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Scoring system for mortality prediction of in-hospital COVID-19 patients in resource-limited settings: a single center cohort study during Delta and Omicron waves

Prognostic scoring of COVID-19 patients

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Abstract: **Objective:** Coronavirus Disease 2019 (COVID-19)-related mortality includes several risk variables that are country-specific in nature. The development of a scoring system is necessary regarding the appearance of novel virus variants. The objective of this research is to develop a prognostic score for COVID-19 patients in resource-constrained settings.

Methods: This study used a retrospective and prospective cohort design to identify variables that influence COVID-19 patients' in-hospital mortality. The receiver operating characteristic (ROC) curve analysis was utilized to determine the laboratory variables cut-off. Cox regression analysis was undertaken to determine the exact variables influencing the survival of COVID-19 patients. A scoring system was created using the best model based on the Hosmer-Lemeshow test (calibration) and the area under the curve (AUC) (discrimination ability).

Results: Based on calibration and discrimination testing, model 2 (immune disorders, unconsciousness, cerebrovascular disease, onset, and oxygen saturation) was rated as the most advantageous model. Model 2 (without age adjustment) had a superior AUC than model 2A (with age). Cut-off was determined at 2, and calculated for onset ≥7 days (AUC=0.816, 95% CI: 0.742,0.890) and <7 days (AUC=0.850, 95% CI: 0.784,0.916). There was no difference in scoring system utilization for subjects recruited during Delta or Omicron waves (P=0.527).

Conclusion: The model (cut-off value ≥2) which incorporated age ≥65 years, immune disorders, decreased consciousness, increased respiratory rate, and oxygen saturation <95% is the best model in our study to predict COVID-19 patient mortality.

Keywords: COVID-19; Prognostic; Scoring System; Survival

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1. Introduction

Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) was originally identified in Wuhan, China, and has been labeled a Coronavirus disease 2019 (COVID-19) pandemic since March 2020 (1,2). According to a study, the illness resulted in an excess of 18.2 million deaths between January 2020 and December 2021 (3). Meanwhile, the case fatality rate (CFR) of COVID-19, which has affected more than 680 million people worldwide, is approximately one percent (4). However, the CFR rate owing to COVID-19 in Indonesia alone (2.7%) is considerably higher than the global average (5). This also lists Indonesia as the major contributor to COVID-19 mortality in Southeast Asia (48.82%) (6).

Patients with severe or critical clinical symptoms are more likely to succumb from COVID-19 than those with milder conditions (7). As a result, it is necessary to conduct an assessment of variables that can forecast the fatality of COVID-19 and tailor it to the distinct characteristics of each nation, since it is determined that there were variations in the risk factors that contributed to patient death in different countries, which may have been caused by variations in the study demographic (8-10).

In Indonesia, publications on the identification of precise COVID-19 risk factors, which are then converted into a score to predict mortality in COVID-19 patients are currently limited to the first round of COVID-19 in 2020 (11). The scoring needs to be updated following the real situation because of the alterations that result from the emergence of several variants, notably the one named Omicron, which is currently the most prevalent COVID-19 variant (12). This is because each variant differs in clinical characteristics, outcomes, and immune system evasion (13).

Consequently, the objective of this study is to create a prognostic score for COVID-19 patients in environments with limited resources and during more recent periods of COVID-19 waves by using demographic, clinical, and laboratory risk factors that may have an impact on the survival of COVID-19 patients. It is intended that by using this system, hospitals will be able to screen COVID-19 patients early on in their hospital stays, make patient care simpler, and lower the morbidity and mortality rates of COVID-19 cases.

2. Methods

2.1. Study design

This single-center study used a retrospective and prospective cohort design with data from patients hospitalized at Dr. Mohammad Hoesin Hospital (a tertiary-level hospital). Patients were selected through consecutive sampling from July 2021 to September 2022. The required information was acquired from the medical records to identify the variables that influence COVID-19 patients' in-hospital mortality. This study was approved by the ethical review committee of Dr. Mohammad Hoesin Hospital, (statute number: 86/keprsmh/2022). Adult inpatients (aged ≥18 years) who had positive SARS-CoV-2 detection on reverse transcriptase polymerase chain reaction (RT-PCR) testing (confirmed COVID-19 cases) were included. This study excluded COVID-19 individuals with insufficient medical records data. All included patients were monitored from admission to discharge or in-hospital mortality. They were divided into two categories: survivors and non-survivors.

2.2. Data collection

We calculated the minimum sample size using a 95% confidence level and an 80% statistical power, yielding 49 people for each group. We gathered demographic information (age and sex), comorbidities (hypertension, diabetes mellitus, heart disease, immune disorder, cerebrovascular disease, malignancy, pregnancy, kidney disease, and tuberculosis), clinical symptoms (cough, rhinorrhea, sore throat, shortness of breath, nausea and vomiting, headache, fever, diarrhea, anosmia, and abdominal pain), physical examinations (respiratory rate, pulse rate, body temperature, blood pressure, body mass index (BMI), consciousness, and oxygen saturation), laboratory examinations (hematology, clinical chemistry, and serology), vaccination status, disease onset, and radiological findings (pneumonia based on X-ray examination). Retrospective data collection was done before July 2022 while prospective data collection was conducted from July 2022 onwards.

2.3. Statistical analysis

A descriptive analysis was done to assess the distribution of the COVID-19 patient characteristics based on outcome (survival). Categorical data were displayed as n (%). Chi-squared was used to analyze the association between the independent variable and the outcome. Patients' age was classified as 18-65 years or >65 years. Incomplete vaccination records were described as not having full-dose vaccination (at least two doses). Comorbidities and complaints were assessed as yes or no (according to the history taking process). Onset was determined as ≥7 days or <7 days. Furthermore, the physical examination included respiratory rate (>24 or ≤24/minute), pulse rate (>110 or ≤110 beats/minute), temperature (>37.3 or ≤37.3 °C), systolic blood pressure (SBP) (≥140 or <140 mmHg), diastolic blood pressure (DBP) (≥80 or <80 mmHg), unconsciousness (Glasgow coma scale <15, yes or no), body mass index (≥23 or <23 kg/m^2), and oxygen saturation (<95 or ≥95 %). We also determined the findings of pneumonia on X-ray (yes or no). For laboratory values, receiver operating characteristic (ROC) curve analysis was used to determine the cut-off.

Bivariate analysis was undertaken to determine the exact variables influencing the survival of COVID-19 patients. In the multivariate analysis, variables that had a P-value of less than 0.25 in the bivariate analysis (based on the chi-squared test) were included. Cox regression and the proportional hazards model were the multivariate analysis methods used to determine mortality risk. Complete modeling was done using the hierarchically well formulated (HWF) principle, followed by interaction and confounding assessment (a positive result when multivariate analysis with the suspected confounding factor included revealed a hazard ratio (HR) difference greater than 10% from the original HR), and final model generation. Investigation results were displayed using the HR and 95% Confidence Interval (95% CI). At the end, factors with a two-sided P-value <0.05 were denoted as the significant predictors of mortality. Furthermore, evaluation of the clinical and statistical model quality was done.

The Hosmer-Lemeshow test was used to evaluate the calibration value, and the area under the curve (AUC) was used to test the discrimination ability. If the observed and expected values differ, the calibration is effective. Meanwhile, if the AUC value is larger than or equal to the minimum predicted value (>80%), the discrimination quality is considered good. A scoring system was created using the best model. Additionally, researchers performed a two-sample Z test of proportions to see if the predictor model obtained does not provide differences for usage in samples from Delta and Omicron waves. The analysis was carried out using Medcalc version 19.3.1 (MedCalc Software Ltd, Ostend, Belgium) and STATA

Table 1 Demographic characteristics of COVID-19 patients and hazard ratio calculation

Parameters	N (%)	Outcome		P-value[a]	HR (95% CI)	P-value[b]
		Non-survive (n (%))	Survive (n (%))			
Age, n=145						
• 18-65 ears	106 (73.10)	43 (33.85)	63 (78.75)	0.089	1.107	0.704
• > 65 years	39 (26.90)	22 (66.15)	17 (21.25)		(0.655,1.869)	
Gender, n=145						
• Male	58 (40)	28 (43.1)	30 (37.5)	0.495	1.216	0.437
• Female	87 (60)	37 (56.9)	50 (62.5)		(0.742,1.994)	
Incomplete vaccination, n=133						
• Yes	76 (57.14)	39 (66.10)	37 (50)	0.062	1.262	0.398
• No	57 (42.86)	20 (33.90)	37 (50)		(0.736,2.166)	
Hypertension, n=145						
• Yes	51 (35.2)	30 (46.2)	21 (26.35)	**0.013**	1.377	0.204
• No	94 (64.8)	35 (53.8)	59 (73.75)		(0.840,2.257)	
Diabetes mellitus, n=145						
• Yes	25 (17.2)	11 (16.9%)	14 (17.5)	0.927	0.823	0.558
• No	120 (82.8)	54 (83.1%)	66 (82.5)		(0.427,1.583)	
Heart disease, n=145						
• Yes	30 (20.7)	16 (24.6%)	14 (17.5)	0.293	1.074	0.807
• No	115 (79.3)	49 (75.4%)	66 (82.5)		(0.607,1.898)	
Immune disorder, n=145						
• Yes	8 (5.5)	6 (9.2)	2 (2.5)	0.140	2.784	**0.018**
• No	137 (94.5)	59 (90.8)	78 (97.5)		(1.189,6.518)	
Cerebrovascular disease, n=145						
• Yes	18 (12.4)	16 (24.6)	2 (3.5)	**< 0.001**	3.193	**<0.001**
• No	127 (87.6)	49 (75.4)	78 (97.5)		(1.800,5.666)	
Kidney disease, n=145						
• Yes	32 (22.1)	19 (29.2%)	13 (16.3)	0.061	1.424	0.199
• No	113 (77.9)	46 (70.8%)	67 (83.8)		(0.830,2.442)	
Tuberculosis, n=145						
• Yes	5 (3.4)	3 (4.6)	2 (2.5)	0.657	1.384	0.584
• No	140 (96.6)	62 (95.4)	78 (97.5)		(0.433,4.422)	
Malignancy, n=145						
• Yes	24 (16.6)	9 (13.8)	15 (18.8)	0.429	0.597	0.155
• No	121 (83.4)	56 (86.2)	65 (81.2)	0.174	(0.293,1.216)	0.773
Pregnancy, n=145						
• Yes	17 (11.7)	5 (7.7)	12 (15.0)	0.174	1.145	0.773
• No	128 (88.3)	60 (92.3)	68 (85.0)		(0.456,2.875)	
Shortness of breath, n=145						
• Yes	98 (67.6)	54 (83.1)	44 (55.0)	**<0.001**	2.284	**0.199**
• No	47 (32.4)	11 (16.9)	36 (45.0)		(1.194,4.370)	
Nausea and/or vomiting, n=145						
• Yes	29 (20.0)	17 (26.2)	12 (15.0)	0.095	1.412	0.223
• No	116 (80.0)	48 (73.8)	68 (85.0)		(0.810,2.458)	
Abdominal pain, n=145						
• Yes	25 (17.2)	8 (12.3)	17 (21.3)	0.156	0.663	0.278
• No	120 (82.8)	57 (87.7)	63 (78.7)		(0.316,1.392)	
Cough, n=145						
• Yes	76 (52.4)	30 (46.2)	46 (57.5)	0.174	0.585	**0.038**
• No	69 (47.6)	35 (53.8)	34 (42.5)		(0.353,0.970)	
Rhinorrhea, n=145						
• Yes	8 (5.5)	2 (5.5)	6 (7.5)	0.297	0.515	0.358
• No	137 (94.5)	63 (96.6)	74 (92.5)		(0.126,2.117)	
Sore throat, n=145						
• Yes	6 (4.1)	2 (3.1)	4 (5.0)	0.761	0.814	0.775
• No	139 (95.9)	63 (96.9)	76 (95.0)		(0.199,3.337)	
Fever, n=145						
• Yes	60 (41.4)	26 (40.0)	34 (42.5)	0.761	0.846	0.514
• No	85 (58.6)	39 (60.0)	46 (57.5)		(0.513,1.396)	
Headache, n=145						
• Yes	19 (13.1)	11 (16.9)	8 (10.0)	0.219	1.320	0.403
• No	126 (86.9)	54 (83.1)	72 (90.0)		(0.689,2.529)	

Table 1 Demographic characteristics of COVID-19 patients and hazard ratio calculation (continued)

Parameters	N (%)	Outcome		P-value[a]	HR (95% CI)	P-value[b]
		Non-survive (n (%))	Survive (n (%))			
Diarrhea, n=145						
• Yes	4 (2.8)	2 (3.1)	2 (2.5)	0.833	1.325	0.697
• No	141 (97.2)	63 (96.9)	78 (97.5)		(0.322,5.457)	
Anosmia, n=145						
• Yes	6 (4.1)	3 (4.6)	3 (3.8)	1.000	0.992	0.989
• No	139 (95.9)	62 (95.4)	77 (96.2)		(0.310,3.169)	
Onset, n=126						
• ≥ 7 days	44 (34.9)	17 (27.4)	27 (42.2)	0.082	0.459	**0.007**
• < 7 days	82 (65.1)	45 (72.6)	37 (57.8)		(0.262,0.805)	
Respiratory ratete (breaths/minute), n=145						
• >24	52 (35.9)	32 (49.2)	20 (25.0)	**0.002**	1.622	0.052
• ≤24	93 (64.1)	33 (50.8)	60 (75.0)		(0.996,2.641)	
Pulse rate (beats/minute), n=145						
• >110	29 (20)	17 (26.2)	12 (15.0)	0.095	1.362	0.275
• ≤110	116 (80)	48 (73.8)	68 (85.0)		(0.782,2.371)	
Temperature (°C), n=145						
• >37.3	25 (17.2)	10 (16.9)	15 (18.8)	0.594	0.754	0.413
• ≤37.3	120 (82.8)	55 (83.1)	65 (81.2)		(0.383,1.484)	
SBP (mmHg), n=144						
• ≥140	53 (36.8)	31 (48.4)	22 (27.5)	**0.015**	1.245	0.386
• <140	91 (63.2)	33 (51.6)	58 (72.5)		(0.759,2.040)	
DBP (mmHg), n=144						
• ≥80	117 (81.3)	47 (73.4)	70 (87.5)	**0.032**	0.553	**0.038**
• <80	27 (18.7)	17 (26.6)	10 (12.5)		(0.317, 0.967)	
Unconsciousness, n=145						
• Yes	33 (22.8)	29 (44.6)	4 (5.0)	**<0.001**	5.202	**<0.001**
• No	112 (77.2)	36 (55.4)	76 (95.0)		(3.089,8.761)	
Body mass index (kg/m2), n=109						
• ≥23	60 (55)	23 (51.5)	37 (57.8)	0.559	1.015	0.961
• <23	49 (45)	22 (48.9)	27 (42.2)		(0.561,1.836)	
Oxygen saturation (%), n=131						
• < 95	60 (45.8)	41 (67.2)	19 (27.1)	**<0.001**	2.247	**0.003**
• ≥ 95	71 (54.2)	20 (32.8)	51 (72.9)		(1.312,3.845)	
Pneumonia on X-ray, n=123						
• Yes	69 (56.10)	40 (72.72)	29 (42.65)	**0.001**	2.007	**0.022**
• No	54 (43.90	15 (27.28)	39 (57.35)		(1.106,3.644)	

[a]: Chi squared test; [b]: Hazard ratio (HR), P<0.05; DBP: Diastolic blood pressure; SBP: Systolic blood pressure; TB: Tuberculosis

version 15 (College Station, Texas 77845, USA).

3. Results

3.1. Demographic and clinical characteristics

In our study, there were 145 patients: 65 non-survivors and 80 survivors. The COVID-19 patient outcome was not statistically significantly associated with the age or gender of the subjects (P=0.089 and P=0.495, respectively). The onset and history of COVID-19 vaccination were also unrelated to patient outcomes (P=0.082 and P=0.062, respectively). In contrast, pneumonia findings on X-ray were associated with COVID-19 patients' outcome (P<0.001).

According to comorbidities, COVID-19 patient outcome were substantially correlated with both cerebrovascular disease and hypertension (P=0.013 and P<0.001, respectively). For physical symptoms, shortness of breath was the only one with a significant association (P<0.001) with COVID-19 patient outcome.

Physical examination revealed a significant association between COVID-19 patient outcomes and respiratory rate, oxygen saturation, and decreased consciousness (P=0.002, P<0.001, and P<0.001, respectively). Furthermore, diastolic blood pressure was also associated with COVID-19 outcome (P=0.032). Systolic blood pressure, on the other hand, did not follow this pattern.

Shortness of breath, immune disorder, cerebrovascular disease, respiratory rate, oxygen saturation, onset, and chest X-ray finding, all significantly impacted the survival rate of COVID-19 patients, according to bivariate analysis with Cox regression. Meanwhile, for the physical examination, only consciousness, diastolic blood pressure, and oxygen saturation had significant effects on COVID-19 patient survival. Table 1 displays data findings on demographic and clinical

Table 2 Laboratory characteristics of COVID-19 patients and hazard ratio calculation

Parameters	N (%)	Outcome		P-value[a]	HR (95% CI)	P-value[b]
		Non-survive (n (%))	Survive (n (%))			
Hemoglobin (g/dL), n=145						
< 11.05	71 (49.0)	40 (50.0)	31 (41.7)	0.782	0.795	0.361
≥ 11.05	74 (51.0)	40 (50.0)	34 (52.3)		(0.486,1.300)	
Leukocyte count (x10^3 cells/uL), n=145						
≥ 11.04	72 (49.7)	37 (56.9)	35 (43.8)	0.115	1.817	0.019
< 11.04	73 (50.3)	28 (43.1)	45 (56.3)		(1.104,2.990)	
Thrombocyte count (x10^3 cells/uL), n=145						
< 265.5	73 (50.3)	31 (47.7)	42 (52.5)	0.565	1.037	0.887
≥ 265.5	72 (49.7)	34 (52.3)	38 (47.5)		(0.631,1.704)	
Neutrophil-lymphocyte ratio (NLR), n=139						
≥ 8.35	68 (48.9)	40 (62.5)	28 (37.3)	0.003	1.762	0.029
< 8.35	71 (51.1)	24 (37.5)	47 (62.7)		(1.061, 2.925)	
Absolute lymphocyte count (ALC), n=139						
<1.105	67 (48.2)	35 (54.7)	32 (42.7)	0.157	1.091	0.729
≥1.105	72 (51.8)	29 (45.3)	43 (57.3)		(0.666,1.790)	
Urea (mg/dL), n=138						
≥ 35	67 (48.6)	39 (60.9)	28 (37.8)	0.007	2.026	0.006
< 35	71 (51.4)	25 (39.1)	46 (62.2)		(1.219,3.367)	
Creatinine (mg/dL), n=138						
≥ 0.915	66 (47.8)	33 (51.6)	33 (44.6)	0.414	1.535	0.094
<0.915	72 (52.2)	31 (48.4)	41 (55.4)		(0.929, 2.535)	
Alanine transaminase (ALT) (U/L), n=112						
≥28	57 (50.9)	28 (52.8)	29 (49.2)	0.697	0.982	0.949
<28	55 (49.1)	25 (47.2)	30 (50.8)		(0.571,1.688)	
Aspartate transaminase (AST) (U/L), n=112						
≥ 35.5	54 (48.2)	30 (56.6)	24 (40.7)	0.092	1.279	0.376
< 35.5	58 (51.8)	23 (43.4)	35 (59.3)		(0.742,2.206)	
Albumin (g/dL), n=112						
< 2.95	58(51.3)	32 (59.3)	26 (44.1)	0.107	1.147	0.626
≥ 2.95	55 (48.7)	22 (40.7)	33 (55.9)		(0.662 – 1.986)	
Ferritin (ng/mL), n=81						
≥ 786.45	45 (55.6)	31 (66.0)	14 (41.2)	0.027	1.879	0.041
< 786.45	36 (44.4)	16 (34.0)	20 (58.8)		(1.025,3.441)	
Procalcitonin (ng/mL), n=66						
≥ 0.375	40 (60.6)	33 (75.0)	7 (31.8)	0.001	2.454	0.010
< 0.375	26 (39.4)	11 (25.0)	15 (68.2)		(1.236,4.872)	
C-reactive protein (CRP) (mg/L), n=118						
≥ 65.1	56 (47.5)	34 (63.0)	22 (34.4)	0.002	1.800	0.038
< 65.1	62 (52.5)	20 (37.0)	42 (65.6)		(1.032,3.139)	

[a]: Chi squared test; [b]: Hazard ratio (HR)
Cut-off was determined by using the receiver operating characteristic (ROC) curve

traits.

3.2. Laboratory examination characteristics

Cut-off for laboratory examination was determined using the ROC analysis (Figure 1). According to COVID-19 patient outcomes, hematological markers in the form of neutrophil-lymphocyte ratio (NLR) have a significant association (P=0.005), with an increase in NLR being observed in 62.5% of patients who do not survive and 37.3% of patients who do. Nevertheless, none of the other hematological variables were significantly associated with patient outcomes.
Serology and clinical chemistry revealed that urea, C-reactive protein (CRP), and procalcitonin had a significant association with COVID-19 patient outcome (P=0.007, P=0.002, and P=0.001, respectively). Our study also discovered a significant association between ferritin and patient outcomes (P=0.027).
Bivariate analysis using Cox regression revealed that laboratory tests for leukocytes, NLR, urea, CRP, ferritin, and procalcitonin had a significant impact on the mortality of COVID-19 patients. Data about laboratory variables are presented in table 2.

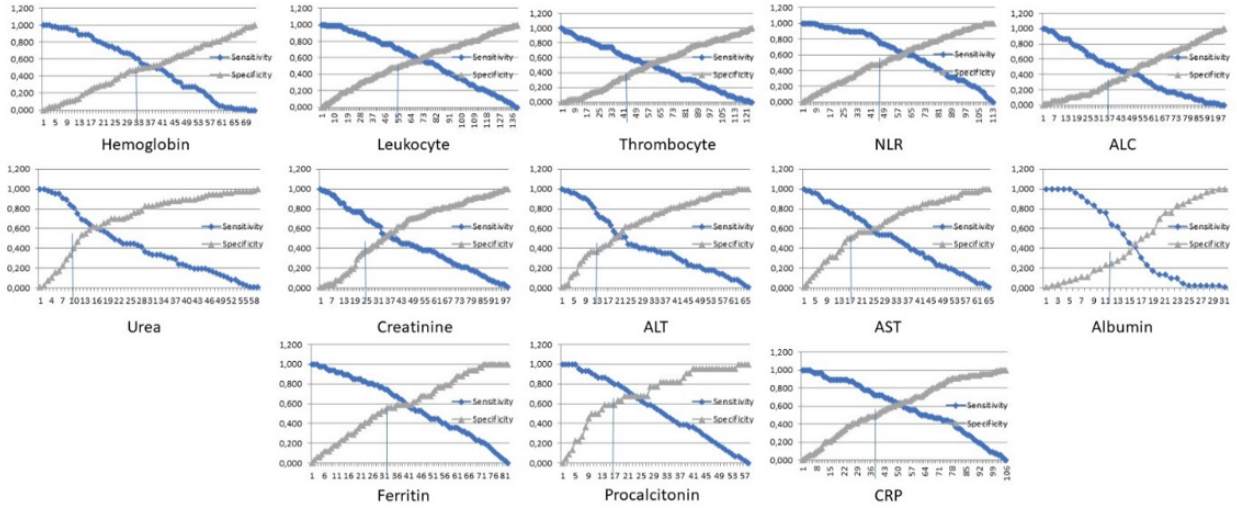

Figure 1 ROC analysis

ALC: Absolute lymphocyte count; ALT: Alanine transaminase; AST: Aspartate transaminase; CRP: C-reactive protein; NLR: Neutrophil-lymphocyte ratio

Table 3 Comparison of the quality of prognostic models

Model	Variables	Statistics		Quality parameters
		Calibration (Hosmer-Lemeshow test)	Discrimination (AUC)	
Model 1	1. Consciousness 2. Immune disorder 3. Respiratory rate 4. Onset	Good P=0.616 (P>0.05)	Moderate 0.786	Cutoff point ≥2, sensitivity=77%, specificity=67%, NPV=75%, PPV=70%, AUC=0.756 (95% CI: 0.674,0.837)
Model 2	1. Immune disorder 2. Consciousness 3. Respiratory rate 4. Oxygen saturation 5. Onset	Good P=0.921 (P> 0.05)	Strong 0.872	Cutoff point ≥2, sensitivity=95%, specificity=51%, NPV=91%, PPV=67%, AUC=0.816 (95% CI: 0.742,0.890)
2A	1.Immune disorder 2. Consciousness 3. Respiratory rate 4. Oxygen saturation 5. Onset 6. Age	Good P=0.450 (P>0.05)	Strong 0.876	Cutoff point ≥2, sensitivity=92%, specificity=58%, NPV=87%, PPV=69%, AUC=0.777 (95% CI: 0.694,0.861)
Model 3	1. Shortness of breath 2. Immune disorder 3. Cerebrovascular disease 4. Onset	Good P=0.709 (P>0.05)	Moderate 0.772	Cutoff point ≥1, sensitivity=94%, specificity=31%, NPV= 83%, PPV=57%, AUC=0,610 (95% CI: 0.518,0.703)

AUC: Area under the curve; NPV: Negative predictive value; PPV: Positive predictive value

3.3. Comparison of the quality of prognostic models

Based on calibration and discrimination testing, some of the generated models will be chosen as the best prognostic models. Table 3 displays the information. All models in our study had good calibration values, while only model 2 had strong discrimination capability.

Model 2 was then rated as the most advantageous among the other models based on clinical and statistical factors. Subsequently, a confounding test was performed on model two, which used the age parameter because it had been statistically and clinically proven to impact mortality. Then, model two was adjusted for age after the confounding test with age revealed that this variable impacted patients' mortality. Model 2 (without age) had a superior AUC than model 2A (with age), hence model 2 was selected for the interaction test. According to the interaction test findings, model 2 with age and gender variables did not interact (P>0.05). However,

Table 4 Prognostic score

No	Predictor	Categories	Score (onset)	
			< 7 days	**≥ 7 days**
1	Immune disorder	Yes	1	1
		No	0	0
2	Respiratory rate	>24 x/minute	1	1
		≤ 24 x/minute	0	0
3	Onset	≥ 7 days		1
		< 7 days	0	
4	Unconsciousness	Yes	2	2
		No	0	0
5	Oxygen saturation (%)	< 95	1	1
		≥ 95	0	0
	Total score		5	6

a model that included disease onset was constructed after the discovery of positive interaction. Thus, model was determined using two onset period as described previously.

We also tested the consistency of prognostic model to be used during the Delta and Omicron era of COVID-19 pandemic. The two sample Z test of proportions was undertaken, and there was no difference in scoring system utilization for subjects recruited during Delta or Omicron waves for model 2 (P=0.527), model 1 (P=0.404), and model 3 (P=0.096). It means that the developed model can be used freely regardless of the pandemic period.

3.4. Prognostic score development

The obtained model 2 needs to be streamlined for application in routine medical practice; hence a scoring system is developed. Scores for each variable were calculated using the coefficient (B) and standard error (SE) values. In model 2, there was an interaction between onset and respiratory rate, therefore scores were calculated for onset ≥7 days and <7 days at cut-off points of 2. The sensitivity, specificity, and accuracy for model 2 with an onset of ≥7 days were 95%, 51%, and 73% (AUC=0.816, 95% CI: 0.742,0.890). Meanwhile, the sensitivity, specificity, and accuracy for model 2 with an onset of <7 days were 92%, 63%, and 78% (AUC=0.850, 95% CI: 0.784,0.916). Table 4 displays the prognostic scores.

4. Discussion

This study enrolled 145 participants between July 2021 and September 2022. Specifically, cerebrovascular disease and hypertension were the only comorbidities that were found to be significantly linked to COVID-19 patients' mortality. According to a systematic study of 423,117 individuals, those with hypertension have a higher risk of death (prevalence odds ratio (pOR)=1.57; 95% CI: 1.27,1.8, and prevalence hazard ratio (pHR)=1.18, 95% CI: 1.01,2.07) (14). The risk of death was also elevated by cerebrovascular disease (OR=3.45, 95% CI: 2.46,4.84, P<0.001) (15).

The outcome of COVID-19 cases is also associated with the clinical symptoms present at the time of admission. Shortness of breath was discovered to be the primary death-related complaint in this study (P<0.001). Breathing difficulties appear as the virus spreads through the bloodstream, particularly to organs that express angiotensin converting enzyme 2 (ACE2), leading to poor gas exchange, thrombosis, endothelial dysfunction, and lung lesions that can progress into acute respiratory distress syndrome (ARDS) (16).

In this study, it was discovered that the proportion of COVID-19 patients who died and experienced tachypnea was 49.7%, which was higher than the proportion of tachypnea in those who survived (25%). Patients with a respiratory rate >22 times per minute had a 1.9-3.2 times higher likelihood of dying than those with a respiratory rate ≤20 times per minute, according to previous research (17).

Additionally, the measurement of another respiratory parameter, oxygen saturation, revealed that hypoxemia occurred in 67.2% of patients who died while it occurred in only 27.1% of patients who survived. In comparison to COVID-19 patients with normoxemia status, hypoxemia patients (oxygen saturation <92%) have a strong association with a risk of death that is elevated by 1.8-4.0 times (17).

Reduced consciousness was experienced by 44.6% of patients who did not survive. An earlier investigation revealed a substantial association between COVID-19 patient mortality and decreasing consciousness. Patients with Glasgow coma scale (GCS) values between 9 and 14 (HR=46.76, P<0.001) and 9 (HR=65.86, P<0.001) are at an increased risk of dying, and abrupt decrease of consciousness was associated with shorter periods of survival for COVID-19 patients (18). Diastolic blood pressure measures, meanwhile, are strongly related to COVID-19 patients' outcomes (P=0.032). Another study discovered a significant association (P=0.033) between diastolic blood pressure and patient mortality, but its level was higher in patients who survive (19).

Several laboratory testing was significantly associated with mortality in our study. The NLR examination has a significant association with the outcome of COVID-19 patients. NLR levels >9.47 were determined to be cut-offs that were substantially linked with in-hospital mortality in Ethiopian research, according to results of multivariate logistic regression analysis (adjusted odds ratio (AOR)=4.73, 95% CI: 1.19,33.68,

P<0.02) (20). Renal function testing using urea has demonstrated a statistically significant correlation with patient outcome (P<0.001; r=0.435) (21). Meanwhile, serological analysis revealed a strong association between COVID-19 patient outcome and CRP, ferritin, and procalcitonin. The risk of mortality is increased with HR values of 12.82 and 12.30 for procalcitonin (≥0.10 ng/mL) and CRP (≥52.14 mg/L), respectively (22). Meanwhile, ferritin has a greater capacity to predict mortality than severity in COVID-19 patients, with an AUC value of 0.69 (vs. 0.66 for severity) (23).

In this study, three models were obtained and evaluated for their quality. Model 2 was identified as the most operational prognostic factor in this investigation, with calibration values of P=0.921, AUC=0.872, 95% sensitivity, and 51% specificity. From a clinical standpoint, model 2 is relatively feasible (can be completed with limited expenses and human resource capabilities) because it only requires an effortless history taking and physical examination (24). This model can also be performed in basic healthcare facilities (25).

World health organization (WHO) developed the 4C mortality score for COVID-19 patients (9). Age, gender, comorbidities, respiratory rate, peripheral oxygen saturation, state of consciousness, urea, and CRP levels are all factors in this mortality index (score range: 0-21). In contrast to patients with a score of three or less, who had a mortality risk of just 1%, patients with a score of ≥15 had a 62% mortality risk. A score named the scoring system of COVID-19 (CSS) was developed in China (8) by incorporating characteristics such as advanced age, coronary heart disease, lymphocyte percentage, procalcitonin, and D-dimer as independent determinants of patient mortality. Patients were divided into two groups: those with low (scoring 0-2) and high (score >2) mortality risk. These data revealed that numerous variables contributed to patient mortality across different nations (26).

An Indonesian multicenter study that looked at eight predictor variables, including age, chronic kidney disease, obstructive lung disease, weakness, dyspnea, impaired consciousness, NLR=5.8, and critical status, came up with a predictive score. The cut-off point score for that study was 6, and the AUC was 0.847, with a 76.3% sensitivity, and a 78.2 % (11). The study used samples from the original SARS-CoV-2 variation from July 2020 to January 2021, whereas the present investigation used specimens from the SARS-CoV-2 Delta and Omicron variants from July 2021 to September 2022. These different times lead to distinct COVID-19 traits, which could result in different clinical profiles of the participants (27). Based on the result of the two sample Z tests of proportions, which demonstrates no difference for either the Delta or Omicron variations in any of the examined prognostic models, this score can be applied to numerous COVID-19 variants sufferers.

In this study, age, consciousness, immune disorders, oxygen saturation, respiratory rate, and disease onset were the six evaluated variables. In general, the mortality models in this investigation differed slightly from previously published models, although generally incorporated information on comorbidity status, clinical symptoms, and physical examinations (28). The most often utilized model was oxygen saturation (8 models), which was followed by immune disorders (7 models), shortness of breath (4 models), cerebrovascular illness (3 models), onset (1 model), and level of consciousness (1 model). After cohort validation from some prior research, the AUC value in this study (range of three models: 0.772-0.876) falls within the AUC range from previously published studies (AUC: 0.74-0.98) (29).

5. Limitations

This study's limitations are related to COVID-19 patient management, which may impact internal validity. Substantial variations will most likely be caused by differences in previous treatment profiles, either independently or from other hospitals. This significant variance in treatment will have an impact on the variables in this investigation, which will have an impact on the findings of this study. Additionally, history-taking derived from subjective patient responses may contain bias in the form of selection bias and recall bias (30,31). The happy hypoxia phenomenon in COVID-19 slows patient visits to medical facilities and conceals the onset of the patient's illness (32).

6. Conclusion

This study discovered three prognostic models, with the best model including predictive variables such as age ≥65 years, co-occurring immune disorders, decreased consciousness, increased respiratory rate (>24 breaths/minute), and oxygen saturation <95%. The model was stratified for onset ≥7 days and <7 days with a cut-off value of 2 in the scoring system. The prognosis model needs validation in multicenter trials for broad implementation in clinical practice. Future research also needs to homogenize elements that may impact the study findings, such as patient care.

7. Declarations

7.1. Acknowledgement

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7.2. Authors' contribution

Conceptualization: PL; Methodology: PL, KM, IAL, ZH; Software: PL and TPU; Validation: PL, KM, TPU; Formal analysis: PL and TPU; Investigation: PL; Resources: PL, KM, IAL; Data curation: PL, KM, ZH; Writing—original draft preparation: PL, KM, TPU; Writing—review and editing: PL and TPU; Visualization: PL and TPU; Supervision: KM, IAL, ZH. All authors have read and approved the final version of the manuscript.

7.3. Conflict of interest

None declared.

7.4. Funding

None.

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