

HYPERTENSION AND FLUORIDE IN DRINKING WATER: CASE STUDY FROM WEST AZERBAIJAN, IRAN

Mina Aghaei,^a Sima Karimzade,^b Mehdi Yaseri,^a Hasan Khorsandi,^b Ebrahim Zolfi,^c
Amir Hossein Mahvi,^{a,d,*}

Tehran and Urmia, Iran

SUMMARY: Hypertension is a major public health challenge in Iran and its detection and control are vitally important to reduce the risk of myocardial infarction and cerebrovascular accident. Fluoride can be a risk factor for hypertension and, in this cross-sectional study, the effects on the prevalence of hypertension of high (3.94 mg F/L) and low (0.25 mg F/L) fluoride exposure via drinking water were investigated in two areas in West Azerbaijan province, Iran. The number of persons studied, aged 20–65 yr, was 897 (male: 453; female: 444) in the high fluoride area and 1981 (male: 945; female: 1036) in the low fluoride area. Cases were excluded who had aetiological factors known to contribute to hypertension, such as smoking, age >65 yr, a family history of hypertension, lack of mobility, cardiovascular disease, and obesity. In the high fluoride area, compared to the low fluoride area, hypertension, without known aetiological factors, was increased ($p < 0.05$) in females aged 50–59 yr and decreased ($p < 0.05$) in the combined group of males and females aged 40–49 yr. Because of the varying results of the studies in this topic, further research is recommended.

Keywords: Drinking water; Fluoride; Hypertension; West Azerbaijan; Iran.

INTRODUCTION

Fluorine, the most electronegative of all elements, has not only remarkable chemical qualities but also physiological properties of importance for human health.¹ Human exposure to the fluoride ion (F) can occur through air via inhalation, dermal contact, and ingestion of soil, food, dental products, and drinking water.² Drinking water is usually the main pathway for F to enter the human body.^{3–5} Although the topical use of F has been seen to have a beneficial cariostatic effect, the systemic ingestion of F may cause a broad range of adverse health effects ranging from damage to teeth and bones, to impacts on the soft tissues, and to death.²

Hypertension, diagnosed when the blood pressure is $\geq 140/90$ mm Hg most of the time, is one of the most common cardiovascular diseases and an important identifiable risk factor for atherosclerosis that can increase the risk of cerebrovascular accident (stroke), myocardial infarction (heart attack), heart failure, aortic aneurysms, and peripheral arterial disease.⁶ A high level of F in drinking water can be harmful with accumulation over time in both the hard and soft tissues including the cardiovascular system.^{7,8} Although F intoxication has been reported to cause hypertension, chronic ischemic heart disease, and an altered

^aSchool of Public Health, Tehran University of Medical Sciences, Tehran, Iran; ^bSchool of Public Health, Urmia University of Medical Sciences, Urmia, Iran; ^cDepartment of Environmental Health Engineering, Urmia University of Medical Sciences, Urmia, Iran; ^dCenter for Solid Waste Research, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran; *For correspondence: Assistant Professor Amir Hossein Mahvi, Center for Solid Waste Research, Institute for Environmental Research, Tehran University of Medical Sciences, Tehran, Iran; E-mail: ahmahvi@yahoo.com.

heart rate, there is no clear evidence of an increased prevalence of hypertension associated with exposure to F in water, food, and air.^{5,6,9-18}

The mechanism of F toxicity effect on the cardiovascular system is complex and not well understood. Although many studies have been carried out on F in Iran, few have been epidemiological studies on the relationship between human F exposure and the prevalence of hypertension.¹⁹⁻²⁷ Thus, the main objective of the present research was to examine the relationship between the prevalence of hypertension in people who exposed to high and low levels of F in drinking water in West Azerbaijan province, in northwest Iran.

MATERIAL AND METHODS

Study areas: Two study areas was selected in West Azerbaijan Province, in the northwest part of Iran, with almost the same socioeconomic status and dietary habits but different natural concentrations of F in drinking water (Figure 1).²⁸

Determination of the water fluoride levels: The data on the drinking water F concentration in the cities being studied were obtained from the Water and Wastewater Company of West Azerbaijan. Potable water samples were also collected from both of the areas and the F levels in the water sample determined by the SPADNS (Sulfo Phenyl Azo Dihydroxy Naphthalene Disulfonic Acid) colorimetric method, in the chemistry laboratory, in the Department of Environmental Health Engineering, the Urmia University of Medical Sciences.

Data on prevalence of hypertension: The data on the prevalence of hypertension, people with a systolic pressure of ≥ 140 mm Hg and a diastolic pressure of ≥ 90 mm Hg, were derived from the health records of the areas being investigated. Based on the health records, 78 people (24 males, 54 females; mean age 60.9 ± 11.5 yr) in the high F area and 162 people (55 males, 107 females; mean age 59.3 ± 14.3 yr) in the low F area were identified as having hypertension. Cases were excluded who had aetiological factors known to contribute to hypertension, such as smoking, age > 65 yr, a family history of hypertension, lack of mobility, cardiovascular disease, and obesity, based on the interview history the and monthly progress reports in the documentation of the health centers. The major source of exposure of the residents in both study areas to F was through drinking water from wells and springs.

Statistical analysis: The SPSS (version 22.0, IBM Co., Chicago, IL) was used to analyze the data. To compare the proportion with hypertension in the two areas, in each of five age groups, we used the Chi-Square or Fisher exact test. To compare the total proportion with hypertension in the two areas, adjusted for the age and sex, we used logistic regression analysis.

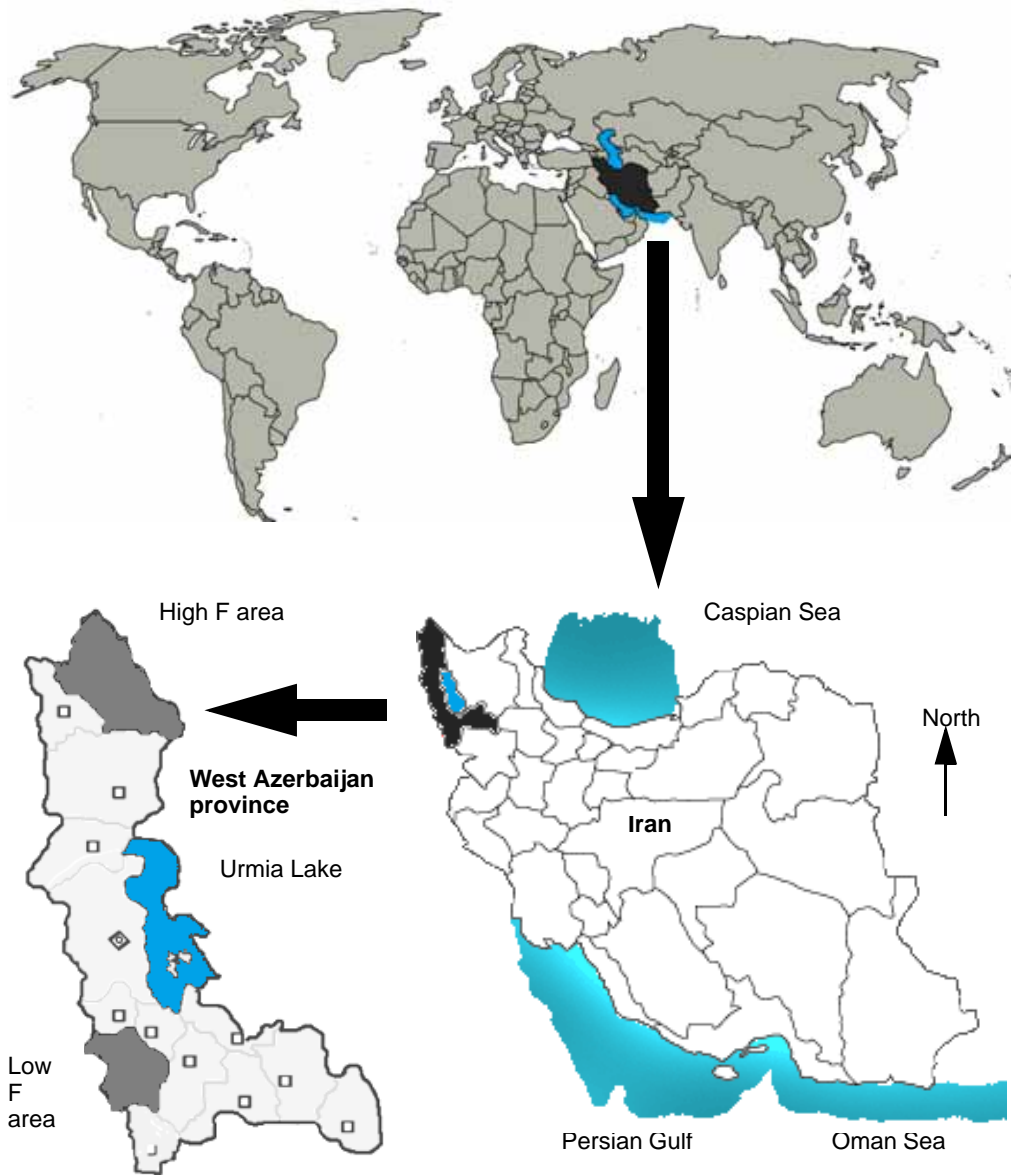


Figure 1. Map of the high and low fluoride areas that were studied in West Azerbaijan province, Iran.

RESULTS

The F level in the high F area of ≈ 3.94 mg/L was higher than the “desirable” upper limit guideline of 1.5 mg/L set by the World Health Organization in 1984 and reaffirmed in 1993, while that of the low F area of ≈ 0.25 mg/L was less than the WHO upper limit guideline (Table 1).²⁹

Table 1. Fluoride level in drinking water (mg/L) in the two studied areas

Area	Fluoride concentration (mg/L)	Total number with hypertension in the region
High fluoride region	≈3.94	78
Low fluoride region	≈0.25	162

The proportion of cases of hypertension with known aetiological factors was 63% (102/162) in the low F area and 58% (45/78) the high F area, leaving the proportion with hypertension without known aetiological factors as 37% (60/162) and 42% (33/78) in the low and high F areas, respectively. The proportion with hypertension, without known aetiological factors, tended to be higher in females than in males, to increase with age, and to be lower in the high F area in those aged 40–49 yr but higher at ages 60–65 yr (Figure 2 and Table 2).

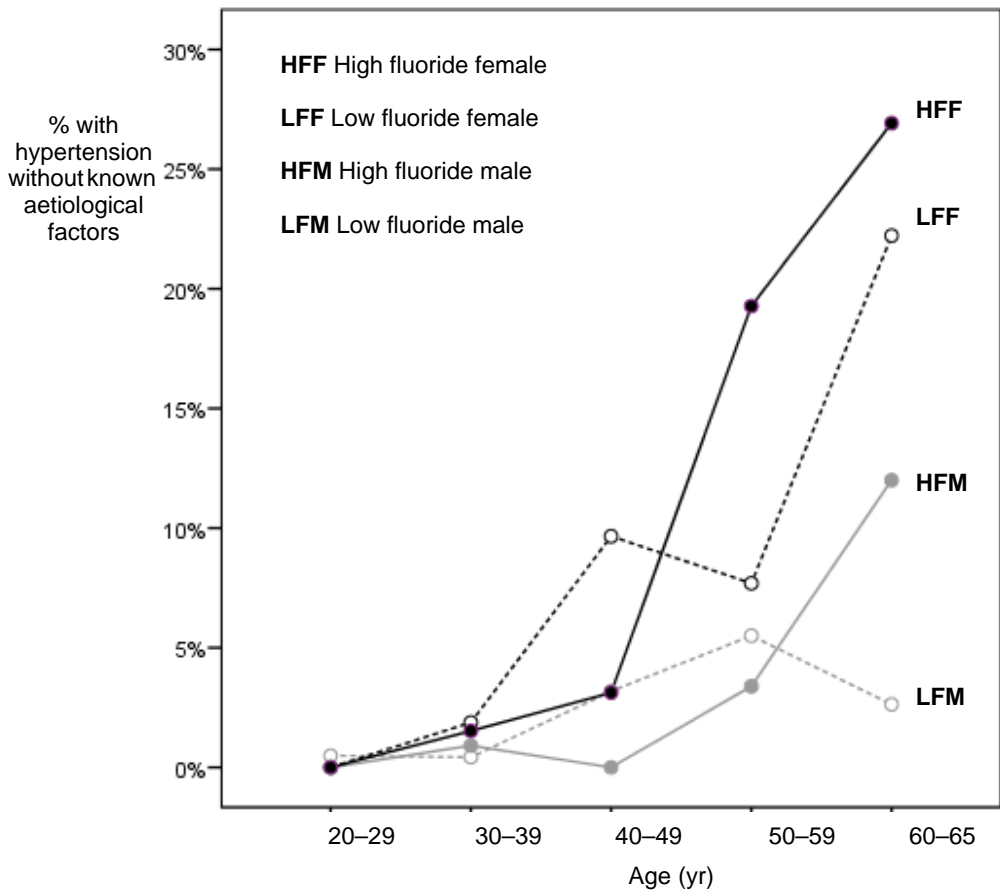


Figure 2. Percentage of the 93 persons (60 from the low fluoride area and 33 from the high fluoride area) with hypertension, without known aetiological factors, by age and gender.

Table 2. Comparison of the prevalence of hypertension, without known aetiological factors, (%) in the different age groups in the two areas with different drinking water fluoride levels

Sex	Age (yr)	Fluoride status						Difference	p*
		Low			High				
		Population	n	%	Population	n	%		
Male	20-29	406	2	0.5%	196	0	0.0%	0.5%	1.000
	30-39	235	1	0.4%	110	1	0.9%	-0.5%	0.537
	40-49	157	5	3.2%	63	0	0.0%	3.2%	0.325
	50-59	109	6	5.5%	59	2	3.4%	2.1%	0.714
	60-65	38	1	2.6%	25	3	12.0%	-9.4%	0.289
Female	20-29	420	0	0.0%	140	0	0.0%	0.0%	†
	30-39	213	4	1.9%	131	2	1.5%	0.4%	1.000
	40-49	176	17	9.7%	64	2	3.1%	6.5%	0.112
	50-59	182	14	7.7%	83	16	19.3%	-11.6%	0.011
	60-65	45	10	22.2%	26	7	26.9%	-4.7%	0.774
Male and female	20-29	826	2	0.2%	336	0	0.0%	0.2%	1.000
	30-39	448	5	1.1%	241	3	1.2%	-0.1%	1.000
	40-49	333	22	6.6%	127	2	1.6%	5.0%	0.033
	50-59	291	20	6.9%	142	18	12.7%	-5.8%	0.069
	60-65	83	11	13.3%	51	10	19.6%	-6.4%	0.338
Male	20-65	945	15	1.6%	453	6	1.3%	0.3%	0.817
Female	20-65	1036	45	4.3%	444	27	6.1%	-1.7%	0.187
Male and female	20-65	1981	60	3.0%	897	33	3.7%	-0.7%	0.424 0.556 [‡]

*Based on the Chi-Square test or the Fisher exact test as appropriate. The Fisher exact test was used for all the analyses apart from that for the total for males and females aged 20-65 yr where the numbers were too large for the Fisher's exact test and the chi-square approximation was performed instead. †One row in the Fisher's exact test grid is filled with zeros. In this situation, chi-square analysis is impossible as at least one of these values must be positive. ‡Adjusted for the age and sex based on the logistic regression analysis.

DISCUSSION

In this study, we investigated the effects of F on the prevalence of hypertension in people, aged 20–65 yr, living in areas with high and low levels of F in the drinking water. We found the prevalence of hypertension, in those without known aetiological factors, was 3.7% and 3% in the high and low F exposure areas, respectively. Based on chi-square statistical analysis, we found in the high fluoride area, compared to the low fluoride area, hypertension was increased ($p < 0.05$) in females aged 50–59 yr and decreased ($p < 0.05$) in the combined group of males and females aged 40–49 yr. No significant difference in the prevalence of hypertension related to F exposure was found in any of the male only groups.

Haghighat et al. found statistically significant negative correlations between the annual average concentration of drinking water F and hypertension prevalence of females ($p = 0.013$) and overall ($p = 0.025$), but no clear association for males ($p = 0.063$).¹¹

In an assessment of the relationship between excess F intake from drinking water and essential hypertension in adults living in F endemic areas, Sun et al. found that subjects with relatively low F levels in their drinking water (normal, mild, and moderate groups) had a lower risk of hypertension compared to the high F exposure groups.⁵

Amini et al. found statistically significant positive correlations between the mean concentrations of F in the ground water resources (GWRs) and the prevalence of hypertension for males, females, and the total of males and females.⁹ In addition, they found statistically significant positive correlations between the mean concentrations of F in the GWRs and the mean systolic blood pressure for males and a borderline correlation for females. In contrast, Varol et al. found no significant differences in the systolic and diastolic blood pressures between fluorosis patients and controls.¹⁴ Xu et al. found, in patients with skeletal fluorosis, that the severity of abnormal cardiac function and cardiac arrhythmias was directly related to the severity of the skeletal fluorosis.⁸ Varol et al. found that the elastic properties of ascending aorta were impaired in people with endemic fluorosis.¹³ Aortic strain and aortic distensibility were significantly lower in the fluorosis patients than in the controls.¹³

CONCLUSION

At present, there is no precise and clear evidence that prolonged exposure to increased levels of F, via water, food, and air, increases hypertension and chronic heart disease.² Since the blood pressure is affected by numerous factors other than F, controlling these other aetiological factors may provide the best approach for reducing the prevalence of hypertension. However, further studies from other areas on the relationship between F exposure and hypertension, also taking account of the other aetiological factors in hypertension, are recommended.

REFERENCES

- 1 World Health Organization. Fluoride and human health. Geneva: WHO; 1970. pp. 165-7.
- 2 Fordyce FM. Fluorine: human health risks. In: Nriagu JO, editor. Encyclopedia of Environmental Health. Vol. 2. Burlington: Elsevier; 2011. pp. 776-85.

- 3 Dobaradaran S, Mahvi AH, Dehdashti S, Abadi DVR. Drinking water fluoride and child dental caries in Dashtestan, Iran. *Fluoride* 2008;41(3):220-6.
- 4 Edzwald JK, editor. *Water quality & treatment: a handbook on drinking water*. New York: American Water Works Association, American Society of Civil Engineers, McGraw-Hill Professional; 2011.
- 5 Sun L, Gao Y, Liu H, Zhang W, Ding Y, Li B, et al. An assessment of the relationship between excess fluoride intake from drinking water and essential hypertension in adults residing in fluoride endemic areas. *Sci Total Environ* 2013;443:864-9.
- 6 Varol E, Varol S. Water-borne fluoride and primary hypertension [guest editorial review]. *Fluoride* 2013;46(1):3-6.
- 7 Scarpa M, Vianello F, Riqo A, Viqlino P, Bracco F, Battistin L. Uptake and life time of fluoride ion in rats by ¹⁹F-NMR. *Magn Reson Imaging* 1993;11(5):697-703.
- 8 Xu R, Xu R. Electrocardiogram analysis of patients with skeletal fluorosis. *Fluoride* 1997;30(1):16-8.
- 9 Amini H, Taghavi Shahri SM, Amini M, Ramezani Mehrian M, Mokhayeri Y, Yunesian M. Drinking water fluoride and blood pressure? An environmental study. *Biol Trace Elem Res* 2011;144(1-3):157-63.
- 10 Varol E, Varol S. Does fluoride toxicity cause hypertension in patients with endemic fluorosis? *Biol Trace Elem Res* 2012;150:1-2.
- 11 Haghghat GA, Yunesian M, Amini H. Hypertension and drinking water fluoride? Is there a relationship? [abstract]. *Fluoride* 2012; 45(3 Pt 1): 167.
- 12 Li Y, Berenji G, Shaba WF, Tafti B, Yevdayev E, Dadparvar S. Association of vascular fluoride uptake with vascular calcification and coronary artery disease. *Nucl Med Commun* 2012;33(1):14-20.
- 13 Varol E, Akcay S, Ersoy IH, Ozaydin M, Koroglu BK, Varol S. Aortic elasticity is impaired in patients with endemic fluorosis. *Biol Trace Elem Res* 2010;133(2):121-7.
- 14 Varol E, Akcay S, Ersoy H, Koroglu BK, Varol S. Impact of chronic fluorosis on left ventricular diastolic and global functions. *Sci Total Environ* 2010; 408(11):2295-8.
- 15 Karademir S, Akcam M, Kuybulu AE, Olgar S, Oktem F. Effects of fluorosis on QT dispersion, heart rate variability and echocardiographic parameters in children. *Anadolu Kardiyol Derg* 2011;11(2):150-5.
- 16 Liu H, Gao y, Sun L, Li M, Li B, Sun D. Assessment of relationship on excess fluoride intake from drinking water and carotid atherosclerosis development in adults in fluoride endemic areas, China. *International Journal of Hygiene and Environmental Health* 2014: 217(2-3): 413-20.
- 17 Ostovar A, Dobaradaran S, Ravanipour M, Khajeian AM. Correlation between fluoride Level in drinking water and the prevalence of hypertension: an ecological correlation study. *Int J Occup Environ Med* 2013;4:216-7.
- 18 Adali MK, Varol E, Aksoy F, Icli A, Ersoy IH, Ozaydin M, et al. Impaired heart rate Recovery in Patients with Endemic Fluorosis. *Biol Trace Elem Res* 2013;152:310-5.
- 19 Mahvi A. Survey of fluoride concentration in drinking water sources and prevalence of DMFT in the 12 years old students in Behshar City. *J Med Sci* 2006;6(4):658-61.
- 20 Dobaradaran S, Mahvi AH, Dehdashti S. Fluoride content of bottled drinking water available in Iran. *Fluoride*. 2008;41(1):93-4.
- 21 Amouei AI, Mahvi AH, Mohammadi AA, Asgharnia HA, Fallah SH, Khafajeh AA. Fluoride concentration in potable groundwater in rural areas of Khaf city, Razavi Khorasan Province, Northeastern Iran. *Int J Occup Environ Med* 2012;3(4):201-3.
- 22 Dobaradaran S, Mahvi AH, Dehdashti S, Dobaradaran S, Shoara R. Correlation of fluoride with some inorganic constituents in groundwater of Dashtestan, Iran. *Fluoride* 2009;42(1):50-3.
- 23 Nouri J, Mahvi AH, Babaei A, Ahmadvpour E. Regional pattern distribution of groundwater fluoride in the Shush aquifer of Khuzestan County, Iran. *Fluoride* 2006;39(4):321-5.
- 24 Mahvi AH, Zazoli MA, Younecian M, Esfandiari Y. Fluoride content of Iranian black tea and tea liquor. *Fluoride* 2006;39(4):266-8.
- 25 Karimzade S, Aghaei M, Mahvi AH. Investigation of intelligence quotient in 9–12-year-old children exposed to high-and low-drinking water fluoride in West Azerbaijan province, Iran. *Fluoride* 2014;47(1):9-14.
- 26 Boldaji MR, Mahvi A, Dobaradaran S, Hosseini S. Evaluating the effectiveness of a hybrid sorbent resin in removing fluoride from water. *International Journal of Environmental Science and Technology* 2009;6(4):629-32.
- 27 Rahmani A, Rahmani K, Dobaradaran S, Mahvi AH, Mohamadjani R, Rahmani H. Child dental caries in relation to fluoride and some inorganic constituents in drinking water in Arsanjan, Iran. *Fluoride* 2010;43(3):179-86.
- 28 Karimzade S, Aghaei M, Mahvi AH. IQ of 9–12-year-old children in high- and low-drinking water fluoride areas in west azerbaijan province, Iran: further information on the two villages in the study and the confounding factors considered [letter to the editor]. *Fluoride* 2014;47(3):266-71.
- 29 WHO. Fluoride in drinking-water: background document for development of WHO Guidelines for drinking-water quality. WHO/SDE/WSH/03.04.96, English only. Geneva: WHO; 2004. Available from: http://www.who.int/water_sanitation_health/dwq/chemicals/fluoride.pdf