

Study on the utilities of the role of biomarkers like albumin, C-reactive protein (CRP), procalcitonin (PCT), and blood urea nitrogen to serum albumin (B/A) ratio in the prediction of development of complications, prognosis, and need of ICU during the course of community-acquired pneumonia (CAP)

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Abstract

Context: Community-acquired pneumonia (CAP) is a serious illness. Early studies of community-acquired pneumonia reported that nonsurvivors had higher blood urea nitrogen levels and lower serum albumin levels than survivors. Therefore, elevation of the blood urea nitrogen to serum albumin (B/A) ratio may classify patients with community-acquired pneumonia who are becoming critically ill.

Aim: To study the role of biomarkers in the prediction of development of complications, prognosis and need of ICU during the course of community-acquired pneumonia (CAP).

Settings and Design: This is a retrospective study.

Material and Method: The present study was conducted in the department of Biochemistry. 200 patient's data, required for the study was collected from the online LIS system, Chest- Medicine ward and medical ICU department.

Statistical Analysis Used: Statistical analysis was performed by Pearson's correlation coefficient (r) and ROC plots.

Results: B/A, PCT, and CRP are statistically significantly positively correlated with the severity of the CAP, decided on the base of PSI and CURB-65 scoring system. (Correlation coefficient $r=0.7368$, 0.6412 and 0.8064 respectively. $P<0.0001$). These biomarkers also have good sensitivity and specificity for deciding need of the ICU during the course of CAP.

Conclusions: In our present study, we found an expressive and unaided positive correlation between B/A (BUN-Blood urea nitrogen/Albumin) ratio and severity of CAP. Both serum biochemical markers, blood urea nitrogen and albumin, are commonly used and can be measured promptly. Thus, our study suggests that the B/A ratio on admission can be a rapid, simple, cost-effective and predictable prognostic and severity indicator for CAP.

Keywords: Blood urea nitrogen to serum albumin ratio, Pneumonia Severity Index, CURB-65, community-acquired pneumonia, mortality, severity

1. Introduction

Community-Acquired Pneumonia (CAP), is an important cause of morbidity and mortality worldwide. [1] Pneumonia is an infection of the pulmonary parenchyma. It can vary from inactive to eruptive in presentation and from mild to fatal in severity.

Community-acquired pneumonia (CAP) represents a significant therapeutic trial to physicians, as they have to decide whether the patient is to be treated in a clinic or need any ICU setting. Therefore, it is vital to assess the severity of the disease, as it forms a starting point in the management design and helps in settle agreeable patient outcomes.

The need for an intensive care unit (ICU) is also a crucial problem for clinicians to deal during the course of

CAP. [2] CURB-65 (confusion, urea nitrogen, respiratory rate, blood pressure, ≥ 65 years) and Pneumonia Severity Index (PSI) are the most oftentimes used scoring scales to assess the disease severity. [3] These scoring tools are useful to clinch between hospitalization and outpatient treatment with an oral antibiotic. The inflammatory reaction [4-6] was reported as a primary reason for hypoalbuminemia. [7-9] The rate of the albumin synthesis is decreased in the acute phase of inflammation. The endotoxin from Gram-negative bacteria, cytokines like IL-6, chemokines cause capillary leakage of albumin. Hypoalbuminemia is a forecaster of poor prognosis in hospitalized and critically ill patients. [10] A high BUN level is one of the components of both the CURB-65 score and PSI. BUN levels show a decrease in renal

perfusion and indirectly presume the severity of pneumonia. The patients who have pneumonia have usually dehydrated that result from the increase of BUN excretion from the kidneys. We investigated whether the ratio of these two easily measurable parameters (BUN and albumin) predicts the prognosis of CAP or not.

C-reactive protein is an acute-phase protein synthesized in the liver. Previous studies have shown that inflammatory markers may have a huge role to play in assessing the severity of CAP. [11, 12] There are some studies, also shown that PCT levels correlate with the severity of pneumonia. Significantly higher PCT levels have been observed in patients with a higher PSI score or with complications or death than those with an uncomplicated clinical sequel. [13] But, CRP and PCT are costly biomarkers compared to BUN and albumin. So, in this study, we tried to set up the use of economically and simple biomarkers for the prediction of the CAP severity.

1.1 Aim and Objectives

- To evaluate the role of the albumin and blood urea nitrogen to serum albumin (B/A) ratio in the prediction of development of complications, need of ICU.
- To study the role of biomarkers like CRP and Procalcitonin in the prediction of development of complications, prognosis and need of ICU during the course of community-acquired pneumonia (CAP).

2. Material and Method

The present study was conducted in the Department of Biochemistry of a University Medical College. It is a retrospective study.

All the data required for the study was collected from the online LIS system, Chest-Medicine ward, and medical ICU department.

200 Patients with ≥ 18 years, admitted from the community, had at least two clinical signs and symptoms

related to pneumonia (fever > 38°C, cough, chest pain, dyspnea, or crackles on auscultation), and presented new infiltration on chest radiography were included in this study.

Patients were excluded if they had any immunocompromised state or any chronic organ failure.

- Albumin, CRP, BUN, and PCT were analyzed by auto-analyzer, and the ratio of B/A were calculated for all participants.
- BUN was estimated by colorimetric kinetic test with urease and glutamate dehydrogenase method. Albumin was estimated by colorimetric assay with endpoint BCG method.
- CRP was estimated by latex particle-enhanced turbidimetric assay.
- PCT was estimated by electrochemiluminescent immunoassay (sandwich principle).

The analysis was performed using the commercially available statistical Software STATA (14.2), and Excel 2016. The P value of less than 0.05 was considered statistically significant. Pearson correlation coefficient was used to test the strength of association between Albumin, CRP, BUN PCT, B/A, PSI, CURB-65 and other variables. Receiver operating characteristic (ROC) plots were used to determine the cut-off values for various parameters.

Ethical clearance was obtained by institution’s Human Research Ethics Committee.

3. Results

There were 69 females and 131 males in this study. The mean age of the participants was 47.23 ± 13.76 years.

Albumin was statistically negatively correlated with all variables like CRP, PCT, BUN, PSI and CURB-65 (r= -0.8133, -0.6534, -0.8500, -0.9693, -0.9693, P<0.0001) respectively. But, when we measured correlation between rests of other variables apart from albumin, they were statistically positively correlated (P<0.0001). (Table 1)

Table 1: Correlation between various biochemical variables and CAP severity

Variables between which correlation measured		Correlation coefficient (r)	Significance level (P)	95% confidence interval for (r)
Albumin	BUN	-0.8500	<0.0001	-0.8845 to -0.8064
Albumin	CRP	-0.8133	<0.0001	-0.8555 to -0.7603
Albumin	CURB-65	-0.9693	<0.0001	-0.9767 to -0.9597
Albumin	PCT	-0.6534	<0.0001	-0.7263 to -0.5660
Albumin	PSI	-0.9693	<0.0001	-0.9767 to -0.9597
BUN	CURB-65	0.8365	<0.0001	0.7893 to 0.8738
BUN	PCT	0.9399	<0.0001	0.9213 to 0.9542
BUN	PSI	0.8365	<0.0001	0.7893 to 0.8738
BUN	CRP	0.9844	<0.0001	0.9795 to 0.9882
B/A	CURB-65	0.7368	<0.0001	0.6662 to 0.7943
B/A	CRP	0.9699	<0.0001	0.9604 to 0.9772
B/A	PSI	0.7368	<0.0001	0.6662 to 0.7943
B/A	PCT	0.9691	<0.0001	0.9594 to 0.9766
CRP	CURB-65	0.8064	<0.0001	0.7517 to 0.8500
CRP	PCT	0.9620	<0.0001	0.9501 to 0.9712
CRP	PSI	0.8064	<0.0001	0.7517 to 0.8500
PCT	CURB-65	0.6412	<0.0001	0.5516 to 0.7163
PCT	PSI	0.6412	<0.0001	0.5516 to 0.7163

All the biochemical variables were compared for their sensitivity, specificity, positive predictive values (PPV) and negative predictive values (NPV) by ROC plots for CAP severity by the need of ICU and other complications. (Table 2)

Among these all, routing biomarker B/A ratio, which has the proficient sensitivity (97.1), specificity (100) and AUC= 0.999 (area under the curve) compared to other special biochemical parameters.

Table 2: The predictive values of biochemical parameters for CAP severity (Need for ICU or not)

Parameter	Cut off value	Sensitivity	Specificity	PPV	NPV	AUC	P value	95% confidence interval
Albumin	3.4	97.1	100	100	93.94	0.999	<0.0001	0.979 to 1.000
BUN	23.36	91.3	100	100	83.78	0.994	<0.0001	0.971 to 1.000
B/A	6.68	97.1	100	100	93.94	0.999	<0.0001	0.979 to 1.000
CRP	50	97.1	100	100	93.94	0.999	<0.0001	0.980 to 1.000
CURB-65	2	100	100	100	100	1.000	<0.0001	0.982 to 1.000
PCT	0.83	100	100	100	100	1.000	<0.0001	0.982 to 1.000
PSI	2	100	100	100	100	1.000	<0.0001	0.982 to 1.000
UREA	8.3	91.3	100	100	83.78	0.994	<0.0001	0.971 to 1.000

(Albumin in gm/dl, BUN in mg/dl, CRP in mg/L, PCT in ng/ml, UREA in mmol/L)

4. Discussion

Community-acquired pneumonia (CAP) is one of the most common infectious diseases and is an important cause of mortality and morbidity worldwide. Typical bacterial pathogens that cause the CAP are Streptococcus pneumoniae (penicillin-sensitive and -resistant strains), Haemophilus influenza (ampicillin-sensitive and -resistant strains), and Moraxella catarrhalis (all strains penicillin-resistant).

CAP is usually acquired via inhalation. Sometimes, CAP results from secondary bacteremia from a distant source, such as Escherichia coli. Aspiration pneumonia, the form of CAP is caused by multiple pathogens. [14]

Some reports indicate that several laboratory biomarkers such as procalcitonin, D-dimer, CRP, cortisol, B-type natriuretic peptide, and mid-regional proatrial natriuretic peptide correlate well with severity of CAP. However, use of these parameters routinely in patients with CAP is difficult because of the high cost. [15-18]

In the fundamental management of patients with suspected CAP, the clinician is challenged with diagnostic and prognostic risks, each trial interrelated to a specific management decision. This accentuates the importance of prompt, accurate diagnosis and severity of illness which approaches to decisions regarding the extremity of management. [19, 20]

200 patients with CAP were enrolled in this study. The current study asserts that B/A ratio with 97.1 % sensitivity and 100 % specificity with AUC of 0.999 is a better marker for the deciding severity, need of ICU and development of any complications during the course of CAP.

But, Ananda-Rajah MR *et al.* authors were not in agreement with our results, as they show that, CURB-65 is neither sensitive nor specific for predicting mortality in CAP patients. [21]

Shah BA *et al.* demonstrated that both PSI and CURB-65 were found to have equal sensitivity to predict death from CAP. Specificity of CURB-65 was higher than that of PSI. However, PSI was more sensitive in predicting ICU admission than CURB-65, which is also not harmonized with our findings. [3]

There are also some other studies regarding the involvement of biomarkers, other scoring systems and their validity for the severity in CAP. They had, in some manner similar and in other ways dissimilar findings. [22-24]

5. Conclusion

The B/A ratio on admission is a simple but reliable and cost-effective biomarker in the prediction of severity CAP, compared to other costly biomarkers like PCT and CRP.

Conflict of interest: None.

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