

Prognostication of COVID-19 patients using ROX index and CURB-65 score - A retrospective observational study

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ABSTRACT

Objectives: Coronavirus disease-2019 (COVID-19) disease has overwhelmed the healthcare infrastructure worldwide. The shortage of intensive care unit (ICU) beds leads to longer waiting times and higher mortality for patients. High crowding leads to an increase in mortality, length of hospital stays, and hospital costs for patients. Through an appropriate stratification of patients, rational allocation of the available hospital resources can be accomplished. Various scores for risk stratification of patients have been tried, but for a score to be useful at primary care level, it should be readily available at the bedside and be reproducible. ROX index and CURB-65 are simple bedside scores, requiring minimum equipment, and investigations to calculate. Methods: This retrospective, record-based study included adult patients who presented to the ED from May 1, 2020 to November 30, 2020 with confirmed COVID-19 infection. The patient's clinical and demographic details were obtained from the electronic medical records of the hospital. ROX index and CURB-65 score on ED arrival were calculated and correlated with the need for hospitalization and early (14-day) and late (28-day) mortality. Results: 842 patients were included in the study. The proportion of patients with mild, moderate and severe disease was 46.3%, 14.9%, and 38.8%, respectively. 55% patients required hospitalization. The 14-day mortality was 8.8% and the 28-day mortality was 20.7%. The AUROC of ROX index for predicting hospitalization was 0.924 (p < 0.001), for 14-day mortality was 0.909 (p < 0.001) and for 28-day mortality was 0.933 (p < 0.001). The AUROC of CURB-65 score for predicting hospitalization was 0.845 (p < 0.001), for 14-day mortality was 0.905 (p < 0.001) and for 28-day mortality was 0.902 (p < 0.001). The cut-off of ROX index for predicting hospitalization was \leq 18.634 and for 14-day mortality was \leq 14.122. Similar cut-off values for the CURB-65 score were ≥ 1 and ≥ 2 , respectively. **Conclusion:** ROX index and CURB-65 scores are simple and inexpensive scores that can be efficiently utilised by primary care physicians for appropriate risk stratification of patients with COVID-19 infection.

Keywords: COVID-19, CURB-65 score, prognostic score, risk-stratification, ROX index

Introduction

India has registered the second-highest number of COVID-19 infections in the world. By the beginning of December 2020,

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India had almost 9.49 million COVID-19 cases and over 1,38,000 deaths, which increased to over 34 million cases and over 4,58,000 deaths by the end of October 2021.^[1]

COVID-19 disease primarily involves the lungs with manifestations ranging from mild pneumonia to severe ARDS. Hypoxia is a common presenting feature and is paradoxically well-tolerated by the patients. This phenomenon termed 'happy hypoxemia'

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occurs because there is a disconnect between the severity of hypoxia and the signs of respiratory distress.^[2:4]

Patients with moderate and even severe COVID-19 disease may appear well at the initial presentation but have a propensity to deteriorate rapidly. So, a scoring system which is based on clinical assessment, requires minimum equipment and is applicable on first presentation at primary care level can help in rational allocation of resources. ROX index and CURB-65 are simple bedside scores, requiring minimum equipment, to calculate.

ROX index is defined as the ratio of oxygen saturation measured by pulse oximetry/FiO₂ to respiratory rate. It is a validated index in patients with acute hypoxemic respiratory failure who are on high flow nasal cannula therapy to predict the success or failure of the therapy in terms of the requirement of intubation.^[5,6] Recently, the ROX index has also found relevance as a prognostic marker for patients in sepsis, with the median ROX index lower in non-survivors than survivors.^[7]

CURB-65 is an internationally validated tool to predict the severity and mortality of patients with community-acquired pneumonia. It is a five-point score comprising five parameters- Confusion, Urea >7 mmol/L, Respiratory rate \geq 30/min, low systolic (<90 mm Hg), or diastolic (\leq 60 mm Hg) blood pressure and age \geq 65 years. A higher CURB-65 score correlates with higher mortality.^[8]

CURB-65 score is reported to have a good predictive value for mortality among patients with COVID-19.^[9] It was also proposed to be used as the reference prognostic tool for COVID-19 pneumonia in Spain.^[10]

In this study, we aimed to assess the predictive value of the ROX index and CURB-65 score in estimating early (14-day) and late (28-day) mortality among patients presenting to the emergency department with confirmed COVID-19 infection.

Materials and Methods

This is a retrospective observational study which was electronic records based (e-hospital^{@NIC}). It was conducted at an urban tertiary care hospital. Data were collected from May 1, 2020 to November 30, 2020. In this study, we assessed the predictive value of ROX index and CURB-65 score in estimating early mortality (14-day) and late mortality (28-day) among patients presenting to the ED with confirmed COVID-19 infection. We also assessed the predictive ability of ROX index and CURB-65 score in determining the need of hospitalization among patients with COVID-19.

Adult patients 18 years of age or older who presented to the ED who were positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by either real-time reverse transcriptase polymerase chain reaction (rRT-PCR) or Rapid Antigen Testing (RAT) were included in the study. Pregnant

females, patients with incomplete medical records, and patients who expired shortly after ED arrival and who did not receive any laboratory testing were excluded from the study.

The sample size was determined by the time window of the study. The study was approved by the institutional ethical committee (Letter Number - AIIMS/IEC/21/658).

This manuscript adheres to the STROBE guidelines.

Methodology

All patients who presented to the ED during the study period were screened for eligibility based on the inclusion and exclusion criteria. Their clinical and demographic details were obtained from the electronic medical records of the hospital (e-hospital^{@NIC}).

Scores were calculated from the first measurement performed upon arrival at the ED. ROX index was calculated using the formula $(\text{SpO}_2/\text{FiO}_2)/\text{RR}$. CURB-65 score was calculated using 5 parameters-

- 1. Age ≥ 65 years
- 2. Confusion.
- 3. Urea >7 mmol/L
- 4. Respiratory Rate \geq 30.
- Systolic Blood Pressure <90 mm Hg or Diastolic Blood Pressure ≤60 mm Hg.

The primary outcome of the study was 28-day mortality.

Patients who were intubated within 24 hours of arrival to the ED were noted. Patient outcome (survival/mortality) on day 14 and day 28 from the day of admission was collected from medical records. A research investigator performed a structured telephonic follow-up for patients who were discharged before 28 days.

Statistical analysis

The data was analyzed with the help of SPSS software version 24. Categorical variables were presented in number and percentage (%), and continuous variables were presented as mean (SD) and median (IQR) depending on the distribution of the data after assessing normality by Shapiro-Wilk test. Categorical variables were analyzed with Chi-squared test or Fisher's exact test. Continuous variables were analyzed using Wilcoxon-Mann-Whitney U test. The receiver operating characteristic curves were plotted to predict the need of hospitalization and the risk of early (14-day) and late (28-day) mortality and the area under the curves was computed. The optimal ROX index and CURB-65 score cut-offs were determined by optimising sensitivity and specificity favouring sensitivity for the purpose of mortality and specificity for the purpose of hospitalization. The level of significance was set at P < 0.05.

Results

842 patients were included in the study. The baseline characteristics of the patients are summarized in Table 1. 55% (n = 463) patients required hospitalization and 29.8% (n = 251) patients required ICU admission. The 14-day mortality was 8.8% (n = 74) and 28-day mortality was 20.7% (n = 174). Table 2 summarizes the outcome parameters of the study population.

The association of various parameters with 14-day mortality is summarized in Table 3. The strength of association (Point-Biserial

Table 1: Baseline characteristics of the patients with COVID-19 who presented to the Emergency Department Parameters Mean±SD/Median (IQR)/Frequency % Age (Years) 48.00 (32.25-62.00) Gender Male 562 (66.7%) Female 280 (33.3%) Clinical Category Mild 390 (46.3%) Moderate 126 (14.9%) 327 (38.8%) Severe Co-Morbidities None 482 (57.2%) 2 (0.2%) Bronchial Asthma 14 (1.7%) Chronic Kidney Disease 15 (1.8%) Chronic Liver Disease Chronic Obstructive Pulmonary Disease 37 (4.4%) Coronary Artery Disease 53 (6.3%) Diabetes Mellitus 147 (17.5%) Hypertension 177 (21.0%) Hypothyroidism 5 (0.6%) Malignancy 4 (0.5%) Pulmonary Kochs 3 (0.4%) Sarcoidosis 1 (0.1%) Stroke 18 (2.1%)

Correlation) of ROX index with 14-day mortality was 0.42 and that of CURB-65 score was 0.49, signifying a large effect size in both the cases.

The association of various parameters with 28-day mortality is summarized in Table 4. The strength of association (Point-Biserial Correlation) of ROX index with 28-day mortality was 0.64 and that of CURB-65 score was 0.63, also signifying a large effect size in both the cases.

The area under the Receiver Operating Characteristic curve (AUROC) for ROX Index for predicting hospitalization was 0.924 (95% CI: 0.906-0.942), thus demonstrating excellent diagnostic performance [Figure 1]. It was statistically significant (p = <0.001). The obtained cut-off for ROX index for hospitalization was 18.634 [Table 4]. The AUROC for CURB- 65 score for predicting hospitalization was 0.845 (95% CI: 0.822-0.868), thus demonstrating good diagnostic performance [Figure 1]. It was also statistically significant (p = <0.001). The obtained cut-off of CURB-65 score for predicting hospitalization was 1. [Table 5]. The diagnostic performance of ROX Index (AUROC = 0.924) was significantly better than that of CURB-65 score (AUROC = 0.845) (DeLong's Test P = <0.001).

The performance of various diagnostic parameters in predicting 14-day mortality is summarised in Table 6. Both ROX index and CURB-65 score demonstrate excellent diagnostic performance in predicting 14-day mortality with an AUROC of 0.909 (95% CI: 0.88-0.938) (p = <0.001) for ROX index and 0.905 (95% CI: 0.881-0.929) (p = <0.001) for CURB-65 score [Figure 2]. Figure 3 shows the ROC curves of SpO₂ and respiratory rate at presentation with 14-day mortality.

There was no significant difference in the diagnostic performance of ROX Index and CURB- 65 score in predicting 14-day mortality. (DeLong's Test P = 0.782). However, the diagnostic performance of ROX index in predicting 14-day



Figure 1: Receiver Operating Characteristic curves for ROX index and CURB-65 score for predicting hospitalization among COVID-19 patients



Figure 2: Receiver Operating Characteristic curves for ROX index and CURB-65 score for predicting 14-day mortality among COVID-19 patients



Figure 3: Receiver Operating Characteristic curves for SpO, and Respiratory Rate for predicting 14-day mortality among COVID-19 patients

Table 2: Outcome parameters of the study population				
Parameters	Frequency (%)			
Intubated in the Emergency	23 (2.7%)			
Disposition				
Home/Facility Isolation	379 (45.0%)			
Hospitalization	463 (55.0%)			
Intensive Care Unit	251 (29.8%)			
High Dependency Unit	212 (25.2%)			
14-Day Mortality	74 (8.8%)			
28-Day Mortality	174 (20.7%)			

mortality (AUROC = 0.909) was significantly better than that of respiratory rate (AUROC = 0.841) (DeLong's Test P = <0.001) and SpO₂ at presentation (AUROC = 0.816) (DeLong's Test P = <0.001). The diagnostic performance of CURB-65 score also (AUROC = 0.905) was significantly better than that of respiratory rate (AUROC = 0.841) (DeLong's Test P = <0.001) and SpO₂ at presentation (AUROC = 0.816) (DeLong's Test P = <0.001) and SpO₂ at presentation (AUROC = 0.816) (DeLong's Test P = <0.001).

The performance of various parameters in predicting 28-day mortality among patients with COVID-19 are summarized in Table 7. Both ROX index and CURB-65 score demonstrate excellent diagnostic performance in predicting 28-day mortality with an AUROC of 0.933 (95% CI: 0.917-0.949) (p = <0.001) for ROX index and 0.902 (95% CI: 0.883-0.92) (p = <0.001) for CURB-65 score [Figure 4]. The diagnostic performance of ROX Index was significantly better than that of CURB- 65 score (DeLong's Test P = <0.001). Figure 5 shows the ROC curves of SpO, and respiratory rate at presentation with 28-day mortality.

The diagnostic performance of ROX Index in predicting 28-day mortality (AUROC = 0.933) was significantly better than that of respiratory rate (AUROC = 0.907) (DeLong's Test P = <0.001) and SpO₂ at presentation (AUROC = 0.900) (DeLong's Test P = <0.001). However, there was no significant difference in the diagnostic performance of CURB-65 - score and SpO₂ at presentation (DeLong's Test P = 0.907) and respiratory rate (DeLong's Test P = 0.564).

Parameters	14-Day Mortality					
	Yes (n=74)	No (n=768)				
Age (Years)***	72 (66.25-76.75)	46 (30.75-59)	< 0.0011			
Gender			0.351 ²			
Male	53 (71.6%)	509 (66.3%)				
Female	21 (28.4%)	259 (33.7%)				
General Physical Examination						
Pulse Rate (BPM)***	108.5 (102.25-115)	94 (88-106)	< 0.0011			
Systolic Blood	100 (88.5-113.5)	120 (110-126)	< 0.0011			
Pressure (mmHg)***						
Diastolic Blood	70 (64.5-78)	74 (70-80)	0.002^{1}			
Pressure (mmHg)***						
Mean Arterial Pressure (mmHg)***	82 (73-89.75)	90 (84-94)	< 0.0011			
Temperature (F)	98.9 (98.73-99.2)	98.9 (98.1-99)	0.081^{1}			
Glasgow Coma Scale***	15 (10.25-15)	15 (15-15)	< 0.0011			
SpO ₂ at presentation (%)***	75.5 (58-86)	95 (88-98)	< 0.0011			
Respiratory Rate (Breaths/min)***	36 (30-38)	22 (19-30)	< 0.0011			
ROX Index***	4.92 (4.07-10.02)	20.78 (13.77-23.57)	< 0.0011			
ROX Index on day of intubation	3.27 (2.53-4.52)	3 (3-4)	0.4151			
CURB-65						
Confusion***	23 (31.1%)	0 (0.0%)	$< 0.001^{3}$			
High Urea***	51 (68.9%)	205 (26.7%)	$< 0.001^{2}$			
High Respiratory Rate ***	61 (82.4%)	213 (27.7%)	$< 0.001^{2}$			
Low BP***	20 (27.0%)	79 (10.3%)	$< 0.001^{2}$			
Advanced Age***	60 (81.1%)	104 (13.5%)	$< 0.001^{2}$			
Total Score***	3 (2-4)	0 (0-2)	< 0.0011			
Intubated in the Emergency (Yes)***	23 (31.1%)	0 (0.0%)	< 0.001 ³			
Day of Intubation***	3 (1-5)	5 (3-5)	< 0.0011			

Parameters	28-Day Mortality					
	Yes (<i>n</i> =174)	No (<i>n</i> =668)				
Age (Years)***	61.5 (49.25-73)	45 (30-58)	< 0.0011			
Gender			0.050^{2}			
Male	127 (73.0%)	435 (65.1%)				
Female	47 (27.0%)	233 (34.9%)				
General Physical Examination						
Pulse Rate (BPM)***	109 (103-114.75)	93 (87-102.25)	< 0.0011			
Systolic Blood	100 (88-114)	120 (110-126)	< 0.0011			
Pressure (mmHg)***						
Diastolic Blood	70 (64-78)	76 (70-80)	< 0.0011			
Pressure (mmHg)***						
Mean Arterial Pressure (mmHg)***	82 (72.25-88.5)	91 (86-95)	< 0.0011			
Temperature (F)***	98.9 (98.6-99.2)	98.65 (98-99)	0.001^{1}			
Glasgow Coma Scale***	14.24±2.00	15.00 ± 0.00	< 0.0011			
SpO ₂ at presentation (%)***	68 (50-81.5)	96 (90-98)	< 0.0011			
Respiratory Rate (Breaths/min)***	36 (32-39)	21 (19-27)	< 0.0011			
ROX Index***	7.38 (5.05-9.29)	21.43 (16.01-24.34)	< 0.0011			
ROX Index on day of intubation	3 (3-4.11)	3 (3-4)	0.6031			
CURB-65						
Confusion***	23 (13.2%)	0 (0.0%)	< 0.0013			
High Urea***	124 (71.3%)	132 (19.8%)	$< 0.001^{2}$			
High Respiratory Rate***	151 (86.8%)	123 (18.4%)	$< 0.001^{2}$			
Low BP***	53 (30.5%)	46 (6.9%)	$< 0.001^{2}$			
Advanced Age ***	84 (48.3%)	80 (12.0%)	$< 0.001^{2}$			
Total Score***	2 (2-3)	0 (0-1)	< 0.0011			
Intubated in the Emergency (Yes)***	23 (13.2%)	0 (0.0%)	< 0.0013			

***Significant at P<0.05, 1: Wilcoxon-Mann-Whitney U Test, 2: Chi-Squared Test, 3: Fisher's Exact Test

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Figure 4: Receiver Operating Characteristic curves for ROX index and CURB-65 score for predicting 28-day mortality among COVID-19 patients



Figure 5: Receiver Operating Characteristic curves for SpO₂ and Respiratory Rate for predicting 28-day mortality among COVID-19 patients

Table 5: Predictive value of ROX index and CURB-65 score for hospitalization among COVID-19 patients						
Parameter	AUROC (95% CI)	Р	Cut-off	Sensitivity	Specificity	Relative Risk (95% CI)
ROX index	0.924 (0.906-0.942)	(<0.001)	≤18.634	80%	97%	4.73 (3.97-5.69)
CURB-65	0.845 (0.822-0.868)	(<0.001)	≥ 1	74%	92%	2.86 (2.55-3.24)

Discussion

This single-centre study was conducted in a cohort of 842 patients who presented with confirmed COVID-19 infection to the Emergency department of an urban tertiary care hospital. Of these, 55% patients required hospitalization and 29.8% patients required ICU admission. The 14-day mortality of the study population was 8.8% and 28-day mortality was 20.7%.

The 28-day mortality in our cohort was similar to the cohort of de Souza R *et al.* (22.64%; India),^[11] Fan *et al.*, (20.3%; China)^[12] and Artero A *et al.* (20.9%; Spain),^[13] but it was higher than Ahmad S *et al.*, (11%; India)^[14] and Gianstefani *et al.* (14.8%; Italy).^[15]

CURB-65 is a simple five-point score that is a strong predictor of 30-day mortality in patients with Community Acquired Pneumonia (CAP). This score has been validated in multiple

Table 6: Predictive value of various parameters for 14-day mortality among COVID-19 patients									
Parameter	AUROC (95% CI)	Р	Cut-off	Youden's index	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy
SpO ₂ at presentation (%)	0.816 (0.783-0.849)	< 0.001	≤87	61.6	86.5% (77-93)	75.1% (72-78)	25.1% (20-31)	98.3% (97-99)	76.1% (73-79)
Respiratory Rate (Breaths/min)	0.841 (0.81-0.871)	< 0.001	≥25	61.0	98.6% (93-100)	62.4% (59-66)	20.2% (16-25)	99.8% (99-100)	65.6% (62-69)
ROX Index	0.909 (0.88-0.938)	< 0.001	≤14.122	64.2	90.5% (81-96)	73.7% (70-77)	24.9% (20-31)	98.8% (97-100)	75.2% (72-78)
CURB-65 score	0.905 (0.881-0.929)	< 0.001	≥ 2	67.7	95.9% (89-99)	71.7% (68-75)	24.7% (20-30)	99.5% (98-100)	73.9% (71-77)

Table 7: Predictive v	value of various	parameters for
28-day mortality	among COVID	-19 patients

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Parameter	AUROC (95% CI)	Р
SpO ₂ at presentation (%)	0.9 (0.879-0.921)	< 0.001
Respiratory Rate (Breaths/min)	0.907 (0.888-0.927)	< 0.001
ROX Index	0.933 (0.917-0.949)	< 0.001
CURB-65 Score	0.902 (0.883-0.92)	< 0.001

populations.^[8,16,17] CURB-65 score was found to have a good diagnostic performance to predict hospitalization and an excellent diagnostic performance in predicting 14-day mortality and 28-day mortality among patients with COVID-19 in our study. Previous studies have also demonstrated a good diagnostic performance of the CURB-65 score in predicting mortality among COVID-19 patients.^[9,18,19]

In our study, the cut-off value of the CURB-65 score for predicting hospitalization among COVID-19 patients was ≥1. The cut-off value predicting 14-day mortality among COVID-19 patients was ≥ 2 . These values imply that patients presenting to the ED with a CURB-65 score of ≥ 1 on arrival require hospitalization, and those with a score of ≥ 2 on arrival are at a high risk of mortality and thus should preferably receive intensive care. Previous studies by Guo J et al., and Carriel J et al., have also reported that a CURB-65 score ≥ 2 could serve as a cut-off value to predict in-hospital mortality among patients with COVID-19.^[18,20] However, according to the CAP guidelines in the pre-COVID era, a CURB-65 score of 0 and 1 was associated with low mortality, and this subset of patients was eligible to be treated as outpatients. Patients with a score of 2 required hospital admission, and those with a score of 3 and above had high mortality and required Intensive care unit admission.^[8]

All the five parameters comprising the CURB-65 score were significantly associated with early (14-day) and late (28-day) mortality in our study. Previous studies have also demonstrated that a higher respiratory rate,^[21] the presence of acute kidney injury,^[22] shock,^[23] higher age,^[24] and neurological involvement^[25] are associated with higher mortality among COVID-19 patients.

ROX index is a simpler score to calculate than even the CURB-65 score. ROX index was found to have an excellent diagnostic performance to predict hospitalization and to predict 14-day mortality and 28-day mortality among patients with COVID-19 in our study. These findings are similar to the findings of previous

studies. In a study by Tang M *et al.*, the ROX index could identify patients with severe COVID-19 disease.^[26] In the study by Prower E *et al.*,^[27] the ROX index could be used to predict deterioration in terms of cardiac arrest, unplanned critical care admission, or death among patients with COVID-19. In the study by Gianstefani *et al.*, the ROX index was found to be significantly associated with mortality in patients with COVID-19.^[15]

In our study, the cut-off value of the ROX index for predicting hospitalization among COVID-19 patients was \leq 18.634. The cut-off value predicting 14-day mortality was \leq 14.122, thus implying the need for intensive care. These findings are quite similar to the study by Prower E *et al.*, where a ROX index <18 showed a positive correlation with severe COVID-19.^[27] However, in the study by Gianstefani *et al.*,^[15] ROX index \leq 25.7 could be used to predict hospitalization, and \leq 22.3 could be used to predict 30-day mortality. The patient cohort of their study was older with a mean age of 61.5 ± 19 years as opposed to the patient cohort of our study. Since age is an independent predictor of mortality among patients with COVID-19,^[7] and lower values of ROX index signify a more severe disease, the lower cut-off values of the ROX index in our study can possibly be attributed to this demographical parameter.

In our study, the diagnostic performance of the ROX index in predicting both early (14-day) and late (28-day) mortality was significantly better than its constituent parameters - namely SpO_2 and respiratory rate. Similarly, the diagnostic performance of the CURB-65 score was significantly better than both SpO_2 and respiratory rate in predicting early mortality. ROX index also outperformed the CURB-65 score in predicting late mortality among patients with COVID-19.

To the best of our knowledge, this is the only study where the predictive value of the ROX index in assessing mortality among patients with COVID-19 in an Indian population has been assessed.

There are certain limitations of our study - the first being that it is a retrospective, single-centre study. Secondly, the scores were calculated just at arrival, and thus dynamicity of these scores with the disease process could not be evaluated. Thirdly, these results cannot be extrapolated to children and pregnant females. Larger, multicentric studies are needed to validate the use of these scores and their cut-off values, especially in the light of evolving disease process.

Conclusion

COVID-19 pandemic has caused an enormous strain on healthcare facilities worldwide. In such a setting, simple risk stratification scores can prove invaluable to reduce patient morbidity and mortality. In our study, we assessed ROX index and CURB-65 scores among patients with confirmed COVID-19 on arrival to the ED and found that they had a good diagnostic performance in predicting both hospitalization as well as early (14-day) and late (28-day) mortality. Thus, these scores can be utilized by primary care physicians for early and appropriate risk stratification of patients with COVID-19 pneumonia.

Key-points

- 1. ROX index and CURB-65 score are simple scores that can be utilised by Primary Care Physicians for easy risk-stratification of patients with COVID-19 pneumonia.
- 2. ROX index and CURB-65 score can be utilised by Physicians in a healthcare setting with minimal infrastructure.

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Conflicts of interest

There are no conflicts of interest.

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