Role Of Expanded Curb-65 Score In Predicting The Severity Of Community Acquired Pneumonia.

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Abstract:
Introduction:
Assessment of severity and site of care decisions for community-acquired pneumonia patients (CAP) are very important for patients' safety and optimal use of resources. Late admission to the intensive care unit (ICU) leads to increase the rate of mortality in CAP. We aimed to evaluate the effectiveness of the new expanded CURB-65 score in comparison with CURB-65 in predicting CAP patient outcomes.
Materials and Methods:
This was a cross sectional study which includes 90 patients presented with CAP in Government hospital for chest and communicable disease, AMC, Visakhapatnam
Results:
The study included 90 patients hospitalized with CAP of which mean (SD) age distribution is 51.49±16.63 years, with 64.4% being men and 83.3% of CAP patients had associated comorbidities. All patients (100%) had elevated serum LDH (> 230U/L), 87.8% had hypoalbuminemia, 8.9% had thrombocytopenia, and 4.44% had elevated BUN values within 24 hours of admission. Regarding outcomes, the ICU admission rate was 36.7%, the 30-day mortality rate was 14.4%, and 35.6% required mechanical ventilation. There was a significant association between tachypnea (respiratory rate >30/min), confusion, and thrombocytopenia (Platelet Count < 100×103/mm3) with 30-day mortality, according to univariate analysis. The current study found that as 30-day mortality for Expanded CURB score of (0-2), (3-4) and (5-8) is 0,4%and 9% respectively, requirement of mechanical ventilation and ICU admission rate were 2%,22%, 8% and2%,23%,8% respectively. Length of hospital stay increase as the score increase with median length of hospital stay being 7 days.
Conclusion:
Compared to CURB-65 and other assessment tools, the Expanded-CURB-65 score, which extends independent risk factors to 8 variables in assessing CAP severity, significantly improves identifying high-risk patients and thereby helps in early institution of appropriate therapy.
Keywords: CAP, Expanded CURB 65 score, 30-day Mortality, ICU admission and Mechanical Ventilation

I.   Introduction:

Community-acquired pneumonia is a leading cause of hospitalization, accounting for approximately 3.5 million deaths per year worldwide and being the leading cause of mortality among infectious diseases[1]. Because disease presentation can range from mild to severe, necessitating intensive care unit treatment, early diagnosis and determination of the adequate level of care are critical for improving outcomes. Pneumonia severity index (PSI), CURB 65 and SMART COP are used to justify hospitalization and predict mortality. In both PSI and CURB 65 scores, age and patient complications are more heavily weighted and this understates the degree of severity in young patients and incorrectly labels the elderly patients as having severe disease[2]. To overcome this, Expanded CURB-65 scoring system was developed by Liu LJ et al., which assesses the severity of CAP based on factors such as confusion, urea > 7mmol/L, respiratory rate >30/min, BP systolic < 90mmHg or diastolic < 60mmHg, age > 65, serum LDH >230μ/l, albumin <3.5g/dl, and platelet count <100×109/L. This score expands eight independent risk factors that are closely related to CAP patient mortality, significantly identifying high-risk patients. There are only a few studies on Expanded CURB 65 in literature. This score is relatively simpler and expands the independent risk factors in predicting the severity of CAP, which supports the need for the present study.

Objectives:

To evaluate the effectiveness of Expanded CURB 65 in predicting the severity, outcome of patients with CAP and to compare Expanded CURB 65 with CURB 65 to know the predictive specificity of CAP.

II.   Materials And Methods:

This was a cross sectional study which includes 90 patients presented with CAP in Government hospital for chest and communicable diseases, AMC, Visakhapatnam from June 2018 to January 2019

Patients of age ≥ 18 years and with radiological evidence of infiltrates and/or clinical signs and symptoms of pneumonia were included. Patients who had antibiotic use in last two weeks prior to admission, those diagnosed to have HIV and those on immunosuppressive treatment were excluded from the study.

Patients admitted with CAP who met the criteria outlined above were included in the study. Demographic information, clinical history, and co-morbidities were documented. Within 24 hours of admission, a physical examination, radiological findings, and laboratory values such as the complete blood count, renal and liver function tests, platelet counts, serum albumin, serum LDH, random blood sugar, sputum for gram staining, and culture were collected. The study was conducted after receiving approval from the institutional ethics committee.

Statistical Analysis:

Data was entered into a Microsoft Excel spreadsheet version 2013 and then exported to SPSS version 17. The analysis was performed using both Microsoft Excel spreadsheet and SPSS. The continuous data were described in terms of mean and standard deviation OR median and interquartile ranges. Nominal data have been described in terms of frequency and percentage. Chi-Square test was used to test the association between the variables. The odds ratio and confidence interval were calculated to determine the strength of association between various risk factors. ROC curves with AUC were generated. A p-value of <0.05 was considered statistically significant.

III.   Results:

The study included 90 patients hospitalized with CAP. The study group had a mean (SD) age of 51.49±16.63 years, with 64.4% men and 35.6% women. 83.3% of CAP patients had comorbidities, primarily COPD (60%), alcoholism (28.9%), and diabetes (23.3%), with 10% of patients having multiple comorbidities. (Table 1)

Table 1: Baseline Variables

VARAIBLES	N	(%)
Age ≥ 65 years	27	30%
Male	58	64.4%
Comorbidities		
COPD	54	60%
Diabetes Mellitus	21	23.3%
CKD	8	8.9%
CVA	1	1.1%
Alcoholism	26	28.9%
Malignancy	3	3.33%
Distribution of Symptoms		
Fever	76	84.40%
Cough with expectoration	85	94.40%
Chest pain	68	75.60%
Dyspnea	77	85.60%
Physical examination findings		
Confusion	12	13.30%
Respiratory rate ≥ 30	49	54.40%
Systolic BP< 90mmHg or Diastolic BP ≤ 60 mmHg	86	95.5%
30-day mortality rate	13	14.40%

In the current study, most predominant examination finding was hypotension (95.5%). 94.4% of the patient's sputum culture specimen demonstrated no growth.

Table 2: Patients outcomes

outcomes	Frequency	Percentage
ICU admission	33	36.70%
Need for mechanical ventilation	32	35.60%
30-day mortality rate	13	14.40%
Length of hospital stay(days) median :7 ± 3.32 days		

In this study, regarding outcomes, the ICU admission rate was 36.7%, the median length of hospital stay was 7 days, the 30-day mortality rate was 14.4%, and 35.6% required mechanical ventilation (Table 2)

Table 3: Laboratory findings

Parameters	Frequency	Percentage
BUN > 19mg/dl	4	4.44%
Serum LDH> 230U/L	90	100%
Platelet counts < 100×10³/mm³	8	8.90%
Albumin < 3.5g/dl	79	87.80%

In this study, all 90 patients (100%) had elevated serum LDH (> 230U/L), 87.8% had hypoalbuminemia, 8.9% had thrombocytopenia, and 4.44% had elevated BUN values within 24 hours of admission (table 3).

Table 4: Serum LDH, Thrombocytopenia and Hypoalbuminemia in different risk class of CURB 65 and Expanded CURB 65 Score in CAP patients.

	CURB 65 score N (%)			Expanded CURB 65 score N (%)		
	0-1	2	3-5	0-2	3-4	5-8
N (%)	49(54.4%)	35(38.9%)	6(6.7%)	11(12.2%)	69(76.7%)	10(11.1%)
S.LDH> 230U/L,N (%)	49	35	6	11	69	10
Thrombocytopenia N (%)	3(6.1%)	4(11.4%)	1(16.7%)	0	3(4.3%)	5(50%)
Hypoalbuminemia N (%)	43(87.8%)	31(88.6%)	5(83.3%)	5(45.5%)	65(94.2%)	9(90%)

The hypoalbuminemia and thrombocytopenia increases with the higher CURB 65 score. There was a statistically significant difference between both the subgroups of Expanded CURB-65 was significantly associated with hypoalbuminemia (p-value < 0.01). Hypoalbuminemia is lower in Expanded CURB-65 score (0-2) 45.5% than in CURB-65 score (0-1) 87.8%, while it is higher in Expanded CURB-65 score (5-8) 90% than in CURB-65 score (3-5) 83.3%.

There was a significant difference in thrombocytopenia between the two subgroups of Expanded CURB-65 (p-value<0.01). Expanded CURB-65 score (0-2) had no thrombocytopenia compared to CURB-65 score (0-1) 6.1%. However, thrombocytopenia was higher in Expanded CURB-65 score (5-8) at 50% compared to CURB-65 score (3-5) at 16.7%. There was no statistically significant difference between the two subgroups for serum LDH levels greater than 230U/L

Table 5: LOS, 30-day mortality, need for mechanical ventilation and ICU admission in a subgroup of CURB 65 and Expanded CURB 65 score

	CURB 65 score			Expanded CURB 65 score		
	0-1	2	3-5	0-2	3-4	5-8
N (%)	49(54.4%)	35(38.9%)	6(6.7%)	11(12.2%)	69(76.7%)	10(11.1%)
LOS(Median IQR)	6(5-8)	8(6-10)	10.5(7.5-12.75)	5(5-7)	7(5.5-9)	9.5(5.5-12.75)
30-day mortality	1(2.0%)	7(20%)	5(83.3%)	0	4(5.8%)	9(90.0%)
Mechanical ventilation	10(20.4%)	18(51.4%)	4(66.6%)	2(18.2%)	22(31.9%)	8(80.0%)
ICU admission	11(22.4%)	18(51.4%)	4(66.6%)	2(18.2%)	23(33.3%)	8(80.0%)

In terms of patient outcome, there is no 30-day mortality in Expanded CURB-65 score (0-2), whereas the 30-day mortality rate in CURB-65 score (0-1) is 2%. The 30-mortality rate was 90% in Expanded CURB-65 score (5-8) versus 83.3% in CURB-65 score (3-5).

In terms of ICU admission, Expanded CURB-65 with a score (0-2) had 18.2% fewer ICU admissions than CURB-65 score (0-1) 22.4%, whereas ICU admission was higher in Expanded CURB-65 score (5-8) 80% than CURB-65 score (3-5) 66.6%.

In terms of mechanical ventilation, Expanded CURB-65 score (0-2) has a lower need for mechanical ventilation (18.2%) than CURB-65 score (0-1) (20.4%), whereas the need for mechanical ventilation was greater in Expanded CURB-65 score (5-8) 80% compared to CURB-65 score (3-5) 66.6%. Length of hospital stay increases as score increase.

Table 6: Univariate analysis of risk factors associated with the 30-day mortality rate in CAP patients

|	OR	95% Cl	P value
Age ≥ 65	2.286	0.688-7.591	0.169
BUN >20	3.125	0.263-37.190	0.377
RR ≥ 30	5.645	1.173-27.172	**0.032***
S. Albumin < 3.5	1.791	0.210-15.306	1.000
Platelet Count <1 lakh	32.142	5.432-190.205	**0.001***
Systolic BP <90	0.981	0.275-3.504	0.977
Diastolic BP <60	1.286	0.363-4.560	0.697
Confusion	29.20	6.491-131.366	**0.001***
DM	1.569	0.430-5.727	0.493
CKD	0.833	0.094-7.394	0.870
COPD	1.600	0.453-5.652	0.463

Risk factors for increased 30-day mortality rate include tachypnea (respiratory rate >30/min), confusion, and thrombocytopenia (Platelet Count < 100×103/mm3) showed significance, according to univariate analysis

Table 7: Sensitivity and specificity in prediction of 30-day mortality, requirement of mechanical ventilation and ICU admission by expanded curb 65 and curb 65 score:

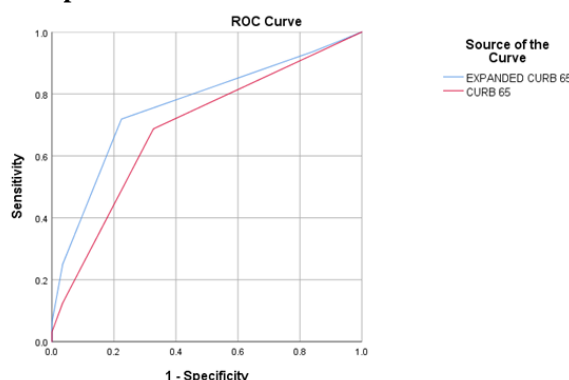| z	CURB 65 score			Expanded CURB 65 score		
	Cut off	Sensitivity%	Specificity%	Cutoff for prediction	Sensitivity %	Specificity%
30-day mortality	>1	92.3	62.3	>3	100	70.1
Requirement of mechanical ventilation	>1	71	67.8	>3	74.2	78
ICU admission	>1	66.7	66.7	>3	69.7	77.2

The cut-off for prediction of 30-day mortality, requirement of mechanical ventilation and ICU admission by expanded curb 65 and curb 65 score was >3 and >1 respectively

Fig: 7 The receiver operating curve (ROC) for prediction of 30-day mortality by Expanded CURB 65 and CURB 65 score.
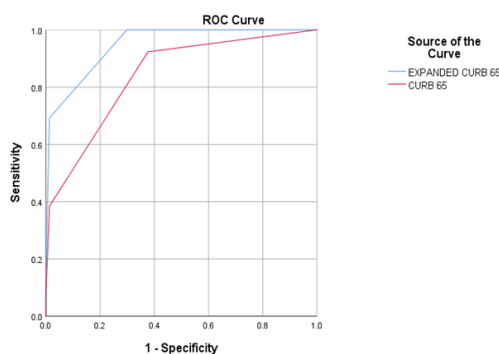

Both scores are reliable predictors of 30-day mortality. Expanded CURB 65 is a stronger predictor of 30-day mortality.

Fig: 8 The receiver operating curve (ROC) for prediction for the need for mechanical ventilation of by Expanded CURB 65 and CURB 65 score.

This demonstrates that both scores are more accurate predictors of the need for mechanical ventilation.

Fig: 9 The receiver operating curve (ROC) for prediction of ICU admission by Expanded CURB 65 and CURB 65 score.
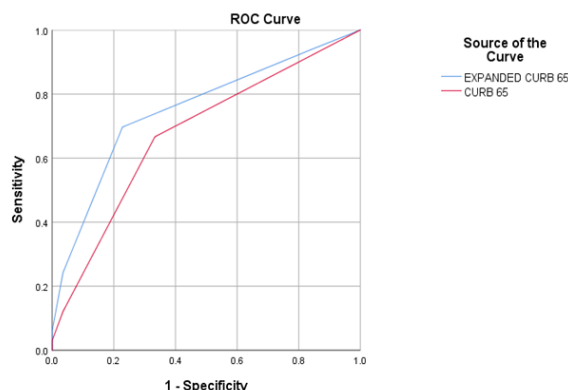
Table 8: AUC and P value of 30-day mortality, requirement of mechanical ventilation and ICU admission by expanded curb 65 and curb 65 score:

	Expanded CURB 65 AUC and P-value for ROC	CURB 65 AUC and P-value from ROC
30-day mortality	0.949(p value<0.001)	0.840(p value<0.001)
Need for mechanical ventilation	0.772(p value<0.001)	0.703(p value<0.001)
ICU admission	0.751(p value<0.0001)	0.676(p-value 0.001)

This demonstrates that Expanded CURB 65 score is a better predictor of ICU admission.

IV.   Discussion:

Community-acquired pneumonia is the leading cause of death and morbidity worldwide. High mortality and clinical deterioration in community-acquired pneumonia can be attributed to a variety of factors, including respiratory failure, worsening of pre-existing comorbidity, or hospital-acquired illness. There is no single clinical prediction to assess the progression of CAP. The degree of severity of community-acquired pneumonia and site of care decisions are critical for improving clinical outcomes. In this study, the average age of CAP patients was 51.49±16.63 years, with 30% of patients were over the age of 65. 83.3% of CAP patients had comorbidities, the majority of which were COPD (60%). Our findings are consistent with those of Ewig et al., who found COPD to be a major comorbidity (43.9%).

The demographic distribution of the current study is similar to that of Ewig et al.[4], Shehata SM et al.[5] and in Lim et al. but the prevalence of comorbidities is higher in the present study than in previous studies.

In our study, COPD was the most common comorbidity associated with CAP. According to Jackson ML et al. studies, COPD has a strong association with CAP[6]. Borden J et al. studies found that the incidence of CAP in patients with COPD was eighteen times greater than in non-COPD patients[7]. COPD increases the risk of CAP due to change in the lung microbiome, abnormal lung immunity and pathogen virulence[3]

Lactate dehydrogenase (LDH) is a cytoplasmic enzyme that is highly expressed in tissues. According to Tao et al., LDH was linked to death in patients with viral pneumonia[8] Lactate modulates macrophages' inflammatory response, and its suppression has anti-inflammatory effects by downregulating several inflammatory mediators[9].

Liu et al. found that elevated serum LDH levels (> 230 u/L), thrombocytopenia (platelet count < 105/mL), and hypoalbuminemia (albumin level < 3.5 g/dL) were independent risk factors for death in CAP patients on multivariate analysis.[10]

In a cross-sectional study by Hendy M R et al. found that serum LDH levels with a cut-off value of 511U/L predicts the most serious outcome in patients with CAP, with a sensitivity of 76.9% and specificity of 65.3%[11]

In the current study, all 90 patients (100%) had serum LDH levels greater than 230 U/L and found that serum LDH at a cut-off value of 614U/L predicts a poor outcome in CAP patients with a sensitivity of 78.8% and specificity of 71.9%.

All of the patients in study had serum LDH levels greater than 230 U/L, which is most likely due to associated comorbidities in the current studies than in previous studies.

Viasus et al. found that 37.7% of 3463 CAP patients had serum albumin levels below 3g/dl within 24 hours of hospitalization and concluded serum albumin levels below 3 g/dl to be predictors of ICU admission and 30-day mortality[12].This study also showed that decreases in serum albumin at that point of hospitalization significantly raise the risk of complications, more time to reach clinical stability and prolonged length of hospitalization with a median of 8 days. According Irfan et al.'s studies, low serum albumin levels (<2.2 g/dl) and abnormal liver function tests were linked to higher mortality rates[13]. Malnutrition, liver dysfunction, and infections cause hypoalbuminemia.
Hypoalbuminemia was common among hospitalized patients with CAP.[14]

During acute infection, endotoxins from Gram-negative bacteria, cytokines, and IL-6 inhibit albumin synthesis in hepatocytes while increasing albumin catabolism, resulting in reduced circulatory albumin levels. In this study, 87.80% of CAP patients had median albumin value of 3.01g/dl, within 24 hours of hospitalization and found that serum albumin levels < 3.1g/dl to be predictors of ICU admission and 30-day mortality, which was consistent with Viasus et al. studies.The current study suggests that as the Expanded CURB 65 score increases, so does hypoalbuminemia. Hypoalbuminemia occurs in approximately 94.2% of Expanded CURB 65 scores (3-4) and 90% of scores (5-8). This result shows that, though 30-day mortality increases with hypoalbuminemia, the relationship did not reach statistical significance. In our current study, 8.90% of patients had thrombocytopenia (platelet counts $< 100\times10^3$/mm3). Among CAP patients who died within 30 days, 46% had thrombocytopenia, and 21% had thrombocytopenia when they were admitted to the ICU. ROC analysis revealed that a platelet counts of $<161\times10^3$ cells/mm3 predicts

30-day mortality, ICU admission with sensitivity and specificity of 84.62%, 48.5% and of 88.31%, 93% respectively.

In univariate analysis of risk factors linked to 30-day mortality in CAP, thrombocytopenia (platelet counts < 100×103/mm3) was found to be strongly associated with 30-day mortality. The presence of thrombocytopenia increases with the increase in Expanded CURB 65 score. Patients with thrombocytopenia are at a higher risk of major bleeding, acute renal injury, and extended ICU stay[15].

Brogly et al. found that 25% of ICU-admitted CAP patients had thrombocytopenia of $<150\times10^9$/L. and concluded thrombocytopenia $<50\times10^9$/L was an independent predictor of mortality[16].

This study found that 36.7% of patients with CAP were admitted to the intensive care unit, the overall median length of hospital stay was 7 days, the 30-day mortality rate was 14.4%, and 35.6% required mechanical ventilation. This is analogous to a prospective study conducted by Shehata SM et al[5].

This study found that duration of hospital stay increases with an increase in Expanded CURB 65 score; the median LOS of Expanded CURB 65 score (0-2), (3-4), and (5-8) is 5, 7, and 9 days, respectively. This finding was consistent with a previous study conducted by Liu et al.,

In the current study, the 30-day mortality rate in different risk classes of two scoring systems (Expanded CURB 65 score (0-2), (3-4), (5-8) was 0, 5.8%, 90% respectively, and CURB 65 score (0-1), (2), (3-5) was 2%, 20%, and 83.3% respectively) was higher than in previous studies done by Shehata et al.[5] and Liu et al. [10] This discrepancy could be attributed to the current study's smaller sample size and higher prevalence of comorbidities. Our current study found that Expanded CURB 65 scores (0-2) and (3-4) had lower 30-day mortality rates than CURB 65 scores (0-1) and (2), while Expanded CURB 65 scores (5-8) had higher mortality than CURB 65 scores (3-5). The 30-day mortality rate differed significantly between the Expanded CURB 65 score subgroups.

After analyzing the discriminative power of both scoring systems in predicting the need for 30-day mortality, ICU admission and need for mechanical ventilation in CAP patients, the Expanded CURB 65 score with cut off score > 3 is superior when compared to CURB 65 score.

The current study's findings are consistent with those of Liu et al.,[10] who found that the overall sensitivity and specificity of Expanded CURB-65 were superior to other score systems such as PSI and CURB-65, in predicting 30-day mortality.

V. Conclusions:

Expanded CURB 65 score, includes eight independent risk factors which predicts the severity of CAP. As the score increases, there is an increased chance of ICU admissions, need for mechanical ventilation, length of hospital stay and risk for 30-day mortality. Expanded CURB 65 score is simple, objective, and relatively accurate than CURB 65 score in identifying high-risk patients, thereby helps in the early institution of therapy.

VI. Limitations:

Sample size of the study was relatively small, therefore multi-centric studies with large sample size are needed to validate the results. And the study was conducted in the tertiary care center, thereby limiting the generalizability of the results.

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