Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/pdbs6426

ROLE OF SERUM ALBUMIN AND COPEPTIN IN SEVERITY OF COMMUNITY-ACQUIRED PNEUMONIA

Dr. Lava[1*], Dr. C. Prashanth[2], Dr. Vaibhav C Padashetty[3], Dr. U Sohan Kukkillaya[4], Dr. Kirankumara[5], Dr. Anusree C[6]

[1*]Postgraduate student, Mysore Medical College & Research Institute (MMC & RI Mysore), Karnataka
[2]Professor & HOD
[3](DM Pulmo ESIC Delhi)
[4,5,6](PG MMC&RI Mysore)

[*]**Corresponding Author:** Dr. Lava
[*]Postgraduate student, Mysore Medical College & Research Institute (MMC & RI Mysore), Karnataka

Abstract

Background: Community-acquired pneumonia (CAP) is a significant cause of morbidity and mortality worldwide. Early risk stratification is crucial for effective management. Traditional clinical scoring systems may be enhanced by objective biomarkers such as serum copeptin, a marker of physiological stress, and serum albumin, a negative acute-phase reactant.

Aim: To evaluate the role of serum copeptin and albumin as markers of disease severity and predictors of outcome in patients with CAP.

Methods: This observational study was conducted over six months at Mysore Medical College and Research Institute, including 100 adult patients diagnosed with CAP. Patients were classified based on Pneumonia Severity Index (PSI) scores into three groups (Class 3, 4, and 5). Serum copeptin and albumin levels were measured on admission and compared across severity groups and clinical outcomes. ROC curve analysis was performed to determine the diagnostic accuracy of both markers.

Results: Mean serum copeptin levels increased significantly with PSI class (PSI 3: 11.63 ng/mL; PSI 5: 30.23 ng/mL). Non-survivors had a mean copeptin level of 32.37 ng/mL compared to 18.46 ng/mL in survivors. A cutoff of 23.7 ng/mL predicted severe CAP with 90.63% sensitivity and 92.65% specificity. Serum albumin levels decreased with increasing severity (PSI 3: 3.45 g/dL; PSI 5: 3.03 g/dL). Non-survivors had lower albumin (2.56 g/dL) compared to survivors (3.39 g/dL), with a mortality prediction cutoff of 2.87 g/dL (sensitivity 88.2%, specificity 94%).

Conclusion: Serum copeptin is a highly sensitive and specific biomarker for predicting severity and mortality in CAP. Serum albumin, while less specific, provides supportive prognostic information. Both markers are independent of age and sex and can enhance clinical decision-making when used alongside established severity scores.

Keywords: Community-acquired pneumonia, Serum copeptin, Serum albumin, Biomarkers, PSI, Prognosis

Introduction

Community-acquired pneumonia (CAP) remains one of the leading infectious causes of morbidity and mortality worldwide, accounting for an estimated 4 million new cases annually in India alone, and contributing significantly to hospital admissions and the global healthcare burden [1,2]. CAP is defined as an acute infection of the pulmonary parenchyma in individuals who have not been recently hospitalized or resided in long-term care facilities. It is typically associated with clinical features such as cough, fever, dyspnea, and sputum production, along with radiographic evidence of new pulmonary infiltrates [3].

The clinical presentation of CAP ranges widely, from mild illness to severe respiratory failure, sepsis, and death. Early and accurate severity assessment is essential to determine the appropriate site of care, initiate timely antimicrobial therapy, and guide the intensity of clinical monitoring. Tools like the Pneumonia Severity Index (PSI) and CURB-65 are commonly used for risk stratification, but they have limitations—particularly in their reliance on subjective clinical findings and baseline comorbidities [4].

In recent years, increasing attention has been directed toward identifying objective biomarkers that can supplement these scoring systems and improve prognostic accuracy. Copeptin, a 39-amino acid glycopeptide derived from the C-terminal portion of pre-provasopress in (the precursor of arginine vasopressin), is released in equimolar amounts with vasopressin during physiological stress. It serves as a stable surrogate marker for vasopressin, which is otherwise difficult to measure due to its short half-life and instability [5]. Elevated copeptin levels have been associated with increased disease severity and mortality in various acute conditions, including lower respiratory tract infections, heart failure, and sepsis [6,7].

Serum albumin, a well-established negative acute-phase reactant synthesized by the liver, also plays an important role in the assessment of inflammatory conditions. In CAP, systemic inflammation leads to decreased hepatic synthesis, increased catabolism, and capillary leakage, resulting in hypoalbuminemia. Low serum albumin levels have been linked to adverse clinical outcomes, including prolonged hospitalization, higher severity scores, and increased mortality [8,9].

The objective of this study is to evaluate the role of serum copeptin and albumin levels in assessing disease severity and predicting clinical outcomes in patients with community-acquired pneumonia. It also aims to determine whether these biomarkers can be reliably utilized in routine clinical settings to enhance early risk stratification.

Materials and Methods

Study Design and Setting

This was a prospective **observational study** conducted over a period of **six months** at the Department of Respiratory Medicine, **Mysore Medical College and Research Institute (MMC & RI), Mysuru**, Karnataka.

Study Population

A total of **100 adult patients** diagnosed with **community-acquired pneumonia (CAP)** were enrolled in the study. CAP was defined as **new or progressive pulmonary infiltrates on chest radiograph**, accompanied by **at least two of the following clinical features**:

- Fever
- Cough
- Purulent sputum production
- Leukocytosis (white blood cell count >10,000/mm³)

Inclusion Criteria

- Patients aged **18 years and above**
- Both **male and female** patients
- Confirmed diagnosis of **CAP**

Exclusion Criteria
Patients were excluded if they had:
- Chronic kidney disease (CKD)
- Chronic alcoholic or non-alcoholic liver disease
- Human immunodeficiency virus (HIV) infection
- Pulmonary tuberculosis
- Burns
- Malabsorption syndromes or malnutrition
- Pregnancy or lactation

Severity Assessment
All patients were evaluated using:
- **Pneumonia Severity Index (PSI)**
- **CURB-65** scoring system

Based on **PSI scores**, patients were classified into three groups:
- **Group 1**: PSI class 3
- **Group 2**: PSI class 4
- **Group 3**: PSI class 5

Biomarker Measurement
On admission, **serum copeptin** and **serum albumin** levels were measured using standard laboratory techniques:
- **Copeptin** levels were reported in **ng/mL**
- **Albumin** levels were reported in **g/dL**

The relationship between biomarker levels and pneumonia severity (as defined by PSI class) as well as patient outcomes (improvement or mortality) was analyzed.

Statistical Analysis
Descriptive statistics (mean and standard deviation) were calculated for biomarker levels across severity groups and outcomes. Receiver Operating Characteristic (ROC) curve analysis was performed to determine optimal cutoff values for predicting severity and mortality. Sensitivity and specificity values were derived accordingly.

Results
Patient Demographics
The study included 100 patients diagnosed with community-acquired pneumonia. The majority of patients were aged between 31 and 70 years, with distribution across various age brackets as shown in Figure 1.

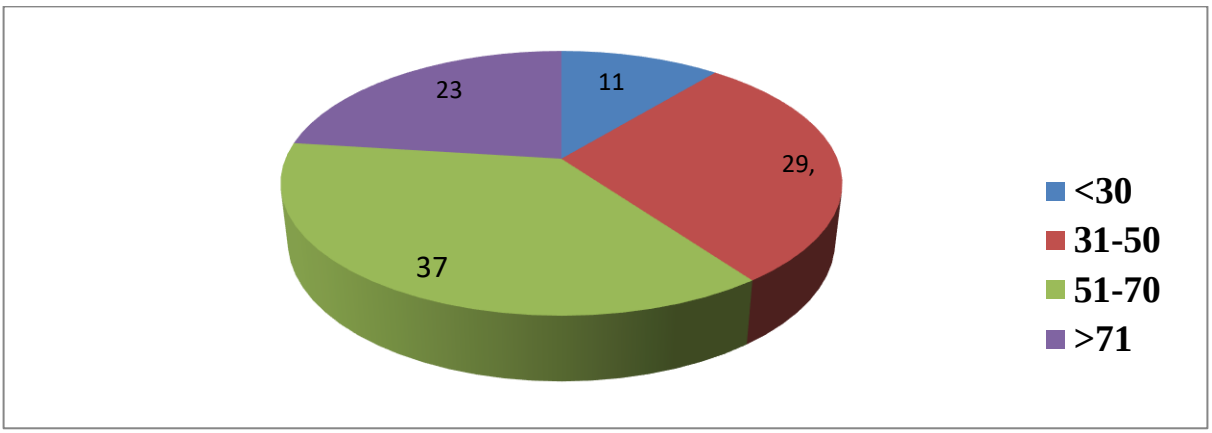

Figure 1. *Age-wise distribution of patients diagnosed with community-acquired pneumonia.*

Severity Classification (PSI Groups)
Patients were categorized into three groups based on **Pneumonia Severity Index (PSI)** scores:
- **Group 1 (PSI Class 3):** 29 patients
- **Group 2 (PSI Class 4):** 39 patients
- **Group 3 (PSI Class 5):** 32 patients

Serum Copeptin and Severity of CAP
There was a significant upward trend in serum copeptin levels with increasing PSI class, suggesting a positive correlation between copeptin and disease severity.

Table 1. Serum Copeptin Levels by PSI Class

PSI Class	Count (n)	Mean Copeptin (ng/mL)	Standard Deviation
3.00	29	11.63	4.23
4.00	39	19.95	3.48
5.00	32	30.23	6.92
Total	**100**	**20.83**	**8.85**

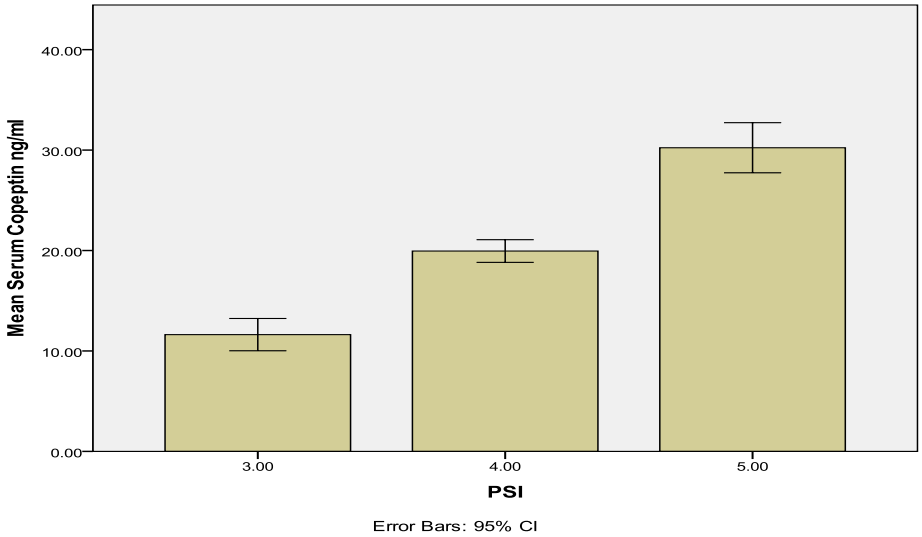

Figure 2. *Mean Serum Copeptin in Different PSI Groups*

Serum Albumin Levels and Severity
An inverse relationship was observed between serum albumin levels and PSI class, with albumin levels decreasing as disease severity increased. This trend reflects the inflammatory and catabolic impact of severe CAP.

Table 2. Serum Albumin Levels by PSI Class

PSI Class	Count (n)	Mean Albumin (g/dL)	Standard Deviation
3.00	29	3.45	0.40
4.00	39	3.28	0.50
5.00	32	3.03	0.55
Total	**100**	**3.25**	**0.52**

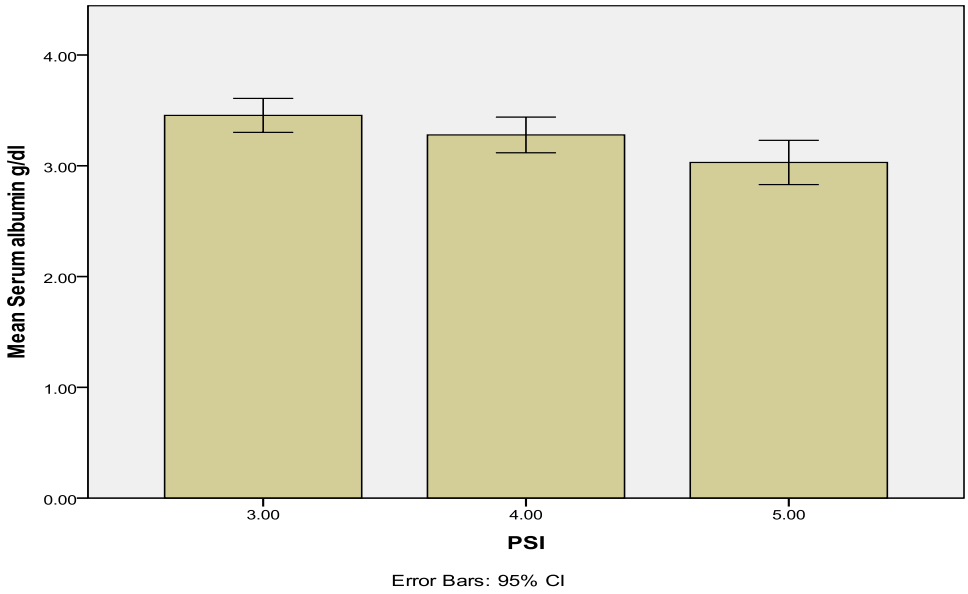

Figure 3. *Mean serum albumin levels across PSI groups with 95% confidence intervals.*

Serum Copeptin and Clinical Outcomes

Outcomes were assessed in relation to serum copeptin levels. Among the 100 patients:

- **17 patients (17%) died**
- **83 patients (83%) recovered**

Patients who succumbed to the illness had **markedly elevated copeptin levels** compared to survivors, reinforcing its value as a prognostic marker.

Outcome	Count (n)	Mean Copeptin (ng/mL)	Standard Deviation
Mortality	17	32.37	6.64
Improved	83	18.46	7.26
Total	**100**	**20.83**	**8.85**

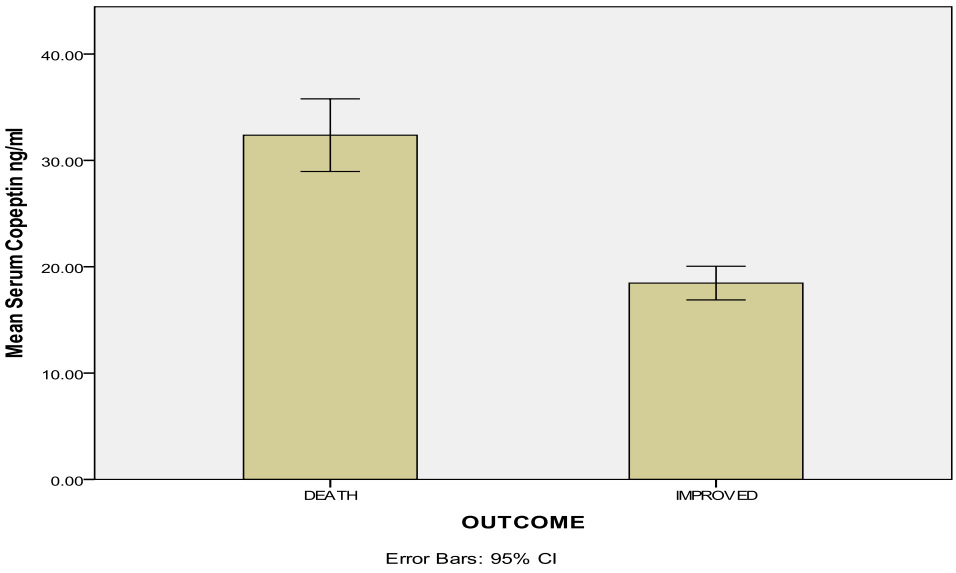

Figure 4. *Mean serum copeptin levels in mortality vs improved outcome groups.*

Table 4. Serum Albumin Levels by Clinical Outcome

Outcome	Count (n)	Mean Albumin (g/dL)	Standard Deviation
Mortality	17	2.56	0.36
Improved	83	3.39	0.42

Total	**100**	**3.25**	**0.52**

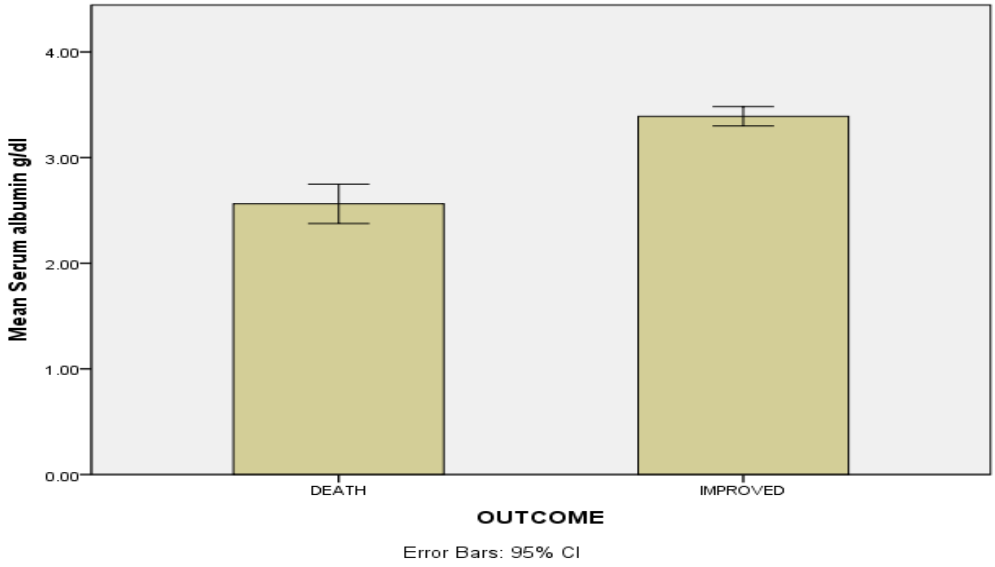

Figure 5. *Mean Serum Copeptin Levels by Clinical Outcome (Mortality vs Improvement) with 95% Confidence Intervals*

ROC Curve Analysis: Diagnostic and Prognostic Accuracy

1. Prediction of CAP Severity

- **Copeptin** demonstrated excellent discriminative power for severity at a cutoff of **23.7 ng/mL**, with:
  - Sensitivity: **90.63%**
  - Specificity: **92.65%**
- **Albumin** showed moderate performance at a cutoff of **3.24 g/dL**:
  - Sensitivity: **65.63%**
  - Specificity: **58.82%**

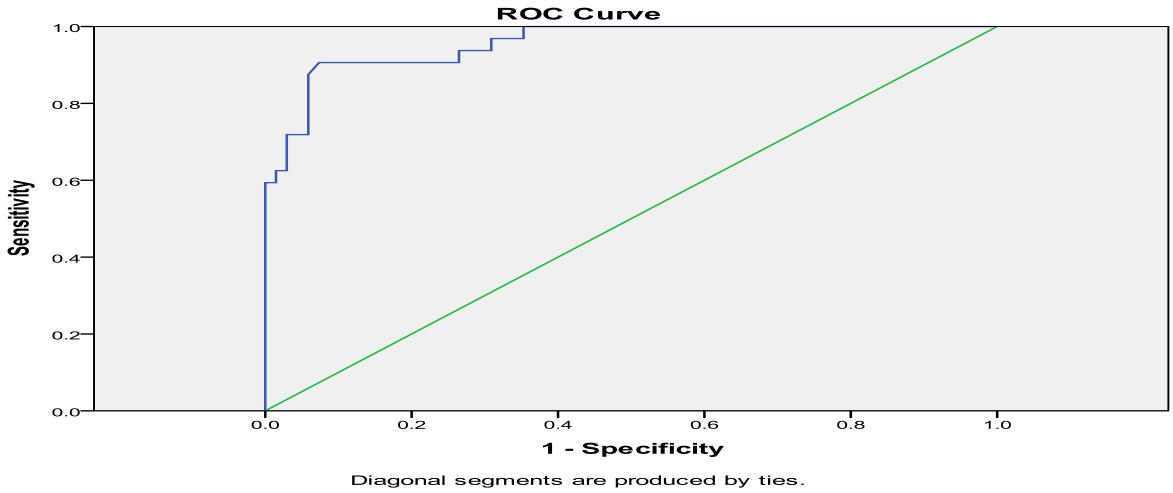

Figure 6. *ROC Curve for serum copeptin in predicting CAP severity.*

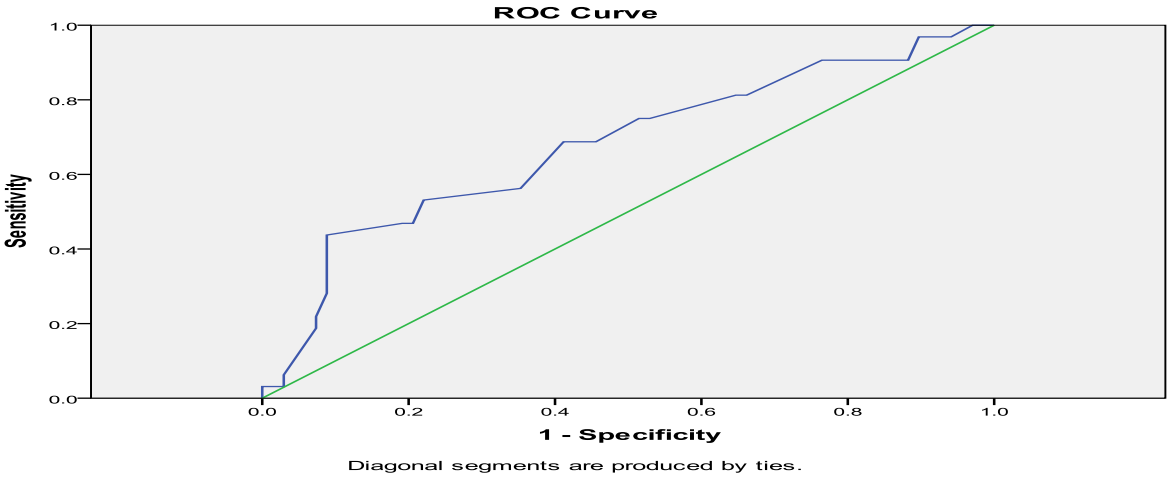

Figure 7. *ROC Curve for serum albumin in predicting CAP severity.*

2. Prediction of Mortality

- **Serum Copeptin**: Patients with copeptin levels ≥ **26.8 ng/mL** were at a significantly higher risk of death.
  - **Sensitivity**: 82.4%
  - **Specificity**: 91.6%
- **Serum Albumin**: Patients with albumin levels ≤ **2.87 g/dL** were more likely to experience mortality due to CAP.
  - **Sensitivity**: 88.2%
  - **Specificity**: 94%

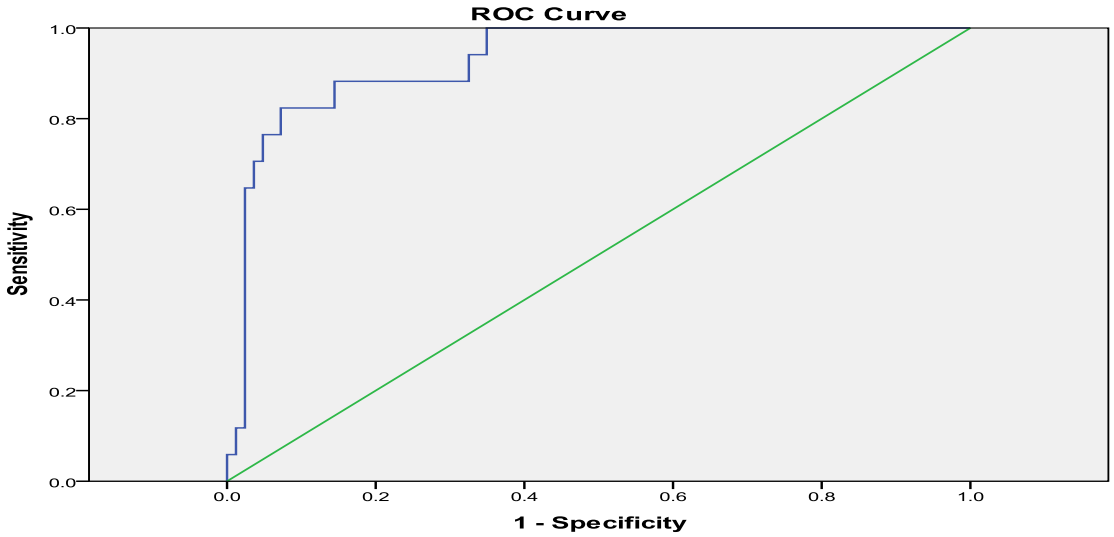

Figure 8. *ROC Curve for serum copeptin in predicting mortality.*

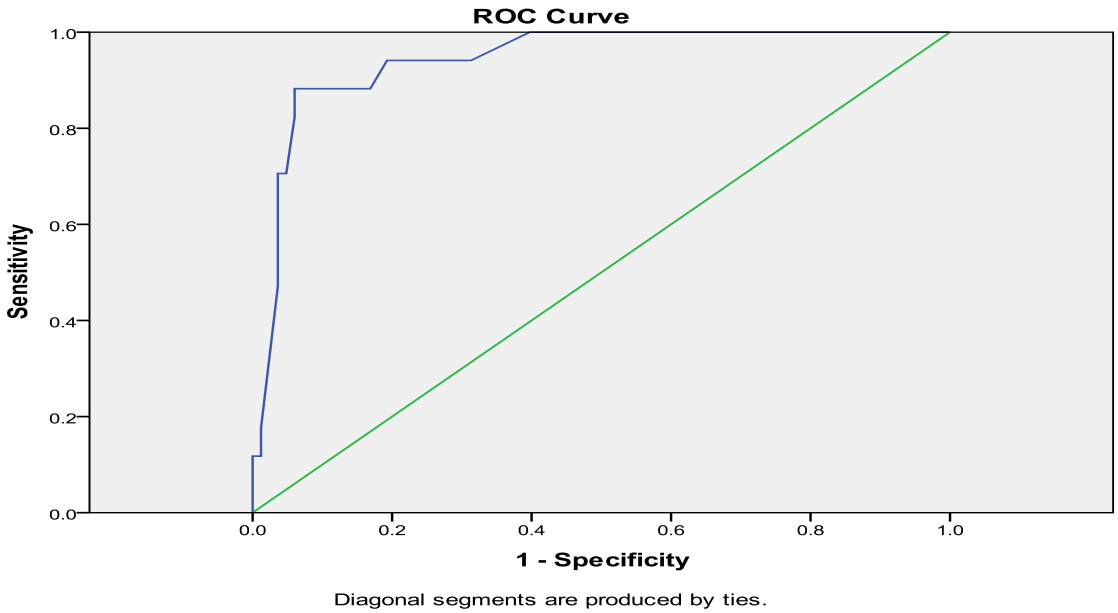

Figure 9. *ROC Curve for Serum Albumin in Predicting Mortality in CAP Patients*

Discussion

This study evaluated the prognostic utility of serum copeptin and serum albumin in assessing the severity and outcomes of community-acquired pneumonia (CAP). The findings suggest that copeptin is a highly sensitive and specific biomarker for predicting both disease severity and mortality, whereas hypoalbuminemia serves as a supportive but less specific indicator of poor prognosis.

Copeptin and Disease Severity

Serum copeptin levels increased significantly across PSI classes, rising from 11.63 ng/mL in PSI class 3 to 30.23 ng/mL in PSI class 5. This strong positive correlation underscores the biomarker's relevance in gauging disease severity. These observations are consistent with previous studies by Krüger et al., which demonstrated that copeptin levels were markedly elevated in patients with severe CAP and were associated with increased risk of ICU admission and mortality [1]. As a surrogate marker for arginine vasopressin, copeptin reflects physiological stress, hemodynamic instability, and systemic inflammation—hallmarks of severe pulmonary infection.

Further supporting its clinical value, ROC curve analysis revealed that a copeptin cutoff of 23.7 ng/mL predicted severe CAP with a sensitivity of 90.63% and specificity of 92.65%. These results align with findings by Katan et al., who reported that copeptin reliably stratified patients with lower respiratory tract infections by outcome risk [2].

Copeptin and Mortality Prediction

Non-survivors in the study exhibited significantly elevated copeptin levels (mean: 32.37 ng/mL) compared to survivors (mean: 18.46 ng/mL). A copeptin cutoff of 26.8 ng/mL predicted mortality with a sensitivity of 82.4% and specificity of 91.6%. These findings reinforce copeptin's potential as an early and objective prognostic marker—especially valuable in settings where traditional clinical scores may underestimate early decompensation.

Serum Albumin and CAP Outcomes

Serum albumin levels were inversely related to disease severity, decreasing progressively from 3.45 g/dL in PSI class 3 to 3.03 g/dL in PSI class 5. Non-survivors also had markedly lower albumin levels (2.56 g/dL) than survivors (3.39 g/dL). Albumin is a well-recognized negative acute-phase reactant, and its decline reflects the severity of systemic inflammation, increased catabolism, and capillary leak seen in severe infections. These findings are consistent with earlier studies linking hypoalbuminemia with adverse outcomes in CAP [3,4].

While albumin demonstrated only moderate diagnostic performance for predicting disease severity (sensitivity 65.63%, specificity 58.82%), its prognostic utility was more pronounced in predicting mortality. An albumin cutoff of 2.87 g/dL showed strong sensitivity (88.2%) and specificity (94%), indicating that significantly low albumin levels are associated with life-threatening illness.

Integration with Modified CURB-65

Emerging evidence supports the integration of biomarkers into existing clinical scoring tools to enhance prognostic accuracy. Modified versions of the CURB-65 score, incorporating markers such as copeptin or procalcitonin, have been shown to improve prediction of severe disease and mortality. For instance, biomarker-enhanced CURB-65 models have demonstrated superior stratification of high-risk patients, particularly those requiring ICU-level care [5]. Given the robust predictive performance of copeptin observed in this study, it may serve as a valuable addition to modified clinical algorithms and decision-making frameworks for CAP management.

Clinical Implications

The addition of copeptin and albumin measurement to traditional scoring systems like PSI and CURB-65 can significantly enhance early risk stratification. Copeptin, in particular, may help identify high-risk patients prior to clinical deterioration, allowing for timely ICU referral, closer monitoring, and aggressive therapeutic intervention. Albumin, while less specific, provides supportive prognostic information and may help identify patients at risk for prolonged recovery or poor nutritional and inflammatory status.

Limitations

This was a single-center study with a relatively small sample size (n = 100), which may limit the generalizability of the findings. Additionally, only baseline biomarker levels were assessed. Serial measurements could provide deeper insights into dynamic changes and prognostic trends. Finally, limited access to copeptin assays and associated costs may present challenges for widespread implementation, especially in resource-constrained settings.

Conclusion

This study underscores the clinical value of serum copeptin and albumin as biomarkers for assessing disease severity and predicting outcomes in community-acquired pneumonia (CAP). The cumulative use of serum copeptin and albumin has high specificity, sensitivity compared to an independent marker. Serum copeptin demonstrated a strong positive correlation with increasing disease severity and was significantly elevated in non-survivors, exhibiting high sensitivity and specificity for both severity and mortality prediction. These findings highlight copeptin's potential as a reliable early indicator of systemic stress and clinical deterioration. Serum albumin, although less specific, was consistently lower in patients with more severe illness and adverse outcomes, reflecting its role as an adjunctive marker of systemic inflammation and nutritional status. Both biomarkers were found to be independent of age and sex, supporting their applicability across diverse patient populations.

Incorporating copeptin and albumin into standard assessment tools such as PSI and CURB-65 may enhance early risk stratification, improve clinical decision-making, and guide the intensity of care required. Further large-scale, multicentric studies are warranted to validate these findings and explore the feasibility of integrating these biomarkers into routine CAP management protocols.

References

1. Jain S, Self WH, Wunderink RG, et al. Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults. *N Engl J Med.* 2015;373(5):415–427.
2. World Health Organization. The top 10 causes of death. WHO Fact Sheets. 2023.
3. Fine MJ, Auble TE, Yealy DM, et al. A Prediction Rule to Identify Low-Risk Patients with Community-Acquired Pneumonia. *N Engl J Med.* 1997;336:243–250.

4. Morgenthaler NG, Struck J, Alonso C, Bergmann A. Assay for the measurement of copeptin, a stable peptide derived from the precursor of vasopressin. *Clin Chem.* 2006;52(1):112–119.
5. Krüger S, Ewig S, Papassotiriou J, et al. Copeptin as a biomarker in acute lung diseases. *Eur Respir J.* 2008;32(3):597–604.
6. Katan M, Morgenthaler N, Widmer I, et al. Copeptin, a stable peptide derived from the vasopressin precursor, correlates with the individual stress level. *Neuro Endocrinol Lett.* 2008;29(3):341–346.
7. Lee JH, Park YS, Choi JS, et al. Hypoalbuminemia at admission predicts poor clinical outcomes in patients with community-acquired pneumonia. *J Crit Care.* 2011;26(2):181–186.
8. Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. *Semin Dial.* 2004;17(6):432–437.