



Contents lists available at ScienceDirect

International Journal of Cardiology Cardiovascular Risk and Prevention

journal homepage: www.journals.elsevier.com/international-journal-of-cardiology-cardiovascular-risk-and-prevention



Low sodium intake and cardiovascular disease mortality among adults with hypertension

Elsie Kodjoe

Harvard T.H.Chan School of Public Health, USA

ARTICLE INFO

Keywords:

Blood pressure
Cardiovascular disease
Diet
Hypertension
Mortality
Salt
Sodium chloride

ABSTRACT

Background: Though high sodium intake is linked to an increased risk of hypertension and cardiovascular diseases, the relationship between sodium intake and mortality remains controversial. Given that medications used to treat hypertension can potentially lower blood sodium levels and alter electrolyte balance, it begs the question whether a further reduction in dietary sodium below the recommended daily intake of 2300 mg is beneficial among adults with hypertension.

Objective: To evaluate the effect of low sodium intake on cardiovascular disease (CVD) mortality and all-cause mortality among adults with hypertension.

Design: A retrospective cohort study was conducted using data from the Continuous NHANES (1999–2010) linked to mortality files from the National Death Index. Using sodium intake categorized as low <2300 mg/day and high ≥ 2300 mg/day, the baseline demographic and health characteristics of participants were determined. Hazard ratios (HR) for CVD and all-cause mortality were determined through cox proportional hazard regression analysis adjusted for age, sex, race, total dietary calories, body mass index, physical activity, smoking, diabetes, alcohol consumption, and total serum cholesterol while considering the complex survey design.

Results: Of the 8542 adults with hypertension, 71.01% consumed sodium higher than the recommended daily intake of 2300 mg. The mean age was 54 years, 52.3% were female and 73.1% were white. Over 12.7 years of follow-up, there were 971 deaths, with 232 deaths from CVD. The low sodium intake group had a nonsignificant 5% higher risk of CVD mortality, [Adjusted HR 1.05, 95% CI (0.7–1.6), p-value 0.82]. Similarly, there was a nonsignificant 17% higher risk for all-cause mortality for the low sodium intake group, [Adjusted HR 1.17, 95% CI (1.0–1.4), p-value 0.10]. There was no effect modification by age, race, or sex.

Conclusion: The findings of an inverse association between sodium intake and mortality among adults with hypertension seen here, though not statistically significant warrant further investigation.

1. Introduction

Sodium is a very important electrolyte in the body. It is key to maintaining homeostasis, fluid balance, nerve conduction, and muscle function. The American Heart Association recommends that the general population consume sodium <2300 mg per day while high-risk individuals such as persons living with hypertension, blacks, and those middle-aged or older consume sodium <1500 mg per day [7]. Advocates of low sodium intake among persons living with hypertension argue that low sodium intake leads to low blood pressure resulting in low cardiovascular disease mortality [5][13]. Ardent critics argue that, beyond blood pressure reduction, low sodium intake has a more complicated

effect and leads to activation of the RAAS system, increasing the level of aldosterone, adrenaline, and noradrenaline which can undermine cardiovascular benefits [8]. Studies evaluating the effect of low sodium on cardiovascular disease mortality or all-cause mortality among adults with hypertension are limited.

2. Methods

This study was a retrospective cohort study using data from the Continuous NHANES (1999–2010) linked to mortality files from the National Death Index. This data represented a total follow-up period of 12.7 years. The National Health and Nutrition Examination Survey

Abbreviations: CVD, Cardiovascular disease; NHANES, National Health and Nutrition Examination Survey; RAS, Renin Angiotensin Aldosterone System; HR, Hazards ratio; NCHS, National Center for Health Statistics.

E-mail address: elsie.fenny@gmail.com.

<https://doi.org/10.1016/j.ijcrp.2022.200158>

Received 15 July 2022; Received in revised form 13 October 2022; Accepted 25 October 2022

Available online 1 November 2022

2772-4875/© 2022 The Author. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

(NHANES) is a survey conducted by the National Center for Health Statistics (NCHS), a part of the Centers for Disease Control and Prevention (CDC) in the United States of America (USA). The survey assesses the health and nutritional status of a nationally representative sample of about 5000 adults and children in the USA. The survey includes interviews and physical examinations, and it oversamples persons 60 and older, African Americans, and Hispanics.

This study included 8542 adult men and women 20 years and older representing 53.4 million non-institutionalized adults in the United States of America. Adults with a systolic blood pressure of ≥ 140 mmHg or diastolic blood pressure of ≥ 90 mmHg or both were included in the study. Participants with no prior history of heart disease or stroke were excluded from the study.

The main exposure was self-reported sodium intake dichotomized as “low sodium intake” (<2300 mg/day) and “high sodium intake” (≥ 2300 mg/day). The primary outcome was CVD mortality, defined as time to death from heart disease or stroke from the baseline physical examination. The secondary outcome was all-cause mortality, defined as time to death from any cause.

Characteristics of the study population were presented as count and percentage for categorical variables and mean and standard deviation for continuous variables. The association between sodium intake and cardiovascular disease mortality and all-cause mortality was determined using time-to-event analysis. Univariable and multivariable analysis was conducted using cox proportional hazard regression analysis. The multivariable analysis controlled for the following confounders: age, sex, race, diabetes, serum cholesterol, physical activity, BMI, smoking, alcohol consumption, and total calories. The proportional hazard assumption was tested using log-log survival plots. Interaction terms were used to determine effect modification by age dichotomized ($<65, \geq 65$ years), race and sex. Sensitivity analysis was conducted using sodium intake as a continuous variable. All the analyses considered the complex survey design with weights appropriately assigned.

3. Results

There were 8542 adults with hypertension representing 53.4 million non-institutionalized adults in the USA. 71.01% consumed sodium higher than the recommended daily intake of 2300 mg. The mean age was 54 years, 52.3% were female, and 73.1% were white. Those who consumed high sodium were more likely to be younger, male, white, overweight, consume more calories, drink alcohol, diabetic, smoke, physically active, and have lower cholesterol. [Table 1](#).

Over the 12.7 years of follow-up, there were 971 deaths. 232 (23.89%) deaths were from CVD. Low sodium intake had a significant 42% higher risk of CVD mortality [HR 1.42, 95% CI (1.0–1.9), p-value 0.03 and a significant 53% higher risk for all-cause mortality [HR 1.53, 95% CI (1.3–1.8), p-value <0.001] after the crude analysis. However, after controlling of confounders, low sodium intake had a nonsignificant 5% higher risk of CVD mortality, [adjusted HR 1.05, 95% CI (0.7–1.6), p-value 0.82] and a nonsignificant 17% higher risk of all-cause mortality [adjusted HR 1.17, 95% CI (1.0–1.4), p-value 0.10]. [Table 2](#). (See [Figs 1 and 2](#)). There was no effect modification by age, race, or sex.

4. Discussion

The effect of sodium intake on mortality remains controversial despite the clear association between high sodium intake and an increase in blood pressure. The Institute of Medicine in 2013, reported a link between high sodium intake and a greater risk of CVD. However, it was noted that there was insufficient evidence to conclude that low sodium intake of <2300 mg/day was beneficial to at-risk populations or the general population. They also reported that low sodium intake of <1840 mg/day in mid to late-stage coronary heart failure patients with low ejection fraction rates undergoing aggressive therapy had a negative

Table 1

Baseline characteristics by sodium group.

	Sodium <2300 mg	Sodium ≥ 2300 mg	Total
	N = 2913	N = 5629	N = 8542
Age (years) mean (SE)	58.13 (0.41)	52.67 (0.34)	54.25 (0.30)
Sex N (%)			
Male	978 (30.5)	3089 (54.8)	4067 (47.7)
Female	1935 (69.5)	2540 (45.2)	4475 (52.3)
Dietary calories (kcal) mean (SE)	1343.78 (13.7)	2430.68 (16.0)	2115.55 (14.9)
Body mass index (kg/m ²) N (%)			
<18.5	33 (1.1)	47 (0.9)	80 (0.9)
18.5–24.99	664 (24.7)	1062 (18.3)	1726 (20.2)
25–29.99	1014 (33.7)	1949 (34.1)	2963 (34.0)
30–34.99	681 (21.6)	1381 (24.7)	2061 (23.8)
≥ 35	521 (18.9)	1190 (22.1)	1711 (21.2)
Race N (%)			
White	1281 (68.6)	2999 (75.0)	4280 (73.1)
Black	706 (15.2)	1227 (11.5)	1933 (12.6)
Hispanic	843 (11.8)	1195 (8.9)	2038 (9.8)
Other	83 (4.4)	208 (4.7)	291 (4.6)
Smoking N (%)			
Yes	1297 (46.8)	2832 (49.4)	4129 (48.6)
No	1616 (53.2)	2797 (50.6)	4413 (51.4)
Diabetes N (%)			
Yes	508 (12.7)	822 (11.2)	1330 (11.7)
No	2405 (87.3)	4807 (88.8)	7212 (88.3)
Physical activity N (%)			
Yes	1114 (44.7)	2518 (50.2)	3632 (48.6)
No	1799 (55.3)	3111 (49.8)	4910 (51.4)
Alcohol consumption N (%)			
Yes	1675 (61.7)	4001 (73.4)	5676 (60.8)
No	1238 (38.3)	1628 (26.6)	2866 (26.9)
Total cholesterol (mg/dl) Mean (SE)	209.21 (1.0)	205.33 (0.8)	206.46 (0.7)

*Continuous variables are reported as mean and standard error.

*Categorical variables are reported as total number and percentages.

*Diabetes – Self-reported history of diabetes.

*Physical activity- Self reported moderate activity for at least 10 min which causes light sweating such as brisk walking.

*Smoking – Self reported history of smoking at least 100 cigarettes.

*Alcohol – Self reported history of at having at least 12 alcohol drinks per year.

*All results consider the complex sampling design.

Table 2

Crude and multivariable adjusted analysis showing the effect of sodium intake on CVD mortality and all-cause mortality.

Mortality outcome	Sodium Measure mg/day	Hazard ratio	95% confidence interval	P value
Cardiovascular disease mortality	<2300	Crude	1.42	(1.0–1.9)
		Adjusted	1.05	(0.7–1.6)
All-cause mortality	<2300	Crude	1.53	(1.3–1.8)
		Adjusted	1.17	(1.0–1.4)

*All models were adjusted for age, sex, race, total dietary calories, body mass index, physical activity, smoking, history of diabetes alcohol consumption and total serum cholesterol.

^a Statistically significant.

effect on outcomes.

The findings from this study are consistent with that of Alderman et al. who found a non-significant inverse relationship between low sodium intake and CVD and all-cause mortality [1–3]. Both studies used dietary sodium as exposure and the NHANES database and therefore have some similarities in the population demographics. This study, however, focused only on the hypertensive population. Some studies have also found a U or J-shaped association between sodium intake and mortality [5] [10] [11] [12] indicating that both high and low sodium

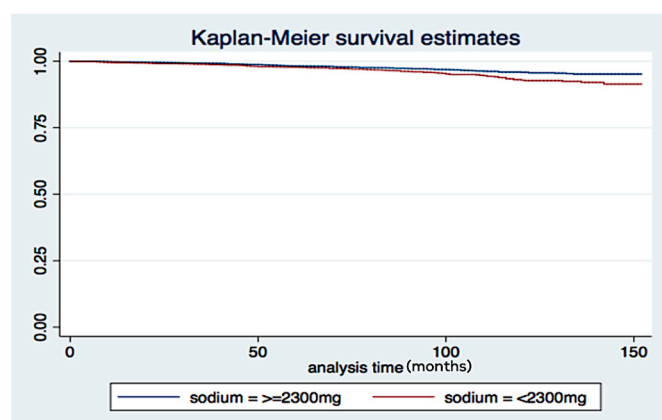


Fig. 1. Kaplan Meier curve showing the effect of sodium intake on CVD mortality.

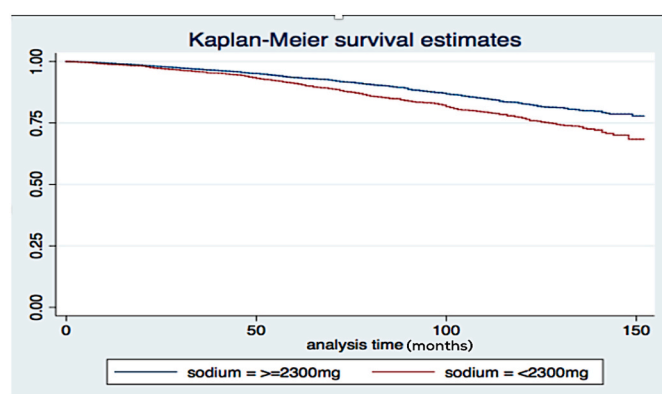


Fig. 2. Kaplan Meier curve showing the effect of sodium intake on all-cause mortality.

intake is associated with an increased risk of mortality. Although Yang et al. used the NHANES data for analysis, they found that higher sodium intake was significantly associated with increased all-cause mortality but not CVD mortality [4].

The varied associations between sodium intake and mortality have been attributed to the challenge with the accurate measurement of body sodium using the gold standard of the 24hr urinary sample. Nancy Cook et al. in the Trials of Hypertension Prevention, used urinary sodium excretion as exposure and found a direct relationship between sodium intake and mortality though this was not statistically significant [9]. The study was also conducted among a prehypertensive younger population (mean age 43yrs) with a male predominance of 68% while this study analyzed a hypertensive, older population (mean age 54yrs) with a female predominance of 52.3%. Therefore, the difference in demographics and sodium assessment may account for the difference in findings. Other studies have also found that this direct relationship occurred in the hypertensive population while the inverse occurred in those without hypertension [6].

The effect of dietary sodium consumption on CVD and all-cause mortality has been explored among other chronic disease patient groups. A cohort study by Ekinci et al. among type 2 diabetics found that CVD and all-cause mortality increased with lower urinary sodium excretion [10]. Furthermore, among type 1 diabetics with end stage renal disease, there was a U-shaped association between urinary sodium excretion and all-cause mortality [11].

4.1. Strengths

The study used a large sample size based on a nationally representative sample of noninstitutionalized adults in the USA. The long follow-up ensured a large number of outcomes. Furthermore, the temporal relationship between sodium intake and mortality was ascertained due to the study design. The exclusion of individuals with prior cardiovascular disease limited the possibility of reverse causation. There was also the availability of many confounding variables in the data for multivariable-adjusted analysis.

4.2. Limitations

Self-reported sodium intake in a dietary recall does not reflect actual sodium levels in the blood. 24 hr urinary sodium excretion is considered the “gold standard”. However, this information is not available in the continuous NHANES. Furthermore, the hidden and varied amounts of sodium in processed food from brand to brand may lead to under-reporting or overreporting of sodium intake. Self-reported sodium is subject to recall bias. Sodium intake during the baseline study does not reflect the changes in consumption over time which could impact the outcome. Finally, socioeconomic status, a known confounder for CVD mortality was not controlled for.

5. Conclusions

70% of adults with hypertension in the United States consume sodium higher than the recommended intake of <2300 mg/day. The inverse association between low sodium and mortality seems to be confounded. The inverse association is stronger for all-cause mortality compared to CVD mortality. The finding of an inverse association between sodium intake and mortality among adults with hypertension seen here, though not statistically significant warrants further investigation.

Credit author statement

This study was carried out as my final practicum during my MPH program at the Harvard. T H Chan School of Public Health. Therefore Dr. Elsie Kodjoe was responsible for conceptualization, methodology, data formal analysis, writing, reviewing and editing.

Funding disclosure

This research was not funded

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The author wishes to acknowledge the Harvard. T. H Chan School of Public Health and the NHANES.

References

- [1] Niels Graudal, Gesche Jürgens, Bo Baslund, Michael H. Alderman, Compared with usual sodium intake, low- and excessive-sodium diets are associated with increased mortality: a Meta-analysis, *Am. J. Hypertens.* 27 (9) (2014) 1129–1137.
- [2] Hillel W. Cohen, Susan M. Hailpern, Michael H. Alderman, Sodium intake and mortality follow-up in the third National Health and Nutrition Examination Survey (NHANES III), *J. Gen. Intern. Med.* 23 (9) (2008) 297–302.
- [3] Michael H. Alderman, Hillel W. Cohen, P.H. Shantha Madhavan, Dietary sodium intake and mortality: the national health and nutrition examination survey (NHANES I), *Lancet* 351 (9105) (1998) 781–785.

- [4] Quanhe Yang, Tiebin Liu, Elena V. Kuklina, Sodium and potassium intake and mortality among US Adults prospective data from the third National Health and Nutrition Examination Survey, *JAMA Arch Intern Med* 171 (13) (2011) 1183–1191, <https://doi.org/10.1001/archinternmed.2011.257>.
- [5] Frank M. Sacks, Laura P. Svetkey, William M. Vollmer, Lawrence J. Appel, George A. Bray, David Harsha, Eva Obarzanek, Paul R. Conlin, Edgar R. Miller, Denise G. Simons-Morton, Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet, *N. Engl. J. Med.* 344 (2001) 3–10.
- [6] Andrew Mente, Martin O'donnel, Sumathy Ranjeragan, Gilles Dagen, Iear Scott, Prof Mathew McQueen, Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies, *Lancet* 388 (10043) (2016) 465–475.
- [7] American Heart Association, website, www.heart.org.
- [8] Carol Kotliar, Pablo Kemny, Sergio Gonzalez, Carlos Castellaro, Forcada Pedro, Sebastian Obregon, Lack of RAAS inhibition by high salt intake is associated with arterial stiffness in hypertensive patients, *J. Renin-Angiotensin-Aldosterone Syst. JRAAS* 15 (4) (2014) 498–504.
- [9] Nancy R. Cook, Lawrence J. Appel, Paul K. Whelton, Sodium intake and all-cause mortality over 20 Years in the Trials of hypertension prevention, *J. Am. Coll. Cardiol.* 68 (15) (2016) 1609–1617.
- [10] Elif I. Ekinci, Sophie Clarke, Merlin C. Thomas, John L. Moran, Karey Cheong, Richard J. MacIsaac, Jerums George, Dietary salt intake and mortality in patients with type 2 diabetes, *Diabetes Care* 34 (3) (2011) 703–709.
- [11] Merlin C. Thomas, John Moran, Carol Forsblom, Valma Harjutsalo, Lena Thorn, Aila Ahola, Johan Waden, Nina Tolonen, Markku Saraheimo, Daniel Gordin, Per-Henrik Group, Finn Diane Study Group, The association between dietary sodium intake and ESRD and all-cause mortality in patients with type 1 diabetes, *Diabetes Care* 34 (4) (2011) 861–866.