National Board of Examination - Journal of Medical Sciences

Volume 1, Issue 7, Pages 413–424, July 2023

DOI 10.61770/NBEJMS.2023.v01.i07.003

ORIGINAL ARTICLE

Correlation of admission S. Na+ and S. Cl- with severity and hospital stay in ADHF patients

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Accepted: 23-June-2023 / Published Online: 18-July-2023

Abstract

Background: Electrolyte imbalances, particularly hyponatremia and hypochloremia, are common in ADHF patients and can influence disease severity and outcomes. Understanding the correlation between admission S. Na^+ and S. Cl^- levels with ADHF severity and hospital stay is crucial for optimizing patient management.

Aim: This study aimed to investigate the correlation between admission S. Na^+ and S. Cl^- levels with disease severity and length of hospital stay in ADHF patients.

Discussion: Diagnostic studies based on sodium and chloride are not only widely available but also, practicable and relatively inexpensive in comparison to other modalities. A total of 150 ADHF patients were included in the study. The mean admission S. Na^+ and S. Cl^- levels were assessed in relation to NYHA functional class and EF. Statistical analysis revealed significant correlations between admission S. Na^+ and S. Cl^- levels and NYHA class, as well as EF.

Conclusion: The correlation of admission S. Na^+ and S. Cl^- levels with disease severity and hospital stay in ADHF patients provides important insights. Monitoring and managing electrolyte imbalances, particularly S. Na^+ and S. Cl^- may have implications for optimizing patient care and improving outcomes in ADHF.

Keywords: Hyponatremia, hypochloremia, ADHF, Ejection Fraction, NYHA.

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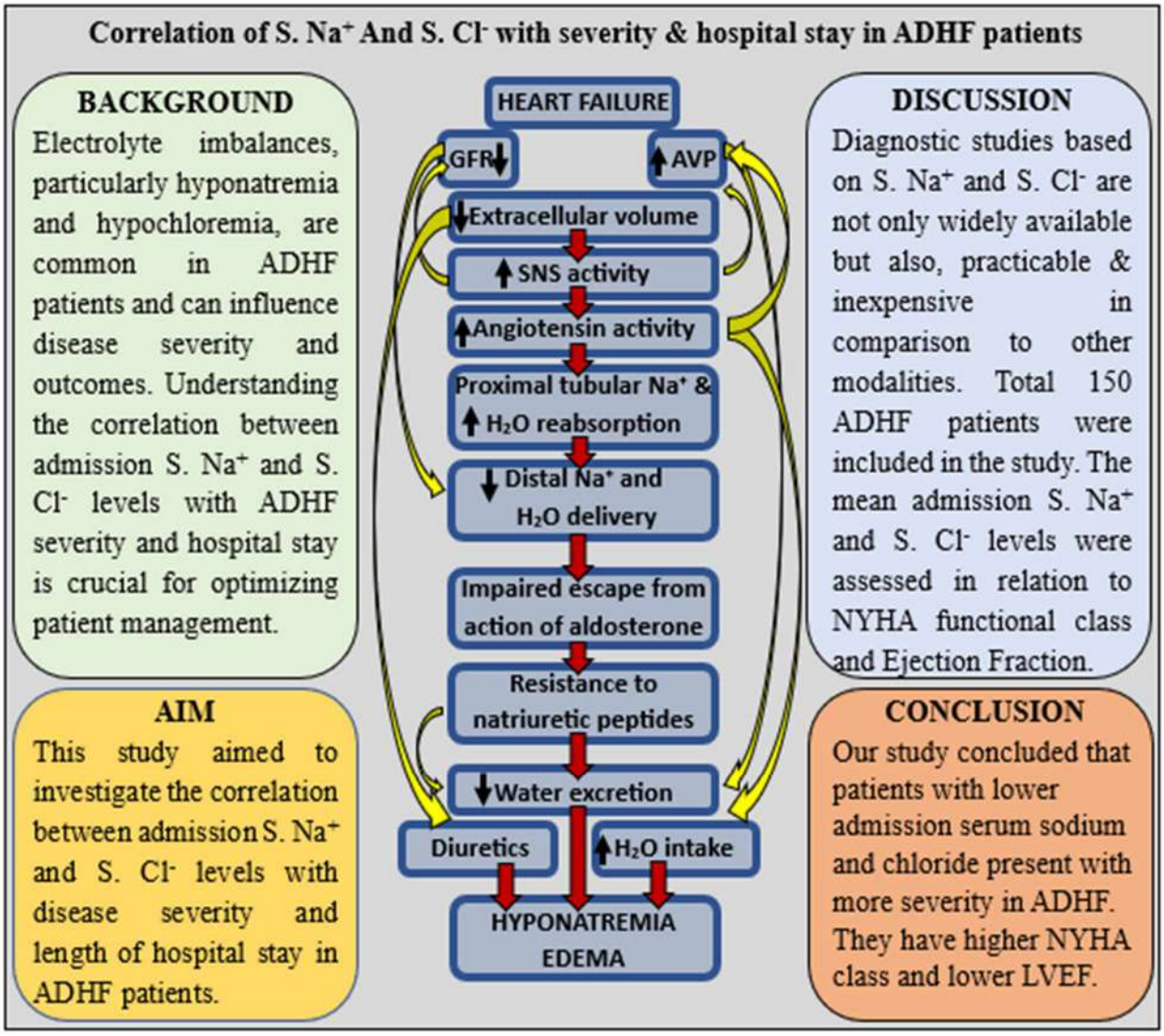
Graphical Abstract



Abbreviations-

ADHF	:	Acute Decompensated Heart Failure
LV	:	Left Ventricle
LVEF	:	Left Ventricular Ejection Fraction
2D-ECHO	:	2-Dimensional Echocardiography
NYHA	:	New York Heart Association
HFpEF	:	Heart Failure with preserved Ejection Fraction
S. Na^+	:	Serum Sodium
S. Cl^-	:	Serum Chloride
HFrEF	:	Heart Failure with reduced Ejection Fraction

Introduction

Heart failure is an evolving non-communicable epidemic in India, but the burden can be felt all over the world since it has been labelled as the new pandemic of the 21st century. During the protracted course of heart failure, it is common for patients to develop electrolyte imbalances, the most common of which are hyponatremia and hypochloremia [1].

Upregulation of maladaptive neurohormonal systems is associated with ventricular dysfunction in patients with heart failure. In heart failure, an imbalance of either of these electrolytes is a contributing factor in morbidity [2].

When a patient is admitted to the hospital with acute decompensated heart failure, hyponatremia is a known reason for the patient to have a prolonged hospital stay [3].

Pathophysiology of Heart Failure

Heart failure may be considered as an advancing condition that usually begins when a key event occurs destroying myocardium, resulting in the insufficiency of cardiac myocytes' ability to generate force required for normal supply of blood [4]. This is triggered by a key incident, frequently acute onset like MI, or sometimes of insidious onset like hypertension. Sometimes, it has an inherited onset, like several genetic cardiomyopathies. Myocardial disease is typically the most frequent cause of heart failure; however, heart rate or rhythm disorders, endocardial disorders, valvular pathologies, or pericardial abnormalities can also lead to cardiac dysfunction [5]. HFrEF pathogenesis involves a few pathogenetic mechanisms, including ischemia-related damage, abnormal myocyte calcium cycling, dysregulated neurohumoral stimulation, immunological stimulation, increased hemodynamic overload, extracellular matrix anomalies, ventricular remodeling, genetic mutations, and accelerated apoptosis. Pathogenesis of HFpEF is diastolic dysfunction, etiology of which has been substantially attributed to accumulation of extracellular matrix (i.e., myocardial fibrosis) due to activation of renin angiotensin aldosterone system [6].

Consequently,

- Increase in peripheral resistance leads to elevated LV after-load which further decreases cardiac function.
- Enhanced contractility, Heart rate, and LV afterload can aggravate or provoke coronary ischemia.
- Angiotensin II, aldosterone and catecholamines cause myocyte loss by apoptosis and myocardial hypertrophy and fibrosis [7].

Classification of Heart Failure

American College of Cardiology/American Heart Association 2022 guidelines define heart failure as a complex clinical syndrome with symptoms and signs that result from any structural and functional impairment of ventricular filling or ejection of blood [8]. ADHF term is defined for both, patients coming with de novo and those with worsening of previously chronic stable Heart failure [9]. Heart failure is classified according to New York Heart Association and patients are placed in four categories, based on limitation in physical activity or ejection fraction as shown in Tables 1 and 2 [8, 10].

Table 1. NYHA Functional Classification.

Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnoea (shortness of breath).
Class II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea (shortness of breath).
Class III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnoea.
Class IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest. If any physical activity is undertaken, discomfort increases.

Table 2. Classification of HF by LVEF

Type of HF according to LVEF	Criteria
HFrEF (HF with reduced EF)	LVEF ≤40%
HFimpEF (HF with improved EF)	Previous LVEF ≤40% and a follow-up measurement of LVEF >40%
HFmrEF (HF with mildly reduced EF)	LVEF 41%-49% Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, non-invasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous or provokable increased LV filling pressures (e.g., elevated natriuretic peptide, non-invasive and invasive hemodynamic measurement)

Hyponatremia in ADHF

Hyponatremia is defined as S. $Na^+ \leq 135$ mEq/L representing an excess water relative to total body solute. Severity of hyponatremia is divided as follows:

1. Mild: S. Na^+ = 130-135 mmol/L
2. Moderate: S. Na^+ = 125-129 mmol/L
3. Severe: S. Na^+ = 125 mmol/L [11]

Hyponatremia in heart failure is a multifaceted process. It involves the increased release of arginine vasopressin and inadequate tubular flow in the distal regions of the nephron, leading to excessive water retention and the progression of

hyponatremia in ADHF [12]. The severity of hyponatremia in ADHF is often proportional to the degree of cardiac dysfunction and serves as an indicator of advanced disease severity. Understanding the mechanisms and implications of hyponatremia in heart failure is crucial for improved patient outcomes [13].

Hypochloremia in ADHF

Chloride is a crucial anion found both in extracellular and intracellular compartments of the body. In patients with CHF, low blood chloride concentration is commonly observed and is associated with unfavorable outcomes [14]. Hypochloremia, regardless of sodium levels, has been found to carry a higher risk of death and hospitalization for heart failure compared to hyponatremia alone [15]. The occurrence of low chloride levels in ADHF can be attributed to similar mechanisms as hyponatremia, such as neurohormonal activation and the use of loop diuretics [16].

Nevertheless, there is a scarcity of studies and the potential of chloride as an independent prognostic marker is yet to be firmly established.

Methodology

All 150 eligible participants above the age of 18 years, admitted to the medicine wards and meeting the inclusion criteria, underwent a thorough evaluation. A detailed history was obtained, including information on symptom onset, precipitating factors, and use of diuretics, among other relevant factors. Comprehensive physical examinations were conducted, recording findings such as jugular venous pressure, chest auscultation, and the presence of peripheral edema. All participants underwent relevant investigations, including Complete Blood Count, Renal Function tests, Liver Function Test, and serum electrolyte analysis based on their presenting symptoms. Additional investigations, such as Chest X-Ray PA view, Electrocardiogram, and 2D ECHO, were performed as necessary.

Inclusion criteria

- The study enrolled individuals aged 18 years and above, who had a documented discharge diagnosis of ADHF resulting from diverse causes.
- It also encompassed patients who had previously been diagnosed with heart failure and presented to the emergency department in a decompensated state.

Exclusion criteria

- Age < 18 years.
- Additionally, patients who received chronic dialysis therapy, had sepsis, showed signs of acute coronary syndrome or myocarditis (based on their medical history, elevated troponin levels, and/or dynamic ECG changes), had incomplete hospital records, were pregnant, or had a malignancy were also excluded from the study.
- Furthermore, individuals who were unwilling to participate in the study were not included.

Measurement of S. Na^+ and S. Cl^- levels was carried out by collecting a venous sample in a plain vial, which was then processed using a biochemical analyzer (AU-480). In

our study, hyponatremia was defined as S. Na^+ levels ≤135 mmol/L, and hypochloremia was defined as S. Cl^- levels ≤96 mmol/L.

The duration of hospital stay was calculated as the number of days from admission to discharge of the patient in the inpatient department.

Results

This observational study was conducted among 150 patients at Government Multispecialty Hospital, Sector 16, Chandigarh. The study participants had a mean age of 60.71 ± 12.77 years, ranging from 36 to 89 years. Most participants (47, 31.3%) fell into the age group of 51-60 years, followed by (30, 20.0%) in the group of 41-50 years.

Among the 150 participants, (109, 72.7%) had diabetes mellitus, and (120, 80%) had hypertension. A history of heart failure was present in (62, 42.2%) of the enrolled patients, and (78, 52%) were on diuretics. Additionally, (17, 11.3%) had a history of alcohol intake, and (44, 29.3%) had a history of tobacco use. Other baseline investigations are documented as shown in Tables 4, 5 and 6.

Table 3. Distribution of study population according to NYHA

		Frequency	Percent
NYHA in class numbers	Class-III	27	18.0%
	Class-IV	123	82.0%
	Total	150	100.0%

Table 4. Baseline parameters and investigations of the participants

	N	Mean	Standard Deviation	Median	Minimum	Maximum
SBP (in mmHg)	150	163.09	26.27	167.00	90.00	230.00
DBP (in mmHg)	150	95.17	14.31	96.00	60.00	130.00
PR (in bpm)	150	112.61	10.54	112.00	94.00	140.00
Hb (in gm/dL)	150	10.86	2.35	11.00	5.70	16.10
TLC (per cubic mm)	150	9055.53	3629.26	8820.00	3800.00	31400.00

Table 5. Pattern of distribution of study population according to EF

		Frequency	Percent
EF	Preserved	45	30.0%
	Mild reduced	53	35.3%
	Reduced	52	34.7%
	Total	150	100.0%

Table 6. Correlation of admission S. Na^+ and S. Cl^- according to NYHA

		NYHA in class numbers		Mann-Whitney U (Z)	p-value
		Class-III	Class-IV		
Admission Serum Sodium (mEq/L)	N	27	123	2.884	.004
	Mean	133.15	128.31		
	SD	6.61	8.51		
	Median	133.00	130.00		
Admission Serum Chloride(mEq/L)	N	27	123	3.550	<.001
	Mean	102.96	97.10		
	SD	2.93	8.06		
	Median	103.00	101.00		

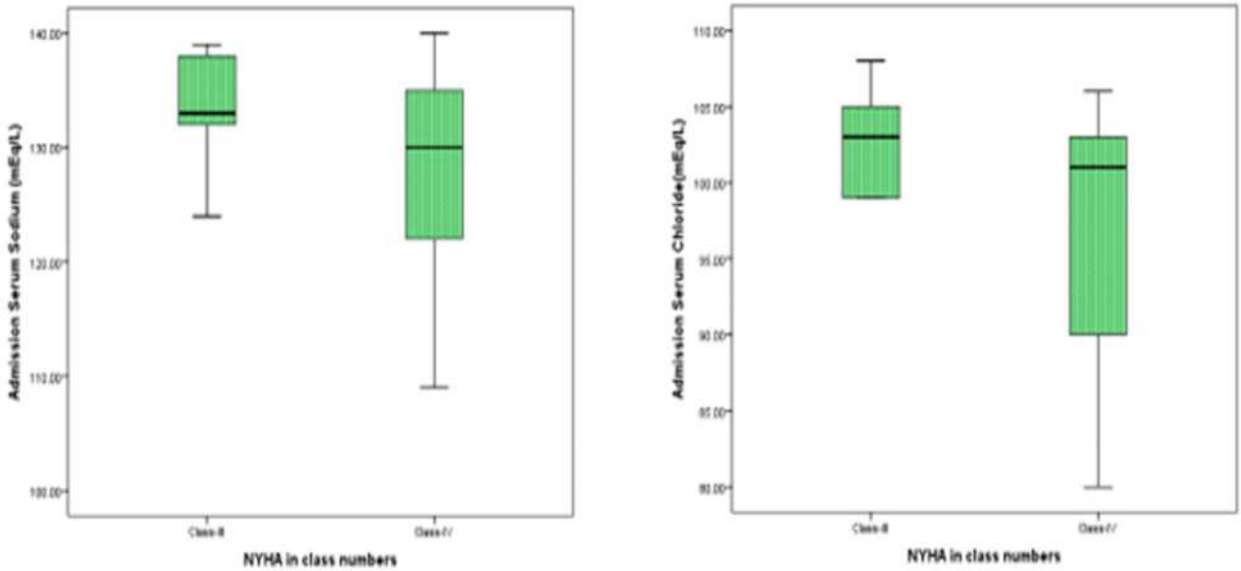


Figure 1. Box and whisker plot of admission S. Na^+ and S. Cl^- with NYHA class 3 and 4.

The mean admission S. Na^+ levels for patients classified as NYHA Class III were observed to be 133.15 ± 6.61 mEq/L, while for patients in NYHA Class IV, the mean admission S. Na^+ levels were 128.31 ± 8.51 mEq/L. Similarly, the mean admission S. Cl^- levels for NYHA Class III patients were 102.96 ± 2.93 mEq/L, and for NYHA Class IV patients, the mean admission S. Cl^- levels were 97.10 ± 8.06 mEq/L. These findings indicate a statistically significant correlation between NYHA classification and admission S. Na^+ and S. Cl^- levels as shown in Table 6 and Figure 1.

Table 7. Correlation of admission S. Na^+ and S. Cl^- according to Ejection Fraction

		EF			Kruskal Wallis (χ2)	p-value
		Preserved	Mild reduced	Reduced		
Admission Serum Sodium (mEq/L)	N	45	53	52	44.084	<.001
	Mean	132.53	131.00	124.42		
	SD	9.22	7.32	6.43		
	Median	137.00	134.00	126.00		
Admission Serum Chloride(mEq/L)	N	45	53	52	46.798	<.001
	Mean	101.31	101.66	91.85		
	SD	4.88	5.63	7.71		
	Median	102.00	103.00	90.00		

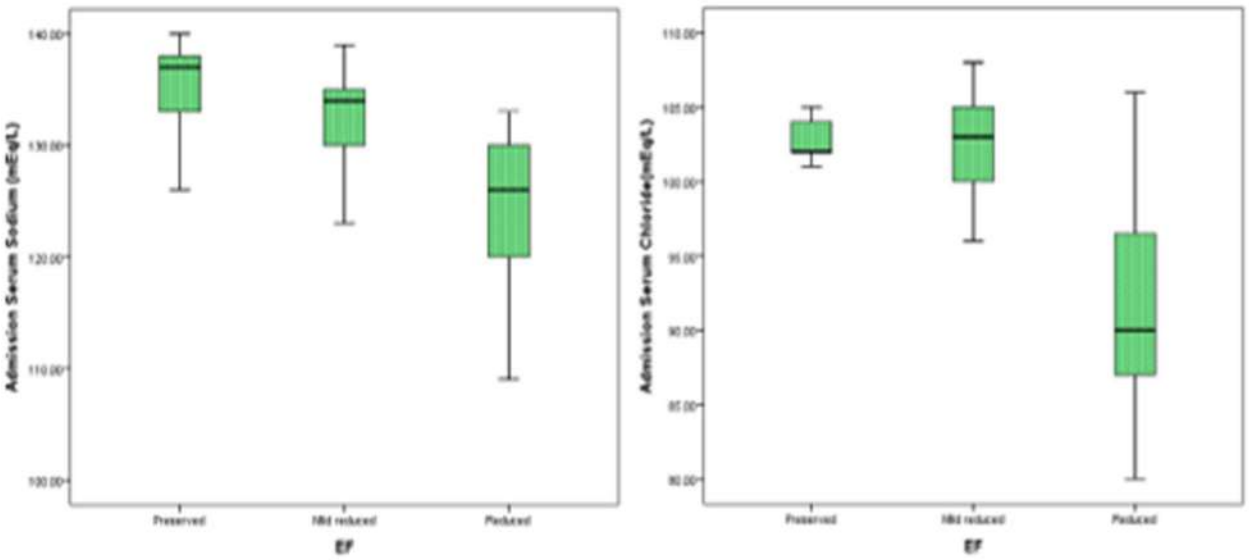


Figure 2. Box and whisker plot of admission S. Na^+ and S. Cl^- with Ejection Fraction

Furthermore, in relation to ejection fraction, the mean admission S. Na^+ levels were found to be 132.53 ± 9.22 mEq/L for preserved EF, 131.00 ± 7.32 mEq/L for mildly reduced EF, and 124.42 ± 6.43 mEq/L for reduced EF. Similarly, the mean admission S. Cl^- levels were 101.31 ± 4.88 mEq/L for preserved EF, 101.66 ± 5.63 mEq/L for mildly reduced EF, and 91.85 ± 7.71 mEq/L for reduced EF. These results establish a statistically significant association between admission S. Na^+, S. Cl^-, and EF as shown in Table 8 and Figure 2.

Table 8. Distribution of admission S. Na^+ and S. Cl^- with hospital stay duration

		Hospital Stay duration (in days)					Kruskal Wallis ($\chi 2$)	p-value
		3 days	4 days	5 days	6 days	7 days		
Admission Serum Sodium (mEq/L)	N	9	34	45	35	27	13.042	<.001
	Mean	132.44	133.35	130.44	125.74	125.19		
	SD	9.46	4.39	7.76	10.04	7.50		
	Median	139.00	135.00	133.00	129.00	124.00		
Admission Serum Chloride (mEq/L)	N	9	34	45	35	27	28.101	<.001
	Mean	104.11	103.06	99.22	93.69	94.00		
	SD	2.09	2.70	5.11	9.92	8.27		
	Median	103.00	104.50	101.00	96.00	90.00		

Moreover, it was observed that patients with lower admission S. Na^+ and S. Cl^- levels had a longer hospital stay duration. The mean admission S. Na^+ was lowest (125.19 ± 7.50 mEq/L) for a hospital stay duration of 7 days (p-value < 0.001). Similarly, the mean admission S. Cl^- was lowest (93.69 ± 9.92 mEq/L) for a hospital stay duration of 6 days (p-value < 0.001). This suggests that patients with lower S. Na^+ and S. Cl^- levels upon admission tend to have a prolonged hospital stay as shown in Table 8.

Furthermore, a positive linear correlation was observed between S. Cl^- and S. Na^+ levels, which was statistically significant (R2 linear = 0.325, p < 0.001). This finding highlights the relationship between these two electrolytes and their interplay in heart failure patients as shown in Figure 3.

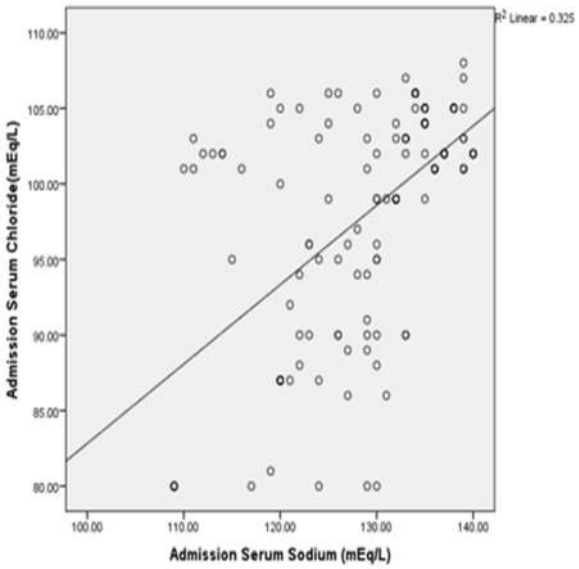


Figure 3. Scatter plot of correlation of admission serum sodium and chloride

Strengths

This study establishes a correlation between the values of admission S. Na^+ and S. Cl^- which has been found to be cost-effective and readily accessible, even at primary health care centers.

Limitations

• No follow-up of cases was conducted in this study.

• Additionally, logistic issues prevented the inclusion of prognostic markers such as BNP and NT-pro BNP for analysis.

Conclusion

Our study concluded that patients with lower admission serum sodium and chloride present with more severity in acute decompensated heart failure. They have higher NYHA functional class and lower LVEF. Also, there was a significant degree of negative correlation between hospital stay duration and admission serum sodium and chloride. Admission serum sodium was better marker for severity in ADHF. Admission serum chloride was better marker to predict hospital stay duration in ADHF. These results provide valuable insights into the association between electrolyte levels, NYHA classification, EF, and hospital stay duration in heart failure patients. Understanding these relationships can aid in better risk stratification and management strategies for improved patient outcomes.

Future Scope

The correlation study between admission serum sodium and serum chloride levels and their association with disease severity and hospital stay in ADHF patients provides valuable insights for future research. There is a need to further investigate the underlying mechanisms responsible for electrolyte imbalances in ADHF and their impact on the severity of the condition and hospitalization outcomes.

Prospective studies can be conducted to assess the potential of admission S. Na^+ and S. Cl^- as prognostic markers for predicting the duration of hospital stay and guiding treatment strategies for ADHF patients. Further research is needed to explore the role of chloride in predicting outcomes and its potential as a standalone prognostic indicator in heart failure.

With the advancements in the field of cardiology, there is an increasing need to explore and develop non-invasive techniques that can provide valuable prognostic information without resorting to invasive procedures.

Non-invasive approaches, such as echocardiography, utilization of cardiac biomarkers like BNP and NT-proBNP, as well as the use of wearable devices, show great potential in predicting the progression of heart failure, gauging response to treatment, and determining overall prognosis for patients. These non-invasive tools offer valuable insights into various aspects of cardiac function, hemodynamics, and fluid status, enabling timely interventions and personalized management strategies.

By incorporating these non-invasive techniques into future research and clinical practices, we can significantly improve risk stratification, enhance patient outcomes, and potentially reduce the duration of hospital stays specifically for individuals diagnosed with ADHF.

Ethics declarations

Funding This study did not receive any funding.

Conflict of interest

The authors declare that they have no competing interests.

Ethics approval, Consent to participate, Consent to publish, Availability of data and material, Code availability

Not applicable.

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