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FREQUENCY OF HYPONATREMIA AND HOSPITAL OUTCOMES IN PATIENTS WITH PNEUMONIA

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Abstract

Background: *Hyponatremia (serum sodium <135 mmol/L) is a common electrolyte disturbance in community-acquired pneumonia (CAP) and has been associated with adverse outcomes. However, robust data from Pakistan and other low- and middle-income countries remain limited. This study aimed to determine the frequency of admission hyponatremia and evaluate its independent association with hospital outcomes in Pakistani patients hospitalized with CAP.*

Methods: *This retrospective cohort study included 400 adult patients admitted to a tertiary care hospital with community-acquired pneumonia. Patients were categorized as hyponatremic or normonatremic based on admission serum sodium levels. Clinical outcomes assessed included in-hospital mortality, ICU admission, need for invasive mechanical ventilation, and length of hospital stay. Multivariable logistic regression was used to evaluate the independent association between hyponatremia and in-hospital mortality after adjusting for age, sex, CURB-65 score, comorbidities, and serum creatinine.*

Results: *Hyponatremia was present in 126 of 400 patients (31.5%). Compared with normonatremic patients, hyponatremic patients had significantly higher in-hospital mortality (10.3% vs. 2.2%; $p < 0.001$), greater ICU admission rates (20.6% vs. 10.9%; $p = 0.010$), and longer hospital stays (median 10 vs. 7 days; $p < 0.001$). Mechanical ventilation was more frequent among hyponatremic patients but did not reach statistical significance (11.1% vs. 6.2%; $p = 0.088$). After multivariable adjustment, hyponatremia remained independently associated with in-hospital mortality (adjusted OR 5.71, 95% CI 2.02–16.13; $p = 0.001$).*

Conclusion: *Admission hyponatremia is common in hospitalized CAP patients and independently predicts higher mortality, ICU admission, and prolonged hospitalization. To our knowledge, this study provides the first evidence from*

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Pakistan demonstrating the independent prognostic value of hyponatremia in CAP after adjusting for established severity indices, supporting its use as a simple, low-cost risk stratification tool in resource-limited settings

1. INTRODUCTION

The most prevalent electrolyte imbalance among hospital inpatients is hyponatraemia, which is defined as serum sodium <135 mmol/L. It affects up to one in three hospitalised adults, compared to about 5% of the general population [1]. Longer hospital stays, increased resource consumption, and increased mortality are linked to even mild hyponatraemia [2, 3]. These findings imply that determining hyponatraemia may help with risk assessment in a variety of circumstances.

Hyponatraemia is a common finding in patients admitted with community-acquired pneumonia (CAP). The reported prevalence is between 25% and 33% of cases [4,5]. As an example, 28.8% of CAP admissions in a Swiss tertiary care series had hyponatraemia [5]. Notably, compared to normonatremic patients, CAP patients with hyponatraemia typically experience more severe illness, including longer hospital stays and a higher need for ICU care and mechanical ventilation [6, 7]. Hyponatraemia is an independent predictor of poor outcomes in pneumonia, according to multivariable analyses. For instance, a large study found that admission hyponatraemia (<130 mmol/L) conferred a >2-fold adjusted odds of in-hospital death [5].

Pneumonia and hyponatraemia are related through a variety of mechanisms. In pulmonary infections, the syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a common cause. Non-osmotic ADH release is triggered by lung inflammation, cytokines (particularly interleukin-6), and hypoxia. Additional factors include gastrointestinal losses or mild hypovolemia from inadequate intake, which results in dilutional hyponatraemia [8]. In all cases, hyponatraemia in pneumonia appears to reflect the severity of the underlying illness. Although active management of hyponatraemia has been suggested by some authors, it is still unknown whether correcting sodium improves outcomes [9]. In CAP, hyponatraemia is therefore primarily considered a prognostic indicator.

To the best of our knowledge, no previous study in Pakistan has rigorously evaluated the independent prognostic significance of admission hyponatremia in hospitalized community-acquired pneumonia (CAP) patients while adequately adjusting for validated disease severity indices and renal function. Although hyponatremia is increasingly recognized as a prognostic marker in CAP, existing evidence is derived predominantly from high-income settings, thereby limiting its generalizability to low- and middle-income countries. Available South Asian data remain sparse and inconsistent, with prior studies frequently limited by heterogeneous definitions of hyponatremia and inadequate adjustment for important confounding variables, including the CURB-65 score and renal dysfunction [10,11]. Consequently, whether admission hyponatremia independently predicts adverse clinical outcomes or merely reflects overall disease severity in this population remains uncertain. By addressing these important methodological limitations, the present study aims to provide robust locally relevant evidence regarding the prevalence and prognostic implications of admission hyponatremia among Pakistani patients hospitalized with CAP.

Accordingly, this retrospective cohort study was conducted at a tertiary-care hospital in Pakistan to determine the frequency of admission hyponatremia in adult patients with community-acquired pneumonia and to evaluate its independent association with hospital outcomes. The primary outcome was in-hospital mortality, while secondary outcomes included ICU admission, requirement for invasive mechanical ventilation, and length of hospital stay.

2. Methods

2.1. Study Design and Setting

The Department of Medicine at Abbasi Shaheed Hospital, a tertiary care teaching facility, conducted this retrospective cohort study. The study included adult patients admitted with

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community-acquired pneumonia between January 2025 to May 2025. A standardised data extraction form was used to extract data from hospital medical records. To reduce selection bias, all eligible patients enrolled consecutively throughout the study period. The study's design and reporting followed the STROBE guidelines for cohort studies (12).

2.2. Participants

During the study period, adult patients (aged ≥18 years) who were admitted with a primary diagnosis of community-acquired pneumonia (CAP) were successively included. According to American Thoracic Society guidelines, CAP was defined as the presence of radiographic evidence of a new pulmonary infiltrate on chest radiograph or computed tomography along with clinical features consistent with lower respiratory tract infection (e.g., fever, cough, sputum production, or dyspnoea) (13).

Exclusion criteria included missing admission serum sodium measurements, hospital-acquired or ventilator-associated pneumonia, radiographic confirmation of pneumonia, and incomplete outcome data. To avoid duplication, only the first hospitalisation was included when multiple admissions occurred during the study period. Comorbid conditions such as chronic kidney disease, heart failure, liver disease, thyroid disorders, and medications that affect sodium balance were identified and included as covariates in the multivariable analysis.

2.3. Exposure Measurement and Classification

The primary exposure variable was serum sodium levels measured within the first 24 hours of hospitalisation. To reduce the impact of therapeutic interventions, the analysis was conducted using the first available sodium value. The hospital's central laboratory used a standardised indirect ion-selective electrode method for all measurements.

According to established clinical guidelines, a serum sodium concentration of less than 135 mmol/L was considered hyponatraemia, and a concentration of more than 135 mmol/L was considered normonatremia. Hyponatraemia was further classified into mild (130–134 mmol/L), moderate (125–129 mmol/L), and severe (<125 mmol/L) categories for secondary analyses in order to assess possible dose–response relationships (14,15).

Sodium values were interpreted in light of pertinent clinical and biochemical parameters to lower the possibility of misclassification, especially in situations where measured sodium levels are known to be impacted (such as hyperglycaemia).

2.4. Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes included admission to the intensive care unit (ICU) at any time during hospitalisation, the need for invasive mechanical ventilation, and the length of hospital stay, which was defined as the number of days from admission to discharge or in-hospital death.

2.5. Baseline and Covariate Data

Age, sex, and pre-existing conditions like diabetes mellitus, heart failure, and chronic obstructive pulmonary disease that were recorded in medical records at the time of admission were among the baseline characteristics. The CURB-65 score, which was computed at admission, was used to evaluate the clinical severity of pneumonia.

Serum creatinine, C-reactive protein (CRP), and white blood cell (WBC) count were among the laboratory parameters measured within the first 24 hours of admission. These variables were selected a priori based on clinical relevance and prior literature and were included as potential confounders in multivariable analyses.

2.6. Sample Size

The sample size was calculated with the primary goal of determining the prevalence of hyponatraemia among patients with community-acquired pneumonia. With a 95% confidence level, a 5% margin of error, and an expected prevalence of 30%, a minimum sample size of 323 patients was needed (16).

Given the retrospective design, all eligible patients who met the inclusion criteria during the study period were included, resulting in a final sample size of 400 patients. This sample size was deemed

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adequate to allow for the comparison of clinical outcomes across exposure groups and to guarantee accurate prevalence estimation.

According to previous research, assuming mortality rates of 2% and 10%, respectively, the available sample offered roughly 80% statistical power (two-sided $\alpha = 0.05$) to identify a clinically significant difference in in-hospital mortality between hyponatremic and normonatremic patients (17, 18).

2.7. Statistical Analysis

The Shapiro-Wilk test was used to determine whether continuous variables were normal. The results are displayed as mean ± standard deviation (SD) or median (interquartile range [IQR]), depending on the situation. For continuous variables, the independent t-test or Mann-Whitney U test was used for between-group comparisons; for categorical variables, the chi-square test or Fisher's exact test was used.

The relationship between hyponatraemia and in-hospital mortality was assessed using multivariable logistic regression analysis. The model was adjusted for predetermined covariates, such as age, sex, CURB-65 score, diabetes mellitus, heart failure, chronic obstructive pulmonary disease, and serum creatinine, with hyponatraemia serving as the main exposure. The findings are presented as odds ratios (ORs) with 95% confidence intervals (Cis).

Unadjusted chi-square tests were used to analyse secondary binary outcomes (ICU admission and invasive mechanical ventilation), and the results are shown as proportions with matching p-values. The Mann-Whitney U test was used to analyse the non-normally distributed length of hospital stay, which is reported as median (IQR).

The Hosmer-Lemeshow goodness-of-fit test and Nagelkerke R2 were used to evaluate the multivariable logistic regression model's performance. All analyses were conducted using a complete-case approach (19,20). A p-value of less than 0.05 was regarded as statistically significant, and all tests were two-sided. IBM SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA) was used to conduct statistical analyses.

2.8. Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki (21). Ethical approval was obtained from the Institutional Review Board (IRB) of Abbasi Shaheed Hospital (Ref: DIR/ASH/SECT/641/2025).

Given the retrospective design and use of de-identified routinely collected clinical data, informed consent was waived by the Institutional Review Board. No direct patient contact was involved. All data were anonymized prior to analysis and handled confidentially throughout the study.

3. Results

3.1. Study Population

487 patients with community-acquired pneumonia who were admitted underwent eligibility screening. Of these, 87 patients were excluded because of incomplete outcome data (n = 12), hospital-acquired or ventilator-associated pneumonia (n = 29), missing admission serum sodium (n = 34), and age <18 years (n = 12). Out of the 400 patients in the final study cohort, 274 (68.5%) had normonatremia and 126 (31.5%) had hyponatraemia (Figure 1).

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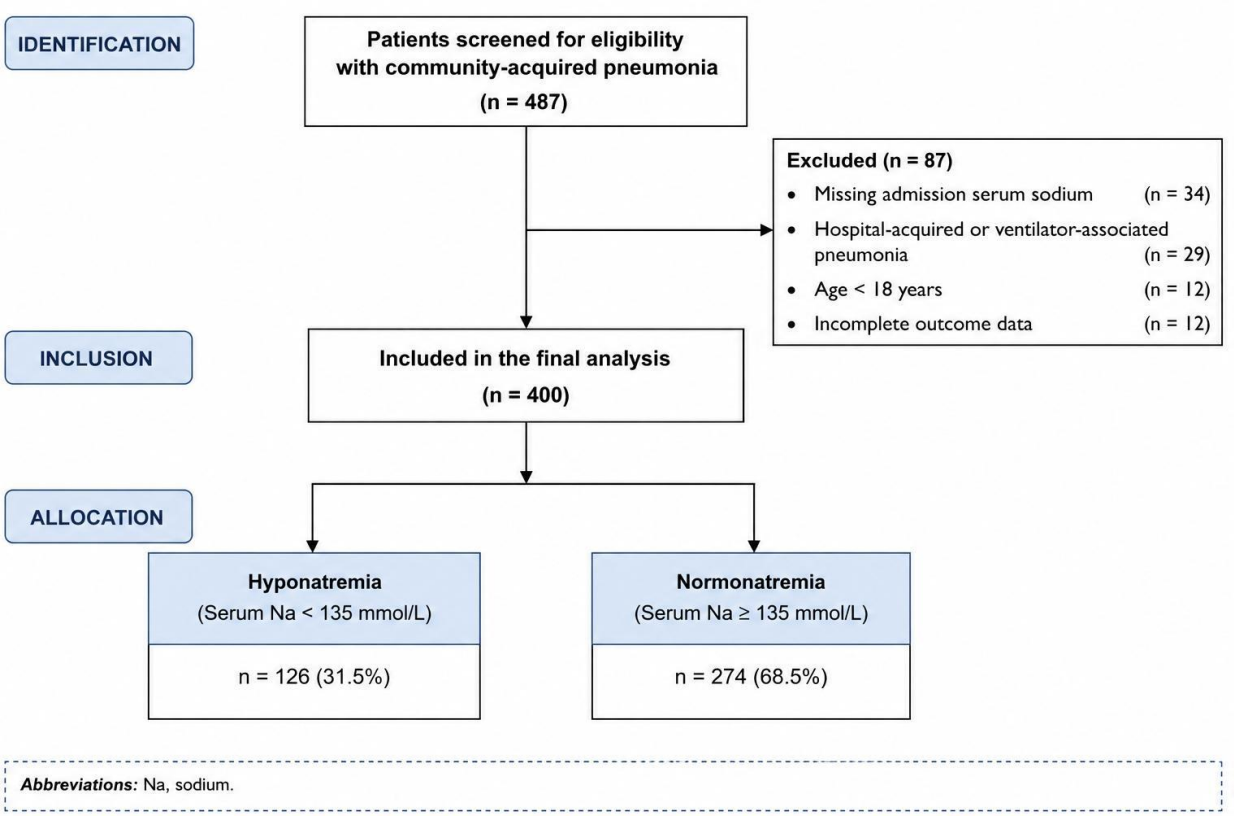

Figure 1: Flow Diagram of the Inclusion and Exclusion Process for Patients with Community-Acquired Pneumonia

3.2. Baseline Characteristics

Baseline characteristics of the study population are shown in Table 1. The hyponatraemia and normonatremia groups had comparable median ages and sex distributions. Diabetes mellitus, heart failure, and chronic obstructive pulmonary disease were among the comorbidities that were similar in both groups.

Inflammatory markers and renal function parameters such as C-reactive protein, white blood cell count, serum creatinine, and estimated glomerular filtration rate were not significantly different between groups. The group definition showed differences in serum sodium levels ($p < 0.001$). The hyponatraemia group had longer hospital stays ($p < 0.001$).

Table 1 Baseline Characteristics of Patients with Pneumonia by Hyponatremia Status (n = 400)

Variable	No Hyponatremia (n = 274)	Hyponatremia (n = 126)	*p* – value
Age (years), median (IQR)	66 (58 – 74)	67 (59 – 75)	0.433
Male gender, n (%)	159 (58.0)	76 (60.3)	0.666
Diabetes, n (%)	87 (31.8)	43 (34.1)	0.638
COPD, n (%)	54 (19.7)	19 (15.1)	0.266
Heart Failure, n (%)	36(13.1)	23 (18.3)	0.180
Serum Sodium (mmol/L), median (IQR)	138 (137-140)	130 (128 – 132)	< 0.001

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CRP (mg/L), mean ± SD	111.3 ± 37.6	114.0 ± 39.9	0.513
WBC (x10^9/L), mean ± SD	11.68 ± 4.04	11.85 ± 4.21	0.693
Creatinine (mg/dL), median (IQR)	1.0 (0.9 – 1.2)	1.0 (0.9 – 1.2)	0.163
eGFR (ml/min/1.73m^2), median (IQR)	88 (75 – 96)	86 (73 -94)	0.090
Length of stay (days), median (IQR)	7 (5 – 10)	10 (7 – 14)	< 0.001

3.3. Hospital Outcomes

Clinical outcomes are summarized in Table 2. The hyponatraemia group had a longer median hospital stay (10 [IQR 7–14] vs. 7 [IQR 5–10] days; p < 0.001) than the normonatremia group.

Patients with hyponatraemia had greater rates of ICU admission and in-hospital mortality (20.6% vs. 10.9%, p = 0.010; and 10.3% vs. 2.2%, p < 0.001, respectively). Although the hyponatraemia group required more invasive mechanical ventilation, this difference was not statistically significant (11.1% vs. 6.2%; p = 0.088).

Table 2 Hospital Outcomes by Hyponatremia Status

Outcome	No Hyponatremia (n = 274)	Hyponatremia (n = 126)	*p* – value
ICU admission, n (%)	30 (10.9)	26 (20.6)	0.010
Mechanical ventilation, n (%)	17 (6.2)	14 (11.1)	0.088
In- hospital death, n (%)	6 (2.2)	13 (10.3)	< 0.001

3.4. Outcomes by Severity of Hyponatremia

Of the 126 hyponatraemia patients, 62 (49.2%) had mild hyponatraemia, 41 (32.5%) had moderate hyponatraemia, and 23 (18.3%) had severe hyponatraemia.

In-hospital mortality rates for mild, moderate, and severe hyponatraemia were 4.8% (3/62), 9.8% (4/41), and 17.4% (4/23), respectively. Additionally, patients with more severe categories of hyponatraemia had higher ICU admission rates. Since no formal test for trend was conducted, these results are presented descriptively (Figure 2).

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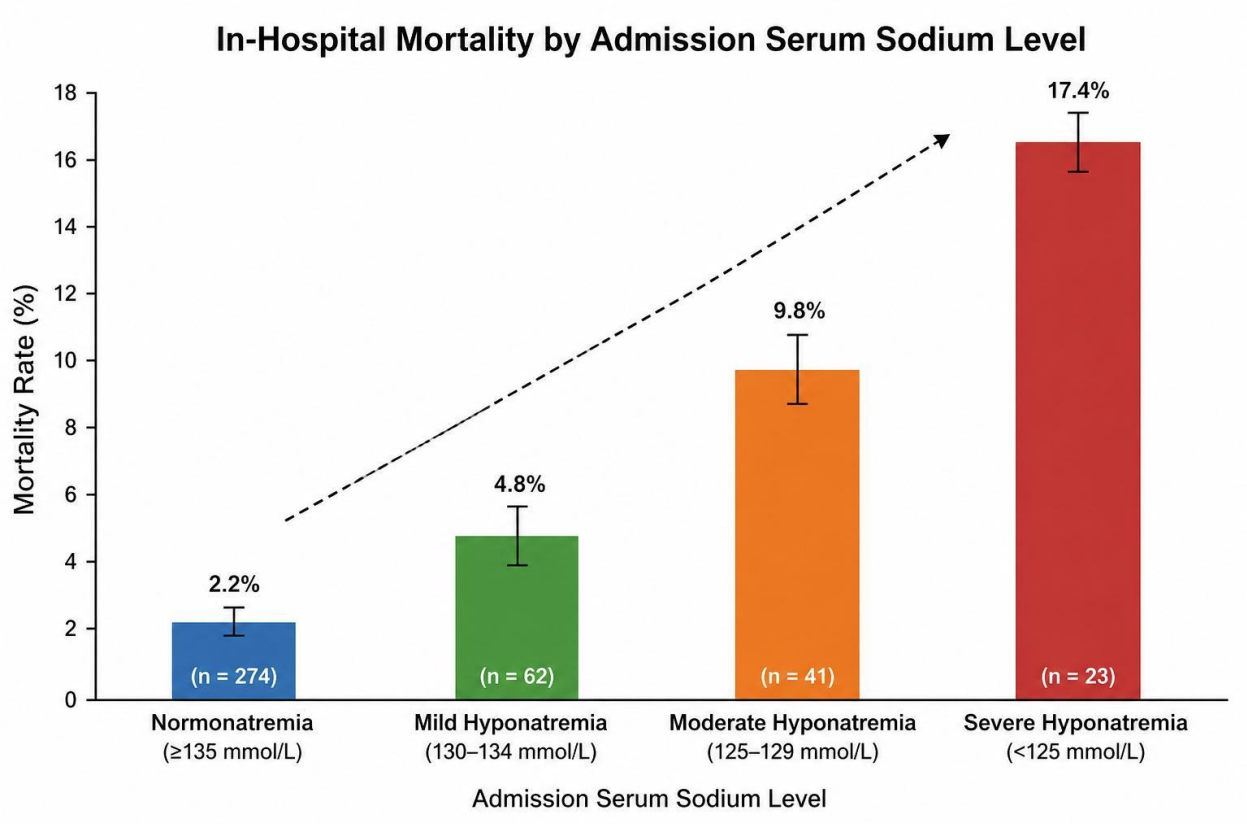

Figure 2: In-Hospital mortality by admission sodium levels

3.5. Length of Hospital Stay

Hospital stays for hyponatremic patients were significantly longer than those for normonatremic patients (median 10 vs. 7 days; $p < 0.001$). The results are presented descriptively with between-group comparison because this outcome has a non-normal distribution.

3.6. Multivariable Analysis of In-Hospital Mortality

Hyponatraemia was linked to higher odds of in-hospital mortality in unadjusted analysis (OR 5.13, 95% CI 1.93–13.70; $p = 0.001$). After controlling for age, gender, CURB-65 score, diabetes, chronic obstructive pulmonary disease, heart failure, and serum creatinine, hyponatraemia remained associated with in-hospital mortality (adjusted OR 5.71, 95% CI 2.02-16.13; $p = 0.001$) (Table 3).

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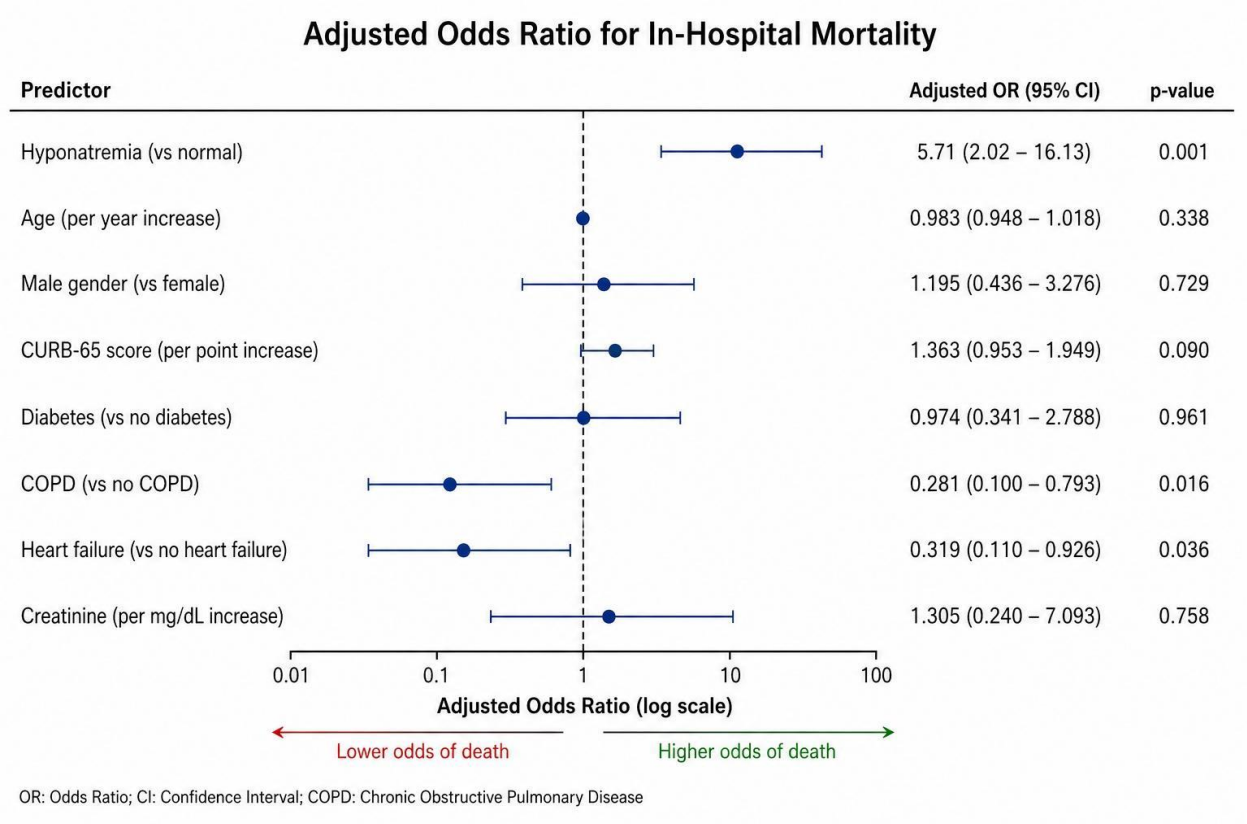

Figure 3: Adjusted Odds Ratios for Predictors of In-Hospital Mortality in Patients with Community-Acquired Pneumonia

Heart failure (adjusted OR 0.32, 95% CI 0.11–0.93; p = 0.036) and COPD (adjusted OR 0.28, 95% CI 0.10–0.79; p = 0.016) were also linked to mortality in the modified model. The model had a moderate explanatory power (Nagelkerke R2 = 0.210) and an acceptable fit (Hosmer–Lemeshow p = 0.572) (Figure 3).

Table 3 Logistic Regression for In-Hospital Death

Predictor	Crude OR (95% CI)	*p* – value	Adjusted OR (95% CI)	*p*– value
Hyponatremia (vs normal)	5.13 (1.93 – 13.70)	0.001	5.71 (2.02 – 16.13)	0.001
Age in years	_	_	0.983 (0.948 – 1.018)	0.338
Male gender	_	_	1.195 (0.436 – 3.276)	0.729
CURB65 score	_	_	1.363 (0.953 – 1.949)	0.090
Diabetes	_	_	0.974 (0.341 – 2.788)	0.961
COPD	_	_	0.281 (0.100 – 0.793)	0.016

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Heart Failure	_	_	0.319 (0.110 – 0.926)	0.036
Creatinine	_	_	1.305 (0.240 – 7.093)	0.758

4. Discussion

To the best of our knowledge, this is the first study from Pakistan to evaluate the independent prognostic significance of admission hyponatremia in hospitalized patients with community-acquired pneumonia (CAP) after rigorous adjustment for validated disease severity indices and renal function. Our findings demonstrate that hyponatremia is independently associated with adverse hospital outcomes, including significantly higher in-hospital mortality, greater ICU utilization, and prolonged hospitalization. Importantly, the association with mortality persisted after controlling for age, comorbidities, renal function, and CURB-65 score, with hyponatremia conferring a more than five-fold increased risk of in-hospital death (adjusted OR 5.71, 95% CI 2.02–16.13). These results suggest that admission serum sodium may provide incremental prognostic information beyond conventional severity scores and support its potential role in early risk stratification of CAP patients in resource-limited settings.

The prevalence of hyponatremia in our cohort (31.5%) is consistent with previous studies reporting admission hyponatremia in approximately 28%–30% of patients with community-acquired pneumonia [22,23]. Comparable prevalence rates have also been reported in other South Asian cohorts [24,25], indicating that hyponatremia is a frequent and reproducible biochemical abnormality in CAP across diverse healthcare settings.

While most prior studies were conducted in high-income countries and often lacked consistent adjustment for key confounders, our study extends the existing evidence by demonstrating that hyponatremia retains independent prognostic value in a Pakistani LMIC population even after adjustment for standardized severity indices and renal function [10,11]. This broadens the generalizability of previous observations and supports the potential utility of serum sodium as an adjunctive, low-cost prognostic marker in settings where advanced diagnostic tools may be limited.

Hyponatremic and normonatremic groups were similar with regard to age, sex, and inflammatory markers such as CRP and white blood cell count. Although renal function was slightly worse in hyponatremic patients, this was accounted for in the multivariable analysis. In our cohort, the lack of significant differences in conventional inflammatory markers suggests that the prognostic significance of hyponatremia may not be explained solely by systemic inflammation. This interpretation is consistent with previous studies demonstrating that hyponatremia is independently associated with adverse clinical outcomes and greater disease severity in patients with pneumonia[26,27].

Consistent with previous studies, hyponatremia was associated with substantially worse clinical outcomes, including increased mortality and prolonged hospital stay, and has also been linked to greater illness severity among patients with community-acquired pneumonia [27,28]. These findings align with observations in both pneumonia-specific and general medical cohorts [26,29], suggesting that hyponatremia identifies a subgroup of CAP patients with heightened clinical vulnerability. Although invasive mechanical ventilation was more frequent among hyponatremic patients, this difference did not reach statistical significance, possibly due to limited statistical power or institution-specific thresholds for escalation of respiratory support.

A key finding of our study is that the association between hyponatremia and mortality remained significant after multivariable adjustment (adjusted OR 5.71). This is consistent with earlier reports [26,30] and, importantly, extends them by showing that serum sodium adds prognostic value beyond that provided by the CURB-65 score and renal function. In resource-constrained settings where CURB-65 is commonly used, incorporating

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admission sodium levels could refine risk assessment without adding substantial cost or complexity.

Moreover, we observed a progressive increase in mortality with worsening severity of hyponatremia, from 4.8% in mild cases to 17.4% in severe cases. Although a formal test for trend was not performed, this gradient is in line with previous studies reporting a dose-response relationship between lower sodium levels and mortality [31,32], and suggests that the degree of hyponatremia carries additional clinical relevance.

The mechanisms linking hyponatremia to poor outcomes in CAP are likely multifactorial. Pulmonary infections are well-known triggers of SIADH via inflammatory cytokines such as interleukin-6 and hypoxia-induced non-osmotic ADH release [33]. Additional factors include fever, hypovolemia, and reduced oral intake. Beyond being a marker of illness severity, hyponatremia may directly contribute to adverse outcomes through neurological effects such as impaired consciousness, reduced respiratory drive, and diminished airway protective reflexes, thereby increasing the risk of aspiration and respiratory failure [34]. These pathophysiological considerations lend biological plausibility to the observed associations with ICU admission and mortality.

4.1. Strengths and Limitations

The strengths of our study include a well-defined cohort, the use of admission sodium values prior to therapeutic interventions, consecutive patient inclusion to minimize selection bias, and adjustment for important confounders including CURB-65 and renal function. The study was conducted in accordance with STROBE reporting guidelines for observational research [12].

Several limitations should be acknowledged. The retrospective, single-center design limits causal inference and may affect generalizability to other settings. We lacked data on the etiology and specific treatment of hyponatremia, precluding mechanistic or interventional analyses. The relatively small number of death events resulted in wide confidence intervals around the effect estimate, and formal trend testing for the severity gradient was not performed. Additionally, serial sodium measurements were not available, so we could not assess the impact of sodium normalization on outcomes.

4.1. Implications and future perspectives

From a clinical perspective, our findings suggest that admission serum sodium an inexpensive, universally available test can aid in the early risk assessment of patients hospitalized with CAP. Integrating sodium levels into existing clinical assessment frameworks may help identify high-risk patients who require closer monitoring or earlier escalation of care. These results are particularly relevant for resource-limited settings where advanced severity scoring systems may be underutilized. Prospective studies are needed to validate these observations and to determine whether targeted correction of hyponatremia can improve clinical outcomes.

Declaration of Statements

Funding

The authors did not receive any support from any organization for the submitted work.

Competing Interests

It is declared that there are no competing interests that might have impacted presentation of the work.

Consent for Participation & Publication

Not required.

Availability of Data and Material

The authors obtained routine laboratory records and direct observation of patients admitted in ICU and ward, which included their daily electrolyte reports and ventilation needs during their course of treatment. The recorded data was manual for research purposes and were not stored as identifiable individual patient records. Thus, the datasets are not publicly displayed to maintain patient confidentiality and nature of the study.

Code Availability

Not required.

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Large Language Model

The authors declare that no generative AI tools were used, except for Grammarly.com for basic checking in the writing of this manuscript.

Author Contributions

M.L.: Conceptualization, study design, data acquisition, critical revision of the manuscript, and final approval of the version to be published.

A.S.R.: Conceptualization, supervision, critical revision of the manuscript, and final approval of the version to be published.

A.M.: Conceptualization, study design, data acquisition, data interpretation, critical revision of the manuscript, and final approval of the version to be published.

Q.J.: Study design, data interpretation, critical revision of the manuscript, and final approval of the version to be published.

N.A.: Data analysis, manuscript drafting, critical revision of the manuscript, and final approval of the version to be published.

S.A.: Data acquisition, critical revision of the manuscript, and final approval of the version to be published.

A.J.: Data acquisition, critical revision of the manuscript, and final approval of the version to be published.

S.A.G.: Data acquisition, critical revision of the manuscript, and final approval of the version to be published.

All authors meet the ICMJE authorship criteria. All authors made substantial contributions to the work, approved the final version of the manuscript, and agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

5. Conclusions

Hyponatremia was a common finding in hospitalized patients with community-acquired pneumonia, affecting 31.5% of cases. It was significantly associated with adverse in-hospital outcomes, including prolonged hospital stay, higher ICU admission rates, and increased mortality. Importantly, these associations remained significant after adjustment for age, sex, CURB-65 score, comorbidities, and renal function, indicating that admission hyponatremia is an independent predictor of poor prognosis in CAP. Routine assessment of serum sodium may therefore be useful for early risk stratification in hospitalized pneumonia patients.

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