

Dysnatraemia in Heart Failure: A Descriptive Study

Huvappa Ganiger¹, A G Ravishankar²

¹Junior Resident, Department of Medicine, Mysore Medical College and Research Institute, Mysore, Karnataka, India, ²Professor and Head, Department of Medicine, Mysore Medical College and Research Institute, Mysore, Karnataka, India

Abstract

Background: Sodium concentrations affect three-dimensional conformations of proteins and enzymes and thus, play a critical role in maintaining electrical gradients across cellular membranes and in muscular excitation. It is within the realms of possibility that these small changes in sodium concentrations may have attenuated deleterious effects on cardiac muscle function in patients with heart failure.

Objectives: The objectives were to estimate proportion of dysnatraemia in heart failure and to look for correlation between the serum sodium levels with left ventricular ejection fraction (LVEF), systolic blood pressure (SBP), blood urea, and serum creatinine levels.

Materials and Methods: The study included 50 patients of heart failure of any cause and severity admitted to K.R. Hospital.

Results: The prevalence of dysnatraemia was 30%, 24% had hyponatremia and 6% had hypernatremia. Mean diastolic blood pressure (DBP) was lower in patients with hyponatremia. Mean SBP was lower in patients with hypernatremia. Mean LVEF was lower in patients with hypernatremia. The mean LVEF was lower in patients with low normal sodium levels (135-139 mmol/L) ($P < 0.019$), whereas LVEF was preserved in patients with high normal sodium levels (140-145 mmol/L). Pulmonary artery hypertension (PAH) was present in 88.33% of patients with hyponatremia ($P < 0.0495$). Mean blood urea and mean serum creatinine were higher in patients with hypernatremia. Mean glomerular filtration rate (GFR) was lower in patients with hypernatremia.

Conclusion: Dysnatraemia is a common occurrence in patients with heart failure, with hyponatremia being common. The hypernatremia is associated with lower LVEF, lower SBP, higher blood urea and higher serum creatinine, and lower estimated GFR. The hyponatremia is associated with PAH and lower DBP. LVEF is preserved in patients with high normal sodium levels.

Key words: Blood urea, Glomerular filtration rate, Heart failure, Hypernatremia, Hyponatremia, Left ventricular ejection fraction, Serum creatinine, Sodium, Systolic blood pressure

INTRODUCTION

Development of symptomatic heart failure carries a poor prognosis. Community-based studies indicate that 30-40% of patients die within 1 year of diagnosis, and 60-70% die within 5 years mainly from worsening heart failure.¹

Normal serum sodium level ranges from 135 to 145 mmol/L. The sodium concentrations affect three-dimensional conformations of proteins and enzymes

and, thus, play a critical role in maintaining electrical gradients across cellular membranes and in muscular excitation.² It is within the realms of possibility that these small changes in sodium concentrations may have attenuated deleterious effects on cardiac muscle function in patients with chronic heart failure. Several studies have indicated the relationship between admission serum sodium concentration and clinical outcomes in patients hospitalized for heart failure.³⁻¹⁸ Both hyponatremia and hypernatremia indicate a markedly compromised prognosis in heart failure regardless of left ventricular ejection fraction (LVEF). Within the normonatremic patients, patients with the high normal range (i.e., 140-145 mmol/L) carries good prognosis compared with those with the low normal range (i.e., 135-139 mmol/L). It has been found that hyponatremia was independently associated with higher urea levels, higher New York Heart Association

Access this article online



www.ijss-sn.com

Month of Submission : 07-2015
Month of Peer Review : 08-2015
Month of Acceptance : 08-2015
Month of Publishing : 09-2015

Corresponding Author: Dr. Huvappa Ganiger, At and Post-Jakanur, Taluq-Badami, Bagalkot - 587 201, Karnataka, India.
 Phone: +91-8884356336. E-mail: Dr.huvappaganiger@yahoo.in

(NYHA) class, lower systolic blood pressure (SBP), and lower ejection fraction. Emergency admissions were also correlated with hyponatremia.¹⁹ The hyponatremia also predicts cardiorenal syndrome which occurs in heart failure. Due to complex physiology of heart failure, the effects of loop diuretics on serum sodium can be difficult to accurately predict thus making frequent monitoring of serum sodium very important.²⁰

Hence this study was done to know the prevalence of dysnatraemia in heart failure as studies on prevalence of hyponatremia in heart failure are lacking, and to find out the correlations between serum sodium measured at the time of admissions with other variables as mentioned in objectives.

Aims and Objectives

1. To measure the serum sodium levels at the time of admission and to estimate proportion of dysnatraemia in heart failure patients
2. To correlate between serum sodium levels measured at the time of admission with the LVEF as determined by two-dimensional (2D) echocardiogram during hospital stay
3. To correlate between the serum sodium levels with other variables such as SBP, blood urea levels, and serum creatinine levels at the time of admission in heart failure patients.

MATERIALS AND METHODS

The present study was conducted on 50 patients with heart failure of any cause and severity admitted to cardiology ward, K.R Hospital, Mysore attached to Mysore Medical College and Research Institute during the period of November 2012-August 2014.

Inclusion Criteria

The patients diagnosed with heart failure that are older than 18 years of age.

Exclusion Criteria

1. The patients with conditions causing hyponatremia like - Vomiting, diarrhea, salt-losing nephropathy, diabetic ketoacidosis, cirrhosis, nephrotic syndrome, syndrome of inappropriate antidiuretic hormone secretion, glucocorticoid deficiency
2. The patients with conditions causing hyponatremia such as - Chronic kidney disease and diabetic insipidus.

Method of Study

The study was of descriptive or exploratory in nature. Purposive sampling technique was used as a sampling method. Data was collected using a pretested proforma

meeting the objectives of the study. The cases for the study were selected in accordance with the above-mentioned inclusion and exclusion criteria. The purpose of the study was explained to the patient, and informed consent obtained. Detailed history, clinical examination and the following investigations such as electrocardiogram, chest X-ray posterior-anterior view, renal function tests, 2D echocardiogram, and other relevant tests were carried out.

In the present study, blood urea was measured using the urease glutamate dehydrogenase method and serum creatinine was measured using Jaffey kinetic method. Estimated glomerular filtration rate (GFR) was calculated using Cockcroft-Gault equation. The serum sodium was measured using easy lyte plus analyzer (method used - direct measurement by ion selective electrode). LVEF was calculated using the modified Simpson's rule. The pulmonary artery systolic pressure was estimated using tricuspid regurgitation jet method. In the present study, patients with pulmonary artery systolic pressure more than 35 mmHg are considered to have pulmonary artery hypertension (PAH).

Statistical Methods

Data was analyzed statistically using descriptive statistics, Chi-square test, product-moment correlation, and cross-tabulations using SPSS (version 20.0).

RESULTS

In the present study, 50 patients of heart failure were included; all of them were in decompensate state at the time of admission (NYHA 4 Class). The serum sodium measured at the time of admission were categorized into normal (135-145 mmol/L), hyponatremia (<135 mmol/L), and hypernatremia (more than 145 mmol/L) (Table 1). The age of patients ranged from 28 to 85 years with mean age of 58.18 ± 13.64 years. Male to female ratio in the present study of heart failure patients was 1:1. In our study, ischemic heart disease was the most common risk factor for heart failure (68%) followed by chronic obstructive pulmonary disease (COPD)/asthma (48%), hypertension (28%), and diabetes mellitus (28%).

Mean SBP was lower in patients with heart failure with hypernatremia (120.0 ± 36.0 mmHg) compared to those with hyponatremia (129.2 ± 27.5 mmHg) and those with normal sodium values (129.0 ± 20.7 mmHg).

Mean diastolic blood pressure (DBP) was lower in patients with heart failure with hyponatremia (80.0 ± 12.8 mmHg) compared to those with hypernatremia (83.3 ± 25.2 mmHg) and those with normal sodium values (81.4 ± 14.2 mmHg).

Table 1: General characteristics of study population

Variable	Hyponatremia (<135 mmol/L)	Normonatremia (135-145 mmol/L)	Hypernatremia (>145 mmol/L)
Number of patients	12	35	03
Women (n)	07	18	00
Mean age	54.75±13.34	58.48±13.92	68.33±7.63
IHD (n)	06	25	03
DM (n)	01	13	00
COPD/asthma (n)	09	15	03
Mean HR	99.7±10.8	101.7±9.3	102.0±7.2 (<i>P</i> <0.81)
Mean SBP	129.2±27.5	129.0±20.7	120.0±36.0 (<i>P</i> <0.808)
Mean DBP	80.0±12.8	81.4±14.2	83.3±25.2 (<i>P</i> <0.925)
Mean LVEF	47.25±14.6	39.82±13.7	30.33±7.2 (<i>P</i> <0.096)
PAH	10	18	00 (<i>P</i> <0.0495)
Mean blood urea	43.33±7.4	43.26±21.6	45.67±7.8 (<i>P</i> <0.977)
Mean serum creatinine	1.01±0.22	1.08±0.27	1.23±0.11 (<i>P</i> <0.375)
Mean GFR	54.86±14.8	56.37±40.53	42.27±6.8 (<i>P</i> <0.802)

IHD: Ischemic heart disease, DM: Diabetes mellitus, COPD: Chronic obstructive pulmonary disease, HR: Heart rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, LVEF: Left ventricular ejection fraction, PAH: Pulmonary artery hypertension, GFR: Glomerular filtration rate

Table 2: LVEF among high normal and low normal sodium groups

Variable	Sodium categories	
	High normal (140-145 mmol/L) (n=14)	Low normal (135-139 mmol/L) (n=21)
Mean LVEF (%)	50±11.3	33±10.3 (<i>P</i> <0.019)

LVEF: Left ventricular ejection fraction

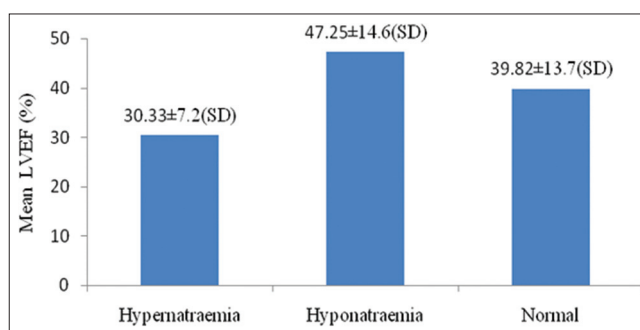
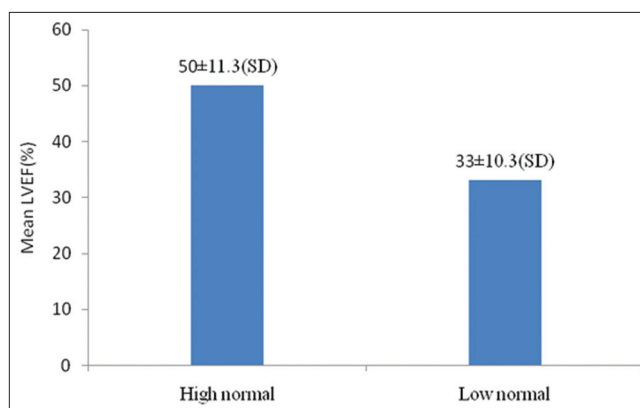
The mean LVEF was lower in patients with heart failure with hypernatremia (30.33% ± 7.2%) compared to those with hyponatremia (47.25% ± 14.6%) and those with normal sodium values (39.82% ± 13.7%) (Table 2 and Graph 1).

The mean LVEF was lower in patients with heart failure with low normal sodium values (33% ± 10.3%) compared to those with high normal sodium values (50% ± 11.3%) which was statistically significant (*P* < 0.019) (Graph 2).

PAH was present in 28 (56%) patients in the present study. PAH was present in 83.33% of patients with hyponatremia and 51.43% of patients with normal sodium values in the present study which was statistically significant (*P* < 0.0495) (Graph 3).

The mean blood urea was higher (45.67 ± 7.8 mg/dL) in patients with heart failure who had hypernatremia compared to those who had hyponatremia (43.33 ± 7.4 mg/dL) and those who had normal sodium values (43.26 ± 21.6 mg/dL).

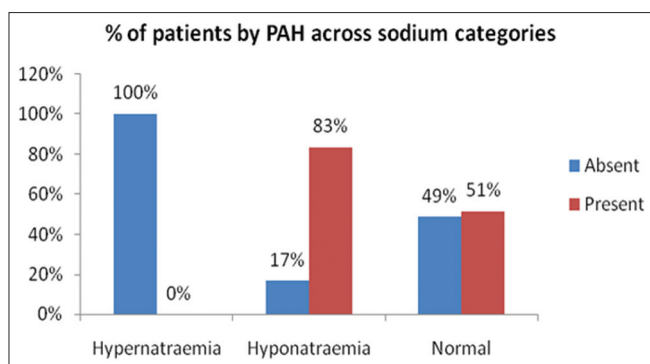
The mean serum creatinine was higher (1.23 ± 0.11 mg/dL) in patients with heart failure who had hypernatremia compared to those who had hyponatremia (1.01 ± 0.22 mg/dL) and those who had normal sodium values (1.08 ± 0.27 mg/dL). Mean GFR was lower (42.27 ± 6.8 ml/min) in patients with heart failure who had

**Graph 1: Left ventricular ejection fraction among different sodium groups****Graph 2: Left ventricular ejection fraction among high normal and low normal sodium groups**

hypernatremia compared to those who had hyponatremia (54.86 ± 14.8 ml/min) and those who had normal sodium values (56.37 ± 40.53 ml/min).

DISCUSSION

Heart failure patients with hyponatremia seem to exhibit a pathophysiological profile that is different from heart failure patients without hyponatremia, as it reflects a greater



Graph 3: Pulmonary artery hypertension among different sodium groups

activation of the rennin-angiotension aldosterone system, the arginine vasopressin system, and the sympathetic nervous system. Both hyponatremia and hypernatremia indicate a markedly compromised prognosis in heart failure regardless of LVEF.

The mean age of study population was 58.1 ± 13.6 years in our study. In Deubner *et al.* study, median age was 73 years.

The prevalence of dysnatraemia was 30% in our study; 24% had hyponatremia and 6% had hypernatremia.

Deubner *et al.* study had 17% prevalence of dysnatraemia, 7.2% hyponatremia, and 9.8% hypernatremia. The prevalence of hyponatremia is more in our study as all patients were in decompensated state with NYHA Class 4. The prevalence of hyponatremia increases to 20-30% when the patient is admitted with acute heart failure. The incidence of higher prevalence of hyponatremia would be attributable to the loop diuretics which patients were already on for heart failure prior to admission.

The studies which included patients with decompensated heart failure had a higher prevalence of hyponatremia. Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure (OPTIME-CHF) trial had 27% prevalence of hyponatremia. ESCAPE trial study had 24% prevalence of hyponatremia similar to our study. OPTIMIZE-HF registry had 26% prevalence of hyponatremia.

Studies on prevalence of hypernatremia are not done, except for Deubner *et al.* prevalence of hypernatremia in their study was more compared to our study; this is probably because in their study there were no exclusion criteria other than acute *de novo* heart failure. The increased prevalence of hypernatremia in their study was may be because of associated renal dysfunction.

The mean age of patients in hypernatremia group was more (68.3 ± 7.6 years) compared to that in normal

sodium group (58.4 ± 13.9 years) which was statistically not significant ($P < 0.11$), may be because of small study group. In Deubner *et al.* study median age of hypernatremia group was 76 years, and that of normal sodium group was 72 years. This suggests that prevalence of hypernatremia increases in elderly patients with heart failure due to age-related reduction in renal reserve.

Mean SBP was lower in patients with heart failure who had hypernatremia ($P < 0.808$). Mean DBP was lower in patients with heart failure who had hyponatremia ($P < 0.925$).

In the previous study of Balling *et al.*, hyponatremia was independently associated with lower SBP compared to patients with normal sodium values.²¹ However, in our study, we did not find such association, infact in our study hypernatremia was associated with lower SBP. This may be because of small sample size further studies are needed to find a casual relationship.

All patients with hypernatremia had decreased LVEF. In fact mean LVEF was more in hyponatremia group than with group with normal sodium range which was not statistically significant ($P < 0.096$) may be because of small sample size. This suggests that hyponatremia occurs irrespective of whether the systolic function normal or decreased, others factors might contribute to the pathogenesis of hyponatremia in patients with preserved LVEF.

The mean LVEF was lower in patients with heart failure with low normal sodium values ($33\% \pm 10.3\%$) compared to those with high normal sodium values ($50\% \pm 11.3\%$) which was statistically significant ($P < 0.019$). This shows that in patients with high normal sodium LVEF was preserved and was decreased in patients with low normal sodium group. In Deubner *et al.* study median, LVEF was 40% in low normal sodium group and 41% in high normal sodium group. In their study, the prognosis was better in patients with high normal sodium compared to those with low normal sodium.

PAH was present in 28 (56%) patients, out of which 10 (35.7%) had hyponatremia rest 18 had sodium in the normal range. PAH was present in 83.33% hyponatremia group compared to 51.43% in the group with sodium in the normal range, which was statistically significant ($P < 0.049$). Interestingly in a patient with hyponatremia and PAH, COPD/asthma was present in 8 patients (80.0%), and LVEF was preserved in 6 patients (60%). This indicates increased neurohormonal activation and thereby hyponatremia may occur in heart failure patients with associated PAH irrespective of systolic dysfunction severity compared to those without PAH. This also suggests that patient with heart failure with PAH are at more risk for hyponatremia. Increased sympathetic activation has recently been

demonstrated in PAH and is thought to correlate with disease severity and impact hemodynamics in a similar manner to left heart failure. In a study conducted by Campo *et al.*, in patients with PAH, hyponatremia was present in 45.2%. In their study, hyponatremia predicted poor prognosis in patients with PAH admitted for right heart failure.²²

In a previous study by Deubner *et al.*, hyponatremia was associated with higher blood urea and serum creatinine levels with lower GFR. In our study, hypernatremia was associated with higher blood urea and serum creatinine levels with lower GFR. This is probably because of small sample size and strict exclusion criterias in our study. The mean age of patients with hypernatremia was the more compared to patients with hyponatremia in our study, which might have lead to an age-related reduction in renal reserve.

CONCLUSION

Dysnatraemia is a common occurrence in patients with heart failure, with hyponatremia being common which needs to be recognized. The hypernatremia is commonly associated with lower LVEF, lower SBP, higher blood urea and higher serum creatinine, and lower GFR. The hyponatremia is commonly associated with PAH and lower DBP. LVEF is preserved in patients with high normal sodium levels.

The sample size in our study was small compared to previous studies hence we couldn't get significant *P* values. Further large studies are required to confirm these associations.

The study was restricted to cross-sectional study due to logistical issues; hence the prognostic importance of dysnatraemia in heart failure patients could not be assessed.

REFERENCES

- Mann DL, Chakinala M. Heart failure, and corpulmonale. In: Harrison's Principles of Internal Medicine. 18th ed., Ch. 234. New York: McGraw-Hill; 2012. p. 1902.
- Rose BD, Post TW. Clinical Physiology of Acid-Base and Electrolyte Disorders. 5th ed. New York: McGraw-Hill; 2001.
- Filippatus TD, Elisaf MS. Hyponatraemia in patients with heart failure. *World J Cardiol* 2013;5:317-28.
- Klein L, O'Connor CM, Leimberger JD, Gattis-Stough W, Piña 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.
- Gheorghide M, Rossi JS, Cotts W, Shin DD, Hellkamp AS, Piña 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.
- Gheorghide M, Abraham WT, Albert NM, Stough WG, Greenberg BH, O'Connor CM, *et al.* Relationship between admission serum sodium concentrations and clinical outcomes in patients hospitalized for heart failure: An analysis from the OPTIMISE-HF registry. *Eur Heart J* 2007;28:980-8.
- Ghosh S, Smith J, Dexter J, Carroll-Hawkins C, O'Kelly N. Mild hyponatraemia and short outcomes in patients with heart failure in the community. *Br J Cardiol* 2011;18:133-7.
- Bettari L, Fiuzat M, Shaw LK, Wojdyla DM, Metra M, Felker GM, *et al.* Hyponatremia and long-term outcomes in chronic heart failure – An observational study from the duke databank for cardiovascular diseases. *J Card Fail* 2012;18:74-81.
- Fonarow GC, Heywood JT, Heidenreich PA, Lopatin M, Yancy CW; ADHERE Scientific Advisory Committee and Investigators. Temporal trends in clinical characteristics, treatments, and outcomes for heart failure hospitalizations, 2002 to 2004: Findings from Acute Decompensated Heart Failure National Registry (ADHERE). *Am Heart J* 2007;153:1021-8.
- DeWolfe A, Lopez B, Arcement LM, Hebert K. Low serum sodium as a poor prognostic indicator for mortality in congestive heart failure patients. *Clin Cardiol* 2010;33:E13-7.
- Vazquez R, Bayes-Genis A, Cygankiewicz I, Pascual-Figal D, Grigorian-Shamagian L, Pavon R, *et al.* The MUSIC Risk score: A simple method for predicting mortality in ambulatory patients with chronic heart failure. *Eur Heart J* 2009;30:1088-96.
- Schrier RW, Sharma S, Shechekochikhin D. Hyponatraemia: More than just a marker of disease severity? *Nat Rev Nephrol* 2013;9:37-50.
- Konishi M, Haraguchi G, Ohigashi H, Sasaoka T, Yoshikawa S, Inagaki H, *et al.* Progression of hyponatremia is associated with increased cardiac mortality in patients hospitalized for acute decompensated heart failure. *J Card Fail* 2012;18:620-5.
- Velavan P, Khan NK, Goode K, Rigby AS, Loh PH, Komajda M, *et al.* Predictors of short term mortality in heart failure - Insights from the Euro Heart Failure survey. *Int J Cardiol* 2010;138:63-9.
- Baldasseroni S, Orso R, Orso F, Bianchini BP, Carbonieri E, Cirò A, *et al.* Relation between serum sodium levels and prognosis in outpatients with chronic heart failure: Neutral effect of treatment with beta-blockers and angiotensin-converting enzyme inhibitors. Data from the Italian Network on Congestive Heart Failure (IN-CHF database). *J Cardiovasc Med (Hagerstown)* 2011;12:723-31.
- Sato N, Gheorghide M, Kajimoto K, Munakata R, Minami Y, Mizuno M, *et al.* Hyponatremia and in-hospital mortality in patients admitted for heart failure (from the ATTEND registry). *Am J Cardiol* 2013;111:1019-25.
- Rusinaru D, Tribouilloy C, Berry C, Richards AM, Whalley GA, Earle N, *et al.* Relationship of serum sodium concentration to mortality in a wide spectrum of heart failure patients with preserved and with reduced ejection fraction: An individual patient data meta-analysis(†): Meta-Analysis Global Group in Chronic heart failure (MAGGIC). *Eur J Heart Fail* 2012;14:1139-46.
- Levy WC, Mozaffarian D, Linker DT, Sutradhar SC, Anker SD, Cropp AB, *et al.* The Seattle Heart Failure Model: Prediction of survival in heart failure. *Circulation* 2006;113:1424-33.
- Deubner N, Berliner D, Frey A, Güder G, Brenner S, Fenske W, *et al.* Dysnatraemia in heart failure. *Eur J Heart Fail* 2012;14:1147-54.
- Romanovsky A, Bagshaw S, Rosner MH. Hyponatremia and congestive heart failure: A marker of increased mortality and a target for therapy. *Int J Nephrol* 2011;2011:732746.
- Balling L, Schou M, Videbaek L, Hildebrandt P, Wiggers H, Gustafsson F; Danish Heart Failure Clinics Network. Prevalence and prognostic significance of hyponatraemia in outpatients with chronic heart failure. *Eur J Heart Fail* 2011;13:968-73.
- Campo A, Mathai SC, Le Pavec J, Zaiman AL, Hummers LK, Boyce D, *et al.* Outcomes of hospitalisation for right heart failure in pulmonary arterial hypertension. *Eur Respir J* 2011;38:359-67.

How to cite this article: Ganiger H, Ravishankar AG. Dysnatraemia in Heart Failure: A Descriptive Study. *Int J Sci Stud* 2015;3(6):81-85.

Source of Support: Nil, **Conflict of Interest:** None declared.