoride exposure.

The effects of fluoride exposure, as well as dental and skeletal fluorosis, have been extensively studied (34, 35). However, limited research has explored the association between fluoride levels and anthropometric parameters or blood pressure. In this study, a significant negative correlation was observed between the consumption of water with low to moderate fluoride levels and DBP. Koh et al.'s study also demonstrated a significant negative association between drinking water fluoride levels and SBP after adjusting for variables such as age, sex, race, and income (36). Similarly, the findings of Guo et al.'s study supported the negative association between water fluoride concentration and SBP (37). Furthermore, the study by Pérez-Galicia et al. reported that exposure to high levels of fluoride was associated with an increase in left ventricular mass (LVM), with variations observed between genders (38). Conversely, several studies have reported a positive association between water fluoride concentration and elevated blood pressure, suggesting that fluoride exposure might contribute to hypertension in certain populations (8, 39). Early experimental animal studies have demonstrated that high levels of fluoride exposure can cause alterations in the liver's lipid membrane and disrupt thyroid hormone levels in rats. Additionally, these studies suggest that fluoride exposure may increase inflammatory cytokine responses in the aorta of rabbits, as well as enhance cardiotoxicity and lipid peroxidation (40). The mechanism by which fluoride affects overweight and obesity is not yet fully understood. However, studies in rodents have shown that fluoride can disrupt lipid metabolism and adipogenesis, with exposure in mice leading to an increase in blood lipids. Additionally, fluoride's effects on the liver and endocrine glands, such as the thyroid and parathyroid, can result in metabolic disturbances and weight gain (13).

However, it is important to note that the results of the present study revealed a direct relationship between anthropometric markers and water fluoride levels. Additionally, the study indicated that factors such as age, smoking, and education level can moderate the effects of fluoride exposure. In contrast, most studies conducted on adult populations have not observed an association between fluoride exposure and anthropometric indices. For instance, Yousefı et al.'s study found no significant relationship between fluoride levels in drinking water and BMI or WC indices (8). Additionally, in a similar study conducted by Mohammadi et al., no significant relationship was observed between the fluoride concentration in drinking water and anthropometric parameters (5). In contrast, studies conducted on children and adolescents, which not only examined fluoride concentrations in drinking water but also assessed fluoride levels in biomarkers such as urine and blood, have demonstrated a positive relationship between fluoride levels in water and various biological and anthropometric markers. Specifically, Liu et al. found that as the fluoride concentration in water increased in areas with low to moderate fluoride levels, the BMI Z-score of children and adolescents also increased. The study further indicated that the father's gender and education level could influence this relationship (13). The conflicting results observed across various studies may be attributed to differences in gender, age, and race distributions among the study populations. Additionally, these inconsistencies could stem from variations in sample size, levels of fluoride exposure, and inherent differences in population susceptibilities and vulnerabilities. Long-term cumulative effects of fluoride exposure may also contribute to these disparities in findings. These factors suggest that a combination of biological, environmental, and methodological variables may influence the observed outcomes in different studies (41). These findings suggest that fluoride may contribute to the development of obesity and related metabolic disorders. However, further research is required to fully understand the underlying mechanisms.

This study provides a comprehensive analysis of fluoride consumption in urban and rural areas with varying fluoride levels (low, moderate, and high), comparing the findings to Iran's national standards and WHO recommendations, which strengthens the reliability of the results. Using a large adult sample and a structured questionnaire ensured sufficient statistical power for effect detection, enhancing the accuracy and validity of the findings. Several confounding factors were considered, including demographics, chronic disease history, fluoride exposure from different sources, and physical activity, improving the study's reliability. Advanced statistical methods were applied to control for confounding, allowing for a thorough exploration of variable relationships. The study's inclusion of both urban and rural areas with diverse geographical characteristics increased the generalizability of the findings and provided a more holistic understanding of environmental factors influencing fluoride exposure and health outcomes.

The limitations of this study include the lack of biomarker measurements, such as fluoride levels in blood and urine, which hindered the precise estimation of fluoride exposure. Additionally, only fluoride levels in water were measured, and the potential effects of other environmental pollutants were not considered. Additionally, the reliance on self-reported data may have introduced recall bias. Furthermore, geographical and cultural differences across regions could have influenced the results, and the limited sampling to specific areas makes it difficult to generalize the findings to broader populations. The study was cross-sectional, which limits the ability to fully investigate causal relationships. Longitudinal studies are required to confirm and better understand the temporal dynamics of these findings.

The results of the decision tree models indicate the complexity and heterogeneity of the association between fluoride concentration in drinking water and anthropometric indices and blood pressure in the adult population. These models were able to reveal different and meaningful patterns of association that were hidden in the overall analyses by separating participants based on demographic, behavioral, and environmental variables. Specifically, in the BMI model, diabetes status was identified as the main differentiating factor, with an inverse relationship with fluoride in diabetics and a positive relationship with fluoride in non-diabetics. The determining role of income level also

reflects the interaction of socioeconomic factors in this relationship. In the WC model, calcium supplementation and physical activity were influential factors, indicating that fluoride can be associated with increased WC in the absence of calcium supplementation or in the presence of regular physical activity. Overall, the decision tree results indicate that the effect of fluoride on health indicators is not uniform and linear, but can be different and sometimes contradictory depending on individual and environmental characteristics. These findings emphasize the necessity of considering individual and contextual differences in environmental and epidemiological studies and justify the use of multivariate analysis approaches such as decision tree models.

5. Conclusion

The results of the present study showed that increased fluoride levels in drinking water, even within the limits recommended by the Iranian National Standard and the WHO, are associated with changes in BMI, WC, and DBP in adults. In addition to exposure intensity, the effects of fluoride are significantly influenced by physiological contexts, lifestyle, and water chemistry. The use of decision tree models (GLM-Tree) in this study, unlike traditional models with linear moderators, allowed the identification of complex interactions and heterogeneity of effects and was particularly effective in distinguishing high-risk subgroups. Given the cross-sectional nature of the study design, no definitive conclusions can be drawn about causal relationships; therefore, future studies with longitudinal and experimental designs are recommended to more accurately examine the effects of fluoride on anthropometric indices and blood pressure. Also, examining other routes of fluoride exposure, such as tea consumption, fluoride-rich foods, hygiene products (such as toothpaste), and measuring fluoride levels in biomarkers, could play an important role in completing future assessments.

Declarations

Acknowledgements

The authors would like to gratefully acknowledge the research deputy of Shahid Sadoughi University of Medical Sciences, Yazd, and also Zarand Health Center and South Okhrasan Water and Wastewater Company.

Ethical approval

The present study has the code of ethics IR.SSU.SPH.REC.1402.197 of Shahid Sadoughi University of Medical Sciences, Yazd.

Consent to participate

All procedures performed in studies involving human participants were in accordance with institutional committee ethical standards. This study has been approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd.

Data availability statement

The supporting data are available from the corresponding authors upon reasonable request.

Authors contributions

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by **A.D, H.A, A.M, M.E, S.M, and H.F.** The first draft of the manuscript was written by **H.N** and all authors commented on the previous versions of the manuscript. All authors read and approved the final manuscript. Conceptualization was performed by **A.D, H.A, A.M, M.E, S.M, H.F**; Methodology by **A.D, H.A, A.M, M.E, S.M, H.F**; Formal analysis and investigation by **M.E, H.F, H.N, A.D**; Writing-original draft preparation by **H.A., M.E, S.M,** Writing-review and editing by **A.D, H.A, A.M, M.E, S.M, H.F.**

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Figures

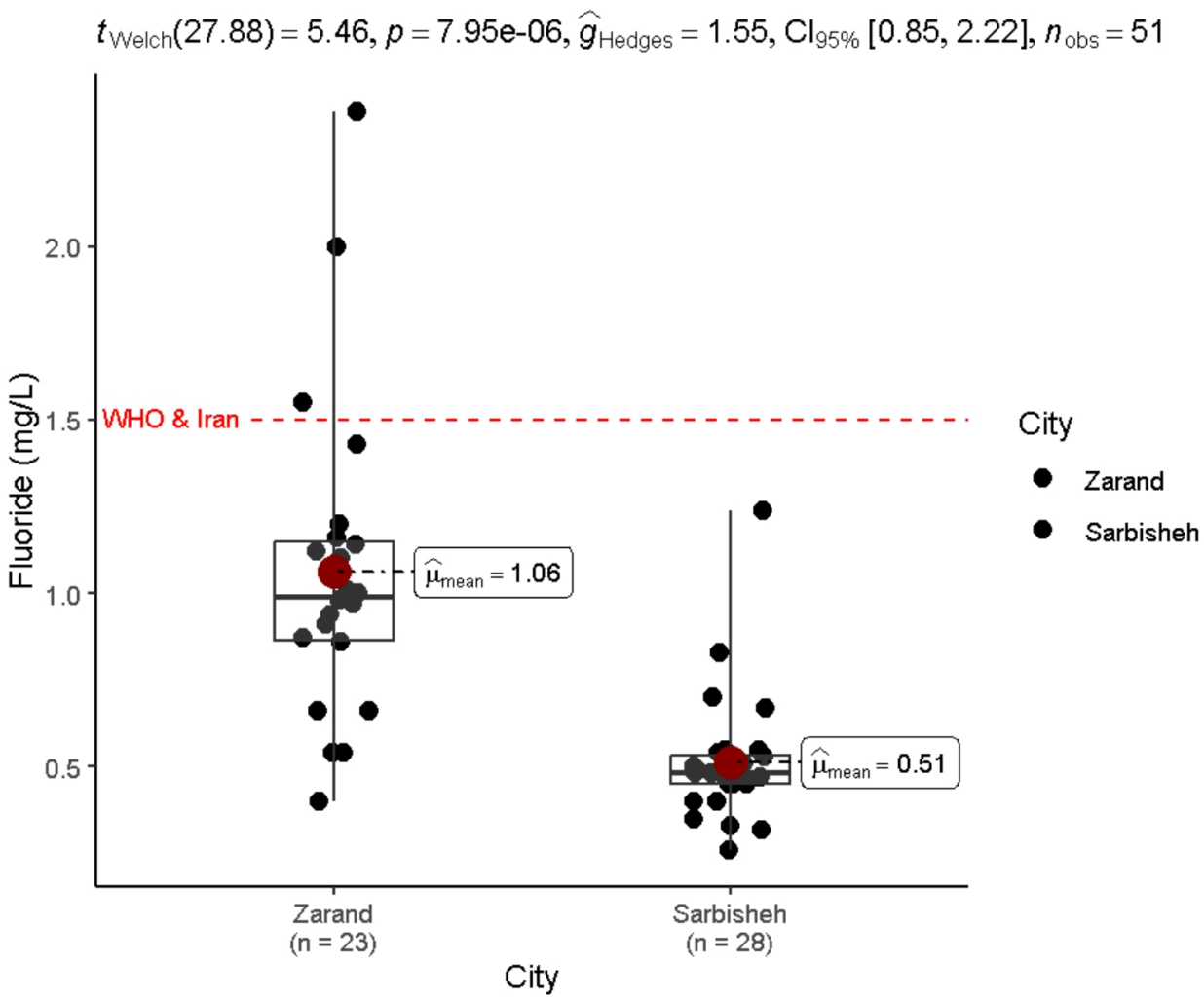


Figure 1

Comparison of Average Water Fluoride Levels in Zarand and Sarbisheh Cities

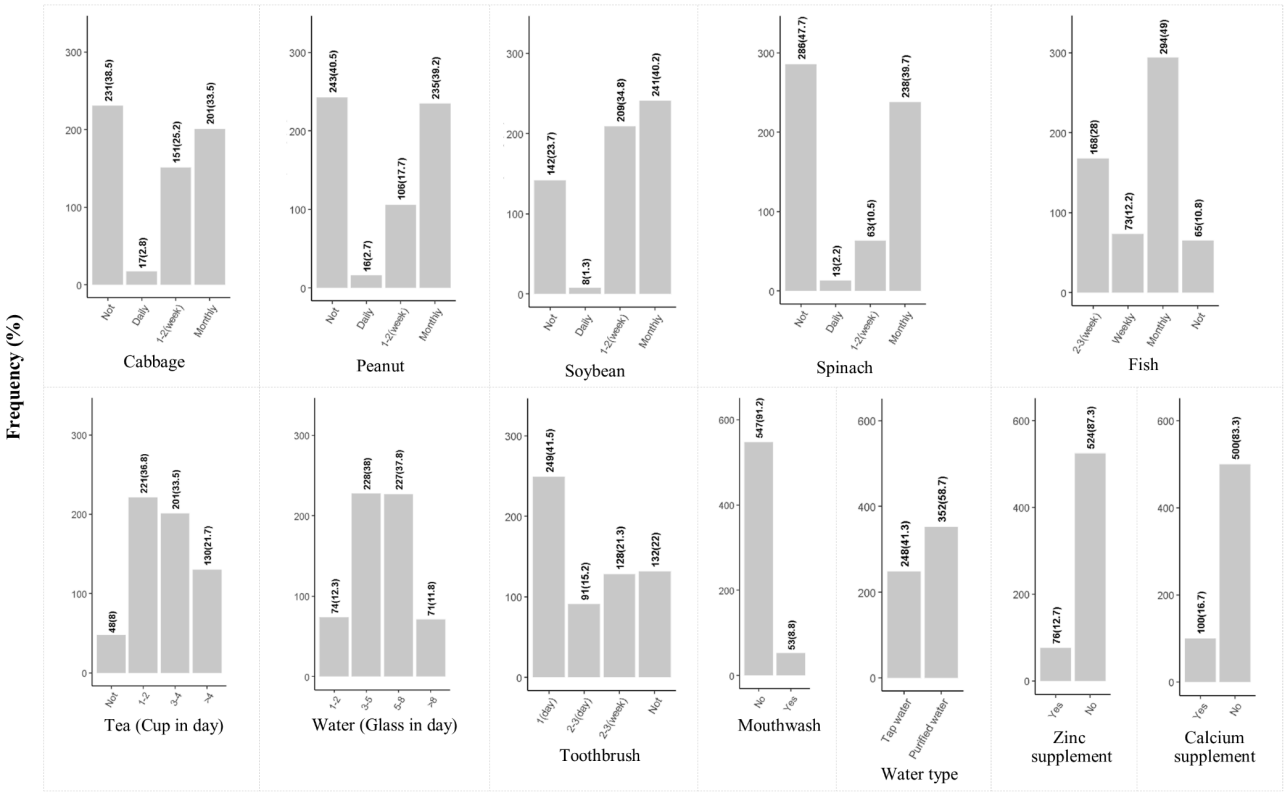


Figure 2

Factors influencing fluoride exposure among study participants

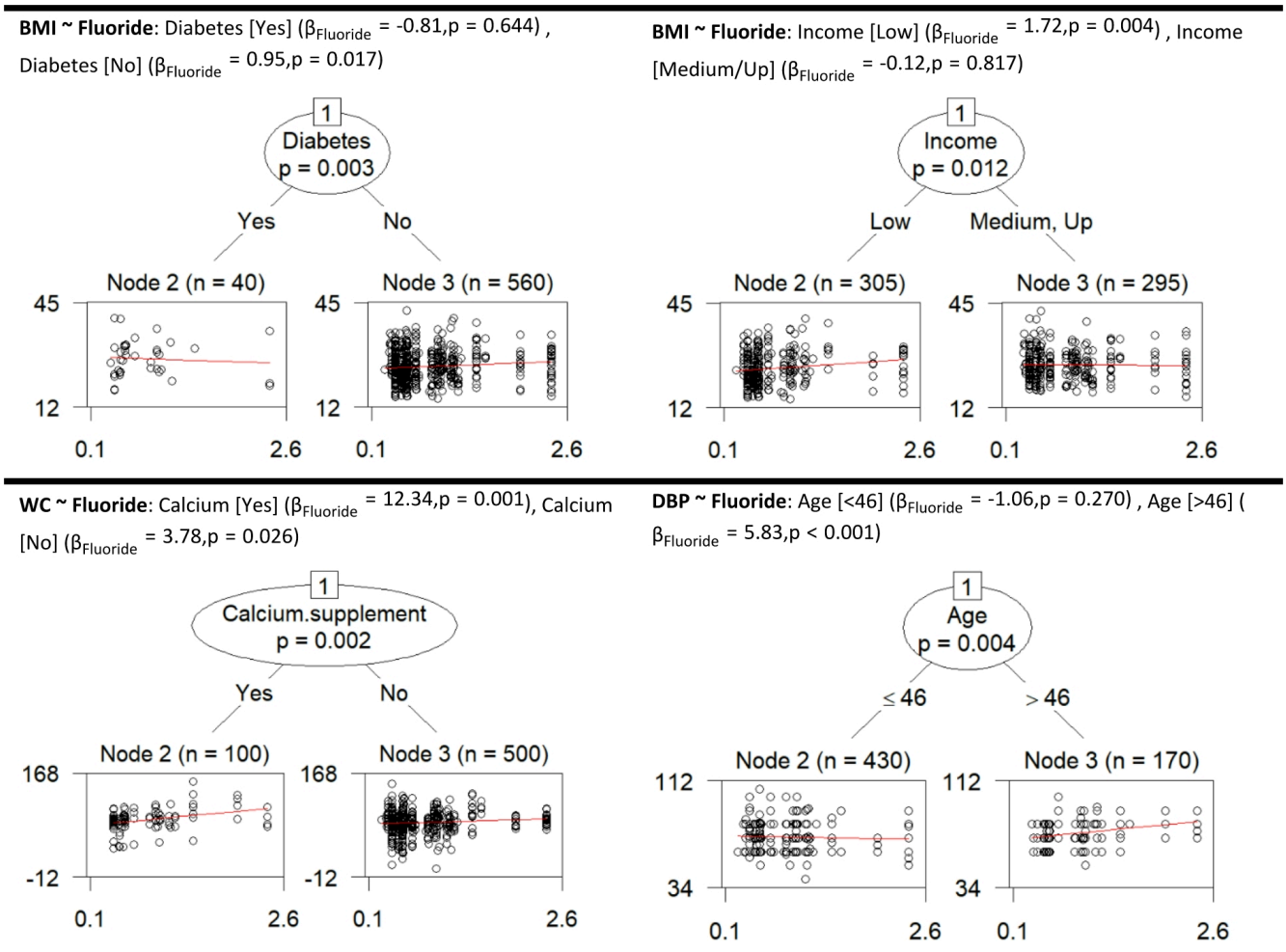


Figure 3

Relationship between anthropometric parameters, blood pressure and water fluoride by adjustments for confounding variables.