Dysnatraemia in Heart Failure: A Descriptive Study

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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 hypernatremia was independently associated with higher urea levels, higher New York Heart Association
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(NYHA) class, lower systolic blood pressure (SBP), and lower ejection fraction. Emergency admissions were also correlated with hypernatremia. 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.

Hence this study was done to know the prevalence of dysnatremia in heart failure as studies on prevalence of hypernatremia 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 dysnatremia 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 hypernatremia 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 hypernatremia (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).
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 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
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. 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 hypernatremia 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 hypernatremia occurs irrespective of whether the systolic function normal or decreased, others factors might contribute to the pathogenesis of hypernatremia in patients with preserved LVEF.

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). 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 hypernatremia rest 18 had sodium in the normal range. PAH was present in 83.33% hypernatremia 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 hypernatremia 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 hypernatremia 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 criteria 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 hyponatremia 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


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