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Application of Call Score in Predicting Progression Risk in Covid- 19 Patients: A Retrospective Study

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ABSTRACT

Background: The outbreak of COVID 19 pandemic has influenced more than 180 countries in the world. The number of cases and high rate of transmission have warranted need of newer diagnostic criteria for predicting the progression risk of the disease. For the purposes of prevention and treatment, it is essential to identify people who naturally have a higher risk of developing severe or even life-threatening illnesses after contracting the virus. This is especially important in light of the lack of a clinically proven drug that specifically targets SARS-CoV-2. **Materials and Methods:** A retrospective study was conducted in 219 patients who were admitted in the Department of General Medicine (IPD and OPD), Sree Narayana Institute of Medical Sciences, Ernakulam, Kerala, during the period from January 2021 to June 2022. Over the course of, 18 months consecutive patients with COVID-19 that tested positive for RAT and met the inclusion and exclusion criteria were evaluated. A CALL SCORE was used as a triage technique to find those who were most likely to experience serious events. The score was worked out considering factors like prevalent comorbidities, age of the patient (under 60 and over 60), serum levels of LDH, and lymphocytes. The association between the parameters of the scoring system like the age, comorbidities, lymphocytopenia and LDH levels with the CALL score risk categories were calculated using the Chi Square test with P value <0.5. The data were entered in MS Excel sheet and analyzed using SPSS software. **Results:** The analysis showed that there is a significant association between each of the parameters and CALL Score risk categories thereby recognizing the severity of the conditions of patients who are RAT-positive COVID-19 early, and initiating treatment in accordance with the severity of the conditions.

Keywords: CALL score, COVID-19, LDH, Age, Comorbidities

I. Introduction

An unprecedented event named “Covid-19” occurred in the month of December 2019 with an extraordinary increase in the number of pneumonia cases in the adult population from Wuhan, China. The number of cases accumulated at an alarming rate, even though quick action was taken by the government and health officials. Subsequently, by January 2020 respiratory samples were collected to identify the microorganism that was causing the pneumonia, that led to respiratory failure. Accordingly, new zoonotic agent, known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified[1]. SARS-CoV2 was communicated via respiratory droplets from one individual to another, causing a pandemic at global level affecting more than 500 million people by March 2022, with more than 6.0 million documented deaths in 191 nations.[2] It was observed that the mortality rate of the 2019 coronavirus disease (COVID-19) increased in elderly patients who also have concomitant conditions such diabetes, hypertension, cardiovascular disease, and cerebrovascular illness[4]. The process of patient treatment, hospitalization, or admission to the intensive care unit (ICU) can be decided based on a number of known scoring systems that are utilised in the management of patients with numerous critical conditions.[5] New scoring systems are still being developed for COVID-19, one of which is the CALL score developed by *Ji et al.*[6] that was derived based on patients’ comorbidities (C), age (A), lymphocyte count (L), and serum lactate dehydrogenase (LDH) levels (L) at the time of admission, to detect a patient population at high risk of disease development. Three independent high-risk indicators identified for the advancement of COVID-19 were advanced age (>60 years), a high level of LDH (give the high value), and a low lymphocyte count (1.0 x10^9/L), and the CALL score helps with its prognosis. According to studies, the recently developed predictive CALL score model for COVID-19, may be able to predict the course of the illness and hospital fatalities. [5, 6,7]

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II. Materials and Methods

A retrospective study was carried out in the Department of General Medicine (IPD and OPD), Sree Narayana Institute of Medical Sciences, Chalakka, North Kuthiyathode (PO), Kunnukara, Ernakulam District, Kerala from January 2021 to June 2022.

Study Design: Retrospective study

Study Location: This was a tertiary care teaching hospital-based study done in Department of General Medicine, at Sree Narayana Institute of Medical Sciences, Chalakka, North Kuthiyathode (PO), Kunnukara, Ernakulam District, Kerala.

Study Duration: January 2021 to June 2022.

Sample size: 219 patients.

Sample size calculation: Sample size was calculated based on the sample sizes specified in the current literature.

Subjects and selection method: Consecutive patients with RAT positive COVID - 19 satisfying the inclusion and exclusion criteria

Inclusion criteria:

(1) Adults (over 18 years of age)
(2) COVID 19 cases confirmed by RAT and admitted in SNIMS COVID isolation facility
(3) Patients who consented to participate in the study

Exclusion criteria:

(1) Missing data on clinical characteristics.
(2) Missing data on laboratory characteristics.
(3) Pregnant women who were RAT positive

Procedure methodology:

All patients who were RAT positive and admitted to the Sree Narayana Institute of Medical Sciences, Chalakka were assessed for the study.

A "CALL Score" was applied to identify people at risk of developing severe events and used as a triage tool. The following parameters were considered for developing the score.

1) Comorbidities
2) Age of patient (<60years and >60 years)
3) LDH level
4) Lymphocytopenia

Call scoring for predicting the disease progression of patients with COVID-19 was estimated as detailed below:

(1) Comorbidity: Without - 1, With - 4
(2) Age: ≤60 years – 1, >60 years - 3
(3) Lymphocyte: >1.0 × 109/L - 1, ≤1.0 × 109/L - 3
(4) LDH: ≤250 U/L – 1, 250–500 U/L- 2 , >500 U/L – 3

Table 1. Classification based on the total of CALL Score

4–6 points	Low risk	CLASS A
7–9 points	Intermediate risk	CLASS B
10–13 points	High risk	CLASS C

Data Collection Method:

Manual collection of the data as printouts from the machines. The data were then entered in an Excel table for further statistical analysis.

Ethical Considerations:

Clearance was obtained from the Ethics Committee, Sree Narayana Institute of Medical Sciences before the commencement of the study. All patients were enrolled only after obtaining informed consent.

Statistical analysis:

The data were analyzed using SPSS version 20 (SPSS Inc., Chicago, IL). Student's t-test was used to ascertain the significance of differences between mean values of two continuous variables and confirmed by nonparametric Mann Whitney test. In addition, paired t-test was used to determine the difference between baseline and 2 years after regarding biochemistry parameters, and this was confirmed by the Wilcoxon test which was a nonparametric test that compares two paired groups. Chi-square and Fisher exact tests were performed to test the differences in proportions of categorical variables between two or more groups. The level $P < 0.05$ was considered as the cutoff value or significance.

III. Results

The general characters of the patients selected for the study and their relationship with CALL score categories are summarized in Tables 2 to 6.

More than half of the participants belonged to the age group of >60 years (53.4%) \and 46.6% had above 60 years age. Majority of the study participants (75.8%) had comorbidities. More than half of the participants had LDH of 250-500 µ/L (53%); 32.9% of participants had LDH below 250 µ/L; and 14.2% had LDH above 500 µ/L. Half of the study participants (50.2 %) had Lymphocytopenia of ≤ 1.0 ×109/L.

Days to hospitalization of patients ranged from 2 to 31 days with a mean of 10.25 days. Number of deaths ranged from 2 to 25 with a mean of 9.68. CALL score ranged from 4 to 13 with a mean of 9.68. Half of the study participants belonged to high-risk category; 31.5% belonged to intermediate risk category and only 17.8% had low risk.

There was a significant difference in CALL Scores with respect to age, comorbidities, LDH and lymphocytopenia levels since the p value < 0.05 (Mann Whitney U test) in all these cases. Patients above 60 years had CALL score of 11.01 belonging to high risk (Class C) category. Patients with comorbidity had a high mean CALL score of 10.32 belonging to high-risk (Class C) category. Patients with high LDH above 250 – 500 had mean CALL score of 10.08 and patients with more than LDH of 500 had the highest mean CALL score of 11.81. Patients with high lymphocytopenia above 1X 109/L had mean CALL score of 7.46 and patients with lymphocytopenia of more than 1X 109/L had the highest mean CALL score of 10.85.

Association of age and illness with CALL score risk factors

It was observed that there is a strong association between high age, the prevalence of comorbidities, high LDH and high Lymphocytopenia levels of the patients with frequency of CALL Score risk categories since as evidenced by the Chi-square test (Table 6).

No patients of above 60 years belonged to low-risk category, and 44.3% of patients (97 numbers) belonged to high risk category. Only 6.4% (14 numbers) of patients below 60 years belonged to high-risk category.

No patients with comorbidities had low risk, whereas 49.3 % (108 persons) had high risk. Patients with more than 250 LDH levels (104 persons, 47.5%) had the high risk for COVID 19; whereas no such patients belonged to low risk category.

It was generally observed that Low levels of Lymphocytopenia had high association for COVID 19 risk. When 89 persons (40.6%) of Lymphocytopenia less than 1X109/L belonged to high risk category, only 13 persons (5.9%) had low risk.

Table 2 - Distribution of patients based on CALL score parameters

Parameters	Frequency	Percent
1. Age <60 years	102	46.6
>60 years	117	53.4
Total	219	100.0
2. Comorbidities		
• Without comorbidity	53	24.2
• With comorbidity	166	75.8
Total	219	100.0
3. LDH <250	72	32.9
250-500	116	53.0
>500	31	14.2
Total	219	100.0
4. Lymphocytopenia 1 x 109/L	109	49.8
<1 X 109/L	110	50.2
Total	219	100.0

Table 3 Hospitalization period and death of patients

Variables	Range Min	Max	Mean	Standard deviation	Median
No. of days in hospital	2	31	10.25	5.49	9
No of deaths	0	25	9.68	6.57	8
CALL Score	2	13	9.16	2.75	10

Table 4 – CALL Scores

Category	Frequency	Percent
Low risk – (4 to 6 points) Class A	39	17.8
Intermediate risk – (7 to 9 points) Class B	69	31.5
High risk – (10 to 13 points) Class C	111	50.7
Total	219	100.0

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Table 5 – Distribution of CALL score categories

Parameters	**Mean ± SD**	**Range**	**Median**	**P Value**
Age < 60 years > 60 years	7.01±2.11 11.01±1.67	4.0 – 11.0 7.0 – 13.0	8.0 12.0	<0.001
Comorbidities • With comorbidity • Without comorbidity	 5.53±1.77 10.32±1.86	 4.0 – 10.0 7.0 – 13.0	 6.0 10.0	 <0.001
LDH • <250 • 250 – 500 • >500	 6.54 ± 1.77 10.08±1.86 11.81±1.53	 4.0 – 11.0 7.0 – 12.0 9.0 – 13.0	 6.0 10.0 13.0	 <0.001
Lymphocytopenia 1 x 109/L <1.0 X 109/L	 7.46±2.19 10.85±2.16	 4.0 – 11.0 6.0 – 13.0	 8.0 12.0	 <0.001

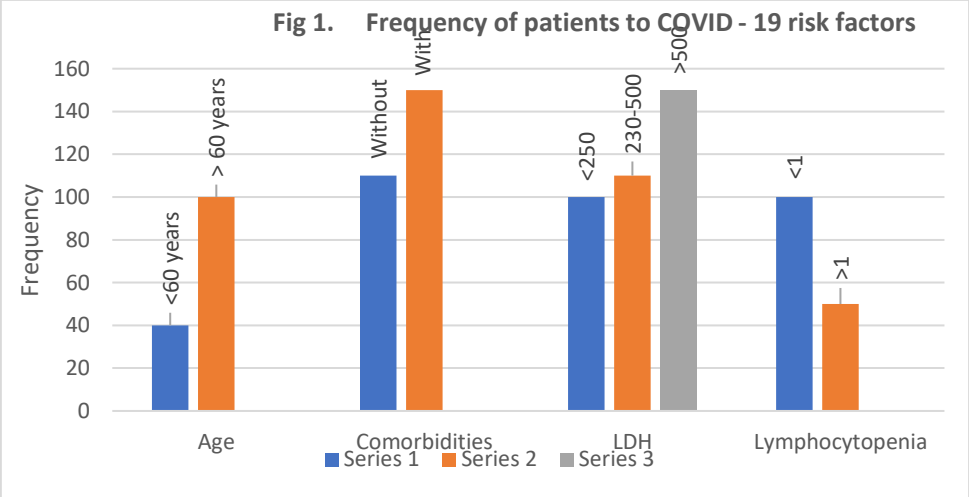

Table 6 – Association of CALL Scores factors with frequency of COVID–19 risk

Call Parameter	Call- risk category			Total %	X^2 value	P value
	Low risk	Intermediate risk	High risk			
Age <60 years >60 years	 39 0	 49 20	 14 97	 46.6% 53.4%	 12.75%	 0.001
Total	**39**	**69**	**111**	**219**		
Comorbidities: Without comorbidities With comorbidities	39 0	11 58	3 108	24.2% 75.8%	 152.68%	 <0.001
Total	**39**	**69**	**111**	**219**		
LDH <250 250-500 >500	39 0 0	26 39 4	7 77 27	32.9% 53.0% 14.1%	 121.26	 <0.001
Total	**39**	**69**	**111**	**219**		
Lymphocytopenia 1.0x <1.0x 109	 26 13	 61 8	 22 89	 49.8% 50.2%	 85.48	 <0.001
Total	**39**	**69**	**111**	**219**		

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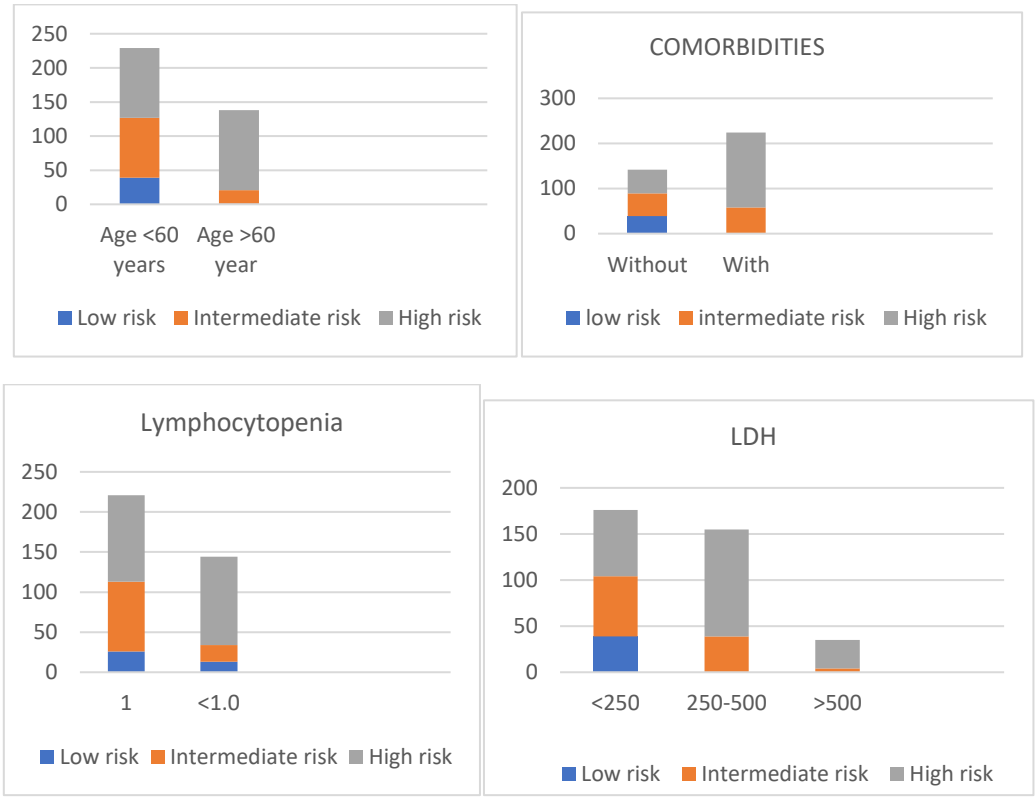

Figure 2 - Call score categories of patients as influenced by age and illness factors

IV. Discussion

Considering the high infectivity and fatality rates of COVID-19 pneumonia, the significance of early disease identification is to be emphasized. A straightforward scoring system employing standard blood tests is essential because early diagnosis and segregation would be beneficial and they might shed insight on the patient's condition and inflammatory process. Previous research works on these aspects indicated that poorer recovery and mortality of COVID-19-infected patients were associated with advanced age, lymphopenia, and high levels of LDH. The existence of comorbidity, on the other hand remains debatable as a separate risk factor. However, a number of studies asserted that the existence of comorbidities constituted a separate risk factor.[49,49–56]

The present study is a hospital-based, retrospective study using a purposive sampling method conducted amongst patients diagnosed with Covid-19 disease by RAT admitted or presented to OPD of departments. From this study of 219 participants, 102 (46.6%) were below the age of 60 years and 117 (53.4%) were > 60 years. The mean CALL score based on the age distribution for those < 60 years of age was 7.01 with a standard deviation of 2.11, Class A (Low Risk). Whereas the mean CALL score based on the age distribution for those >60 years of age was 11.03 with a standard deviation of 1.67, that is Class C (High risk) in the CALL scoring system. There is a statistically significant difference in CALL Score with respect to age since the p-value < 0.05(Mann Whitney U test). Among the 219 participants, 53 (24.2%) had no comorbidities and 166 (75.8%) had any kind of comorbidities like hypertension, diabetes, hypothyroidism, coronary artery disease, chronic kidney disease and other comorbidities were found. The mean CALL score for those participants without comorbidities was 5.53 with a standard deviation of 1.77, Class A (Low Risk). Whereas, the mean CALL score for those with any kind of comorbidities was 10.32 with a standard deviation of 1.86, that is Class C (High risk) in the CALL scoring system. There was a significant difference in CALL Score with respect to comorbidities since the p value < 0.05(Mann Whitney U test).

Kamran *et al.*[7] have reported that the CALL score was an accurate predictor of illness progression and mortality. Guan *et al.*[50]observed that the number of comorbidities was a significant risk factor for composite outcomes (ICU hospitalization, invasive ventilation, or death), in addition to the fact that patients with any comorbidity had inferior clinical results[50] . In COVID-19, community-acquired pneumonia scores were found to be more predictive of death and progression than particular COVID-19 scoring systems, according to Guan *et al*[50].; as a result, they proposed using the CALL score to assess if outpatient therapy is appropriate[57]. Further, Ji *et al.*[6] discovered in their study that >96% of subjects with CALL scores of 4-6 points did not advance to serious illness (Class A). According to several studies, the CALL score is an effective prognosticator for predicting the progression to severe COVID-19, identifying critically ill

patients who need to be admitted to the ICU, in-hospital mortality, deteriorating disease, and associated death[6].

In the current study, more than half of the study participants had LDH of 250-500 µ/L (53%). Out of 219 participants, 70 (32.9%) participants had LDH levels of ≤ 250 µ/L, 116(53%) participants showed LDH levels of 250-500 µ/L and 31(14.2%) participants showed LDH levels of >500 µ/L. The mean CALL score for those participants with LDH levels <=250 u/L is 6.54 with a standard deviation of 1.77. The mean CALL score for participants with LDH levels 250-500 u/L is 10.08 with a standard deviation of 1.86. There was a significant difference in CALL Score with respect to LDH since the p-value < 0.05(Kruskal Wallis H test.)

In the study, it was discovered that patients with COVID-19 who had elevated LDH levels had a six-fold higher risk of suffering a serious illness and a 16-fold higher risk of dying. Half of the subjects in the current investigation had lymphocyte counts below 1.0 109/L. Out of 219 participants, 109(49.8%) participants had lymphocyte count of >1.0 ×109/L and 110 (50.2%) participants had a count of 1.0 ×109/L) is 7.46 with a standard deviation of 2.19. There is a significant difference in CALL Score with respect to Lymphocytopenia since the p-value < 0.05(Mann Whitney U test). These results are in agreement with the earlier reports of Henry *et al*.[12]who assessed the relationship between high LDH levels at the earliest time point during hospitalization and illness outcomes in patients with COVID-19 and found that the patients with bad outcomes have a lower lymphocyte count than those with good outcomes. Additionally, it was clear from the subgroup analysis that patients with severe COVID-19, ARDS, who received ICU care had lower lymphocyte counts.[59]

In the present study the mean CALL score was found to be 9.16 with a standard deviation of 2.75 with a min score being 4 and a maximum being 13. Out of the 219 participants half of them had high risk. When 39 (17.8%) participants came under the Low-Risk category, 69 (31.5%) fell under the Intermediate risk category and 111 (50.7%) participants under the High-risk category. The association between the parameters of the scoring system like the age, comorbidities, lymphocytopenia and LDH levels with the CALL score risk categories were calculated using the Chi Square test with p-value. There was a strong association between high age, prevalence of comorbidities, high LDH and high Lymphocytopenia levels of the patients with frequency of CALL Score risk categories. No patients of above 60 years belonged to low risk category, and 44.3% of patients (97 numbers) belonged to high risk category. Only 6.4% (14 numbers) of patients below 60 years belonged to high risk category. No patients with comorbidities had low risk, whereas 49.3 % (108 persons) had high risk. Patients with more than 250 LDH levels (104 persons, 47.5%) had the high risk for COVID 19; whereas no such patients belonged to low risk category. It was generally observed that Low levels of Lymphocytopenia had high association for COVID 19 risk. When 89 persons (40.6%) of Lymphocytopenia less than 1X109/L belonged to high risk category, only 13 persons (5.9%) had low risk.

Bajgain *et al*.[58] published a detailed review paper on COVID 19 methodologies. The analysis included 27 studies with a total of 22,753 patient cases from significant hotspots around the globe. CVD (8.9%), HTN (27.4%), diabetes (17.4%), COPD (7.5%), cancer (3.5%), CKD (2.6%), and other (15.5%) were the most common comorbidities in the general population. China (Hypertension 39.5%), South Korea (Coronary artery disease (CAD 25.6%), Italy (Hypertension 35.9%), the United States (Hypertension 38.9%), Mexico (Other 42.3%), the United Kingdom (Hypertension 27.8%), and Iran (Diabetes 35.0%) had the highest rates of major comorbidity in the study. 84.1% of the study's fatal cases had one or more coexisting conditions. According to this analysis of the literature, COVID-19-positive patients throughout the major centers of the world most frequently had hypertension, followed by diabetes and cardiovascular illnesses. Increased illness severity was associated with having one or more comorbidities.[58]

V. Conclusion

For the purposes of prevention and treatment for COVID-19, it is essential to identify people who naturally have a higher risk of developing severe or even life-threatening illnesses after contracting the virus. This is especially important in light of the lack of a clinically proven drug that specifically targets SARS-CoV-2. For extremely unwell patients, only symptomatic and intensive care have been considered. Articulating the high-risk characteristics in such a situation will assist clinicians in developing an early and simpler therapeutic strategy for patients.

This study would be helpful in recognizing the severity of the conditions of patients who are RAT positive for COVID19 early, and initiating treatment in accordance with the severity of the patient's conditions. A quantitative approach, such as a score, will aid in the systematic evaluation of patients and facilitate communication between various facilities on various outcomes. The score may also be used to categorize patients into subgroups for proper utilization of medical resources and establish various treatment plans based on the intensity or extent of symptoms. With its user-friendly features, the CALL model, which only uses four clinical characteristics, aids the doctor in forecasting mortality and offering the proper treatment in light of the pandemic conditions.

Various research on CALL scores have shown ambiguous results, which may be attributable to sample numbers or demographic variations. To confirm the CALL score and understand the influence of comorbidities, prospective

multicentered studies in large demographic samples are still required.

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