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Association of dietary calcium, magnesium, sodium, and potassium intake and hypertension: a study on an 8-year dietary intake data from the National Health and Nutrition Examination Survey

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ABSTRACT

BACKGROUND/OBJECTIVES: There has been an increased interest in determining calcium magnesium, sodium, and potassium's distinct effects on hypertension over the past decade, yet they simultaneously regulate blood pressure. We aimed at examining the association of dietary calcium, magnesium, sodium, and potassium independently and jointly with hypertension using National Health and Nutrition Examination Survey data from 2007 to 2014.

MATERIALS/METHODS: The associations were examined on a large cross-sectional study involving 16684 US adults aged >20 years, using multivariate analyses with logistical models.

RESULTS: Sodium and calcium quartiles assessed alone were not associated with hypertension. Potassium was negatively associated with hypertension in the highest quartile, 0.64 (95% confidence interval [CI], 0.48–0.87). When jointly assessed using the high and low cut-off points, low sodium and corresponding high calcium, magnesium, and potassium intake somewhat reduced the odds of hypertension 0.39 (95% CI, 0.20–0.76). The sodium-to-potassium ratio was positively associated with hypertension in the highest quartile 1.50 (95% CI, 1.11–2.02). When potassium was adjusted for sodium intake and sodium-to-potassium ratio assessed among women, increased odds of hypertension were reported in the highest quartile as 2.02 (95% CI, 1.18–3.34) and 1.69 (95% CI, 1.12–2.57), respectively. The association of combined minerals on hypertension using dietary goals established that men meeting the reference intakes for calcium and exceeding for magnesium had reduced odds of hypertension 0.51 (95% CI, 0.30–0.89). Women exceeding the recommendations for both calcium and magnesium had the lower reduced odds of 0.30 (95% CI, 0.10–0.69).

CONCLUSIONS: Our results suggest that the studied minerals' association on hypertension is stronger when jointly assessed, mostly after gender stratification. As compared to men, women increased their risk of hypertension even with a low sodium intake. Women would

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Data Availability

The National Health and Nutrition Examination Survey (NHANES) data used to support the findings is a program of studies designed to assess the adult's and children's health and nutritional data and status from a representative sample of the non-institutionalized US population. The survey combines interviews and physical examinations. NHANES is a major program of the National Center for Health Statistics (NCHS), which is part of the Centers for Disease Control and Prevention (CDC) available from <https://www.cdc.gov/nchs/nhanes/Default.aspx>.

Conflict of Interest

The authors declare no potential conflicts of interest.

Authors Contributions

Conceptualization: Cheteu Wabo TM, Wu XY; Formal analysis: Cheteu Wabo TM, Boah M; Investigation: Cheteu Wabo TM, Ngo Nkondjock VR, Shah I; Methodology: Cheteu Wabo TM, Boah M; Supervision: Sun CH, Wu XY; Validation: Wu XY, Sun CH, Cheteu Wabo TM; Writing - original draft: Cheteu Wabo TM; Writing - review & editing: Cheteu Wabo TM, Wu XY, Sun CH, Boah M, Ngo Nkondjock VR, Kosgey Cheruiyot J, Amporfro Adjei D, Shah I.

also reasonably reduce their risk of developing hypertension by increasing calcium and magnesium intake. In comparison, men would somewhat be protected from developing hypertension with calcium intake meeting the dietary goals and magnesium exceeding the nutritional goals.

Keywords: Calcium-to-magnesium ratio; sodium-to-potassium ratio; hypertension; odds ratio; NHANES

INTRODUCTION

High blood pressure is a risk factor for cardiovascular disease, causing premature death worldwide for decades. It is called the "silent killer" because people often do not realize they have it until they suffer from a related condition [1]. Worldwide, 7.6 million premature deaths (about 13.5% of the total globally) and 92 million (6.0% of the total globally) of all Disability-adjusted life years (DALYs) were attributed to high blood pressure [2,3]. Its asymptomatic nature makes its prevalence likely to rise in the coming years. If nothing is done, by 2025, the number of individuals with hypertension will be as high as approximately 1.17 billion, representing almost three-fourths of the world's hypertension population [3,4]. Hypertension is the first and fourth leading cause of death in the United States and is responsible for at least 30% of deaths. According to the American Heart Association, 34% of American adults have hypertension, and more than 1 in 3 American adults have more than one type of cardiovascular disease [5]. Less than 25% of the hypertensives in the United States have their blood pressure under control [6], which indicates that high priority should be given to high blood pressure management.

The management of hypertension requires both pharmacological and non-pharmacological interventions. Non pharmacological interventions help to reduce the daily dose of anti-hypertensive drugs and delay progression from pre-hypertension to hypertension. When hypertension is confirmed, the first approach is lifestyle change before starting pharmacological therapy or in combination afterward [7]. As a first-line initiative in the diet approach to stop hypertension, reducing sodium intake to reduce blood pressure has long been an interest in public health research. Restriction of sodium consumption plays an essential role in lowering blood pressure [8-11]. Several experimental, clinical, and observational studies have explored the single effects of other micronutrients such as calcium, magnesium, and potassium on high blood pressure. The National Health and Nutrition Examination Survey (NHANES) 1988–1994 found a significant inverse association between the high level of magnesium intake and hypertension [12]. Park et al., [13], in a study on Korea National Health and Nutrition Examination Survey (KNHANES III), found calcium and potassium inversely associated with systolic blood pressure (SBP) and diastolic blood pressure (DBP) and did not associate sodium intake with SBP or DBP. Beydoun M.A et al. also found that a 100 mg/day decrease in Mg was associated with a reduced risk of hypertension [14]. The association between calcium and hypertension has been less compelling in the literature. However, A 16 trials review found that increasing calcium intake slightly reduces both systolic and diastolic blood pressure in normotensive people, particularly in young people, suggesting a role in preventing hypertension [15]. Kim et al. [16] found dietary calcium intake negatively associated with blood pressure. A large cross-sectional study in adult women found an inverse association between calcium and hypertension [17].

Dietary interventions have also demonstrated potassium's blood pressure-lowering properties in humans. A US based multi-centre randomized controlled trial showed that a high-potassium dietary intervention was associated with a significantly reduced mean of blood pressure [18]. A third meta-analysis reported that high potassium intake is inversely associated with blood pressure in hypertensive populations [19]. Nevertheless, controlling high blood pressure goes beyond a one-dimensional focus on a single micronutrient because they are all intimately related and collectively affect several metabolic functions in the body. For example, a potassium deficient diet promotes sodium retention, thus increases bloodstream leading to high blood pressure. When sodium becomes too high and potassium too low, bloodstream increases high blood pressure is one result. When dietary potassium is high, kidneys excrete more salt and water, increasing potassium excretion and reducing blood pressure [9,20]. Magnesium regulates calcium magnesium exchanges through the N-methyl-D-aspartate (NMDA) receptor. It stabilizes the membrane of the nerve fiber and makes it less excitable. Low magnesium levels increase intracellular calcium through NMDA resulting in hyperexcitability, hyper-muscular contractility, which leads to hypertension [21,22]. Therefore, using a single mineral to analyze the risk of developing hypertension may not accurately determine its actual risk.

Assessing each nutrient intake while considering others as potential confounders when modeling will undoubtedly avoid underestimating or overestimating their daily intake when estimating the risk of developing hypertension. Consequently, in this study, our goal was to evaluate the association between sodium, potassium, calcium, and magnesium individually and jointly using two ratios (Ca: Mg, Na: K), adjusting for each nutrient, as well as relevant cut-off points (Dietary references intakes levels, quartiles) and hypertension. Since the intake of the studied minerals is different across sex, we further examined the association between minerals intake and hypertension by sex. Additionally, we adjusted for potential confounding variables (age, sex, city, ethnicity, body mass index (BMI), physical activity, and other characteristics) using 8 years of NHANES data (2007–2014).

MATERIALS AND METHODS

Data source

Our data source is from the NHANES, a program of studies designed to assess adults' and children's health and nutritional data and status from a representative sample of the non-institutionalized US population. The survey combines interviews and physical examinations. NHANES is a major program of the National Center for Health Statistics (NCHS), part of the Centers for Disease Control and Prevention (CDC). The NHANES interview includes demographic, socioeconomic, dietary, and health-related questions [23].

A total of 22,833 adults men and non-pregnant women > 20 years of age participated in the mobile examination center (MEC) from 2007 to 2014. Were excluded from the study the following participants:

- Unreliable information on the first 24-hour dietary recall (2,403)
- Kidney diseases/dialysis patients/diabetes (638)
- Energy intake < 500 kcal/day (182) and > 4,500 kcal/day (243)
- Missing/incomplete BP values (536)
- Patients Taking hypertensive medications & patients with missing dietary intake data (2,147)

Our final data set used was 8,062 men, 8,622 women totaling 16,684 Participants.

Definition of the outcome

Our outcome was high blood pressure. We used the average of up to three blood pressure readings obtained under standard conditions during a single physical examination at the mobile examination center. We defined hypertension as an average of systolic blood pressure ≥ 140 mmHg and/or the average of diastolic blood pressure ≥ 90 mmHg [1]. Participants were classified as having hypertension if their systolic blood pressure, diastolic blood pressure, or both exceeded the above values. If they indicated a health care provider ever told them they had high blood pressure, and if they have not been told they have high blood pressure but were found to have a mean systolic blood pressure ≥ 140 mmHg and/or a mean diastolic blood pressure ≥ 90 mmHg [24]. Participants taking anti-hypertensive medications are not included in this study.

Covariates

Our study's covariates included age, gender, race/ethnicity (non-Hispanic white, non-Hispanic black, other Hispanic, Mexican-American, or others race); energy intake, BMI; educational level, smoking status (current smoker, former smoker, or never smoked); and heavy use of alcohol: defined as self-reported consumption of more than two drinks per day for men and more than one drink per day for women (heavy user or not heavy user) [25].

The 2018 Physical Activity Guideline for Americans recommendations for all adults was utilized as a basic assessment of physical activity. Throughout the Guidelines, reference is made to four levels of aerobic physical activity: inactive, insufficiently active, active, and highly active. In this study, we grouped them into three levels:

- Inactive or insufficiently active: is not getting any moderate- or vigorous- intense physical activity beyond basic movement from daily life activities or doing some moderate- or vigorous-intense physical activity but less than 150 minutes of moderate-intensity physical activity a week or 75 minutes of vigorous-intensity physical activity or the equivalent combination.
- Active is doing the equivalent of 150 minutes to 300 minutes of moderate-intensity physical activity a week. This level meets the key guideline target range for adults.
- Highly active is doing the equivalent of more than 300 minutes of moderate-intensity physical activity a week. This level exceeds the key guideline target range for adults.

Dietary and supplemental sodium, potassium, calcium, and magnesium intake measures

Data on dietary sodium, potassium, calcium, and magnesium intake were assessed using two days of 24-hour dietary recalls. The NHANES Day 2 dietary recall was collected by telephone approximately 3 to 10 days after the MEC exam. The US Department of Agriculture (USDA) Food and Nutrient Database for Diet Studies (FNDDS) assigned nutrients values to foods. We used the average total magnesium, calcium, sodium, and potassium nutrients intakes from the two days of 24-hour recalls. We also assessed magnesium, calcium, sodium, and potassium supplementation intake by including the use of antacids to measure daily supplemental intake of magnesium, calcium, sodium, and potassium. Total, sodium (mg/day), potassium (mg/day), calcium (mg/day) and magnesium (mg/day) intake variables for non-supplements users were calculated by summing the total daily intake from dietary. For supplements users, sodium, calcium, magnesium, and potassium intake was calculated, summing the total daily intake from diet, supplemental intake, and antacid sources.

Statistical analysis

Statistical analyses were completed on a calculated 8-year sample weight of the complex sample design of NHANES. The association between hypertension and each potential risk factor was assessed using chi-square (χ^2) tests for categorical variables and the Student's t-test for continuous variables. Blood pressure as a continuous variable was plotted against different dietary intakes to ascertain the linearity.

Because of the non-linearity of our variables of interest (minerals and blood pressure), we used magnesium, calcium, sodium, and potassium and their ratio (Ca: Mg, Na: K) quartiles to evaluate their associations with hypertension. Adjusted odds ratios (ORs) were estimated using multivariable logistic regression analysis comparing the high quartiles Q4, Q3, and Q2 to the lowest quartile Q1. We defined two multivariable models to independently examine the association between our outcomes and our independent variables. Respectively, we adjusted for age, sex, ethnicity, energy intake, family income, educational level, smoking status, physical activity, BMI as a continuous variable (model 1). Additionally, we adjusted for total magnesium (for the model including calcium quartiles), total calcium (for the model including magnesium quartiles), total sodium (for the model including potassium quartiles), or total potassium (for the model including sodium quartiles) for model 2. We also categorized calcium, magnesium, sodium, and potassium into “high” and “low” cut-off points using their highest (fourth) quartile and lowest three quartiles, respectively, for each nutrient. Thus, we defined few combinations according to high and low intake as follows: high sodium/high potassium, high sodium/low potassium, low sodium/high potassium, low sodium/low potassium dietary intake for sodium and potassium. Dietary calcium and magnesium combinations groups were: High calcium/high magnesium, high calcium/low magnesium, low calcium/high magnesium, low calcium/low magnesium intake. We then combined calcium, magnesium, sodium, and potassium using high low levels as follows: low calcium, low magnesium, low sodium, and low potassium; low calcium, low magnesium, low sodium, and high potassium; low calcium, low magnesium, high sodium, and low potassium; low calcium, low magnesium, high sodium, and high potassium; low calcium, high magnesium, low sodium, and low potassium; low calcium, high magnesium, low sodium, and high potassium; low calcium, high magnesium, high sodium, and low potassium; low calcium, high magnesium, high sodium, and high potassium; high calcium, high magnesium, low sodium, and low potassium; high calcium, high magnesium, low sodium, and high potassium; high calcium, high magnesium, high sodium, and low potassium; high calcium, high magnesium, high sodium, and high potassium.

Sodium, potassium, calcium, and magnesium intake were also examined based on the dietary recommendations for each nutrient (below dietary goals or meeting dietary goals or above dietary goals based on 2015–2020 Dietary Guidelines recommendations) [26] and the combinations of sodium and potassium, calcium and magnesium groups meeting, above or below the recommendations explored.

A 2-side *P*-value < 0.05 was regarded as an indication of statistical significance. All statistical analyses were conducted using STATA version 13.3.

Ethics statement/ethical considerations

NHANES III is approved by the NCHS Institutional Review Board (IRB), prior to the data collection, informed consent was obtained from participants. The NCHS IRB (after 2004)/ and the NCHS Research Ethics Review Board (ERB) (the year 2007 to 2010) approved the NHANES 2005 to 2006 (Protocol #2005-06 for the NHANES 2005 to 2010 and protocol #2011-17 for the NHANES 2011 to 2017) <https://wwwn.cdc.gov/nchs/nhanes/Default.aspx>.

RESULTS

General characteristics of the study population

The population consisted of 16,684 adults with an average age of approximately 60 years (SE \pm 0.22). More than half of the study population were female (51.68%). Almost half of the adults were non-Hispanic white (46.36%), non-Hispanic black 20.58%, and Mexican American 14.38%. The overall average dietary calcium, magnesium, sodium, and potassium intake and their ratios were 874.50 mg/day, 272.20 mg/day, 3,348.13 mg/day, 2,424 mg/day, 3.40, and 1.50, respectively. The percentages of hypertensive participants meeting the dietary goals were 15.44%, 16.91%, 27.32%, 2.61%, respectively, for calcium, magnesium, sodium, and potassium. Among them, only 14.68% of men and 13.02% of women met the recommendations for calcium intake, 20.39% of men and 11.42% of women met recommendations for magnesium intake, 20.47% of men, and 41.58% of women met the recommendations for sodium intake, only 3.94% of men and 0.65% of women met recommendations for potassium (**Table 1**).

The overall hypertension prevalence was 42.85%, in which 51.59% of females and 48.41% of males were more likely to be obese (49.20%). Hypertensive participants had the overall weighted lower calcium (792.87 mg/day), magnesium (260.06 mg/day), sodium (3,246.08

Table 1. Characteristics of participants by hypertension status

| Demographics | Hypertension | No hypertension | P-value |
|----------------------------------|---------------|-----------------|---------|
| Age | | | < 0.01 |
| Mean | 57.65 | 42.60 | |
| SE | 0.22 | 0.27 | |
| Sex | | | 0.32 |
| Male | 3,472 (48.41) | 4,590 (47.45) | |
| Female | 3,677 (51.59) | 4,945 (52.55) | |
| Ethnicity/race | | | < 0.01 |
| Mexican American | 806 (25.47) | 1,593 (9.53) | |
| Non-Hispanic white | 3,429 (39.35) | 4,305 (68.41) | |
| Non-Hispanic black | 1,846 (47.75) | 1,587 (8.97) | |
| Other Hispanic | 622 (28.97) | 1,030 (5.97) | |
| Other race | 446 (29.79) | 1,020 (7.11) | |
| Education level | | | < 0.01 |
| Less than 9th | 819 (6.29) | 797 (4.44) | |
| 9–11 grade | 1,125 (12.51) | 1,266 (10.13) | |
| High school diploma/GED | 1,791 (24.86) | 1,999 (20.38) | |
| Some college/associate | 2,040 (31.78) | 2,780 (30.29) | |
| College graduate or above | 1,367 (24.56) | 2,684 (34.75) | |
| Family income | | | < 0.01 |
| < \$20,000 | 1,860 (27.85) | 1,989 (15.82) | |
| \$20,000–\$44,999 | 2,147 (32.15) | 2,712 (25.51) | |
| \$45,000–\$64,999 | 921 (13.79) | 1,246 (15.62) | |
| > \$65,000 | 1,750 (26.20) | 2,931 (43.05) | |
| Smoking status | | | < 0.01 |
| Never smoked | 3,629 (50.56) | 5,550 (65.34) | |
| Current smoker | 1,282 (17.51) | 2,036 (20.18) | |
| Former smoker | 2,238 (31.94) | 1,948 (21.40) | |
| Alcohol consumption | | | < 0.01 |
| Mild consumption | 728 (16.17) | 857 (12.17) | |
| Heavy consumption | 3,464 (83.83) | 5,694 (87.83) | |
| Physical activity | | | < 0.01 |
| Inactive or inefficiently active | 675 (12.53) | 710 (8.53) | |
| Active | 883 (19.80) | 1,403 (19.75) | |
| Hyperactive | 3,174 (67.67) | 5,429 (71.72) | |

(continued to the next page)

Table 1. (Continued) Characteristics of participants by hypertension status

| Demographics | Hypertension | No hypertension | P-value |
|---|---------------|-----------------|---------|
| Body mass index (kg/m²) | | | |
| SE | 0.12 | 0.10 | < 0.01 |
| Mean | 30.87 | 27.73 | |
| Under weight | 63 (0.93) | 178 (1.66) | < 0.01 |
| Normal weight | 1,277 (17.69) | 3,161 (34.28) | |
| Overweight | 2,279 (32.18) | 3,276 (34.89) | |
| Obese | 3,530 (49.2) | 2,920 (29.16) | |
| Dietary components | | | |
| Calcium (mg/d) | | | |
| Mean | 836.56 | 897.70 | < 0.01 |
| SE | 7.27 | 6.33 | |
| Magnesium (mg/d) | | | |
| Mean | 260.06 | 279.60 | < 0.01 |
| SE | 1.91 | 2.22 | |
| Ca:Mg Ratio | | | |
| Mean | 3.41 | 3.39 | 0.58 |
| SE | 0.02 | 0.02 | |
| Sodium (mg/d) | | | |
| Mean | 3,246.08 | 3,410.70 | < 0.01 |
| SE | 22.41 | 19.03 | |
| Potassium (mg/d) | | | |
| Mean | 2,335.21 | 2,480.01 | < 0.01 |
| SE | 16.92 | 14.48 | |
| Na:K Ratio | | | |
| Mean | 1.51 | 1.49 | 0.16 |
| SE | 0.011 | 0.009 | |
| Calcium (mg/d) | | | |
| Bellow RDA | 5,482 (73.35) | 6,620 (67.45) | < 0.01 |
| Meeting RDA | 989 (15.44) | 1,623 (17.93) | |
| Above RDA | 678 (11.21) | 1,292 (14.62) | |
| Magnesium (mg/d) | | | |
| Bellow RDA | 5,486 (74.21) | 6,510 (66.39) | < 0.01 |
| Meeting RDA | 1,128 (16.91) | 2,015 (22.55) | |
| Above RDA | 535 (8.88) | 1,010 (11.06) | |
| Sodium (mg/d) | | | |
| Meeting UL | 2,240 (27.32) | 2,305 (21.95) | < 0.01 |
| Above UL | 4,909 (72.68) | 7,230 (78.05) | |
| Potassium (mg/d) | | | |
| Bellow AI | 6,988 (97.39) | 9,249 (97.02) | 0.30 |
| Meeting AI | 161 (2.61) | 286 (2.97) | |

Values are presented as number (%).

For male between 20–70 years old, Below RDA is Ca < 1,000 mg/day, Meeting RDA Ca = 1,000 mg/day, Above RDA Ca > 1,000 mg/day; For male above 70 years old, Ca RDA: Below RDA is Ca < 1,200 mg/day, Meeting RDA is Ca = 1,200 mg/day, Above RDA is Ca > 1,200 mg/day. For female between 20–50 years old, Ca Below RDA is Ca < 1,000 mg/day, Meeting RDA is Ca = 1,000 mg/day, Above RDA is Ca > 1,000 mg/day. For female above 50 years old, Below RDA is Ca < 1,200 mg/day, Meeting RDA is Ca = 1,200 mg/day, Above RDA is Ca > 1,200 mg/day.

For male between 20–30 years old Mg Below RDA is Mg < 400 mg/day, Meeting RDA is Mg = 400 mg/day, Above RDA is Mg > 400 mg/day, For male above 30 years old, Below RDA is Mg < 420 mg/day, Meeting RDA is Mg = 420 mg/day, Above RDA is Mg > 420 mg/day; For female between 20–30 years old, Below RDA is Mg < 310 mg/day, Meeting RDA is Mg = 310 mg/day, Above RDA is Mg > 310 mg/day, For female above 30 years old, Below RDA is Mg < 320 mg/day, Meeting RDA Mg = 320 g/day, Above RDA Mg > 320 mg/day.

UL for Na is < 2,300 mg/day; AI for K is > 4,700 mg/day.

GED, general educational development.

mg/day) and potassium (2,335.21 mg/day) intake and highest calcium-to-magnesium (3.41) and sodium to potassium (1.51) ratio (**Table 2**). Baseline characteristics of the participants across the average dietary sodium, potassium, calcium, and magnesium intake showed a difference by hypertension status. Sodium weighted mean (SE) intake was higher among normotensive male (3,964 ± 28.60) participants. Lower potassium intake mean (SE) was

among hypertensive females (2,094 ± 20.74). The higher calcium intake mean (SE) was among normotensive males (948 ± 7.16). The mean (SE) lower magnesium intake was among hypertensive females (225 ± 1.58). The highest mean of sodium-to-potassium ratio was found among hypertensive of other races 1.60 (0.03). Calcium-to-magnesium among hypertensive females (3.55 ± 0.03) (Table 2).

Table 2. Calcium, magnesium, sodium, potassium, sodium-to-potassium ratio and calcium-to-magnesium ratio means intake by hypertension status and selected characteristics

| Variables | Sample | | Ca (mg/day) | | Mg (mg/day) | | Ca: Mg | | Na (mg/day) | | K (mg/day) | | Na: K | |
|--------------------|--------------|-------|----------------|-----------------|---------------|---------------|----------------|-----------------|-------------------|-------------------|-------------------|-------------------|----------------|-----------------|
| | Hypertensive | | Hypertensive | | Hypertensive | | Hypertensive | | Hypertensive | | Hypertensive | | Hypertensive | |
| | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No | Yes | No |
| All | 7,149 | 9,535 | 792.87 | 870.12 | 260.06 | 279.68 | 3.41 | 3.39 | 3,246.08 | 3,410.7 | 2,335.21 | 2,480.01 | 1.51 | 1.49 |
| Age (yrs) | | | | | | | | | | | | | | |
| ≤ 50 | 1,723 | 6,432 | 884 (10.70) | 894 (5.57)* | 272 (2.68) | 279 (1.47) | 3.38 (0.03) | 3.36 (0.01)* | 3,558 (34.86) | 3,489 (17.82)* | 2,514 (29.89) | 2,492 (17.72)* | 1.58 (0.02) | 1.53 (0.01) |
| > 50 | 5,426 | 3,103 | 761 (5.07) | 814 (7.34) | 243 (1.49) | 266 (2.23) | 3.34 (0.01) | 3.27 (0.02)* | 3,061 (33.74) | 3,131 (34.44) | 2,262 (20.29) | 2,453 (28.79) | 1.48 (0.01) | 1.41 (0.01) |
| Gender | | | | | | | | | | | | | | |
| Male | 3,472 | 4,590 | 834 (7.54) | 948 (7.16) | 276 (2.03) | 305 (1.91) | 3.13 (0.02) | 3.23 (0.01) | 3,776 (34.40) | 3,964 (28.60) | 2,592 (24.40) | 2,746 (20.15) | 1.59 (0.01) | 1.58 (0.01)* |
| Female | 3,677 | 4,945 | 753 (5.67) | 797 (5.34) | 225 (1.58) | 247 (1.47) | 3.55 (0.02) | 3.42 (0.02) | 2,748 (21.74) | 2,910 (20.48) | 2,094 (20.74) | 2,239 (17.43) | 1.43 (0.01) | 1.42 (0.01)* |
| Race | | | | | | | | | | | | | | |
| Mexican American | 806 | 1,593 | 825 (14.19) | 907 (10.97) | 268 (3.95) | 296 (3.11) | 3.21 (0.04) | 3.19 (0.03)* | 3,218 (70.70) | 3,457 (54.84) | 2,433 (48.52) | 2,599 (28.69) | 1.40 (0.01) | 1.40 (0.01)* |
| Non-Hispanic white | 3,429 | 4,305 | 846 (7.06) | 906 (6.85) | 253 (1.89) | 272 (1.87) | 3.54 (0.02) | 3.53 (0.02)* | 3,273 (26.85) | 3,396 (25.26) | 2,363 (20.15) | 2,482 (19.62) | 1.51 (0.01) | 1.50 (0.01)* |
| Non-Hispanic black | 1,846 | 1,587 | 695 (8.65) | 790 (11.06) | 233 (2.55) | 252 (2.70) | 3.14 (0.03) | 3.25 (0.03) | 3,084 (34.92) | 3,332 (37.86) | 2,118 (29.08) | 2,253 (24.33) | 1.57 (0.01) | 1.58 (0.01)* |
| Other Hispanic | 622 | 1,030 | 770 (14.22) | 875 (12.8) | 252 (4.26) | 273 (3.48) | 3.22 (0.05) | 3.34 (0.04)* | 3,015 (69.04) | 3,310 (44.23) | 2,390 (45.91) | 2,536 (42.02) | 1.35 (0.02) | 1.40 (0.02)* |
| Other race | 446 | 1,020 | 757 (16.68) | 778 (11.79)* | 266 (5.40) | 291 (3.83) | 3.05 (0.06) | 2.82 (0.03) | 3,491 (91.03) | 3,663 (63.66) | 2,353 (62.80) | 2,533 (45.54) | 1.60 (0.03) | 1.55 (0.02)* |
| Body mass index | | | | | | | | | | | | | | |
| Under weight | 63 | 178 | 732 (56.13) | 861 (36.47)* | 214 (11.8) | 269 (8.61) | 3.47 (0.18) | 3.29 (0.10)* | 2,770 (199.68) | 3,083 (128.2) | 2,095 (161.54) | 2,529 (120.3) | 1.48 (0.11) | 1.32 (0.04)* |
| Normal weight | 1,277 | 3,161 | 785 (11.18) | 869 (7.81) | 249 (3.14) | 283 (2.32) | 3.35 (0.04) | 3.26 (0.02) | 2,926 (53.62) | 3,359 (29.65) | 2,259 (33.46) | 2,489 (26.19) | 1.42 (0.02) | 1.47 (0.01)* |
| Overweight | 2,279 | 3,276 | 788 (8.17) | 886 (7.70) | 254 (2.33) | 280 (2.08) | 3.30 (0.02) | 3.32 (0.02)* | 3,206 (34.61) | 3,465 (30.78) | 2,349 (29.47) | 2,536 (23.17) | 1.49 (0.02) | 1.48 (0.01)* |
| Obese | 3,530 | 2,920 | 800 (6.77) | 854 (9.49) | 249 (1.86) | 261 (2.01) | 3.37 (0.02) | 3.42 (0.02)* | 3,395 (37.59) | 3,423 (32.34) | 2,357 (22.58) | 2,398 (20.88) | 1.56 (0.01) | 1.53 (0.01)* |
| Smoking status | | | | | | | | | | | | | | |
| Never smoked | 3,629 | 5,550 | 800 (6.58) | 871 (5.64) | 249 (1.83) | 276 (1.58) | 3.39 (0.02) | 3.32 (0.01)* | 3,182 (31.02) | 3,379 (21.41) | 2,313 (23.19) | 2,485 (15.97) | 1.49 (0.01) | 1.47 (0.01)* |
| Current smoker | 1,282 | 2,036 | 778 (11.65) | 862 (10.85) | 246 (3.14) | 262 (2.64) | 3.32 (0.04) | 3.43 (0.03)* | 3,344 (50.62) | 3,451 (42.71) | 2,357 (33.99) | 2,391 (31.97) | 1.53 (0.02) | 1.56 (0.02)* |
| Former smoker | 2,238 | 1,948 | 789 (8.23) | 876 (9.77) | 254 (2.34) | 287 (2.88) | 3.29 (0.02) | 3.24 (0.03)* | 3,293 (44.60) | 3,456 (46.24) | 2,357 (23.28) | 2,547 (36.96) | 1.53 (0.02) | 1.48 (0.02) |
| Alcohol status | | | | | | | | | | | | | | |
| Mild consumption | 728 | 857 | 817 (16.04) | 897 (15.06) | 277 (4.37) | 310 (5.07) | 3.09 (0.04) | 3.07 (0.04)* | 3,639 (67.71) | 3,829 (60.61) | 2,610 (59.53) | 2,800 (54.63) | 1.54 (0.03) | 1.53 (0.02)* |
| Heavy consumption | 3,464 | 5,694 | 810 (6.92) | 880 (5.82) | 257 (1.92) | 277 (1.54) | 3.32 (0.02) | 3.34 (0.01)* | 3,311 (27.54) | 3,442 (24.52) | 2,373 (21.67) | 2,478 (16.16) | 1.51 (0.01) | 1.50 (0.01)* |
| Physical activity | | | | | | | | | | | | | | |
| Inactive | 675 | 710 | 782 (14.57) | 827 (16.04) | 251 (4.20) | 257 (4.10) | 3.30 (0.05) | 3.38 (0.05)* | 3,143 (61.86) | 3,178 (50.45)* | 2,306 (54.21) | 2,554 (39.93)* | 1.46 (0.03) | 1.48 (0.02)* |
| Active | 883 | 1,403 | 799 (13.06) | 839 (10.09) | 252 (3.41) | 278 (2.99) | 3.35 (0.04) | 3.20 (0.03) | 3,214 (64.96) | 3,279 (48.01) | 2,369 (46.49) | 2,437 (44.21) | 1.49 (0.03) | 1.47 (0.02)* |
| Hyperactive | 3,174 | 5,429 | 826 (7.42) | 908 (6.20) | 265 (2.05) | 286 (1.72) | 3.42 (0.02) | 3.41 (0.03)* | 3,404 (33.38) | 3,512 (23.88) | 2,440 (23.39) | 2,310 (18.49) | 1.52 (0.01) | 1.49 (0.01)* |

*non-significant differences $P > 0.05$.

The association of sodium, potassium, calcium, and magnesium on hypertension risk

When assessed individually and in combination using dietary goals cut-off points, sodium, potassium, and calcium intake were not associated with hypertension risk. Magnesium intake above the diet recommendations was negatively associated with hypertension risk among women (OR, 0.64; 95% confidence interval [CI], 0.40–0.95). Men with the same magnesium intake had low but not statistically significant odds of hypertension. Participants meeting recommendations for calcium and above recommendations for magnesium had a significant low odds of hypertension (OR, 0.61; 95% CI, 0.39–0.96). The association remained significant only among men meeting recommendations for calcium and above recommendations for magnesium with a lower odds of hypertension (OR, 0.51; 95% CI, 0.30–0.89). Women above dietary goals for calcium and magnesium had the lowest odds of hypertension (OR, 0.30; 95% CI, 0.10–0.69). The association among men with the same intake was positive but not significant. Using RDA for potassium and sodium, no significant association was found with hypertension (**Table 3**). Different groupings of calcium, magnesium, sodium, and potassium were computed by dividing values into high and low intakes based on the highest quartile and the lower three quartiles for each nutrient.

Table 3. Multivariate analysis for references intakes of sodium, potassium, calcium and magnesium with hypertension

| | H | NH | All individuals | | Men | | Women | |
|--------------------------------------|-------|-------|-----------------|-----------|------|-----------|-------|-----------|
| | | | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Sodium (mg/day) | | | | | | | | |
| Meeting | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| Above Na | 4,909 | 7,230 | 0.97 | 0.80–1.10 | 0.86 | 0.69–1.06 | 1.05 | 0.86–1.30 |
| Potassium (mg/day) | | | | | | | | |
| Meeting | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| Below | 6,988 | 9,249 | 1.01 | 0.67–1.58 | 1.14 | 0.80–1.70 | 0.73 | 0.27–1.99 |
| Meeting Na meeting K | | | | | | | | |
| Meeting Na Bellow K | 2,236 | 2,297 | 5.58 | 0.91–33.5 | - | - | 3.06 | 0.33–29 |
| Above Na Meeting K | 157 | 278 | 5.51 | 0.88–34.1 | - | - | 5.53 | 0.46–66 |
| Above Na Bellow K | 4,752 | 6,952 | 5.51 | 0.90–31.1 | - | - | 3.06 | 0.34–28 |
| Magnesium (mg/day) | | | | | | | | |
| Below Mg RDA | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| Met Mg RDA | 1,128 | 2,015 | 0.80 | 0.67–0.96 | 0.83 | 0.63–1.05 | 0.79 | 0.61–1.03 |
| Above Mg RDA | 535 | 1,010 | 0.78 | 0.62–1.00 | 0.84 | 0.66–1.20 | 0.64 | 0.40–0.95 |
| Calcium (mg/day) | | | | | | | | |
| Below Ca RDA | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| Met Ca RDA | 989 | 1,623 | 0.90 | 0.75–1.11 | 0.77 | 0.59–1.01 | 1.06 | 0.75–1.51 |
| Above Ca RDA | 678 | 1,292 | 0.96 | 0.77–1.20 | 0.93 | 0.71–1.10 | 0.99 | 0.65–1.49 |
| Below RDA Ca Below RDA Mg | | | | | | | | |
| Meeting Ca RDA Meeting Mg RDA | 313 | 541 | 0.80 | 0.54–1.13 | 0.64 | 0.39–1.04 | 0.98 | 0.54–1.77 |
| Meeting Ca RDA above Mg RDA | 125 | 251 | 0.61 | 0.39–0.96 | 0.51 | 0.30–0.89 | 0.80 | 0.34–1.86 |
| Above Ca RDA Above Mg RDA | 237 | 483 | 0.88 | 0.50–1.30 | 1.47 | 0.80–2.68 | 0.30 | 0.10–0.69 |
| Meeting Ca RDA Meeting Mg RDA | | | | | | | | |
| Below RDA Ca Below RDA Mg | 4,712 | 5,353 | 1.24 | 0.84–1.83 | 1.44 | 0.91–2.35 | 0.94 | 0.50–1.75 |
| Meeting Ca RDA above Mg RDA | 125 | 251 | 0.76 | 0.46–1.25 | 0.81 | 0.45–1.49 | 0.81 | 0.30–2.15 |
| Above Ca RDA Above Mg RDA | 237 | 483 | 1.10 | 0.64–1.88 | 1.48 | 0.84–2.66 | 0.36 | 0.13–1.02 |

The model was adjusted for sex age ethnicity energy intake, household income body mass index (as continuous variable), education smoking status, physical activity, drinking status.

For male between 20–70 years old, Below RDA is Ca < 1,000 mg/day, Meeting RDA Ca = 1,000 mg/day, Above RDA Ca > 1,000 mg/day, For male above 70 years old; Ca RDA: Below RDA is Ca < 1,200 mg/day, Meeting RDA is Ca = 1,200 mg/day Above RDA is Ca > 1,200 mg/day. For female between 20–50 years old Ca Below RDA is Ca < 1,000 mg/day, Meeting RDA is Ca = 1,000 mg/day, Above RDA is Ca > 1,000 mg/day, For female above 50 years old, Below RDA is Ca < 1,200 mg/day, Meeting RDA is Ca = 1,200 mg/day Above RDA is Ca > 1,200 mg/day.

For male between 20–30 years old Mg Below RDA is Mg < 400 mg/day, Meeting RDA is Mg = 400 mg/day, Above RDA is Mg > 400 mg/day, For male above 30 years old, Below RDA is Mg < 420 mg/day, Meeting RDA is Mg = 420 mg/day, Above RDA is Mg > 420 mg/day For female between 20–30 years old, Below RDA is Mg < 310 mg/day, Meeting RDA is Mg = 310 mg/day, Above RDA is Mg > 310 mg/day, For female above 30 years old, Below RDA is Mg < 320 mg/day, Meeting RDA Mg = 320 mg/day, Above RDA Mg > 320 mg.

UL for Na is < 2,300 mg/day AI for K is > 4,700 mg/day.

H, number of hypertensive participants; NH, non hypertensive participants; OR, odds ratio; CI, confidence interval; Ref, referent values.

Magnesium intake was divided into high (≥ 322 mg/day) and low (< 322 mg/day) groups, and calcium intake was dichotomized into high ($\geq 1,036$ mg/day) and low ($< 1,172$ mg/day) groups. Sodium intake was dichotomized into high ($\geq 3,029$ mg/day) and low ($< 3,029$ mg/day), and potassium intake was dichotomized into high ($\geq 2,207$ mg/day) and low ($< 2,207$ mg/day) groups.

All individuals with high calcium and magnesium intake had a lower significant odds of hypertension (OR, 0.81; 95% CI, 0.67–0.98). Individuals with low sodium $< 3,029$ mg/day, high potassium $\geq 2,207$ mg/day intake also had a lower risk of hypertension, but the statistical significance was marginal (OR, 0.81; 95% CI, 0.65–1.01). Low calcium, low magnesium, high sodium, and high potassium intake was positively associated with hypertension in all individuals (OR, 1.34; 95% CI, 1.04–1.74). The association was confirmed among women (OR, 1.56; 95% CI, 1.05–2.32) (Table 4). In all individuals, high calcium, high magnesium, low sodium, high potassium intake was negatively associated with hypertension (OR, 0.39; 95% CI, 0.20–0.76). Because of the small sample size, other combinations of the four minerals using the high and low cut-off points were not reported.

We did not find an association between the highest and the lowest quartiles of sodium intake and hypertension for all individuals, neither in the first model nor when adjusted for total potassium (model 2). Among women, high sodium intake (fourth quartile) was positively associated with increased odds of hypertension when adjusted for total potassium Q4 vs. Q1 (OR, 2.04; 95% CI, 1.18–3.54) (Table 5).

There was an inverse association between higher intakes of potassium and hypertension when adjusted for total sodium. The odds of hypertension decreased with increasing

Table 4. Multivariate analysis of hypertension by sodium, potassium, calcium, and magnesium combinations using high and low cut-off points

| | H | NH | All individuals | | Men | | Women | |
|---|-----|-------|-----------------|-----------|------|-----------|-------|-----------|
| | | | OR | 95% CI | OR | 95% CI | OR | 95% CI |
| Low calcium and low magnesium | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| Low calcium and high magnesium | 704 | 1,165 | 0.85 | 0.69–1.04 | 0.86 | 0.69–1.08 | 0.82 | 0.57–1.17 |
| High calcium and low magnesium | 728 | 1,147 | 0.99 | 0.77–1.29 | 0.84 | 0.59–1.20 | 1.15 | 0.81–1.64 |
| High calcium and high magnesium | 773 | 1,531 | 0.81 | 0.67–0.98 | 0.81 | 0.61–1.09 | 0.74 | 0.49–1.11 |
| Low sodium and low potassium | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| Low sodium and high potassium | 747 | 1,171 | 0.81 | 0.65–1.01 | 0.86 | 0.63–1.17 | 0.76 | 0.55–1.04 |
| High sodium and low potassium | 723 | 1,195 | 1.08 | 0.91–1.27 | 1.01 | 0.80–1.28 | 1.18 | 0.85–1.62 |
| High sodium and high potassium | 768 | 1,486 | 0.92 | 0.76–1.11 | 0.85 | 0.68–1.06 | 1.18 | 0.74–1.88 |
| Low calcium, low magnesium, low sodium and low potassium | | | 1.00 | Ref | | Ref | 1.00 | Ref |
| Low calcium, low magnesium, low sodium and high potassium | 646 | 812 | 1.04 | 0.78–1.40 | 1.00 | 0.65–1.54 | 1.07 | 0.72–1.57 |
| Low calcium, low magnesium, High sodium and low potassium | 930 | 1,152 | 1.04 | 0.84–1.29 | 0.92 | 0.64–1.31 | 1.17 | 0.81–1.70 |
| Low calcium, low magnesium, high sodium, and high potassium | 809 | 1,092 | 1.34 | 1.04–1.74 | 1.15 | 0.78–1.68 | 1.56 | 1.05–2.32 |
| Low calcium, high magnesium, low sodium, and low potassium | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| Low calcium, high magnesium, low sodium and high potassium | 194 | 320 | 0.56 | 0.25–1.26 | - | - | - | - |
| Low calcium, high magnesium, High sodium and low potassium | 35 | 32 | 1.35 | 0.32–5.64 | - | - | - | - |
| Low calcium, high magnesium, High sodium and high potassium | 406 | 732 | 0.72 | 0.31–1.65 | - | - | - | - |
| High calcium high magnesium Low sodium, and low potassium | | | 1.00 | Ref | 1.00 | Ref | 1.00 | Ref |
| High calcium high magnesium Low sodium high potassium | 100 | 192 | 0.39 | 0.20–0.76 | - | - | - | - |
| High calcium high magnesium High sodium low potassium | 24 | 34 | 1.77 | 0.52–5.93 | - | - | - | - |
| High calcium high magnesium High sodium high potassium | 622 | 1,275 | 0.73 | 0.25–2.07 | - | - | - | - |

The model was adjusted for sex, age, ethnicity, energy intake, household income body mass index (as a continuous variable), education, smoking status, physical activity, drinking status. High magnesium ≥ 322 mg/day and low magnesium < 322 mg/day, high calcium $\geq 1,036$ mg/day low calcium intake $< 1,172$ mg/day. High sodium intake $\geq 3,029$ mg/day low sodium intake $< 3,029$ mg/day, and high potassium intake $\geq 2,207$ mg/day and low potassium intake $< 2,207$ mg/day. The model was adjusted for sex, age, ethnicity, energy intake, household income body mass index (as a continuous variable), education, smoking status, physical activity, drinking status.

H, hypertensive participants; NH, non hypertensive participants; OR, odds ratio; CI, confidence interval; Ref, referent values.

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Table 5. Multivariate analysis of hypertension by sodium, potassium, and sodium-to-potassium ratio quartiles

| | H | NH | Total mg/day | Model 1 | | Model 2 | |
|------------------|-------|-------|--------------|---------|-----------|---------|-----------|
| | | | | OR | 95% CI | OR | 95% CI |
| Sodium | | | | | | | |
| All individuals | | | | | | | |
| Quartile 1 | | | < 2,335 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,700 | 2,185 | 2,335–3,118 | 0.89 | 0.71–1.10 | 0.89 | 0.72–1.11 |
| Quartile 3 | 1,624 | 2,260 | 3,118–4,082 | 1.01 | 0.78–1.32 | 1.03 | 0.79–1.34 |
| Quartile 4 | 1,384 | 2,502 | > 4,082 | 1.10 | 0.84–1.35 | 1.10 | 0.87–1.40 |
| Men | | | | | | | |
| Quartile 1 | | | < 2,335 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,700 | 2,185 | 2,335–3,118 | 0.86 | 0.61–1.22 | 0.87 | 0.61–1.22 |
| Quartile 3 | 1,624 | 2,260 | 3,118–4,082 | 0.91 | 0.64–1.30 | 0.93 | 0.65–1.32 |
| Quartile 4 | 1,384 | 2,502 | 4,082 | 0.91 | 0.64–1.29 | 0.93 | 0.65–1.33 |
| Women | | | | | | | |
| Quartile 1 | | | < 2,335 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,700 | 2,185 | 2,335–3,117 | 0.91 | 0.66–1.26 | 0.91 | 0.60–1.37 |
| Quartile 3 | 1,624 | 2,260 | 3,117–4,078 | 1.09 | 0.76–1.56 | 1.53 | 0.98–2.38 |
| Quartile 4 | 1,384 | 2,502 | > 4,078 | 1.31 | 0.91–1.89 | 2.04 | 1.18–3.54 |
| Potassium | | | | | | | |
| All individuals | | | | | | | |
| Quartile 1 | | | < 1,850 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,389 | 1,945 | 1,850–2,409 | 0.97 | 0.75–1.26 | 0.92 | 0.72–1.21 |
| Quartile 3 | 1,310 | 2,025 | 2,409–3,086 | 0.78 | 0.59–1.02 | 0.75 | 0.54–0.94 |
| Quartile 4 | 1,206 | 2,126 | > 3,086 | 0.64 | 0.48–0.87 | 0.40 | 0.40–0.77 |
| Men | | | | | | | |
| Quartile 1 | | | < 1,850 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,389 | 1,945 | 1,850–2,409 | 1.25 | 0.79–1.98 | 1.20 | 0.76–1.89 |
| Quartile 3 | 1,310 | 2,025 | 2,409–3,086 | 0.77 | 0.49–1.19 | 0.70 | 0.45–1.09 |
| Quartile 4 | 1,206 | 2,126 | > 3,086 | 0.70 | 0.44–1.11 | 0.61 | 0.37–0.99 |
| Women | | | | | | | |
| Quartile 1 | | | < 1,850 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,389 | 1,945 | 1,850–2,409 | 0.81 | 0.57–1.14 | 0.77 | 0.54–1.09 |
| Quartile 3 | 1,310 | 2,025 | 2,409–3,086 | 0.79 | 0.55–1.14 | 0.72 | 0.49–1.05 |
| Quartile 4 | 1,206 | 2,126 | > 3,086 | 0.59 | 0.38–0.92 | 0.52 | 0.33–0.84 |
| NaK | | | | | | | |
| All individuals | | | | | | | |
| Quartile 1 | | | < 1.03 | 1.00 | Ref | - | - |
| Quartile 2 | 1,305 | 1,892 | 1.03–1.31 | 1.11 | 0.88–1.42 | - | - |
| Quartile 3 | 1,266 | 1,932 | 1.31–1.63 | 1.32 | 1.01–1.73 | - | - |
| Quartile 4 | 1,186 | 2,011 | > 1.63 | 1.50 | 1.11–2.02 | - | - |
| Men | | | | | | | |
| Quartile 1 | | | < 1.03 | 1.00 | Ref | - | - |
| Quartile 2 | 1,305 | 1,892 | 1.03–1.31 | 0.88 | 0.64–1.21 | - | - |
| Quartile 3 | 1,266 | 1,932 | 1.31–1.63 | 1.29 | 0.94–1.78 | - | - |
| Quartile 4 | 1,186 | 2,011 | > 1.63 | 1.33 | 0.91–1.93 | - | - |
| Women | | | | | | | |
| Quartile 1 | | | < 1.03 | 1.00 | Ref | - | - |
| Quartile 2 | 1,305 | 1,892 | 1.03–1.31 | 1.48 | 1.01–2.15 | - | - |
| Quartile 3 | 1,266 | 1,932 | 1.31–1.63 | 1.28 | 0.89–1.83 | - | - |
| Quartile 4 | 1,186 | 2,011 | > 1.63 | 1.69 | 1.12–2.57 | - | - |

Model 1: age, sex, ethnicity, energy intake, family income, education level, body mass index as a continuous variable, physical activity, alcohol intake and smoking status.

Model 2: Model 1+ total potassium (for the model including Na quartiles), total sodium (for the model including K quartiles).

H, hypertensive participants; NH, non hypertensive participants; OR, odds ratio; CI, confidence interval; Ref, referent values.

potassium intake, with a significant low OR for all individuals in all models. Sodium free adjusted model was only significant in the higher potassium intake quartile (OR, 0.64; 95% CI, 0.48–0.87). When adjusted for total sodium intake, two quartiles were significant. The sodium adjusted model highest quartile had the lower OR, Q4 vs. Q1 (OR, 0.40; 95% CI,

0.40–0.77). The association remained significant for both sex in model 2. Women in model 2 had the lowest odds of hypertension (OR, 0.52; 95% CI, 0.33–0.84).

Sodium-to-potassium ratio was positively associated with hypertension among all individuals with significant increased OR in the two highest quartiles Q3 vs. Q1 (OR, 1.32; 95% CI, 1.01–1.73), Q4 vs. Q1 (OR, 1.50; 95% CI, 1.11–2.02). The association remained positive and significant among women with a high OR in the lowest and the highest quartile Q2 vs. Q1 (OR, 1.48; 95% CI, 1.01–2.15), Q4 vs. Q1 (OR, 1.69; 95% CI, 1.12–2.57) (**Table 5**).

We found no association between calcium and hypertension in all models for all individuals. However, a significant positive association between calcium and hypertension was found among women when adjusting for magnesium with a high OR in the highest quartile Q4 vs. Q1 (OR, 1.80; 95% CI, 1.03–3.16). The calcium-to-magnesium ratio was positively associated with hypertension with a significant increased odds among all individuals in the third quartile Q3 vs. Q1 (OR, 1.29; 95% CI, 1.02–1.62). When stratified by sex, no association was found between calcium-to-magnesium ratio and hypertension risk. We did not find any significant association between magnesium intake and hypertension (**Table 6**).

Calcium intake among supplement users was positively associated with hypertension in model 2 Q2 vs. Q1 (OR, 1.42; 95% CI, 1.04–1.93). There was no significant association between other minerals, their ratio, and hypertension among supplements users of both sexes (**Table 7**). Because of the small sample size, women using calcium, magnesium supplements, and all sodium, potassium supplements users are not reported.

DISCUSSION

This study aimed to evaluate the association between sodium, potassium, calcium, and magnesium individually and jointly using two ratios (Ca: Mg, Na: K), adjusting for each nutrient, as well as relevant cut-off points (Dietary references intakes levels, quartiles) and hypertension. Our results showed no significant association between sodium and hypertension when assessed alone. However, we found a positive association with hypertension among women in the highest quartile when adjusted for total potassium intake and when using sodium-to-potassium ratio. As much as men in the fourth quartile had higher sodium intake, their sodium-to-potassium ratio and potassium-adjusted sodium intake did not yield a significant positive association. When assessed alone, potassium intake was negatively associated with hypertension. Further adjusted for total sodium intake, the negative association remained with a lower odds of hypertension. Both men and women in the highest quartile had reduced odds when adjusting for total sodium intake.

Our sodium and potassium total findings are consistent with Xu et al. [27]. They found a significant positive association between sodium intake and hypertension in the fifth sodium quintile when adjusting for total potassium. They also found a significant negative association between potassium and hypertension in the fifth potassium quintile when adjusted for total sodium [27]. Our findings are also similar to Whelton et al. [28]. They found a strong effect of potassium in lowering blood pressure in participants exposed to a high sodium intake, concluding that blood pressure reduction from potassium depends on the concurrent sodium intake. The higher the sodium intake, the better the blood pressure-lowering effect of increased potassium intake. It highlights that sodium and potassium are

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Table 6. Multivariate analysis of hypertension by calcium, magnesium and calcium-to-magnesium ratio levels for non-supplements users

| | H | NH | Total mg/day | Model 1 | | Model 2 | |
|------------------|-------|-------|--------------|---------|-----------|---------|-----------|
| | | | | OR | 95% CI | OR | 95% CI |
| Calcium | | | | | | | |
| All individuals | | | | | | | |
| Quartile 1 | | | < 557 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,092 | 1,579 | 557–799 | 0.96 | 0.75–1.23 | 0.99 | 0.77–1.27 |
| Quartile 3 | 956 | 1,713 | 799–1,106 | 0.83 | 0.62–1.12 | 0.88 | 0.65–1.20 |
| Quartile 4 | 894 | 1,778 | > 1,106 | 0.92 | 0.68–1.24 | 1.03 | 0.75–1.43 |
| Men | | | | | | | |
| Quartile 1 | | | < 557 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,092 | 1,579 | 557–799 | 0.81 | 0.54–1.23 | 0.82 | 0.54–1.24 |
| Quartile 3 | 956 | 1,713 | 799–1,106 | 0.69 | 0.47–1.03 | 0.70 | 0.47–1.05 |
| Quartile 4 | 894 | 1,778 | > 1,106 | 0.71 | 0.46–1.09 | 0.73 | 0.46–1.15 |
| Women | | | | | | | |
| Quartile 1 | | | < 557 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,092 | 1,579 | 557–799 | 1.13 | 0.80–1.58 | 1.28 | 0.93–1.77 |
| Quartile 3 | 956 | 1,713 | 799–1,106 | 0.96 | 0.63–1.45 | 1.23 | 0.79–1.90 |
| Quartile 4 | 894 | 1,778 | > 1,106 | 1.29 | 0.77–2.18 | 1.80 | 1.03–3.16 |
| Magnesium | | | | | | | |
| All individuals | | | | | | | |
| Quartile 1 | | | < 198 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,315 | 1,696 | 198–262 | 1.28 | 0.99–1.68 | 1.27 | 0.98–1.63 |
| Quartile 3 | 1,143 | 1,838 | 262–342 | 0.88 | 0.68–1.12 | 0.86 | 0.67–1.10 |
| Quartile 4 | 1,003 | 1,992 | > 342 | 0.83 | 0.60–1.12 | 0.79 | 0.58–1.08 |
| Men | | | | | | | |
| Quartile 1 | | | < 198.5 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,315 | 1,696 | 198.5–262 | 1.44 | 0.90–2.29 | 1.42 | 0.90–2.25 |
| Quartile 3 | 1,143 | 1,838 | 262–342 | 0.95 | 0.64–1.39 | 0.92 | 0.63–1.35 |
| Quartile 4 | 1,003 | 1,992 | > 342 | 0.97 | 0.62–1.50 | 0.92 | 0.62–1.38 |
| Women | | | | | | | |
| Quartile 1 | | | < 198.5 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 1,315 | 1,696 | 198.5–262 | 1.15 | 0.78–1.67 | 1.05 | 0.78–1.65 |
| Quartile 3 | 1,143 | 1,838 | 262–342 | 0.81 | 0.55–1.18 | 0.77 | 0.53–1.20 |
| Quartile 4 | 1,003 | 1,992 | > 342 | 0.69 | 0.43–1.09 | 0.70 | 0.41–1.11 |
| Ca:Mg | | | | | | | |
| All individuals | | | | | | | |
| Quartile 1 | | | < 2.32 | 1.00 | Ref | - | - |
| Quartile 2 | 1,025 | 1,614 | 2.32–3.05 | 0.92 | 0.71–1.19 | - | - |
| Quartile 3 | 1,043 | 1,597 | 3.05–3.95 | 1.29 | 1.02–1.62 | - | - |
| Quartile 4 | 934 | 1,703 | > 3.95 | 1.11 | 0.84–1.48 | - | - |
| Men | | | | | | | |
| Quartile 1 | | | < 2.32 | 1.00 | Ref | - | - |
| Quartile 2 | 1,025 | 1,614 | 2.32–3.05 | 0.77 | 0.56–1.05 | - | - |
| Quartile 3 | 1,043 | 1,597 | 3.05–3.95 | 1.10 | 0.84–1.44 | - | - |
| Quartile 4 | 934 | 1,703 | > 3.95 | 0.94 | 0.67–1.33 | - | - |
| Women | | | | | | | |
| Quartile 1 | | | < 2.32 | 1.00 | Ref | - | - |
| Quartile 2 | 1,025 | 1,614 | 2.32–3.05 | 1.27 | 0.80–2.02 | - | - |
| Quartile 3 | 1,043 | 1,597 | 3.05–3.95 | 1.64 | 0.94–2.86 | - | - |
| Quartile 4 | 934 | 1,703 | > 3.95 | 1.46 | 0.84–2.51 | - | - |

Model 1: age, sex, ethnicity, energy intake, family income, education level, BMI as a continuous variable, physical activity, alcohol intake, smoking status.

Model 2: Model 1+ total magnesium (for the model including Ca quartiles), total calcium (for the model including Mg quartiles).

H, hypertensive participants; NH, non hypertensive participants; OR, odds ratio; CI, confidence interval; Ref, referent values.

equally crucial in controlling blood pressure since the effects of either sodium or potassium on blood pressure are stronger in the presence of the other.

Nevertheless, it is vital to keep sodium at a lower and reasonable amount for a better health outcome, as shown by other studies [29–33]. Women in our study had the highest significant

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Table 7. Multivariate analysis of hypertension by calcium, magnesium and calcium-to-magnesium ratio levels for supplements users

| | H | NH | Total mg/day | Model 1 | | Model 2 | |
|------------------------------------|-----|-----|--------------|---------|-----------|---------|-----------|
| | | | | OR | 95% CI | OR | 95% CI |
| Calcium supplements users | | | | | | | |
| All Individuals | | | | | | | |
| Quartile 1 | | | < 532 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 775 | 717 | 532–701 | 1.19 | 0.87–1.62 | 1.42 | 1.04–1.93 |
| Quartile 3 | 737 | 763 | 701–927 | 1.03 | 0.81–1.29 | 1.04 | 0.77–1.40 |
| Quartile 4 | 704 | 793 | > 927 | 1.08 | 0.76–1.53 | 1.20 | 0.82–1.78 |
| Men | | | | | | | |
| Quartile 1 | | | < 532 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 775 | 717 | 532–701 | 1.12 | 0.73–1.72 | 1.03 | 0.81–1.29 |
| Quartile 3 | 737 | 763 | 701–928 | 1.19 | 0.87–1.62 | 1.01 | 0.64–1.61 |
| Quartile 4 | 704 | 793 | > 928 | 0.78 | 0.52–1.18 | 1.08 | 0.76–1.53 |
| Women | | | | | | | |
| Quartile 1 | | | < 532 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 775 | 717 | 532–701 | - | - | - | - |
| Quartile 3 | 737 | 763 | 701–928 | - | - | - | - |
| Quartile 4 | 704 | 793 | > 928 | - | - | - | - |
| Magnesium supplements users | | | | | | | |
| All Individuals | | | | | | | |
| Quartile 1 | | | < 157 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 605 | 567 | 157–200 | 1.10 | 0.72–1.69 | 1.15 | 0.75–1.75 |
| Quartile 3 | 555 | 618 | 200–260 | 0.99 | 0.64–1.54 | 1.01 | 0.64–1.57 |
| Quartile 4 | 510 | 661 | > 260 | 1.06 | 0.70–1.61 | 1.17 | 0.75–1.84 |
| Men | | | | | | | |
| Quartile 1 | | | < 157 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 605 | 567 | 157–200 | 0.68 | 0.36–1.28 | 0.73 | 0.39–1.35 |
| Quartile 3 | 555 | 618 | 200–260 | 0.74 | 0.37–1.48 | 0.80 | 0.41–1.55 |
| Quartile 4 | 510 | 661 | > 260 | 0.79 | 0.45–1.38 | 0.97 | 0.54–1.73 |
| Women | | | | | | | |
| Quartile 1 | | | < 157 | 1.00 | Ref | 1.00 | Ref |
| Quartile 2 | 605 | 567 | 157–200 | - | - | - | - |
| Quartile 3 | 555 | 618 | 200–260 | - | - | - | - |
| Quartile 4 | 510 | 661 | > 260 | - | - | - | - |
| Ca:Mg | | | | | | | |
| All individuals | | | | | | | |
| Quartile 1 | | | < 2.5 | 1.00 | Ref | - | - |
| Quartile 2 | 566 | 573 | 2.5–3.3 | 1.24 | 0.91–1.68 | - | - |
| Quartile 3 | 556 | 583 | 3.3–4.4 | 1.18 | 0.82–1.68 | - | - |
| Quartile 4 | 601 | 538 | > 4.4 | 1.19 | 0.87–1.62 | - | - |
| Men | | | | | | | |
| Quartile 1 | | | < 2.5 | 1.00 | Ref | - | - |
| Quartile 2 | 566 | 573 | 2.5–3.3 | 1.12 | 0.79–1.59 | - | - |
| Quartile 3 | 556 | 583 | 3.3–4.4 | 1.04 | 0.67–1.61 | - | - |
| Quartile 4 | 601 | 538 | > 4.4 | 1.09 | 0.73–1.64 | - | - |
| Women | | | | | | | |
| Quartile 1 | | | < 2.5 | 1.00 | Ref | - | - |
| Quartile 2 | 566 | 573 | 2.5–3.3 | - | - | - | - |
| Quartile 3 | 556 | 583 | 3.3–4.4 | - | - | - | - |
| Quartile 4 | 601 | 538 | > 4.4 | - | - | - | - |

Ref: reference values.

Model 1: age, sex, ethnicity, energy intake, family income, education level, body mass index as a continuous variable, physical activity, alcohol intake, smoking status.

Model 2: Model 1+ total magnesium (for the model including Ca quartiles), total calcium (for the model including Mg quartiles).

H, hypertensive participants; NH, non hypertensive participants; OR, odds ratio; CI, confidence interval; Ref, referent values.

odds of hypertension for sodium intake and sodium-to-potassium ratio. The somewhat lower odds of hypertension for potassium intake among women can be explained because they are more salt-sensitive [34–36]. Spahn et al. [37] and Pilic et al. [38] have demonstrated that the benefits of dietary potassium on blood pressure are more potent in salt-sensitive individuals.

A small increase in sodium intake in these individuals can easily increase their risk of developing high blood pressure.

Our findings on the association between sodium-to-potassium ratio and hypertension have also been documented in previous studies [8-10,30,39], but conflicted with Sharma et al. [40], Chmielewski and Catmody [41]. They did not find any association between high blood pressure and sodium-to-potassium ratio neither in quartiles nor using high and low-level cut-off points. The association was significant among women in spite of their lower sodium intake which concurred with experimental and clinical studies [36,38,42] supporting the results by specific physiological mechanisms in salt-sensitive female mice. Salt sensitive female mice have a lower renin-angiotensin system activity compared to males. In female mice, the increase of adrenal aldosterone synthetase expression, the high aldosterone retention level is salt-induced. Female mice also develop salt-induced impairment of endothelium-dependent relaxation by the rise of an endogenous competitive inhibitor of endothelial NO called asymmetric dimethylarginine, which inhibits vasodilatation, favors vasoconstriction, and increase blood pressure [43-47]. These findings suggest that women may require to reduce their sodium intake more than men to reduce their risk of developing high blood pressure.

When assessing calcium and magnesium intake individually using dietary goals cut-off points, we established that only magnesium intake was negatively associated with hypertension in all individuals and among women. Women above dietary goals for magnesium had reduced lower odds of hypertension at 36%. When jointly assessed, women above dietary goals for calcium and magnesium had 70% lower reduced odds of hypertension, and men meeting the nutritional goals for calcium and above dietary goals for magnesium intake had 49% reduced odds of hypertension. All individuals with high calcium ($\geq 1,036$ mg) and high magnesium intake (≥ 322 mg) had a 19% reduced odds of hypertension. Women in the highest calcium quartile ($> 1,453$ mg/day) had a high odds of hypertension when calcium intake was adjusted for total magnesium. No significant sex difference was observed with calcium-to-magnesium ratio. Calcium intake was positively associated with hypertension among supplement users in the lower quartile when adjusted for supplements user's total magnesium intake.

Our calcium and magnesium results conflict with previous epidemiological studies reporting a greatest reduced odds at 41% among women who met the dietary goals for both calcium and magnesium and suggested men's calcium and magnesium intake to be above and meeting the dietary goals respectively to be potentially protected from developing other chronic diet-related diseases [48]. In the same study, men with a magnesium intake of ≥ 386 mg/day and calcium intake of $\geq 1,224$ mg/day had a significant low odds of metabolic syndrome. However, in our case, no gender difference was found. High calcium $\geq 1,036$ mg/day and high magnesium ≥ 322 mg/day intake is negatively associated with hypertension for all individuals. Limited epidemiological evidence supports a positive association of calcium with hypertension. In our study, low calcium intake is positively associated with hypertension among supplements users who in the first quartile, had a calcium intake below the dietary goals. These findings are consistent with several clinical trials and epidemiological studies showing that low calcium intake increases blood pressure [49-52].

Stratified by sex, when adjusted with total magnesium, calcium intake in the highest calcium quartiles ($> 1,453$ mg/day) was positively associated with hypertension. The association of

calcium intake with hypertension has always been conflicting [50]. It is well known that the cardioprotective effects of calcium are more potent when associated with magnesium [53]. Therefore, the two nutrients should be balanced for the best health outcome. Low magnesium status impairs calcium metabolism affecting blood pressure. Low magnesium increases neuro mediators secretion, causing hyperexcitability of NMDA receptor, promoting calcium ions massive entry, giving rise to hyperexcitability hyper-muscular contractility, leading to high blood pressure [21,22]. The positive association in the highest calcium quartile among women in our study could be explained by the fact that women had the lowest dietary magnesium intake mean of 225 mg/day. Our findings suggest that women need to increase their calcium and magnesium intake to benefit from the cardioprotective effects of calcium on hypertension, as we reported in the combined effects of calcium and magnesium intake among women using RDA cut-off points. Women above dietary goals for both calcium and magnesium had a 70% reduced odds of hypertension. Our calcium and magnesium findings suggest that calcium intake meeting the nutritional goals with magnesium intake above the dietary goals may be adequate to protect men from developing high blood pressure. In contrast, women may need to increase calcium and magnesium to be protected from developing high blood pressure.

The relationship between combinations of different intake levels of sodium, potassium, magnesium, and calcium using the high and low cut-off points has not been well studied. We found a negative association with a significant reduced odds of 61% between low sodium, high potassium, high calcium, high magnesium intake, and high blood pressure. This Adjusted odds ratio was lower than when combining only calcium and magnesium or sodium and potassium intake using high and low cut-off points. Our findings suggest that increasing calcium ($\geq 1,036$ mg/day), magnesium (≥ 322 mg/day), and potassium intake ($\geq 2,207$ mg/day) while reducing sodium ($< 3,029$ mg/day) intake may protect from developing hypertension. Similar to our findings, some scientists [54,55] indicate that increasing calcium, magnesium, and potassium intake while decreasing sodium intake lowers blood pressure. The negative association we observed between low sodium, high calcium, magnesium, and potassium intake with hypertension was also consistent with Houston [53]. They explained the outcome by the crucial role of magnesium intake in combining the studied minerals in blood pressure control. Magnesium is a modulator of sodium, calcium, and potassium movements across numerous tissues [53,56]. Increasing magnesium, potassium, and calcium, intake coupled with a reduced sodium intake is an effective anti-hypertensive drug in treating hypertension and more effective in lowering blood pressure than a single mineral intake [53,55].

Assessing the independent relationship of key minerals involved in blood pressure regulation and hypertension vis a vis their combined relationship with hypertension determined using the ratios (Ca: Mg, Na: K) and adjusted for each key mineral at different cut-off points is one strength of this study. The study also used a representative sampling period of 8 years (2007-2014) from NHANES, which is believed to produce valid and reliable results.

However, some issues should be considered when interpreting these results. The use of 24-hour dietary recall interviews for dietary assessment is known to over or underestimate actual intake. The 24-h dietary recall does not account for day-to-day variation. Moreover, we could not determine the contribution of mineral intake from different sources of drinking water and sodium, potassium from table salt, which could have changed the total intake of each mineral and, therefore, impacted the outcome. Finally, in observational cross-sectional studies, it is difficult to determine whether the outcome followed exposure in time or exposure resulted from the outcome.

In summary, our study suggests that the studied minerals' association with hypertension is stronger when jointly assessed. Gender stratification also had a significant effect on the reported association. As compared to men, women increased their risk of hypertension even with a lower sodium intake. Women would also reasonably reduce their risk of developing hypertension by increasing calcium and magnesium intake. In comparison, men would somewhat be protected from developing hypertension with calcium intake meeting the dietary goals and magnesium exceeding the nutritional goals. High calcium, magnesium, potassium, and low sodium intake somewhat reduces the risk of developing hypertension in all individuals. However, additional prospective studies using other reliable dietary intake assessment methods in a different population are needed to validate our findings.

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