



CRACKING THE CODE: UNVEILING SERUM CHLORIDE AS A PROGNOSTIC BEACON FOR HEART FAILURE AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: Congestive heart failure is a pathologic state in which abnormal cardiac function results in the failure of the heart to pump blood at the requisite rate for metabolism or to pump blood from an increased filling pressure. Heart failure (HF) is associated with multiple serum electrolyte abnormalities, including hyponatraemia, hypokalaemia, and hypochloraemia besides acid-base disturbances. We aimed to study the effect of admission serum chloride levels on the duration of hospital stay in HF patients and their correlation with serum sodium levels. **Material and Methods:** This was a Prospective study conducted in Department of General Medicine, SMS Medical College and attached group of hospitals, Jaipur. Sample of 75 cases was calculated for detailed history of the patients. **Result:** In the present study we included 75 patients. The mean age for the study was 59.13 years with 48 male and 27 female patients. patients were grouped into three categories according to serum chloride level. 18 patients were in Group A (Chloride level <96 meq/L), 25 patients were in Group B (Chloride level 96-101 meq/L) and 32 patients were in Group C (Chloride level > 101 meq/L). In our study the median duration of stay of patients in ICU in Category A was 17 days whereas, the median duration of stay of patients in ICU in Category B was 11 days and the median duration of stay of patients in ICU in Category C was 7 days. **Conclusion:** Hypochloremia has high prevalence in critical ill ICU patients. Admission serum chloride levels are independently and inversely associated with increased duration of stay in acute decompensated heart failure. This effect is independent of the sodium levels at presentation. Although sodium levels are important, more robust prognostic information can be inferred from serum chloride levels.

KEYWORDS : Heart Failure, Chloride levels.

INTRODUCTION

Congestive heart failure is a pathologic state in which abnormal cardiac function results in the failure of the heart to pump blood at the requisite rate for metabolism or to pump blood from an increased filling pressure.¹ Earlier Heart failure used to be defined as hemodynamic disorder only, which may explain the symptoms of HF but not sufficient to explain the progression of heart failure.

Heart failure (HF) is associated with multiple serum electrolyte abnormalities, including hyponatraemia, hypokalaemia, and hypochloraemia besides acid-base disturbances.² Most of the literature in HF till recently has primarily focused on hyponatremia as the major predictor of short and long-term morbidity and mortality. As ventricular dysfunction progresses to symptomatic HF, up-regulation of maladaptive neurohormonal systems may limit solute and free water delivery to the distal nephron, increasing free water absorption and potentially reducing serum sodium and chloride levels.³ These electrolyte perturbations may be exacerbated through the use of decongestive therapies in acute and chronic HF (e.g., loop and thiazide diuretics).⁴ The finding of hyponatremia in the patient with HF is a well-established, strong predictor of short- and long-term morbidity and mortality irrespective of left ventricular (LV) systolic function.⁵

when the concept of volume depletion and chloride responsive metabolic alkalosis became clear. Recent studies have shown that serum chloride levels provide stronger prognostic information for HF than serum sodium levels, and that patients with hypochloraemia have relatively high short and long-term mortality.⁶ Some investigators have even used hypertonic saline solution to successfully treat acute Heart failure. In 2015, Grodin et al. reported that serum chloride level on admission is a robust and independent predictor of mortality in acute Heart failure, and it may even have a stronger prognostic value than sodium.⁷ The present study assessed the effect of admission serum chloride levels on the duration of hospital stay in HF patients and their correlation with serum sodium levels.

MATERIALS AND METHODS

This was a Prospective study conducted in Department of General Medicine, SMS Medical College and attached group of hospitals, Jaipur. Sample of 75 cases was calculated for detailed history of the patients including past treatment and personal history to identify possible etiologies and a thorough clinical examination to identify the evidence of acute decompensated heart failure was taken. The patients were classified according to ADMISSION CHLORIDE LEVELS and divided in 3 groups. Group A: S. chloride level <96, Group B: 96-101 and Group C: >101.

The role of chloride in volume hemostasis was appreciated

Patients was subjected to the routine work up for ADHF

including:

1. Serial Serum Chloride Level, Serum Sodium Level
2. Hb, Urine Routine, Renal Function Tests.
3. Pro Bnp Level,
4. Lvef%
5. Systolic Blood Pressure
6. Bun; Creatinine;
7. Length Of Stay [Days]

Inclusion Criteria:

1. Patients >18 years of age.
2. k/c/o ADHF due to dilated cardiomyopathy /ischemic cardiomyopathy.
3. Patients with established diagnosis of ADHF.

Exclusion Criteria:

1. Patient on chronic dialysis therapy.
2. Pregnant and lactating women.
3. Patient has malignancy.
4. Patient <18 year of age.
5. Patient has sepsis.

Statistical Analysis:

Chi square test was used to analyze nonparametric or categorical data. For analysis of ordinal scale data, Student's t test was used. Spearman correlation coefficient will be calculated to observe correlation between variables. P < 0.05 was taken as significant. All the data will be computed on Microsoft Office 2007 and statistical analysis was done using appropriate statistical tool.

OBSERVATIONS AND RESULTS

In the present study, 75 patients were included. The mean age for the study was 59.13 years with 48 male and 27 female patients.

Table 1: Baseline Characteristics of Cases

	mean	SD
Duration of stay(Days)	11.12	4.89
NA+ (meq/L)	136.57	4.63
K+ (meq/L)	4.34	0.64
SBP(mmofHg)	122.53	18.26
DBP(mmofHg)	74.4	9.63
Urea(mg/dl)	56.72	38.96
Creatinine(mg/dl)	1.55	1.2
OT(U/L)	74.85	94.51
PT(U/L)	98.61	195.12
PROBNP(pg/ml)	6615.92	3398.3
LVEF%	37.36	9.6
HB(g/dl)	11.81	2.28
CL-(meq/L)	100.72	6.75

In the above table 1, it was found that mean duration of stay was 11.12 days and other laboratory parameter were shown. In table 2, patients were divided according to serum chloride levels at admission. No significant difference was found between these group in any baseline characteristics.

Table 2: Baseline Characteristics According To Admission Serum Chloride Levels (categorical Variables).

	<96		96-101		>101		Total	%	P value
Male	13	72.22	16	41.03	19	105.56	48	64	0.638
Female	5	27.78	9	23.08	13	72.22	27	36	
DM	10	55.56	10	25.64	10	55.56	30	40	0.081
Inotrope use	8	44.44	9	23.08	9	50	26	34.67	0.313
Smoking	5	27.78	6	15.38	9	50	20	26.67	0.425
Alcohol	3	16.67	3	7.69	3	16.67	9	12	0.903
CAD	2	11.11	5	12.82	9	50	16	21.33	0.112
HTN	2	11.11	6	15.38	5	27.78	13	17.33	0.983

Table 3: Correlation Of Duration Of The Stay And Continuous Parameters.

	"rho"	p value
Age	0.494	<.001
NA+	-0.364	0.001
K+	0.108	0.358
SBP	-0.109	0.353
DBP	-0.103	0.38
Urea	0.13	0.266
Creatinine	0.144	0.218
OT	0.24	0.038
PT	0.17	0.144
PROBNP	-0.173	0.137
LVEF	-0.096	0.412
HB	-0.166	0.154
CL-	-0.889	<.001

Table 4: Multiple Linear Regression Model To Assess The Independent Effect Of Various Variables On Duration Of Stay

	Unstandardized Coefficients		Standardized Coefficients	t	Sig.	95.0% Confidence Interval for B	
	B	Std. Error				Beta	Lower Bound
CL	-0.616	0.063	-0.852	-9.847	0	-0.741	-0.491
Age	0.072	0.043	0.12	1.697	0.094	-0.013	0.157
NA+	0.064	0.086	0.061	0.745	0.459	-0.107	0.235
SBP	0.017	0.019	0.063	0.886	0.379	-0.021	0.055
Inotrope Use	1.333	0.611	0.13	2.181	0.033	0.112	2.554
Smoking	-0.041	0.752	-0.004	-0.055	0.957	-1.543	1.461
CAD	0.484	0.757	0.041	0.639	0.525	-1.028	1.996
Alcohol	-0.286	0.908	-0.019	-0.315	0.754	-2.099	1.528
HTN	0.036	0.843	0.003	0.043	0.966	-1.648	1.721

In table 3, Spearman Correlation was used to test as duration of the stay was non-parametric. There corresponding r value and p value are shown above.

In the present study, Spearman Correlation was calculated between CL- and NA+ levels. We found that r value was 0.48 and p value was <0.001.

In table 4, Multiple Linear regression model was used to assess the independent effect of various variables on Duration of Stay.

In the present study, Normality test was used for Duration of stay data, p value was found to be 0.001 with degree of freedom 75.

On multiple linear regression after adjusting the age, SBP, Beta blocker, Inotrope, and sodium at admission, only serum Chloride at admission had significant negative relation with hospital stay. The results showed 1 unit increase in chloride level was associated with 6.1% (p=0.000) decrease in hospital stay (95% CI: 7.4% to 4.9%).

Figure 1: Scatter Plot showing relation between hospital stay and CL Levels.

DISCUSSION

Relatively few studies have been performed in past to formally assess the usefulness of admission Serum Chloride Levels as Predictor of Stay Duration in Acute Decompensated Heart Failure (ADHF). The present study was conducted on patients of ADHF admitted in SMS and attached hospitals, Jaipur and to demonstrate the utility of Serum Chloride Levels as Predictor of Stay Duration.

In present study the median age of cases was 60 years and mean age was 59.13 ± 8.09 years. In our study the patients

were grouped into three categories according to serum chloride level. 18 patients were in Group A (Chloride level <96 meq/L), 25 patients were in Group B (Chloride level 96-101 meq/L) and 32 patients were in Group C (Chloride level > 101 meq/L). Similarly A Goyal et al.⁸ (2020) in their study divided the patients into three categories according to serum chloride level-Group A (Chloride level <96 meq/L), Group B (Chloride level 96-101 meq/L) and Group C (Chloride level > 101 meq/L). In present study the three groups were comparable on parameters of DM, Hypertension, Smoking, alcohol, CAD, and inotrope use and application of t test showed that the difference among the 3 groups were not statistically significant on these parameters.⁹ patients have DM in all 3 groups and application of t test showed that this difference was not statistically significant. Similarly A Goyal et al.⁸ (2020) in their study found that three groups were comparable on parameters of DM, Hypertension, Smoking, alcohol, CAD, and inotrope use and application of t test showed that the difference among the 3 groups were not statistically significant on these parameters which is consistent with our results.

In present study the median age in Category A was 67, median age in Category B was 62 and the median age in Category C was 54.5 and application of t test showed that this difference was statistically significant. Abhishek Goyal et al.⁸ (2020) in their study found that the median age was higher in the patients with low serum chloride levels. In study of Grodin et al.⁷ (2015) the mean age in group A was 64.9 (53.8 to 74.8) years, in group B was 59.2 (48.3 to 72.7) years, and in group C was 64.5 (52.3 to 75.6) years.

In present study the median duration of stay of patients in ICU in Category A was 17 days whereas, the median duration of stay of patients in ICU in Category B was 11 days and the median duration of stay of patients in ICU in Category C was 7 days and application of t test showed that this difference was statistically significant. Similarly Abhishek Goyal et al.⁸ (2020) in their study found that the duration of hospital stay differed significantly among the three tertiles. The median lengths of hospital stay in tertiles 1 (Chloride level <96), 2 (Chloride level 96-101), and 3 (Chloride level >101), were 8, 7, and 6 days, respectively (p = 0.011).

The most important finding of present study is the inverse relation between serum chloride levels and the duration of hospital stay; that is, low admission chloride levels are associated with a prolonged hospital stay in patients with ADHF. This effect is independent of the sodium levels at presentation. Various studies have investigated the effect of Chloride levels on cardiovascular morbidity and mortality.⁶ Grodin et al.⁷ (2015) found that admission serum chloride levels were independently and inversely associated with mortality in a multivariate model (hazard ratio per unit change: 0.93, p < 0.001). Kataoka proposed the 'chloride theory' in which they stated that the serum chloride level is the primary determinant of changes in the plasma volume and the renin-angiotensin-aldosterone system (RAAS) and an indirect determinant of changes in the antidiuretic hormone system.¹⁰

In present study, it was found that as Chloride level increases the sodium level also increases. There were significant differences among the Sodium level in the three Categories. Similarly, A Goyal et al.⁸ (2020) in their study found significant differences among the three categories. In their study the median Na⁺ level in Category A was 130, in Category B was 136 whereas in Category C it was 139 which is consistent with our results.

In present study when we analyze the correlation of duration of stay in ICU with various continuous parameters we found that age, admission Sodium level and admission serum

Chloride level are predictors of Stay Duration in Acute Decompensated Heart Failure and Chloride level (<.001) shows more strong correlation with duration of stay in ICU than Sodium level (0.001). However, duration of stay in ICU does not show correlation with Potassium level, RFT, LFT, LVEF, Pro-BNP, and Haemoglobin level. Similarly A Goyal et al.⁸ (2020) in their study found that that duration of stay in ICU does not show correlation with gender, Hypertension, DM, Smoking, and CAD but shows positive correlation with Inotrope use. They found that on multiple linear regression after adjusting the age, SBP, Beta blocker, Inotrope, and sodium at admission, Chloride at admission had significant negative relation with hospital stay.

The findings of present study suggests that lower chloride levels during admission were associated with higher hospital stay and offers important insights into interpretation of electrolytes in ADHF. Our findings suggest that although sodium levels are important, more robust prognostic information can be inferred from serum chloride levels. Although low sodium has consistently been shown to be a strong predictor of short- and long- term morbidity and mortality in patients with both systolic and diastolic HF.

CONCLUSION

Hypochloremia has high prevalence in critical ill ICU patients. Admission serum chloride levels are independently and inversely associated with increased duration of stay in acute decompensated heart failure. This effect is independent of the sodium levels at presentation. Although sodium levels are important, more robust prognostic information can be inferred from serum chloride levels. Studies involving role of Chloride in ADHF patients are warranted in order to understand prognosis and impact of dyschloremia.

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