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Comparison of Various Clinical Scoring Systems in Predicting Progression and Outcome in COVID 19 Infection

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Authors' contributions

This work was carried out in collaboration among all authors. Authors HP and AM designed the study, performed the statistical analysis, wrote the protocol and first draft of the manuscript. Authors RG and Jeevana managed the analysis of the study and literature searches. All authors read and approved the final manuscript.

Article Information

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ABSTRACT

Aim: Comparison of various scoring systems and to find the better one for predicting the progression of disease in COVID-19 infection.

Study Design: Observational.

Place and Duration: Department of General medicine, Dhiraj hospital, a tertiary care center, located in Gujarat, India over period of 4 month (May-august 2020).

Methodology: We included consecutive 300 adult patients of Asian ethnicity with COVID 19 infection, admitted in the hospital in ICU and Ward, who signed for participation. Various clinical scoring systems evaluated and compared for predictability of progression in COVID-19 infection which included two well-established and widely used systems- CURB-65 and qSOFA and two

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recent models, one being novel scoring model- CALL score used exclusively for COVID19 patients and other, the modified version of NEWS2 system. These scores were calculated for each confirmed COVID-19 positive patient on admission. WHO clinical disease severity grading was used to stratify patients and as reference for comparison with other scores.

Results: Of the 300 patients, 197(65.6%) were male and 103(34.3%) were female with mean age of 49.74±15.69 years. 95(31.6%) patients had co-morbidities, hypertension being the most common (21%) followed by diabetes (14.3%). Using WHO clinical disease severity, 160 (53.3%) patients had mild disease, 68(22.6%) had moderate and 72(24%) had severe disease. The four scoring systems were applied and compared for predictability. NEWS2 system had higher discriminative power(AUC,0.69; 95%CI, 45.5 -72.9%) followed by qSOFA (AUC,0.41; 95%CI, 35.3-48.2%), CALL score had lower discrimination (AUC,0.40; 95%CI, 33.5-46.9%) and CURB-65 had the poor values (AUC,0.35; 95%CI, 29.3-42.1%) in predicting the progression of disease in admitted patients. NEWS2 had sensitivity and specificity of 69.7% and 100% respectively.

Conclusion: In this study, four clinical scoring systems were compared on admission and NEWS2 system of risk stratification was found more accurate and better in predicting the disease progression in COVID19 positive patients.

Keywords: Scoring; COVID-19; NEWS2; pneumonia; severity.

1. INTRODUCTION

COVID-19 is caused by a novel coronavirus, named severe acute respiratory syndrome coronavirus 2. Beginning in December 2019, it was first emerged in Wuhan City, Hubei Province, Central China. Genetic sequencing of virus suggest that it is a beta-coronavirus closely linked to SARS virus [1]. WHO declared Corona virus infection as pandemic on March 11th 2020 [2]. As of 2nd September 2020, there have been 26,071,864 confirmed cases of Covid-19, including 864,040 deaths, as reported by the WHO. The highest number of cases has been reported from USA, followed by Spain and Italy. As of date, India has a reported 3,847,588 cases with a total of 67,476 deaths [3]. Symptomatic transmission of the virus is by close contact through respiratory droplets, by direct contact with infected persons, or by contact with contaminated objects and surfaces [4]. The incubation period for COVID-19 is 5-6 days, but can be up to 14 days [5]. The disease severity can vary from asymptomatic, mild, moderate to severe [6]. COVID-19 develop only mild (40%) or moderate (40%) disease in most of the people, approximately 15% develop severe disease that requires oxygen support, and 5% have critical disease with complications such as respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multiorgan failure, including acute kidney injury and cardiac injury Older age, smoking and underlying [7]. noncommunicable diseases (NCDs), such as diabetes. hypertension. cardiac disease. chronic lung disease and cancer, have been reported as risk factors for severe disease and death.

Multivariable analyses done by Zouh F et al. have confirmed older age, higher sequential organ failure assessment (SOFA) score and Ddimer > 1 µg/L on admission were associated with higher mortality [8]. CURB 65 and qSOFA are already used in pneumonia and critically ill patients for predicting outcome since years. CALL score was introduced by Ji Dong to predict the progression risk in COVID 19 patients with pneumonia [9]. Specifically for COVID 19 infection recently NEWS (National Early Warning System) score was also launched by The Royal College of Physicians (RCP) in 2012 to improve the identification, monitoring and management of unwell patients in hospital. It is based on a logistic regression model designed to predict inhospital patient mortality within 24 hours of a set of vital sign observations. Originally consisting of pulse rate, respiratory rate, blood pressure, temperature and oxygen saturation, it was updated in 2017 to NEWS2, which incorporated new onset of confusion and a separate scoring system for oxygen saturation in patients with type 2 respiratory failure. A high NEWS2 score appears to predict poor survival in patients admitted to critical care facilities; a low score predicts good survival [10]. The purpose of the study was to compare various clinical risk scoring systems and to find the better score to predict the risk, severity and progression of the disease in different population and age groups and to compare new COVID 19 scoring systems with well-established scoring systems (gSOFA & CURB 65).

2. METHODOLOGY

This was an observational study conducted at Dhirai Hospital in the Department of General Medicine after IEC approval with 300 adult consecutive RT PCR diagnosed adult COVID 19 patients admitted in a span of 4 months were included in the study. Patients who refused to participate and did not give consent were excluded. On admission detailed demographic data, presenting history, comorbidity status, contact history and relevant examination findings were noted. All necessary radiological investigations as per protocol were performed on admission. Four scoring systems qSOFA, CURB 65, CALL score and NEWS 2 score were applied for all patients on admission and patients were categorized into mild, moderate and severe category as per WHO guidelines [11]. We assessed the predictive performance of four scores - CURB-65, qSOFA, CALL and NEWS 2 for admitted patients with COVID 19 infection. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with 95% confidence interval (CI) were calculated for each score. The AUC (area under curve) was estimated to compare the accuracy of all four scores in predicting the progression of disease. The area measured denotes 'Discrimination' - the ability of each score to correctly predict the progression and outcome in mild, moderate and severe disease (defined according to WHO grading). We used Receiver Operating characteristic Curves (ROC) for portraying the performance results for each score. An α -error (p-value) of less than 0.05 was considered statistically significant for all statistical tests. The software used for analysis was IBM SPSS version 23.

3. RESULTS

observational study enrolled 300 This consecutive in-hospital adult patients, who were COVID 19 RT PCR positive. Out of which, 197 (65.66%) were male and 103 (34.33%) were female. The age of patients ranged from minimum of 18 years to maximum of 98 years with mean age of 49.74±15.69 years, and that of male patients was 49.74±16.49 and of female was 49.82±16.29. We found that 95(31.66%) patients had comorbidities, among which the most common was hypertension (21%) followed by diabetes (14.3%). Out of 300 patients, 160 (53.33%) were having mild disease, 68(22.66%) were found to have moderate disease and 72

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(24%) had severe disease according to WHO grading of severity in COVID 19 infection (Fig. 1A). We also observed that the ICU stay for critical patients varied between two to twenty-two days with average of 10 ± 6.6 days.

3.1 Score Performance and Comparison with Present Grading System by WHO (Table 1)

We calculated and assessed four scoring systems, two being well-established and commonly used systems for pneumonia and sepsis i.e.; CURB-65 and qSOFA respectively. And two newly developed scoring systems for assessment of patients with COVID -19 infection i.e.; CALL score and NEWS2 scoring system. CURB65 is a very well validated pneumonia scoring system for risk evaluation and stratification of patients. According to this score, patient is stratified into need for hospitalization or not, and if needed then admission in ICU is required or not. In our study as shown in Fig. 1B, CURB 65 predicted that 274(91.33%) patients out of 300 had score 0-1 indicating that they were at no risk and needed outpatient treatment whereas 21(7%) patients had score of 2 they require in-hospital indicating that management and only 5(1.66%) patients had severe disease with score of more than 2 requiring intensive care management. qSOFA scoring system was used at the bedside to quickly evaluate patients who might need care in a step-up unit. When calculated for our patients, we found that 292(97.33%) patients had score of 1 or less indicating mild disease and low risk of mortality whereas it predicted that only 8 (2.66%) patients needed intensive care management and had risk of adverse outcomes (Fig. 1C). While the CALL model, a novel scoring system, was used first time in Wuhan, china after the outbreak of COVID-19, to predict disease severity. In our study we found that, CALL score model predicted that 207(69%) patients out of 300, had low risk with 10% chance of progression into severe disease(score of 4-6), 72(24%) patients had a score of 7-9, indicating intermediate risk with 10-40% probability of developing severe disease, and 21(7.1%) patients had a score of more than 10, indicating high risk with over 50% probability of developing severe disease as shown in Fig. 1D.

The NEWS2 scoring system was developed by the NHS in the UK and is used to predict outcome of patients and the need for step up

need for urgent care and immediate step up to

care or care at the same level. Through this score patients were assessed and the decision was then made regarding need for step up care or continuation of care at the same level. Out of the 300 patients, 226 patients (75%) had a NEWS2 score of 4 or less, classifying them into low score, indicating the need for ward-based care. 8(2.6%) patients had a medium score, indicating that the particular patient had to be monitored closely so as to recognize early if there would be a need for step up care. 65 (21.66%) patients had high score, indicating the

Out of Among these four scores calculated using patient information on admission, we found that NEWS2 score had highest discrimination (AUC,0.69; based 95%CI, 45.5 – 72.9%), followed by qSOFA

intensive care unit (Fig. 1E).

(AUC,0.41; 95%CI, 35.3-48.2%), CALL score had lower discrimination (AUC,0.40; 95%CI, 33.5-46.9%) and CURB-65 had the poor values (AUC,0.35; 95%CI, 29.3-42.1%) in predicting the progression of disease in admitted patients.

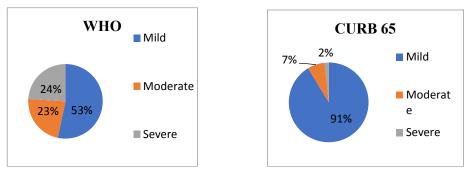
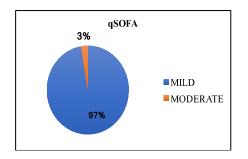


Fig. 1A. WHO grading of severity







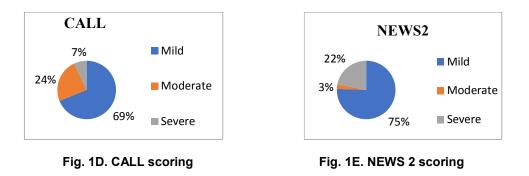


Fig. 1. Showing Grading of severity according to WHO (1A) and predictability of severity by four scoring systems (1B-1E)

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Variable	AUC	CI	p value	Sensitivity	Specificity	PPV	NPV
CURB65	.357	.293421	0.000	57.3% (51.21%-63.23%)	100% (86.77% - 100%)	100%	18.18% (16.23%- 20.31%
qSOFA	0.418	0.353-0.482	0.014	53.77% (47.86%-59.59%	100% (63.06%-100%)	100%	5.59% (4.98%-6.28%)
ĊALL	0.402	0.335-0.469	0.004	66.18% (59.3% -72.6%)	78.49% (68.76% - 86.34%)	87.26% (82.11% - 91.09%)	51.05% (45.60%-56.4%)
NEWS	0.692	0.455-0.729	0.006	69.78% (63.32% - 75.7%)	100% (95.2% - 100%)	100%	52.45% (47.49% to 57.36%)

Table 1. AUC; CI; sensitivity, specificity, PPV, NPV for four scores

As described in the Table 1, the area under curve (AUC) showed the predictability of these scoring systems for true positive and false positive cases. The AUC closer to 1 shows good predictability. And we can see that among these 4 scoring systems, NEWS2 showed better predictability of disease progression as discussed above.

Also, as shown above in the Table 1, that all four scoring systems have high specificity but less sensitivity. NEWS2 scoring had better and balanced sensitivity and specificity. The sensitivity of the score system helps to identify (predicts) patients at risk of severity whereas specificity of the score system identifies the survivors. The specificity of NEWS2 scoring system was found to be 100%, similarly that of CURB-65 and qSOFA was found to be 100% too and that of CALL score was 78.49%, which denotes that all these scoring systems can predict correctly the patients at no/low risk of progression. Whereas, the sensitivity was found to be 69.78% for NEWS2 followed by 66.18% for CALL score, then 57.3% for CURB-65 and 53.77% for qSOFA. So, in order for the scoring system to predict the progression of disease and determine its severity it needed to have good sensitivity and NEWS2 had sensitivity of 69.78%, highest among all.

PPV of the scoring system gives information about the patients which the scoring system truly predicted to be at risk precisely, while NPV depicts in how many patients it didn't predict the severity when compared to actually who had milder disease and less risk of progression. So, based on this, we found that NEWS2 had 100% PPV and 52.45% NPV i.e.; it predicted 52.45% patients at low risk of progression, falsely omitting 47.55% patients, on comparing these values with other scoring systems, we found that NEWS2 seemed to be a better scoring system in predicting the risk of disease progression, followed by CALL scoring system which had 87.2% PPV and 51.05% NPV, CURB65 and qSOFA being the poorer predictive scoring systems for COVID19 infection. The similar finding has been portrayed in ROC curves for each score as shown below (Figs. 2A-2D). Fig. 2A is showing the ROC curve constructed from clinical prediction rules, computed using false positive rate (1-specificity) on x axis and true positive rate (sensitivity) on y-axis, similarly, Figs. 2B-2D are plotted for CALL score, qSOFA and CURB-64 respectively.

4. DISCUSSION

COVID 19 infection has created panic among people and healthcare system, increasing the burden on limited resources especially in countries like India. Initially when disease appeared in hospitals and clinics of Wuhan city of china, very less was known, and was found to be highly contagious with varying spectrum of presentation ranging from asymptomatic to severe respiratory failure leading to death. Still overall mortality and morbidity is not certain in many countries of the world. In highly populated countries like ours where people inhabitate in close proximities, spread is easy and difficult to control leading to increased hospitalization creating overutilization of healthcare resources and poor management of patients. In such situations it becomes very important to triage the patients based on our clinical judgement most importantly and secondly with the help of predicting scores used previously and those developed new.

Therefore, we conducted this study to evaluate the predictability of four scoring systems, two being old and widely used scores in pneumonia and sepsis and other two being recently developed for assessment of COVID positive patients. WHO recommendations for screening and early triage of patients with COVID-19 based on clinical severity scoring has been very valuable in hospitals across the globe [12]. We also graded our patients based on this clinical severity grading system as they presented in emergency or out-patient department. It is based on the symptoms and signs of pneumonia (fever, cough, dyspnea, tachypnea), sepsis, septic shock and oxygen saturation levels measured on presentation. This severity grading has been very useful, as it is solely based on clinical evaluation and oxygen saturation. Especially in centers which are situated in remote and rural areas of countries like India when prompt investigations and imaging studies are not possible, this grading is very helpful in early triage of patients and initiating treatment accordingly. CURB-65, has been a well- known clinical scoring system recommended by British Thoracic Society for assessment of severity of pneumonia [13]. A score of 2 or more indicates need for hospitalization and in-patient management. It was developed to stratify patients with community-acquired pneumonia. It only helps to decide the action required for that patient to treat as out-patient or to consider hospitalization. As it has been widely used since years as pneumonia

severity scoring system and COVID-19 infection is commonly seen manifesting as viral pneumonia, we ought to implement it for our patients to testify if it can be useful for evaluation of disease progression in COVID-19 patients. But instead we found it less sensitive with very low NPV (18.18%) and poor discrimination power (AUC:0.35), suggesting that it is of less use in predicting the disease severity. Though it includes age>65 years and respiratory rate as one of the parameters but it doesn't include oxygen saturation as a parameter, which is an important monitoring tool in patients with COVID-19 pneumonia. Similarly, qSOFA, also known as quick SOFA score, has been recommended as an essential bedside tool to asses organ dysfunction in patients with sepsis [14]. The gSOFA score of more than 2 means that the treating clinician must enhance monitoring and investigate for organ dysfunction. It includes altered mental status (GCS<15), tachypnea hypotension (Systolic blood (RR>22) and pressure; SBP < 100 mmHg) as measuring tools. It is best used for evaluation of patients with sepsis with signs of impending shock. But among these three parameters, only respiratory rate >22 is the marker that can guide clinicians while evaluating patients with COVID-19 pneumonia, this doesn't give information about hypoxemia and need for oxygen supplementation. In our study, we found qSOFA to be less useful, as it had less discriminative power (AUC;0.41) and was less sensitive. It predicted only 2.66% patients requiring need for intensive care management whereas according to WHO clinical disease severity, 23% patients had severe disease requiring intensive management.

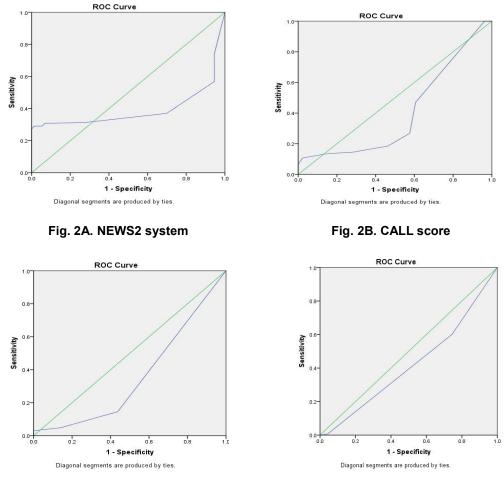
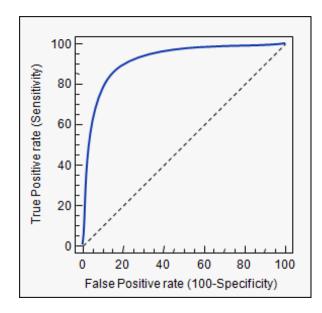




Fig. 2D. CURB 65

Fig. 2. Showing ROC curves for each of the four scores



(a)

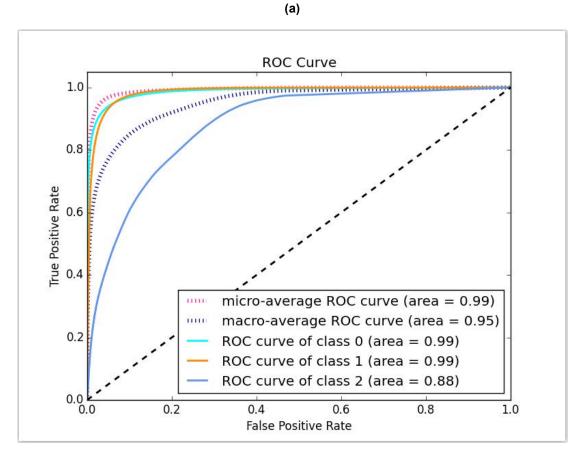




Fig. 3.

In the study done in China which concluded CALL scoring model highly accurate and an optimal predictive tool for progression of disease [9]. CALL scoring model of disease progression developed for predicting severity in patients with COVID 19 pneumonia includes four parameters - comorbidity, older age, lower lymphocyte count and higher Lactate dehydrogenase (LDH). In our study, we observed that, CALL model has less sensitivity (66.1%) and less specificity as well (78.4%), making it less useful in identifying severe patients. As it has been observed that ARDS is common in patients with COVID 19 pneumonia, this scoring model doesn't include parameters like respiratory rate and oxygen saturation, for monitoring respiratory distress, hence this score cannot demonstrate the inhospital progression to severe disease with respiratory failure.

NEWS2, a standardized clinical scoring system developed as the latest version of original NEWS system, has been used for the better and early detection of deterioration in acutely ill patients [10]. NEWS was developed in 2012 first and later was updated in December 2017, by the Royal College of Physicians (RCP), London and has been incorporated into the health care system of NHS hospitals across England [10]. It is based aggregate score of six physiological on parameters - respiration rate, oxygen saturation, systolic blood pressure, heart rate, temperature and level of consciousness. NEWS2 includes a new SpO₂(oxygen saturation) scoring scale for patients with/at risk of type II respiratory failure, which assigns weights at lower SpO₂ thresholds than NEWS. NEWS2 score of 5 or 6 has been considered a key threshold that may indicate deterioration and should prompt for urgent response by clinician. In February 2020, for the first time it was mentioned about the use of adapted version of NEWS2 scoring (age>65 years) by Liao et al. in the article stating the experience and preparation of intensive care units for the epidemic of COVID 19 infections in Sichuan Province of China [15]. It has been evident that Respiratory failure is the hallmark in COVID-19 patients and later in the course of disease circulatory failure can also occur [16]. Also, in a Scandinavian study by Myrstad M, et al published in July 2020, found that 'NEWS2 system was superior than gSOFA and other clinical risk scores for prediction of severe disease' [17]. When we studied and applied this system in our patients, we also found promising results in severity prediction and decision making in these patients. We found that NEWS2 scoring

system had good sensitivity and specificity and better discriminative power (AUC:0.69) as well. Hence, when compared to rest of the scoring systems, NEWS2 proves to be a better tool as it includes hypoxemia and supportive oxygen treatment, providing all the important parameters to assess patient in emergency and on admission for COVID-19 pneumonia. Therefore, we can state that it is the most accurate scoring system in predicting the deterioration of patients, favoring the recommendations by the Chinese study of Liao et al.

As there have been case reports [18] about 'silent hypoxemia' and we also observed in our patients that there is presence of hypoxemia without evident symptoms of respiratory distress, we highly recommend the monitoring of oxygen saturation as one of the most important parameters in risk stratification. CURB-65, gSOFA and CALL model could not accurately predict the overall risk of disease progression and were found less helpful in triage of patients in our study. So, we highly suggest that their utilization in clinical practice for evaluation of COVID19 patients should be used only with utmost care and awareness. Therefore, scoring systems like CURB-65, qSOFA and CALL model, are less able to predict the severity of disease and risk of progression in patients with COVID 19 pneumonia when compared to NEWS2 system.

A recently done retrospective study, comparing various scoring systems by Fan, Guohui, et al. [19] concluded the ADROP, a modified CURB65 score, as a reliable tool for risk stratification for COVID 19 patients. We didn't include this model in our comparison of scoring system, but it can be extrapolated further with future studies. There is need for more studies to be done on larger population across the globe to validate these scoring systems. Also, further studies can be done in future to find the validity of NEWS2, a very promising scoring system for other respiratory diseases. But based on our observation, we recommend use of NEWS2 system for prediction of disease progression in COVID 19 patients.

5. CONCLUSION

NEWS2 scoring system has been found the most accurate and helpful in predicting the disease progression and also guiding us to triage the patient and identify earlier to manage in critical care. Needless to mention, there is no replacement for clinical judgement and examination by the treating doctor in identifying the critical patient and decision making.

CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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