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Exposure to perchlorate, nitrate and thiocyanate was associated with the prevalence of hypertension

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Abstract

Background Our study aims to examine the relationships between exposure to perchlorate, nitrate, and thiocyanate and the risk of hypertension.

Methods A total of 21,321 participants were selected from the National Health and Nutritional Examination Survey (NHANES). We used logistic regressions models to explore the odds ratio of urinary perchlorate, nitrate, and thiocyanate on the risk of hypertension and restricted cubic splines to check the nonlinearity.

Results 2851 (13.4%) individuals were diagnosed with hypertension. Multivariable logistic regression analysis suggested that urinary perchlorate and nitrate were inversely associated with hypertension, and thiocyanate has a positive correlation. Compared with the lowest quartile, the highest quartile of odds ratios was 0.86 (0.74–1.00; $P=0.048$) for perchlorate, 0.79 (0.67–0.94; $P=0.007$) for nitrate, and 1.47 (1.25–1.73; $P<0.001$) for thiocyanate. Restricted cubic splines showed that urinary perchlorate was nonlinearly associated with hypertension ($P=0.0014$).

Conclusions Higher exposure to perchlorate and nitrate were associated with a lower risk of hypertension, while a positive association was observed for urinary thiocyanate.

Keywords Perchlorate, Nitrate, Thiocyanate, Hypertension, NHANES

Introduction

Hypertension is a global health problem, accounting for 9.4 million deaths worldwide [1]. Globally, the prevalence of hypertension was 24.1% and 20.1% in men and women respectively [2]. Besides, hypertension was one of the leading risk factors for cardiovascular diseases and chronic kidney disease [3, 4].

Perchlorate, nitrate, and thiocyanate are environmentally endocrine-disruptors, which could be detected in drinking water, food and some electronic products [5–7]. It was reported that urinary nitrate was inversely correlated with obesity, while thiocyanate increased the risk of obesity [8]. And higher urinary perchlorate levels are associated with an increased prevalence of diabetes mellitus [9]. However, it remains unknown about the

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relationship between exposure to perchlorate, nitrate, and thiocyanate with the risk of hypertension.

Methods

Study population

Among a total of 24,508 participants from NHANES, we excluded individuals without data on urinary perchlorate, nitrate and thiocyanate ($n=1,228$), hypertension ($n=1,954$) and urinary creatinine ($n=5$). Finally, we included 21,321 in the present study (Fig. 1). The study protocol was approved by the National Center for Health Statistics (NCHS).

Urinary perchlorate, nitrate and thiocyanate

Urine concentrations of perchlorate, nitrate and thiocyanate are measured by LC-MS/MS [10]. The value

lowering the limit of detection is the detection limit divided by the square root of two.

Variables collection

Common information on age, sex, race, education level, poverty income ratio (PIR), alcohol consumption, smoking status, physical activity and disease history were obtained from the questionnaires. Diabetes was defined as a history of diabetes, fasting plasma glucose ≥ 7.0 mmol/L, or HbA1c $\geq 6.5\%$. Hypertension was defined as self-reported doctor diagnosis of hypertension, blood pressure $\geq 140/90$ mmHg, or the use of anti-hypertensive medicine [11].

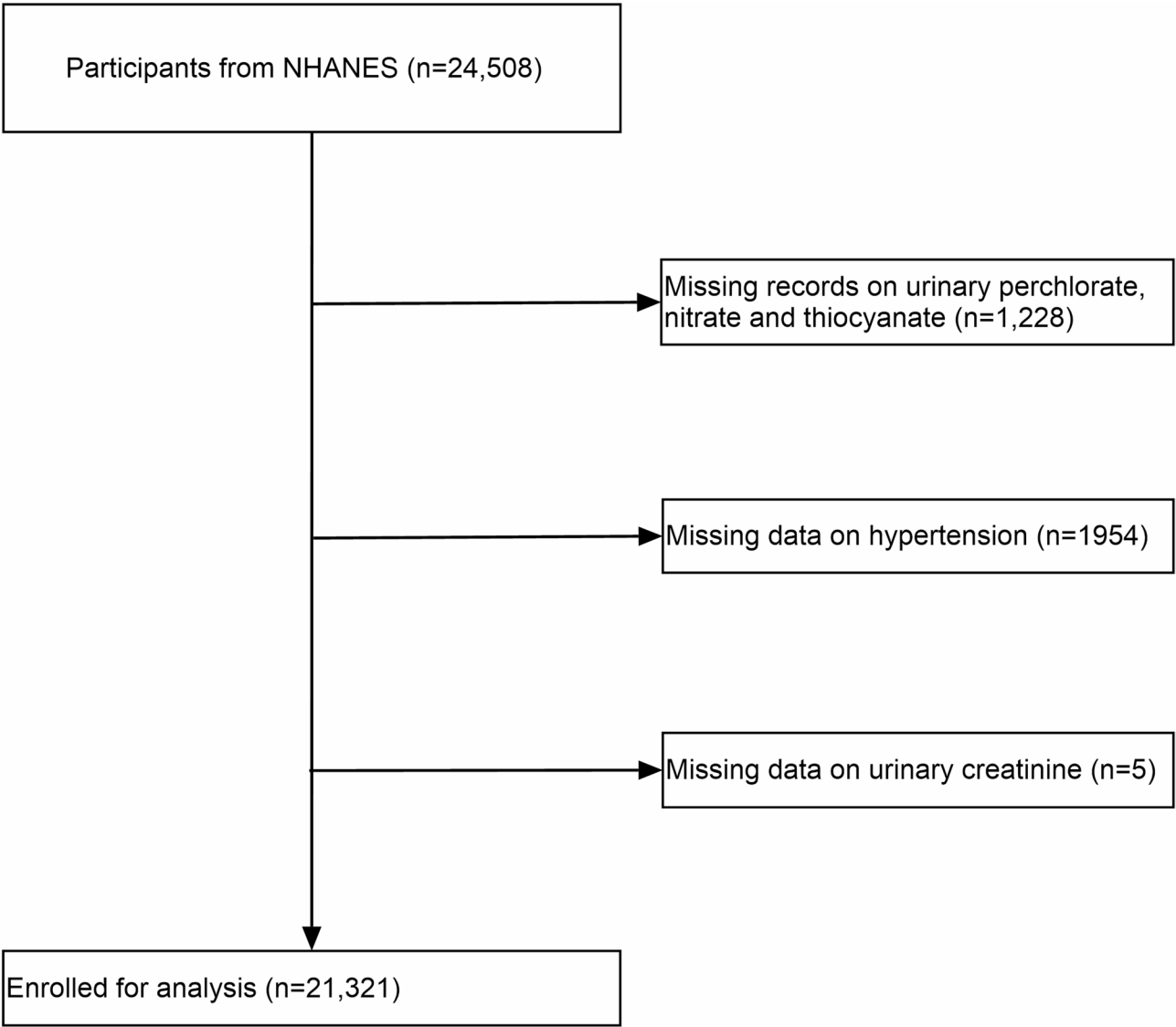


Fig. 1 The flow chart of participant selection

Statistical analysis

Continuous variables were presented as the mean \pm standard deviation while categorical variables were presented as the number (percentage). Multivariable logistic regression models were used to explore the relationship between urinary perchlorate, nitrate and thiocyanate with the risk of hypertension. Restricted cubic splines were used to estimate the dose-response relationship between urinary perchlorate, nitrate and thiocyanate with hypertension. Data were analyzed using R software version 3.6.0. P value < 0.05 was considered as statistically significant.

Results

The present study included 21,321 participants, of whom 2851 (13.4%) was diagnosed as hypertension. The characteristics of population according to hypertension were

shown in Table 1. Hypertensive individuals had a lower level of urinary perchlorate ($P = 0.07$), nitrate ($P < 0.001$) and thiocyanate ($P < 0.001$).

Associations of urinary perchlorate with the prevalence of hypertension are shown in Table 2. Compared to the lowest quartile, the odds ratios (ORs) of the highest quartile were 0.73 (95% confidence interval [CI], 0.65–0.82; $P < 0.001$), 0.83 (0.73–0.95; $P = 0.008$), 0.84 (0.73–0.96; $P = 0.013$) and 0.86 (0.74–1.00; $P = 0.048$). For urinary nitrate shown in Table 3, the ORs across the increasing quartiles were 0.89 (95% CI, 0.79–1.01; $P = 0.079$), 0.79 (0.68–0.91; $P = 0.002$) and 0.79 (0.67–0.94; $P = 0.007$) in the fully-adjusted model. For urinary thiocyanate (Table 4), the highest quartile was positively associated with the presence of hypertension compared with the lowest quartile (OR 1.47 [1.25–1.73]; $P < 0.001$). Restricted cubic splines (Fig. 2) also suggested that

Table 1 Characteristics of the study population according to the presence of hypertension

Variable	Overall (n = 21321)	Non-HBP (n = 18470)	HBP (n = 2851)	P value
Male (%)	10,601 (49.7)	9080 (49.2)	1521 (53.3)	< 0.001
Age, years	38.16 \pm 22.30	34.63 \pm 21.04	61.07 \pm 15.68	< 0.001
Race (%)				< 0.001
Non-Hispanic white	8678 (40.7)	7380 (40.0)	1298 (45.5)	
Non-Hispanic black	4985 (23.4)	4177 (22.6)	808 (28.3)	
Mexican American	4395 (20.6)	4017 (21.7)	378 (13.3)	
Others	3263 (15.3)	2896 (15.7)	367 (12.9)	
Education (%)				< 0.001
Less than high school	4042 (27.4)	3073 (25.7)	969 (34.5)	
High school or equivalent	3460 (23.4)	2758 (23.1)	702 (25.0)	
College or above	7264 (49.2)	6126 (51.2)	1138 (40.5)	
PIR (%)				< 0.001
< 1	4799 (24.2)	4264 (24.8)	535 (20.4)	
1 ~ 3	8145 (41.1)	6923 (40.3)	1222 (46.5)	
> 3	6871 (34.7)	6000 (34.9)	871 (33.1)	
BMI, kg/m ²	26.9 \pm 7.1	26.5 \pm 7.01	29.7 \pm 7.2	< 0.001
Drinking, %	2052 (50.4)	1626 (50.7)	426 (49.2)	0.463
Smoking, %				0.146
Never	8000 (71.5)	6573 (71.2)	1427 (72.6)	
Past	542 (4.8)	463 (5.0)	79 (4.0)	
Current	2653 (23.7)	2193 (23.8)	460 (23.4)	
Activity, %				< 0.001
Inactive	2359 (20.0)	2060 (19.9)	299 (20.5)	
Moderate	4412 (37.4)	3761 (36.4)	651 (44.7)	
Vigorous	5024 (42.6)	4518 (43.7)	506 (34.8)	
CVD, %	1526 (10.3)	1006 (8.4)	520 (18.5)	< 0.001
Diabetes, %	2426 (11.4)	1667 (9.0)	759 (26.6)	< 0.001
sBP, mmHg	118.0 \pm 17.8	113.1 \pm 12.0	151.9 \pm 13.5	< 0.001
dBp, mmHg	65.4 \pm 14.9	63.9 \pm 13.8	76.1 \pm 17.8	< 0.001
Creatinine, mg/dL	126.3 \pm 78.5	128.4 \pm 79.1	112.5 \pm 73.2	< 0.001
Perchlorate, μ g/L	3.56 [1.97, 6.27]	3.62 [2.01, 6.35]	3.16 [1.80, 5.68]	0.07
Nitrate, mg/L	47.7 [27.8, 73.6]	49.1 [29.0, 75.2]	37.6 [22.0, 61.9]	< 0.001
Thiocyanate, mg/L	1.13 [0.55, 2.30]	1.15 [0.57, 2.30]	0.96 [0.46, 2.27]	< 0.001

Data are presented as n (%), and mean \pm SD or median [lower quartile, upper quartile]. PIR, poverty income ratio. BMI, body mass index; CVD, cardiovascular disease; sBP, systolic blood pressure; dBp, diastolic blood pressure

Table 2 Association of urinary perchlorate with the presence of hypertension

Subgroup	Cases	N	Model 1		Model 2		Model 3		Model 4	
			OR[95%CI]	P	OR[95%CI]	P	OR[95%CI]	P	OR[95%CI]	P
Q1	813	5355	Ref	-	Ref	-	Ref	-	Ref	-
Q2	775	5336	0.95 [0.85, 1.06]	0.339	0.91 [0.80, 1.02]	0.109	0.90 [0.80, 1.02]	0.103	0.90 [0.80, 1.02]	0.110
Q3	647	5313	0.77 [0.69, 0.87]	< 0.001	0.76 [0.67, 0.86]	< 0.001	0.77 [0.67, 0.88]	< 0.001	0.78 [0.68, 0.89]	< 0.001
Q4	616	5317	0.73 [0.65, 0.82]	< 0.001	0.83 [0.73, 0.95]	0.008	0.84 [0.73, 0.96]	0.013	0.86 [0.74, 1.00]	0.048

Model 1: non-adjusted

Model 2: adjusted for creatinine, age and gender

Model 3: Model 1 + education, PIR, BMI, drinking, smoking, activity, CVD and diabetes

Model 4: Model 2 + mutual adjustment of log-transformed urinary perchlorate, nitrate and thiocyanate

OR, odds ratio; CI, confidence interval; CVD, cardiovascular diseases

Q1: 1.21; Q2: 2.74; Q3:4.76; Q4: 12.8

Table 3 Association of urinary nitrate with the presence of hypertension

Subgroup	Cases	N	Model 1		Model 2		Model 3		Model 4	
			OR[95%CI]	P	OR[95%CI]	P	OR[95%CI]	P	OR[95%CI]	P
Q1	987	5338	Ref	-	Ref	-	Ref	-	Ref	-
Q2	781	5323	0.76 [0.68, 0.84]	< 0.001	0.95 [0.84, 1.07]	0.416	0.92 [0.81, 1.03]	0.153	0.89 [0.79, 1.01]	0.079
Q3	587	5334	0.55 [0.49, 0.61]	< 0.001	0.89 [0.78, 1.03]	0.112	0.82 [0.71, 0.94]	0.005	0.79 [0.68, 0.91]	0.002
Q4	496	5326	0.45 [0.40, 0.51]	< 0.001	0.95 [0.81, 1.11]	0.491	0.83 [0.71, 0.97]	0.022	0.79 [0.67, 0.94]	0.007

Model 1: non-adjusted

Model 2: adjusted for creatinine, age and gender

Model 3: Model 1 + education, PIR, BMI, drinking, smoking, activity, CVD and diabetes

Model 4: Model 2 + mutual adjustment of log-transformed urinary perchlorate, nitrate and thiocyanate

OR, odds ratio; CI, confidence interval; CVD, cardiovascular diseases

Q1: 17.4; Q2: 37.7; Q3: 59.6; Q4: 116.0

Table 4 Association of urinary thiocyanate with the presence of hypertension

Subgroup	Cases	N	Model 1		Model 2		Model 3		Model 4	
			OR[95%CI]	P	OR[95%CI]	P	OR[95%CI]	P	OR[95%CI]	P
Q1	884	5333	Ref	-	Ref	-	Ref	-	Ref	-
Q2	693	5401	0.74 [0.67, 0.82]	< 0.001	0.98 [0.86, 1.10]	0.690	0.97 [0.86, 1.10]	0.685	1.01 [0.90, 1.15]	0.816
Q3	569	5269	0.61 [0.54, 0.68]	< 0.001	1.01 [0.89, 1.15]	0.871	0.99 [0.87, 1.13]	0.908	1.05 [0.92, 1.21]	0.451
Q4	705	5318	0.77 [0.69, 0.86]	< 0.001	1.40 [1.23, 1.58]	< 0.001	1.36 [1.16, 1.59]	< 0.001	1.47 [1.25, 1.73]	< 0.001

Model 1: non-adjusted

Model 2: adjusted for creatinine, age and gender

Model 3: Model 1 + education, PIR, BMI, drinking, smoking, activity, CVD and diabetes

Model 4: Model 2 + mutual adjustment of log-transformed urinary perchlorate, nitrate and thiocyanate

OR, odds ratio; CI, confidence interval; CVD, cardiovascular diseases

Q1: 0.32; Q2: 0.82; Q3: 1.61; Q4: 5.98

urinary perchlorate was nonlinearly related to hypertension (P for nonlinearity = 0.0014), while urinary nitrate was inversely associated with hypertension (P for nonlinearity = 0.6912) while urinary thiocyanate was positively related to hypertension (P for nonlinearity = 0.0563).

Considering the distribution of the predictor variables included extremely low and high values (Supplementary Table 1), we excluded the value below 1% and above 99% and re-analyzed the association between urinary levels of perchlorate (Supplementary Table 2), nitrate (Supplementary Table 3), thiocyanate (Supplementary Table 4). The results were also consistent as previously described.

Discussion

This is the first study to examine the associations between urinary perchlorate, nitrate, and thiocyanate and the prevalence of hypertension. In this study, we found that urinary perchlorate was nonlinearly associated with hypertension, with a lower level increasing the risk of hypertension. Urinary nitrate was inversely associated with hypertension while urinary thiocyanate was positively related to hypertension. The association was independent of traditional hypertension risk factors.

Previous studies suggested that exposure to perchlorate, nitrate and thiocyanate could inhibit thyroid function [12], which may be responsible for regulation of

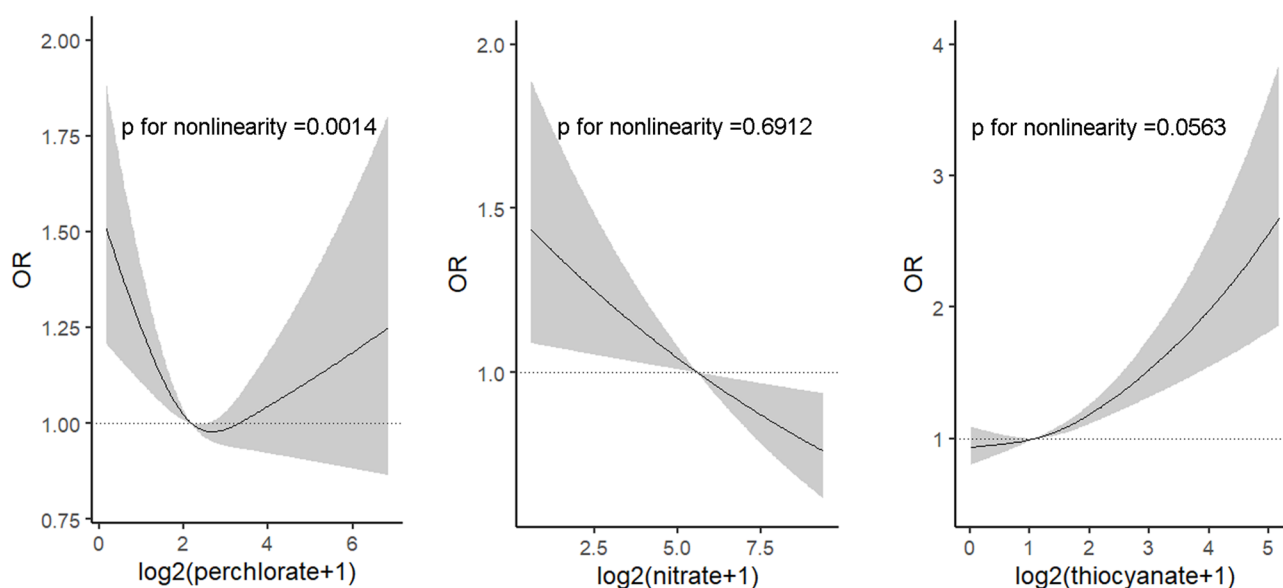


Fig. 2 The dose-response analysis between urinary perchlorate (A), nitrate (B) and nitrate (C) with hypertension

blood pressure. We found that lower level of urinary perchlorate increased the risk of hypertension. However, there was no report about the link between perchlorate exposure and hypertension. Previous studies demonstrated that nitrate supplementation could reduce systolic blood pressure and diastolic blood pressure [13–15]. This was in consistent with our results that urinary nitrate was negatively associated with the prevalence of hypertension. Our results also found that urinary thiocyanate was positively associated with hypertension. Animal study showed that thiocyanate promoted vessel constriction in a dose-dependent manner [16]. Clinical trial also showed that thiocyanate-rich vegetables abolished the anti-hypertensive effect of nitrate-rich vegetable [17].

However, our study also had several limitations. Firstly, urinary perchlorate, nitrate and thiocyanate were measured only once, lack of dynamic biomonitoring. Secondly, this is a cross-sectional study.

Conclusions

In summary, urinary nitrate was inversely associated with hypertension while urinary thiocyanate was positively related to hypertension. Urinary perchlorate was nonlinearly associated with hypertension.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12872-025-04878-3>.

Supplementary Material 1

Acknowledgements

None.

Author contributions

R C and H J S designed the study; X F M and Y C performed the statistical analysis; J P L prepared the figures. All authors approved it.

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Data availability

The datasets were available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Review Board of National Center for Health Statistics and informed consent to participate was obtained from all of the participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Clinical trial number

Not applicable.

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