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External Validation of the Novel ABCD Scoring System for Prediction of In-Hospital Mortality among Severe and Critically Ill COVID-19 Patients: A Prospective Cohort Study

Dina M. Ali*[1] and Khaled Raafat[2]

[1]Department of Tropical Medicine, Faculty of Human Medicine, Zagazig University, Zagazig City, Egypt

[2]Department of Internal Medicine, Faculty of Human Medicine, Ain Shams University, Cairo, Egypt

***E-mail: dalali@zu.edu.eg**

Abstract

COVID-19 is a worldwide public health emergency. The availability of a brief and objective tool predicting the mortality among hospitalized COVID-19 patients might be helpful to direct limited medical resources to patients at higher risk of mortality. The aim of this work was to assess the novel ABCD scoring system as a tool for the prediction of in-hospital mortality among severe and critically ill COVID-19 patients admitted to the quarantine ICU. A prospective cohort study was conducted at Zagazig University Hospitals and comprised one hundred and seventy-nine COVID-19 patients admitted to the ICU. The ABCD score was calculated for all the patients. The primary outcome was the in-hospital mortality among the study participants. The median age of the participants was 63 (range: 18-95). About fifty-one percent (n= 92, 51.4%) were males. Of the total 179 patients, (n= 91, 50.8% survived, and n= 88, 49.2% died). A statistically significant association between the ABCD grading and the mortality outcome was detected (p-value = 0.029). By multiple logistic regression, the ABCD grading was a predictor of mortality in COVID-19 patients where the OR was 2.66 (95% CI: 1.284-5.517) (p-value = 0.008). The AUROC of the ABCD score was 0.608 (95% CI: 0.526-0.691), sensitivity was 61.4%, specificity was 50.5%, PPV was 54.5%, and NPP was 57.5%. To conclude: the ABCD grading system showed a discriminative ability to predict death in critically ill COVID-19 patients. The ABCD grading might be a quick approach for bedside assessment of severe COVID-19 patients, and it could also be used to rule out the probability of additional deterioration in patients in the non-critical zone.

Keywords: COVID-19, Coronavirus Disease, ABCD score, Mortality, Prognosis, Egypt.

1. Introduction

Coronavirus Disease 2019 (COVID-19) is a global public health issue. At the time of writing this manuscript, 444 million cases have been infected, and 5.9 million cases have died worldwide [1]. The main symptoms of the disease are fever, cough, myalgia, and dyspnea. The disease may progress to Acute Respiratory Distress

Syndrome (ARDS) and respiratory failure [2]. The presence of co-morbidities may worsen the clinical outcome [3]. The availability of a simple and objective tool to predict mortality among COVID-19 patients may help guide re-allocation of care and resources for those with expected higher mortality rates [4]. Currently, the researchers are investigating multiple specific and general scores for prediction of COVID-19 severity and outcome, such as the National Early Warning Score (NEWS) [5, 6], Sequential Organ Failure Assessment (SOFA) [7], and CURB 65 scores [8]. Recently, a novel assessment tool for patients presenting to the emergency department of a hospital with COVID-19 symptoms, termed the ABCD scoring system, was suggested. The scoring system components include **(1) A**ge**: ≤** 50 or >50 **(2) B**lood markers: leucocyte counts, lymphocyte counts, Lactate Dehydrogenase (LDH), C-Reactive Protein (CRP), and D-Dimer levels **(3) C**hest X-ray or **C**omputed Tomography (CT) (4) **C**o-morbidities (5) **D**yspnea, defined as respiratory rate >30 or O2 saturation <90% [9]. Therefore, we conducted this study to investigate the potential capability of the novel ABCD scoring system to predict the in-hospital mortality among severe and critically-ill COVID-19 patients admitted to the quarantine Intensive Care Unit (ICU), Zagazig University Hospitals (ZUH), Egypt.

2. Patients and Methods

2.1. Study design and setting

This prospective cohort study was conducted at the quarantine ICU, ZUH, between March and December 2021.

2.2. Study sample

The study included all confirmed COVID-19 patients admitted to the quarantine ICU at ZUH (n=179) during the study period (comprehensive sample). The sample size also followed the recommendations of Palazón-Bru et al. to externally validate scoring systems based on binary logistic regression models [10]. Inclusion criteria: (1) age ≥ 18 years old; (2) male or female; and (3) confirmed COVID-19 infection. Exclusion criteria (1): age <18 years; and (2) pregnant females.

2.3. Study tools

All participants were subjected to thorough history-taking, clinical, laboratory, and radiological assessment. The diagnosis of COVID-19 was established based on positive Real-Time Polymerase Chain Reaction (RT-PCR) for nasopharyngeal swabs and non-contrast chest Computed Tomography (CT). Based on the criteria published by the Egyptian Ministry of Health (MOH), the presence of at least one of the following conditions was included in the definition of severe COVID-19: (1) respiratory distress with a respiratory rate greater than 30 breaths per minute; (2) resting blood oxygen saturation ≤92%; or (3) a partial pressure of arterial blood oxygen (PaO2)/oxygen concentration (FiO2) ≤ 300 mmHg. Critically ill patients were defined as those who have experienced (1) respiratory failure requiring mechanical ventilation; (2) shock; or (3) failure of any other major organ [11]. The ABCD scoring system was calculated for all the study participants at the first day of admission, as shown in supplementary tables (I and II). Each variable was assigned a value of 0 if the answer was no, and a value of 1 if the answer was yes. The maximum possible score is 14 while the lowest possible score is 0 [9].

2.4. Primary outcome

The primary outcome was the assessment of the in-hospital mortality among the COVID-19 ICU patients.

2.5. Ethical consideration

The study protocol was approved by the Review Board of Faculty of Human Medicine, Zagazig University (ZU IRB: No. 9634) and followed the medical research ethical principles listed by Declaration of Helsinki. All patients or their families signed an informed written consent.

2.6. Statistical analysis

The Statistical Package for Service Solution (IBM-SPSS, version 26) was used to manage the data. Kolmogorov-Smirnov single-sample test was used to test the data distribution. Numerical variables were summarized as median and range while categorical variables were described as frequencies and percentages. Comparison between two groups for numerical variables was done using Mann-Whitney-U test. Chi-Square test or Fisher's exact test as appropriate were used to compare qualitative variables. Stepwise logistic regression was applied to the significant variables within the univariate analysis using the forward likelihood ratio method. The odds ratio (OR) and its 95% confidence intervals (CI) were calculated to estimate the risk. Spearman correlation was used to correlate continuous data. The optimal cut-off values were calculated by applying the Receiver Operating Characteristic Curve (ROC) analysis. Probability (p-value) equal to or less than 0.05 was considered significant.

3. Results

3.1. Baseline characteristics of the study participants

One hundred and seventy- nine patients were enrolled in the study. The baseline demographic, clinical, and laboratory characteristics of all patients are shown in Table (1). The median age of the study participants was 63 (18-95). Males comprised (n=92, 51.4%). Of the total 179 patients, n=91 (50.8%) survived and n=88 (49.2 %) died. The age, conscious level, the presence of fever, vital signs, the need for invasive respiratory support, the presence of hepatic co-morbidities, the count of WBCs (total and differential namely neutrophils), CRP, and D- Dimer levels were the statistically significant factors between the survivors and non-survivors.

3.2. The ABCD grades as a predictor of severe COVID-19 mortality

We found a statistically significant association between the in-hospital mortality outcome and the ABCD grades (p value=0.029) as shown in Table (2). A multivariate logistic regression showed that ABCD grades were a highly statistically significant factor for mortality OR=2.66 (95% CI: 1.28-5.517); (p value =0.008) as shown in Table (3). The multivariate logistic regression also revealed that fever (OR=3.46, 95% CI: 1.75-6.84) (p value=0.001) and serum CRP level (OR=2.14, 95% CI: 1.1-4.18) (p value=0.025) were other significant factors for the prediction of in-hospital mortality in patients with severe COVID-19 infection, as shown in Table (3).

3.3. The diagnostic performance of the ABCD score

The diagnostic performance of the ABCD score is shown in Table (4). The cut-off point for discriminating death from survival was 7.5. The sensitivity of the ABCD score was 61.4%, the specificity was 50.5%, PPV was 54.5%, and NPV was 57.5%, with an overall accuracy 55.9%. The AUROC Curve was 0.608 (95% CI: 0.526-0.691) as shown in Figure (1).

3.4. Correlation between the ABCD score and laboratory variables

The correlation between the ABCD score and the laboratory variables revealed a statistically significant correlation between the score and the lymphocytic count (r=-0.188; p value =0.012) and the D- Dimer level (r=0.183 p value= 0.015) as shown in Table (5).

Table (1): Baseline demographic, clinical, and laboratory characteristics of all study participants.

Characteristic	Total (N=179)	Alive (N=91)	Dead (N=88)	P- value
Demographic criteria:				
Age, median (range)	63 (18-95)	61 (18-85)	65 (22-95)	**0.026***
Sex (n, %)				
Female	87(48.6%)	41 (47.1%)	46 (52.9%)	0.334
Male	92 (51.4%)	50 (54.3%)	42 (45.7%)	
Smoking (n, %)				
No	125(69.8%)	65 (52.0%)	60 (48.0%)	0.636
Yes	54 (30.2%)	26 (48.1%)	28 (51.9%)	
Clinical symptoms (n, %):				
Disturbed Conscious Level				
No	164 (91.6%)	91 (55.5%)	73 (44.5%)	**<0.001***
Yes	15 (8.4%)	0 (0%)	15 (100%)	
Fever				
No	110(61.5%)	70 (63.6%)	40 (36.4%)	**<0.001***
Yes	69 (38.5%)	21 (30.4%)	48 (69.6%)	
Fatigue				
No	173 (96.6%)	87 (50.3%)	86 (49.7%)	0.682
Yes	6 (3.4%)	4 (66.7%)	2 (33.3%)	
Vital signs (median, range):				
Heart rate (per minute)	90 (51-190)	88 (51-145)	92 (58-190)	**0.051***
Respiratory rate (per minute)	27 (20-35)	26 (20-35)	29 (20-35)	**<0.001***
Oxygen saturation (%)	79 (55-90)	80 (60-90)	74 (45 -90)	**<0.001***
Respiratory Support (n, %):				
Reservoir mask	100 (55.9%)	78 (78%)	22 (22%)	**<0.001***
CPAP	60(33.5%)	13(21.7%)	47 (78.3%)	
Mechanical Ventilation	19 (10.6%)	0 (0%)	19 (100%)	
Co-morbidities (n, %):				
Hypertension				
No	112 (62.6%)	61 (54.5%)	51 (45.5%)	0.210
Yes	67 (37.4%)	30 (44.8%)	37 (55.2%)	
Diabetes				
No	113 (63.1%)	56 (49.6%)	57 (50.4%)	0.654
Yes	66 (36.9%)	35 (53.0%)	31 (47.0%)	
Renal Disorders				
No	164 (91.6%)	85(51.8%)	79 (48.2%)	0.380
Yes	15(8.4%)	6 (40%)	9 (60%)	
Hepatic Disorders				
No	163 (91.1%)	89 (54.6%)	74 (45.4%)	**0.001***
Yes	16 (8.9%)	2 (12.5%)	14 (87.5%)	
Cardiac Disorders				
No	171 (95.5%)	87(50.9%)	84 (49.1%)	1
Yes	8 (4.5%)	4 (50%)	4 (50%)	
Malignancy				
No	178 (99.4%)	91 (51.1%)	87 (48.9%)	0.76
Yes	1 (o.6%)	0 (0%)	1 (100%)	
Laboratory investigations (median, range):				
WBC's ($\times 10^9$/L)	11.1 (1.1-65)	10.5 (1.1-29)	12.5 (1.3-65)	**0.006***
Neutrophils ($\times 10^9$/L)	10 (0.7-150)	9.0 (0.7-25)	11.5 (1.0-150)	**0.003***
Lymphocytes ($\times 10^9$/L)	0.7 (0.1-3.4)	0.8 (0.1-2.7)	0.6 (0.1-3.4)	0.095
CRP (mg/L)	132 (1-441)	102 (1-438)	168.5 (11.3-441)	**<0.001***
LDH (U/L)	480 (92-1650)	471 (118-1307)	500 (92-1650)	0.163
D-Dimer (mg/L)	1.2 (0.1-16)	0.9 (0.1-8.7)	1.4 (0.2-16)	**0.021***
ICU-LOS (median, range):				
ICU-LOS (Days)	9 (1-30)	10 (4-30)	6 (1-29)	**<0.001***

Table (2): Association between the ABCD grades and COVID-19 mortality.

ABCD Grade	Clinical Outcome		Total	P value
	Survival	Death		
Yellow	73	56	129	**0.029***
Red	18	32	50	
Total	91	88	179	

***P value is statistically significant.**

Table (3): Multivariate analysis of predictors of severe COVID-19 mortality.

Variables	Mortality				
	B	S. E	P-value	OR	95% CI
Fever	1.242	0.348	**<0.001***	3.462	1.750-6.847
CRP	0.765	0.341	**0.025***	2.148	1.102-4.189
ABCD grade	0.979	0.372	**0.008***	2.662	1.284-5.517

***P value is statistically significant.**

Table (4): Diagnostic performance of the ABCD score as a predictor of severe COVID-19 mortality.

Parameters	Cut-off point	AUROC (95% CI)	Sensitivity	Specificity	PPV	NPP	Overall accuracy
ABCD score	7.5	0.608 (0.526- 0.691)	61.4%	50.5%	54.5%	57.5%	55.9%

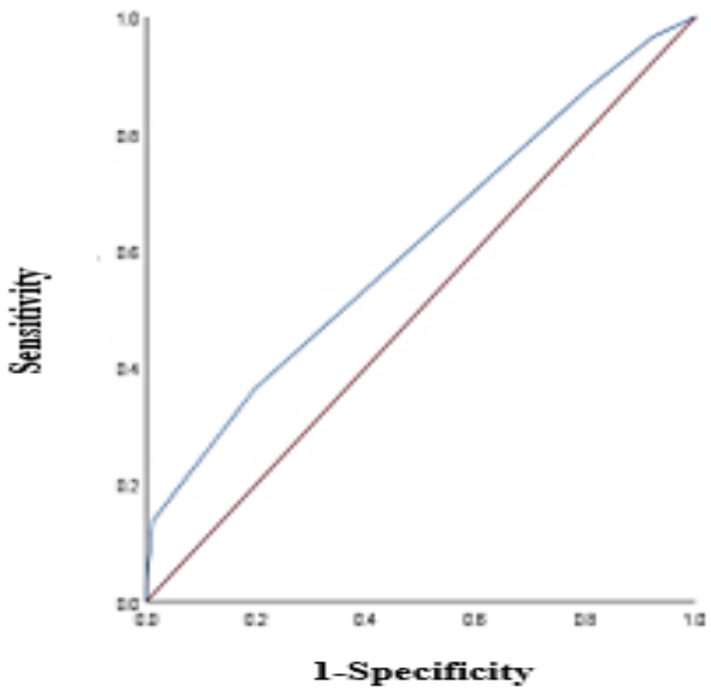

Figure (1): Receiver Operator Characteristic Curve for the ABCD score as a predictor of severe COVID-19 mortality

Table (5): Correlation between the ABCD score and other laboratory findings.

Characteristic	ABCD score	
	Correlation coefficient (r)	P value
WBCs	-.009	0.903
Neutrophils	.010	0.892
Lymphocytes	-.188	**0.012***
CRP	-.063	0.401
LDH	.072	0.407
D-Dimer	.183	**0.015***

***P value is statistically significant.**

4. Discussion

According to our knowledge, this was the first study to externally validate and assess the proposed ABCD scoring system for prediction of in-hospital mortality risk among severe and critically-ill COVID-19 patients. The score was first proposed by Salunke et al. for in-hospital triage of COVID-19 patients admitted to the emergency department. The variables used to calculate the score were given the initials A, B, C, and D, where the letters stand for age, blood markers, co-morbidities, chest X-ray or CT scan, and dyspnea, respectively. Each variable outputs a value of 0 if the answer is no or 1 if the answer is yes. The maximum score is 14 and the minimum is 0 [9]. The authors also suggested categorizing the overall final score using traffic light colors. Green was used to represent mild COVID-19 infection, which was assigned a total score of 0–4. The therapy advised for this group was symptomatic treatment in the ward. A moderate COVID-19 infection was designated as having a score of 4 to 8 and was given the yellow label. Treatments for this group included admission to semi-critical care and oxygen supplementation. The score 4 in the green and yellow groupings, however, overlaps, as we noticed. Consequently, the authors settled on a scale of 5-8 for moderate COVID-19 conditions. Finally, a total score of higher than 8 was recommended to indicate severe COVID-19 infection. The patients in this group were labeled red and the admission to ICU was the advocated regimen [9]. The current study revealed an AUROC of 0.608 (95% CI: 0.526- 0.691) for the ABCD scoring system as a predictor of in-hospital mortality for severe and critically-ill COVID-19 patients. There were no other similar studies available in the literature to compare with. However, numerous COVID-19 specific scores demonstrated higher performance for predicting COVID-19 in-hospital mortality. For example, Marcello Covino et al. conducted a research to evaluate the International Severe Acute Respiratory Infection Consortium- Coronavirus Clinical Characterization Consortium (ISARIC-4C) score, COVID-GRAM critical illness risk score (COVID-GRAM), Quick COVID-19 Severity Index (qCSI), and National Early Warning Score (NEWS).The ISARIC-4C score had the best AUROC of 0.799 (0.738–0.851), followed by COVID-GRAM 0.785 (0.723–0.838), NEWS 0.764 (0.700–0.819), and qCSI 0.749 (0.685–0.806) [12]. Because of the sudden onset of COVID-19 pandemic, the existing ICU prognostic scoring systems (e.g., APACHE II and SOFA) have been also used to COVID-19 patients in order to best distribute limited resources and

treatment. Wang et al. conducted a study to assess the APACHE II scoring system as a predictor of mortality in COVID-19 patients and they reported excellent AUROC of 0.937 [13]. Similarly, Zou et al. reported an AUROC of 0.966 for APACHE II as a prognostic score for COVID-19 mortality [14]. According to a review published by Chu et al. APACHE II reported the highest AUROC curve, in comparison with other scores, for prediction of COVID-19 mortality [15]. However, it is a complicated score formed of 12 variables. In addition, the Sequential Organ Failure Assessment (SOFA) score, which consists of only six variables, has also been demonstrated to be an effective predictor of mortality in COVID-19 patients, with an AUROC of 0.915[16]. The Area Under Receiver Operating Characteristic Curve (AUROC) is generally recognized as an outcome metric for prediction of model accuracy [17]. However, the evaluation of the prognostic scoring systems should not only rely on the AUROC, and it must take into account other factors such as that the intended score should comprise basic accessible variables without complexity in order to enable fast bedside detection of the patients at elevated risk of adverse events.

5 .Implications of the study

The ABCD grading system is objective, easily remembered, and simple to utilize. It might be a useful tool for predicting the in-hospital mortality among severe and critically-ill COVID-19 patients.

6 .Limitation of the study

This was a single center study. Further larger multicenter studies are required.

7 .Conclusion

The ABCD grading system exhibited a discriminative capacity to predict in-hospital mortality for severely ill COVID-19 patients, despite the AUROC of the ABCD score being inconclusive. The ABCD grading method may be a useful rapid choice for bedside assessment of severely and critically-ill COVID-19 patients and it may be used to rule out the possibility of further deterioration in patients designated for a non-critical region.

List of abbreviations:

APACHE II: The Acute Physiology and Chronic Health Evaluation II, **AUROC:** Area Under Receiver Operating Characteristic Curve, **ARDS:** Acute Respiratory Distress Syndrome, **CI:** Confidence Interval**, COVID-19:** Corona Virus Disease-2019**, CRP:** C Reactive Protein**, CT:** Computed Tomography**, CURB-65:** Creatinine, Urea, Respiratory rate, Blood pressure, age ≥65**, ISARIC-4C:** International Severe Acute Respiratory Infection Consortium-Coronavirus Clinical Characterization Consortium, **ICU:** Intensive Care Unit**, LDH:** Lactate Dehydrogenase, **LOS:** Length Of Stay, **NPV:** Negative Predictive Value**, OR:** Odds Ratio**, PPV:** Positive Predictive Value**, ROC Curve:** Receiver Operating Characteristics**, RT-PCR:** Real Time Polymerase Chain Reaction, **SOFA:** Sequential Organ Failure Assessment, **ZUH:** Zagazig University Hospitals.

Authors' contributions:

Dina M. Ali is the principal investigator responsible for the conceptualization, study design, collection of data, analysis and interpretation of data, writing the draft and critical revision of the final manuscript. Khaled Raafat is a co-author responsible for critical revision of the final manuscript for intellectual content.

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Supplementary Table (I): The ABCD Scoring System.

Study Variable	Values	Score	
		0	1
Age (Years)	Young, elderly	0-50	>50
Blood test	Leucopenia	No	Yes
	Lymphocytes (<1500 per mm^3)	No	Yes
	CRP (> 10mg/L)	No	Yes
	LDH (>250 U/L)	No	Yes
	D- Dimer (>0.5mg/L)	No	Yes
Chest x-ray or CT	Ground Glass & bilateral Patchy Shadows	No	Yes
Comorbidities	COPD/Smoker	No	Yes
	Cancer	No	Yes
	Hypertension &Chronic heart disease	No	Yes
	Chronic renal failure	No	Yes
	Diabetes mellitus	No	Yes
Dyspnea	RR>30/min	No	Yes
	O2 saturation <90%	No	Yes
Total Score			

Supplementary Table (II): ABC Grading System.

ABCD score	Category	Recommendations
0-4	**Mild COVID-19**	**Observation: Symptomatic treatment in the ward**
5-8	**Moderate COVID-19**	**Active treatment: Semi-critical care and oxygen supplementation**
>8	**Severe COVID-19**	**Urgent treatment: Admission to intensive care unit**