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Original Research Article

Hypoalbuminemia as Predictor of Thrombotic Events in Patients with Community-Acquired Pneumonia

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Abstract

Introduction: Community-acquired pneumonia (CAP) remains a major cause of morbidity and mortality, particularly among older adults and those with comorbidities. While respiratory complications are well recognized, thrombotic events such as deep vein thrombosis (DVT), pulmonary embolism (PE), stroke, and myocardial infarction (MI) are increasingly acknowledged as significant contributors to adverse outcomes in CAP. Hypoalbuminemia, a common marker of disease severity and inflammation, has been proposed as a potential predictor of thrombotic risk, but remains underexplored in this context.

Materials and Method: This prospective observational study included 100 adult patients with CAP admitted to a tertiary care hospital. Patients were categorized based on serum albumin levels measured within 24 hours of admission into hypoalbuminemia (<3.5 g/dL) and normoalbuminemia (≥3.5 g/dL) groups. The primary outcome was the incidence of in-hospital thrombotic events. Secondary outcomes included length of hospital stay, ICU admission, and in-hospital mortality. Multivariate logistic regression was performed to identify independent predictors of thrombosis.

Results: Hypoalbuminemia was present in 58% of patients. Thrombotic events occurred in 24.1% of the hypoalbuminemic group compared to 9.5% in the normoalbuminemic group ($p = 0.047$). The hypoalbuminemia group also had a significantly longer hospital stay ($p = 0.002$) and higher ICU admission rate ($p = 0.031$). Multivariate analysis confirmed hypoalbuminemia as an independent predictor of thrombotic events (adjusted OR: 2.96; 95% CI: 1.01–8.68; $p = 0.048$).

Conclusion: Hypoalbuminemia is a significant and independent predictor of thrombotic complications in hospitalized CAP patients. Routine albumin measurement may aid in early risk stratification and guide thromboprophylactic strategies.

Keywords: Community-acquired pneumonia, hypoalbuminemia, thrombosis, serum albumin, thrombotic events, ICU admission, risk prediction.

Introduction

Community-acquired pneumonia (CAP) remains a significant public health concern, contributing extensively to global morbidity, mortality, and healthcare resource utilization. It is particularly prevalent among the elderly and individuals with chronic comorbidities, often leading to hospitalization and prolonged clinical recovery.

While the primary complications of CAP include respiratory failure and sepsis, increasing evidence has highlighted the risk of extrapulmonary manifestations, notably thrombotic events such as venous thromboembolism (VTE), pulmonary embolism (PE), ischemic stroke, and myocardial infarction. These complications substantially impact short- and long-term outcomes, further aggravating the disease burden associated with CAP [1]. One of the key biomarkers gaining clinical attention in this context is serum albumin, the most abundant plasma protein in the human body. Synthesized by hepatocytes, albumin serves multiple essential physiological functions: it maintains colloid osmotic pressure, buffers pH, transports endogenous and exogenous substances, scavenges oxygen free radicals, and exerts significant anti-inflammatory and antithrombotic effects [2].

The antithrombotic properties of albumin are attributed to its ability to bind antithrombin, inhibit platelet aggregation, and neutralize activated coagulation factors such as factor Xa [2,3]. Hypoalbuminemia, commonly defined as a serum albumin concentration below 3.5 g/dL, can develop

in a range of clinical settings including acute and chronic liver disease, malnutrition, nephrotic syndrome, sepsis, and systemic inflammation [2,4]. In acutely ill patients, hypoalbuminemia frequently reflects both impaired hepatic synthesis and increased capillary leakage, and is considered a marker of disease severity. In CAP, hypoalbuminemia has been independently associated with prolonged hospitalization, increased need for mechanical ventilation, ICU admission, and higher 30-day mortality [5–9].

Notably, a serum albumin level <30 g/L has been associated with a two-fold increase in mortality risk and thrombotic complications in acutely ill patients [3]. Recent studies have also explored the potential mechanistic role of hypoalbuminemia in promoting thrombotic complications. It is hypothesized that reduced albumin levels contribute to a prothrombotic state through multiple pathways: reduced oncotic pressure leading to hemoconcentration, diminished anticoagulant buffering capacity, endothelial dysfunction, and dysregulation of coagulation cascades [3].

In a multicenter observational study of hospitalized patients with CAP, the incidence of thrombotic events was significantly higher in those with hypoalbuminemia than in normoalbuminemic individuals (26 vs. 11 events per 1,000 patient-days), and the condition was independently associated with thrombotic risk (HR 3.19; 95% CI 1.48–6.89) [1]. Furthermore, inverse correlations between serum albumin levels and inflammatory/thrombotic markers such as C-reactive protein (CRP) and D-dimer have been demonstrated [3].

Although thrombotic risk is increasingly recognized in CAP, it remains underrepresented in existing prognostic scoring tools like CURB-65 and the Pneumonia Severity Index (PSI), which currently do not include serum albumin as a risk marker. Given the simplicity, cost-effectiveness, and accessibility of serum albumin testing, establishing hypoalbuminemia as a predictor of thrombotic complications could enable more effective risk stratification and targeted prophylaxis in CAP management [8].

Materials and Methods

This was a prospective observational study conducted at, a tertiary care teaching hospital A total of 100 adult patients admitted with community-acquired pneumonia (CAP) were enrolled consecutively during the study period, based on predefined inclusion and exclusion criteria.

Eligibility Criteria

Inclusion Criteria

- Age ≥18 years
- Clinical and radiological diagnosis of community-acquired pneumonia at the time of hospital admission
- Serum albumin levels measured within the first 24 hours of admission
- Availability of complete hospitalization records

Exclusion Criteria

- Hospital-acquired or ventilator-associated pneumonia
- Chronic liver disease, nephrotic syndrome, active malignancy
- Prior use of albumin infusion or long-term corticosteroids/immunosuppressants
- Patients discharged against medical advice or lost to follow-up

Data Collection: Baseline demographic details (age, sex), clinical presentation, comorbidities (e.g., diabetes, hypertension, chronic kidney disease), and laboratory parameters including serum albumin, CRP, D-dimer, hemogram, and coagulation profile were recorded at the time of admission. Serum albumin levels were measured using the bromocresol green method in the hospital's central clinical biochemistry laboratory.

Patients were categorized into two groups based on their serum albumin levels:

- **Hypoalbuminemia Group**: Albumin <3.5 g/dL
- **Normoalbuminemia Group**: Albumin ≥3.5 g/dL

All patients were monitored throughout their hospital stay for the development of thrombotic events, which included:

- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)
- Acute ischemic stroke
- Acute myocardial infarction (MI)

Diagnosis of thrombotic events was confirmed through standard diagnostic tools such as Doppler ultrasonography, CT pulmonary angiography, ECG with cardiac enzymes, and neuroimaging (CT/MRI), as appropriate.

Study Outcomes

Primary Outcome: Incidence of in-hospital thrombotic events in patients with hypoalbuminemia compared to normoalbuminemic patients.

Secondary Outcomes

- Length of hospital stay
- ICU admission requirement
- In-hospital mortality

Statistical Analysis: Data analysis was performed using SPSS version [21] (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), based on distribution. Categorical variables were summarized as frequencies and percentages. The Chi-square test or Fisher's exact test was used for comparison of categorical variables, and Student's t-test or Mann–Whitney U test was applied for continuous variables, as appropriate.

To evaluate the independent association between hypoalbuminemia and thrombotic events, multivariate logistic regression analysis was conducted. Variables with $p < 0.1$ in univariate analysis were included in the multivariate model. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A p-value < 0.05 was considered statistically significant.

Results

A total of 100 patients with community-acquired pneumonia were enrolled in the study. The mean age of the study population was 61.4 ± 15.2 years, with a male predominance (62%). Among these, 58 patients (58%) had hypoalbuminemia (serum albumin <3.5 g/dL), while 42 patients (42%) had normal serum albumin levels (≥3.5 g/dL). The mean serum albumin level in the hypoalbuminemia group was 2.9 ± 0.4 g/dL compared to 3.8 ± 0.3 g/dL in the normoalbuminemia group, which was statistically significant ($p < 0.001$). Although comorbidities such as diabetes mellitus and hypertension were more frequently observed in the hypoalbuminemia group, these differences were not statistically significant ($p = 0.342$ and $p = 0.761$, respectively). The two groups were comparable in terms of age and sex distribution. Out of the total 100 patients, 18 (18%) developed thrombotic complications during their hospital stay. These included cases of deep vein thrombosis (DVT), pulmonary embolism (PE), ischemic stroke, and myocardial infarction (MI). The incidence of thrombotic events was significantly higher in the hypoalbuminemia group, where 14 out of 58 patients (24.1%) developed thrombotic events, compared to only 4 out of 42 patients (9.5%) in the normoalbuminemia group ($p = 0.047$). Specific thrombotic events in the hypoalbuminemia group included 5 cases of DVT, 3 of PE, 4 of ischemic stroke, and 2 of MI, while the normoalbuminemia group had 2 cases of DVT, 1 of PE, and 1 of MI, with no reported strokes. Patients with hypoalbuminemia had a significantly longer mean hospital stay compared to those with normal albumin levels (10.2 ± 3.8 vs. 7.5 ± 2.6 days; $p = 0.002$). Additionally, ICU admission was more frequently required in the hypoalbuminemia group (27.6%) compared to the normoalbuminemia group (9.5%), with this difference reaching statistical significance ($p = 0.031$).

In-hospital mortality was higher in patients with hypoalbuminemia (13.8%) compared to those with normal albumin levels (4.8%), although this difference was not statistically significant ($p = 0.127$).A multivariate logistic regression analysis was performed to identify independent predictors of thrombotic events, adjusting for potential confounding variables such as age, sex, diabetes mellitus, and D-dimer levels. Hypoalbuminemia was found to be an independent predictor of thrombotic events during hospitalization, with an adjusted odds ratio (OR) of 2.96 (95% CI: 1.01–8.68; $p = 0.048$). Other variables, including age >65 years, diabetes mellitus, and elevated D-dimer levels (>500 ng/mL), were not found to be statistically significant predictors in the final model.

Table 1: Baseline Characteristics of the Study Population (N = 100)

Variable	Total (n = 100)	Hypoalbuminemia (n = 58)	Normoalbuminemia (n = 42)	p-value
Age (mean ± SD)	61.4 ± 15.2	63.1 ± 14.8	59.2 ± 15.7	0.173
Male sex (%)	62 (62%)	37 (63.8%)	25 (59.5%)	0.683
Diabetes mellitus (%)	41 (41%)	26 (44.8%)	15 (35.7%)	0.342
Hypertension (%)	47 (47%)	28 (48.3%)	19 (45.2%)	0.761
Serum albumin (g/dL)	—	2.9 ± 0.4	3.8 ± 0.3	<0.001***

Table 2: Incidence of Thrombotic Events and Secondary Outcomes

Outcome	Hypoalbuminemia (n = 58)	Normoalbuminemia (n = 42)	p-value
Any thrombotic event (%)	14 (24.1%)	4 (9.5%)	0.047*
• DVT	5	2	—
• PE	3	1	—
• Stroke	4	0	—
• MI	2	1	—
ICU admission (%)	16 (27.6%)	4 (9.5%)	0.031*
Length of stay (mean ± SD)	10.2 ± 3.8	7.5 ± 2.6	0.002**
In-hospital mortality (%)	8 (13.8%)	2 (4.8%)	0.127

Table 3: Multivariate Logistic Regression for Predictors of Thrombotic Events

Variable	Adjusted OR	95% CI	p-value
Hypoalbuminemia	2.96	1.01 – 8.68	0.048*
Age > 65 years	1.32	0.55 – 3.14	0.524
Diabetes mellitus	1.44	0.61 – 3.42	0.397
D-dimer > 500 ng/mL	2.08	0.89 – 4.84	0.091

Discussion

In the present study, hypoalbuminemia (serum albumin <3.5 g/dL) was noted in 58% of hospitalized CAP patients, with a significantly lower mean albumin level in the hypoalbuminemic group (2.9 ± 0.4 g/dL) compared to the normoalbuminemic group (3.8 ± 0.3 g/dL, $p < 0.001$). This is consistent with findings by Hedlund et al. (1995) [8], who reported hypoalbuminemia in 43% of CAP admissions and demonstrated that it was associated with more severe disease and slower recovery. Similarly, Herrmann et al. (1992) [10] found that patients with serum albumin <3.5 g/dL had significantly higher mortality and longer hospital stays. Our study population had a mean age of 61.4 years, with 62% being male—comparable to study's in studies like Lim et al. (2003) [11] and Falcone et al. (2011) [12], which evaluated disease severity and predictors of outcome in CAP. The high prevalence of hypoalbuminemia in our study supports the hypothesis by Levitt and Levitt (2016) [13], who suggested that systemic inflammation impairs hepatic albumin synthesis and increases vascular leakage, leading to reduced serum levels during acute illness. Our study found that 18% of CAP patients developed thrombotic events, with significantly more events in the hypoalbuminemia group (24.1%) than in the normoalbuminemia group (9.5%, $p = 0.047$). This parallels the findings of Valeriani et al. (2024) [14], who reported thrombotic events in 18.6% of hypoalbuminemic patients vs. 8.5% of normoalbuminemic ones in a study of 231 CAP cases, with a hazard ratio of 3.19 (95% CI: 1.48–6.89) for thrombosis in those with albumin <3.5 g/dL.In our study, the events included DVT, PE, ischemic stroke, and MI. Cangemi et al. (2014) [15] demonstrated that 15% of CAP patients experienced myocardial infarction, with platelet activation playing a major role. Similarly, Violi et al. (2017) [16] found 11% of CAP patients developed cardiovascular events, and that hypoalbuminemia increased this risk. Our findings also support Loffredo et al. (2016) [17], who reported endothelial dysfunction and impaired vascular reactivity in CAP patients with low serum albumin.

We observed longer hospital stays among hypoalbuminemic patients (10.2 ± 3.8 vs. 7.5 ± 2.6 days, $p = 0.002$), and more frequent ICU admissions (27.6% vs. 9.5%, $p = 0.031$). These findings mirror those of Herrmann et al. (1992) [10], who showed that low serum albumin predicted longer length of stay and poorer clinical outcomes. In-hospital mortality was also higher in the hypoalbuminemia group (13.8%) compared to the normoalbuminemia group (4.8%), although this difference was not statistically significant ($p = 0.127$). Violi et al. (2017) [16], however, reported a significantly increased short-term mortality in hypoalbuminemic CAP patients (18% vs. 9%, $p < 0.01$), reinforcing the adverse prognostic implications. Multivariate analysis in our study revealed that hypoalbuminemia independently predicted thrombotic events, with an adjusted odds ratio of 2.96 (95% CI: 1.01–8.68; $p = 0.048$). This supports the results of Chi et al. (2019) [18], who analyzed acutely ill patients in the APEX trial and reported a doubling of VTE risk in the lowest serum albumin quartile (adjusted OR: 2.02; 95% CI: 1.49–2.73).Other predictors in our model, such as age >65 years (OR: 1.32), diabetes (OR: 1.44), and D-dimer >500 ng/mL (OR: 2.08), did not reach statistical significance, which may be due to our smaller sample size. Ay et al. (2015) [19] similarly noted that competing risks may obscure traditional predictors and emphasized the importance of incorporating biomarkers into VTE risk models. The findings reinforce the mechanistic insights proposed by Violi et al. (2017) [16] and Loffredo et al. (2016) [19], who linked hypoalbuminemia with platelet activation, impaired endothelial function, and thrombo-inflammation. Moshage et al. (1987) [21] previously described how systemic inflammation downregulates albumin synthesis, further linking inflammation to thrombotic predisposition.

Conclusion

This prospective observational study demonstrated that hypoalbuminemia is an independent predictor of thrombotic complications in patients hospitalized with community-acquired pneumonia. It was associated with higher rates of thrombotic events, prolonged hospital stay, and increased ICU admissions. Multivariate analysis confirmed its role as a risk factor, suggesting that routine serum albumin measurement—a simple and cost-effective test—can aid in early identification of high-risk patients. Incorporating albumin into prognostic models may guide timely thromboprophylaxis and improve outcomes. Further large-scale studies are needed to validate these findings and standardize albumin-guided risk assessment in CAP.

Limitations of the Study: This study was limited by its single-centre setting and relatively small sample size, which may restrict generalizability. Its observational design prevents establishing causality. Albumin levels were assessed only at admission, and serial measurements could have provided additional insights. Although confounders were adjusted, unmeasured variables such as nutrition, liver function, and medication use may still have influenced results. Moreover, thrombotic events were evaluated only during hospitalisation, without long-term follow-up, possibly underestimating their true incidence. Multicenter studies with larger cohorts and extended follow-up are warranted.

References

1. Cangemi R, Calvieri C, Falcone M, Cipollone F, Ceccarelli G, Pignatelli P, et al. Comparison of thrombotic events and mortality in patients with community-acquired pneumonia and COVID-19: a multicenter observational study. Thromb Haemost. 2022;122:257–266.
2. Gatta A, Verardo A, Bolognesi M. Hypoalbuminemia. Intern Emerg Med. 2012;7(Suppl 3):S193–S199.
3. Violi F, Novella A, Pignatelli P, Castellani V, Tettamanti M, Mannucci PM, et al. Low serum albumin is associated with mortality and arterial and venous ischemic events in acutely ill medical patients: Results of a retrospective observational study. Thromb Res. 2023;225:1–10.
4. Weaving G, Batstone GF, Jones RG. Age and sex variation in serum albumin concentration: an observational study. Ann Clin Biochem. 2016;53:106–111.
5. Cao Y, Su Y, Guo C, He L, Ding N. Albumin level is associated with short-term and long-term outcomes in sepsis patients admitted in the ICU: a large public database retrospective research. Clin Epidemiol. 2023;15:263–273.
6. Takegawa R, Kabata D, Shimizu K, Hisano S, Ogura H, Shintani A, et al. Serum albumin as a risk factor for death in patients with prolonged sepsis: an observational study. J Crit Care. 2019;51:139–144.
7. Hu J, Lv C, Hu X, Liu J. Effect of hypoproteinemia on the mortality of sepsis patients in the ICU: a retrospective study study. Sci Rep. 2021;11:24379.
8. Hedlund JU, Hansson LO, Ortqvist AB. Hypoalbuminemia in hospitalized patients with community-acquired pneumonia. Arch Intern Med. 1995;155:1438–1442.
9. Cangemi R, Carnevale R, Nocella C, Calvieri C, Bartimoccia S, Frati G, et al. Low-grade endotoxemia is associated with cardiovascular events in community-acquired pneumonia. J Infect. 2024;88(2):89–94.
10. Herrmann FR, Safran C, Levkoff SE, Minaker KL. Serum albumin level on admission as a predictor of death, length of stay, and readmission. Arch Intern Med. 1992;152(1):125–30.
11. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax. 2003;58(5):377–82.
12. Falcone M, Venditti M, Shindo Y, Kollef MH. Healthcare-associated pneumonia: diagnostic criteria and distinction from community-acquired pneumonia. Int J Infect Dis. 2011;15(8):e545–50.
13. Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. Int J Gen Med. 2016;9:229–55.
14. Valeriani E, Cangemi R, Carnevale R, Romiti GF, Pannunzio A, Pignatelli P, Violi F. Hypoalbuminemia as predictor of thrombotic events in patients with community-acquired pneumonia. Int J Cardiol. 2024;404:131942. doi:10.1016/j.ijcard.2024.131942
15. Cangemi R, Casciaro M, Rossi E, Calvieri C, Bucci T, Calabrese CM, et al. Platelet activation is associated with myocardial infarction in patients with pneumonia. J Am Coll Cardiol. 2014;64(18):1917–25.
16. Violi F, Cangemi R, Falcone M, Taliani G, Pieralli F, Vannucchi V, et al. Cardiovascular complications and short-term mortality risk in community-acquired pneumonia. Clin Infect Dis. 2017;64(11):1486–93.
17. Loffredo L, Cangemi R, Perri L, Catasca E, Calvieri C, Carnevale R, et al. Impaired flow-mediated dilation in hospitalized patients with community-acquired pneumonia. Eur J Intern Med. 2016;36:74–80.
18. Chi G, Gibson CM, Liu Y, Hernandez AF, Hull RD, Cohen AT, et al. Inverse relationship of serum albumin to the risk of venous thromboembolism among acutely ill hospitalized patients: analysis from the APEX trial. Am J Hematol. 2019;94(1):21–8.
19. Ay C, Posch F, Kaider A, Zielinski C, Pabinger I. Estimating risk of venous thromboembolism in patients with cancer in the presence of competing mortality. J Thromb Haemost. 2015;13(3):390–7.
20. Moshage HJ, Janssen JA, Franssen JH, Hafkenscheid JC, Yap SH. Study of the molecular mechanism of decreased liver synthesis of albumin in inflammation. J Clin Invest. 1987;79(6):1635–41.