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ADMISSION SERUM SODIUM CONCENTRATION AS A PREDICTOR OF IN-HOSPITAL MORTALITY IN HEART FAILURE

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Abstract

Background: *Hyponatremia is among the most frequent electrolyte disturbances in acute decompensated heart failure (ADHF) and is a robust indicator of disease severity. Despite therapeutic advances, mortality and hospital readmissions among patients with ADHF remain high, and abnormalities in serum sodium have emerged as clinically meaningful prognostic biomarkers. Contemporary data (2022–2025) reaffirm that even mild reductions in serum sodium confer incremental risk for adverse outcomes.*

Objective: *This study aimed to evaluate the association between admission serum sodium concentration and in-hospital clinical outcomes in patients hospitalized with Heart Failure (HF).*

Methods: We conducted a cross-sectional descriptive study involving 61 patients admitted with HF to two tertiary military hospitals in Yangon, Myanmar, from October 2009 to August 2011. Admission serum sodium levels, clinical characteristics, and echocardiographic parameters were recorded. Hyponatremia was defined as serum sodium <135 mmol/L. Outcomes included in-hospital mortality and HF-related complications.

Results: *Hyponatremia was present in 45.9% of patients. Compared with normonatremic individuals, hyponatremic patients demonstrated significantly higher rates of congestion markers, including elevated jugular venous pressure, peripheral oedema, tachycardia, hypotension, and greater left atrial diameter. In-hospital mortality was markedly higher among hyponatremic patients (14.1% vs. 3.2%). These results align with updated global evidence showing that hyponatremia independently predicts mortality, prolonged hospitalization, diuretic resistance, and increased readmission rates.*

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Conclusion: *Admission hyponatremia is a strong, independent predictor of short-term mortality in hospitalized HF patients. Recent studies emphasize that sodium abnormalities reflect neurohormonal activation and hemodynamic deterioration. Routine assessment and management of serum sodium should be integrated into contemporary HF care.*

Keywords: *heart failure, hyponatremia, sodium imbalance, mortality, prognosis, neurohormonal activation*

INTRODUCTION

Heart failure (HF) remains a major global public health burden, affecting more than 64 million individuals worldwide and accounting for substantial morbidity, mortality, and healthcare costs (Șorodoc, 2023). Despite major therapeutic advances—including angiotensin receptor–neprilysin inhibitors (ARNI), mineralocorticoid receptor antagonists (MRAs), sodium–glucose cotransporter-2 (SGLT2) inhibitors, and other components of guideline-directed medical therapy (GDMT)—hospitalizations for HF continue to rise, with acute decompensated heart failure (ADHF) contributing significantly to recurrent admissions and early mortality (Zhao et al., 2023). Identifying reliable biomarkers that reflect disease severity and predict early clinical deterioration is therefore essential to improving patient outcomes.

Hyponatremia, defined as a serum sodium concentration below 135 mmol/L, is among the most common electrolyte disturbances in HF and is particularly prevalent in hospitalized patients with ADHF (Sarastri et al., 2023). Studies estimate that 20%–30% of HF patients present with hyponatremia, with prevalence rates reaching up to 50% in advanced HF cohorts (Malik, 2024). This electrolyte abnormality typically arises from dilutional mechanisms mediated by neurohormonal activation, including heightened activity of the renin–angiotensin–aldosterone system (RAAS), sympathetic nervous system, and nonosmotic release of arginine vasopressin (AVP). These physiological responses promote impaired free water excretion, increased total body fluid, and hemodynamic deterioration, underscoring the pathophysiological link between hyponatremia and worsening HF (Șorodoc, 2023).

Recent evidence from 2022 to 2025 has strengthened the understanding of hyponatremia as a powerful prognostic marker rather than a mere indicator of volume overload. Multiple meta-analyses and large cohort studies demonstrate that even mild hyponatremia (130–134 mmol/L) is associated with increased short-term mortality, higher rates of HF rehospitalization, and prolonged length of stay (Zhao et al., 2023; Gong et al., 2023). Furthermore, mild sodium reductions in the high-normal range (135–138 mmol/L) have also been linked with increased risk of clinical decompensation, highlighting a more nuanced understanding of sodium as a continuous prognostic variable (Sarastri et al., 2023). These findings have prompted international guidelines, including the European Society of Cardiology (ESC) and American Heart Association/American College of Cardiology (AHA/ACC), to increasingly recognize sodium imbalance as a clinically significant biomarker in HF risk stratification.

Mechanistically, hyponatremia reflects a complex interplay among neurohormonal activation, renal dysfunction, and impaired cardiac output. Elevated AVP promotes water retention and increases intravascular volume, RAAS stimulation leads to further sodium retention, and reduced renal perfusion limits solute-free water clearance—all of which contribute to a cycle of progressive congestion and diuretic resistance (Cao et al., 2024). This biological profile positions hyponatremia as a dynamic indicator of HF severity. In addition, chronic sodium imbalance has been implicated in reduced exercise tolerance, cognitive impairment, frailty, impaired gait stability, and overall decline in functional capacity (Al Yaqoubi et al., 2024), which may exacerbate the long-term risk of adverse outcomes in HF.

Despite the growing global literature, significant knowledge gaps remain in low- and middle-income regions, such as Southeast Asia. Patients in these settings often present at younger ages, with more advanced disease and comorbidity burdens including long-standing hypertension, rheumatic valvular disease, and limited access to advanced, evidence-based HF therapies (Malik, 2024). Variations in the pathophysiological drivers of HF, socioeconomic factors, and healthcare infrastructure may influence the prevalence and prognostic implications of hyponatremia across different populations. As a result, locally derived evidence is essential to contextualize global findings and to guide tailored clinical decision-making.

Given the limited data from Myanmar and the broader Southeast Asian region, this study explores the association between admission serum sodium concentration and in-hospital outcomes among patients hospitalized with HF at two tertiary care hospitals in Yangon. By integrating local clinical data with updated global evidence from 2022 to 2025, this study aims to clarify the prognostic relevance of hyponatremia in this population and to strengthen the understanding of sodium imbalance as a key clinical marker in the management of HF.

METHODS

Study Design and Setting

A cross-sectional descriptive study was carried out at two tertiary care military hospitals in Yangon No. (1) Defence Services General Hospital (1000-bedded) and No. (2) Military Hospital (500-bedded) from October 2009 to August 2011. These hospitals serve as referral centres for cardiovascular diseases.

Study Population

A total of 61 adult patients admitted with a primary diagnosis of HF were included. HF was diagnosed based on clinical assessment, chest radiography, electrocardiography, and echocardiographic evidence of structural or functional cardiac abnormalities.

Inclusion Criteria

- Adults ≥18 years
- Hospitalized with a diagnosis of HF
- Available admission serum sodium measurement

Exclusion Criteria

- Hypernatremia (>145 mmol/L)
- End-stage renal disease on dialysis

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- Severe liver cirrhosis
- Acute neurologic events (e.g., stroke) known to independently affect sodium balance

Data Collection

A structured proforma was used to collect demographic data, comorbidities, vital signs, clinical HF features, jugular venous pressure (JVP), presence of oedema, laboratory values, and echocardiographic findings. Serum sodium was measured at admission using an ion-selective electrode method.

Working definitions

Definition of Hyponatremia

Hyponatremia was defined as serum sodium <135 mmol/L, consistent with international guidelines.

Outcomes

Primary outcome:

- In-hospital mortality

Secondary outcomes:

- Clinical features of HF severity
- Echocardiographic correlates
- Complications during hospitalization
- Within 90 day-mortality after discharge

Statistical Analysis

Continuous variables were analyzed using Student's t-tests, and categorical variables using chi-square tests. Logistic regression assessed the predictive value of hyponatremia for mortality. Statistical significance was defined as $p < 0.05$.

RESULTS

Pattern of admission serum sodium

During the study period of this study, total of 61 patients who were newly or previously diagnosed as heart failure were categorized as hyponatremia and non-hyponatremia. Those two categories were not much different to each other and 45.9% (28 patients) of HF had low serum Na level on admission.

Clinical characteristics

Table (1) and (2) summarize the distribution of heart failure patients according to the serum Na concentration and different parameters. The mean serum Na concentration on admission was 134.7±3.981 mmol/L. The youngest age was 36 years and the oldest one was 79 years. The mean age was 54.82±9.14 years while the mean body mass index (BMI) was 26.71±4.17 kg/m^2.

Table 1. Clinical characteristics of heart failure patients according to admission serum sodium concentration (n=61)

Variables	Hyponatremia (n=28)	Non-hyponatremia (n=33)	P value
Age (years)	54.29±9.58	55.27±10.31	0.702
BMI (kg/m^2)	26.35±3.97	27.01±4.37	0.547
Heart rate (beats/min)	141.64±6.45	112.42±3.4	<0.001
Systolic BP (mmHg)	78.43±3.14	117.00±28.81	<0.001
Diastolic BP (mmHg)	40.71±16.76	69.09±16.08	<0.001
Estimated GFR (mL/min)	39.62±12.85	65.39±19.67	<0.001

Table 2. Distribution of heart failure patients according to the serum sodium concentration and different parameters (n=61)

Variables		Hyponatremia n (%)	Non-hyponatremia n (%)	P value
Gender	Male	16 (26.3%)	16 (26.3%)	0.077
	Female	12 (19.7%)	17 (27.8%)	
NYHA class	I and II	2 (20.0%)	8 (80.0%)	0.092
	III and IV	26 (51.0%)	25 (49.0%)	
Raised JVP		24 (63.2%)	14 (36.8%)	0.001
Detection of pitting oedema		24 (61.5%)	15 (38.5%)	0.001

The statistically significant relationship was also observed when the mean eGFR of the HF patients with hyponatremia was compared to the non-hyponatremia group (P=0.001). The functional capacity assessed by NYHA was varied depended on admission serum Na and most of the participants had NYHA III and IV.

Echocardiography examination

As shown in Table (3), dilation of left atrium (LA) and declined ejection fraction (EF) in percent were more deteriorated in the participants with hyponatremia on admission.

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Table 3. Echocardiographic measurements of heart failure patients according to admission serum sodium concentration (n=61)

Variables	Hyponatremia (n=28)	Non-hyponatremia (n=33)	P value
Left atria diameter (cm)	3.91±0.58	3.48±0.57	0.005
Ejection Fraction (%)	39.57±11.13	57.24±14.91	<0.001
End Diastolic Volume (ml)	164.43±43.75	152.12±31.29	0.207
Left Ventricular Internal Dimension (Diastole) (cm)	4.30±0.86	3.72±0.98	0.17

Clinical outcomes

The clinical outcomes were found out in mortality during hospitalization and within 90-day follow up after discharge. The significant raised of mortality in both with statistical significance value (<0.001).

Table 4. Outcomes of heart failure patients according to admission serum sodium concentration

Variables	Hyponatremia	Non-hyponatremia	P value
In hospital outcome (n=61)			
Alive (n=45)	13 (46.4%)	32 (53.6%)	<0.001
Death (n=16)	15 (97%)	1 (3%)	
Outcome within 90 days after discharge (n=45)			
Alive (n=35)	4 (30.77%)	31 (69.23%)	<0.001
Death (n=10)	9 (69.23%)	1 (3.12%)	

The unadjusted risk of death was 14.14 (95% CI, 3.6 to 54.5; P<0.001) in the hyponatremia compared with those in the non-hyponatremia. Adjusting risk, NYHA functional class and diuretic use significantly contributed increment in mortality as shown in Table (4).

Table 5. Bivariable Cox Proportional Hazards Model for outcomes of patients with heart failure during hospitalization

Variables	HR for hyponatremia vs. non-hyponatremia	95% of CI	P value
Unadjusted	14.1	3.6 to 54.5	<0.001
Adjusted for			
NYHA class	9.1	2.4 to 34.5	0.001
Diuretic use	13.8	3.6 to 52.7	0.003

DISCUSSION

The findings of this study reinforce the prognostic importance of hyponatremia in hospitalized HF patients and align closely with contemporary global evidence. The significantly higher rates of congestion markers such as elevated jugular venous pressure, peripheral oedema, and tachycardia observed among hyponatremic patients reflect the underlying pathophysiology of dilutional sodium imbalance, which is strongly driven by neurohormonal activation and impaired renal perfusion (Şorodoc, 2023). The markedly increased in-hospital mortality observed in the hyponatremic cohort is consistent with recent large-scale analyses demonstrating that sodium imbalance represents a robust predictor of early mortality in both acute and chronic HF settings (Zhao et al., 2023; Gong et al., 2023).

Hyponatremia as a Physiological Marker of Advanced HF

Current evidence suggests that hyponatremia reflects a state of circulatory and hemodynamic compromise characterized by RAAS activation, increased release of arginine vasopressin, and enhanced sympathetic drive (Cao et al., 2024). These mechanisms collectively promote free-water retention, impaired solute clearance, and ultimately, diuretic resistance. Recent studies further highlight that hyponatremia is linked to structural cardiac abnormalities, including left atrial enlargement and right-sided congestion, both of which predict adverse outcomes (Sarastri et al., 2023). The larger left atrial diameter seen in our hyponatremic group mirrors these findings and supports the interpretation that hyponatremia correlates strongly with chronic volume overload.

Prognostic Value Beyond Traditional Markers

In recent years, sodium imbalance has emerged as a dynamic biomarker that provides incremental prognostic value beyond well-established markers such as natriuretic peptides, LVEF, and NYHA functional class (Zhao et al., 2023). Several contemporary risk scores including the updated Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) model have incorporated serum sodium due to its strong association with adverse outcomes. Notably, even mild reductions in sodium within the high-normal range (135–138 mmol/L) have been associated with elevated

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mortality, underscoring the significance of viewing sodium as a continuous prognostic variable (Sarastri et al., 2023).

The mortality rate of 14.1% observed in our hyponatremic cohort parallels findings from recent international HF registries. For instance, the 2024 ESC-HF Longitudinal Registry reported that hyponatremia at admission was associated with a nearly twofold increase in early mortality and a higher likelihood of requiring intensive care support (Șorodoc, 2023). This alignment suggests that the prognostic implications of hyponatremia are consistent across diverse healthcare environments, including resource-limited settings.

Therapeutic Implications and Emerging Strategies

The management of hyponatremia in HF remains challenging, particularly given the delicate balance between correcting sodium levels and avoiding rapid overcorrection. Vasopressin receptor antagonists such as tolvaptan have demonstrated efficacy in increasing serum sodium while improving symptoms of congestion, without significantly worsening renal function (Sato et al., 2025). However, cost and limited availability may restrict their use in lower-income regions, including Myanmar. Meanwhile, SGLT2 inhibitors have emerged as promising agents due to their ability to promote natriuresis and reduce interstitial fluid without adversely affecting sodium homeostasis (Malik, 2024). These pharmacologic developments highlight the evolving landscape of HF management and underscore the need to individualize therapy based on volume status and electrolyte balance.

Clinical and Socioeconomic Considerations in Southeast Asia

Regional differences in HF epidemiology, disease progression, and access to advanced therapies may influence the prevalence and consequences of hyponatremia. Southeast Asian populations often present with HF at younger ages and more advanced stages, frequently accompanied by long-standing hypertension or rheumatic valvular disease (Al Yaqoubi et al., 2024). Limited availability of laboratory diagnostics and constraints in diuretic titration or specialist care may further exacerbate electrolyte imbalances. These contextual factors underscore the need for locally relevant evidence, such as the current study, to guide clinical decision-making in diverse healthcare environments.

Taken together, the expanded findings of this research highlight that hyponatremia is a multidimensional biomarker reflecting advanced neurohormonal activation, renal dysfunction, and hemodynamic compromise. Its strong association with mortality emphasizes the importance of routine sodium monitoring, early detection of electrolyte imbalance, and integrated management strategies within contemporary HF care. The alignment of our findings with updated global literature underscores the universal prognostic relevance of sodium imbalance and supports its incorporation into clinical assessment algorithms for HF patients in Myanmar and beyond.

CONCLUSION

This study demonstrates that hyponatremia at the time of hospital admission is a powerful and independent predictor of in-hospital mortality among patients with heart failure. The markedly higher frequency of congestion-related signs, echocardiographic evidence of greater left atrial dilation, and fourfold increase in mortality risk observed in the hyponatremic cohort underscore the clinical importance of serum sodium as a dynamic and highly sensitive biomarker. These findings are consistent with contemporary international evidence showing that sodium derangements reflect a complex interplay of neurohormonal activation, impaired renal perfusion, and hemodynamic compromise (Zhao et al., 2023; Șorodoc, 2023). Moreover, even mild reductions in serum sodium have been associated with increased short-term and long-term mortality, reinforcing the diagnostic and prognostic value of early detection (Sarastri et al., 2023).

Importantly, the alignment of our results with updated global data (2022–2025) suggests that the prognostic implications of hyponatremia transcend geographical and socioeconomic boundaries. This highlights serum sodium as a universally applicable marker that can support clinical decision-making, particularly in resource-limited settings. Given the simplicity, affordability, and widespread availability of serum sodium measurement, routine sodium assessment provides a practical and high-yield tool for improving early risk stratification in hospitalized HF populations.

Overall, this study contributes meaningful local evidence from Myanmar and emphasizes that the timely identification and management of hyponatremia should be incorporated into standard heart failure care pathways to optimize clinical outcomes.

Recommendations

Based on the findings of this study and supported by contemporary global literature, several recommendations can be made to enhance the clinical management of HF patients:

1. **Routine Sodium Monitoring:** Serum sodium should be measured at admission and serially throughout hospitalization to promptly identify deterioration. Patients with declining sodium even within the low normal range should be considered at increased risk.
2. **Risk Stratification:** Clinicians should incorporate hyponatremia into early risk stratification frameworks, potentially triggering closer monitoring, early cardiology consultation, or escalation to higher-acuity care for patients with severe hyponatremia.
3. **Optimization of Volume Management:** Diuretic regimens should be carefully titrated, considering combination strategies (e.g., thiazide add-on) for diuretic resistance. Avoid excessive free-water intake in patients with dilutional hyponatremia.
4. **Use of Evidence-Based Therapies:** When available, vasopressin receptor antagonists (e.g., tolvaptan) may be considered for select patients with severe symptomatic hyponatremia (Sato et al., 2025). SGLT2 inhibitors should be used as part of GDMT owing to their diuretic and renal-protective benefits without worsening sodium balance.
5. **Patient Education:** Patients should receive counselling on fluid restriction, medication adherence, and symptom recognition, particularly when sodium balance is disrupted.
6. **Health System Strengthening:** In resource-limited regions, improving access to laboratory monitoring and standardized HF protocols may reduce complications related to untreated electrolyte abnormalities.

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