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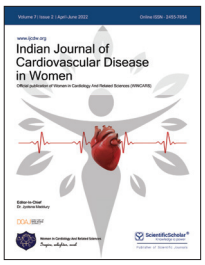

Cardiovascular *Original Article*

Hyponatremia in Acute Decompensated Heart Failure as a Predictor of Acute Cardiorenal Syndrome Type-1

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ABSTRACT

Objectives: Acute cardiorenal syndrome (CRS type-1) refers to an acute worsening of heart function, leading to acute kidney injury (AKI), frequently complicating acute decompensated heart failure (ADHF). This study aims to investigate whether hyponatremia, is a surrogate marker for the development of AKI in patients admitted with ADHF.

Materials and Methods: Sample size – 100 patients with ADHF. Age – More than 18 years. Investigations – 2D-ECHO, N-terminal pro-brain natriuretic peptide, kidney function test, estimated glomerular filtration rate, USG abdomen, complete blood picture, chest X-ray, and complete urine examination.

Results: On analysis of data, 63.5% (n=33) of patients who had hyponatremia (n=45) eventually developed AKI during hospital stay, whereas 36.5% (n=19) of patients who did not have hyponatremia (n=36) developed AKI. Hyponatremia was found to be a statistically significant (P = 0.001) predictor of increased incidence of AKI in a predetermined group of patients with HF in our study, and ADHF patients with hyponatremia have a 5.21-fold higher risk of developing AKI (95% CI, 2.20–12.36) than ADHF patients without hyponatremia.

Conclusion: Hyponatremia predicts complications while admission in heart failure patients like type-I CRS and it has also been shown that comorbidities could play an important role in the presence or absence of hyponatremia and could even influence the length of hospital stay attributed to lower serum sodium levels which need further clinical trials.

Keywords: Hyponatremia, Acute decompensated heart failure, Acute cardiorenal syndrome type-1

ABSTRACT IMAGE

Hyponatremia in Acute Decompensated Heart Failure as a Predictor of Acute Cardiorenal Syndrome Type-1

The objectives of this study were to investigate whether hyponatremia, is a surrogate marker for the development of AKI in patients admitted with ADHF.

Sample size – 100 patients with ADHF. Age – More than 18 years. Investigations – 2D-ECHO, N-terminal pro-brain natriuretic peptide, kidney function test, estimated glomerular filtration rate, USG abdomen, complete blood picture, chest X-ray, and complete urine examination.

Analysis of Hyponatremia & AKI in ADHF patients using Chi-square Test

AKI	Hyponatremia present		Hyponatremia absent		*P*-value
	n	%	*n*	%	
AKI Present	33	63.5	19	36.5	<0.001*
AKI Absent	12	25.0	36	75.0	

AKI: Acute kidney injury, ADHF: Acute decompensated heart failure

Descriptive analysis for LVEF and NT Pro BNP among study participants

Variable	*n*	Mean	SD	Median	Min	Max
LVEF	100	30	4.96	30	13	43
NT Pro BNP	100	3284.76	3555.82	1570	234	15890

LVEF: Left ventricular ejection fraction

Hyponatremia predicts complications while admission in heart failure patients like type-I CRS and it has also been shown that comorbidities could play an important role in the presence or absence of hyponatremia and could even influence the length of hospital stay attributed to lower serum sodium levels which need further clinical trials.

INTRODUCTION

Acute cardiorenal syndrome (CRS type-1) is the development of acute kidney injury (AKI) and renal dysfunction in a patient with an acute cardiac disease, typically acute decompensated heart failure (ADHF).[1] Acute kidney damage (AKI) that develops in this situation has repeatedly been linked to higher all-cause death rates over the short- and long-term, as well as cardiovascular mortality, and to a quicker progression of more advanced renal disease.[2]

AKI's pathogenesis in the context of ADHF is complex and multifaceted. Hemodynamic variables, neurohormonal activation, and congestion are three major contributory mechanisms. Quantification of hemodynamic disturbance is possible; however, the level of fluid overload and the exposure of the kidney to numerous activated neurohormonal systems is difficult to quantify clinically.

The most common electrolyte disorder that is frequently seen in ADHF patients as well as in a variety of therapeutic settings is hyponatremia.[3] Low sodium levels have been linked to mortality and recurrent hospitalizations for decompensation, according to numerous investigations on patients with heart failure (HF).

Compared to outpatients with stable disease, hospitalized patients with deteriorating HF have a much higher prevalence of hyponatremia[4] and volume overload. AKI may also be more likely to occur in the kidneys due to neurohormonal activation, renal vasoconstriction, and decreased renal blood flow, in addition to the impact of hyponatremia on survival, severe volume overload, and related venous congestion.[5] Therefore, the purpose of this study is to investigate the hypothesis that hyponatremia may portend the onset of AKI in the setting of ADHF.

Study participants

With 100 participants experiencing ADHF, we conducted prospective observational research. All study participants provided written fully informed consent. This study was done between June 2022 and August 2022 and accepted by the Ethics Committee of NIMS Hospital. We included patients with Ages >18 years and all patients with ADHF with or without AKI. However, we excluded patients with previous acute or chronic kidney disease, acute myocardial infarction, and patients with structural kidney diseases.

At the beginning of the study, 148 ADHF patients in total were enrolled. Patients having missing information on their age, gender, or clinical outcome (n = 13) were not included in the study.

Patients who had undergone nephrectomy, kidney transplantation, or chronic renal disease (n = 18), as well as patients who had any of these procedures in the past, were also eliminated. In addition, patients with AKI that were thought to have been brought on by medication toxicity, contrast and confirmed severe sepsis, structural kidney disorders, and acute myocardial infarction were not included in the study. These individuals (n = 11) were not included, because it was not possible to link ADHF with certainty to the change in serum creatinine. The final analysis included 100 participants. AKI and ADHF were present in one group (52 participants), but ADHF was absent in the second group (48 participants).

MATERIALS AND METHODS

After receiving properly informed consent, patients meeting the inclusion and exclusion criteria will be enrolled in this study. Before the trial, a medication history including diuretics and nephrotoxic medications will be obtained.

We looked at the relationship between hyponatremia and AKI in two distinct cohorts: (1) Patients with AKI in ADHF and (2) patients without AKI in ADHF.

AKI is defined as an increase of >0.3 mg/dL in creatinine from baseline. Sodium levels below 136 mmoL/L are considered hyponatremia. Between June and August 2022, adults (>18 years of age) with ADHF were enrolled. Electronic medical records were used to obtain clinical data. The permitted error was ±2%, and $\alpha = 0.05$ bilateral when estimating the sample size using the formula for calculating the sample size of cross-sectional studies. The estimated sample size was 100.

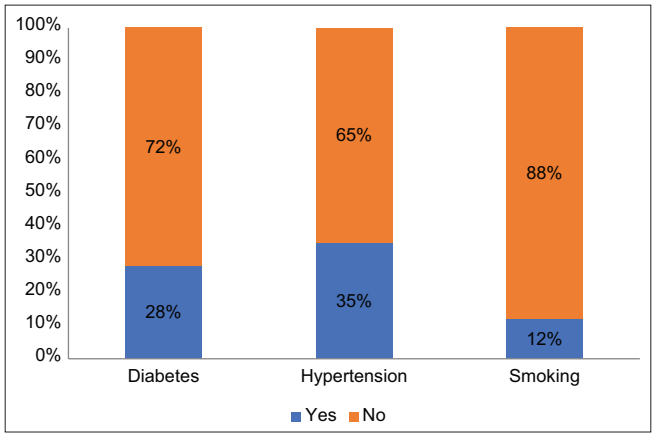

Figure 1: Distribution of characteristics among study patients.

RESULTS

The study included 100 patients in total, of whom 75 (75%) were men and 25 (25%) were women. The participants' average age was 51.60 years. It was noted that 26 (26%) participants were between the ages of 21 and 40, 42 (42%) were between the ages of 41 and 60, and 32 (32%) were over the age of 60 [Table 1]. Depending on whether AKI was present or not, we split the study population into two groups [Table 2].

The mean N-terminal pro-brain natriuretic peptide (NT Pro-BNP) levels were 3284 pg/mL and the mean left ventricular ejection fraction (LVEF) was 30% [Table 3]. In our study, 17 diabetic patients (32.7%), 21 hypertensive patients (40.4%), and eight chromic smokers (15.4%) all suffered from AKI; however, none of these percentages were statistically significant [Table 4].

One finding was that hyponatremia affected 45% of the study participants [Table 2]. It was noted that 12% of the

Table 1: Age and gender distribution among study participants.

Age and gender distribution among study participants			
Variables	**Category**	***n***	**%**
Age	21–40 yrs.	26	26
	41–60 yrs.	42	42
	61–80 yrs.	32	32
		Mean	**SD**
Gender	Mean	51.60	14.07
	Range	23–80	
	Males	75	75
	Females	25	25

SD: Standard deviation

Table 2: Incidence of AKI and hyponatremia among study patients.

Incidence of AKI and hyponatremia among study patients			
Variables	**Category**	***n***	**%**
AKI	Absent	48	48
	Present	52	52
Hyponatremia	Absent	55	55
	Present	45	45

AKI: Acute kidney injury

Table 3: Descriptive analysis for LVEF and NT Pro BNP among study participants.

Descriptive analysis for LVEF and NT Pro BNP among study participants						
Variable	***n***	**Mean**	**SD**	**Median**	**Min**	**Max**
LVEF	100	30	4.96	30	13	43
NT Pro BNP	100	3284.76	3555.82	1570	234	15890

LVEF: Left ventricular ejection fraction

Table 4: Association between co-morbidities and AKI.

Association between comorbidity and AKI among ADHF participants using Chi-square test						
Variable	**Category**	**AKI Present**		**AKI Absent**		***P*-value**
		n	**%**	***n***	**%**	
Diabetes	Yes	17	32.7	11	22.9	0.28
	No	35	67.3	37	77.1	
Hypertension	Yes	21	40.4	14	29.2	0.24
	No	31	59.6	34	70.8	
Smoking	Yes	8	15.4	4	8.3	0.28
	No	44	84.6	44	91.7	

AKI: Acute kidney injury, ADHF: Acute decompensated heart failure

study group had a history of smoking, 35% of patients had hypertension, and 28% of patients had diabetes mellitus [Figure 1]. According to data analysis, AKI finally developed in 63.5% of patients with hyponatremia during a hospital stay, but only 36.5% of individuals without hyponatremia [Table 5].

In comparison to ADHF patients without hyponatremia, those with hyponatremia have a 5.21-fold higher chance of getting AKI (95% CI, 2.20–12.36), and this conclusion was statistically significant ($P < 0.001$) [Table 6].

After correcting for age, gender, comorbidities, and habits as potential confounders, ADHF patients with hyponatremia are 5.07 times more likely to develop AKI (95% CI, 2.05–12.55) than ADHF patients without hyponatremia. This finding was statistically significant at $P < 0.001$ [Table 7].

DISCUSSION

Acute CRS type-1 and ADHF coexistence are a serious condition linked to significantly higher morbidity and mortality in people with HF.[6-9] The inability to identify patients with a high risk of developing CRS type-1 early enough to start therapies is a significant obstacle to improving clinical outcomes in ADHF patients.

Patients with ADHF often experience hyponatremia. According to Lee *et al*.,[10] chronic HF patients who have hyponatremia had increased mortality rates. Patients with ADHF experience this as well.

A 19.7% admission rate for patients with hyponatremia (Na 135 mMoL/L) was found in the analysis of the OPTIMIZE-HF registry. Both registries and clinical trials, such as outcomes of a prospective trial of intravenous milrinone for exacerbations of chronic heart failure[3] (27%) and ESCAPE[4] (24%), have similar rates of hyponatremia. When comparing hyponatremia to normal sodium levels, a lower blood sodium concentration is linked to increased mortality during hospitalization and after discharge as well as a higher likelihood of readmission for ADHF after 6 months.

Our study's key findings were that hyponatremia in HF patients was linked to increased problems during a hospital stay. With ADHF, 45% of patients exhibited hyponatremia (among which 33 patients had AKI, and 12 patients did not have AKI).

Patients with ADHF from a range of age groups, genders, and comorbidities are included in our sample. Some of these variations could play a role in the development of AKI. Even though comorbidities were more prevalent in individuals with AKI, they did not significantly affect the outcomes statistically. Other studies have demonstrated that chronic comorbidities independently increase the mortality rates of patients with newly diagnosed HF[11] and also in the ambulatory HF population.[12]

Table 5: Analysis of hyponatremia and AKI in ADHF patients.

Analysis of Hyponatremia & AKI in ADHF patients using Chi-square Test					
AKI	**Hyponatremia present**		**Hyponatremia absent**		***P*-value**
	n	**%**	***n***	**%**	
AKI Present	33	63.5	19	36.5	<0.001*
AKI Absent	12	25.0	36	75.0	

AKI: Acute kidney injury, ADHF: Acute decompensated heart failure

Table 6: Risk of AKI among hyponatremia patients.

Univariate logistic regression analysis to calculate the risk of AKI in ADHF patients with hyponatremia				
Variable	**OR**	**95% CI**		***P*-value**
		Lower	**Upper**	
AKI	5.21	2.20	12.36	<0.001*

OR: Odds ratio, CI: Confidence interval, AKI: Acute kidney injury, ADHF: Acute decompensated heart failure

Table 7: Multivariate logistic regression model to estimate the risk of AKI among hyponatremia in ADHF patients after adjusting for possible confounders.

Multivariate logistic regression model to estimate the risk of AKI among hyponatremia in ADHF patients after adjusting for possible confounders				
Variables	**OR**	**95% CI for OR**		***P*-value**
		Lower	**Upper**	
Age (>50)	0.39	0.16	0.99	0.07
Gender (Males)	1.58	0.56	4.46	0.39
Diabetes	1.14	0.39	3.32	0.81
Hypertension	0.96	0.36	2.55	0.93
Smoking	1.92	0.47	7.94	0.37
AKI	5.07	2.05	12.55	<0.001*

AKI: Acute kidney injury, ADHF: Acute decompensated heart failure

Hyponatremia was found to be a statistically significant ($P< 0.001$) predictor of increased incidence of AKI in a predetermined group of patients with HF in our study, and ADHF patients with hyponatremia have a 5.21-fold higher risk of developing AKI (95% CI, 2.20–12.36) than ADHF patients without hyponatremia. Future trials with hyponatremic patients and HF should include data on comorbidities to validate the results that we acquired in this study. Older people have more comorbidities, and the percentage of patients with intact ejection fraction is higher.

Study limitations

The incidence of rehospitalizations and all-cause mortality were not investigated due to the limited sample volume

and short duration of the study, as well as the fact that a sizable proportion of patients presented without baseline information on their baseline creatinine concentration and estimated glomerular filtration rate.

Finally, because the study focused mostly on in-patients of tertiary hospitals, it is possible that the results cannot be generalized to patients in community hospitals or any other study setting.

Despite these drawbacks, this study sheds light on how hyponatremia affects patients with ADHF who may develop CRS type-1. Our research can contribute to the body of knowledge regarding the value of serum sodium levels and their relationship to worsening renal failure.

CONCLUSION

Hyponatremia predicts complications while admission in HF patients like type-I CRS and it has also been shown that comorbidities could play an important role in the presence or absence of hyponatremia and could even influence the length of hospital stay attributed to lower serum sodium levels which need further clinical trials.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Ronco C, McCullough P, Anker SD, Anand I, Aspromonte N, Bagshaw SM, *et al*. Cardio-renal syndromes: Report from the consensus conference of the acute dialysis quality initiative. Eur Heart J 2010;31:703-11.
2. Newsome BB, Warnock DG, McClellan WM, Herzog CA, Kiefe CI, Eggers PW, *et al*. Long-term risk of mortality and end-stage renal disease among the elderly after small increases in serum creatinine level during hospitalization for acute myocardial infarction. Arch Intern Med 2008;168:609-16.
3. Klein L, O'Connor CM, Leimberger JD, Gattis-Stough W, Pina IL, Felker GM, *et al*. Lower serum sodium is associated with increased short-term mortality in hospitalized patients with worsening heart failure: Results from the Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) study. Circulation 2005;111:2454-60.
4. Gheorghiade M, Rossi JS, Cotts W, Shin DD, Hellkamp AS, Pina IL, *et al*. Characterization and prognostic value of persistent hyponatremia in patients with severe heart failure in the ESCAPE Trial. Arch Intern Med 2007;167:1998-2005.
5. Damman K, Voors AA, Hillege HL, Navis G, Lechat P, van Veldhuisen DJ, *et al*. Congestion in chronic systolic heart failure is related to renal dysfunction and increased mortality. Eur J Heart Fail 2010;12:974-82.
6. Yoo BS, Park JJ, Choi DJ, Kang SM, Hwang JJ, Lin SJ, *et al*. Prognostic value of hyponatremia in heart failure patients: An analysis of the Clinical Characteristics and Outcomes in the Relation with Serum Sodium Level in Asian Patients Hospitalized for Heart Failure (COAST) study. Korean J Intern Med 2015;30:460.
7. Omar HR, Charnigo R, Guglin M. Prognostic significance of discharge hyponatremia in heart failure patients with normal admission sodium (from the ESCAPE Trial). Am J Cardiol 2017;120:607-15.
8. Sato Y, Yoshihisa A, Oikawa M, Nagai T, Yoshikawa T, Saito Y, *et al*. Hyponatremia at discharge is associated with adverse prognosis in acute heart failure syndromes with preserved ejection fraction: A report from the JASPER registry. Eur Heart J Acute Cardiovasc Care 2019;8:623-33.
9. Wang J, Zhou W, Yin X. Improvement of hyponatremia is associated with lower mortality risk in patients with acute decompensated heart failure: A meta-analysis of cohort studies. Heart Fail Rev 2019;24:209-17.
10. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: Derivation and validation of a clinical model. JAMA 2003;290:2581-7.
11. Jong P, Vowinckel E, Liu PP, Gong Y, Tu JV. Prognosis and determinants of survival in patients newly hospitalized for heart failure: A population-based study. Arch Intern Med 2002;162:1689-94.
12. Clarke B, Howlett J, Sapp J, Andreou P, Parkash R. The effect of comorbidity on the competing risk of sudden and nonsudden death in an ambulatory heart failure population. Can J Cardiol 2011;27:254-61.

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