

Impact of Serum Sodium Levels at the time of Admission on Length of Hospital Stay and In-Hospital Mortality among Heart Failure Patients

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ABSTRACT

Objective: To determine the length of hospital stay and the in-hospital mortality amongst heart failure patients in relation to their serum sodium levels on admission.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Army Cardiac Center, Lahore Pakistan, from Jul to Dec 2019.

Methodology: One forty three patients admitted with acute heart failure were included. At the time of admission, serum sodium levels were recorded along with other clinical and demographic data. The information was analyzed using SPSS v23, and various statistical associations were drawn comparing variables amongst the two sample groups, hyponatremic and normonatremic patients. The length of hospital stay, in days, and in-hospital mortality were also determined.

Results: From a total of 143 patients, there were 95(66.4%) males and 48(33.6%) females, with a mean age of 64±11.6 years. The mean serum sodium level at admission was 134.5±5.9 mmol/L. Hyponatremia was recorded in 64(44.8%) patients. The in-hospital mortality for hyponatremic patients was 7.8%, which was higher as compared to normonatremic patients, 5.1% ($p=0.50$). The length of hospital stay was marginally longer for patients with lower sodium levels at 5.0±3.3 days as compared to normal sodium levels, at 4.8±3.7 days ($p=0.47$).

Conclusion: Hyponatremia at presentation is a remarkable finding amongst HF patients. While the results deemed statistically insignificant, hyponatremia was associated with both, a longer length of hospital stay as well as an increased in-hospital mortality.

Key words: Heart failure, Hyponatremia, In-hospital mortality.

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INTRODUCTION

Heart Failure (HF) is a global cause of morbidity and mortality, with an estimated prevalence of more than 37.7 million individuals worldwide.¹ As admission rates for HF continue to surge, there is an increasing burden on the healthcare system. A substantial percentage of these admissions culminate in in-hospital mortality. This renders it essential to identify precipitating factors that could increase mortality rates in these patients.

The presence of concurrent electrolyte disorders with HF are one of the precipitants leading to adverse events during hospital admissions. The most common electrolyte abnormalities present in HF patients are hyponatremia, hypokalemia/hyperkalemia, and hypomagnesemia.^{2,3} While disorders of potassium and magnesium have been frequently studied previously,³ hyponatremia needs further research as it is the most

prevalent abnormality seen in all hospitalized patients.⁴

Hyponatremia, defined as a serum sodium concentration of less than 135 mmol/L, is known to be a predictor of unfavorable outcomes in hospitalized patients with HF. A few previously done studies have recognized hyponatremia as an independent factor of increased short and long term mortality.⁵ In fact, it is present in about 20% patients admitted with acute heart failure and develops in another 15-25% during the treatment phase.⁶

The pathophysiology of hyponatremia in HF can be owing to both, the activation of several neuro-humoral mechanisms, and due to drugs used during treatment, such as diuretics. Chronic activation of the rennin-angiotensin-aldosterone system (RAAS) with simultaneous stimulation of the sympathetic nervous system, results in a counter-productive effect including cardiac remodeling and water and sodium retention.⁷ Additionally, excessive use of diuretic medications to treat fluid overload in HF can exacerbate the

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activation of the RAAS,⁸ resulting in a vicious cycle of serum over-dilution and hence, hyponatremia.

While there exists abundant data to prove this in the West, there is scarce data stating the effects of hyponatremia in HF patients from developing countries with limited resources. Therefore, the aim of this study was to inquire whether hyponatremia proves to be an independent factor of increased length of hospital stay (LOHS) as well as in-hospital mortality in our region.

METHODOLOGY

The prospective longitudinal study was conducted at the Army Cardiac Centre (ACC), Lahore, Pakistan from July to December, 2019. Following approval from the Ethical Review Committee (Reference Number 25/Estb/ACC), 143 patients were included using a non-probability, consecutive sampling technique after receiving their thorough consent for participation. Demographic data, serum electrolyte levels at admission (including serum sodium, potassium, magnesium and chloride), relevant past medical history, and data regarding co-morbid conditions (diabetes mellitus, hypertension, ischemic heart disease, and smoking) was recorded.

Inclusion Criteria: All patients ≥ 18 years with a diagnosis of acute HF by a cardiologist on admission, or those already on HF treatment (ACE-inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, digoxin, diuretics, inotropes) for more than 6 months now presenting with worsening of symptoms, were included.

Exclusion Criteria: Patients diagnosed with any malignancy, currently carrying a pregnancy, having clinical signs of systemic infections or those on hemodialysis were excluded due to their multifactorial pathologies. In addition, patients with incomplete labs at admission and those with extreme variations in other measured electrolytes levels, e.g., serum potassium values of < 3.5 or > 5.5 mmol/L were also excluded from the study, as these electrolyte imbalances can also act as individual factors contributing to adverse events during hospitalization.

Each patient fulfilling the criteria was assigned to one of the following two groups: hyponatremia if sodium < 135 mmol/L, and normonatremia if sodium ≥ 135 mmol/L (but less than 150 mmol/L). All laboratory investigations were carried out under supervision of a pathologist using the same equipment. 3 mL of venous blood was collected from a peripheral

site for each patient into an evacuated tube without any anticoagulant. The blood samples were analyzed within 30 minutes of collection by the automatic electrolyte analyzer JOKOH Ex-D (Japan).

All data was then entered and analyzed using SPSS v 23. Continuous data was presented as Mean \pm SD. Nominal data, with categorical variables was presented as percentages and the Chi square test was used to compare variables amongst the two groups. Student's *t*-test was used to compare means of the groups. The *p* value of ≤ 0.05 denoted a statistically significant relationship.

Length of hospital stay (LOHS) was calculated for each patient (in days) from date of admission to the date of either of three outcomes, namely: discharge from the hospital or death/in-hospital mortality or the patient left against medical advice (LAMA). In-hospital mortality was defined as death occurring from any cause prior to discharge from the hospital.

RESULTS

Amongst a total of 143 patients who were part of the study, there were 95(66.4%) males and 4 (33.6%) females, between the ages of 34-95 years, with a mean age of 64 ± 11.7 years. From these 64 patients were reported hyponatremics on admission, including 41(64.1%) males and 23(35.9%) females ($p=0.59$). Therefore, there was no statistically significant relationship between hyponatremia and gender.

All patients had their sodium values recorded at admission whose results ranged from 117-148 mmol/L Figure-1.

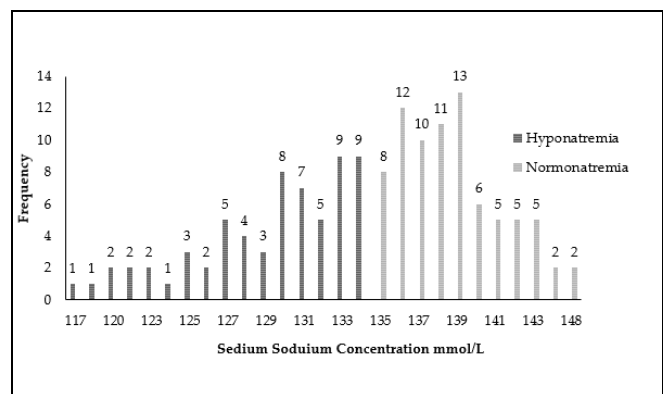


Figure-1: Serum Sodium Levels at Admission (n=143)

With a mean serum sodium value of 134.5 ± 5.9 mmol/L. From the total sample population, 64(44.8%) HF patients comprising of 41 males and 23 females Table-I

Table-I: Co-morbidities in Hyponatremic and Normonatremic patients with Heart Failure (n=143)

Co-morbidities	Hyponatremia (n = 64)	Normonatremia (n = 79)	p-value
Diabetes Mellitus	42	39	.051
Hypertension	36	47	.69
Ischemic Heart Disease	47	57	.86
Smoking	10	15	.60

Had hyponatremia at presentation. 3 patients suffered from severe Hyponatremia i.e., serum sodium ≤ 120 mmol/L. There was no statistical significance between the co-morbidities amongst the two groups, as shown in Table-II.

Table-II. In-Hospital Mortality and Length of Hospital Stay (LOHS) in Heart Failure Patients (n=143)

Outcome	Normonatremia (n = 79)	Hyponatremia (n = 64)	p-value
Deaths	4	5	0.50
In-Hospital Mortality	5.1%	7.8 %	0.50
Mean Length of Hospital Stay (LOHS) (days)	4.8 \pm 3.7	5.0 \pm 3.3	0.47

*LAMA=left against medical advice

The fate of each patient after admission was stratified into three possible outcomes, as shown in Figure-2. It was observed that 75(94.9%) normonatremic HF patients were discharged by doctors. On the other hand, the number of discharged patients who had hyponatremia at presentation was 56 (87.5%), in addition to which, 3(4.7%) patients left against medical advice and follow up was not possible. The percentage in-hospital mortality for hyponatremic patients was 7.8%, which was higher compared to normonatremic patients who had an in-hospital mortality of 5.1% ($p=0.50$).

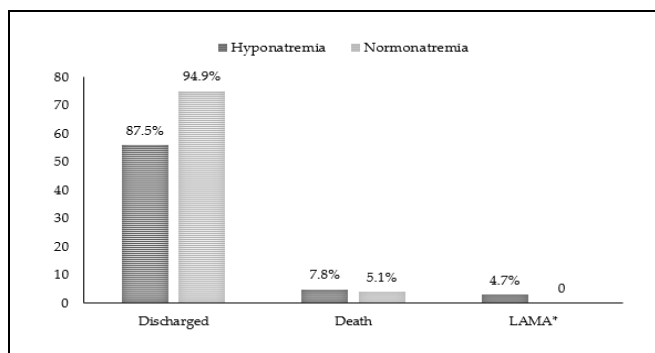


Figure-II: In-patient outcomes in Hyponatremic and Normonatremic patients

The LOHS was slightly longer for patients with lower sodium levels at 5.0 ± 3.3 days ($p=0.47$) as compared to normal sodium levels, at 4.8 ± 3.7 days. Nonetheless, this was a statistically insignificant finding.

DISCUSSION

Hyponatremia is the commonest electrolyte abnormality seen in hospitalized patients, and has been repeatedly reported amongst HF patients.⁹⁻¹¹ Some of the factors which lead to hyponatremia being prevalent in HF patients include co-existing chronic kidney disease, and use of treatment modalities like a chronic salt-restricted diet, and diuretics (furosemide and spironolactone), together with the use of ACE Inhibitors.^{10,12} This was proven in our study, which revealed that the mean sodium level at presentation in HF patients was 134.48 mmol/L, which falls in the hyponatremic range. A similar study design conducted by Ali *et al.* reported to have a mean serum sodium level of 136.9 mmol/L, which differed from our mean as it falls into the normonatremic range.¹⁰

In terms of prevalence, 44.8% patients in our study admitted for HF presented with hyponatremia. This percentage was higher as compared to another regional study by Farooq *et al.* where 35.3% of the admitted cohort had hyponatremia.¹⁰ It was also higher in comparison to some international studies like the OPTIMIZE-HF registry (United States) which reported 19.7%, and Acute Decompensated Heart Failure Syndromes (ATTEND) registry (Japan) which reported 11.6% hyponatremics.^{7,14} While these global studies depicted hyponatremia at admission obtained from hospital records, a study by Louise *et al.* showed 17% referred to outpatient heart failure clinics were hyponatremic, from which 51% concluded in either a hospital admission or death.¹⁵

The sinister nature of this electrolyte abnormality has been associated with worse hospital outcomes, including a longer LOHS and increased in-hospital mortality, both short and long term.^{9,10} The in-hospital mortality of hyponatremic patients in our study was 7.8% which was higher in comparison to normonatremic patients, 5.1% however, the results were statistically insignificant. Nonetheless, the results were in synchrony with a local study by Farooq *et al.* who also had similar findings that were also statistically insignificant.¹⁶

Moreover, another adverse outcome documented in hyponatremic patients is an increased LOHS.¹⁷ The exact mechanism as to why hyponatremia results in a

poorer prognosis in HF patients and increased LOHS remains unclear and no single definitive explanation has been put forth. However, one study suggests that pathophysiological profiles of HF patients with hyponatremia can differ from those with normal serum sodium levels due to a more severe activation of the rennin-angiotensin-aldosterone, or the sympathetic nervous system, or vasopressin release.¹⁸

LIMITATION OF STUDY

The study was conducted in a single tertiary care urban hospital so it may not portray a true representation of all HF patients hospitalized in Pakistan. To counter this, more studies need to be conducted involving various hospitals at all levels of healthcare dealing with HF patients. Furthermore, only serum sodium levels at admission were taken into account so the effects of persistent or resolved hyponatremia could not be determined. Lastly, a larger sample size would have produced more reliable and generalizable results.

CONCLUSION

Hyponatremia at presentation is a common finding amongst HF patients. While the results deemed statistically insignificant, hyponatremia was associated with both, a longer length of hospital stay as well as an increased in-hospital mortality rate.

Conflict of Interest: None.

Author's Contribution

Following authors have made substantial contributions to the manuscript as under:

MA & MC: Conception, study design, drafting the manuscript, approval of the final version to be published.

NI & WS: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

OG & AM: Critical review, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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