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C- Reactive Protein to Serum Albumin Ratio as Prognostic Factor in Hospitalized Elderly Patients with Community-Acquired Pneumonia at Tertiary Care Institute of Northern India

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KEYWORDS

C-reactive protein, albumin, CRP/albumin ratio, community-acquired pneumonia, elderly, CURB-65, prognostic marker, inflammation, risk stratification

ABSTRACT:

Background: Community-acquired pneumonia (CAP) is a major cause of morbidity and mortality among the elderly. Early identification of prognostic markers is essential for improving clinical outcomes. The C-reactive protein to albumin ratio (CAR) has emerged as a potential marker reflecting both inflammation and nutritional status.

Objectives: To evaluate the prognostic value of CAR and compare it with the CURB-65 score in predicting clinical outcomes among elderly patients hospitalized with CAP.

Methods: This prospective observational study included 100 elderly patients (>65 years) with CAP. Clinical and laboratory parameters, including CRP, serum albumin, complete blood count, and CURB-65 score, were recorded on admission (Day 1) and on Day 7. Patients were categorized into "symptom resolved" and "symptom unresolved" groups based on clinical assessment at Day 7. The association of CAR and other hematological parameters with clinical outcomes was analyzed using univariate and multivariate analysis. Receiver operating characteristic (ROC) curves were constructed to compare the prognostic accuracy of CAR and CURB-65.

Results: The mean CAR decreased significantly from Day 1 to Day 7 in patients whose symptoms resolved ($p < 0.0001$). Patients in the symptom unresolved group had significantly higher CAR, total leukocyte count, and neutrophil percentage, and lower lymphocyte percentage and hemoglobin levels compared to those with resolved symptoms. ROC analysis showed CAR had superior prognostic accuracy (AUC = 0.828) compared to CURB-65 (AUC = 0.722). Multivariate analysis identified CAR,

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red cell distribution width (RDW), hemoglobin, neutrophil percentage, and lymphocyte percentage as significant independent predictors of symptom resolution.

Conclusion:
The CRP to albumin ratio is a reliable and accessible prognostic marker in elderly patients with CAP. It outperforms the CURB-65 score in predicting symptom resolution and can serve as a valuable tool for early risk stratification and personalized management in geriatric care settings.

INTRODUCTION

Community-acquired pneumonia (CAP) remains a leading cause of morbidity and mortality among the elderly population worldwide, particularly in low- and middle-income countries like India [1,2]. With aging, individuals become more susceptible to infections due to immunosenescence, the presence of multiple comorbidities, and reduced physiological reserve, making pneumonia a serious threat in this group [3,4]. Elderly patients with CAP often present with atypical features, which may delay diagnosis and appropriate treatment, further contributing to adverse outcomes [5].

Prognostic tools such as the CURB-65 score, which incorporates confusion, urea level, respiratory rate, blood pressure, and age ≥65 years, have been commonly employed to stratify severity and guide clinical decisions in CAP [6]. However, these tools, while helpful, may not fully capture the dynamic inflammatory and nutritional status of elderly patients, which are crucial determinants of disease outcome [7].

C-Reactive Protein (CRP) is a widely recognized acute-phase reactant synthesized by the liver in response to systemic inflammation, particularly bacterial infections [8]. Elevated CRP levels are often correlated with the severity of CAP and adverse clinical outcomes [9]. Conversely, serum albumin, a negative acute-phase reactant, reflects both nutritional status and systemic inflammation. Hypoalbuminemia has been independently associated with prolonged hospitalization, complications, and mortality in pneumonia [10,11].

The CRP to albumin ratio (CAR) has emerged as a novel composite biomarker combining the prognostic utility of both inflammation (CRP) and nutritional status (albumin). Studies have shown that CAR may serve as a more robust indicator of disease severity, prognosis, and treatment response in various inflammatory and infectious conditions, including sepsis, malignancy, and COVID-19 [12–14]. However, limited data exist regarding its utility in elderly patients with community-acquired pneumonia, particularly in the Indian population.

Given the growing burden of CAP in the aging population and the need for accessible, reliable prognostic markers, this study aimed to evaluate the CRP to albumin ratio as a prognostic indicator in hospitalized elderly patients with CAP. The study also sought to correlate CAR with clinical outcomes, compare it with the CURB-65 score, and analyze its relationship with other inflammatory and hematological markers.

MATERIALS AND METHODS

Study Design and Setting

This prospective follow-up study was conducted at the Department of Medicine, Integral Institute of Medical Sciences and Research (IIMSR), Lucknow. The study population comprised patients aged more than 60 years, admitted with a diagnosis of community-acquired pneumonia (CAP).

Study Duration

The total duration of the study was 18 months, comprising 12 months for data collection and 6 months for data analysis.

Sample Size Calculation

The sample size was calculated using the standard formula for estimating a proportion in a population:

n=Z2×p(1−p)d2n = \frac{Z^2 \times p (1 - p)}{d^2}n=d2Z2×p(1−p)

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Where:

- n = required sample size
- Z = Z-score corresponding to 95% confidence level (1.96)
- p = estimated population proportion (0.5)
- d = margin of error (0.08)

n=(1.96)2×0.5×(1−0.5)(0.08)2=3.8416×0.250.0064=0.96040.0064=150.0625n = \frac{(1.96)^2 \times 0.5 \times (1 - 0.5)}{(0.08)^2} = \frac{3.8416 \times 0.25}{0.0064} = \frac{0.9604}{0.0064} = 150.0625n=(0.08)2(1.96)2×0.5×(1−0.5) =0.00643.8416×0.25=0.00640.9604=150.0625

Adjusting for a non-response rate of 20%:

Final Sample Size=150×(1+0.20)=180\text{Final Sample Size} = 150 \times (1 + 0.20) = 180Final Sample Size=150×(1+0.20)=180

Study Participants

A total of 180 patients fulfilling the inclusion and exclusion criteria were enrolled.

Inclusion Criteria

- Age > 60 years.
- Clinical features of CAP, including at least one respiratory symptom (cough, expectoration, dyspnea, tachypnea, or pleuritic chest pain).
- Presence of at least one of the following: auscultatory findings suggestive of pneumonia or signs of infection (WBC >11×10⁹/L or <4×10⁹/L, or core body temperature >37.7°C).
- Radiological evidence of new infiltrates on chest X-ray.

Exclusion Criteria

Patients with comorbid conditions or diseases that could affect serum albumin or C-reactive protein (CRP) levels were excluded:

- Congestive heart failure (NYHA Class III or IV).
- Chronic kidney disease (creatinine clearance <30 mL/min).
- Severe dehydration, ascites, anasarca, or liver cirrhosis.
- Proteinuria ≥ 2+ or ≥ 300 mg/24 hours.
- Autoimmune diseases with/without immunosuppressive therapy.
- Terminal stage malignancy.
- Acute myocardial infarction.

Clinical Evaluation

All patients underwent detailed clinical history-taking and examination to identify any coexisting illnesses and to rule out conditions meeting exclusion criteria.

Laboratory Investigations

- C-Reactive Protein (CRP): Quantified using Particle-Enhanced Turbidimetric Immunoassay (PETIA) in the Biochemistry section of the Central Clinical Laboratory, IIMSR, Lucknow.
- Serum Albumin: Measured by the bromocresol green dye-binding method in the same laboratory.

CRP and serum albumin were measured on Day 1 (admission), Day 3, and Day 7 of hospitalization. A decrease in serum albumin level >10% from baseline was considered significant.

Outcome Assessment

Clinical progression or resolution of pneumonia was assessed on Day 7 or at the time of discharge.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The following statistical methods were employed:

- Student's t-test: To compare means between two groups.

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- Spearman Correlation: To assess the correlation between non-parametric variables.
- Regression Analysis: To determine predictive factors associated with outcomes.
- Sensitivity and Specificity: Calculated where applicable.

A p-value <0.05 was considered statistically significant, with the following thresholds for interpretation:

- $p > 0.05$: Not significant
- $p < 0.05$: Significant
- $p < 0.01$: Highly significant
- $p < 0.001$: Very highly significant

RESULTS AND OBSERVATIONS;

Table 1: Demographic Characteristics of the Study Population

Age Mean (S.D.)	65.22±4.44	
Gender	Number	Percentage
- Female	92	51.11%
- Male	88	48.89%

The mean age of the study population was 65.22 years with a standard deviation of 4.44 years, indicating that most participants were in the early elderly age group. The gender distribution was nearly equal, with females comprising 51.11% (n=92) and males 48.89% (n=88) of the total sample, suggesting a balanced representation of both sexes.

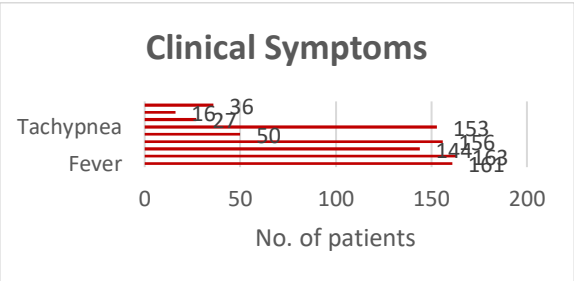

Figure 1: Graphical representation of Clinical Symptoms Among the Study Population

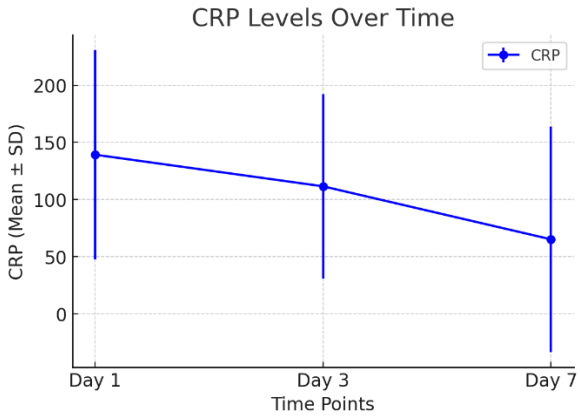

Figure: 2 Graphical representations of Trend of C-Reactive Protein (mg/L) Levels Over Time

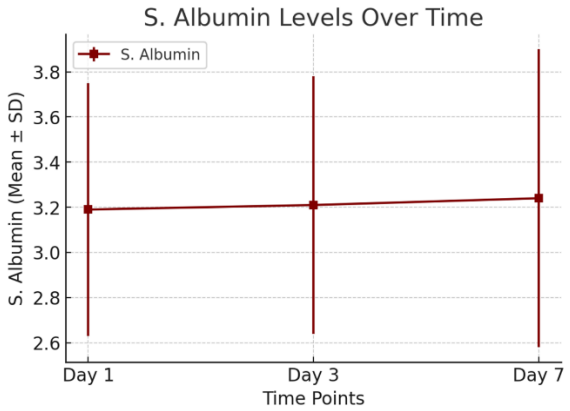

Figure: 3 Graphical representations of Serial Measurement of Serum Albumin (g/dL) on Day 1, Day 3, and Day 7

Table 5: Serial Measurement of Serum C-Reactive Protein to Serum Albumin Ratio on Day 1, Day 3, and Day 7

S.C- reactive protein to serum albumin ratio	Mean ± SD
DAY1	47.17±35.34
DAY3	39.00±34.31
DAY7	26.97±44.30

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The C- reactive protein to serum albumin ratio demonstrated a declining trend from Day 1 to Day 7, indicating a potential improvement in the inflammatory and nutritional status of the patients over time. On Day 1, the mean ratio was 47.17 ± 35.34, reflecting a high inflammatory burden relative to the nutritional reserve at admission. By Day 3, the ratio decreased to 39.00 ± 34.31, and further dropped to 26.97 ± 44.30 by Day 7.

Table 3: Baseline Hematological and Biochemical Blood Parameters of the Study Population

Blood Parameters	Mean ± SD
RDW (%)	14.24±2.5
S. UREA (mg/dl)	46.29±27.97
HEMOGLOBIN (g/dl)	10.37±1.76
Total Leucocyte Count (cells/mm³)	15832.78±5537.96
Neutrophil (%)	82.06±9.87
Lymphocytes (%)	15.06±10.62
Neutrophil to Lymphocytes Ratio	10.26±9.84
Platelet's count (lakh/mm³)	2.12±0.87

Table 4: Vital Signs and Physical Examination Findings at Presentation

Vital Signs and Physical Examination	Mean ± SD
Heart Rate (bpm)	100.41±20.36
Systolic Blood Pressure (mmHg)	111.74±20.45
Diastolic Blood Pressure (mmHg)	70.29±10.95
Temperature (°F)	99.45±1.59
Respiratory Rate (per minute)	23.84±5.60

Table:5 CURB-65 Score Distribution, Mortality Risk, and Symptom Resolution Status Among the Study Population

CURB-65 Score	Predicted Mortality	n (Patients)	% of Total Patients	Symptoms Resolved (n)	Symptoms Not Resolved (n)
0 or 1	1.5%	85	47.22%	76	9
2	9.2%	73	40.56%	48	25
≥3	22%	22	12.22%	6	16
Total	—	180	100%	130 (72.22%)	50 (27.78%)

Table:6 Comparison of CRP, Serum Albumin, and CRP/Albumin Ratio Between Patients With and Without Symptom Resolution

Parameter	Day	Symptoms Not Resolved (Mean ± SD)	Symptoms Resolved (Mean ± SD)	t-value	p-value	Significance

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C-Reactive Protein (mg/L)	Day 1	181.04 ± 106.53	108.68 ± 61.22	4.524	<0.0001	Very Highly Significant
	Day 3	200.78 ± 72.41	77.29 ± 52.87	7.544	<0.0054	Highly Significant
	Day 7	201.84 ± 94.73	12.65 ± 10.55	10.872	0.0031	Very Highly Significant
Serum Albumin (g/dL)	Day 1	2.62 ± 0.40	3.42 ± 0.44	7.369	<0.0001	Very Highly Significant
	Day 3	2.55 ± 0.35	3.46 ± 0.42	9.117	0.0001	Very Highly Significant
	Day 7	2.37 ± 0.28	3.57 ± 0.40	13.461	0.0061	Very Highly Significant
CRP to Albumin Ratio	Day 1	71.63 ± 42.96	32.08 ± 17.19	6.318	<0.0001	Very Highly Significant
	Day 3	81.47 ± 33.61	22.66 ± 15.36	8.717	0.0021	Very Highly Significant
	Day 7	87.68 ± 43.99	3.62 ± 3.16	10.439	0.0031	Very Highly Significant

Table: 7 Comparison of Hematological Parameters and CURB-65 Score Between Patients With and Without Symptom Resolution

Parameter	Symptoms Not Resolved (Mean ± SD)	Symptoms Resolved (Mean ± SD)	t-value	p-value	Significance
Red Cell Distribution Width (%)	15.06 ± 2.05	13.92 ± 2.59	1.89	0.014	Significant
Serum Urea (mg/dL)	65.72 ± 32.20	38.82 ± 22.11	3.772	0.0011	Very Highly Significant
Hemoglobin (g/dL)	9.21 ± 2.18	10.82 ± 1.32	3.46	0.001	Very Highly Significant
Total Leucocyte Count (cells/mm³)	20878.00 ± 5067.43	13892.31 ± 4375.12	5.715	0.0111	Highly Significant
Neutrophil	87.32 ± 6.28	80.03 ± 10.27	3.317	0.002	Very Highly

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Parameter	Symptoms Not Resolved (Mean ± SD)	Symptoms Resolved (Mean ± SD)	t-value	p-value	Significance
(%)					Significant
Lymphocyte (%)	8.56 ± 6.25	17.55 ± 10.90	3.919	0.0061	Very Highly Significant
Neutrophil to Lymphocyte Ratio	15.74 ± 11.59	8.15 ± 8.19	2.929	0.005	Highly Significant
Platelet Count (lakh/mm³)	1.91 ± 0.95	2.20 ± 0.83	1.259	0.213	Not Significant
CURB-65 Prognostic Score	2.26 ± 1.29	1.40 ± 0.70	3.209	0.002	Very Highly Significant

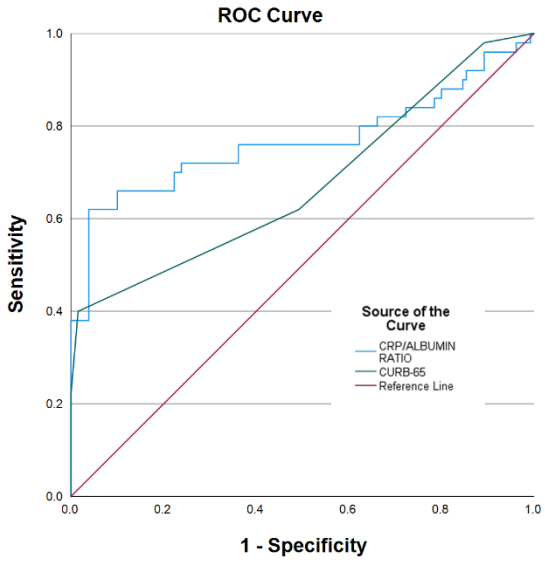

Figure: 4 Graphical representations of ROC Analysis of CRP/Serum Albumin Ratio and CURB-65 Score for Predicting Symptom Resolution

Table; 8 Regression analysis for the predictor of Resolved symptoms with C- reactive protein to Serum Albumin ratio and other inflammatory marker

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1[a]	C- reactive protein	.328	.092	12.702	1	.001	1.388

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C- reactive protein to Serum Albumin ratio	-.930	.255	13.273	1	.001	.394
Red Cell Distribution Width (RDW)	1.173	.403	8.492	1	.004	3.233
Hemoglobin	1.047	.388	7.295	1	.007	2.848
Total Leucocyte Count	.000	.000	.727	1	.394	1.000
Neutrophil	.984	.330	8.887	1	.003	2.675
Lymphocytes	1.106	.348	10.097	1	.001	3.023
Neutrophil To Lymphocyte Ratio	.085	.061	1.944	1	.163	1.089
Platelet Count	1.110	.638	3.026	1	.082	3.034
Constant	123.700	39.616	9.750	1	.002	.000

Table 9: Spearman correlation of resolved symptoms with CURB-65, C- C-reactive protein to Serum Albumin ratio, and other inflammatory markers

	Spearman's rho	Significance (2-tailed)	95% Confidence Intervals (2-tailed)	
			Lower	Upper
C C-reactive protein Albumin ratio	-.553	<.001*	-.647	-.442
CURB-65	-.395	<.001*	-.511	-.264
Red cell distribution width (RDW)	-.205	.006*	-.341	-.061
Hemoglobin	.414	<.001*	.285	.528
Total leucocyte Count	-.567	<.001*	-.658	-.458
Neutrophil	-.332	<.001*	-.456	-.195
Lymphocytes	.381	<.001*	.248	.499

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Neutrophil to lymphocyte ratio	-.347	<.001*	-.469	-.211
Platelet count	.146	.050	.000	.286

A strong negative correlation was observed between the C- C-reactive protein to Serum Albumin ratio and symptom resolution ($\rho = -0.553$, $p<0.001$), indicating that higher ratios are associated with poorer outcomes. Similarly, the total leukocyte count ($\rho = -0.567$, $p<0.001$) and CURB-65 score ($\rho = -0.395$, $p<0.001$) also showed significant negative correlations, suggesting that increased systemic inflammation and higher severity scores are linked to delayed recovery.

Other markers like neutrophil percentage ($\rho = -0.332$, $p<0.001$), neutrophil-to-lymphocyte ratio ($\rho = -0.347$, $p<0.001$), and RDW ($\rho = -0.205$, $p=0.006$) also had significant negative correlations with symptom resolution, though to a lesser extent.

On the other hand, hemoglobin ($\rho = 0.414$, $p<0.001$) and lymphocyte percentage ($\rho = 0.381$, $p<0.001$) demonstrated moderate positive correlations, implying that higher hemoglobin levels and a better lymphocyte response are associated with improved clinical outcomes. Platelet count showed a weak positive correlation ($\rho = 0.146$, $p=0.050$), at the threshold of significance.

DISCUSSION

Community-acquired pneumonia (CAP) remains a leading cause of morbidity and mortality among the elderly population worldwide. Prognostic markers that can aid in risk stratification and guide therapeutic decisions are crucial for improving clinical outcomes in this vulnerable group [1]. In the present study, we evaluated the prognostic value of the C-reactive protein (CRP) to serum albumin ratio (CAR) in elderly patients admitted with CAP.

Our findings demonstrate a significant decline in the CRP to albumin ratio from Day 1 to Day 7 among patients who showed symptom resolution. The ratio was significantly higher in patients with unresolved symptoms compared to those who recovered. These results are consistent with previous studies, which have established that elevated CAR values are associated with increased inflammatory burden and poor prognosis in various infections, including CAP [2,3].

CRP is a well-established acute-phase reactant synthesized by the liver in response to inflammation, infection, or tissue injury, and its levels increase rapidly during the early phase of infection [4]. In contrast, serum albumin is a negative acute-phase protein whose synthesis decreases during systemic inflammation, reflecting both the nutritional and inflammatory status of the patient [5]. The CAR, as a combined marker, thus serves as a more reliable prognostic tool than either parameter alone.

Several studies have validated the clinical utility of CAR in predicting outcomes in pneumonia. A retrospective study by Ranzani et al. reported that higher CAR values on admission were associated with increased severity of pneumonia and longer hospital stays [6]. Similarly, Lee et al. found that CAR was an independent predictor of 30-day mortality in patients with CAP [7]. Our findings align with these reports, underscoring the relevance of CAR as a prognostic biomarker.

The CURB-65 score, widely used for pneumonia severity assessment, also showed significant correlation with symptom resolution in our study. However, ROC curve analysis revealed that the CAR had superior predictive ability compared to CURB-65 in determining symptom resolution. This suggests that CAR may be a more sensitive indicator of disease trajectory, particularly in the elderly, where atypical presentations may undermine clinical scoring systems [8].

Furthermore, our study highlights the significance of other hematological parameters, such as neutrophil-to-lymphocyte ratio (NLR), hemoglobin levels, and RDW, in influencing outcomes. Elevated NLR and total leukocyte counts were significantly associated with unresolved symptoms, corroborating previous findings that link systemic inflammation to poorer prognosis [9]. Conversely, higher lymphocyte percentages and

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hemoglobin levels showed positive correlations with recovery, likely reflecting better immune competence and oxygen-carrying capacity, respectively [10,11].

Multivariate regression analysis identified the CRP/albumin ratio, RDW, hemoglobin, neutrophil percentage, and lymphocyte percentage as significant independent predictors of symptom resolution. These findings suggest that an integrative approach using both inflammatory and hematologic markers can provide a more comprehensive assessment of disease severity in elderly CAP patients.

Despite the strengths of our study, including its prospective design and serial measurements, it has some limitations. Being a single-center study may limit the generalizability of results. Additionally, long-term outcomes beyond discharge were not evaluated.

CONCLUSION;

The CRP to serum albumin ratio is a valuable, cost-effective, and easily accessible biomarker that can help predict clinical outcomes in elderly patients with community-acquired pneumonia. Incorporating CAR into routine assessment protocols, alongside established tools like CURB-65, could enhance early risk stratification and optimize management strategies in this high-risk population

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