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Original Research Article

Correlation of CALL score with disease progression in COVID-19 patients

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ABSTRACT

Background: Many prognostic models have been introduced to predict the disease progression in an individual with COVID-19, CALL score is one among them. The objective of the study was to evaluate the role of comorbidity, high age, low lymphocyte count, high lactate dehydrogenase (CALL) score in predicting disease progression and mortality in COVID 19 patients.
Methods: Total 105 patients were divided into - stable group (CALL≤6) and progressive group (CALL>6), Chi-square test and ROC analysis is applied to predict the outcomes like oxygen requirement, ICU requirement (high flow nasal oxygen), invasive ventilation requirement, increase in respiratory rate ≥30 Cpm and death/recovery with CALL score in both the groups.
Results: ROC analysis was done to predict outcome based on CALL score in both groups which showed sensitivity 100% (91.6% to 100%), specificity of 8.2% (2.7 to 18.1%), PPV – 44% (42.16 to 45.86%) and NPV – 100%.
Conclusions: Using the CALL score model with cut off of 6 points, clinicians can predict the progression risk in terms of higher respiratory rate ≥30 cpm, oxygen requirement, requiring ICU, death/ recovery.

Keywords: CALL score, COVID-19, Disease progression

INTRODUCTION

Coronavirus Disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), often produces asymptomatic or mild disease in the majority of patients, but roughly 10% – 15% of patients develop severe disease.[1,2] Severe cases raise demand for hospital beds and may result in a medical care shortage. The healthcare system can benefit from predictive models that evaluate the probability of progressing disease in this case. Early detection and management of patients at high risk may help to reduce the need for hospitalization, mechanical ventilation, and even death.[3] Numerous risk variables, including patient characteristics (age, underlying diseases) and laboratory indicators (CRP, ferritin, lymphocyte count, neutrophil/lymphocyte ratio), have been identified in prior research for prediction of disease severity.[4,5]

Various prediction models were created during the early pandemic period. Severity of pneumonia can be assessed using the Pneumonia Severity Index (PSI), CURB-65,12 SMART-COP13 and MuLBSTA14 scores at the admission time.[6,7] The CALL score, which was

developed by Ji et al using four clinical parameters (comorbidity - age - lymphocyte count - lactate dehydrogenase [LDH]), was claimed to be the optimal predictor of progression with an AUC value of 0.91 (with a 95 percent confidence interval [CI] of 0.86-0.94) when used to differentiate hospitalized COVID-19 patients with stable (n=168) and progressive (n=40) diseases.[8] This study was one of the first and most well-known studies to develop a predictive model for COVID-19 patients admitted to the hospital. 8 The purpose of this study was to assess the CALL score's performance in patients with COVID-19 in Bangalore Medical College Hospital setting.

METHODS

Study population

The study was conducted in Bangalore Medical College and Research Institute, Bangalore. From September to October 2020, 105 adult patients (no age criteria) with COVID-19 confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) were included in this retrospective, non-interventional study. The Bangalore Medical College Institutional Ethical Review Board waived informed consent. Patients were classified as stable (CALL ≤6) or progressing (CALL >6). In both groups, the chi-square test and receiver operating characteristic analysis are used to predict outcomes such as oxygen demand, ICU requirement (high flow nasal oxygen), invasive ventilation requirement, rise in respiratory rate ≥30 Cpm, and death/recovery.

Data collection

Following informed consent, the patients' characteristics (age, gender, and comorbidities), vital signs, and laboratory values, such as complete blood count, CRP, ferritin, LDH, RR, and O2 demand, were collected. The following information was also obtained: ICU admission, invasive ventilation necessity, and outcome. These laboratory parameters were checked at admission and every other day while the patient was in the hospital. The patient's O2 saturation was determined using pulse oximetry in room air and validated by arterial blood gas analysis. The progression of illness was monitored by infectious disease specialists on a daily basis while the patients were hospitalized.

Inclusion criteria

Patients diagnosed with COVID-19 infection by RT-PCR technique or rapid antigen testing. Mild to moderate COVID-19 disease at presentation. Patients willing to sign informed consent. Patient of either sex and any age.

Exclusion criteria

Patient not will to give informed consent. Patients with severe COVID-19 disease at presentation.

Statistical analysis

Kolmogorov smirnov, skewness kurtosis, and histogram plots were used to examine the distribution of numerical variables. The numerical variables that did not have a normal distribution were reported using the median, interquartile range, lowest and maximum values. Frequencies and percentages were used to report categorical variables. Chi-Square and Fisher's exact tests were used to assess categorical variables. The Mann-Whitney U test was used to compare the distribution of numerical variables among independent groups. According to Ji et al study the CALL score was derived using the number of comorbidities, age, LDH, and lymphocyte count factors.[6] The CALL score's ability to predict progressive COVID-19 was examined using receiver operating characteristic (ROC) analysis, and the area under curve (AUC) value was provided with a 95 percent confidence interval. CALL score = 6 was utilized as the cut off value, and sensitivity, specificity, negative and positive predictive values, and likelihood ratios were provided with a 95 percent confidence range.

A p-value of 0.05 or less was judged statistically significant. All analyses were carried out using IBM Statistical package for social sciences (SPSS) version 21 software.

RESULTS

Clinical characteristics of patients

Overall, 105 patients with PCR-confirmed mild to moderate COVID-19 cases were included in the study. The median age was 48 (IQR, 28), 14 (13.3%) were older than 65 years, and 3 (2.9%) were less than 15 years. Significant association was observed between age groups and CALL Score (Table 1).

Out of 105 subjects, 49 (46.70%) patients were female. No significant association was found between gender and CALL score as p>0.05 (Table 2).

Of 105 patients, 54 (51.4%) had at least one comorbidity (hypertension, diabetes mellitus, asthma, COPD, CLD, CVD, cancer or HIV) and significant correlation was observed between presence of comorbidity and CALL score (Table 3).

Lymphocyte count was categories as <1000 units and >1000 units. It was observed that 82(78.1%) had >1000 lymphocyte count. Significant correlation was observed between lymphocyte and CALL score (Table 3).

LDH was categorized in two different cut offs 250 unit, and 500 unit. When LDH >500 was considered as cut off, significant association was noted with CALL score (Table 3).

Table 1: Distribution of the subjects based on age.

Age (in years)		Call score		Total	Chi-square value	P value
		Progressive	Steady			
16 to 25	Count	2	9	11	41.07	0.00*
	%	1.9%	8.6%	10.5%		
26 to 35	Count	3	16	19		
	%	2.9%	15.2%	18.1%		
36 to 45	Count	6	4	10		
	%	5.7%	3.8%	9.5%		
46 to 55	Count	21	7	28		
	%	20.0%	6.7%	26.7%		
56 to 65	Count	15	5	20		
	%	14.3%	4.8%	19.0%		
Above 65	Count	14	0	14		
	%	13.3%	0.0%	13.3%		
Less than 15	Count	0	3	3		
	%	0.0%	2.9%	2.9%		
Total	Count	61	44	105		
	%	58.1%	41.9%	100.0%		

*significant

Table 2: Distribution of the subjects based on gender.

Gender		Call-class		Total	Chi-square value	P value
		Progressive	Steady			
Females	Count	30	19	49	0.37	0.54
	%	28.60%	18.10%	46.70%		
Males	Count	31	25	56		
	%	29.50%	23.80%	53.30%		
Total	Count	61	44	105		
	%	58.10%	41.90%	100.00%		

Table 3: Cross tabulation of the parameters based on CALL score.

Variables			CALL score		Total	Chi- square value	P value
			Progressive	Steady			
Comorbidity	No	Count	9	42	51	66.64	0.00*
		%	8.60%	40.00%	48.60%		
	Yes	Count	52	2	54		
		%	49.50%	1.90%	51.40%		
Lymphocyte count	<1000	Count	21	2	23	13.34	0.00*
		%	20.00%	1.90%	21.90%		
	> 1000	Count	40	42	82		
		%	38.10%	40.00%	78.10%		
LDH	<250	Count	26	25	51	2.06	0.15
		%	24.80%	23.80%	48.60%		
	>250	Count	35	19	54		
		%	33.30%	18.10%	51.40%		
LDH	<500	Count	55	44	99	4.59	0.032*
		%	52.40%	41.90%	94.30%		
	>500	Count	6	0	6		
		%	5.70%	0.00%	5.70%		
RR >30	No	Count	14	34	48	30.39	0.00*
		%	13.30%	32.40%	45.70%		
	Yes	Count	47	10	57		
		%	44.80%	9.50%	54.30%		

Continued.

Variables			CALL score		Total	Chi- square value	P value
			Progressive	Steady			
O2 Requirement	No	Count	20	35	55	22.4	0.00*
		%	19.00%	33.30%	52.40%		
	Yes	Count	41	9	50		
		%	39.00%	8.60%	47.60%		
ICU Requirement	No	Count	56	44	100	3.78	0.052
		%	53.30%	41.90%	95.20%		
	Yes	Count	5	0	5		
		%	4.80%	0.00%	4.80%		
Invasive Ventilation	No	Count	57	44	101	3	0.08
		%	54.30%	41.90%	96.20%		
	Yes	Count	4	0	4		
		%	3.80%	0.00%	3.80%		
Outcome	Discharge	Count	56	44	100	3.78	0.052
		%	53.30%	41.90%	95.20%		
	Death	Count	5	0	5		
		%	4.80%	0.00%	4.80%		

Table 4: Odd's ratio for estimating the risk of progression of illness.

Variables	OR	95% CI		P value
		Lower	Upper	
Co-morbidity	0.008	0.002	0.04	<0.05
Lymphocyte count	11.02	2.42	50.09	<0.05
RR >30	0.08	0.035	0.22	>0.05
O2 requirement	0.12	0.051	0.31	>0.05

Table 5: Performance of CALL score for prediction of progressive disease.

Area under the curve				
Area	Std. Error	P value	Asymptotic 95% CI	
			Lower bound	Upper bound
0.771	.096	0.042*	0.582	0.959

Cut off for respiratory rate was considered to be 30. Out of 105 subjects, 48(45.7%) had RR <30. Significant association was noted between RR and CALL Score (Table 3).

Oxygen requirement during stay in hospital was present in 50(47.60%) subjects and it was significantly corelated to CALL score as p<0.05 (Table 3).

No statistical significance was observed between ICU requirement and requirement of invasive ventilation versus CALL score. Death was observed in only 5 (2%) patients.

Odd's ratio was calculated for estimating the risk of progression of illness. Comorbidity: OR 0.008 95% CI (0.002-0.04) p<0.05, Lymphocyte Count: OR- 11.02, 95% CI (2.42-50.09) p<0.05, RR >30: OR 0.08 95% CI (0.035-0.22) p>0.05, O2 requirement: OR 0.12 95% CI (0.051-0.31) p>0.05 (Table 4).

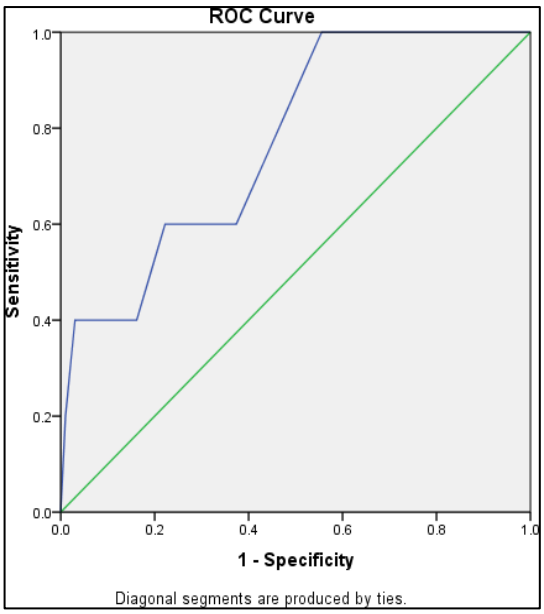

Figure 1: ROC analysis to predict outcome based on CALL score.

Sensitivity- 100% (91.96% to 100%). Specificity- 8.20% (2.72 % to 18.1%). Positive Likelihood ratio- 1.09 (1.01 to 1.17) Negative Likelihood ratio- 0.00. PPV- 44% (42.16% to 45.86%). NPV- 100%.

The AUC value for CALL score for predicting progression to severe COVID-19 was 0.771 (95% CI 0.582-0.959) (Table 5).

When the cut-off point was selected as 6, ROC analysis was done to predict outcome based on CALL score in both groups which showed sensitivity 100% (91.6% to 100%), specificity of 8.2% (2.7 to 18.1%), PPV – 44% (42.16 to 45.86%) and NPV – 100%.

DISCUSSION

The clinical and laboratory parameters of progressive and stable COVID-19 patients were compared in this study, and the performance of the CALL score was assessed in Bangalore Medical College hospital settings.

When compared to prior studies, the subjects in this study were of lower age gorup.[8] Furthermore, more than half of the patients were males, and 51.4 percent had one or more comorbidities. According to these patient features, the patient sample has a less severe clinical course when compared to earlier investigations on hospitalised patients.[9] As a result, mortality was recorded in 2% of patients. Nonetheless, the patient groups differed significantly in terms of male gender, low lymphocyte count, LDH, RR, and O2 demand. These findings were consistent with earlier research.[10-12]

In this study, the sensitivity value of the CALL score for the prediction of progressive disease was reasonably high (sensitivity: 100% (91-100)) when compared to the original study that developed the CALL score (sensitivity: 95% (83.1–99.4)).[6] Another study by Sultan et al concluded that sensitivity of CALL score was 80% (68-91).[13]

This result in the patient cohort can be explained in part by a high level of progressing illness. In addition, during the start of the pandemic, we hospitalised milder and younger patients with no comorbidities due to a lack of knowledge about the disease's natural course. Finally, COVID-19 strains and patient genotypes may differ between nations and hospitals.[14] These characteristics may account for the comparatively high performance of the CALL score in the patient population.

Various COVID-19 predictive models were developed during the pandemic and are now available in academic literature to improve medical decision making.[7] The CALL score was found to be a good predictive measure for in-hospital mortality and disease progression in this investigation. According to Ji et al., a large proportion of patients with higher CALL scores in this research group exhibited disease progression. A CALL score with a cut off valve of nine points showed positive and negative predictive valves of 78.3 percent and 11.9 percent, respectively.[7] According to Ji et al., the three factors of CALL score; age greater than 60 years, lymphocyte count fewer than 1000, and higher LDH, were reliable predictors of worsening illness state.[7]

The study has a number of limitations. There were a restricted number of people with the progressing condition. Clinical conditions and hospitalisation criteria for patients differed significantly from the original CALL score study. Prospective research in many locations and countries are required. Other infectious pathogens that could elicit COVID-19-like clinical presentations (for example, influenza) were not ruled out using laboratory approaches.

CONCLUSION

With the CALL score model, doctors can estimate the progression risk in terms of greater respiratory rate >30cpm, oxygen need, ICU admission, and death/recovery based on a cut-off of 6 points. As a result, the CALL score contributes to the efficient utilization of available medical resources by identifying patients who are more prone to deteriorate and, as a result, enabling them to receive early intensive therapy, hence minimizing mortality and morbidity.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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