Original Article

Hypoalbuminemia predicts intensive care need among adult inpatients with community acquired pneumonia: a cross sectional study

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Abstract
Introduction: Various scales helped physicians to decide the site of care of pneumonia patients, but had certain limitations. Literature review suggested that serum albumin and B/A ratio predict the site of care but more evidences were required. Therefore, the study was aimed to evaluate the role of serum albumin and B/A ratio in the prediction of intensive care need among patients with community acquired pneumonia.
Methodology: The cross-sectional analytical study enrolled 134 adult inpatients with pneumonia from Sir Ganga Ram Hospital, Lahore, Pakistan during September 2014 to December 2016. Serum albumin, creatinine and urea levels were estimated; and BUN, B/A ratio and CURB-65 scores were calculated to predict the need of ICU.
Results: Overall mean age was 50 ± 21 years, and 54.5% patients were females. The patients (19.4%) who required treatment in ICU had significantly lower albumin levels (p = 0.001); elevated BUN levels (p = 0.003), B/A ratio (p = 0.001) and CURB-65 score (p = 0.038); and longer hospital stay (p = 0.002). Hypoalbuminemia showed significant association with the requirement of ICU (OR: 7.956; p = 0.001). The optimal cut-off point of serum albumin to predict ICU need was 3.4 g/dL (50% sensitivity; 89% specificity). Low serum albumin was revealed as a good predictor of requiring treatment in ICU (AUC 0.718).
Conclusions: Hypoalbuminemia was a good predictor of requiring ICU treatment. Elevated B/A ratio and BUN levels showed significant association with ICU need. Serum albumin estimation before hospitalization might be used independently or additional with established criteria to decide the site of care.

Key words: Blood urea nitrogen; hypoalbuminemia; hospitalization; intensive care unit; pneumonia.

Introduction

Community acquired pneumonia (CAP) remained one of the major reasons for hospitalization among adult patients [1]. In the United States (US), about one million adult pneumonia patients get hospitalized each year [2]. In Pakistan, overall frequency of self-reported lifetime pneumonia was 10% [3]; and treatment cost of hospitalization depending upon the severity of disease ranged from 80-598 USD [4]. Therefore, taking decision about the site of care is very crucial as the avoidable hospital admissions put significant burden on limited resources [5,6] Infectious Diseases Society of America (IDSA) and American Thoracic Society (ATS) recommend CURB-65 and Pneumonia Severity Index (PSI) scales for the initial assessment of severity of pneumonia [5]. Same recommendations have been endorsed by Pakistan Chest Society for making decision about the site of care [6]. However, there are certain limitations of using these scales. For example,

in CURB-65 scale assessment for the presence or absence of confusion may vary from physician to physician. Whereas PSI scale requires more than twenty parameters to calculate scores that costs more time and money.

Few retrospective and observational studies used biochemical markers such as serum albumin, and blood urea nitrogen to serum albumin (B/A) ratio to evaluate their role in the prediction of ICU admission [7-9]. Elevated B/A ratio as an independent factor had significant association with ICU need among Japanese patients with pneumonia [7]. Both, elevated B/A ratio and low serum albumin predicted the risk of requiring ICU treatment; however low serum albumin was a better predictor than B/A ratio among Turkish patients [8]. Low serum albumin also showed significant association with ICU admission among Spanish patients [9].

A review study on CAP in Pakistan included eleven studies published from 2003 to 2013 and reported that most of them were observational, retrospective, clinical and microorganisms' specific. It was suggested that more comprehensive studies were essentially required to revise the in-practice treatment guidelines for adult Pakistani patients with CAP [10]. A recent nationwide study from Pakistan reported 39.7% disagreement between physician's decisions regarding the site of care and the recommendations of CURB-65 scale [11].

Limited data on severity and prognosis of community acquired pneumonia from Pakistan and other studies on the prediction of ICU requirement suggested evaluating the role of serum albumin and B/A ratio in the prediction of ICU admission among adult CAP patients.

Methodology
Bioethical Clearance
Ethical approval was obtained from the Institutional Ethical Review Board, Fatima Jinnah Medical University/ Sir Ganga Ram Hospital, Lahore on 30th September 2014 (No.1177 I.E.R.B). Informed written consent was also obtained from all participants.

Study Design, Setting and Duration
The cross-sectional analytical study was carried out at Sir Ganga Ram Hospital, Lahore; and data was collected from September 2014 to December 2016.

Sampling Technique and Inclusion Criteria
Total 134 newly admitted CAP patients who were not taking antibiotics for last 14 days were selected by convenient sampling method. Other inclusion criteria were adult ($\geq$ 18 years) and of both genders.

CAP diagnosis depended upon history of high grade fever with pleuritic chest pain, shortness of breath and cough. Laboratory findings included infiltration on chest X-ray; Leucocytosis, and sputum examination.

The patients with fever, dehydration, confusion, and positive chest X-ray were admitted in the ward. While those who required support on ventilator were admitted in the ICU. CURB-65 score had also been considered for ICU admissions.

CAP patients who had chronic kidney disease, advanced liver disease, sepsis, or who were on immunosuppressive drugs were excluded from the study.

Lab Investigations
Blood urea was estimated by Glutamate dehydrogenase (GLDH) method [12]; serum creatinine by Jaffe-Reaction [13]; and serum albumin by bromocresol green (BCG) method [14]. Blood urea nitrogen (BUN) was calculated by multiplying blood urea level (mg/dL) to 0.47 and B/A ratio by dividing BUN over serum albumin level.

CURB-65 scale
It was used to measure the severity of community acquired pneumonia. It included five parameters i.e. age $\geq$ 65 years; blood urea ($\geq$ 20 mg/dL); respiratory rate ($\geq$ 30 breaths per minute); low blood pressure (SBP $\leq$ 90 mmHg, DBP $\leq$ 60 mmHg); and confusion (present). Each positive parameter had been assigned with one score, and none was given to negative parameter. As per interpretation of CURB-65 scale, the patients who score 0-1 should be treated as outpatient; who score 2 require short hospital stay; who score 3 require indoor treatment; and who score 4-5 require intensive care [15].

Statistical Analysis
Data were entered and analyzed by using Statistical Package for Social Sciences (SPSS) version 20. Qualitative and quantitative variables were described by using number (percentage) and mean $\pm$ standard deviation, respectively. Comparison of variant characteristics underlying study was discussed by using t-test and chi square test. Odds ratios were calculated to measure the risk of ICU admission. Receiver's operative characteristics (ROC) curve was used to predict the need of ICU. Youden index was used to find optimal cut-off points. P-value $\leq$ 0.05 was considered significant.

Results
Mean age of 134 CAP patients was 50 $\pm$ 21 years. Frequency of males and females was 45.5% and 54.5%, respectively. Mean family income was 222 $\pm$ 162 USD per month. Assessment of household arrangements showed that 43.4% patients were residing with 7-20 family members; 11.9% patients were living in a single room house; 22.4% patients had no separate kitchen; and 16.4% patients were using wooden stove for cooking purposes. Frequencies of current and passive cigarette smokers were 29.1% and 38.1%, respectively. Comorbidities included hypertension 10.6%, chronic obstructive pulmonary disease (COPD) 9.1%, and tuberculosis 6.1%. Occurrence rates of bronchial and lobar pneumonia were 59.7% and 40.3%, respectively. While reoccurrence rate of pneumonia within 1 year was 14.9%.

Table 1. Comparison of ICU versus Ward Patients.

	ICU* (n = 26)	Ward (n = 108)	P value
Age (years)	51.0 ± 20.0	50.1 ± 20.9	0.828
Hospital Stay (days)	6.6 ± 4.4	4.4 ± 2.8	0.002
Body Mass Index (Kg/m^2)	21.5 ± 3.8	23.5 ± 5.5	0.094
Systolic blood pressure (mmHg)	117.6 ± 17.9	123.2 ± 21.8	0.226
Diastolic blood pressure (mmHg)	70.1 ± 11.1	76.1 ± 12.8	0.030
Serum creatinine level (mg/dL)	3.8 ± 3.9	1.7 ± 1.0	0.001
Blood urea nitrogen (mg/dL)	41.3 ± 29.1	22.4 ± 13.0	0.003
Serum albumin level (g/dL)	3.0 ± 0.4	3.5 ± 0.7	0.001
BUN* over albumin ratio (mg/g)	14.0 ± 10.1	6.7 ± 3.9	0.001
CURB-65 score	1.7 ± 1.2	1.2 ± 1.0	0.038

*ICU: Intensive Care Unit; BUN: Blood Urea Nitrogen.

Total 19.4% patients were admitted in the ICU and 80.6% patients in the ward. Beside low albumin levels in both groups, ICU admitted patients had further decreased levels when compared with ward patients (p = 0.001). Moreover, ICU patients had elevated mean levels of B/A ratio, BUN and creatinine (p < 0.05); prolonged hospital stay (p 0.002); and higher CURB-65 score (p 0.038) as shown in Table 1.

The frequencies of five factors used in CURB-65 scale showed that raised urea was the commonest factor present in 48.5% patients; followed by elder age in 32.1% patients. Elevated respiratory rate and confusion were observed in 23.1% and 14.9% patients, respectively. Low blood pressure either systolic or diastolic was seen in 8.2% patients. The frequency of patients who met the hospital admission criteria of

CURB-65 scale was 38.8%. There were 36.6% patients who required treatment in the general ward but 22.5% of them received treatment in the ICU. On the other hand, only three patients (2.2%) required treatment in the ICU but one of them received treatment in the general ward. A significant disagreement between physician's decision about the site of care and the recommendations of CURB-65 can be observed in Table 2.

Multivariate analysis revealed that low serum albumin had significant association with ICU admission (p = 0.001); and the patients with albumin levels below 3.5 mg/dL had 8 times greater risk of getting ICU admission (OR = 7.956). Elevated B/A ratio and BUN levels, increased BMI and low diastolic blood pressure also showed significant association (p <0.05) and had

Table 2. CURB-65 Score and Hospital Admission Status.

CURB-65 Score	ICU* (n = 26)	Ward (n = 108)	Total (n = 134)
0	04 (15.4%)	33 (30.6%)	37 (27.6%)
1	09 (34.6%)	36 (33.3%)	45 (33.6%)
2	07 (26.9%)	27 (25.0%)	34 (25.4%)
3	04 (15.4%)	11 (10.2%)	15 (11.2%)
4-5	02 (7.7%)	01 (0.9%)	03 (2.2%)

*ICU: Intensive Care Unit.

Table 3. Risk Factors of ICU* Admission.

	OR value	95% CI		P value
		Lower	Upper	
Age ≥ 65 years	1.357	0.523	3.525	0.525
Body Mass Index < 18 Kg/m^2)	1.221	0.366	4.070	0.719
Systolic Blood Pressure < 90 mmHg	0.803	0.738	0.874	0.351
Diastolic Blood Pressure < 60 mmHg	3.745	0.930	15.083	0.075
Serum Creatinine level ≥ 1.3 mg/dL	1.669	0.667	4.172	0.264
Blood Urea Nitrogen ≥ 20 mg/dL	2.920	1.169	7.295	0.033
Serum Albumin level < 3.5 g/dL	7.956	2.255	28.073	0.001
BUN* over Albumin ratio ≥ 6.75 mg/g	3.480	1.416	8.552	0.005
CURB-65 Score ≥ 04	8.916	0.776	102.40	0.071

*ICU: Intensive Care Unit; BUN: Blood Urea Nitrogen.

Table 4. Cut-off Points to Predict ICU Admission.

	Cut-off	Sensitivity	Specificity	PPV*	NPV*
Albumin	< 3.2 g/dL	65%	65%	65%	65%
	< 3.3 g/dL	57%	81%	75%	65%
	< 3.4 g/dL	50%	89%	82%	64%
BUN*	> 21.2 mg/dL	69%	65%	66%	67%
	> 23.9 mg/dL	61%	71%	68%	70%
	> 26.7 mg/dL	57%	75%	70%	64%
B/A* Ratio	> 7.4 mg/g	57%	68%	64%	61%
	> 10.3 mg/g	53%	80%	73%	63%
	> 13.2 mg/g	50%	92%	86%	65%

PPV: Positive Predictive Value; NPV: Negative Predictive Value; BUN: Blood Urea Nitrogen; B/A ratio: BUN/albumin ratio.

3-4 times higher chances of being admitted in the ICU as shown in Table 3.

The area under the curve (AUC) was 0.718 for serum albumin (95% CI, 0.625-0.812); followed by 0.707 for B/A ratio (95% CI, 0.578-0.836); 0.672 for BUN (95% CI, 0.535-0.809); and 0.614 for CURB-65 score (95% CI, 0.535-0.809) to predict the need of ICU admission, see Figure 1.

The optimal cut-off point for serum albumin to predict the requirement of ICU admission was 3.4 g/dL (50% sensitivity; 89% specificity). The optimal cut-off values for B/A ratio and BUN were 13.2 mg/g (50% sensitivity; 92% specificity) and 21.2 mg/dL (69% sensitivity; 65% specificity), respectively as shown in Table 4.

Discussion

As the hospital admissions put significant burden on resources, therefore taking decision about the site of care is very crucial especially in the developing countries like Pakistan. Out of 134 adult CAP patients, there were 19.4% patients who received ICU treatment

Figure 1. Biochemical Predictors of ICU Admission.
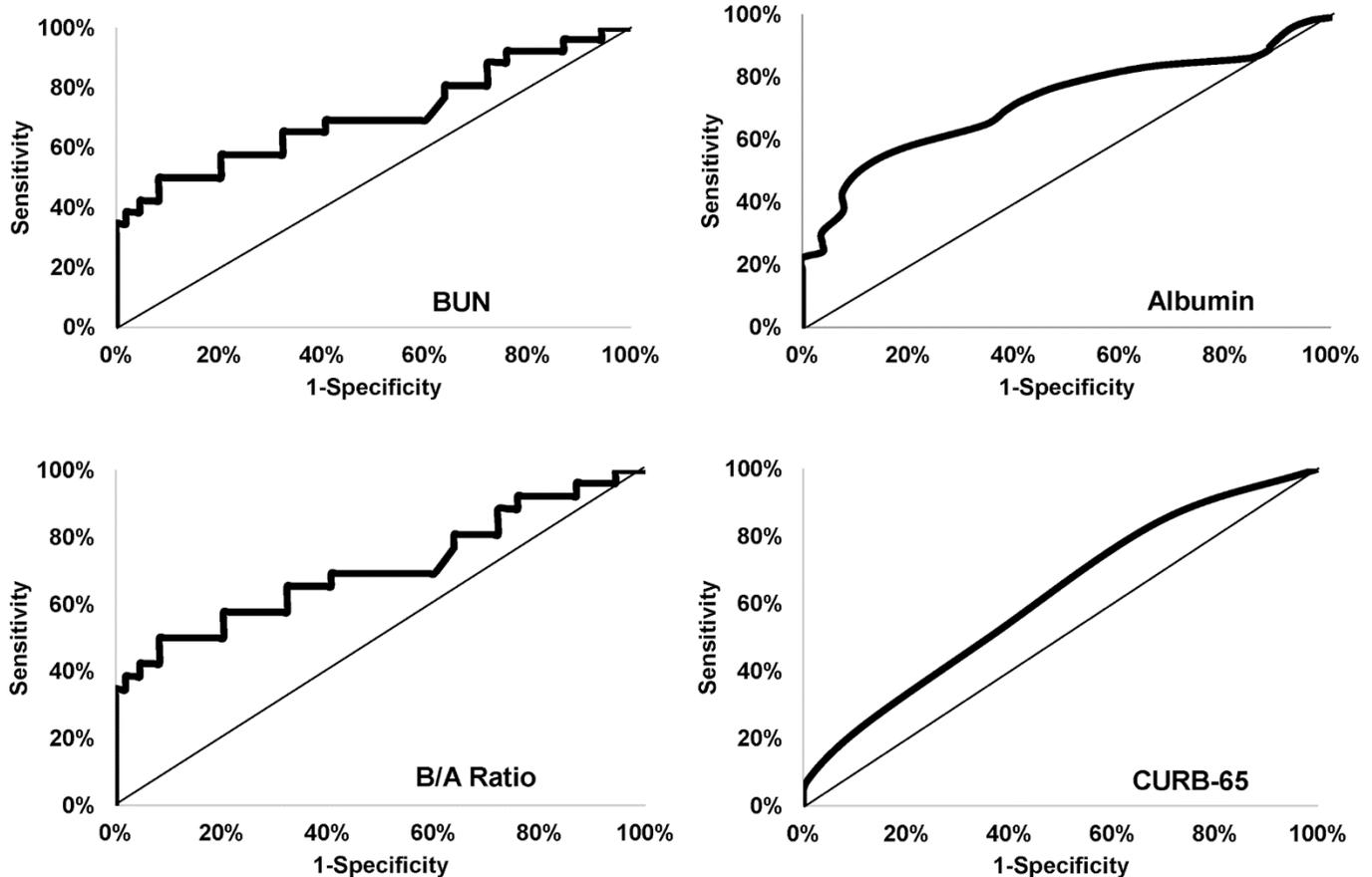
BUN: Blood Urea Nitrogen; B/A ratio: Blood Urea Nitrogen over albumin ratio; CURB: CURB-65 Score.

which was quite higher than the rates reported from other countries. Though the rate of ICU admission observed in present study was little higher than the rate (16.6%) reported from Japan [7]. But it was two times greater than the rates (9.7%) reported from Turkey [8], and (9.0%) from Spain [9]. According to CURB-65 score, only 38.8% patients truly met the hospital admission criteria; and 36.6% patients required admission in the ward. In comparison to 19.4% ICU admissions, only 2.2% patients actually required ICU treatment. It seems that many admissions in the ward and ICU were avoidable. The underlying reason for unnecessary ward and ICU admissions might be non-adherence of physicians to the recommended CURB-65 and PSI scales.

Previous studies had reported that occurrence rate of lobar pneumonia was higher than bronchial pneumonia [16,17]. Unlikely, the rate of lobar pneumonia was lower than bronchial pneumonia in present study. Living in a crowded house (>10 persons in a house) had two times higher risk of getting CAP [18]. Similar household arrangements were seen in the study; where 43.4% patients had 7-20 family members residing within one house. Various studies had reported that smoking was a significant risk factor of CAP [19-23]. It had also been reported that smoking increased the susceptibility to bacterial lung infection among smokers and passive smokers [24]. The number of CAP patients having history of smoking was relatively lower than the frequency of smokers (74%) among Indian CAP patients [17]. Moreover, no association between smoking status and ICU admission was found in the study. The length of hospital stay in the study was 2-3 times shorter than the stay reported by other studies i.e. 8 ± 7 days [25], and 14.62 ± 7.08 days [26].

The ICU admitted patients showed significantly different levels of serum albumin, BUN and B/A ratio from ward admitted patients. Similar significantly different levels had been reported in other studies [7-9]. In the current study, AUC 0.71 for serum albumin revealed that it was a good predictor of requiring ICU admission. A quite comparable AUC 0.72 for serum albumin had been reported by some other studies [8,9]. Similarly, AUC 0.70 for B/A ratio showed that it was also a good predictor of ICU admission. Though it was better than AUC 0.64 reported by Akpinar *et al.* [8], but worse than AUC 0.83 reported by Ugajin *et al.* [7]. The AUC 0.61 for CURB-65 was the poorest among AUC calculated for predictors under investigation. The reason might be that CURB-65 was not considered at the time of admission in the settings. Even then it was comparable to AUC 0.62 reported by Viasus *et al.* [9].

In the present study, the optimal cut-off point of serum albumin to predict ICU admission was 3.4 g/dL, which was equivalent to 3.39 g/dL reported by Akpinar *et al.* [8]. Whereas, the cut-off value 13.5 mg/g of B/A ratio was considerably higher than ratio 9.85 mg/g reported by Ugajin *et al.* [7], and shockingly bigger than ratio 4.15 mg/g reported by Akpinar *et al.* [8]. It was reported that elevated B/A ratio had significant association with ICU need [7]. Another study also concluded that elevated B/A ratio and hypoalbuminemia predicted the requirement of ICU; but hypoalbuminemia was a better predictor than B/A ratio [8]. One more study reported that hypoalbuminemia was significantly associated with ICU admission and prolonged hospital stay [9]. The results of present study validated the findings of previous studies that hypoalbuminemia, elevated BUN and B/A ratio were independent risk factors and showed significant association with ICU requirement.

Conclusions

Hypoalbuminemia was a good predictor of requiring intensive care treatment. Elevated B/A ratio and BUN levels also demonstrated significant association with ICU need. Therefore, serum albumin estimation before hospitalization might be used independently or additional with established criteria to decide the site of care.

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