



Research Paper

Review on evaluation of serum Sodium and serum Potassium in essential Hypertension

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ABSTRACT:

Introduction: Hypertension is a prominent contributor to mortality and morbidity among the adult population on a global scale. The primary risk factor accountable for the development of coronary, cerebral, and peripheral vascular disease is identified. **Aim and Objectives:** The aim of this review is to comprehensively examine the existing research on serum sodium and serum potassium levels in persons specifically diagnosed with essential hypertension, excluding those with secondary hypertension. **Material and methods:** The literature was collected by using predetermined phrases on various online databases such as Google Scholar, PubMed and other journals. Only English literature was included, literature related to secondary hypertension, dietary intake of electrolyte and drug investigation were excluded. **Results:** Literature provide evidence to the significant increase in serum sodium levels in persons diagnosed with primary hypertension, regardless of gender, highlighting the strength and reliability of this correlation. On the other hand, this review article also reveals that a notable decrease in serum potassium concentrations among persons with hypertension, couple with an inverse relationship with the blood pressure. **Conclusions:** This comprehensive review aims to enhance the comprehension of essential hypertension by identifying areas of study that have not been adequately explored, discussing the potential consequences for clinical practice, and suggesting potential directions for future investigations.

Key-words: Primary Hypertension, Serum Sodium, Serum Potassium.

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I. Introduction:

Hypertension is a prominent contributor to mortality and morbidity among the adult population on a global scale. The primary risk factor accountable for the development of coronary, cerebral, and peripheral vascular disease is identified. Primary hypertension accounts for around 90% of cases of hypertension¹.

The prevalence of hypertension is increasingly being recognized as a significant health concern in India. By the time a significant proportion of individuals become cognizant of their hypertensive condition, they have typically progressed to a stage characterized by the presence of end organ damage, such as a potentially fatal stroke, myocardial infarction, or irreversible renal failure. Regrettably, even within affluent nations such as the United States, a staggering fifty million individuals receive a diagnosis of hypertension. Out of the aforementioned population, a majority of 70% exhibit awareness of the condition, while a mere 50% are actively engaged in seeking treatment for the condition. Furthermore, a mere 20% of individuals are effectively managing and controlling the condition².

In addition to the fundamental augmentation of cardiac activity resulting from an overactive sympathetic nervous system, the primary retention of salt and water by the kidney, there exist additional factors that contribute to the development of hypertension. These factors include familial susceptibility as well as high sodium consumption and insufficient potassium excretion.

In a nation such as India, individuals have developed a dietary pattern characterized by high sodium intake and low potassium consumption. Numerous studies have demonstrated a favorable association between

serum potassium levels and blood pressure. It has been demonstrated that reducing salt intake and increasing potassium intake, either individually or in combination, may be efficacious in the prevention or treatment of hypertension. The present investigation was done due to a dearth of independent information on serum sodium and potassium levels in the Indian hypertensive population.

Both potassium and sodium are essential to life. Large amounts of data, however, point to the significance of high dietary sodium as a significant risk factor for HTN^{3,4}. Research has also indicated that dietary potassium may offer some protection, either on its own or through influencing how the body handles sodium⁵. The current article aims to evaluate the evidence from studies on the associations between serum sodium, potassium, or the sodium to potassium ratio.

II. Aim and Objectives

1. The objective of this review is to thoroughly analyze the current body of literature on serum sodium and serum potassium levels in individuals with particularly essential hypertension.

III. Material and methods

This was a literature based study. For this, online database sets were searched to find literature related to serum sodium and serum potassium particularly in essential hypertension. Online data base used for research include Google Scholar, Web of Science, PubMed and other online journals.

The scope of citations was restricted to those that were published exclusively in the English language, without any other search constraints being used. The sodium-to-potassium ratio, serum potassium, essential blood pressure, essential hypertension was all included in the search phrase.

The initial round of screening was assessing the relevance of all titles and abstracts. A comprehensive analysis of the complete text was conducted on all papers that were not rejected during the initial screening process in order to find articles that were pertinent to the research question. To find suitable studies that were not initially obtained through the initial query, a supplemental literature search was conducted. This search involved examining the reference lists of all relevant studies with primary data, as well as any pertinent review articles and meta-analyses.

Eligibility. The inclusion criteria for this study encompassed research that investigated and provided findings on the association between the ratio of serum sodium to potassium, as well as serum sodium or potassium individually, and various health indicators such as essential blood pressure, essential hypertension. These investigations were conducted on individuals who did not have any acute illnesses, and the subjects could be either children or adults. Inclusion of studies was not limited to those examining the sodium-to-potassium ratio exclusively. This decision was primarily made to augment the available information regarding the associations between the ratio and the desired outcomes. However, it is important to note that these studies were unable to directly compare the relative strength of association between the ratio and the individual nutrients. Duplicate research populations were included in the analysis if the studies presented distinct findings. In cases where the findings were not unique, the study with the most thorough and up-to-date data was selected for inclusion. In the event that simultaneous interventions, such as dietary intake, pharmacologic medicines, were investigated, were not considered eligible. After screening, eligible literature was synthesize using narrative approach or integrative review or literature synthesis. The aforementioned approach is frequently employed in literature reviews, when the primary focus lies in the synthesis, comparison, and analysis of findings from several sources in order to derive broad conclusions.

IV. Results and Observations:

During the initial literature search, a total of 1365 studies were identified using the selected phrases. However, subsequent removal of duplicates, non-English articles, and articles pertaining to secondary hypertension, dietary intake, drug evaluation, and pharmaceutical evaluation resulted in only 12 studies that met the eligibility criteria for inclusion in this study.

Salt consumption in food is out of control in our nation. However, it should be noted that primary hypertension is not prevalent among all individuals. The low prevalence of hypertension observed in individuals who consume high quantities of salt may potentially be attributed to the long-term adaptation of the body's renal system to effectively eliminate sodium. However, further molecular investigations are needed to investigate this aspect of chronic adaptation of sodium handling by the kidneys. In addition to genetic susceptibility, excessive sodium intake and inadequate potassium intake, the renal processing of these cations also plays a significant role in the development of essential hypertension^{6,7,8}.

In general, salt consumption tended to be higher in tropical countries as a means to compensate for the loss of sodium through perspiration. In contemporary times, there has been an increase in salt consumption compared to previous eras due to a variety of culinary practices or a combination thereof, as individuals have become more attuned to the palatability of food. The incorporation of various dietary ingredients necessitates

the use of supplementary salt. Consequently, individuals tend to consume quantities that exceed their actual dietary needs, with an average intake of 2 grams per day per person compared to the recommended range of 8-10 grams per day. Excessive salt intake has been found to be a contributing factor in the development of hypertension, particularly in individuals with a hereditary predisposition.

The Analysis of Serum Sodium Levels in Individuals with Essential hypertension

According to a study conducted by Hangshing, T.⁹, the hypertension group had higher levels of serum sodium compared to the control group, despite both groups falling within the normal range. The average and variability of serum sodium levels among the cases were found to be 147.94 ± 2.88 meq/L, whereas in the control group, the corresponding values were 138.86 ± 3.44 meq/L.

The study in Srinagar, Kashmir was conducted by Jan et al.¹⁰. For the study, a total of 135 hypertension patients were selected, along with an equal number of age and sex-matched healthy controls. The serum sodium levels in the hypertension group were measured to be 140 ± 2.90 , whereas in the control group, the levels were determined to be 138.5 ± 1.12 . The hypertensive group had higher levels of serum sodium compared to the control group, which is believed to contribute to the development or maintenance of high blood pressure.

Lever et al.¹¹ conducted a study examining the relationship between arterial pressure and body electrolyte content in a sample of 91 patients diagnosed with essential hypertension and 121 individuals classified as normal controls. The study revealed a favorable correlation between plasma and exchangeable sodium levels and arterial pressure in the patient population. The study reached the conclusion that essential hypertension is likely influenced by two processes. During the initial phases of the condition, the aberrant mechanism responsible for the elevation in blood pressure is mostly associated with potassium rather than sodium. A renal lesion may manifest subsequently, maybe as a result of the hypertensive condition. This particular lesion is distinguished by the resetting of pressure natriuresis, which is evident through an atypical correlation between body sodium levels and arterial pressure. Additionally, individuals with this lesion have heightened vulnerability to the effects of elevated dietary salt consumption.

In an additional study carried out by Williams et al.¹², the authors examined the correlation between body sodium, chlorine, and potassium levels in a cohort of 30 individuals diagnosed with essential hypertension. In this study group, it was observed that there is a positive association between serum salt levels and blood pressure.

Nanji et al.¹³ conducted a separate study which demonstrated a favorable association between serum levels of sodium and hypertension.

Komiya et al.¹⁴ did a study using a sample of Japanese individuals. A total of 3,222 individuals from Japan were included in the study, with 610 participants from Kashiwa City Hospital and 2,612 participants from Shinshu University Hospital. Among these, 741 individuals had essential hypertension, with 256 from Kashiwa City Hospital and 485 from Shinshu University Hospital. The objective of the study was to investigate the potential influence of sodium, renal function, and plasma aldosterone concentration (PAC) on the elevation of blood pressure. The researchers discovered that the apex of the distribution curve for serum sodium was roughly 2 mmol/L greater in the hypertension group in comparison to the control group. The hypertension group exhibited a considerably greater prevalence of elevated blood sodium content (≥ 147 mmol/l).

In an additional examination carried out by Bulpitt¹⁵, a total of 2,328 male participants and 1,496 female participants aged between 35 and 64 years underwent screening for hypertension, alongside the measurement of their plasma sodium and potassium values. The study revealed a positive correlation between plasma sodium levels and blood pressure. Specifically, an elevation of 1 mmol/L in serum sodium was observed to correspond to a 1 mmHg increase in blood pressure for both males and females.

The study conducted by Parfrey et al.¹⁶ in 1981 examined a group of sixteen individuals with mild essential hypertension, characterized by an average diastolic blood pressure ranging from 90-110 mm Hg. Additionally, eight normotensive subjects with a diastolic pressure below 85 mm Hg were included in the study. The participants were randomly assigned to two different dietary interventions in a crossover design, with the trial being observer-blind. For a duration of 12 weeks, the individuals received their regular diets supplemented with 100 mmol of sodium per day, followed by a period of a no added sodium diet supplemented with 100 mmol of potassium daily. In both groups, blood pressure (BP) gradually increased during the high sodium meal. At the 12-week mark, the hypertension group exhibited a statistically significant increase in systolic pressure (mean \pm SD: 8.9 ± 12.6 mm Hg) compared to their pre-diet levels. Conversely, the normotensive group experienced a non-significant increase of 5.3 ± 9.0 mm Hg in systolic pressure. The hypertensive group experienced a significant decrease in blood pressure on the high potassium and sodium-free diet. At the 6-week mark, the average systolic pressure exhibited a decrease of 8.9 ± 11.2 mm Hg compared to the levels observed prior to the diet intervention. Conversely, in the normotensive group, there was an increase of 3.7 mm Hg. This disparity in response between the two groups was found to be statistically significant. During the experiment, a significant association was found between alterations in blood pressure (BP) and variations in the urine sodium-

to-potassium (Na/K) ratio among those in the hypertensive group. The blood pressure of individuals diagnosed with mild essential hypertension is observed to decrease when dietary salt is considerably reduced and potassium intake is increased. However, this effect is not observed in individuals with normal blood pressure levels.

The Analysis of Serum Potassium Levels in Individuals with Essential Hypertension

A study conducted by Hangshing⁹ involved the estimation of serum potassium levels in both control and study groups, with subsequent comparison between the two groups. The hypertension group exhibited a decreased serum potassium level in comparison to the control group, despite the fact that both groups were within the normal range. The average serum potassium level in the study group was determined to be 3.55 ± 0.29 meq/L. The average potassium concentration in the control group was determined to be 4.67 ± 0.22 meq/L.

Bulpitt et al.¹⁵ conducted a study involving a sample of 2328 men and 1496 women, all aged between 35 and 64 years. The participants were subjected to hypertension screening, and their plasma sodium and potassium values were examined. Individuals who were undergoing antihypertensive or diuretic treatment were excluded from subsequent analysis. After controlling for age, body mass index, and other relevant factors, it was observed that plasma potassium had a negative correlation with both systolic and diastolic pressure in both male and female individuals. There was a significant correlation between a reduction of 1 mmol/l in plasma potassium levels and an increase of 7 mmHg in systolic pressure ($P < 0.001$) as well as an increase of 4 mmHg in diastolic pressure ($P < 0.001$) among women. In male individuals, the observed increases were 4 mmHg ($P < 0.01$) and 2 mmHg ($P < 0.05$).

In a study conducted by Lever et al.¹¹, a total of 121 normal participants and 91 hypertension patients were examined. The findings of this investigation revealed a significant inverse correlation between plasma, exchangeable, and total body potassium levels and arterial pressure among the hypertensive patients. The researchers have proposed the subsequent explanation as the underlying factor for essential hypertension. During the initial phases of the condition, there is an aberrant mechanism that leads to an elevation in blood pressure. This process is mostly associated with potassium rather than sodium. A renal lesion may manifest at a later stage, potentially as a result of the hypertension. This particular condition is distinguished by the resetting of pressure natriuresis, which is evident by an aberrant correlation between the sodium content in the body and arterial pressure. Additionally, individuals with this condition are more prone to experiencing an elevated sensitivity to higher levels of dietary salt consumption.

A study was undertaken at the National Institute of Public Health and Environmental Protection in Bilthoven, The Netherlands. A study was conducted to examine the associations between serum cations, namely sodium, potassium, calcium, and magnesium, and blood pressure in a sample of 182 Dutch individuals aged 20-59 years. The combined study revealed a negative correlation between serum potassium levels and diastolic blood pressure. This correlation was observed specifically among women¹⁶.

Another study was conducted in Karachi, Pakistan, in which a sample of thirty individuals with both hypertension and diabetes was selected. An equal number of individuals who were matched in terms of age and sex were chosen as controls for the study. The study group had a mean blood potassium level of 4.59 mmol/L, whereas the control group had a mean serum potassium level of 5.03 mmol/L¹⁷.

A research investigation conducted at the University of Tokyo involved the measurement of plasma electrolytes in a cohort of 82 individuals diagnosed with essential hypertension. The primary objective of this study was to explore the potential association between blood pressure levels and plasma electrolyte concentrations. The researchers detected significant negative correlations between plasma potassium content and 24-hour systolic blood pressure ($r = -0.336$) as well as diastolic blood pressure ($r = -0.298$) in the patient population under study. There is an inverse correlation between plasma potassium content and both daytime and overnight systolic and diastolic blood pressure. There was no observed correlation between the blood pressure levels measured in the office setting and the content of potassium in the plasma. The results of this study demonstrate that there is a negative correlation between plasma potassium concentration and ambulatory blood pressure, including both daytime and night-time blood pressure, in individuals with essential hypertension. These findings suggest that potassium levels may play a role in determining overall blood pressure throughout the day in individuals with essential hypertension¹⁸.

In order to examine the impact of potassium on blood pressure, Luft et al.¹⁹ conducted a study with a total of 431 normotensive individuals and 478 hypertensive individuals. An inverse association between serum potassium and blood pressure was identified, which provides support for our study.

Combined Analysis

The study conducted by Prabhakaran and Heber Anandan²⁰ demonstrated statistically significant differences between the patients and controls. The average serum sodium concentration was found to be $146 \pm$

2.81 mmol/L in males and 148 ± 4.2 mmol/L in females. The average and variability of serum potassium levels among the cases were found to be 3.79 ± 0.179 mmols/L, whereas in the control groups, the corresponding values were 4.25 ± 0.22 mmol/L. The study's findings indicate that hypertension individuals exhibited considerably higher levels of serum sodium, regardless of any accompanying risk factors or gender.

V. Discussion:

Literature research revealed that very limited literature is available on serum sodium and potassium evaluation in essential hypertension. Only 12 studies were found eligible for the current review. The collective findings from the examined research consistently indicate a potential correlation between increased levels of sodium in the bloodstream and the occurrence of essential hypertension. Multiple investigations have demonstrated a positive association^{9,10,11,12,13,14, 15, 16}, suggesting that the disruption of sodium homeostasis may have a contributing role in the pathogenesis of hypertension. The presence of increased levels of sodium in the bloodstream, a crucial electrolyte, has been observed to have an impact on the volume of fluid outside the cells and the resistance within the blood vessels. These factors play a significant role in the regulation for blood pressure.

Nevertheless, the strength of this correlation is influenced by significant differences in the demographics, research approaches and geographic contexts of the studies. The observed variability in research outcomes may be attributed to disparities in dietary salt intake, genetic predispositions and additional environmental factors. Hence, it is crucial to exercise caution when interpreting the observed tendency towards a positive correlation, as it is necessary to consider the potential; impact of confounding variables. In order to enhance the understanding of the complex association between serum sodium levels and critical hypertension, future research attempts should strive to employ more standardized procedures and encompass bigger and more diverse study populations.

In comparison to sodium, the studies evaluated showed notable variability in the findings pertaining to serum potassium levels in essential hypertension. Several studies have documented an inverse relationship between levels of potassium and hypertension^{9,15,11,16,17,18,19,20}, indicating that reduced serum potassium levels may be a contributing factor to high blood pressure.

While this review article contributes to valuable insights to understand the evaluation of serum sodium and serum potassium in case of essential hypertension, this study has discovered a dearth of scientific assessment pertaining to serum sodium, potassium and the impacts of a reduced ratio of sodium to potassium on blood pressure.

VI. Summary and conclusions:

This literature review examines the complex association between serum sodium, serum potassium and primary hypertension, providing detailed insights derived from a thorough study of available research findings. Literature provide evidence to the significant increase in serum sodium levels in persons diagnosed with primary hypertension, regardless of gender, highlighting the strength and reliability of this correlation. On the other hand, this review article also reveals that a notable decrease in serum potassium concentrations among persons with hypertension, couple with an inverse relationship with the blood pressure. The lack of definitive findings necessitates further targeted research on the impact of potassium on blood pressure, taking into account variables such as medication utilization and dietary determinants. The results of this review have practical significance in both academics and therapeutic contexts. Healthcare professionals may get benefits from taking into account serum electrolyte levels as indicators of the risk of hypertension, which could potentially contribute to the development of more individualized and focused treatment approaches. Based on the knowledge acquired from this study, it is recommended that forthcoming research initiatives give precedence to the utilization of standardized procedure, delve into the molecular mechanisms that underlie electrolyte imbalances and take into the account the impact of hereditary factors on individual's responses. These endeavors will not only augment our comprehension of fundamental hypertension but also provide the groundwork for pioneering and more efficacious methodologies in its avoidance and control.

In conclusion, this review represents an available literature finding on evaluation of serum sodium and potassium in essential hypertension and establishes a fundamental basis for subsequent research endeavors.

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