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Original article

Serum Albumin And C-reactive Protein as Prognostic Biomarkers in Hospitalised Patients with Community Acquired Pneumonia

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Abstract

Background: Pneumonia is an infection of the pulmonary parenchyma, causing significant morbidity and mortality. Inflammation potentiates hypoalbuminemia. CRP is an acute phase reactant produced by the liver in response to inflammation, which depends on severity of illness. Serum albumin concentration as a negative acute phase reactant, changes with change in CRP(C-reactive protein) value. ***Objectives:*** To study the prognostic significance of commonly used biomarkers serum Albumin level and C - reactive protein in hospitalized patients with Community Acquired Pneumonia. ***Methodology:*** The prospective study was conducted in a hospital affiliated to Vijayanagara Institute of Medical Science, Ballari. Patients with signs and symptoms of CAP were hospitalized based on a CURB-65 score. After informed consent, all relevant data was collected. Clinical examination and laboratory parameters i.e. Serum albumin & C - reactive protein levels on day 1, 3 & 7/discharge were carried out. The values of serum albumin & C - reactive protein were analyzed with the clinical profile and outcome in these study groups. ***Results:*** In our study, CAP was more commonly seen among the age group of 61-70 yrs (27%). COPD was a major associated co-morbidity (50%) and smoking was an important risk factor (70%). The majority had a CURB 65 score of >3-5 on admission (64%). Out of 50 patients, 26% of them had severe hypoalbuminemia (<2.5 mg/dl) and 58% of them had mild hypoalbuminemia (2.5-3.5 mg/dl) on day 1 of admission. When serum albumin levels at the time of admission were analyzed for the time of discharge, there was significant change (P=0.025) noted, i.e an increase in serum albumin levels were seen in all patients who had clinical signs of resolution. 38% of patients had serum CRP levels <100 mg/l and 40 % had 101-200 mg/l and 22% of them had levels > 200 mg/l. There was decrease in CRP level at the time of discharge (p=0.001). Serum Albumin levels and CRP levels showed significant change from day 1 to the day of discharge (p=0.025 and P=<0.001) respectively. ICU requirement, need for mechanical ventilation and other outcomes correlated well with serum albumin levels (p=0.021, p=0.004, p=0.003 respectively). ***Conclusion:*** Our study showed a history of smoking, COPD and hypoalbuminemia at presentation were major risk factors present for CAP. Patients with severe hypoalbuminemia had high morbidity and mortality in the form of ICU requirement, need for mechanical ventilation, complications and death. CRP serves as an important marker of inflammation whose series levels reduce significantly with cure / resolution of pneumonia. Thus, serum albumin levels and C reactive protein can be used as a prognostic biomarker in community acquired pneumonia.

Keywords: ***Community Acquired Pneumonia, Prognostic markers, Serum Albumin, C-reactive protein.***

Introduction

"Pneumonia" is a Greek word meaning "lungs". Pneumonia is defined as an inflammation of the alveoli, distal airways and interstitium of the lungs [1].

Community acquired pneumonia (CAP) is a common life-threatening infectious disease and remains a common and persistent cause of morbidity and mortality,[2] accounting for nearly 1% of all medical admissions [3]. According to WHO statistics, deaths per 100,000 population in 2004 due to LRTI in India was 89.5, while it was 62.0 in UK [4].

There are many factors which aid in assessing the severity of CAP, like CURB-65 SCORE (i.e. presence of confusion, raised urea, increased respiratory rate, reduced blood pressure and age factor). Although it has been extensively validated and is simple to use, the CURB-65 score has limitations, which forces a clinician to look for an additional severity assessment scale that adds additional sensitivity. It is poor at detecting the need for intensive care, with only 51% of patients requiring admission to intensive care units having CURB-65-defined severe disease (a score of 3+) [5]. In addition, 20% of deaths occur in patients with CURB-65 scores of 2 or lower, and there was a mortality of 8% in the BTS audit for patients with a score of 2.5 Consequently, additional prognostic rules (eg the Infectious Diseases Society of America/ American Thoracic Society (IDSA/ATS) minor criteria and SMART-COP) have been designed, but as yet do not have the simplicity and proven validity of the CURB-65 score. Additional clinical indicators of severe disease, such as bilateral or multilobar consolidation, positive blood cultures, acidosis, hypoalbuminaemia and hypoxia, should be used to support risk stratification by CURB-65 [6]. Numerous biomarkers have also been tested for their utility in improving risk stratification of patients with CAP, including C-reactive protein (CRP), pro-calcitonin (PCT), cytokines and several stress hormones [7]. Of these, CRP and albumin is the most readily available and does provide additional prognostic data.

Both albumin and CRP are acute phase reactant proteins. C-reactive protein (CRP) is synthesized by hepatocytes in response to infection or tissue inflammation [8-10]. Decreased albumin levels during acute infection are also directly caused by the underlying inflammation process, provide an illustration of the severity of infection/inflammation [11-14].

There are various studies showing an association of CRP and albumin levels in assessing the severity of CAP. In levels conducted by Chalmers JD et al [15,16] showed a CRP of <100 mg/l is independently associated with a lower mortality increased 9.6 and >100 mg/l with increased risk of complication by CAP and also raised CRP level was associated with increase complication development Para pneumonic effusion and empyma thoracis.

In a study conducted by Viasus D et al [22] investigated, whether serum albumin levels within 24hr of admission decreased with outcomes in community-acquired pneumonia (CAP) showed levels of serum albumin decreased, and the risk of complications significantly increased (P <.001). Decreased albumin levels were also associated with prolonged time to reach clinical stability (P <.001), prolonged hospital stay (P <.001), ICU admission (P <.001), the need for mechanical ventilation (P <.001) and 30-day mortality (P <.001).

Akpinar E E et al [20] in a prospective observational study in 216 CAP patients, has also shown that low albumin level was an independent predictor for development of complications and need for ICU.

In a recent study by Lee et al [21], it was reported that albumin was associated with 28-day mortality in patients hospitalized with a CAP diagnosis.

Hence, the current study aims to assess the prognostic significance of CRP and albumin level in CAP.

Materials and Methods

Source of data: The Prospective study was conducted in patients admitted to hospital affiliated to Vijayanagara Institute of Medical Science, Ballari, from November 2016 to October 2018.

Method of collection of data: All clinically diagnosed pneumonia patients requiring hospitalization based on CURB-65 scores were admitted and included in study (informed consent taken).

Inclusion criteria:

1. Patients of age>18 years and both sexes
2. 2. Patients with community acquired pneumonia who are hospitalized based on (Pneumonia Outcome Research Trial) PORT/CURB 65 score.

Exclusion criteria:

1. Patients of age<18 years.
2. Patients with chronic liver and kidney disease.
3. Burns
4. Malabsorption syndromes
5. Diabetics
6. Pregnancy and Lactation.

Following which routine hematological investigations were done. Serum albumin & C-reactive protein levels were done on day 1, 3 & 7/discharge. The lab values of serum albumin and C - reactive protein were analyzed with the clinical profile and outcome in these study groups. All the above patients received standard pneumonia treatment in icu/ward according to hospital protocol. The data was compiled & appropriate statistical tests were applied.

Method of Statistical Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented in mean SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5 % level of significance. The Chi-square/ Fisher Exact test has been used to find the significance of study parameters on a categorical scale between two or more groups.

Results

During the study period, 50 patients were admitted with community acquired pneumonia (fitting into inclusion and exclusion criteria). Among them, most patients belong to age group of 61-70 yrs (27 %) followed by 51-60 yrs (25 %). Males (n=36{72%}) were more common than females (n=14{28%}).

In the study group, 26% of the patients belonged to rural areas and 74 % of the patients belonged to urban areas. Clinical symptoms of fever, cough with sputum were noticed in all patients (100 %), and breathlessness was present among 40 patients (80 %). The majority of the patients had a fever of 1-5 days, cough of 6-10 days and sputum production of 1- 5 days. Majority of them were smokers (n=35, 70%). To estimate the severity of pneumonia, CURB 65 scores in the study group were as follows. Scores between 0-1 were seen in 12 % of patients, scores of 2 to 24 % and scores from 3-5 among 64% of them. COPD (n=36, 72%) was the most common associated co-morbidities and 25 patients (69.4%) had asthma, 3 patients had a past history of tuberculosis. 10 patients (22%) required ICU admission, out of which 5 patients (10%) required mechanical ventilator support. Evaluation of vital data at the time of admission showed most patients had a pulse rate of 90-110 bpm (76%), respiratory rate of 20-30 (72%), SBP of <120 mmhg (90), DBP of <80 (88%) and temperature of 100-105F (64 %). Blood investigations showed that the majority of them had a total count of >11,000, blood urea levels of 60-120 (70%) and Hb of < 10 mg/dl (7%). Serum albumin levels on the day of admission and on the day of discharge are analyzed in table 1, which showed that patients who got recovered and discharged had increases in albumin.

Out of 50 patients during the study period, 1 patient died, 5 of the patients went DAMA (Discharge against medical advice), 40 of them resolved completely and 4 had unresolving pneumonia.

Table 1: Albumin and CRP levels of patients studied

Albumin	Day 1	Discharge	% Change	CRP	Day 1	Discharge	% Change
<2.5	26 %(n=13)	19.1%	-6.90%	<100	38	85.1	47.10%
2.5-3.5	58% (n=29)	57.4%	-0.60%	101-200	40	8.5	-31.50%
>3.5	16% (n=8)	23.4%	7.40%	>200	22	6.4	-15.60%
Total	100%(n=50)	100%	P=0.025 *	Total	100	100	P<0.001*

*P<0.001**, Significant, paired Proportion test*

The CRP levels at the time of admission and discharge are analyzed in table 1, which depicts a significant decrease at the time of admission (p=0.001).

But 6 out of 50 patients had their levels increased on the day of discharge. Among these patients, two of them had their pneumonia unresolving, three patients got discharged against advice. One patient showed clinical signs of resolution even with high CRP levels. CRP levels and albumin levels showed a significant correlation at the time of discharge (p=0.006) than at the time of admission (p=0.490) in table 3 and graph 1.

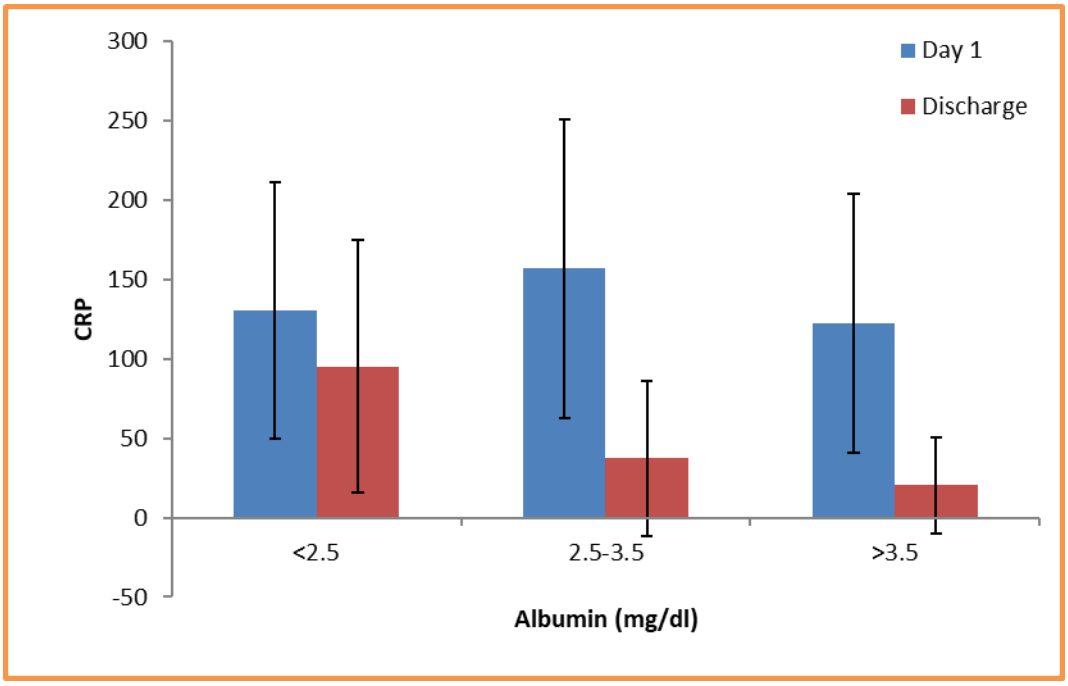
Levels of serum albumin correlated well with the need for ICU & mechanical ventilation, table 4. Among the patients who

required ICU, most of them (53.8%) had severe hypoalbuminemia (levels < 2.5) and 4.8 % of patients with hypoalbuminemia (levels 2.5-3.5) required ICU care (p=0.021). In patients with serum albumin >3.5, the need for ICU was least (10 %). Among 5 patients who required mechanical ventilation (30.8%), all had severe hypoalbuminemia. Statistical analysis showed strong significance (p=0.004).

Correlation of albumin with outcome showed (table 5) strong significance in statistical analysis(p=0.003). 90% of patients with serum albumin levels >3.5 had their pneumonia resolved. 46% of patients with serum albumin <2.5 mg/dl had their pneumonia unresolving. Death was noticed in patients with severe hypoalbuminemia. However, most of the patients with serum albumin levels between 2.5-3.5 mg/dl had their pneumonia resolved.

Table 3: Correlation of CRP with albumin levels

CRP	Albumin (mg/dl)			Total	P value
	<2.5	2.5-3.5	>3.5		
Day 1	130.53±80.72	156.91±94.34	122.65±81.42	143.20±88.14	0.490
Discharge	95.38±79.77	37.60±48.89	20.53±30.43	47.49±60.21	0.006**



Graph 1: Correlation of CRP with albumin levels

Table 4: Correlation of ICU/Mechanical ventilation with albumin levels

	Albumin (mg/dl)			P value
	<2.5 (n=13)	2.5-3.5 (n=27)	>3.5 (n=10)	
Need ICU	7(53.8%)	2(14.8%)	1(10%)	0.021*
Need for mechanical ventilation	4(30.8%)	0(0%)	1(3.8%)	0.004**

Table 5: Correlation of Outcome with Albumin levels

Outcome	Albumin (mg/dl)			Total
	<2.5	2.5-3.5	>3.5	
DAMA	2(15.4%)	2(7.4%)	1(10%)	5(10%)
Death	1(7.7%)	0(0%)	0(0%)	1(2%)
Resolving	6(46.2%)	25(92.6%)	9(90%)	40(80%)
Unresolving	4(30.8%)	0(0%)	0(0%)	4(8%)
Total	13(100%)	27(100%)	10(100%)	50(100%)

*P=0.003**, Significant, Fisher Exact test*

Discussion

Our study included age groups above 18yrs. The majority of the patients in the study were between 61-70 yrs (27%) followed by 51-60 yrs (25%). The lower number of patients were between 21-30 yrs (7%) and the least were of the age group > 80 yrs (6%).

In a study conducted by Kuntjoro Harimurti et al [23], hospitalized elderly patients with CAP had significant positive correlation with raised CRP and hypoalbuminemia.

In the present study processes, we have taken albumin as a negative acute phase reactant, whose levels decrease as inflammatory processes progress in the body.

Out of 50 patients evaluated,
26% of them had severe hypoalbuminemia (<2.5 mg/dl) on day 1 of admission.
58% of them had hypoalbuminemia (2.5-3.5 mg/dl) on day 1 of admission.
Thus, the majority of the patients (84%) had low serum albumin levels at the time of admission.

This shows that hypoalbuminemia is an important risk factor noted among patients with community acquired pneumonia. A study conducted by Dey AB et al [18] also shows albumin as an important risk factor for CAP.

When serum albumin levels were analysed at the time of discharge, there was significant change (P=0.025) noted among patients. Increases in serum albumin levels were seen in all patients who had clinical signs of resolution. Hedlund et al [24] found that serum albumin is decreased until the sixth day of hospitalization, and then it increases again on the ninth day, in patients with CAP.

A study by lokendra dave et al [19] showed the trend that patients with CAP have low levels of serum albumin (mean value 2.91+_0.09 gm/dl) and this value decreases significantly with increasing severity of pneumonia (p<0.001). In pneumonia cases, serum albumin shows a decreasing trend along with increasing severity of disease with statistically significant (p<0.001) difference in mean serum albumin level in all three CAP groups with different levels of severity.

C reactive protein, 38% of patients had serum CRP levels <100mg/dl, 40 % had levels between 101-200mg/dl, and 22% of them had levels more than 200 mg/l. When serum levels were analyzed at the time of discharge, there was significant decrease in the CRP levels (p=0.001).

The study by Hedlund et al [24] found weak but significant negative correlation (r = -0.30. P 0.0003) between CRP and albumin levels at the admission in patients with hospitalized community-acquired pneumonia.

Most patients (74%) stayed in the hospital for 5-6 days, few for >6days (18%) and the rest of them less than 4 days (8%). 78 % of all patients admitted required ICU care and 10% of all required mechanical ventilation. The outcome of the study showed clinical signs of resolution in 80 % of the patients. 5 patients were discharged against advice, 4 patients did not show any features of resolution (unresolving). Levels of serum albumin correlated well with the need for ICU & mechanical ventilation. Among the patients who required ICU, most of them (53.8%) had severe hypoalbuminemia (levels < 2.5) and 4.8 % of patients with hypoalbuminemia (levels 2.5-3.5) required ICU care. (p=0.021)

In patients with serum albumin >3.5, the need for ICU was least (10 %). Among 5 patients who required mechanical ventilation (30.8%), all had severe hypoalbuminemia. Statistical analysis showed strong significance (p=0.004).

Correlation of albumin with outcome showed strong significance in statistical analysis. (p=0.003). 90% of patients with serum albumin levels >3.5 had their pneumonia resolved. 46% of patients with serum albumin <2.5 mg/dl had their pneumonia unresolving. Death was noticed in patients with severe hypoalbuminemia. Patients who went against advice had serum albumin levels <2.5 mg/dl. However, most of the patients with serum albumin levels between 2.5-3.5 mg/dl had their pneumonia resolved.

Akpinar E E et al [20] in a prospective observational study in 216 CAP patients, also have shown that low albumin level was independent predictor for development of complications and need for ICU. The cut-off level of albumin in prediction of ICU need was 3.39 g/dl (sensitivity 71%, specificity 71%). Also, low albumin level was independent predictive factor for the development of complications and the cut-off level of albumin in prediction of development of complications was 3.44.

A study conducted by Jae hyuk lee et al [21] showed albumin and CRP were associated with 28-day mortality in hospitalized patients with CAP (p<0.05).

Viasus D et al [22] investigated whether serum albumin levels within 24hr of admission correlate with outcomes in community acquired pneumonia (CAP). During the study period, 3463 patients with CAP requiring hospitalization were studied. The median value of albumin was 3.1 g/L (IQR 28–35). As levels of serum albumin decrease, the risk of complications significantly increases (P <.001). Decreased albumin levels were also associated with prolonged time to reach clinical stability (P <.001), prolonged hospital stay (P <.001), ICU admission (P <.001), the need for mechanical ventilation (P <.001) and 30-day mortality (P <.001).

Conclusion

From the above results of this study, where 50 patients of CAP were analysed, there were,

- Significant association of CAP to History of smoking, pre-existing COPD and hypoalbuminemia at presentation as risk factors.
- Patients with severe hypoalbuminemia had high morbidity and mortality in the form of ICU requirements and a need for mechanical ventilation.
- CRP serves as an important marker of inflammation whose series levels reduce significantly with cure / resolution of pneumonia.

Thus, serum albumin levels and C reactive protein can be used as a prognostic biomarker in community acquired pneumonia.

Conflict of Interest

The author declares that there is no conflict of interest regarding the publication of the article.

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