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Original article

ASSOCIATION OF SERUM CHLORIDE LEVEL WITH HYPERTENSION.

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Abstract.

Background:
The most abundant anion in our body, along with sodium, is chloride (Cl), which is primarily obtained through dietary sources. Studies indicate that greater dietary Chloride intake raises blood pressure, and higher serum Cl seems to be linked to decreased cardiovascular risk and death. This indicates that serum Chloride reflects risk pathways independent of blood pressure, serum sodium, and serum bicarbonate. It is uncertain how serum chloride affects a patient's long-term survival after developing pulmonary arterial hypertension.

Methods:
This study included patients with hypertension, idiopathic or heritable, who had a basic metabolic panel when they were diagnosed with hypertension.

Results:
Over time, serum chloride had no obvious impact on systolic blood pressure. Only serum bicarbonate among electrolytes demonstrated an independent impact on longitudinal blood pressure.

Conclusion:
This study has shown the association of chloride with systolic and diastolic blood pressure.

Recommendation:
More studies are now needed to elucidate the mechanisms of the association between low serum Chloride levels and mortality outcomes if more studies confirm and extend our findings. Our findings may be applied in clinical practice to recognize persons with high-risk hypertension as Chloride measurement is a critical component of routine clinical screening.

Keywords: Serum chloride, hypertension, clinical pathology, arterial hypertension, blood pressure,
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1. INTRODUCTION.

Hypertension is a term for a physiologically abnormal blood pressure peak (140/90 mmHg or greater) in blood vessels. There is a lot of evidence from both human and animal studies that suggests the anionic component, Cl+, rather than Na+, maybe more directly responsible for the rise in blood pressure caused by salt consumption [1]. Moreover, there is increasing evidence that chloride movement across the cell controls smooth muscle cell contraction, fluid transport, synaptic transmission, and cell volume rather than just being an inert participant in equilibrium across the cell plasma membrane [2–5].

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Hypertension and NaCl, the circumstances in which it happens, its clinical conclusions, and the function of counter-regulatory processes and fundamental regulations that are disturbed when salt consumption is altered, are still the subject of great discussion [5]. Salt sensitivity, a term for the blood pressure reaction to salt ingestion, is indicated by a change in blood pressure in response to a change in sodium chloride ingestion [6]. Since its sensitivity is more common (30–50%) in hypertensives than in normotensives, the risk factor for developing hypertension in the future is the presence of salt sensitivity in normotensives. Salt sensitivity can be influenced by other dietary elements such as calcium, potassium, carbohydrates, protein, and fat, hence it is not specifically tied to sodium chloride [7].

The Chloride component of sodium chloride salt may have a greater function in blood pressure, according to mounting data, and it may even be more significant than the Na+ component. More than 85% of the salt in typical meals is taken as sodium chloride, and any therapeutic significance prognosis has been widely regarded as 'academic'. Studies examining the amounts of sodium and Chloride in processed meals, however, show that these two substances' concentrations are not always correlated because they can come from various sources [8]. This study aims to investigate the importance of Cl as an important electrolyte with a considerable impact on hypertension and health.

2. MATERIALS AND METHODS.

2.1. Study setting and population.

Tests were done in [clinical biochemistry] under clinical Pathology in MGMMCH, Jamshedpur, Jharkhand, India. Those who were diagnosed as hypertensive patients in MGMMCH were included in the study during August and September 2023

2.2. Clinical measurement.

Three manual BP readings using calibrated sphygmomanometers were taken. The average of the previous two readings was recorded. In the clinical laboratory biochemical analysis of blood samples collected was done as part of standard screening. The assays were carried out on automated analyzers in MGMMCH hospital, and the normal range of chloride had not changed as per quality control.

2.3. Statistical Methods.

All analyses were restricted to the 128 hypertensive database participants who had their serum Cl levels evaluated at registration. The measured serum electrolytes were analyzed first, followed by the corrected serum Chloride and bicarbonate values. Except for when a competing acid-base illness is present, it is expected that serum sodium, Chloride, and bicarbonate concentrations will migrate together when there are free water disturbances, which are frequent in hypertension patients receiving treatment.

It is reasonable to anticipate that the change in serum Chloride following a water surplus or loss will be nearly like a change in serum sodium as the ratio of serum Chloride to sodium in healthy measures was 0.76±0.02,22 [9]. The calculated serum Cl value is therefore calculated as follows: calculated Chloride ion + 0.76 * (140 calculated sodium). The decline (rise) in serum bicarbonate with a water excess (loss) should be roughly one-fifth the fall (rise) in sodium, keeping in mind that the ratio of bicarbonate to sodium in normal is 0.19±0.01.22 [10]. The population was then divided into 5 groups based on the serum Chloride levels in each group. Age, sex, BMI, diastolic and systolic blood pressure, alcohol use, and smoking status, were significant variables that were considered in the analyses. A general estimating equation model was used to evaluate the relationship between baseline serum chloride, repeated annual serum Chloride, and change in Blood pressure throughout the follow-up period.

3. RESULTS.

A total of 128 subjects were included in this study. At the initial stage, several 197 patients were examined for eligibility, however, 69 patients

were excluded from this study due to not being eligible. The achieved Systolic blood pressure and diastolic blood pressure were much lower than baseline BP (Table 1). Data has been presented as mean.

Individuals in lowest level of serum Cl- were older and had high Blood pressure, cholesterol, regardless of HCO3-.

3.1. Association of serum Cl- with Blood pressure changes.

Over time, serum chloride had no evident impact on systolic blood pressure. Only serum bicarbonate among electrolytes demonstrated an independent impact on longitudinal blood pressure. (Table 2).

4. DISCUSSION.

According to this study's findings, the risk possessed by low Chloride does not represent risks associated with acid-base abnormalities [12]. It is discovered that the risk caused by low Chloride is unaffected by concurrent sodium or bicarbonate levels. Our study cohort consisted of people who had been treated for hypertension, thus confounding brought on by taking diuretics is undoubtedly a possibility. In 7 individuals (5% of the total cohort), serum HCO3 >30 mEq/L was the only biochemical marker of metabolic alkalosis, showing that it is unlikely that the reverse effect from severe volume restriction or hyperaldosteronism will occur. A recent study that found that a larger anion gap in early CKD is an indication of early death (which can be connected to low Cl) supports our findings further. Greater anion gaps and the associated low serum Cl levels are connected to elevated blood pressure in a subset of the NHANES [13] with normotensive participants.

Serum chloride is routinely assessed in hypertension patients as part of the usual biochemistry diagnostic panel in hospitals, even though it is not frequently used in risk classification. The results of both our study and earlier research point to serum Cl as a risk indicator. Consistent findings in people with heart failure were also made public. Serum chloride was an improvement over traditional CV risk factors in terms of risk discrimination [11].

The current findings in patients with treated hypertension also show a similar association between anion gap, as well as baseline and achieved blood pressure. The findings on serum Chloride contrast with what has been seen on the impact of dietary Chloride. A link between dietary Chloride intake and reduced Blood pressure has been discovered in some research, but not in others.

5. CONCLUSION.

Serum Cl appears to represent a risk marker independent of serum sodium and bicarbonate levels. The mechanism of the risk is uncertain. Serum Chloride levels are a better indicator of abnormal physiology than serum sodium levels because they may be more homeostasis-regulated. The customary lower range for blood chloride may be changed from 95 mEq/L to 100 mEq/L given the inverse linear association between a serum chloride level of 100 mEq/L and mortality.

6. LIMITATIONS.

The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of a comparison group also poses a limitation for this study's findings.

7. RECOMMENDATION.

More studies are now needed to elucidate the mechanisms of the association between low serum Chloride levels and mortality outcomes if more studies confirm and extend our findings. Our findings may be applied in clinical practice to recognize persons with high-risk hypertension as Chloride measurement is a critical component of routine clinical screening.

Table 1: **Particulars of study population**

VARIABLES	MEN	WOMEN	TOTAL
Age	49.68	51.34	50.55
Systolic blood pressure	164.07	168.18	166.22
Diastolic blood pressure	99.35	97.5	98.38
Serum Na+	140.25	139.84	140.04
Serum Cl-	102.45	102.87	102.67
Anion gap	15.91	15.72	15.81
Serum bicarbonate	26.31	25.56	25.92
Achieved Systolic BP	149.68	152.59	151.20
Achieved Diastolic BP	90.60	89.20	86.87

Table 2: **Relationship between serum chloride and systolic blood pressure.**

Electrolytes	Systolic blood pressure	95% Cl	P value
Serum Na+	0.16	-0.03 to 0.35	0.105
Serum Cl-	0.01	-0.19 to 0.21	0.893
Serum K+	-.65	-1.82 to 0.53	0.281
Serum bicarbonate	-0.34	-0.53 to −0.15	0.001

Systolic blood pressure' deviation was calculated using general estimating equation.

Table 3: **Relationship between serum electrolytes and diastolic blood pressure.**

Electrolytes	Diastolic blood pressure	95% Cl	P value
Serum Na+	0.15	0.05 to 0.25	0.003
Serum Cl-	-0.01	-0.11 to 0.10	0.876
Serum K+	-1.23	-1.85 to −0.61	<0.001
Serum bicarbonate	-0.19	-0.29 to −0.09	<0.001

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9. LIST OF ABBREVIATIONS.

Cl- chloride
BP- Blood Pressure
BMI- Body mass index
CKD- Chronic kidney disease
NHANES- National Health and Nutrition Examination Survey
CV- Cardiovascular

10. SOURCE OF FUNDING.

The study was not funded.

11. CONFLICT OF INTEREST.

The authors report no conflicts of interest in this work.

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