Original Article

Journal of Public Health Research

Journal of Public Health Research
2023, Vol. 12(4), 1–8

DOI: 10.1177/22799036231204323
journals.sagepub.com/home/phj
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Association between fluoride exposure and blood pressure

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Abstract

Objectives: This study investigated whether fluoride was associated with an increased prevalence of high blood pressure (BP) among adolescents in the United States.

Methods: The study sample consisted of 2015–2016 National Health and Nutrition Examination Survey participants aged 13–17 years. Independent-samples *t*-tests, Chi-square tests, and regression models were used to analyze the data.

Results: A total of 814 participants met the study criteria. The findings showed that the proportion of patients with high levels of water or plasma fluoride in the high BP group was higher than that in the normal BP group. However, after adjusting for sociodemographic covariates, neither water nor plasma fluoride levels were significantly associated with a high BP.

Conclusions: This study did not find an association between either water or plasma fluoride levels and high BP. Further study is needed to exclude a dose dependent effect at higher levels of fluoride.

Keywords

Fluoride, hypertension, dental, medical

Date received: 18 February 2023; accepted: 22 August 2023

Introduction

Fluoride is a naturally occurring mineral found both in water and soil. Its role in oral health first became apparent at the turn of the century when McKay and Black[1] observed brown stains on the permanent teeth of several of his patients and that these teeth were more resistant to dental caries.[2] Dr. McKay and others suspected that these brown stains originated from something either in or missing from drinking water. Water sample studies later determined that drinking water containing high levels of naturally occurring fluoride was responsible.[3,4] In the 1940s, the first community water fluoridation programs began to study if the controlled addition of sodium fluoride in naturally fluoride-deficient water supplies reduced caries. These programs, located in Muskegon, Michigan; Newburgh and Kingston, New York; Brantford and Sarnia, Ontario, Canada; and Evanston and Oak Park, Illinois, found fluoridation reduced dental caries and established that adding a controlled amount of fluoride to drinking water was a cost-effective public health measure to reduce dental caries.[5]

Starting in 1962, the U.S. Public Health Service recommended a fluoride concentration in water of 0.7–1.2 mg/L to prevent dental caries. In 2015, the United States (US) Department of Health and Human Services updated and reduced its recommendation to 0.7 mg/L because of the increased availability of fluoride from other sources, such as juice,[6] soda,[7] infant formula,[8] and fluoridated toothpaste. In communities whose fluoride content fails to reach the 0.7 mg/L fluoridation standardization, the American Academy of Pediatric Dentistry[9] recommends prescribing fluoride supplements to high-risk children over 6 months of age.

Fluoride reduces cavities by strengthening the dental enamel, making it more resistant to dental caries.

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Demineralization occurs when an individual consumes fermentable carbohydrates, such as fruits and pasta. Organic acids from oral bacteria begin to dissolve enamel and over time can form a cavity.[10] Remineralization arrests or even reverses a caries lesion and fluoride enhances the remineralization process by helping calcium and phosphate ions to rebuild the tooth surface.[11] These remineralized crystals are more acid-resistant than the original enamel and help protect the tooth from decay. Fluoride also reduces the formation of acids by plaque bacteria.[12]

Epidemiologic evidence validates the oral health benefits of fluoride. Several systematic reviews support both the clinical and cost-effectiveness of fluoridation.[13–20] Drinking fluoridated reduces tooth decay by approximately 25% in children and adults[21,22] and every dollar spent on fluorination yields as much as $32 in reduced dental care expenses.[23]

While many concerns regarding fluorination such as neurotoxicity,[24] bone fragility, and increased risk of bone cancer[25–27] have been largely disproven at the recommended levels of water fluoride concentration, there is little research exploring a possible link between fluoride and hypertension. A Chinese-based study[28] raised the possibility of a positive correlation between fluoride exposure and blood pressure (BP) while others did not find similar associations. A recent systematic review[29] also found that the evidence is suggestive but insufficient to establish a correlation between fluoride exposure and BP. About 73% of those in the US receive fluoridated water. The prevalence of fluoridation and the public health burden of hypertension makes it important to further explore a possible link between fluoride exposure and BP.

This study used a nationally representative sample of adolescents in the US to explore associations between fluoride exposure and hypertension. This study contributes to the literature by updating and expanding earlier research about whether fluoride exposure is linked to hypertension. The results should help policymakers and healthcare professionals to maximize the balance between the potential risks and known benefits of fluoride exposure.

Methods

Data source

The study used 2015-2016 data from the National Health and Nutrition Examination Survey (NHANES). NHANES is a survey aimed at determining the health and nutritional status of all Americans, including adults and children. It consists of both interviews and physical tests and uses complex sampling and weighting techniques to develop a nationally representative sample to assess the health and nutrition of the noninstitutionalized population of the United States. Health interviews are performed at the respondents' homes, and health measurements are carried out in equipped mobile centers that travel across the country. Data collection for this continuous program began in 1999 and surveys about 5000 persons each year.

This research study restricted the analysis to adolescents aged 13–17 years who completed both the NHANES interview and physical examination ($n=870$). We excluded participants who did not have at least 1 systolic BP and diastolic BP measurement ($n=56$). After these exclusions, a total of 814 participants were included in the analysis. The study followed the "data use restrictions" published on the NHANES website.[30] More details regarding NHANES study procedures can be found at https://www.cdc.gov/nchs/nhanes/index.htm.

Measures

Outcome measure. The key outcome measure was BP which was assessed by trained personnel at the NHANES mobile examination centers (MECs). Before taking BP, the upper arm circumference of each participant was measured and used to guide the proper cuff size. Three BP measurements were obtained at 30-second intervals after 5 min of seated rest. The mean of all available measurements was used to define systolic BP and diastolic BP for each participant. Among participants included in the current analysis, 0.4% ($n=3$) had one systolic BP or diastolic BP measurement, 3.9% ($n=32$) had two, and 95.7% ($n=779$) had three. The BP variable was categorized as either normal or high BP with high BP defined as either elevated or hypertensive based on age norms outlined in the *"2017 American Academy of Pediatrics Clinical Practice Guideline"* (Supplemental Appendix 1).[31]

Predictor. This study utilized two continuous variables, plasma, and water fluoride levels as predictors. Both plasma and water fluoride concentrations were analyzed at the MECs by laboratory personnel. To measure plasma fluoride concentrations, each sample was measured twice using the ion-specific electrode and hexamethyldisiloxane method and the two results averaged. Fluoride concentrations in water samples were also measured twice using an ion-specific electrode[21] and averaged.

Based on the US Public Health Service recommended water fluoride concentration of 0.7 mg/L,[24] fluoride levels in water were categorized as 0.00–0.30 (reference level), 0.31–0.50 (level 1), 0.51–0.70 (level 2), and >0.70 (level 3). We also transformed plasma fluoride levels into a four-category variable, which was 0.00–0.30 (reference level), 0.31–0.40 (level 1), 0.41–0.50 (level 2), and >0.50 (level 3).

Covariates. This study adjusted for sociodemographic factors collected by the NHANES survey. Race/ethnicity categories include Hispanic, non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, and non-Hispanic other). The

National Center for Health Statistics (NCHS) calculated the poverty-to-income ratio (PIR) as a ratio of self- or proxy-reported family income to the federal poverty level based on family size. A PIR of less than 1.00 indicates that the family income was below the poverty level. The PIR was grouped as less than 1.30, 1.30–3.49, and 3.50 or greater, consistent with categories frequently used by the NCHS.[32] Body mass index (BMI), calculated as weight in kilograms divided by height in meters squared and rounded to 1 decimal place, was categorized as underweight (BMI = <5th percentile), normal (BMI = 5th–<85th percentile), overweight (BMI = 85th–<95th percentile), and obese (BMI ≥ 95th percentile) based on age- and sex-specific growth charts developed by the Centers for Disease Control and Prevention in 2000.[33]

Statistical approach. Descriptive statistics were calculated for participants' characteristics, fluoride exposure factors, and BP. Independent-samples *t*-tests for continuous measurements and Chi-square tests for categorical data were used to explore differences in participant characteristics according to whether they had high BP. Then, binary logistic regression models were used to analyze associations between fluoride exposure and BP. Unadjusted models were first run for water fluoride levels and plasma fluoride levels. Then, adjusted models were run to calculate adjusted odds ratios (AOR) and 95% confidence intervals (95% CI) after adjusting for socio-demographics. All analyses were conducted with SPSS Software (Version 28) and statistical significance was set at two-sided p values <0.05.

Results

Demographic characteristics

The total sample consisted of 814 participants with an average age of 14.96 years (95% CI = 14.87–15.06). Among the participants who met the study criteria, 85.3 % had normal BP and 14.7% had high BP. Just over half (51.7%) were male and Hispanics represented the largest Race/Ethnicity group (33%). In addition, 360 (45.1%) participants were exposed to water with low fluoride levels (<0.3 mg/L) and 433 (59.8%) participants had low plasma fluoride levels (<0.3 μmol/L). The mean ratio of family income to the poverty level was 2.08 (95% CI = 1.97–2.18) and more than half (55.4%) of the participants had a normal BMI. Table 1 summarizes the study population characteristics.

Table 1. Demographic characteristics (NHANES, 2015–2016).

Variable	Mean (95% CI)	*n* (%)
Age (year)	14.96 (14.87–15.06)	
Gender, *n* (%)		
Male		421 (51.7)
Female		393 (48.3)
Race/Ethnicity		
Hispanic		269 (33)
Non-Hispanic White		239 (29.4)
Non-Hispanic Black		183 (22.5)
Non-Hispanic Asian		75 (9.2)
Non-Hispanic Other		48 (5.9)
BMI		
Underweight		22 (2.7)
Normal		448 (55.4)
Overweight		173 (21.4)
Obesity		165 (20.4)
Ratio of family income to poverty	2.08 (1.97–2.18)	
<1.30		292 (39.1)
1.30–3.49		304 (40.8)
≥3.5		150 (20.1)
Water fluoride (mg/L)	0.45 (0.42–0.47)	
<0.3		360 (45.1)
0.31–0.50		129 (16.2)
0.51–0.70		145 (18.2)
>0.70		164 (20.6)
Plasma fluoride (μmol/L)	0.32 (0.3–0.33)	
<0.3		433 (59.8)
0.31–0.40		150 (20.7)
0.41–50		89 (9.5)
>0.50		72 (9.9)
Blood pressure		
Normal		694 (85.3)
High blood pressure		120 (14.7)

Comparison between the high BP and normal BP groups

Table 2 shows the characteristics of the sample divided into a high BP group and a normal BP group. Individuals with high BP were more likely to be older, male, Hispanic, and obese than participants without high BP. Figure 1 displays water fluoride and plasma fluoride levels between the high BP and normal BP groups. The results indicate a greater proportion of individuals exposed to higher levels of water fluoride or higher plasma fluoride levels in the high BP group compared to the normal BP group.

Relationship between fluoride exposure and high BP

Figures 2 and 3 summarize the multivariate logistic regression analysis of the association between fluoride exposure and high BP. As shown in the univariate plasma fluoride logistic regression analysis (model 1), the patients with the highest levels of plasma fluoride (>0.5 μmol/L) (OR: 2.039, 95% confidence interval (95% CI): 1.107–3.757, and $p = 0.022$) had an increased risk of high BP in contrast to those with low plasma fluoride levels <0.3 μmol/L. After adjusting for age and gender (model 2), the risk of high BP in patients with plasma fluoride level >0.5 μmol/L

Table 2. Comparison of the characteristics between high BP and normal BP groups (NHANES, 2015–2016).

Variable	Normal BP group (*n* = 694)	High BP group (*n* = 120)	Statistic	*p*-value
Age (year), mean (95% CI)	14.9 (14.79–15)	15.35 (15.11–15.59)	*t*=−3.29	**0.001**
Gender, *n* (%)				
Male	336 (48.4)	85 (70.8)	−0.16	<**0.001**
Female	358 (51.6)	35 (29.2)		
Race/Ethnicity, *n* (%)				
Hispanic	227 (32.7)	42 (35)	0.119	**0.021**
Non-Hispanic White	212 (30.5)	27 (22.5)		
Non-Hispanic Black	144 (20.7)	39 (32.5)		
Non-Hispanic Asian	69 (9.9)	6 (5)		
Non-Hispanic Other	42 (6.1)	6 (5)		
BMI, *n* (%)				
Underweight	22 (3.2)	–	0.252	<**0.001**
Normal	406 (58.8)	42 (35.6)		
Overweight	149 (21.6)	24 (20.3)		
Obesity	113 (16.4)	52 (44.1)		
Ratio of family income to poverty, *n* (%)				
<1.30	254 (40)	38 (34.2)	0.067	0.185
1.30–3.49	250 (39.4)	54 (48.6)		
≥3.5	131 (20.6)	19 (17.1)		
Water fluoride (mg/L)				
<0.3	306 (44.9)	54 (46.2)	0.080	0.164
0.31–0.50	118 (17.3)	11 (9.4)		
0.51–0.70	120 (17.6)	25 (21.4)		
>0.70	137 (20.1)	27 (23.1)		
Plasma fluoride (μmol/L)				
<0.3	376 (61)	57 (52.8)	0.089	0.128
0.31–0.40	128 (20.8)	22 (20.4)		
0.41–50	57 (9.3)	12 (11.1)		
>0.50	55 (8.9)	17 (15.7)		

All *p*-value<0.05 are in bold.

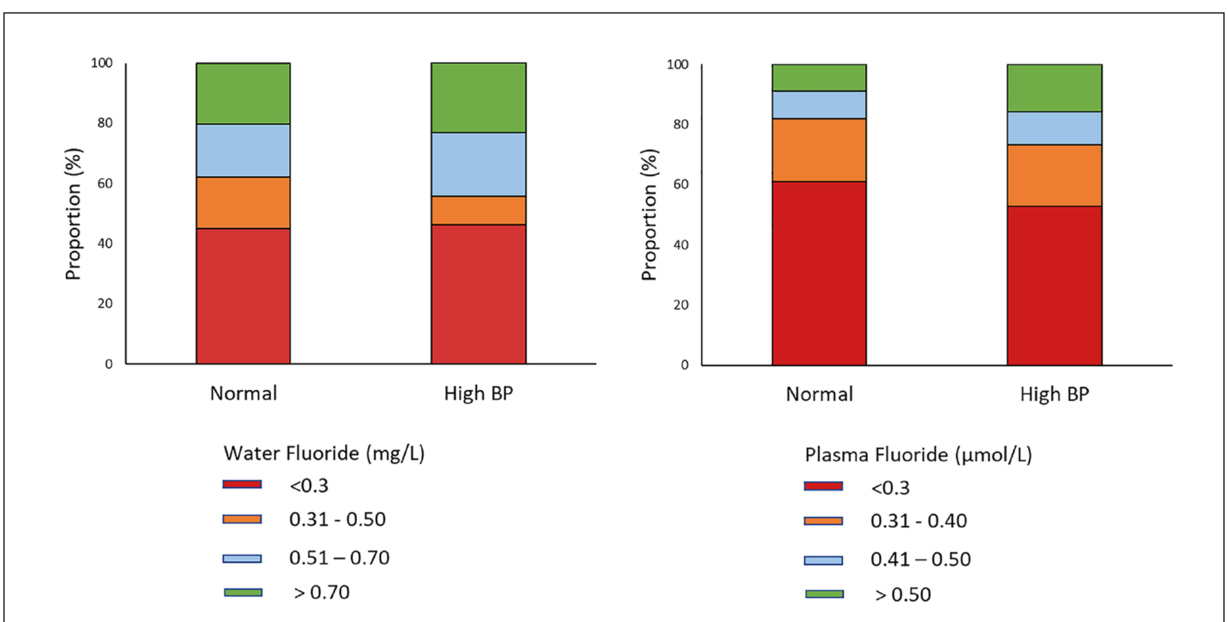
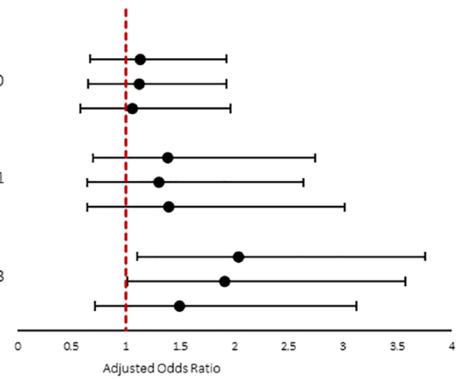


Figure 1. The water fluoride and plasma fluoride level distribution of high blood pressure and normal blood pressure groups.

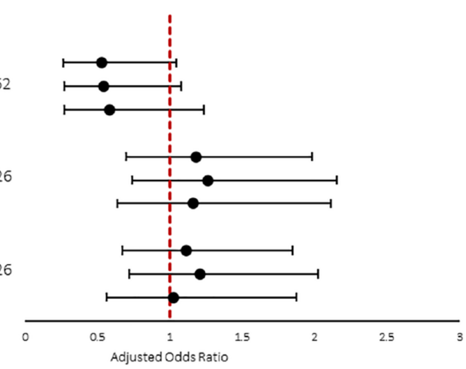
Exposure	Model 1 OR (95%CI)	*P* value	Model 2 OR (95%CI)	*P* value	Model 3 OR (95%CI)	*P* value
Plasma Fluoride (µmol/L)						
<0.3	Ref		Ref		Ref	
0.31-0.40	1.134 (0.667-1.929)	0.643	1.120 (0.650-1.931)	0.682	1.065 (0.578-1.962)	0.840
0.41-0.50	1.389 (0.702-2.747)	0.345	1.306 (0.647-2.633)	0.456	1.393 (0.643-3.019)	0.401
>0.50	**2.039 (1.107-3.757)**	**0.022**	**1.907 (1.016-3.579)**	**0.045**	1.496 (0.717-3.121)	0.283



Note. Bold indicates p <.05.
Group
Model 1: Univariate logistic regression analysis for plasma fluoride levels.
Model 2: Multivariate logistic regression analysis after adjustments for age and gender.
Model 3: Multivariate logistic regression analysis after adjustments for the covariates including age, gender, race/ethnicity, BMI, and PIR.

Figure 2. Multivariate logistic regression forest plot of the association between water fluoride levels and high blood pressure risk.

Exposure	Model 1 OR (95%CI)	*P* value	Model 2 OR (95%CI)	*P* value	Model 3 OR (95%CI)	*P* value
Water Fluoride (mg/L)						
<0.3	Ref		Ref		Ref	
0.31-0.50	0.528 (0.267-1.045)	0.067	0.541 (0.270-1.082)	0.082	0.585 (0.276-1.240)	0.162
0.51-0.70	1.181 (0.703-1.984)	0.531	1.266 (0.743-2.156)	0.386	1.160 (0.638-2.112)	0.626
>0.70	1.117 (0.675-1.849)	0.668	1.209 (0.722-2.026)	0.471	1.029 (0.564-1.877)	0.926



Group
Model 1: Univariate logistic regression analysis for water fluoride levels.
Model 2: Multivariate logistic regression analysis after adjustments for age and gender.
Model 3: Multivariate logistic regression analysis after adjustments for the covariates including age, gender, race/ethnicity, BMI, and PIR.

Figure 3. Multivariate logistic regression forest plot of the association between plasma fluoride levels and high blood pressure risk.

was increased (OR: 1.907, 95% CI: 1.016–3.579, and $p = 0.045$) compared to those with a reference level of plasma level (<0.3 µmol/L). Model 3 shows that after adjusting for age, gender, race/ethnicity, BMI and PIR, the relationships between BP and water fluoride levels (Figure 2), and between BP and plasma fluoride levels (Figure 3) no longer remained statistically significant.

Discussion

The majority of dental, medical, and public health organizations, including the American Dental Association, American Academy of Pediatrics, US Public Health Service, and the World Health Organization[34] recommend community water fluoridation. Considered one of the ten great public health achievements of the 20th century, the CDC regards fluoride as a critical element for maintaining health so long as levels are within the standard range.[35] In contrast, several studies suggest that excessive fluoride exposure adversely affects human health.[36,37] In short, when fluoride consumption exceeds the recommended limit individuals are potentially at risk for health harms.

While the effects of excessive fluoride exposure have been investigated, the relationship between lower levels of fluoride exposure and human health has received less attention.[38] In this study, we examined the association of fluoride exposure from both water and plasma and BP. Using data extracted from a nationally representative sample, this study found that after controlling for sociodemographic covariates, neither water nor plasma fluoride levels were associated with high BP.

In contrast, earlier studies report a positive relationship between fluoride exposure and BP.[39,40] Animal studies that found that fluoride induces oxidative stress and activates the expression of nuclear factor kappa beta in cardiac and renal tissue offer a plausible mechanism for BP[41] for a link between fluoride exposure and BP. However, our results align with others who also found no association between lower levels of fluoride.[42,43] Unlike Liu et al.[44] who identified a significant association of fluoride for girls in Mexico City, our study did not demonstrate sex differences.

One reason that our results differed from other studies is that most evidence linking fluoride to hypertension derives from countries with increased fluoride in the ground water.[28] In these studies, the risk of elevated BP appears to increase for individuals living in fluorosis-endemic areas.[29,40,43,45,46] It may be that the connection of fluoride to high BP is dose-dependent and most individuals in the US fall below the threshold needed to increase BP. Further study is needed to explore if dose dependency is an issue and what levels should trigger action by public health officials.

Conversely, Guo et al.[47] found an inverse association between water fluoride and childhood BP levels. Although their study also used NHANES data, it differed from our study by including younger aged children and data from before the 2015 DHHS recommendation to lower water fluoride concentrations from 1.2 to 0.7 mg/L.[24]. In addition, Guo et al.[47] examined changes in systolic and diastolic blood pressure while our study categorized BP as either normal or high BP. However, their finding of an inverse relationship between BP and fluoride levels in combination with our finding that fluoride was not associated with high BP should provide additional reassurance to those concerned about fluoride increasing BP.

Limitations of this study

Several limitations need to be considered. First, this study was cross-sectional rather than longitudinal, thus causality could not be strongly inferred by the associations between fluoride exposure and BP. Second, three measurements of BP were taken at one visit. To diagnose hypertension in children and adolescents, guidelines recommend calculating the mean of multiple BP measurements taken during two or more visits[31] and a reading at a single visit may misclassify a child's BP status. Third, due to the lack of additional data on antihypertensive treatment, hypertension was defined solely by BP measurements. Finally, higher fluoride exposure was associated with an increased risk of high BP but this association did not achieve statistical significance. It may be that the sample size in the high BP group was insufficient to detect small differences.

Conclusions

Using data from a US national database, this study did not find an association between either water or plasma fluoride levels and high BP. However, the data could not exclude the possibility of a link at levels seen in fluorosis-endemic areas outside of the US. Further study is needed to exclude a dose-dependent effect at higher levels of fluoride.

Acknowledgments

The authors thank the Clinical Outcomes Research and Education at Roseman University of Health Sciences College of Education and the Analytic Galaxy for the support of this study.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Supplemental material

Supplemental material for this article is available online.

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