

# Predictive Performance of the National Early Warning Score 2 for Stratification of Critically Ill COVID-19 Patients

© Faraz Ahmed Baig<sup>1</sup>, © Amna Hamid<sup>2</sup>

<sup>1</sup>Ziauddin University, Department of Pathology, Karachi, Pakistan

<sup>2</sup>Memon Medical Institute & Hospital, Department of Nephrology, Karachi, Pakistan

## Abstract

**Aim:** To validate the ability of National Early Warning Score 2 (NEWS2) for predicting the severity of Coronavirus disease-2019 (COVID-19). In addition, we also intend to examine the impact of pre-existing comorbidities to produce an advanced COVID-19 disease.

**Materials and Methods:** A multicenter prospective cohort was performed on 108 patients having moderate-intensity COVID-19 infection during October 2020 and November 2021. NEWS2 parameters were recorded on admission to generate an output score, which then classified in accordance with the NEWS2 reference scale into low, medium, and high-risk categories. Each patient was followed till discharge or death for the clinical progression of COVID-19. The measures of validity and area under the curve (AUC) for NEWS2 threshold scores were calculated to predict the clinical deterioration of COVID-19.

**Results:** Overall, 29.6% patients developed an advanced disease, out of which 21.8% patients died during treatment. NEWS2 score of 6 or more showed the highest sensitivity (78.1%), specificity (94.8%), and the AUC (0.838) for predicting an adverse outcome. Among comorbidities, the majority showed an increased risk of clinical deterioration.

**Conclusion:** NEWS2 score of 6 or more at baseline showed good predictive ability to stratify patients with poor outcomes who may later require escalated care. However, we recommend more research to confirm our findings.

**Keywords:** COVID-19, Coronavirus disease-2019, NEWS2, sensitivity

## Introduction

The Coronavirus disease-2019 (COVID-19) pandemic is a big challenge for global healthcare systems (1). Although most Severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) patients remained asymptomatic, some of those develops deteriorating disease, which often end up with a fatal outcome (2). The recent estimates indicated that almost 4% of critically ill COVID-19 patients eventually die while receiving intensive care unit (ICU) care (3). Accumulating data suggested that advanced age and pre-existing comorbidities are the main factors involved in the progression of COVID-19. Hence, assessing the risk factors on admission is crucial in determining the possibility of progression in COVID-19 disease (4). Besides, few clinical scoring systems have been evaluated for predicting the clinical deterioration in COVID-19 patients (5).

At the moment, no established method is available for early stratification of high-risk COVID-19 patients. Such risk stratification allows physicians to escalate care for potentially aggressive cases (6). The National Early Warning Score 2 (NEWS2) is a clinical tool used in ICU's to assist health care workers in stratification of high-risk septicemic patients who could be benefited by intensive management and monitoring (7). NEWS2 scale is based on six parameters which includes; temperature, respiratory rate, pulse, blood pressure, consciousness level and oxygenation saturation (8).

Recently, the application of the NEWS2 algorithm for early stratification of severe COVID-19 patients has been proposed (9). The assessment of oxygen and ventilation parameters are the main reasons to recommend NEWS2 in COVID-19 disease compared to some other scoring methods (8).



**Corresponding Author:** Faraz Ahmed Baig MD, Ziauddin University, Department of Pathology, Karachi, Pakistan  
**Phone:** +923453316575 **E-mail:** faraz.baig@zu.edu.pk **ORCID ID:** orcid.org/0000-0002-0787-6019

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Each NEWS2 parameter is scored in an order of 0 to 3, reflecting the degree of severity. The cumulative NEWS2 score ranges from 0 to 23, which is computed by the addition of all parametric scores. The cumulative score is sub-categorized as; low risk (1 to 4), medium risk (5 to 6) and high risk ( $\geq 6$ ) infection (8). However, these risk levels are primarily meant for evaluating the status of patients suffering from sepsis (10).

Nevertheless, there is a dearth of literature on the ability of NEWS2 to predict clinical outcomes in COVID-19, but also the power of NEWS2 scores for stratification of high-risk COVID-19 patients is unclear. Moreover, NEWS2 has been studied mostly in the United Kingdom and its validation in non-caucasian population is a subject of further research. We therefore determined the accuracy of NEWS2 for stratification of risk levels in COVID-19 patients on admission. We also sought to examine the potential of pre-existing comorbidities for clinical deterioration during hospitalization.

## Materials and Methods

### Study Design and Setting

A multicenter prospective cohort was designed comprising 108 patients with proven COVID-19 infection using SARS-CoV-2 PCR assay. The ethical approval was sought from the Ethic Review Committee Ziauddin University, Karachi, Pakistan (ERC #1701219FHPAT, date: 10.02.2020) in line with the Helsinki Declaration 2013. The subjects were selected from four major tertiary care hospitals located in District East, Karachi, Pakistan. The subjects received in-patient care between October 2020 and November 2021. Written informed consent was obtained from all subjects to use their data. All information were coded and kept confidential.

### Participants

The patients were selected by applying non-probability consecutive sampling model. All cases were recently admitted for the treatment of COVID-19. The disease spectrum i.e., mild, moderate, severe and critical was determined on admission in accordance with CDC guidelines, which describes mild disease as no shortness of breath and moderate disease if oxygen saturation ( $\text{SpO}_2$ )  $\geq 94\%$ . While severe disease is diagnosed when  $\text{SpO}_2 < 94\%$ ,  $\text{PaO}_2/\text{FiO}_2 < 300$  mmHg and respiratory rate  $> 30$  breaths/min whereas, the cases presented with respiratory failure and multi-organ dysfunction are characterized as critical (11). Based on this guideline, our inclusion criteria were newly admitted adult patients with moderate COVID-19 disease. Patients who already developed severe to critical illnesses at the time of admission were excluded from the selection. Also, the cases with mild disease were excluded as they do not require in-patient care.

Each i.e. subject was followed to determine the clinical course of COVID-19 during hospitalization, i.e. of moderate infection to a severe and critical state or death. The demographic data such as age, residence and gender along with presenting symptoms, the vital signs including blood pressure, pulse, respiratory rate and oxygen saturation were recorded at the time of admission. Additionally, the level of consciousness was assessed in accordance with Glasgow Coma Scale (GCS) i.e.  $\text{GCS} > 13$  for alert.

### Procedure

The NEWS2 score was calculated using MDCalc online assessment tool (12). The six parameters, which includes: respiratory rate, oxygen saturation ( $\text{SpO}_2$ ), supplemental oxygen, pulse rate, level of consciousness, and temperature recorded on admission were entered in MDCalc to generate the final scores by an automated preset algorithm. All scores were then organized and distributed among the three NEWS2 categories i.e. 4, 5, and  $\geq 6$  indicating low, medium and high-risk levels, respectively.

### Statistical Analysis

We classified the outcome according to their clinical spectrum as described in the aforementioned CDC guidelines. Those who remained on a moderate course throughout hospitalization constitute the good outcome or control group while poor outcome or case group was comprised of those participants who progressed to severe or critical disease and those who eventually died. The sensitivity, specificity, positive, negative predictive values, and accuracy for the NEWS2 risk thresholds were estimated to predict worsening of COVID-19. The ROC curve was generated and the area under the curve (AUC) was calculated.

The impact of comorbidities to causing an advanced disease was assessed by relative risk at 95% confidence interval (CI) and the strength of association was determined by p value. The p value  $< 0.05$  was considered statistically significant. All statistical analyzes were performed using MedCalc statistical software version 20.

## Results

Our data showed that 32 (29.6%) out of 108 cohorts developed an advanced COVID-19 disease during hospitalization, thus classified as a case or poor outcome group. Of which 16 (50%) patients progressed to severe illness, 9 (28.1%) developed critical disease, and 7 (21.8%) died during treatment. We found 76 (70.3%) patients remained on a moderate course and eventually recovered, hence considered as controls or good outcome group. Table 1 shows the number of subjects within the case and control groups based on the clinical outcome. Our demographic data revealed male predominance ( $n=61$ ). Furthermore, most

participants (75.9%) were aged over 60 years. The minimum age in our series was 18 years, while the maximum age was recorded as 81 years. The overall median age was 67.5 years.

The NEWS2 data showed that scores on admission were ranged from 4 to 14. The median for the score was 9.6. We observed that most patients in the control or good outcome group (89.4%) had an initial NEWS2 score below 6 and some patients (10.5%) were scored 6 or above on admission. Conversely, the majority of subjects (78.1%) in the case or poor outcome category presented with initial scores 6 or more while only few (21.8%) were scored lower than 6 on admission. This accounts for sensitivity (78.1%), specificity (89.4%), positive predictive value (45.1%), and negative predictive value (97.3%) for the score 6 and above. Similarly, the highest accuracy (88.3%) was observed for the scores over 6 to predict deteriorating illness. These validity estimates were also supported by the receiver operating curve that indicated highest

AUC (0.838) for scores 6 and above (Figure 1). In comparison, the admission scores 4 and 5 showed low diagnostic value in risk stratification of COVID-19 patients. Table 2 presents the validity estimates of the NEWS2 threshold points for risk assessment on admission.

On the analysis of comorbidities, we found that the overwhelming majority (85%) of cohorts had some forms of pre-existing illness. At 95% CI, increasing age, hypertension, diabetes, renal, hepatic, and cardiovascular disorders showed a greater risk for an advanced disease or poor outcome. These factors were also significantly associated with poor outcomes in COVID-19 on descriptive statistics. However, asthma and chronic obstructive lung disease had higher odds to produce an aggressive disease, but no association with the severity of COVID-19 was observed. Table 3 describes statistical estimates of pre-existing comorbidities with the clinical progression of COVID-19.

**Table 1. Distribution of NEWS2 scores among COVID-19 cases and controls**

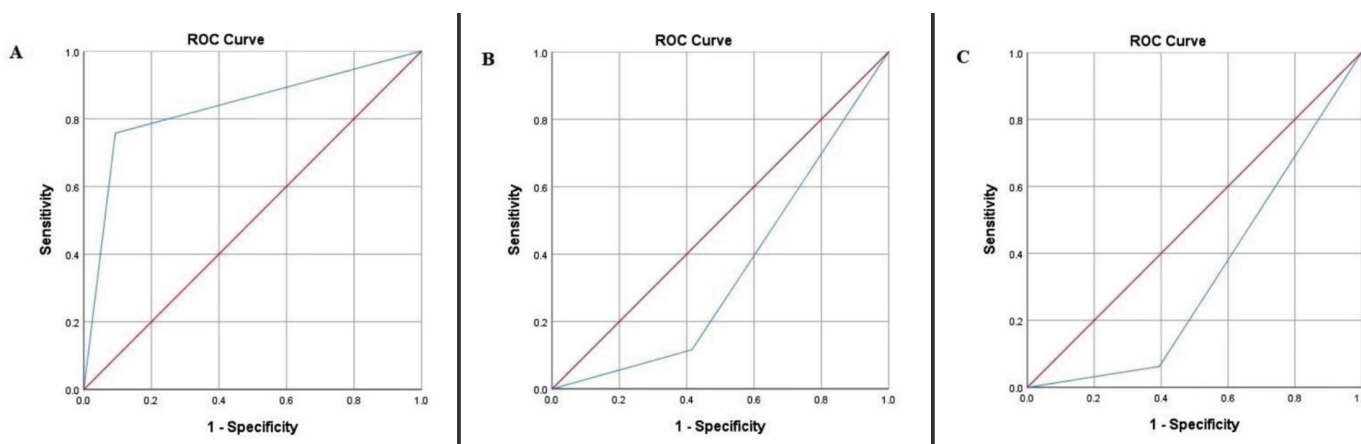
NEWS2 Scores <sup>a</sup>	COVID-19 disease <sup>a</sup>			
	Controls (good outcome group)		Cases (poor outcome group)	
	Moderate disease (n=76)	Severe disease (n=16)	Critical disease (n=9)	Death (n=7)
4	30	2	0	0
5	38	4	1	0
6 and above	8	10	8	7

<sup>a</sup>NEWS2 cut-off scores for risk levels, <sup>a</sup>Clinical spectrum based on CDC guidelines, COVID-19: Coronavirus disease-2019, NEWS2: National Early Warning Score 2

**Table 2. Predictive performance of NEWS2 scores on admission for risk stratification in Coronavirus disease-2019**

NEWS2 Scores <sup>†</sup>	Sensitivity (%)	Specificity (%)	PPV <sup>‡</sup> (%)	NPV <sup>‡</sup> (%)	AUC <sup>†</sup>	Accuracy (%)
4	6.2	60.5	1.7	85.3	0.334	55
5	15.6	50	3.3	84.2	0.328	46.5
6 and above	78.1	89.4	45.1	97.3	0.838	88.3

<sup>†</sup>: NEWS2 cut-off scores for risk levels, <sup>‡</sup>: Positive predictive value, <sup>‡</sup>: Negative predictive value, <sup>†</sup>: Area under the curve



**Figure 1.** Receiver operating curve (ROC) with reference line (red) comparing the sensitivities for (A) NEWS2 score 6 and above, (B) score 5 and (C) score 4 representing high, medium and low risk of clinical deterioration in Coronavirus disease-2019 patients

Factors	p value*	Relative risk*	95% CI
Age	0.0001	3.562	2.085 to 6.085
Hypertension (n=20)	0.007	2.902	1.333 to 6.320
Chronic renal disease (n=18)	0.0006	4.750	1.953 to 11.551
Diabetes (n=17)	0.006	3.392	1.417 to 8.123
Chronic liver disease (n=13)	0.011	3.800	1.345 to 10.732
Cardiovascular disease (n=12)	0.001	7.125	2.062 to 24.613
Asthma (n=5)	0.152	3.562	0.624 to 20.315
Malignancy (n=4)	0.837	0.791	0.0855 to 7.327
Chronic obstructive lung disease (n=3)	0.196	4.750	0.446 to 50.544

\*: P value <0.05 is statistically significant, \*: RR >1.0 represents positive association, CI: Confidence interval

## Discussion

The lack of prognostic indicators for novel COVID-19 is the biggest dilemma of our agile health system. Early warning systems (EWS) are typically employed in critically ill patients by emergency care physicians to identify candidates who could pose a threat of clinical deterioration. To date, several models of EWS have been developed and tested. Out of these, the Royal College of Physicians proposed NEWS2 as a suitable method for risk stratification in COVID-19 patients (13). Therefore, a cohort was designed on patients from various centers that are designated for COVID-19 testing and treatment to evaluate the performance of NEWS2 in early stratification of high-risk COVID-19 patients.

The NEWS2 scale was implemented after the initial assessment of patients who were suitable for admission. Our findings indicated that a score of 6 or more had reasonably good sensitivity (78.1%) and specificity (89.4%) to predict an aggressive course of disease and thus identified those who later required ICU. We also discovered that a minimum score of 6 at baseline had maximum AUC (0.838) for predicting the poor outcome. Furthermore, increasing age, diabetes, chronic renal, hepatic, and cardiovascular impairments are independent factors associated with greater risk of complications.

Since the start of the pandemic, researchers have evaluated numerous factors for prognostic purposes. In early studies, Chinese authors reported that older age, smoking, inflammatory markers such as; neutrophil to lymphocyte ratio, platelet counts, C-reactive protein, procalcitonin, D-dimer could prove useful in the assessment of high-risk COVID-19 patients (14). Another study observed that Sequential Organ Failure Assessment scores traditionally used for characterization of sepsis could also serve as prognosticator for COVID-19 (14). However, it is evident from recent data that adverse outcomes in COVID-19 results from

pulmonary complications that are aggravated or triggered by pre-existing comorbidities. Since then studies are focused on factors attributed to progression of COVID-19 (14).

Despite these encouraging reports, the tasks to determine the possibility of clinical deterioration is proving to be extremely challenging. In this context, we have previously attempted to correlate the levels of inflammatory markers with severity of disease; however, most of these laboratory investigations are time consuming, costly, and not readily available in smaller setups. Thus, it is critical to determine alternative methods for stratification of risk in COVID-19 patients (15).

The NEWS score was introduced in 2012 to monitor critically ill patients in the ICU. The NEWS2 is an update to the NEWS score with the addition of parameters such as: oxygen saturation and confusion. National Health System (NHS), United Kingdom has been advocating to implement NEWS2 in the management of COVID-19 patients (8). The basis for this NHS recommendation is the NEWS2 parameters which includes; oxygen saturation and also the benefits of NEWS2 seen in critically ill adults during pre-COVID-19 era (8). Subsequently, a Chinese modification of NEWS2 has been evaluated for triaging COVID-19 patients however, the algorithm had numerous calibration issues which compromised its worth in clinical application (16).

In recent studies, a single center retrospective research conducted in UK found that NEWS2 score of 5 or more during hospitalization can predict clinical deterioration with a greater accuracy (7). Later these findings were also supported by Kostakis et al. (17). Another single center cohort from neighboring India concluded that NEWS2 score of 5 and above at admission has an outstanding discriminatory power (AUC of 0.90; 95% CI: 0.82-0.97) for COVID-19 patients that later required mechanical ventilation or suffered death during hospitalization (6).

Contrary to some of the past studies (6,7), in present research we have documented a higher threshold value ( $\geq 6$ ) for predicting worsening of COVID-19 infection, which coincides with NEWS2 risk levels implemented in sepsis. Our finding corroborate with a recent study conducted in neighboring India by Chikhalkar et al. (18) who found that NEWS2 score  $\geq 6$  is a statistically significant cut-off value for predicting adverse outcome on admission with 93.24% sensitivity and 98.91% specificity. This observation was also supported by a recent case control investigation (19). Additionally, in agreement to our finding, Rigoni et al. (20) previously recorded NEWS2 score of 6 and above on admission is the best predictor of progressive disease in COVID-19 patients. The author reported 80% sensitivity and 84.3% specificity, with an AUC of 0.822 (20). However, previous authors recommended more research for validation of their findings in view of retrospective design and use of convenience sampling (18,20). In contrast, this research is a multicenter cohort. We have employed CDC criteria for stratification of poor outcomes and for recruitment of the participants. Furthermore, we have validated the performance of NEWS2 cut-offs for risk assessment to predict poor outcomes in COVID-19 disease.

Several studies demonstrated increased risk of clinical deterioration in COVID-19 cases with pre-existing comorbidities (21). On the assessment of our secondary objective, we found that six of the independent factors were significantly associated with worsening condition. However, the risk analysis yielded all factors has increased odds of poor outcome except malignancy. Surprisingly, pulmonary pathologies revealed no association with disease progression. This could be related to the low prevalence of respiratory disorders in our series. Alternatively, the differences in statistical estimates seen in studies might be due to the heterogeneous selection of outcome parameters.

### Study Limitations

The results of the present research have better external validity due to prospective and multicenter research design. We have estimated the predictive performance of discrete NEWS2 cut-offs, while most authors evaluated the predictive accuracy of a single threshold value in the COVID-19 setting (6,9). In addition, we have employed the relative risk, which is a more robust test than the odds ratio, used in past studies to determine the adverse outcomes in COVID-19 patients. Moreover, being the first study on NEWS2 from Pakistan, our findings will assist in introducing a new clinical algorithm in local setups for stratification of cases that are expected to get worse overtime. This in turn allows physicians to use our medical resources for those who are on the utmost need.

Besides these strengths, there are some limitations to this study. First, our sample size is lower than some other cohorts. Second, we used clinical history and previous laboratory tests for characterizing comorbidities, and fresh diagnostic investigations were not performed for reassessment of their current status.

### Conclusion

NEWS2 score of 6 and above at admission could predict adverse outcomes in COVID-19 patients with high sensitivity (78.1%) and specificity (89.4%). Some of the pre-existing comorbidities are associated with poor outcomes and increased risk of clinical deterioration. We suggest that the NEWS2 score should be assessed in all patients on admission and physicians should be alarmed for the possibility of severe disease in cases with a score greater or equals to 6. However, this conclusion needs to be further validated on a larger scale.

### Ethics

**Ethics Committee Approval:** The study was approved by the Ethic Review Committee Ziauddin University, Karachi, Pakistan (ERC #1701219FHPAT, date: 10.02.2020).

**Informed Consent:** Consent form was filled out by all participants.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: A.H., Concept: F.A.B., Design: F.A.B., Data Collection or Processing: A.H., Analysis or Interpretation: F.A.B., A.H., Literature Search: F.A.B., Writing: F.A.B.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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