European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 09, Issue 07, 2022

ORIGINAL RESEARCH

Serum Electrolytes as Mortality Indicators in Hypertension Cases

Syeda Parveen Fatima[1], Deva Pragna Prashanthi[2]

[1]Assistant Professor, Department of Physiology, Govt Medical College, Jagitial, Telangana, India

[2]Assistant Professor, Department of Biochemistry, Govt Medical College, Jagitial, Telangana, India

ABSTRACT

Background: According to the pressure natriuresis theory, monogenic hypertension, and dietary salt reduction studies, Na+ is a primary predictor of blood pressure and mortality. The evolved response to a salt or water shortfall is more efficient than the response to salt surplus. Cl is the most abundant anion outside of cells and derives from food. The current epidemiological investigation examined the relationship between blood electrolyte levels and hypertension in a salt-consuming community. Fluid and electrolyte balance is necessary for postoperative and critically ill patients' metabolic care, gastrointestinal function, and nutrition. Artificial nutrition should be prescribed with the same care as other nutritional and pharmaceutical needs.

Materials and Methods: Secondary study of epidemiological study was carried out at the Government Medical College, Jagitial, India, which was carried out between the December 2021 to November 2022. Using regression models, the relationship between the amounts of sodium, potassium, chloride, total calcium, phosphate, and magnesium in the serum and blood pressure and the presence or absence of hypertension was investigated.

Results: 81 previously diagnosed hypertension patients were included in this study. 56% of participants experienced electrolyte problems. 62% of hypercalcaemic subjects had hypertension, followed by hypokalaemia (56%) and hypernatremia (54%). Hypercalcemia was linked to IH and PDH. Higher serum calcium quartile increased IH and PDH risk. Serum salt and hypertension were unrelated. PDH U-shaped serum potassium. Higher chloride quartile had lower PDH chances. Highest phosphate quartile was solely related with lower IH probabilities, although higher magnesium lowered IH and PDH odds.

Conclusions: We found a link between IH/PDH and serum calcium, magnesium, and chloride. Patients with IH may have concurrent electrolyte issues, such as hypercalcemia, which may reflect additional underlying etiologies. When prescribing fluid and electrolytes, it's important to understand the relationship between internal and external balance, starvation, and injury to reduce physiological and clinical side effects. Prescriptions need detail and education.

Keywords: Serum electrolytes, mortality, indicators, hypertension, cases.

Corresponding Author: Dr Syeda Parveen Fatima, Assistant Professor, Department of Physiology, Govt Medical College, Jagitial, Telangana, India

INTRODUCTION

The evidence from dietary salt reduction, monogenic forms of hypertension, and the pressure natriuresis hypothesis all point to Na+ as a significant factor in blood pressure (BP) and, consequently, mortality. The main extracellular anion that surrounds Na+ is Cl, which is mostly obtained from food sources. The resulting perception that any clinical significance of the independent effect of Cl on BP and prognosis is essentially academic has led to this.[1-3] However, a substantial amount of research in both humans and animals suggests that the increase in blood pressure in response to salt consumption may be more specifically related to the anionic component, Cl+ rather than Na+. Additionally, there is mounting evidence that chloride movement across the cell plasma membrane regulates cell volume, Trans epithelial fluid transport, smooth muscle cell contraction, and synaptic transmission rather than simply acting as an inert bystander in electrochemical equilibrium across cell membranes.[4,5] The thick ascending limb of Henle cells, which exhibit an increase of cyclo-oxygenase-2 in low Cl solution, and the tumour necrosis factor-induced inflammatory response, which is partially related with low intracellular Cl, provide additional evidence that Cl plays a role in inflammation.[6,7] Extracellular Cl plays a crucial part in the macula densa's control of renin secretion in the kidneys. Recently, it was demonstrated that blocking the vascular endothelial growth factor receptor 3 was linked to elevated BP and selective Cl buildup in the skin of mice. This was independent of Na+ and water content. It has been challenging to separate the independent effects of serum Cl from changes in serum Na+, potassium (K+), and HCO3 since these changes occur concurrently with changes in serum Cl. After adjusting for age, body mass index (BMI), and serum Na+ levels, a serum Cl 100 mEq/L level was linked to a 48% (hazard ratio [HR], 1.48; 95% confidence interval [CI], higher risk of all-cause mortality.[8-11]

Cl was the strongest predictor of all-cause death in patients with heart failure, with an adjusted HR of 0.78 per SD rise in serum Cl, according to a post hoc analysis of the CHARM (Candesartan in Heart Failure-Assessment of Reduction in Mortality and Morbidity) research.[12-14] This suggests that serum Cl independently predicts risk from serum BP and Na+. Despite the fact that Cl has a role in a number of physiological processes in the human body and may be linked to BP, nothing is known about the epidemiological implications of Cl in terms of long-term mortality effects. In this investigation, a sizable hypertensive cohort followed up to examine the link of serum Cl with cause-specific death irrespective of other electrolytes and BP.[15-17]

Objectives of the study

To investigate the effect of serum electrolyte as mortality indicator in the hypertensive patients.

MATERIALS & METHODS

Secondary study of epidemiological study was carried out at the Government Medical College, Jagitial, India, which was carried out between the December 2021 to November 2022. 81 Individuals suffering from hypertension in the India can receive services at the secondary and tertiary levels of care at the district hospital Jagitial. At the Glasgow blood pressure clinic, every patient receives treatment until their blood pressure reaches the desired range; after that, they are given the option to continue receiving care either at the or in primary care.

Data collection

Self-reporting and a questionnaire were used to gather data during an in-person discussion with cardiologists and/or trained nurses about recent medications, dietary habits, smoking,

alcohol usage, and personal and family medical histories. All participants' height and weight were recorded to the nearest 05 cm and 01 kg, respectively, when they were not wearing shoes and wearing light clothing. BMI was computed as height divided by weight.

At each visit, professional hypertension nurses took manual blood pressure readings three times with calibrated mercury sphygmomanometers. The average of the last two readings was recorded at each visit. Patients who were planning to visit the clinic were instructed to continue taking their prescribed medications as they normally would prior to their appointment. At each visit, height and weight were measured with apparatus that was standardised for each patient using the scale. At the beginning of the study as well as at predetermined time intervals, blood was drawn for the purpose of calculating standard hematologic and biochemical indices, which included renal function tests. Serum chloride concentration was determined with the Senacore analyzer (ST 200 Pro) and ion selective electrodes.

Despite the fact that the chloride assays were conducted over an extended period of time, they were carried out in certified hospital laboratories using automated analyzers with careful attention paid to external quality control schemes, and the normal range of chloride that was reported by the laboratories has not changed. The use of tobacco and alcohol was evaluated according to a structured format. Each piece of information was saved to a large central database after being entered into an electronic format.

Statistical Methods

All of the analyses were limited to the participants in the database who were hypertensive and had their serum Cl measured during the registration visit. After performing initial analyses on the measured serum electrolytes, subsequent analyses were carried out on the adjusted serum Cl and HCO3 values. It is normal for the serum concentrations of Na+, Cl, and HCO3 to move in unison in the presence of free water disturbances, which are typical in treated hypertensive patients. The only exception to this rule is when there is also a competing acid–base imbalance present. The Feldman et al. approach was utilised in order to derive the adjusted values for Cl and HCO3. It is possible to estimate, based on the fact that the ratio of serum Cl to serum Na+ in normal controls. Similarly, the decrease (increase) in serum HCO3 with a water excess should be close to one-fifth the decrease (rise) in Na+, when considering the ratio of HCO3 to Na in normal controls. This is because a water excess (deficit) causes an increase in serum HCO3. Accordingly, an adjusted level of serum HCO3 equals a measured level of HCO3+. Anion, where Anion Gap is the difference between the patient's anion gap and the typical anion gap. Na+ is the amount of sodium that was measured.

RESULTS

Demographics

[Table 1] lists the 81 subject’s initial characteristics. The population was overweight, middle-aged, and hypertensive, with a roughly equal mix of males and females (52%). Fifty-five percent of people smoked, and 61.3% said they drank more than six units of alcohol per week. 18.2% of the population indicated concomitant CVD morbidity at the time of registration, which is less than one fifth of the total. Diuretics were used by around one fifth (22.0%) of the population. The SBP and DBP that were reached were much lower than the starting BP. regardless of HCO3 and Na+ levels, those in the lowest percentile of serum Cl were older and had greater prevalences of BP, cholesterol, and CVD. The lowest percentages of people who used alcohol and had an estimated glomerular filtration rate of less than 60 mL/min per 1.73 m^2 were seen in the highest quintile of serum Cl. In line with expectations, serum HCO3 and Na+ displayed an inverse linear correlation across serum Cl quintiles. As a result, with lower serum Cl levels, the mean anion gap was greater.

Table 1: Serum Electrolytes and Systolic Blood Pressure

Serum Electrolytes	GEE β (SBP)*	95% CI β	P Value
Serum Cl−	0.01	−0.19 to 0.21	0.893
Serum Na+	0.16	−0.03 to 0.35	0.105
Serum K+	−0.65	−1.82 to 0.53	0.281
Serum HCO3−	−0.34	−0.53 to −0.15	0.001

Table 2: Values of Electrolytes

	β	95 % CI	P value	Adjusted R^2	β	95 % CI	P value	Adjusted R^2
Sodium	0·03	0·00, 0·06	0·042	29·0%	0·04	0·01, 0·07	0·021	20·1%
Potassium	−0·02	−0·05, 0·01	0·134		−0·05	−0·08, −0·01	0·004	
Chloride	−0·01	−0·04, 0·02	0·575		−0·002	−0·04, 0·03	0·886	
Total calcium	0·08	0·05, 0·11	<0·001		0·10	0·06, 0·13	<0·001	
Phosphate	−0·10	−0·14, −0·07	<0·001		−0·06	−0·10, −0·03	<0·001	
Magnesium	−0·03	−0·06, 0·00	0·039		−0·03	−0·06, 0·00	0·059	

Table 3: Association between serum electrolyte and mortality rate

Variables		Outcomes		
	Alive	Dead	X2	P value
Blood Pressure				
Normal	21	5	0.650	0.424
Abnormal	60	18		
Electrolyte Status				
Normal	58	910	0.313	
Abnormal	23	13		0.625
Gender				
Male	65	12	5.870	0.018
Female	16	10		
Age				
25-50	17	2	12.455	0.003
51-70	45	11		
71+	19	11		

DISCUSSION

Blood Cl 100 mEq/L was a significant independent predictor of all-cause mortality as well as CVD and non-CVD mortality in a large cohort of 81 hypertensive patients followed up. This connection was irrespective of concurrent serum Na+ and HCO levels and diuretic usage. Serum Cl is frequently tested in hypertension patients and is a component of the standard

screening biochemistry panel in outpatient clinics, but it is not a component of routine risk strati- fication. Our findings and those of other studies indicate that serum Cl is a risk signal.[18,19] Using C-statistics, net reclassification improvement, and integrated discrimination improvement, risk discrimination analyses demonstrate that adding serum chloride enhanced risk discrimination over and above conventional CV risk variables. It is necessary to confirm that the net reclassification improvement was 4.6% in several investigations. Uncertainty surrounds the mechanism through which low serum Cl promotes mortality. Our findings imply that the danger provided by low Cl is independent of concurrent Na+ or HCO levels and does not reflect hazards related to hyponatremia or acid-base disturbances. As treated hypertension individuals made up our study cohort, confounding caused by the use of diuretics is probably a possibility. The link between low Cl and mortality persisted even after the analyses were stratified for diuretic usage, even though only 22% of our patients were taking diuretics at the time that serum Cl was tested during the initial visit. Additionally, we modified Cl levels for free water variations that are frequently brought on by the use of diuretics.[20,21] Contrary to what has been seen about the impact of dietary Cl, our findings on serum Cl. On the relationship between dietary serum Cl and blood pressure in animal experiments with experimental diet alteration, there are conflicting results in the literature. While some studies show a correlation between dietary Cl intake and BP, other studies show no such correlation. The fact that Bartter syndrome is characterised by normal blood pressure despite its associations with selective Cl- deficiency and salt wasting is also pertinent to note. However, it is unclear if dietary Cl elevates blood pressure by any other means except affecting the way that Cl is absorbed by the kidneys. The intriguing discovery that when this immune mechanism was blocked, there was selective Cl accumulation in the skin salt-sensitive hypertension would suggest that our findings may have a more complex underpinning mechanism than just renal salt balance, which is supported by mounting evidence that the immune system plays an extra renal regulatory role in maintaining Na+ homeostasis.[20-22] The longitudinal measurements of blood pressure and electrolytes, as well as the study's large cohort of approximately 13 000 hypertensive people with median survival duration of 32 years, are its strong points. Our work has certain limitations, including the fact that it was an observational study of a treated hypertensive cohort, thus even though hypertension affects about 27% of adults; the findings may not be generalizable. Additionally, we lack any assessments of the renin-aldosterone status, arterial blood gases, or urine electrolytes. In this investigation, we have simply looked at mortality. Finally, unmeasured factor-related residual confounding may still present.

CONCLUSION

A risk indicator that seems to be independent of serum Na+ and HCO levels is serum Cl. Uncertainty surrounds the risk's underlying mechanism. Simple explanation: Serum Cl+ levels, which may be more homeostatically regulated than Cl+ levels, indicate aberrant physiology better than serum Na+ levels. Further research is now required to clarify the underlying mechanisms underlying the link between low serum Cl levels and mortality outcomes, assuming future studies confirm and extend our findings. However, because Cl measurement is a standard component of clinical screening, our findings may be useful in identifying high-risk hypertension patients in clinical settings. The typical lower limit of the reference range for blood chloride may be redefined from 95 mEq/L to 100 mEq/L in light of the inverse linear connection between serum chloride level 100 mEq/L and mortality.

REFERENCES

1. De Bacquer D, De Backer G, De Buyzere M, Kornitzer M. Is low serum chloride level a risk factor for cardiovascular mortality? *J Cardiovasc Risk*. 1998;5:177–184.
2. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA, Swedberg K, Wang D, Yusuf S, Michelson EL, Granger CB; CHARM Investigators. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol. 2007;50:40–47.
3. Paul L, Jeemon P, Hewitt J, McCallum L, Higgins P, Walters M, McClure J, Dawson J, Meredith P, Jones GC, Muir S, Dominiczak AF, Lowe G, McInnes GT, Padmanabhan S. Hematocrit predicts long-term mortality in a nonlinear and sex-specific manner in hypertensive adults. Hypertension. 2012;60:631–638.
4. Feldman M, Soni NJ, Dickson B. Use of sodium concentration and anion gap to improve correlation between serum chloride and bicarbonate con- centrations. J Clin Lab Anal. 2006;20:154–159.
5. Harrell FE Jr, Califf RM, Pryor DB, Lee KL, Rosati RA. Evaluating the yield of medical tests. JAMA. 1982;247:2543–2546.
6. Pencina MJ, D'Agostino RB Sr, D'Agostino RB Jr, Vasan RS. Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond. Stat Med. 2008;27:157–172; discus- sion 207.
7. Abramowitz MK, Hostetter TH, Melamed ML. The serum anion gap is altered in early kidney disease and associates with mortality. Kidney Int. 2012;82:701–709.
8. Whitescarver SA, Ott CE, Jackson BA, Guthrie GP Jr, Kotchen TA. Salt-sensitive hypertension: contribution of chloride. Science. 1984;223:1430–1432.
9. Wyss JM, Liumsiricharoen M, Sripairojthikoon W, Brown D, Gist R, Oparil S. Exacerbation of hypertension by high chloride, moderate sodium diet in the salt-sensitive spontaneously hypertensive rat. Hypertension. 1987;9(6 Pt 2):III171–III175.
10. Duran C, Thompson CH, Xiao Q, Hartzell HC. Chloride channels: often enigmatic, rarely predictable. Annu Rev Physiol. 2010;72:95–121.
11. Cheng HF, Wang JL, Zhang MZ, McKanna JA, Harris RC. Role of p38 in the regulation of renal cortical cyclooxygenase-2 expression by extracel- lular chloride. J Clin Invest. 2000;106:681–688.
12. Yang H, Huang LY, Zeng DY, Huang EW, Liang SJ, Tang YB, Su YX, Tao J, Shang F, Wu QQ, Xiong LX, Lv XF, Liu J, Guan YY, Zhou JG. Decrease of intracellular chloride concentration promotes endothelial cell inflammation by activating nuclear factor-κB pathway. Hypertension. 2012;60:1287–1293.
13. Lorenz JN, Weihprecht H, Schnermann J, Skøtt O, Briggs JP. Renin release from isolated juxtaglomerular apparatus depends on macula densa chloride transport. Am J Physiol. 1991;260(4 pt 2):F486–F493.
14. Wiig H, Schröder A, Neuhofer W, et al. Immune cells control skin lymphatic electrolyte homeostasis and blood pressure. J Clin Invest. 2013;123:2803–2815.
15. Hypertension in men. Is the sodium ion alone important? N Engl J Med. 1987;317:1043–1048.
16. Luft FC, Steinberg H, Ganten U, Meyer D, Gless KH, Lang RE, Fineberg NS, Rascher W, Unger T, Ganten D. Effect of sodium chloride and sodium bicarbonate on blood pressure in stroke-prone spontaneously hypertensive rats. Clin Sci (Lond). 1988;74:577–585.
17. Luft FC, Zemel MB, Sowers JA, Fineberg NS, Weinberger MH. Sodium bicarbonate and sodium chloride: effects on blood pressure and electrolyte homeostasis in normal and hypertensive man. J Hypertens. 1990;8:663–670.

18. Shore AC, Markandu ND, MacGregor GA. A randomized crossover study to compare the blood pressure response to sodium loading with and without chloride in patients with essential hypertension. J Hypertens. 1988;6:613–617.
19. Liamis G, Milionis H, Elisaf M. Blood pressure drug therapy and electrolyte disturbances. International Journal of Clinical Practice. 2008 Oct;62(10):1572-80.
20. Sinclair AM, Isles CG, Brown I, Cameron H, Murray GD, Robertson JW. Secondary hypertension in a blood pressure clinic. Archives of internal medicine. 1987 Jul 1;147(7):1289-93.
21. Liamis G, Rodenburg EM, Hofman A, Zietse R, Stricker BH, Hoorn EJ. Electrolyte disorders in community subjects: prevalence and risk factors. The American journal of medicine. 2013 Mar 1;126(3):256-63.
22. Nakimuli A, Nakubulwa S, Kakaire O, Osinde MO, Mbalinda SN, Kakande N, Nabirye RC, Kaye DK. The burden of maternal morbidity and mortality attributable to hypertensive disorders in pregnancy: a prospective cohort study from Uganda. BMC pregnancy and childbirth. 2016 Dec;16(1):1-8.