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Original Article

Development and diagnostic performance of a novel scoring system for predicting COVID-19 severity in a national referral hospital

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Abstract

Coronavirus disease 2019 (COVID-19) shows a wide spectrum of clinical manifestations, ranging from mild illness to severe and critical disease. Early identification of patients at risk of deterioration remains important for timely clinical decision-making. The aim of this study was to develop a novel scoring system for predicting COVID-19 severity in a national referral hospital. This prospective cohort study included patients with confirmed COVID-19 admitted to Dr. M. Djamil Hospital, Padang, Indonesia, from May to December 2021. Demographic, clinical, and laboratory data were collected, and disease severity was classified according to the World Health Organization criteria. Univariate analysis was performed to identify candidate variables, followed by multivariable logistic regression analysis to determine independent predictors of severity. A scoring system was then constructed based on the retained predictors, and its diagnostic performance was evaluated using receiver operating characteristic analysis and the Youden index. Five variables were independently associated with COVID-19 severity: white blood cell count (WBC) ≥10,000/mm^3, absolute lymphocyte count (ALC) <1,500/mm^3, platelet large cell ratio (PLCR) ≥30%, interleukin-6 (IL-6) ≥7 pg/mL, and D-dimer ≥500 ng/mL. These variables were incorporated into a scoring system with a maximum total score of 6. Using a cut-off score of 3.5, the model showed a sensitivity of 96.15% and a specificity of 79.03% for differentiating severe from non-severe COVID-19. This study highlights that a novel scoring system based on WBC, ALC, PLCR, IL-6, and D-dimer performed well in predicting COVID-19 severity and may support early risk stratification in hospitalized patients.

Keywords: COVID-19, novel scoring, prediction, severity, D-dimer

Introduction

Coronavirus disease 2019 (COVID-19), an acute infectious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a systemic disease affecting multiple systems, including the respiratory, cardiovascular, gastrointestinal, neurological, hematopoietic, hemostatic, and immune systems [1]. SARS-CoV-2 enters the host cells through the interaction of its spike protein (S protein) with the angiotensin-converting enzyme 2 (ACE2) receptors. ACE2 receptors are widely expressed in pulmonary alveolar epithelial cells, cardiac myocytes, and vascular endothelial cells and therefore are found in almost all organs, such as the nasopharynx,

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oropharynx, stomach, small intestine, and others. SARS-CoV-2 infection in the lungs leads to extensive disruption of both epithelial and endothelial cell integrity, triggering diffuse alveolar inflammation characterized by heightened release of pro-inflammatory cytokines—including tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6)— and this immune response is highly exaggerated in severe and critical illness, described as a systemic cytokine storm [2]. Cytokine storms are essential in the pathogenesis of severe COVID-19 manifestations such as acute respiratory distress syndrome [3].

Activation of many cytokines can also lead to atrophy of lymphoid organs and failure of lymphocyte turnover [4,5]. A cohort study of 450 patients reported that severe cases were associated with lymphopenia, elevated leukocyte count, and a higher neutrophil-to-lymphocyte ratio [6]. Mean platelet volume (MPV) has been considered a marker of platelet activation and reflects the metabolism and proliferation of megakaryocytes and the production of thrombosis in the bone marrow [7]. During infection, elevated levels of inflammatory cytokines—such as TNF-α, IL-1, IL-3, and IL-6—stimulate thrombopoietin production and enhance megakaryocyte maturation, leading to the release of larger and more reactive platelets into the circulation. These activated platelets exhibit a markedly higher phosphorylation rate compared with smaller, unstimulated platelets [8]. Functionally, platelets play key roles not only in hemostasis but also in modulating inflammatory pathways and contributing to innate immune defense mechanisms [9]. The proportion of circulating large platelets can be quantitatively evaluated using the platelet large cell ratio (P-LCR) parameter [7].

Hypercoagulability is frequently observed among hospitalized patients with COVID-19. Progressive elevation of D-dimer levels has been consistently reported throughout the course of illness and is strongly associated with clinical deterioration [5]. Additional coagulation abnormalities—such as prolonged prothrombin time and activated partial thromboplastin time (aPTT), increased fibrin degradation products, and severe thrombocytopenia—may signal the development of disseminated intravascular coagulation, a life-threatening condition that necessitates careful monitoring and prompt therapeutic intervention [5].

A study reported increased C-reactive protein (CRP) values in COVID-19 patients, which were suspected to be correlated with disease severity and progression [10]. A study showed that the median CRP value was correlated with the severity of COVID-19 and was an independent predictor of mortality [10]. A few studies have also shown an increase in ferritin levels in patients with COVID-19 and elevated ferritin levels may predict inflammatory responses that occur in COVID-19 [11,12]. Another study reported that ferritin levels were significantly higher in severe cases of COVID-19 [13].

The clinical complexity of SARS-CoV-2 infection arises from the highly variable and rapidly evolving manifestations of COVID-19, which may progress unpredictably and lead to severe complications and death. These dynamics underscore the need for reliable early-warning tools capable of identifying patients at risk of deterioration. Motivated by this gap, this study was conducted to develop a novel scoring system designed to predict COVID-19 severity in a national referral hospital. This scoring system aims to accurately identify and stratify patients at risk of progressing to severe disease, thereby supporting timely clinical decision-making and optimizing patient management.

Methods

Study design and patient criteria

This study used an analytical prospective cohort design and was conducted at Dr. M. Djamil Hospital, Padang, Indonesia, from May to December 2021. Dr. M. Djamil Hospital is a national referral hospital that receives patients with COVID-19 from Padang and surrounding regions, including cases requiring advanced diagnostic evaluation and inpatient management. Consecutive sampling was used to recruit patients during the study period. A total of 140 patients with confirmed SARS-CoV-2 infection were included in the study. The diagnosis of SARS-CoV-2 infection was established by real-time polymerase chain reaction (RT-PCR) using nasopharyngeal and/or oropharyngeal swab specimens.

Study variables and data collection

Baseline demographic and clinical data were collected for all patients at enrollment. Recorded variables included age, sex, oxygen saturation, chest X-ray findings, and comorbidities, including diabetes mellitus, hypertension, and cardiovascular disease. Blood specimens consisting of ethylenediaminetetraacetic acid (EDTA), whole blood, and serum were collected for laboratory evaluation. Hematological parameters included hemoglobin, white blood cell count, absolute lymphocyte count, neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet count, mean platelet volume, and platelet large cell ratio. Hemostatic parameters included prothrombin time, activated partial thromboplastin time (aPTT), and D-dimer. Inflammatory and biochemical markers included ferritin, CRP, procalcitonin, and IL-6. Disease severity was assessed according to the World Health Organization criteria and categorized into non-severe and severe groups for analysis [14]. The non-severe group comprised patients with mild and moderate illness, whereas the severe group comprised patients with severe and critical illness [14].

Severity assessment

COVID-19 severity was classified according to the WHO criteria into mild, moderate, severe, and critical illness [14]. Severity determination was performed independently of the prognostic laboratory variables evaluated in this study. Mild illness was defined as symptomatic COVID-19 without evidence of viral pneumonia or hypoxia. Moderate illness was defined as the presence of clinical signs of pneumonia, such as fever, cough, dyspnea, or fast breathing, without features of severe pneumonia, with oxygen saturation at room air of ≥90%. Severe illness was defined as pneumonia with at least one of the following: respiratory rate >30 breaths/minute, severe respiratory distress, or oxygen saturation at room air of <90%. Critical illness included acute respiratory distress syndrome, sepsis, and septic shock. For the purpose of analysis, patients with mild and moderate illness were grouped as non-severe COVID-19, whereas those with severe and critical illness were grouped as severe COVID-19.

Laboratory measurement

EDTA whole blood and serum samples were collected from all patients for laboratory examination. Hematological parameters, including hemoglobin, white blood cell count (WBC), absolute lymphocyte count (ALC), neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet count (PLT), mean platelet volume (MPV), and platelet large cell ratio (PLCR), were measured using a Sysmex XN-1500 hematology analyzer with a fluorescent flow cytometry method (Sysmex Corporation, Kobe, Japan). Hemostasis parameters, including prothrombin time and aPTT, were measured using a Sysmex CS-2500 coagulation analyzer (Sysmex Corporation, Kobe, Japan). D-dimer was measured using an enzyme-linked fluorescent assay on the VIDAS system (bioMérieux, Marcy-l'Étoile, France). Ferritin, procalcitonin (PCT), and IL-6 were measured using a Cobas e411 analyzer with an electrochemiluminescence assay (Roche Diagnostics, Mannheim, Germany). High-sensitivity CRP was measured using the Afinion 2 analyzer (Abbott Diagnostics Technologies, Oslo, Norway).

Statistical analysis for score development and validation

Data were analyzed to identify factors associated with COVID-19 severity and to develop and validate a severity prediction score. Univariate analysis was first performed to assess the association between each demographic and laboratory variable and COVID-19 severity. Variables with $p<0.25$ in the univariate analysis were included in the multivariable logistic regression analysis as candidate predictors. Variables that remained significant in the multivariable model were retained for score development.

The COVID-19 severity scoring system was developed using variables that remained significant in the multivariable logistic regression analysis, whereas the optimal cut-off point was determined using the Youden index analysis. Score weighting was determined by comparing the beta coefficient with its standard error for each retained predictor. The diagnostic performance of the final scoring system was evaluated using receiver operating characteristic (ROC) curve analysis, with sensitivity and specificity reported. A $p<0.05$ was considered statistically significant.

Results

Baseline characteristics and factors associated with COVID-19 severity

The patients were followed for 2–3 weeks after enrollment. Among the 140 patients included in the study, 78 were classified as having severe COVID-19 and 62 as having non-severe COVID-19. Univariate analysis showed that several demographic and laboratory parameters were associated with COVID-19 severity (**Table 1**). Patients aged ≥65 years were more likely to have severe disease than those aged <65 years (p=0.002). Severe disease was more frequent among patients with Hb<10 g/dL (p=0.007), WBC≥10,000/mm^3 (p<0.001), ALC<1,500/mm^3 (p<0.001), NLR≥3.13 (p<0.001), MLR≥0.37 (p<0.001), PLT<150,000/µL (p<0.001), PLCR≥30% (p<0.001), and MPV>10 fL (p=0.001). Coagulation parameters, including prothrombin time ≥13 seconds (p=0.006) and aPTT≥30 seconds (p<0.001), were also significantly associated with severe disease. In addition, liver and inflammatory markers were significantly associated with COVID-19 severity. Patients with aspartate aminotransferase (AST) >38 U/L (p<0.001), alanine aminotransferase (ALT) >41 U/L (p=0.021), ferritin in the risk category (p<0.001), IL-6≥7 pg/mL (p<0.001), and D-dimer ≥500 ng/mL (p<0.001) were more likely to have severe COVID-19 (**Table 1**).

Based on the predefined criterion for model development, variables with p<0.25 were selected as candidate predictors for the subsequent multivariable analysis. These variables included age, hemoglobin, WBC, ALC, NLR, MLR, PLT, PLCR, MPV, prothrombin time, aPTT, AST, ALT, ferritin, IL-6, and D-dimer.

Table 1. Univariate analysis showing risk factors associated with severity of COVID-19 patients

Characteristics	Severe (n=78) f (%)	Non severe (n=62) f (%)	Odds ratio (95%CI)	p-value
Age				0.002*[a]
<65 years	52 (66.7)	56 (90.3)	Ref	
≥65 years	26 (33.3)	6 (9.7)	4.67 (1.78–12.24)	
Sex				1.000
Male	32 (41.0)	25 (40.3)	1.03 (0.52–2.03)	
Female	46 (59.0)	37 (59.7)	Ref	
Total comorbidities				n/a
None	0	42 (67.7)	Ref	
1	15 (19.2)	10 (16.1)	n/a	
>1	63 (80.8)	10 (16.1)	n/a	
Hemoglobin				0.007*[a]
Hb <10 g/dL	14 (17.9)	2 (3.2)	6.56 (1.43–30.09)	
Hb ≥10 g/dL	64 (82.1)	60 (96.8)	Ref	
White blood cells				<0.001*[a]
≥10,000/mm^3	57 (73.1)	12 (19.4)	11.31 (5.06–25.28)	
<10,000/mm^3	21 (26.9)	50 (80.6)	Ref	
Absolute lymphocyte count				<0.001*[a]
<1,500/mm^3	67 (85.9)	23 (37.1)	10.33 (4.55–23.45)	
≥1,500/mm^3	11 (14.1)	39 (62.9)	Ref	
Neutrophil lymphocyte ratio				<0.001*[a]
≥3.13	77 (98.7)	23 (37.1)	130.56 (16.99–1002.96)	
<3.13	1 (1.3)	39 (62.9)	Ref	
Mean monocyte lymphocyte ratio				<0.001*[a]
≥0.37	69 (88.5)	26 (41.9)	10.62 (4.49–25.05)	
<0.37	9 (11.5)	36 (58.1)	Ref	
Platelet				<0.001*[a]
<150,000/uL	19 (24.4)	1 (1.6)	19.64 (2.55–151.45)	
≥150,000/uL	59 (75.6)	61 (98.4)	Ref	
Platelet large cell ratio				<0.001*[a]
≥30%	52 (66.7)	11 (17.7)	9.27 (4.15–20.72)	
<30%	26 (33.3)	51 (82.3)	Ref	
Mean platelet volume				0.001*[a]
>10 fL	60 (76.9)	30 (48.4)	3.56 (172–7.34)	
8–10 fL	18 (23.1)	32 (51.6)	Ref	
Prothrombin time				0.006*[a]
≥13	12 (15.4)	1 (1.6)	11.09 (1.40–87.85)	
<13	66 (84.6)	61 (98.4)	Ref	

Characteristics	Severe (n=78)	Non severe (n=62)	Odds ratio (95%CI)	*p*-value
	f (%)	f (%)		
Activated partial thromboplastin time				<0.001*[a]
≥30	34 (43.6)	9 (14.5)	4.55 (1.97–10.50)	
<30	44 (56.4)	53 (85.5)	Ref	
Aspartate aminotransferase				<0.001*[a]
≤38 u/L	40 (51.3)	53 (85.5)	Ref	
>38 u/L	38 (48.7)	9 (14.5)	5.59 (2.43–12.89)	
Alanine aminotransferase				0.021*[a]
≤41 u/L	44 (56.4)	47 (75.8)	Ref	
>41 u/L	34 (43.6)	15 (24.2)	2.42 (1.16–5.04)	
Procalsitonin				n/a
≥2 ng/mL	30 (38.5)	0	n/a	
<2 ng/mL	48 (61.5)	62 (100.0)	Ref	
Ferritin				<0.001*[a]
Risk (man ≥434 ng/mL; woman ≥159 ng/mL)	74 (94.9)	26 (41.9)	25.62 (8.31–78.94)	
Unrisk (man <434 ng/mL; woman <159 ng/mL)	4 (5.1)	36 (58.1)	Ref	
Interleukin-6				<0.001*[a]
≥7 pg/mL	73 (93.6)	25 (40.3)	21.61 (7.65–61.04)	
<7 pg/mL	5 (6.4)	37 (59.7)	Ref	
D-dimer				<0.001*[a]
≥500 ng/mL	76 (97.4)	24 (38.7)	60.17 (13.50–268.07)	
<500 ng/dL	2 (2.6)	38 (61.3)	Ref	
C-reactive protein				n/a
≥5 mg/L	78 (100.0)	60 (96.8)	n/a	
<5 mg/L	0	2 (3.2)	Ref	

Ref: reference; n/a: not account
*Statistically significant at $p<0.05$
[a]Variable with $p<0.25$ in multivariate modelling

Multivariate analysis assessing factors associated with COVID-19 severity

Multivariable analysis identified five variables that were independently associated with COVID-19 severity (**Table 2**). Patients with WBC≥10,000/mm^3 had higher odds of severe disease compared with those with lower WBC levels (OR: 9.15; 95%CI: 1.51–55.27; p=0.016). Patients with ALC<1,500/mm^3 were also more likely to have severe COVID-19 (OR: 53.58; 95%CI: 4.97–578.14; p=0.001). In addition, PLCR≥30% was independently associated with severe disease (OR: 15.55; 95%CI: 1.47–164.45; p=0.023). Inflammatory and coagulation markers also remained significant in the multivariable model. IL-6≥7 pg/mL was associated with higher odds of severe COVID-19 (OR: 21.23; 95%CI: 2.46–183.17; p=0.05), while D-dimer≥500 ng/mL was also independently associated with severity (OR: 17.14; 95%CI: 1.21–243.24; p=0.036).

These findings indicate that WBC, ALC, PLCR, IL-6, and D-dimer were the most relevant independent predictors and were therefore included in the development of the COVID-19 severity scoring system.

Table 2. Multivariate analysis of candidate variable selection of scoring models for predicting the severity of COVID-19 patients

Variable	Beta coefficient	Standard error (SE)	Odds ratio (95%CI)	*p*-value
Age (≥65 years)	1.058	0.915	2.88 (0.48–17.31)	0.248
Hemoglobin (<10 g/dL)	0.675	1.329	1.96 (0.15–26.59)	0.612
White blood cell count (≥10,000/mm^3)	2.214	0.918	9.15 (1.51–55.27)	0.016*
Absolute lymphocyte count (<1,500/mm^3)	3.981	1.214	53.58 (4.97–578.14)	0.001*
Neutrophil lymphocyte ratio (≥3.13)	3.316	2.383	27.56 (0.26–2941.34)	0.164
Mean monocyte lymphocyte ratio (≥0.37)	-2.147	1.436	0.12 (0.007–1.95)	0.135
Platelet count (<150,000/uL)	1.341	1.311	3.82 (0.29–49.93)	0.306
Platelet large cell ratio (≥30%)	2.744	1.203	15.55 (1.47–164.45)	0.023*
Mean platelet volume(>10 fL)	-1.025	0.996	0.36 (0.05–2.53)	0.303
Prothrombin time (≥13)	2.271	3.778	9.69 (0.06–15913.70)	0.548
Activated partial thromboplastin time (≥30)	-0.211	0.823	0.81 (0.16–4.07)	0.798
Aspartate aminotransferase (>38 u/L)	-0.822	0.844	0.44 (0.08–2.30)	0.330
Alanine aminotransferase (>41 u/L)	-1.040	0.928	0.35 (0.06–2.18)	0.263

Variable	Beta coefficient	Standard error (SE)	Odds ratio (95%CI)	*p*-value
Ferritin (risk: man, ≥434 ng/mL; woman ≥159 ng/mL))	-0.174	1.742	0.84 (0.03–25.52)	0.920
Interleukin-6 (≥7 pg/mL)	3.055	1.100	21.23 (2.46–183.17)	0.05*
D-dimer (≥500 ng/mL)	2.841	1.354	17.14 (1.21–243.24)	0.036*

*Statistically significant at $p<0.05$

Development of the COVID-19 severity scoring system

The COVID-19 severity scoring system was developed based on the results of the Youden index analysis using variables that remained significant in the multivariable logistic regression analysis, namely WBC, ALC, PLCR, IL-6, and D-dimer (**Table 3**). Score assignment was determined by comparing the beta coefficient with its standard error for each predictor. Based on this approach, WBC≥10,000/mm^3 was assigned 1 point, ALC<1,500/mm^3 was assigned 2 points, PLCR≥30% was assigned 1 point, IL-6≥7 pg/mL was assigned 1 point, and D-dimer≥500 ng/mL was assigned 1 point. The maximum total score was 6.

Among the included predictors, ALC had the highest weight in the score, indicating a stronger contribution to predicting severe COVID-19 than the other variables. In contrast, WBC, PLCR, IL-6, and D-dimer each contributed 1 point to the final model (**Table 3**). These variables were subsequently combined into a composite scoring system to classify patients according to the risk of severe COVID-19.

Table 3. Scoring in the prediction of the severity of COVID-19 patients

Variable	Beta coefficient (B)	Standard error(SE)	B/S.E	B/S.E/2.22	Score
White blood cell count (≥10,000/mm^3)	2.12	0.72	2.94	1.33	1
absolute lymphocyte count (<1,500/mm^3)	3.27	0.87	3.76	1.69	2
Platelet large cell ratio (≥30%)	1.53	0.69	2.22	1.00	1
Interleukin-6 (≥7 pg/mL)	2.73	0.85	3.21	1.45	1
D-dimer (≥500 ng/mL)	3.14	1.13	2.78	1.25	1
Total score					6

Diagnostic performance of the COVID-19 severity scoring system

The diagnostic performance of the COVID-19 severity scoring system was evaluated using receiver operating characteristic (ROC) curve analysis, while the optimal cut-off point was determined using the Youden index (**Table 4** and **Figure 1**). The analysis showed that a total score of 3.5 was the optimal threshold for differentiating severe from non-severe COVID-19. At this cut-off point, the scoring system had a sensitivity of 96.15% and a specificity of 79.03%.

These findings indicate that the scoring system had high sensitivity for identifying patients with severe COVID-19, with acceptable specificity for distinguishing them from non-severe cases. Patients with a total score of ≥3.5 were classified as having severe COVID-19, whereas those with a total score of <3.5 were classified as having non-severe COVID-19.

Table 4. Selection of cut-off points determined by the optimal cut-off point at the intersection of the sensitivity and specificity lines in the Youden index curve in determining the total score for predicting the severity of COVID-19 patients

Potential cut-off point	Sensitivity	1 – specificity	Sensitivity	Specificity
-1	1	1	1	0
0.5	1	0.741935484	1	0.258065
1.5	1	0.564516129	1	0.435484
2.5	1	0.338709677	1	0.66129
3.5	0.961538	0.209677419	0.961538	0.790323
4.5	0.692308	0.048387097	0.692308	0.951613
5.5	0.371795	0	0.371795	1
7	0	0	0	1

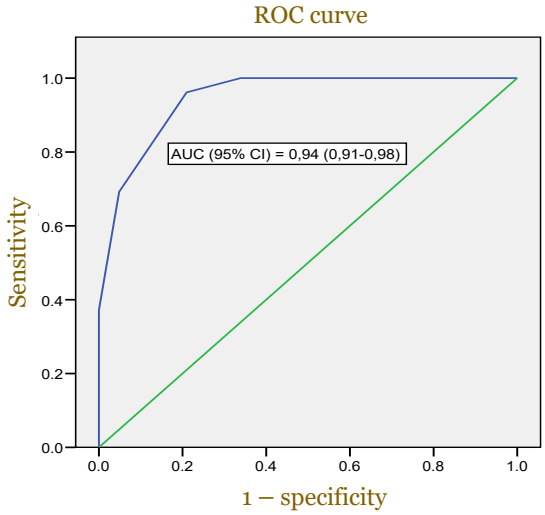

Figure 1. Accuracy of determining the total score to predict the severity of COVID-19 patients.

Discussion

A total of 140 patients with confirmed COVID-19 were included in the analysis and followed for 2–3 weeks to evaluate factors associated with disease severity and to develop a scoring system to predict severe COVID-19. The findings of this study showed that WBC, ALC, PLCR, IL-6, and D-dimer were significant predictors of COVID-19 severity. Based on these parameters, a novel scoring system was developed to help identify patients at higher risk of severe disease. This model may support early risk stratification and timely clinical decision-making in hospitalized patients with COVID-19.

In the present study, WBC≥10,000/mm^3 and ALC<1,500/mm^3 were associated with severe COVID-19 and were included in the final scoring system. A previous study reported that hospitalized patients with confirmed COVID-19 had significantly higher WBC values than outpatients, suggesting that leukocytosis may indicate a higher risk of clinical deterioration [15]. During the early stage of infection, leukocyte and lymphocyte counts may remain normal or slightly decreased. However, disease progression is often accompanied by an exaggerated inflammatory response and cytokine release, which can induce lymphocyte apoptosis and lead to lymphopenia [4,5]. Lymphocytes may also be directly affected by SARS-CoV-2 through angiotensin-converting enzyme 2 receptor-mediated mechanisms, contributing further to lymphocyte depletion [4,5]. In addition, damage to lymphoid organs, such as the spleen and lymph nodes, may impair lymphocyte turnover and worsen lymphopenia. A previous study involving 201 patients with COVID-19 pneumonia showed that lymphopenia was associated with the development of acute respiratory distress syndrome and death [5]. These findings support the role of leukocytosis and lymphopenia as markers of severe systemic inflammation and immune dysregulation in COVID-19.

This study also found that PLCR≥30% was independently associated with severe COVID-19. Platelet activation has been recognized as an important component of COVID-19 pathophysiology. Inflammatory cytokines and endothelial injury may increase platelet consumption and thrombus formation, leading to the release of larger and more reactive platelets into the circulation [16]. A previous study showed that SARS-CoV-2 can directly activate platelets through ACE2, thereby enhancing thrombosis and platelet-mediated inflammatory responses [17]. Another study reported that patients with COVID-19 had hyperreactive platelets, with increased platelet factor 4 and P-selectin expression [18]. PLCR reflects the proportion of large circulating platelets and may therefore indicate platelet activation and increased platelet turnover [19]. Larger platelets have greater prothrombotic potential, higher metabolic activity, and stronger hemostatic function than smaller platelets [19,20,21]. Thus, the association between elevated PLCR and severe COVID-19 observed in this study is biologically plausible and consistent with previous evidence.

IL-6 was another parameter included in the final scoring system, with IL-6≥7 pg/mL associated with severe disease. IL-6 is a pleiotropic cytokine that plays a central role in

inflammation, immune regulation, and the acute-phase response [22,23]. Elevated IL-6 levels have been consistently reported in patients with severe COVID-19 and are considered an important feature of cytokine storm syndrome [22]. Elevated IL-6 levels were more common among critically ill than non-critically ill patients, and IL-6 was an independent predictor of disease progression [22]. The present finding further supports the clinical utility of IL-6 as a marker of hyperinflammation and disease severity in COVID-19.

D-dimer was also identified as an independent predictor of severe COVID-19 in this study. Elevated D-dimer levels reflect activation of coagulation, fibrin formation, and fibrinolysis, and are widely recognized as markers of hypercoagulability [24,25,26]. In COVID-19, an excessive inflammatory response may trigger coagulation abnormalities through endothelial dysfunction, thrombin generation, and impaired anticoagulant pathways [27]. Hypoxia in severe disease may further promote thrombosis through increased blood viscosity and activation of hypoxia-related signaling pathways [27]. Previous studies have shown that elevated D-dimer levels are associated with poor prognosis and mortality in patients with COVID-19 [24,27]. A previous study reported that D-dimer levels above 1,000 ng/mL were associated with poor outcomes [28], while another showed that admission D-dimer levels above 2,000 ng/mL could effectively predict in-hospital mortality [27]. Therefore, the inclusion of D-dimer in the present scoring system is supported by both pathophysiological mechanisms and prior clinical evidence.

Taken together, these findings indicate that the final scoring model incorporates markers representing several important pathways involved in severe COVID-19, including systemic inflammation, immune dysfunction, platelet activation, and coagulation abnormalities. Because these parameters are routinely available or measurable in hospital settings, the proposed scoring system may offer practical value for early identification of patients at risk of severe disease.

This study has several limitations. First, it was conducted at a single national referral hospital, which may limit the generalizability of the findings to other healthcare settings or populations. Second, the sample size was relatively limited, particularly for broader model validation. Third, although the scoring system showed high sensitivity and acceptable specificity, external validation in independent cohorts is still needed before wider clinical application. Future studies are needed to validate this scoring model in larger and more diverse populations and to assess its performance across different clinical settings.

Conclusion

WBC, ALC, PLCR, IL-6, and D-dimer are significant predictors of COVID-19 severity. Based on these parameters, a novel scoring system was developed to predict severe COVID-19 in hospitalized patients. Using a cut-off score of 3.5, the scoring system showed a sensitivity of 96.15% and a specificity of 79.03% for differentiating severe from non-severe COVID-19. A total score of ≥3.5 indicated severe COVID-19, whereas a score of <3.5 indicated non-severe disease. This scoring system may support early risk stratification and clinical decision-making in hospital settings.

Ethics approval

The research has attained ethical approval by the Health Research Ethics Committee, Dr. M. Djamil Hospital, Padang, Indonesia (Ethical Approval No: 170/KEPK/2021).

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Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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