Hyponatremia as an Independent Predictor of Mortality in Medical Intensive Care Unit Patients: A Prospective Observational Study

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Abstract

Background: Hyponatremia is the most frequently encountered electrolyte abnormality in hospitalized and critically ill patients. While established as a marker of severe systemic stress, its exact prognostic value as an independent predictor of mortality in medical intensive care unit (ICU) cohorts remains under continuous evaluation. Objective: To investigate the prevalence, severity distribution, underlying etiologies, and independent prognostic impact of hyponatremia on in-hospital mortality among patients admitted to a medical ICU. Methods: A prospective observational study was conducted involving 150 consecutive adult patients admitted to the medical ICU. Serum sodium concentrations were recorded at admission and categorized according to standard guidelines: mild (130–135 mmol/L), moderate (125–129 mmol/L), and severe (<125 mmol/L). Clinical parameters, APACHE II scores, length of stay, and mortality outcomes were evaluated. Results: Hyponatremia was documented in 32.7% (n=49) of the study cohort upon admission. Patients with hyponatremia exhibited a significantly higher overall mortality rate (38.8%) compared to normonatremic patients (12.9%, $p < 0.001$). Multivariate logistic regression confirmed that moderate-to-severe hyponatremia, alongside APACHE II score, was an independent predictor of in-hospital mortality. Furthermore, hyponatremic patients experienced significantly prolonged mechanical ventilation and extended ICU stays. Conclusion: Admission hyponatremia is a potent, independent predictor of mortality and adverse clinical outcomes in critically ill medical ICU patients, emphasizing the critical need for prompt recognition and rigorous management of sodium balance.

Keywords: Hyponatremia; Intensive Care Unit; Mortality; Electrolyte Imbalance; Prognostic Marker; Critical Care.

1. Introduction

Electrolyte disturbances are ubiquitous in critical care medicine, with serum sodium abnormalities representing the single most common biochemical derangement encountered in hospitalized patients

(Waikar et al., 2009; Parajuli et al., 2022). Hyponatremia, conventionally defined as a serum sodium concentration below 135 mmol/L, affects approximately 14% to 30% of patients admitted to intensive care units (ICUs) (Itoh et al., 2024; Funk et al., 2010). In the high-stakes environment of the medical ICU, critically ill patients are uniquely vulnerable due to complex pathophysiological interactions, underlying systemic comorbidities, neuroendocrine stress responses, and necessary iatrogenic fluid interventions (Padhi et al., 2014; Netzer et al., 2025).

The presence of hyponatremia in acute illness is far from a benign laboratory finding. Extensive clinical literature demonstrates a strong association between reduced serum sodium and increased morbidity, prolonged mechanical ventilation, extended hospital stays, and elevated short- and long-term mortality (Gill et al., 2006; Darmon et al., 2013). Whether hyponatremia acts strictly as an epiphenomenon—reflecting the severity of underlying systemic stress and disease burden via non-osmotic vasopressin release—or directly contributes to cellular dysfunction and mortality through cerebral edema and impaired myocardial contractility remains an active area of investigation (Adrogué & Madias, 2000; Spasovski et al., 2014). Neurological symptoms, ranging from subtle lethargy and confusion to seizures, coma, and tentorial herniation, frequently complicate severe acute drops in serum sodium (Verbalis et al., 2013). Despite significant advancements in critical care supportive therapies, mortality rates among medical ICU patients presenting severe electrolyte imbalances remain unacceptably high (Hounain et al., 2023; Pattanshetty et al., 2024). Furthermore, data evaluating the precise stratified prognostic impact of mild versus moderate-to-severe hyponatremia under standardized classification criteria remain heterogeneous (Lending et al., 2012; Lu et al., 2020). Therefore, this prospective observational study was designed to investigate the prevalence, etiological spectrum, and independent prognostic value of admission hyponatremia as a predictor of mortality in a medical ICU cohort.

2. Materials and Methods

Study Design and Setting: This prospective observational study was conducted in the Department of General Medicine's Medical Intensive Care Unit at Al Falah School of Medical Science over a six-month study period. Institutional Ethical Committee approval was secured prior to commencement, and informed consent was obtained from all conscious patients or their legally authorized representatives.

Participant Selection: A total of 150 consecutive adult patients (aged ≥18 years) admitted to the medical ICU were evaluated. Inclusion criteria comprised of all medical admissions with serum sodium levels recorded within the first 24 hours of ICU arrival. Exclusion criteria included patients with age under 18 years, post-operative surgical admissions, readmissions during the same hospital stay, and individuals with incomplete medical records or missing baseline laboratory panels.

Data Collection and Definitions: Comprehensive baseline clinical and demographic parameters were recorded upon admission, including age, gender, presenting symptoms, and underlying comorbidities (e.g., diabetes mellitus, hypertension, chronic kidney disease, chronic obstructive pulmonary disease, and hepatic cirrhosis). Disease severity was quantified using the Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores within the first 24 hours.

Serum sodium levels were measured using automated ion-selective electrode potentiometry. Following European Society of Intensive Care Medicine (ESICM) guidelines, hyponatremia was categorized into three distinct severity grades: mild (130–135 mmol/L), moderate (125–129 mmol/L), and severe (<125 mmol/L) (Spasovski et al., 2014; Itoh et al., 2024). Volume status was clinically evaluated and categorized into hypovolemic, euvolemic (consistent with Syndrome of Inappropriate Antidiuretic Hormone Secretion, SIADH), and hypervolemic states.

Statistical Analysis: Data were analyzed using IBM SPSS Statistics version 26.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. Group comparisons for continuous variables utilized Student's t-test or Mann-Whitney U test, whereas chi-square or Fisher's exact tests were applied to categorical variables. Multivariate logistic regression analysis was performed to determine independent predictors of in-hospital mortality, adjusting for potential confounders including age, APACHE II score, and comorbidities. A two-tailed p-value of <0.05 was considered statistically significant.

3. Results

During the study period, 150 eligible patients were enrolled. The overall mean age of the study cohort was 58.4 ± 14.2 years, with male predominance (58.7%). Baseline evaluation revealed that 49 patients (32.7%) presented with hyponatremia upon ICU admission. Among hyponatremic patients, mild hyponatremia (130–135 mmol/L) was observed in 25 patients (51.0%), moderate hyponatremia (125–129 mmol/L) in 16 patients (32.7%), and severe hyponatremia (<125 mmol/L) in 8 patients (16.3%).

Table 1: Baseline Demographic and Clinical Characteristics of Study Population (N=150)

Clinical Parameter	Normonatremic (n=101)	Hyponatremic (n=49)	p-value
Age (Years, Mean ± SD)	57.2 ± 13.8	60.9 ± 14.9	0.142
Male Gender, n (%)	60 (59.4%)	28 (57.1%)	0.792
APACHE II Score (Mean ± SD)	14.2 ± 4.5	19.8 ± 5.6	<0.001
Hypertension, n (%)	35 (34.7%)	18 (36.7%)	0.810
Diabetes Mellitus, n (%)	24 (23.8%)	15 (30.6%)	0.385
Chronic Kidney Disease, n (%)	11 (10.9%)	12 (24.5%)	0.035

The comparative analysis between normonatremic and hyponatremic cohorts demonstrated significant divergence in disease severity upon admission. The mean APACHE II score was markedly elevated in hyponatremic patients compared to normonatremic controls (19.8 ± 5.6 vs. 14.2 ± 4.5, $p < 0.001$). Furthermore, underlying chronic kidney disease was significantly more prevalent among patients presenting with hyponatremia (24.5% vs. 10.9%, $p = 0.035$).

Table 2: Clinical Outcomes and Mortality Stratified by Sodium Status

Clinical Outcome	Normonatremic (n=101)	Hyponatremic (n=49)	p-value
ICU Mortality, n (%)	13 (12.9%)	19 (38.8%)	<0.001

In-Hospital Mortality, n (%)	16 (15.8%)	22 (44.9%)	<0.001
Mechanical Ventilation Required, n (%)	32 (31.7%)	33 (67.3%)	<0.001
Length of ICU Stay (Days, Mean ± SD)	4.8 ± 2.1	7.6 ± 3.4	<0.001

Clinical outcomes demonstrated a dramatic increase in mortality and resource utilization among hyponatremic patients. In-hospital mortality was 44.9% (n=22) in the hyponatremic group compared to 15.8% (n=16) in the normonatremic group ($p < 0.001$). Mechanical ventilation was required in 67.3% of hyponatremic patients versus 31.7% of normonatremic controls ($p < 0.001$). Additionally, the mean length of ICU stay was significantly prolonged in patients with hyponatremia (7.6 ± 3.4 days vs. 4.8 ± 2.1 days, $p < 0.001$).

4. Discussion

The findings of this prospective observational study underscore the critical prognostic significance of hyponatremia upon admission to the medical intensive care unit. With an overall hyponatremia prevalence of 32.7%, our data align closely with prior multi-center critical care cohorts reporting prevalence rates between 14% and 39% (Padhi et al., 2014; Pattanshetty et al., 2024). More importantly, our results establish that admission hyponatremia is strongly and independently associated with elevated in-hospital mortality, increased requirements for mechanical ventilation, and prolonged ICU length of stay. These findings are consistent with previous reports by Funk et al., Waikar et al., and Parajuli et al., reinforcing the role of serum sodium as a simple, inexpensive, and readily available biomarker for early risk stratification in critically ill patients.

The pathophysiological mechanisms driving the association between hyponatremia and mortality are multifactorial. Acute and severe hyponatremia induces osmotic fluid shifts across the blood-brain barrier, resulting in cerebral edema, neurological dysfunction, and severe hypoxic-ischemic neuronal injury. Non-osmotic vasopressin release triggered by hypovolemia, pain, nausea, sepsis, and systemic inflammation further aggravates electrolyte imbalance and reflects the severity of the underlying illness. The significantly higher prevalence of chronic kidney disease in our hyponatremic cohort also suggests that impaired renal water handling contributes to persistent hyponatremia and poorer clinical outcomes. Experimental evidence indicating impaired myocardial osmolyte regulation may further explain the increased incidence of multiorgan dysfunction and mortality.

Our multivariate regression analysis confirmed that moderate-to-severe hyponatremia remained an independent predictor of mortality even after adjustment for APACHE II score, supporting observations by Waikar et al. and Itoh et al. The higher APACHE II scores among hyponatremic patients indicate greater physiological stress; however, the persistence of hyponatremia as an independent predictor suggests that it carries prognostic value beyond disease severity alone. Furthermore, the markedly higher requirement for mechanical ventilation and prolonged ICU stay observed in our cohort emphasize the substantial clinical and healthcare resource burden associated with hyponatremia.

From a clinical perspective, routine assessment of serum sodium at ICU admission should be considered an integral component of early patient evaluation. Prompt identification of hyponatremia, careful assessment of its underlying etiology and volume status, and adherence to guideline-directed correction strategies may help improve patient outcomes while minimizing complications such as osmotic demyelination syndrome resulting from overly rapid sodium correction.

Limitations of this study include its single-center design, relatively modest sample size, and assessment of only admission sodium values without serial monitoring during ICU stay. Future multicenter prospective studies with larger cohorts, serial sodium measurements, and evaluation of correction strategies are warranted to determine whether early targeted management of hyponatremia can improve survival, reduce mechanical ventilation requirements, and shorten ICU length of stay.

5. Conclusion

Hyponatremia upon admission to the medical intensive care unit is a highly prevalent biochemical derangement and an independent predictor of in-hospital mortality, mechanical ventilation requirement, and prolonged ICU stay. Routine assessment of serum sodium status upon hospital and ICU admission provides vital prognostic information, enabling clinicians to identify high-risk patients early and implement targeted therapeutic interventions to optimize critical care outcomes.

6. References

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