

## Role of Serum Sodium and Potassium Levels in Hypertensive Patients

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### Abstract

**Background:** In particular, the effectiveness of restricted sodium or increased potassium intake on mitigating hypertension risk has been demonstrated in clinical and observational research. The role that modified sodium or potassium intake plays in influencing the renin-angiotensin system, arterial stiffness, and endothelial dysfunction remains of interest in current research. **Material and Methods:** This is a prospective and observational study has been conducted at the Department of Biochemistry, Shri Ram Murti Smark Institute of Medical Sciences (SRMS IMS), Bareilly U.P. India. Patients either gender above 20 years of age with primary hypertension were included. The subjects were examined clinically and the physical examinations included measurement of height in cms, weight and blood pressure. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. Blood Pressure was measured on the right arm using standard sphygmomanometer with participant seated quietly on a bench with back support after physical rest for 5 minutes. **Results:** A total of 120 subjects were included in the study out of which 60 case group and 60 control group. In our study 73 (60.8%) were male and 47 (39.1%) were females. The most common age group from 61 – 70 years constituted to about 35.0% of the patients. The next age group involved was 51 – 60 years having 26.6% of patients followed by 21.6% and 16.6% in 41 – 50 and 21 – 30 years age groups shown. Mean serum sodium in grade I hypertension is  $144.6 \pm 5.93$  and in grade II hypertension is  $144.6 \pm 7.35$ . It is not statistically significant ('p' value = 1.26). Mean serum potassium in grade I hypertension is  $3.29 \pm 0.32$  and in grade II hypertension is  $3.81 \pm 0.38$  and is not statistically significant ('p' value = 0.96). **Conclusion:** Base-line serum potassium level, but not baseline serum sodium level, was positively related to the risk of incident hypertension in these population.

**Keywords:** Serum sodium, Serum Potassium, Hypertension, Primary hypertension, BMI.

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### Introduction

High blood pressure, also known as hypertension, is one of the most well-known major risk factors for cardiovascular disease (CVD) and stroke.<sup>[1]</sup> Estimates reported by the American Heart Association indicate that in 2007–2010, 33% of all adults aged 20 years in the United States (i.e., 78,000,000) had hypertension.<sup>[2]</sup> According to the American Heart Association, prevalence estimates for hypertension are comparable between men and women, are highest among African Americans (44%), and show that only 53% of all hypertensive adults have their blood pressure under control.<sup>[3]</sup> Given the established relation between hypertension and CVD and stroke, 2 leading causes of morbidity and mortality worldwide, it is critical that simple yet effective interventions for reducing blood pressure be identified. Potentially relevant indicators of CVD and stroke risk also include the renin-angiotensin system,<sup>[4]</sup> arterial stiffness and the augmentation index,<sup>[5,6]</sup> and endothelial dysfunction.<sup>[7]</sup>

Dietary interventions, in particular those based on sodium or potassium intakes, have demonstrated their ability to re-duce blood pressure in humans. For example, the Dietary Approaches to Stop Hypertension (DASH) diet, a U.S.-based multicenter randomized controlled trial (RCT), showed that a high-potassium and high-calcium dietary intervention was associated with significantly reduced mean blood pressure at low, intermediate, and high sodium intakes compared with the control diet.<sup>[8-10]</sup>

Several mechanisms exist by which sodium and potassium can influence blood pressure, and evidence indicates that the interaction between these nutrients plays a dominant role in the development of primary hypertension.<sup>[11]</sup> Specifically, diets characteristic of the modern Western diet—which is high in sodium and low in potassium—produce a biologic interaction with the kidneys, resulting in excessive sodium and insufficient potassium concentrations in the human body; these biologic changes result in vascular smooth muscle cell contraction, followed by an increase in peripheral vascular resistance and higher blood pressure, and finally hypertension.<sup>[12]</sup> The influence of sodium or potassium intake on the renin-angiotensin system, arterial stiffness, and endothelial dysfunction remains under study.<sup>[13]</sup>

The joint effects of low sodium and high potassium in-takes on blood pressure, hypertension, and related factors may be larger than the effects of either sodium or potassium alone.<sup>[14]</sup> Up to the present date, no known study has been undertaken to determine if the sodium-to-potassium role is more strongly associated with blood pressure and related risk factors for CVD than either sodium or potassium alone. The goal of this study was to identify the current research gaps, and to make research recommendations on the basis of the published data regarding the evaluation of these determinants for blood pressure and related factors.

### **Material and Methods**

This is a prospective and observational study has been conducted at the Department of Biochemistry, Shri Ram Murti Smark Institute of Medical Sciences (SRMS IMS), Bareilly U.P. India.

### **Inclusion Criteria**

Patients either gender above 20 years of age with primary hypertension.

### **Exclusion Criteria**

Patients below 20 years. Patients with renal failure, Patients with secondary hypertension. Patients on non-steroidal anti-inflammatory agents, antihypertensive agents.

Their physical examinations included measurement of height in cms, weight and blood pressure. Body mass index (BMI) was calculated as the weight in kilograms divided by the square of the height in meters. Blood Pressure was measured on the right arm using standard sphygmomanometer with participant seated quietly on a bench with back support after physical rest for 5 minutes. The mean value of three consecutive readings was used both at the baseline and the follow-up surveys. Hypertension was defined as a mean systolic blood pressure  $\geq 140$  mmHg, and/ or a mean diastolic blood pressure  $\geq 90$  mmHg, and/or taking antihypertensive medication. Optimal blood pressure was defined as a mean systolic blood pressure  $< 120$  mmHg and a mean diastolic blood pressure  $< 80$  mmHg. Normal blood pressure was defined as a mean systolic blood pressure of 120–129 mmHg and a mean diastolic blood pressure of 80– 84 mmHg. Pre-hypertension was defined as a mean systolic blood pressure of 130–139 mmHg and a mean diastolic blood pressure of 85–89 mmHg.

Diabetes mellitus was defined as fasting blood glucose  $\geq 126$  mg/dl (7.0 mmol/L) or the use of anti-diabetic drugs. Overnight fasting venous blood samples were collected for the measurements of serum glucose, blood lipid, and electrolyte concentrations. Serum potassium and sodium levels were measured by the ion-selective electrode method. Fasting blood

glucose was measured by enzymatic methods. High-density lipoprotein and low-density lipoprotein were measured by the homogeneous assay.

### Results

A total of 120 subjects were included in the study out of which 60 case group and 60 control group.

**Table 1: Showing age and Gender wise distribution of the case group.**

Age Group(Yrs)	Male	Female	Total	Percentage
21 – 30	13	7	20	16.6
41 – 50	17	9	26	21.6
51 – 60	19	13	32	26.6
61 – 70	24	18	42	35.0
Total	73	47	120	100

In [Table 1], 73 (60.8%) were male and 47 (39.1%) were females. The most common age group from 61 – 70 years constituted to about 35.0% of the patients. The next age group involved was 51 – 60 years having 26.6% of patients followed by 21.6% and 16.6% in 41 – 50 and 21 – 30 years age groups shown in [Table 1].

**Table 2: Distribution of cases and controls with respect to Body Mass Index (BMI).**

BMI	Cases		Controls	
	No.	%	No.	%
Underweight <18.5	7	08	8	11
Normal weight 18.5- 22.9	18	34	37	65
Overweight 23-24.9	14	20	12	20
Obese >25	21	38	3	4
Total	60	100	60	100

In our study 36% of cases were obese while in the control group obesity was noticed in 2%. Details are given in following [Table 2].

**Table 3: Distribution of BMI between cases and controls**

BMI	Cases	Controls
Mean	25.39	23.61
S.D	4.16	3.43
'p' value = 0.0001		

The mean body mass index in the case group is  $25.39 \pm 4.16$  and in the control group is  $23.61 \pm 3.43$ . This shows that the difference in Body Mass Index between cases and controls was statistically significant [Table 3].

**Table 4: Distribution of BMI with respect to grade of hypertension.**

BMI	Grade I Hypertension	Grade II Hypertension
<18.5	4	4
18.5-22.9	6	12
23-24.9	5	9
>25	5	15
Total	20	40
'p' value = 0.08		

No significant difference was found for BMI between grade I and grade II hypertension case in [Table 4].

**Table 5: Distribution of cases with respect to grade of hypertension**

Hypertension	No.	Cases%
Grade 1	21	29
Grade 2	39	71

In our study 21 cases were of grade I hypertension and 39 cases were of grade II hypertension in [Table 5].

**Table 6: Serum sodium with respect to gender in grade I and grade II hypertension**

Grade of Hypertension	Males		Females	
	Mean	S.D.	Mean	S.D.
Grade I	143.27	6.32	146.2	8.91
Grade II	145.37	7.79	143.49	7.93

Serum sodium levels in grade II hypertension in males was  $145.37 \pm 7.79$  and in females was  $143.49 \pm 7.93$ . Though sodium values are high in males compared to females but it is not statistically significant ('p' value = 0.83) in [Table 6].

**Table 7: Serum potassium with respect to gender in grade I and grade II hypertension**

Grade of Hypertension	Males		Females	
	Mean	S.D.	Mean	S.D.
Grade I (mEq/L)	3.27	0.32	3.31	0.14
Grade II (mEq/L)	3.84	0.79	3.94	0.18

Serum potassium levels in grade I hypertension in males was  $3.27 \pm 0.32$  and in females was  $3.31 \pm 0.14$ . Not statistically significant ('p' value = 0.58). Serum potassium levels in grade II hypertension in males was  $3.84 \pm 0.79$  and in females was  $3.94 \pm 0.18$ . Not statistically significant ('p' value = 0.97) in [Table 7].

**Table 8: Serum sodium and potassium levels in grade I and grade II hypertension**

Grade of Hypertension	Serum Sodium	Serum Potassium
Grade I	$144.6 \pm 5.93$	$3.29 \pm 0.32$
Grade II	$144.6 \pm 7.35$	$3.81 \pm 0.38$

Mean serum sodium in grade I hypertension is  $144.6 \pm 5.93$  and in grade II hypertension is  $144.6 \pm 7.35$ . It is not statistically significant ('p' value = 1.26). Mean serum potassium in grade I hypertension is  $3.29 \pm 0.32$  and in grade II hypertension is  $3.81 \pm 0.38$  and is not statistically significant ('p' value = 0.96).

## Discussion

As far as we know, there are few epidemiological studies investigating the association between serum potassium level and hypertension with only one cohort study among them.<sup>[15]</sup> The Framingham Heart Study found that adults with serum potassium  $\geq 5.2$  mEq/L had increased risk of hypertension, though the difference was not significant.<sup>[16]</sup> Higher serum potassium level was also associated with increased risk of CVD. The results of Fang, et al.<sup>[17]</sup> suggested that there was an increase in CVD mortality among the population with serum

potassium  $\geq 4.5$  mEq/L, after adjusting for other CVD risk factors. Wannamethee, et al.<sup>[18]</sup> reported an in-crease in mortality risk of 70% in male smokers with serum potassium  $\geq 5.2$  mEq/L.

The results of cross-sectional and case-control studies of serum potassium and hypertension were not consistent with our study. Kesteloot, et al.<sup>[19]</sup> Pikilidou, et al.<sup>[20]</sup> and Rinner, et al.<sup>[21]</sup> found that serum potassium level was negatively associated with blood pressure. Hu, et al.<sup>[22]</sup> suggested that serum potassium level was lower in hypertension group compared with non-hypertension group. However, it is insufficient to infer causality of serum potassium level on future risk of hypertension based on results from cross-sectional and case control studies.

We found an 84% increased risk of hypertension in individuals with baseline serum potassium level  $\geq 4.80$  mEq/L compared with level of 4.20–4.79 mEq/L, in accordance with the trend shown by Framingham Heart Study.<sup>[23]</sup> Our study was similar to that of the Framingham Heart Study with respect to follow-up years, but the participants in our study were older. In addition, the Framingham Heart Study excluded participants with creatinine levels  $\geq 2.0$  mg/dL and potassium levels  $> 6.3$  mEq/L, however, all participants had creatinine levels  $< 2.0$  mg/dL and potassium levels  $\leq 6.3$  mEq/L in our study.

There was no significant association between baseline serum sodium level and risk of hypertension, which was consistent with Framingham Heart Study. While a cross-sectional study from Kesteloot, et al.<sup>[19]</sup> found a negative correlation between serum sodium level and blood pressure. And Hu, et al.<sup>[22]</sup> found no significant difference in serum sodium level between hypertension and non-hyper-tension groups.

Potassium and sodium play important roles in the maintenance of cellular functions, and raised or lowered serum potassium level may be harmful to health.<sup>[24]</sup> Our results found that elevated serum potassium could increase the risk of hypertension. The physiological mechanisms by which higher serum potassium level increase hypertension risk are not fully understood. Renal function may affect the level of serum potassium.<sup>[25]</sup> This indicated that the association between serum potassium and hypertension risk was independent of renal function. Our study found no association between serum sodium and risk of hypertension. The regulation of blood pressure by sodium may be based on dietary intake and renal excretion, independent of serum sodium level.<sup>[26]</sup>

Increased dietary intake of potassium and sodium may subsequently increase potassium and sodium levels in blood.<sup>[27]</sup> The Atherosclerosis Risk in Communities (ARIC) Study measured the dietary and serum potassium levels in 12,209 participants,<sup>[28]</sup> and showed that serum potassium level was higher in the group of high potassium intake. In this study, serum potassium level was divided into 4 groups  $< 4.0$ , 4.0–4.5, 4.5–5.0 and 5.0–5.5 mEq/L, and the dietary potassium intake were  $1.63 \pm 0.43$ ,  $1.65 \pm 0.42$ ,  $1.68 \pm 0.41$  And  $1.70 \pm 0.41$  mg/kcal ( $P < 0.01$ ), respectively. Another research among normotensive individuals showed that with the salt intake from 10 mmol/day increased to 250 mmol/day, plasma sodium levels changed from  $138.5 \pm 0.7$  mmol/day to  $141.5 \pm 1.1$  mmol/day.<sup>[29]</sup>

Salt substitute containing 25% potassium chloride, 65% sodium chloride and 10% magnesium sulfate to replace 100% sodium chloride are currently used in China to reduce sodium intake and increase potassium intake.<sup>[30]</sup> However, our results suggested that an increase in serum potassium might also increase the risk of hypertension. Individuals with normal blood pressure who use such salt substitute over a long period may thus be at increased risk of hyper-tension. In fact, the results from studies with health out-comes were insufficient to draw a conclusion whether low sodium intake is associated with an increased or reduced risk of CVD in general population.<sup>[28-30]</sup>

## Conclusion

The results of this study indicated that elevated serum potassium level might increase the risk of incident hypertension, while serum sodium level was unrelated to hypertension risk. These findings suggested that potassium might not always be beneficial in terms of reducing the risk of hypertension. However, further studies with larger sample size and wider age ranges are needed to clarify the relationships between serum potassium and sodium and the risk of hypertension.

## References

1. Lloyd-Jones DM, Hong Y, Labarthe D, Mozaffarian D, Appel LJ, Van Horn L, Greenland K, Daniels S, Nichol G, Tomaselli GF, et al. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American Heart Association's strategic Impact Goal through 2020 and beyond. *Circulation* 2010; 121:586–613.
2. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, et al. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation* 2013; 127:e6–245.
3. Lambers Heerspink HJ, Perkovic V, and de Zeeuw D. Renal and cardio-protective effects of direct renin inhibition: a systematic literature re-view. *J Hypertens* 2009; 27:2321–31.
4. Schmieder RE, Hilgers KF, Schlaich MP, Schmidt BM. Renin-angiotensin system and cardiovascular risk. *Lancet* 2007; 369:1208–19.
5. Payne RA, Wilkinson IB, Webb DJ. Arterial stiffness and hypertension: emerging concepts. *Hypertension* 2010; 55:9–14.
6. Nürnberger J, Keflioglu-Scheiber A, Opazo Saez AM, Wenzel RR, Philipp T, Schafers RF. Augmentation index is associated with cardiovascular risk. *J Hypertens* 2002; 20:2407–14.
7. Hadi HA, Carr CS, Al Suwaidi J. Endothelial dysfunction: cardiovascular risk factors, therapy, and outcome. *Vasc Health Risk Manag* 2005; 1: 183–98.
8. 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.
9. He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomized trials. *BMJ* 2013; 346:f1325.
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. Drenjancevic-Peric I, Jelakovic B, Lombard JH, Kunert MP, Kibel A, Gros M. High-salt diet and hypertension: focus on the renin-angiotensin system. *Kidney Blood Press Res* 2011; 34:1–11.
12. Millen AM, Norton GR, Majane OH, Maseko MJ, Brooksbank R, Michel FS, Snyman T, Sareli P, Woodiwiss AJ. Insulin resistance and the relationship between urinary Na<sup>+</sup>/K<sup>+</sup> and ambulatory blood pressure in a community of African ancestry. *Am J Hypertens* 2013; 26: 708–16.
13. Hedayati SS, Minhajuddin AT, Ijaz A, Moe OW, Elsayed EF, Reilly RF, Huang CL. Association of urinary sodium/potassium ratio with blood pressure: sex and racial differences. *Clin J Am Soc Nephrol* 2012; 7:315–22. Geerling JC, Loewy AD. Central regulation of sodium appetite. *Exp Physiol*. 2008; 93:177–209.

14. Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJL. The comparative risk assessment collaborating group. Selected major risk factor and global and regional burden of disease. *Lancet* 2002; 360:1347-60.
15. Sharma S, McFann K, Chonchol M, et al. 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: 418–423.
16. Polónia J, Maldonado J, Ramos R, Bertoquini S, Duro M, Almeida C, Ferreira J, Barbosa L, Silva JA, Martins F. Determinacao do consumo del sal numa amostra da populacao Portuguesa adulta pela exercao urnaria de sodio. Sua realcao com rigidez arterial. *Rev Port Cardiol* 2006; 25:801–17.
17. Zhang Z, Cogswell M, Gillespie C, Fang J, Loustalot F, Dai S, Carriquirry AL, Kuklina EV, Hong Y, Merritt R, et al. Association between usual sodium and potassium intake and blood pressure and hypertension among U.S. adults: NHANES 2005–2010.
18. Wannamethee SG, Lever AF, Shaper AG, et al. Serum potassium, cigarette smoking, and mortality in middle-aged men. *Am J Epidemiol* 1997; 145: 598–606.
19. Kesteloot H, Joossens JV. Relationship of serum sodium, potassium, calcium, and phosphorus with blood pressure. *Belgian Interuniversity Research on Nutrition and Health. Hypertension* 1988; 12: 589–593.
20. Pikilidou MI, Lasaridis AN, Sarafidis PA, et al. Blood pressure and serum potassium levels in hypertensive patients receiving or not receiving antihypertensive treatment. *Clin Exp Hypertens* 2007; 29: 563–573.
21. Rinner MD, Spliet-van Laar L, Kromhout D. Serum sodium, potassium, calcium and magnesium and blood pressure in a Dutch population. *J Hypertens* 1989; 7: 977–981.
22. Hu G, Xu X, Liang X, et al. Associations of plasma atrial natriuretic peptide and electrolyte levels with essential hyper-tension. *Exp Ther Med* 2013; 5: 1439–1443.
23. Lago RM, Pencina MJ, Wang TJ, et al. Interindividual variation in serum sodium and longitudinal blood pressure tracking in the Framingham Heart Study. *J Hypertens* 2008; 2121–2125.
24. Worth HG. A comparison of the measurement of sodium and potassium by flame photometry and ion-selective electrode. *Ann Clin Biochem* 1985; 22: 343–350.
25. Foringer JR, Norris C, Finkel KW. Evidence-Based Nephrology, Molony DA & Craig JC, Eds.; Blackwell Publishing Ltd. 2008; Chapter 56, 633–641.
26. Oparil S. Low sodium intake—cardiovascular health benefit or risk? *N Engl J Med* 2014; 371: 677–679.
27. O'Donnell MJ, Yusuf S, Mente A, et al. Urinary sodium and potassium excretion and risk of cardiovascular events. *JAMA* 2011, 306: 2229–2238.
28. Chatterjee R, Yeh HC, Shafi T, et al. Serum and dietary potassium and risk of incident type 2 diabetes mellitus: The Atherosclerosis Risk in Communities (ARIC) study. *Arch Intern Med* 2010; 170: 1745–1751.
29. Stolarz-Skrzypek K, Kuznetsova T, Thijs L, et al. Fatal and nonfatal outcomes, incidence of hypertension, and blood pressure changes in relation to urinary sodium excretion. *JAMA* 2011; 305: 1777–1785.
30. Ellis D, Miyashita Y. Primary hypertension and special aspects of hyper-tension in older children and adolescents. *Adolesc Health Med Ther* 2011; 2:45–62.