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ORIGINAL RESEARCH

Dietary sodium and potassium intake and their association with blood pressure in a non-hypertensive Iranian adult population: Isfahan salt study

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Abstract

Aim: The association of sodium (Na) and potassium (K) intake with blood pressure (BP) is an ongoing debate, especially in central Iran. We aimed to examine the mean Na and K intake, major sources of Na and the relationship between BP and dietary and urinary Na and K.

Methods: This cross-sectional study was performed in central Iran in 2013–2014. A total of 796 non-hypertensive adults aged >18 years were randomly recruited. The semi-quantitative food frequency questionnaire was used to assess dietary Na and K intake. Moreover, 24-hour urine samples were collected to measure 24-hour urinary Na (UNa) and K (UK) as biomarkers. BP was measured twice on each arm using a standard protocol.

Results: The mean Na and K intake were 4309.6 ± 1344.4 and 2732.7 ± 1050.5 mg/day, respectively. Table and cooking salt were the main sources of Na. Odds ratio (OR) (95% confidence interval (CI)) of the crude model in the highest quartile of UNa indicated a significant association with the higher risk of prehypertension (OR (95% CI): 2.09 (1.09–4.05); *P* for trend = 0.007). After adjustment for potential confounders, prehypertension was significantly associated with increasing dietary Na/K ratio (OR (95% CI): 1.28 (1.01–1.57); *P* for trend = 0.046) and UNa/UK ratio (OR (95% CI): 2.15(1.08-4.55); *P* for trend = 0.029).

Conclusions: Increasing dietary and urinary Na/K ratios and UNa were associated with elevated BP and prehypertension occurrence. These findings support the necessity of developing a salt reduction programme in our country.

Key words: blood pressure, diet, urine, Iran, potassium, sodium.

Introduction

Hypertension is a major public health issue affecting almost one quarter of adults worldwide. Its prevalence is on a rapid rise in developing countries[1] and has reached 17.3% among Iranian adult population.[2] Hypertension control has, hence, turned into a global public health priority.[3] Dietary modifications may regulate blood pressure (BP) and subsequently control hypertension.[4] Among dietary factors, high sodium (Na) and low potassium (K) intakes are associated with higher BP[5] and have been reported to increase overall mortality and the risk of cardiovascular diseases in the American population.[6] Na reduction may thus be the most cost-effective approach to hypertension control in both low- and high-income countries.[7] Although several epidemiological and interventional studies have shown BP to be independently associated with Na and K levels,[8,9] a population-based study rejected the relationship between K levels and BP.[8] However, two recent meta-analyses on 22 randomised clinical trials (RCTs) and population-based studies in 21 countries reported an inverse relationship between K levels and BP.[10,11] While most studies have

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measured Na and K intake through dietary assessment methods, such as 24-hour dietary recall or semi-quantitative food frequency questionnaire (FFQ), evaluating the urinary excretion of Na and K using 24-hour urine collection is still considered the most valid and reliable method to determine daily intake of these two elements.[12] Furthermore, population-based studies have failed to establish obvious relationships between Na and K levels and hypertension. Because of the ongoing debate over these relationships,[13,14] especially in Eastern Mediterranean and Middle East regions, the present study aimed to evaluate the associations between dietary Na and K intake and BP using data from the Isfahan salt study in 2013–2014.[15]

Methods

The present study was performed on healthy adults aged >18 years in Isfahan city, Iran in 2013–2014. In order to select the participants using multi-stage cluster sampling, a number of households were first selected, and the study objectives and procedures were explained to them. One adult from each household was then recruited. Sample size was determined according to a previous study,[15] and a total of 796 healthy individuals were enrolled. While the only inclusion criteria was age greater than 18 years, the exclusion criteria were a history of diabetes insipidus, diabetes mellitus, hypertension, a special dietary regimen or fasting at the time of sampling, history of using diuretics, renal insufficiency, menstruation or pregnancy and excessive sweating on the day of urine collection. In addition, we excluded the participants with less than 500 mL urine/day, reporting more than one missed voiding. Male and female subjects who were younger than 50 years with 24-hour urine creatinine (UCr) to body weight ratios of less than 20 and 15 mg/kg/day, respectively, along with those who were aged 50 years and over with UCr to body weight ratios of less than 10 and 7.5 mg/kg/day, respectively. The study was approved by the Research Council of Isfahan Cardiovascular Research Centre (ICRC), a World Health Organization (WHO) collaborative centre, ethics committee. Written informed consent was obtained from all participants. This paper was prepared based on the strengthening the reporting of observational studies in epidemiology (STROBE) statement for cross-sectional studies.

The medical history of all subjects was taken, and clinical examinations followed by blood and urine tests were performed. Height and weight were measured using standard methods. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). BP was measured manually by a trained operator using a mercury sphygmomanometer according to standard protocol,[16] twice from right and left arms in sitting position after five minutes of rest. We kept the BP measurement environment silent to hear Korotkoff sound. The first Korotkoff sound was recorded as the systolic blood pressure (SBP), and the disappearance of the sounds (V phase) was considered the diastolic blood pressure (DBP). The mean of the two BP readings on the arm with higher BP was used in the analyses. According to the Joint National Committee7 (JNC7) and WHO guidelines, prehypertension was defined as an SBP of 130–139 mmHg and/or a DBP of 80–89 mmHg.[1]

Dietary assessment was carried out by a 136-item semi-quantitative FFQ. The FFQ was validated against the gold standards of 24-hour urine samples and 12-monthly 24-hour dietary recalls in 113 participants. The FFQ was also recompleted with a one-year interval to examine its reproducibility. The criterion validity and reproducibility were presented by correlation and intra-class correlation coefficients, respectively. The criterion validity of FFQ for assessment of Na and K was 0.60 and 0.56 compared with 24-hour dietary recall and 0.31 and 0.38 against 24-hour urine Na and K excretions, respectively. The reproducibility was 0.43 and 0.40 for Na and K intake, respectively. The FFQ was coded by giving a gram weight to every portion reported. All dietary data were entered into the Iranian Food Consumption Program (IFCP), designed by ICRC,[17] and analysed. The IFCP calculated nutrient intake and food group servings for all foods reported in the FFQ. It had a research quality nutrient database analysing Na and K for a variety of food items using the Iranian Food Composition Table,[18] which was modified based on the US Department of Agriculture National Nutrient Database. Trained nutritionists assisted in the design and validation of the dietary questionnaire. The FFQ included some questions about dietary supplements and five questions regarding discretionary salt consumption, including salt used at the table and salt for food preparation at home. The salt intake questions comprised using the salt shaker, the weight of the salt package that they usually use, how long before the salt package was consumed, the total number of family members and their age to estimate salt consumption by each participant.

Urine samples were collected from 7 a.m. to 7 a.m. the next day (after excluding the first sample of the first day). The samples were poured into sterile plastic containers labelled with the participants' name and a special code. Inappropriately collected samples along with those with a low volume of urine were excluded from the analysis. If a person was unable to deliver the urine sample to the laboratory, we collected it at his/her home. Venous blood samples were taken on the same day to measure serum biochemical indices, including fasting blood sugar, serum albumin level and lipid profile. Total 24-hour urinary Na (UNa) was calculated by multiplying Na concentration by the urine volume in litres. Urinary chemical parameters including UNa, 24-hour urinary K (UK) and 24-hour UCr were measured. In order to assess the accuracy of urinary samples as 24-hour specimens, we measured the concentration of UCr using Jaffe method (technical SMA 12-60).

Categorical variables were presented as frequencies, mean and standard deviations were used to summarise the values of continuous variables. As our data were fairly complete, a simple approach (i.e. complete-case) was adopted to handle missing data. Chi-square and Student's *t*-tests were used to compare baseline characteristics between normotensive and prehypertensive participants. As the percentage of food contribution in Na intake was not normally

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distributed, we utilised a Mann–Whitney *U* test to compare the two groups. An analysis of variance (ANOVA) test was applied to compare the mean of normally distributed variables. In cases where the data did not have a normal distribution, Kruskal–Wallis tests in UNa, UK and UNa/UK ratio quartiles were used.

Hierarchical logistic regression was used to determine effect sizes according to different categories of confounders. In fact, simple logistic regression was first fitted to evaluate the crude relationships between prehypertension and the quartiles of dietary and urinary Na, K and Na/K ratio. Multiple logistic regression was then applied to find the adjusted associations, considering the reference category as those at the first quartile. The initial adjusted model was defined to comprise age and gender as covariates (Model 1). We fitted Model 2 to assess additional adjustment for BMI (kg/m^2). The confounder effect of 24-hour UCr (mg/day) was additionally adjusted in Model 3. Using the median of dietary and urinary Na, K and Na/K ratio in each quartile in the logistic models, the trend of odds ratios (ORs) were evaluated by finding the P values for each trend. Statistical analyses were performed using SPSS for windows 18.0 (SPSS Inc, Chicago, IL, USA). The significance level was set at $P < 0.05$.

Results

The study sample included 796 individuals (349 men and 447 women). As Table 1 shows, the mean Na and K dietary intake and Na/K ratios in all participants were 4309.6 ± 1344.4, 2732.7 ± 1050.5 mg/day and 1.6 ± 0.8, respectively. The mean 24-hour UNa, UK and UNa/UK ratios in the whole population were 4069.6 ± 1655.3, 2242.9 ± 1636.5 mg/day and 1.8 ± 1.0, respectively. Normotensive and prehypertensive participants had no significant differences in the mean dietary and urinary Na, K and Na/K ratio ($P > 0.05$). However, the mean age, SBP, DBP, BMI (all $P < 0.001$) and UCr ($P = 0.003$) were significantly higher in prehypertensive subjects than in normotensive participants. Moreover, prehypertension was marginally significant more frequently in men than in women ($P = 0.05$). Normotensive and prehypertensive participants had non-significant differences in terms of nuts and seeds, fruits and vegetables, fast food, dairy products, canned food, salty snacks, processed meat, sweats and soft drinks ($P > 0.05$); however, only grain consumption was significantly more in prehypertensive *versus* normotensive ($P = 0.040$).

The main sources of Na intake were table and cooking salt, grains, cheese, fruits and vegetables, other dairy products, meats, fast foods, sweets and soft drinks, salty snacks, canned foods and nuts and seeds (Table 2). There was a non-significant difference between sources of Na intake in normotensive and prehypertensive participants ($P > 0.05$). The mean SBP and DBP were not significantly related with urinary and dietary Na and K levels ($P > 0.05$) (Table 3). However, SBP and DBP significantly increased with higher dietary Na/K ratio ($P = 0.006$ and 0.039, respectively) and UNa/UK ratio ($P < 0.001$ and 0.003, respectively).

According to the obtained ORs (95% confidence interval (CI)) for the crude and adjusted models, there were no

Table 1 Basic characteristics of participants according to blood pressure

	Total	*Normotensive*	*Prehypertensive*	P-*value*[(a)]
Age (years)	38.9 ± 11.4	37.8 ± 11.0	43.6 ± 11.7	<0.001
Gender (male) (%)	349 (43.3)	309 (42.2)	40 (54.1)	0.050
Dietary sodium (mg/day)	4309.6 ± 1344.4	4309.9 ± 1366.9	4308.2 ± 1240.6	0.989
Dietary potassium (mg/day)	2732.7 ± 1050.5	2710.8 ± 1049.0	2832.6 ± 1055.2	0.208
Dietary sodium to potassium ratio	1.6 ± 0.8	1.6 ± 0.9	1.5 ± 0.8	0.409
24-hour urine sodium (mg/day)	4069.6 ± 1655.3	4070.6 ± 1684.4	4065.3 ± 1521.1	0.973
24-hour urine potassium (mg/day)	2242.9 ± 1636.5	2202.7 ± 1609.7	2125.8 ± 1547.6	0.335
24-hour urine sodium to potassium ratio	1.8 ± 1.0	1.8 ± 1.0	1.9 ± 0.9	0.264
Systolic blood pressure (mmHg)	112.0 ± 10.9	108.9 ± 8.5	126.2 ± 9.2	<0.001
Diastolic blood pressure (mmHg)	70.8 ± 8.7	68.1 ± 6.5	83.5 ± 5.7	<0.001
Body mass index (kg/m^2)	25.7 ± 4.4	25.4 ± 4.5	28.4 ± 4.5	<0.001
24-hour urine creatinine (mg/day)	1611.8 ± 555.4	1585.32 ± 557.4	1732.5 ± 531.6	0.003
Dietary intake (g/day):				
Grains	358.6 ± 132.1	353.0 ± 150.6	374.6 ± 157.4	0.040
Nuts and seeds	7.6 ± 10.2	7.6 ± 7.9	7.2 ± 9.5	0.675
Fruits and vegetables	298.2 ± 165.1	294.8 ± 186.5	314.3 ± 141.5	0.151
Fast food	33.9 ± 30.5	33.8 ± 30.9	34.5 ± 29.7	0.176
Dairy products	362.0 ± 218.9	356.5 ± 211.3	387.3 ± 250.1	0.171
Canned food	7.3 ± 10.2	7.5 ± 10.3	6.6 ± 8.3	0.483
Salty snacks	5.1 ± 4.2	5.4 ± 4.5	3.7 ± 7.6	0.064
Processed meat	8.9 ± 6.7	8.9 ± 7.0	8.7 ± 6.9	0.231
Sweats and soft drinks	138.1 ± 114.2	139.0 ± 119.2	136.3 ± 126.6	0.623

[(a)] *P*-value: comparison between normotensive and prehypertensive participants.

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Table 2 Food contribution in sodium intake according to blood pressure

Food item (%)	*Total*	*Normotensive*	*Prehypertensive*	P-*value*[(a)]
Salt at table and preparing food	48.8 ± 14.1	49.1 ± 13.9	48.4 ± 14.9	0.594
Grains	18.1 ± 7.8	18.1 ± 7.9	18.3 ± 7.7	0.723
Cheese	8.8 ± 6.2	8.5 ± 5.9	9.2 ± 7.3	0.327
Fruits and vegetables	7.3 ± 3.5	7.3 ± 3.9	8.7 ± 7.9	0.867
Other dairy products	6.1 ± 3.8	6.1 ± 3.7	6.5 ± 4.1	0.258
Meats	3.8 ± 2.5	3.8 ± 2.6	3.7 ± 2.0	0.739
Fast food	2.1 ± 3.1	2.1 ± 3.1	2.1 ± 3.0	0.857
Sweats and soft drinks	1.6 ± 1.8	1.6 ± 1.9	1.5 ± 1.7	0.316
Salty snacks	0.8 ± 1.4	0.8 ± 1.4	0.6 ± 1.2	0.143
Canned food	0.5 ± 1.0	0.5 ± 1.0	0.5 ± 0.9	0.873
Nuts and seeds	0.1 ± 0.4	0.1 ± .0.4	0.1 ± 0.5	0.416
Others	1.5 ± 1.9	1.9 ± 1.9	1.0 ± 1.2	0.129

[(a)] *P*-value: comparison between normotensive and prehypertensive participants by the Mann–Whitney *U* test.

significant relationships between dietary Na and K levels and Na/K ratio except for the OR (95% CI) of the highest quartile of dietary Na/K ratio against reference in the fully adjusted model (OR (95% CI): 1.28 (1.01–1.57); *P* for trend = 0.046) (Table 4).

As seen in Table 5, OR (95% CI) of the crude model in the highest quartile of UNa indicated a significant association with the higher risk of prehypertension (OR (95% CI): 2.09 (1.09–4.05); *P* for trend = 0.007). The OR increased in Model 1 with adjustment for age and gender (OR (95% CI): 2.35 (1.17–4.71); *P* for trend = 0.005). The ORs in Model 2 with additional adjustment for BMI and Model 3 with additional adjustment for UCr were not significantly related to UNa levels in the second, third and fourth quartiles compared to the first quartile. However, the trend of ORs in these models showed a significant increase (*P* for tend = 0.033 and 0.045, respectively). Nevertheless, there were non-significant associations between prehypertension and UK in the crude and multivariate models (Table 5). The OR of prehypertension was not significantly associated with the UNa/UK ratio in the crude model and the model adjusted for age and gender (model 1). In contrast, the OR (95% CI) of UNa/UK ratio in the Model 2 with additional adjustment for BMI was significantly associated with a higher risk of prehypertension in the highest quartile of the UNa/UK ratio (OR (95% CI): 2.14(1.01–4.55); *P* for trend = 0.030). Similar results were seen in Model 3 with additional adjustment for UCr (OR (95% CI): 2.15 (1.08–4.55); *P* for trend = 0.029) (Table 5).

Discussion

There was a significant positive association between dietary Na/K ratio and prehypertension in the fully adjusted model. The present study also showed significant positive

Table 3 Mean blood pressures based on quartiles of dietary and urinary sodium, potassium and sodium to potassium ratio

	Q1	*Q2*	*Q3*	*Q4*	P-*value*[(a)]
Quartile of sodium intake	<3270	3270–4083	4084–5256	>5256	
Systolic blood pressure (mmHg)	111.7 ± 10.6	112.7 ± 11.6	111.3 ± 10.9	112.3 ± 10.1	0.569
Diastolic blood pressure (mmHg)	70.8 ± 9.1	71.2 ± 8.7	70.4 ± 8.5	71.0 ± 8.3	0.233
Quartile of potassium intake	<2008	2008–2549	2550–3198	>3198	
Systolic blood pressure (mmHg)	111.8 ± 11.5	112.3 ± 9.8	111.1 ± 10.4	112.8 ± 11.6	0.344
Diastolic blood pressure (mmHg)	71.1 ± 9.3	69.9 ± 8.0	70.9 ± 8.6	71.5 ± 8.6	0.213
Quartile of sodium to potassium ratio intake	<1.22	1.22–1.59	1.60–2.03	>2.03	
Systolic blood pressure (mmHg)	109.8 ± 10.8	112.9 ± 10.9	112.0 ± 10.7	113.2 ± 10.4	0.006
Diastolic blood pressure (mmHg)	69.4 ± 9.4	71.4 ± 8.4	71.0 ± 8.7	71.6 ± 10.4	0.039
Quartile of urinary sodium	<2865	2865–3780	3781–5011	>5011	
Systolic blood pressure (mmHg)	112.9 ± 12.3	111.6 ± 11.1	111.6 ± 9.8	111.2 ± 10.4	0.594
Diastolic blood pressure (mmHg)	69.7 ± 8.1	70.9 ± 8.2	71.2 ± 9.1	71.3 ± 9.3	0.202
Quartile of urinary potassium	<1474	1474–2008	2009–2626	>2626	
Systolic blood pressure (mmHg)	112.9 ± 10.7	111.6 ± 10.8	112.7 ± 10.4	111.8 ± 11.9	0.341
Diastolic blood pressure (mmHg)	70.8 ± 8.2	69.5 ± 7.8	71.6 ± 8.7	71.0 ± 8.8	0.247
Quartile of urinary sodium to potassium ratio	<1.39	1.39–1.87	1.88–2.63	>2.63	
Systolic blood pressure (mmHg)	109.2 ± 11.0	112.1 ± 10.6	112.6 ± 11.6	114.0 ± 9.8	<0.001
Diastolic blood pressure (mmHg)	69.2 ± 9.0	71.1 ± 7.8	70.7 ± 8.7	72.4 ± 7.9	0.003

[(a)] *P*-value: for parametric analysis, ANOVA test and for nonparametric analysis, Kruskal–Wallis test was used.

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Table 4 Odds ratios (95% CI) of prehypertension based on quartiles of dietary sodium, potassium and sodium to potassium ratio

					P *for trend*
Quartiles of sodium intake					
Crude model	1	1.29 (0.76–2.20)	1.66 (0.99–2.79)	1.21 (0.70–2.07)	0.052
Model 1[(a)]	1	1.21 (0.69–2.12)	1.50 (0.87–2.60)	1.13 (0.64–1.99)	0.105
Model 2[(b)]	1	1.21 (0.69–2.13)	1.50 (0.87–2.60)	1.13 (0.64–1.99)	0.112
Model 3[(c)]	1	1.17 (0.66–2.05)	1.48 (0.85–2.56)	1.11 (0.63–1.97)	0.115
Quartiles of potassium intake					
Crude model	1	0.75 (0.45–1.23)	0.87 (0.52–1.40)	0.79 (0.35–1.12)	0.161
Model 1[(a)]	1	0.79 (0.46–1.33)	0.85 (0.51–1.43)	0.76 (0.32–1.09)	0.129
Model 2[(b)]	1	0.78 (0.46–1.33)	0.85 (0.51–1.43)	0.76 (0.32–1.08)	0.125
Model 3[(c)]	1	0.78 (0.46–1.32)	0.87 (0.52–1.47)	0.77 (0.33–1.09)	0.131
Quartile of sodium to potassium ratio intake					
Crude model	1	1.18 (0.91–1.50)	1.13 (0.89–1.46)	1.19 (0.94–1.51)	0.123
Model 1[(a)]	1	1.20 (0.92–1.53)	1.15 (0.88–1.45)	1.22 (0.95–1.53)	0.116
Model 2[(b)]	1	1.24 (0.95–1.54)	1.21(0.92–1.51)	1.25 (0.97–1.56)	0.105
Model 3[(c)]	1	1.26 (0.97–1.56)	1.23 (0.95–1.52)	1.28 (1.01–1.57)	0.046

[(a)] Model 1: adjustment for age and gender.
[(b)] Model 2: additional adjustment for body mass index.
[(c)] Model 3: additional adjustment for 24-hour urinary creatinine.

Table 5 Odds ratios (95% CI) of prehypertension based on quartiles of urinary sodium, potassium and sodium to potassium ratio

					P *for trend*
Quartiles of sodium					
Crude model	1	0.79(0.36–1.73)	1.20(0.59–2.45)	2.09(1.09–4.05)	0.007
Model 1[(a)]	1	0.89(0.39–1.99)	1.25(0.59–2.65)	2.35(1.17–4.71)	0.005
Model 2[(b)]	1	0.89(0.38–2.04)	1.15(0.52–2.56)	1.98(0.94–4.16)	0.033
Model 3[(c)]	1	0.85(0.37–1.96)	1.12(0.50–2.49)	1.89(0.89–3.97)	0.045
Quartiles of potassium					
Crude model	1	1.01(0.51–2.03)	0.88(0.43–1.82)	1.39(0.73–2.69)	0.318
Model 1[(a)]	1	0.82(0.40–1.69)	0.70(0.33–1.50)	1.11(0.56–2.18)	0.683
Model 2[(b)]	1	0.64(0.30–1.37)	0.49(0.22–1.12)	0.74(0.35–1.55)	0.564
Model 3[(c)]	1	0.63(0.29–1.37)	0.47(0.21–1.07)	0.68(0.32–1.46)	0.440
Quartile of sodium to potassium ratio					
Crude model	1	0.99(0.48–2.05)	1.19(0.59–2.39)	1.49(0.76–2.93)	0.176
Model 1[(a)]	1	1.04(0.49–2.21)	1.35(0.66–2.79)	1.87(0.93–3.77)	0.051
Model 2[(b)]	1	1.02(0.46–2.25)	1.33(0.63–2.80)	2.14(1.01–4.55)	0.030
Model 3[(c)]	1	1.00(0.45–2.21)	1.31(0.62–2.77)	2.15(1.08–4.55)	0.029

[(a)] Model 1: adjustment for age and gender.
[(b)] Model 2: additional adjustment for body mass index.
[(c)] Model 3: additional adjustment for 24-hour urinary creatinine.

relationships of BP with both UNa and UNa/UK ratio, which are a proxy for unhealthy diet after adjustment for potential confounders such as age, gender, BMI and UCr. However, there was no significant association between K and BP. Moreover, SBP and DBP significantly increased with increasing dietary and urinary Na/K ratios.

Similar to our findings, large-scale observational studies such as INTERSALT,[19] European Prospective Investigation into Cancer in Norfolk[20] and Prospective Urban Rural Epidemiological Study, as well as some recent meta-analyses of RCTs, illustrated a positive relationship between Na and BP that was greater in hypertensive than normotensive populations.[22–26] Other population-based studies reported that reducing Na intake could reduce BP in both hypertensive and normotensive adults.[11,27,28]

The evidence regarding the association between K intake and BP is inconsistent. Contrary to our findings, several epidemiological and clinical trials indicated an inverse relationship between dietary K intake and BP.[20,27–29] The INTERSALT study showed a negative association between UK and BP in a large population from around the world.[20] Several double-blind RCTs reported that reducing K intake increased BP in both hypertensive and normotensive participants.[20,27–29] Moreover, Siani *et al*. concluded that a

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high-K diet decreased the need for antihypertensive medications in patients with normal renal function.[30]

Appel *et al*. suggested that the high natural K content of fruits and vegetables in combination with low Na intake, according to the Dietary Approach to Stop Hypertension (DASH), reduced SBP and DBP in both hypertensive and normotensive participants.[31] However, the exact role of K in the beneficial effects of DASH cannot be determined as the antioxidant content of fruits and vegetables might actually be responsible for BP reduction.[32] Nevertheless, a recent meta-analysis incorporating 22 RCTs reported that a K supplement reduced BP only in adults with primary hypertension.[10] One former meta-analysis including 33 RCTs found that the beneficial effect of dietary K supplementation on SBP and DBP remained in participants with high salt intake.[33] Therefore, K supplementation can be recommended as an appropriate strategy to decrease BP in hypertensive patients who cannot reduce their salt intake.[31] In fact, K intake can, to some extent, blunt the undesirable effects of high Na intake.[34]

However, a systematic review on six RCTs confirmed our findings and indicated that dietary K supplementation had no significant effects on SBP and DBP.[35]

Several potential reasons, including various polymorphisms in some relevant genes and maternal hypertension history, may lead to different reactions of persons to dietary K intake.[36,37] Furthermore, in most previous studies, few participants had stage II hypertension. In the present study, however, no individuals with mild hypertension (SBP and DBP of 140–159 and 90–99 mmHg, respectively) were included. Finally, using the most valid biomarker of Na and K intake in the present study has probably increased the accuracy of our estimations compared to those in previous studies.

Consistent with the findings of previous studies,[14,38,39] the present study showed the incidence of prehypertension to be more strongly related with the UNa/K ratio than with either UNa or UK alone. We found that the OR of prehypertension occurrence was more than doubled in the highest quintile of the UNa/K ratio compared to its lowest quintile. Likewise, the National Health and Nutrition Examination Survey (2001–2006) and another population-based study reported that while the combination of Na and K had a positive relationship with the risk of elevated BP, no such relationships were present in case of Na and K alone.[14,39]

The average Na intake in the present study (167 mEq/day) was about two times higher than the 88 mEq/day (2000 mg/day) recommended by the WHO.[40] Moreover, the average K intake (63 mEq/day) among our participants was slightly lower than the recommended amount (2700–3100 mg/day).[40]

In the present study, the dietary Na/K ratio were 1.6 and 1.5 in normotensive and prehypertensive subjects and UNa/UK ratios were 1.8 and 1.9 in normotensive and prehypertensive participants, respectively. This ratio was 1.65 in the North American population[6] and 1.79 in Brazilian adults.[34] However, much lower values (about 0.06) were reported in the past decades.[41] Therefore, changes in dietary habits along with the adoption of the Western diet, including refined and processed foods, provide huge amounts of salt consumption and decreased their dietary K intake. Such changes will undoubtedly exert adverse health effects.[42,43] High Na intake may not only thicken and narrow the resistance arteries but also inhibit nitric oxide production and release sympathetic systems. These mechanisms will raise BP and lead to the development of hypertension.[44] While the mechanism through which K intake decreases BP is still unclear, induction of nitric oxide synthesis by increasing intracellular K content might be responsible for this effect.[44]

The strengths of the present study were using 24-hour urine collection as the standard approach for the measurement of Na and K intake. To the best of our knowledge, this was the first study in Iran and the Middle East to examine the associations of BP with not only Na and K intake but also 24-hour UNa and UK, which surrogate Na and K intakes in subjects without a diagnosis of hypertension.

As urine samples of a particular day may not accurately reflect one's usual dietary habits, collecting urine samples on a single day can be regarded as a limitation of the current research. Moreover, because of its cross-sectional design, the present study might have been unable to clarify the causality effect.

In conclusion, this population-based cross-sectional study showed elevated BP and prehypertension to be significantly related with increased dietary Na/K ratio, UNa and UNa/K ratio, which can be considered to be surrogates of an unhealthy diet. However, we failed to find significant relationships between BP and dietary Na, K and UK alone. Further clinical trials are thus warranted to investigate the causality effects of dietary Na and K intake on BP. Our findings supported the need for the development of a salt reduction programme in Iran.

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Conflict of interest

The authors have no conflicts of interest to declare.

Authorship

AKH contributed to drafting the article and final approval of the version to be published; ARKH contributed to study concept and design and interpretation of data; NM contributed to study concept and design, interpretation of data, drafting the article data, analysis and interpretation of data and revising content; FN and AF contributed to the analysis and interpretation of data and revising content; AE, JG and NS contributed to study concept and design and revising critically. All authors read and approved the final manuscript.

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References

1 Chobanian AV, Bakris GL, Black HR *et al.* Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 2003; **42**: 120612–52.

2 Shirani S, Kelishadi R, Sarrafzadegan N *et al.* Awareness, treatment and control of hypertension, dyslipidaemia and diabetes mellitus in an Iranian population: the IHHP study. *East Mediterr Health J* 2009; **15**: 1455–63.

3 Perkovic V, Huxley R, Wu Y, Prabhakaran D, MacMahon S. The burden of blood pressure-related disease: a neglected priority for global health. *Hypertension* 2007; **50**: 991–7.

4 Bazzano LA, Green T, Harrison TN, Reynolds K. Dietary approaches to prevent hypertension. *Curr Hypertens Rep* 2013; **15**: 694–702.

5 Elliott P, Walker LL, Little MP *et al.* Change in salt intake affects blood pressure of chimpanzees: implications for human populations. *Circulation* 2007; **116**: 1563–8.

6 Yang Q, Liu T, Kuklina EV *et al.* Sodium and potassium intake and mortality among US adults: prospective data from the Third National Health and Nutrition Examination Survey. *Arch Intern Med* 2011; **171**: 1183–91.

7 Smith-Spangler CM, Juusola JL, Enns EA, Owens DK, Garber AM. Population strategies to decrease sodium intake and the burden of cardiovascular disease: a cost-effectiveness analysis. *Ann Intern Med* 2010; **152**: 481–7.

8 Geleijnse JM, Kok FJ, Grobbee DE. Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomised trials. *J Hum Hypertens* 2003; **17**: 471–80.

9 Gu D, Rice T, Wang S *et al.* Heritability of blood pressure responses to dietary sodium and potassium intake in a Chinese population. *Hypertension* 2007; **50**: 116–22.

10 Aburto NJ, Hanson S, Gutierrez H, Hooper L, Elliott P, Cappuccio FP. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. *BMJ* 2013; **346**: f1378.

11 van Mierlo LA, Greyling A, Zock PL, Kok FJ, Geleijnse JM. Suboptimal potassium intake and potential impact on population blood pressure. *Arch Intern Med* 2010; **170**: 1501–2.

12 Brown IJ, Tzoulaki I, Candeias V, Elliott P. Salt intakes around the world: implications for public health. *Int J Epidemiol* 2009; **38**: 791–813.

13 Weir MR, Fink JC. Salt intake and progression of chronic kidney disease: an overlooked modifiable exposure? A commentary. *Am J Kidney Dis* 2005; **45**: 176–88.

14 Sharma S, McFann K, Chonchol M, Kendrick J. Dietary sodium and potassium intake is not associated with elevated blood pressure in US adults with no prior history of hypertension. *J Clin Hypertens (Greenwich)* 2014; **16**: 418–23.

15 Haghighatdoost F, Sarrafzadegan N, Khosravi A *et al.* Is the association between salt intake and blood pressure mediated by body mass index and central adiposity? *Arch Iran Med* 2013; **16**: 167–71.

16 Frese EM, Fick A, Sadowsky HS. Blood pressure measurement guidelines for physical therapists. *Cardiopulm Phys Ther J* 2011; **22**: 5–12.

17 Touyz RM, Campbell N, Logan A, Gledhill N, Petrella R, Padwal R. The 2004 Canadian recommendations for the management of hypertension: Part III – lifestyle modifications to prevent and control hypertension. *Can J Cardiol* 2004; **20**: 55–9.

18 Rafiei M, Boshtam M, Marandi A, Jalali A, Vakili R. The Iranian Food Consumption Program (IFCP), A unique nutritional sotware in Iran. *Iran J Publ Health* 2002; **31**: 105–7.

19 Dorosti Motlagh AR, Tabatabaei M. *Iranian Food Composition Table*, 1st edn. Tehran, Iran: Donyaye Taghzie Press, 2007.

20 Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. Intersalt Cooperative Research Group. *BMJ* 1988; **297**: 319–28.

21 Khaw KT, Bingham S, Welch A *et al.* Blood pressure and urinary sodium in men and women: the Norfolk Cohort of the European Prospective Investigation into Cancer (EPIC-Norfolk). *Am J Clin Nutr* 2004; **80**: 1397–403.

22 Mente A, O'Donnell MJ, Rangarajan S *et al.* Association of urinary sodium and potassium excretion with blood pressure. *N Engl J Med.* 2014; **371**: 601–11.

23 Aburto NJ, Ziolkovska A, Hooper L, Elliott P, Cappuccio FP, Meerpohl JJ. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ* 2013; **346**: f1326.

24 Graudal NA, Hubeck-Graudal T, Jurgens G. Effects of low-sodium diet *vs*. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). *Am J Hypertens* 2012; **25**: 1–15.

25 He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: cochrane systematic review and meta-analysis of randomised trials. *BMJ* 2013; **346**: f1325.

26 Mozaffarian D, Fahimi S, Singh GM *et al.* Global sodium consumption and death from cardiovascular causes. *N Engl J Med* 2014; **371**: 624–34.

27 Centers for Disease Control and Prevention (CDC). Application of lower sodium intake recommendations to adults – United States, 1999-2006. *MMWR Morb Mortal Wkly Rep* 2009; **58**: 281–3.

28 Donfrancesco C, Ippolito R, Lo Noce C *et al.* Excess dietary sodium and inadequate potassium intake in Italy: results of the MINISAL study. *Nutr Metab Cardiovasc Dis* 2013; **23**: 850–56.

29 Krishna GG, Kapoor SC. Potassium depletion exacerbates essential hypertension. *Ann Intern Med* 1991; **115**: 77–83.

30 Siani A, Strazzullo P, Giacco A, Pacioni D, Celentano E, Mancini M. Increasing the dietary potassium intake reduces the need for antihypertensive medication. *Ann Intern Med* 1991; **115**: 753–9.

31 Appel LJ, Moore TJ, Obarzanek E *et al.* A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med* 1997; **336**: 1117–24.

32 Sacks FM, Svetkey LP, Vollmer WM *et al.* Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med* 2001; **344**: 3–10.

33 Whelton PK, He J, Cutler JA *et al.* Effects of oral potassium on blood pressure. Meta-analysis of randomised controlled clinical trials. *JAMA* 1997; **277**: 1624–32.

34 Rodrigues SL, Baldo MP, Machado RC, Forechi L, Molina Mdel C, Mill JG. High potassium intake blunts the effect of elevated sodium intake on blood pressure levels. *J Am Soc Hypertens* 2014; **8**: 232–8.

35 Dickinson HO, Nicolson DJ, Campbell F, Beyer FR, Mason J. Potassium supplementation for the management of primary hypertension in adults. *Cochrane Database Syst Rev* 2006: CD004641.

36 Kelly TN, Gu D, Rao DC *et al.* Maternal history of hypertension and blood pressure response to potassium intake: the GenSalt study. *Am J Epidemiol* 2012; **176**: S55–63.

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37 Kanbay M, Bayram Y, Solak Y, Sanders PW. Dietary potassium: a key mediator of the cardiovascular response to dietary sodium chloride. *J Am Soc Hypertens* 2013; **7**: 395–400.
38 Du S, Batis C, Wang H, Zhang B, Zhang J, Popkin BM. Understanding the patterns and trends of sodium intake, potassium intake, and sodium to potassium ratio and their effect on hypertension in China. *Am J Clin Nutr* 2014; **99**: 334–43.
39 Campagnoli T, Gonzalez L, Santa CF. Salt intake and blood pressure in the University of Asuncion-Paraguay youths: a preliminary study. *J Bras Nefrol* 2012; **34**: 361–8.
40 Who J, Consultation FE. Diet, nutrition and the prevention of chronic diseases: report of a Joint WHO/FAO Expert Consultation. *World Health Organ Tech Rep Ser* 2003; **916**: 1–149, backcover.
41 Eaton SB, Konner M. Paleolithic nutrition. A consideration of its nature and current implications. *N Engl J Med* 1985; **312**: 283–9.
42 Cook NR, Cutler JA, Obarzanek E *et al.* Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ* 2007; **334**: 885–8.
43 Strazzullo P, D'Elia L, Kandala NB, Cappuccio FP. Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. *BMJ* 2009; **339**: b4567.
44 Adrogue HJ, Madias NE. Sodium and potassium in the pathogenesis of hypertension. *N Engl J Med* 2007; **356**: 1966–78.

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