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Prognostic Significance of Serum Chloride Levels in Congestive Heart Failure

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Abstract

Background: Hypochloraemia is associated with higherrates of short as well as long-term mortality, and that blood chloride levels are a better predictive indicator of heart failure than serum sodium levels. Due to the fact that chloride will not be distally reabsorbed, unlike sodium, loop diuretics do not prevent hypochloremia. Since there haven't been many studies conducted in the western part of Uttar Pradesh, this subject has been chosen for further study. **Material and Methods:** Inclusion criteria-All Patients older than 18 years and admitted with a diagnosis of congestive heart failure including both HFrEF (heart failure with reduced ejection fraction) and HFpEF (heart failure with preserved ejection fraction). Exclusion Criteria - Patients on drugs like corticosteroids, laxatives, bicarbonates, Patients had prior heart transplantation or mechanical circulatory assist device, Patients having sepsis, Patients with COPD with respiratory failure, Patients with pregnancy, or malignancy & Patients who has showed unwillingness to give consent. **Results:** The study was a prospective observational hospital-based study carried out in the Department of Medicine at Teerthanker Mahaveer Medical College and Research Centre. Majority of subjects (>85%) were above 40 years of age. The most common presenting complaint was swelling in lower limbs and shortness of breath (SOB). 79.1% subjects were in NYHA IV category while 20.9% were in NYHA III category. 38.4% of study subjects had heart murmurs. 18.6% of study subjects had hypochloremia while 81.4% had normal chloride levels. **Conclusion:** Several clinical trials investigating serum chloride role in acute and chronic HF have shown hypochloremia to be strongly associated with death, with varied conclusions depending on the severity of the sickness and the research population. Intracellular chloride sensors, which may be therapeutically addressed, affect diuretic resistance.

Keywords: Congestive Heart Failure, Sympathetic Nervous System, Glomerular Filteration Rate.

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Introduction

Heart failure is described as a result of structural or functional impairment of ventricular filling or blood ejection, which in turn causes the cardinal clinical symptoms of dyspnea and fatigue and signs of heart failure, such as edema and rales. Hyponatremia, hypokalemia, and hypomagnesemia are the most typical electrolyte disorders. Metabolic alkalosis causes the acid-base imbalances that are typically seen. These changes are the result of several systems interacting.[1]

Recent research has demonstrated that hypochloraemia is associated with higherrates of short as well as long-term mortality, and that blood chloride levels are a better predictive indicator of heart failure than serum sodium levels.[2] The normal range of serum chloride concentrations is 96–106 mEq/L.[3]

Loop diuretics administered in acute heart failure block the co-transport mechanism involving sodium, potassium and chloride located in loop of Henle within the thick ascending part (LH-TA). Due to the fact that chloride will not be distally reabsorbed, unlike sodium, loop diuretics do not prevent hypochloremia.[4] Low serum levels of chloride may be responsible for diuretic resistance in heart failure as shown in a recent study which observed utilization of very high doses of furosemide in hospital patients.[5] Chloride detection in macula densa (MD) by NKCC2 is responsible for feedback at tubule-glomerular level.[6] The overall chloride amount in the early part of the distal tubule correlates with the rate at which renin is secreted from the macula densa. Diuretic hypo-responsiveness thus occurs via a variety of methods. Given that sodium homeostasis and neurohormonal activation, two crucial routes in heart failure, are directly regulated by chloride.[7] We speculate that serum chloride may have a significant role in prognosis and contribute significantly to the risk that would otherwise be attributed to serum sodium. In the current study, we investigate the prognostic significance of serum chloride as an independent marker in congestive heart failure (CHF)and explain the clinical features associated with low serum chloride. Lower serum chloride has been linked to greater mortality in heart failure and diuretic resistance,

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according to recent studies. Since there haven't been many studies conducted in the western part of Uttar Pradesh, this subject has been chosen for further study.[8]

AIM

- To study the prognostic significance of serum chloride levels in patients with congestive heart failure.

OBJECTIVES

- To assess the levels of serum chloride in congestive heart failure patients with HFrEF (heart failure with reduced ejection fraction) or HFpEF (heart failure with preserved ejection fraction).
- To correlate the levels of serum chloride with the prognosis of Patients with Congestive Heart failure in both the groups separately.

Methodology

Inclusion criteria

All Patients older than 18 years and admitted with a diagnosis of congestive heart failure including both HFrEF (heart failure with reduced ejection fraction) and HFpEF (heart failure with preserved ejection fraction).

Exclusion Criteria

- Patients on drugs like corticosteroids, laxatives, bicarbonates.
- Patients had prior heart transplantation or mechanical circulatory assist device.
- Patients having sepsis.
- Patients with COPD with respiratory failure
- Patients with pregnancy, or malignancy.
- Patients who have showed unwillingness to give consent.

RESULTS

Table 1: Distribution of study participants according to Age

Age (Years)	Frequency (n=86)	Percentage (%)
<41	11	12.8
41-50	24	27.9
51-60	27	31.4
>60	24	27.9

Majority of subjects (>85%) were above 40 years of age. 31.4% of subjects were in the age group 51-60 years followed by 27.9% each above 60 years and in 41-50 years age group.

Table 2: Distribution of study participants according to Presenting complaints

Presenting complaints	Frequency (n=86)	Percentage (%)
Altered sensorium	15	17.4
Chest pain	14	16.3
Chest pain and SOB	14	16.3
SOB	15	17.4
Swelling in lower limbs	10	11.6
Swelling in lower limbs and SOB	18	20.9

The most common presenting complaint was swelling in lower limbs and shortness of breath (SOB) seen in 20.9% of study subjects followed by Altered sensorium in 17.4%, SOB in 17.4%, chest pain and SOB in 16.3%, chest pain in 16.3% and swelling in lower limbs in 11.6%.

Table 3: Distribution of study participants according to Past history

Past history	Frequency (n=86)	Percentage (%)
Smoker	29	33.7
MI	17	19.8
CKD	14	16.3
CVA	7	8.1
DM/HTN/MI 2yrs	1	1.2
No Significant history	18	20.9

33.7% of study subjects were smokers, 19.8% had history of myocardial infarction, 16.3% had history of CKD, 8.1% had had history of CVA and 1.2% had history of DM/HTN.

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Table 4: Distribution of study participants according to Cl levels

Cl levels	Frequency (n=86)	Percentage (%)
Hypochloremia	16	18.6
Normal	70	81.4

[Table 4] shows that out of total 86 subjects, 18.6% of study subjects had hypochloremia while 81.4% had normal chloride levels.

Table 5: Distribution of study participants according to demographic characteristics and Chloride levels

Parameter	Hypochloremia		Normal		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
Age	53.75	7.21	54.41	14.41	54.29	13.33	0.859
Duration of Stay	13.56	2.76	6.83	2.60	8.08	3.71	0.000
Height	1.66	0.09	1.63	0.06	1.64	0.07	0.109
Weight	61.75	7.95	61.10	9.23	61.22	8.97	0.795
BMI	22.37	2.22	22.96	2.86	22.85	2.75	0.443

[Table 5] shows comparative demographic characteristics namely age, duration of stay, height, weight and BMI with Chloride levels. There was statistically significant difference seen with respect to duration of stay with p-value less than 0.05.

Table 6: Distribution of study participants according to Vital Parameters and Chloride levels

Parameter	Hypochloremia		Normal		Total		p-value
	Mean	SD	Mean	SD	Mean	SD	
Systolic BP	130.63	30.21	119.00	31.90	121.16	31.75	0.188
Diastolic BP	81.25	18.21	74.71	18.16	75.93	18.24	0.198
Pulse	99.69	18.34	105.89	29.58	104.73	27.85	0.425
SpO2	76.25	15.61	75.81	14.71	75.90	14.79	0.916
EF	30.94	12.55	31.19	10.31	31.14	10.68	0.934

[Table 6] shows comparative vital parametersnamely systolic and diastolic blood pressure, pulse, SpO2 and Ejection fraction with Chloride levels. There was no statistically significant difference seen with respect to vital parameters (p-value<0.05).

Table 7: Distribution of study participants according to NYHA (Admission) with Cl levels

NYHA (Admission)	Cl levels		Total	p-value
	Hypochloremia	Normal		
III	0	18	18	0.015
IV	16	52	68	

[Table 7] shows distribution of chloride levels with respect to NYHA category at admission. There was statistically significant difference seen with respect to NYHA category at admission (p-value<0.05).

Table 8: Distribution of study participants according to Total Diuretic dose with Cl levels

Cl levels	Total Diuretic Dose (mg)		p-value
	Mean	SD	
Hypo	747.50	229.22	<0.001
Normal	499.00	203.08	

[Table 8] shows distribution of chloride levels with respect to total diuretic dose. There was statistically significant difference seen with respect to total diuretic dose (p-value<0.05).

DISCUSSION

The study was a prospective observational hospital based study carried out in the Department of Medicine at Teerthanker Mahaveer Medical College and Research Centre All the Cases of Congestive Heart Failure during the study period presenting to Department of Medicine were evaluated. Majority of subjects (>85%) were above 40 years of age. 31.4% of subjects were in the age group 51-60 years followed by 27.9% each above 60 years and in 41-50 years age group. Out of 86 subjects, 50% of study subjects were male and 50% of study subjects were female. The most common presenting complaint was swelling in lower limbs and shortness of breath (SOB) seen in 20.9% of study subjects followed by Altered sensorium in 17.4%, SOB in 17.4%, chest pain and SOB in 16.3%, chest pain in 16.3% and swelling in lower limbs in 11.6%. Out of total 86 study subjects at admission, 79.1% subjects were in NYHA IV category while 20.9% were in NYHA III category. Out of total 86 study subjects at

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discharge, 55.8% subjects were in NYHA I category, 40.7% were in NYHA II category and 3.5% were in NYHA III category. 33.7% of study subjects were smokers, 19.8% had history of myocardial infarction, 16.3% had history of CKD, 8.1% had had history of CVA and 1.2% had history of DM/HTN. 44.2% of study subjects had diabetes mellitus and 23.3% had hypertension while 32.6% had both the comorbidities. 26% of study subjects had pallor. 30.2% of study subjects had edema. 15.1% of study subjects had altered consciousness. 38.4% of study subjects had heart murmurs. Of these 26.7% had systolic ejection murmur and 11.6% subjects had mid-diastolic murmur. 73.3% of study subjects had bilateral crepitations,14% had diffuse crepitations and 12.8% subjects had basal crepitations. 18.6% of study subjects had hypochloremia while 81.4% had normal chloride levels. 18.6% of study subjects had RVH & RBBB followed by old anterior wall MI in 18.6%, LVH in 17.4%, RBBB in 9.3% and RVH in 8.1. Pulmonary edema was seen in all subjects. Cardiomegaly was seen in 29.1% and COPD in 10.5% of study subjects. Sodium has been the main subject of a lot of study, both observational and interventional, throughout the past few decades. Evidence-based management recommendations for issues with fluid balance have been heavily ijnfluenced by sodium's role and effects on numerous biological pathways. Lower levels of serum sodium are a major predictor of poor prognosis in heart failure (HF), and risk prediction models usually take this into consideration. However, more recent clinical observations have cast doubt on this enduring sodium-centric viewpoint. Additionally, there is proof that giving patients who have been hospitalised for heart failure and fluid overload hypertonic saline may assist them decongest.[9] Chloride is a potentially potent cardio-renal connection due to its specific biological activities (e.g., modulation of several sodium transport mechanism in renal tubules) that are pertinent to the pathophysiology of fluid balance. “Low serum chloride levels at admission are independently linked to a higher risk of mortality in patients with acute HF, according to a 2015 study by Grodin et al.[10] The common thread is that hypochloremia is a separate risk factor for unfavourable outcomes, and that serum sodium, which was formerly thought to be the main cardiorenal connection, may not be as important in predicting outcomes as chloride.” Low serum chloride levels appear to be associated with negative outcomes via two plausible candidate pathways: diuretic resistance and maladaptive neurohormonal activation. The RAAS hyperactivity has long been known to presage negative effects in the context of heart failure and is a major therapeutic target in these patients.[11,12]

Limitations

Most of the data were obtained through studies where chloride was neither a primary nor a secondary endpoint, despite the fact that a few small interventional trials and plausible biological pathways supporting associated of serum chloride to HF prognosis. Large-scale prospective clinical trials are necessary to establish if hypochloremia is a modifiable risk factor or merely indicates severity of illness and poor prognosis.

CONCLUSION

Considering macula densa relying on chloride to detect load of salt as well as status of volume, chloride is crucial for fluid balance in HF. The WNK pathway most likely contributes to diuretic resistance by serving as intracellular chloride sensor. Despite the fact that several studies involving populations with acute & chronic HF demonstrated hypochloremia as the prognostic marker, trials have overlooked serum chloride as a potential therapeutic target. Several clinical trials investigating serum chloride role in acute and chronic HF have shown hypochloremia to be strongly associated with death, with varied conclusions depending on the severity of the sickness and the research population. Intracellular chloride sensors, which may be therapeutically addressed, affect diuretic resistance.

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