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Routine Biomarkers for COVID-19 Mortality Prediction in Low-Resource Settings

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Abstract

COVID-19 has placed a heavy burden on healthcare systems, especially in resource-limited settings where simple and affordable tools are needed to identify patients at high risk of death. This study aimed to evaluate routine laboratory biomarkers associated with mortality among hospitalized COVID-19 patients. A retrospective cohort study was conducted using medical records of 199 adult patients with RT-PCR-confirmed COVID-19 who were admitted to Sultan Agung Islamic Hospital, Semarang, Indonesia, between December 2020 and August 2021. Patients were selected using consecutive sampling. Hematological, inflammatory, coagulation, and virological parameters measured at admission were analyzed. Differences between survivors and non-survivors were assessed using Chi-square and Mann–Whitney tests, followed by logistic regression analysis to identify independent predictors of mortality. Of the 199 patients, 156 (78.4%) survived. and 43 (21.6%) died. Non-survivors had significantly higher neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelet-to-lymphocyte ratio, C-reactive protein, and D-dimer levels, while lymphocyte, monocyte, and basophil counts were significantly lower ($p<0.05$). Lymphopenia was the strongest independent predictor of mortality (aOR=4.263; 95%CI=1.661–10.945; p=0.003). Routine laboratory parameters, particularly lymphocyte count, may help identify high-risk patients and support early clinical decision-making in resource-limited hospitals.

Introduction

COVID-19 is a contagious disease transmitted by the SARS-CoV-2 virus that spread in late 2019 quickly around the world, infecting millions and causing substantial mortality. Since its emergence in late 2019, the disease has affected millions of people and placed unprecedented pressure on hospitals, particularly during periods of high transmission (Arini *et al*., 2023; WHO Coronavirus (COVID19) Dashboard, 2022). Clinical manifestations may be asymptomatic or mild symptoms to critical *pneumonia*, *ARDS* (*acute respiratory distress syndrome*), organ failure, and death (C. Huang *et al*., 2020). Hospitalization duration in COVID-19 was almost equally divided between stays of ≤2 weeks (54.20%) and >2 weeks (45.80%). Hospitalized COVID-19 patients with severe disease frequently experience prolonged hospital stays and higher mortality rates, highlighting the need for simple laboratory biomarkers that can support early risk stratification and resource allocation in healthcare settings (Rees *et al*., 2020; Zhou *et al*., 2020). LMICs (Low- and middle-income countries), including Indonesia, have been

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disproportionately impacted due to limited healthcare resources and uneven access to diagnostics (Yadav *et al*., 2021). The COVID-19 pandemic affected not only clinical outcomes but also social and public health systems, highlighting the need for effective strategies to identify patients at risk of severe disease (Nugroho *et al*., 2021).

Severe COVID-19 involves complex pathological processes. The virus enters host cells and triggers immune activation that can cause organ damage (Varga *et al*., 2020). These processes accelerate clinical deterioration and increase mortality risk. Furthermore, many survivors experience long-term or delayed complications, including persistent respiratory and cardiovascular problems, which add to the overall disease burden (Carfì *et al*., 2020). COVID-19 diagnosis primarily relies on *RT-PCR* (*reverse transcriptase–polymerase chain reaction*), which estimates viral load by the cycle threshold (CT) value (Corman *et al*., 2020). However, during peak pandemic waves in LMICs, RT-PCR testing was constrained by reagent shortages, limited laboratory networks concentrated in major cities, and prolonged turnaround times (Tan *et al*., 2020). These limitations often delay diagnosis and clinical decision-making, highlighting the need for complementary tools to assess disease severity and predict outcomes early. In this context, simple and widely available biomarkers that can be measured by using routine laboratory tests have emerged as valuable tools for early risk stratification at hospital admission (Eryando & Afrizal, 2024; Lagunas-Rangel, 2020). Several biomarkers, including *NLR* (*neutrophil-to-lymphocyte ratio*), *CRP* (*C-reactive protein*), and *D-dimer,* have been consistently correlated to the COVID-19 severity and mortality (Zeng *et al*., 2020). Elevated levels at admission have been shown to predict poorer outcomes, and combining multiple biomarkers can enhance prognostic accuracy compared with single-marker assessment (Khedar *et al*., 2022). Despite extensive international evidence, data from LMICs remain limited. Few studies have simultaneously evaluated multiple biomarkers in one cohort, and most findings are derived from tertiary hospitals with advanced laboratory capacity, which may not represent typical resource-limited health facilities (Fernandez-Carballo *et al*., 2025).

During the most critical phases of the pandemic, real-world data collection was often limited, and hospitals were overwhelmed, contributing to higher mortality (Gmanyami *et al*., 2024). Consequently, comprehensive information on biomarker patterns, disease progression, and clinical outcomes in resource-limited settings is scarce. The pandemic highlighted the importance of preparedness and evidence-based interventions to strengthen health system responses to future outbreaks (Priyantini *et al*., 2025; Simanjuntak & Simanjuntak, 2023; Sulistyawati & Haifa, 2025). Establishing such data not only informs clinical decision-making but also provides a historical baseline reference for future research, health system planning, and outbreak preparedness. Considering those situations, this study evaluated the effectiveness of potential biomarkers correlated to the mortality among COVID-19 patients in a resource-limited Indonesian hospital. In addition, predictors of survival time were analyzed to provide actionable evidence for early risk stratification. By focusing on the peak pandemic period and routinely available biomarkers, this study aims to contribute both practical clinical insights and a historical benchmark for LMIC healthcare systems.

Method

This analysis was a retrospective cohort analysis at Sultan Agung Islamic Hospital, Semarang, Indonesia (latitude 6°57'20.0" S; longitude 110°27'41.7" E). The hospital is classified as a Class B facility, offering both specialty and selected subspecialty services, serving as the main teaching hospital of Universitas Islam Sultan Agung and functioning as a referral center for COVID-19 patients. Semarang, the capital of Central Java province, has a densely populated area of approximately 373.8 km² with over 1.7 million residents, and has reported among the highest COVID-19 case counts and mortality rates in Indonesia (Wulandari *et al*., 2022). Patients included in this study were adults (≥18 years) with confirmed COVID-19, admitted in December 2020 and August 2021. Consecutive sampling

was employed to extract demographic and laboratory biomarker data from medical records at the time of hospital admission. Inclusion criteria required a positive SARS-CoV-2 result by RdRP (RNA-dependent RNA polymerase) RT-PCR. Patients were excluded if they had conditions likely to confound outcomes, including pregnancy, malignancy, autoimmune disorders, immunodeficiency, burns, hematological diseases, recent surgery, or prior treatment at another hospital. The study population comprised 199 patients, including 107 males (55.1% recovered, 48.8% deceased) and 92 females (44.9% recovered, 51.2% deceased).

Laboratory analyses were performed upon admission to evaluate hematological, biochemical, and molecular markers documented in medical records. Ratios such as NLR, ELR (eosinophil-to-lymphocyte), MLR (monocyte-to-lymphocyte), and PLR (platelet-to-lymphocyte) were measured using fluorescence flow cytometry (FFC). Red blood cell counts were determined by the electronic impedance method, while hemoglobin concentration was measured using a cyanide-free assay on the XN-1000 B3 hematology analyzer (Sysmex Corp., Kobe, Japan). Nasopharyngeal swab samples were analyzed by RT-PCR using the NGenePlex™ nCoV kit, with cycle threshold (CT) values measured on the Roche LightCycler® 480 system (Roche Applied Science, Basel, Switzerland). CRP was quantified applying a latex turbidimetric immunoassay (LTIA) on the TMS 50i Superior automated analyzer (Tokyo Boeki Medisys Inc., Japan) with Nanopia CRP reagents (Sekisui Medical Co., Ltd., Tokyo, Japan). D-dimer levels were measured using the Sysmex CA-660 automated coagulation analyzer (Sysmex Corp., Kobe, Japan).

Laboratory and clinical data were extracted from medical records between 12 and 19 December 2022. Treatments were provided according to the COVID-19 Management Guidelines, 4th Edition, 2022 (Araya *et al*., 2021). Data analysis was performed using IBM SPSS v27.0 (IBM Corp., NY, USA), with $p<0.05$ considered statistically significant. Continuous variables not following normal distribution were compared applying the Mann–Whitney U test, while categorical variables were analyzed with the chi-square test. ROC (Receiver operating characteristic) curves were generated to find out optimal cut-off values for mortality prediction. Variables significantly associated with mortality were further studied by binary logistic regression. The Kaplan–Meier method was used as a survival analysis to estimate time-to-event outcomes for patients. The analysis protocol was accepted by the RSI (Islamic Hospital) Sultan Agung Semarang's Ethics Committee (Letter No. 150/KEPK-RSISA/IX/2022). All data were sourced from anonymized medical records, with access limited to the research team. All procedures were conducted in strict compliance with the Declaration of Helsinki and relevant ethical standards.

Result and Discussion

Initially, 386 patients who had COVID-19 confirmed by RT-PCR were assessed. Among these, 187 patients were excluded due to conditions that could introduce confounding factors, including pregnancy, malignancy, autoimmune or immunodeficiency disorders, burns, hematological diseases, recent surgery, or prior treatment at other hospitals. Consequently, 199 patients met the inclusion criteria for analysis. Of these, 156 patients (78.4%) recovered, whereas 43 patients (21.6%) died during hospitalization (FIGURE 1).

The mean age of deceased patients (50.33 ± 1.34 years) was significantly higher than that of recovered patients (45.10 ± 0.85 years; $p = 0.005$). The duration of hospitalization also differed markedly, with recovered patients averaging 13.29 ± 5.31 days compared to 7.37 ± 4.80 days in deceased patients ($p < 0.001$). No significant differences were obtained between groups of gender ($p = 0.464$) or common symptoms (cough, fever, anosmia, odynophagia, nausea, and vomiting) ($p > 0.05$). However, dyspnea ($p < 0.001$) and diarrhea ($p = 0.048$) were more frequent among patients who died. Laboratory analyses revealed that deceased patients had significantly higher neutrophil percentages (80.60 ± 7.69%), NLR (11.24 ± 17.61), MLR (0.61 ± 0.42), PLR (308.99 ± 244.88), CT values (17.25 ± 4.33), CRP (107.54 ± 82.29 mg/L), and D-dimer

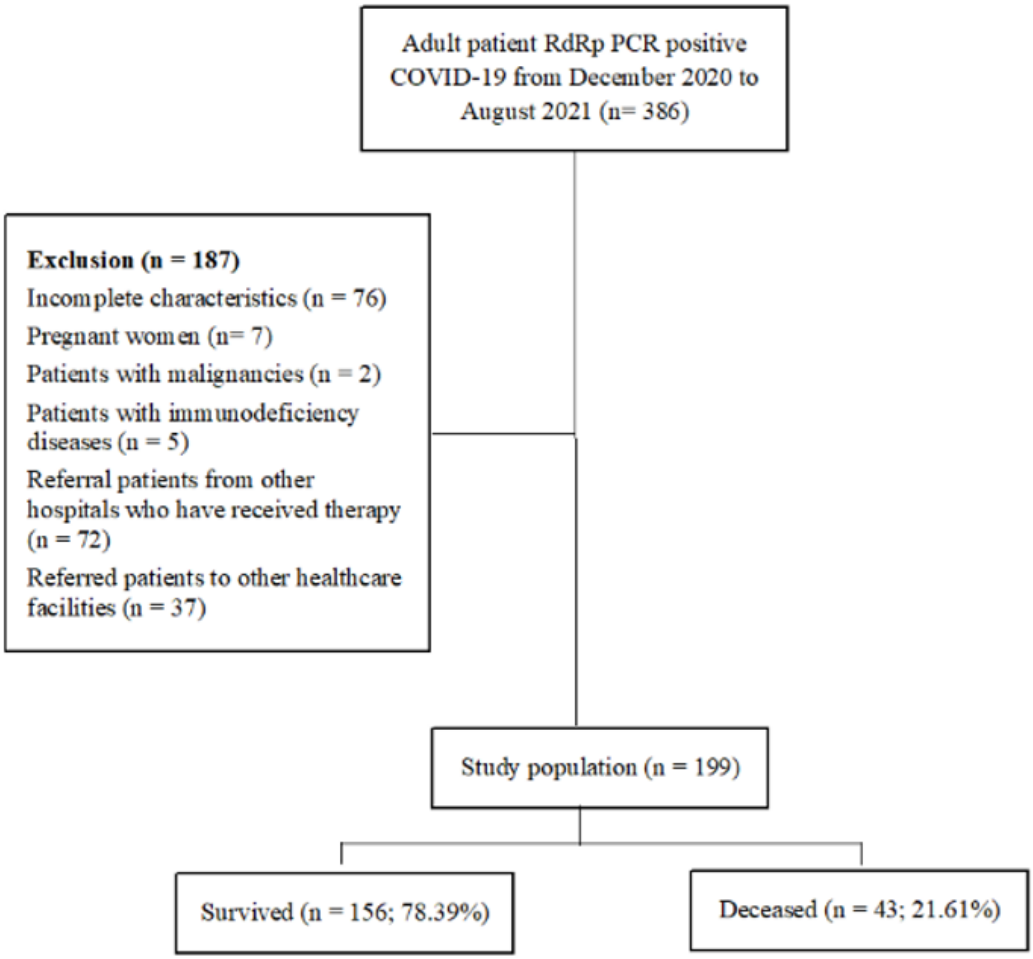

FIGURE 1. Flowchart of Patient Selection Process and Clinical Outcomes

TABLE 1. Demographic Characteristics and Biomarkers of COVID-19 Patients at Sultan Agung Islamic Hospital, Semarang, Indonesia between December 2020 and August 2021.

Characteristics	**Recovered (n = 156)**	**Deceased (n = 43)**	**P value**
Age	45.10	50.33	
18-59	152 (97.4%)	41 (95.3%)	p = 0.479 [a]
≥ 60	4 (2.6%)	2 (4.7%)	
Length of Hospitalization (days)	13.29	7.37	p < 0.001 [b]
Gender			p = 0.464[a]
Female (n=92)	70 (44.9%)	22 (51.2%)	
Male (n=107)	86 (55.1%)	21 (48.8%)	
Fever			p = 0.733[a]
Yes	112 (71.8%)	32 (74.4%)	
No	44 (28.2%)	11 (25.6%)	
Cough			p = 0.48 [a]
Yes	127 (81.4%)	37 (86.0%)	

Characteristics	Recovered (n = 156)	Deceased (n = 43)	P value
No	29 (18.6%)	6 (14%)	
Dyspnea			p <0.001 [a]
Yes	73 (46.8%)	33 (76.7%)	
No	83 (53.2%)	10 (23.3%)	
Diarrhea			p = 0.048 [a]
Yes	45 (28.8%)	6 (14.0%)	
No	111 (71.2%)	37 (86.0%)	
Nausea or Vomiting			p = 0.881 [a]
Yes	38 (24.4%)	10 (23.3%)	
No	118 (75.6%)	33 (76.7%)	
Anosmia			p = 0.593 [a]
Yes	15 (9.6%)	3 (7.0%)	
No	141 (90.4%)	40 (93.0%)	
Painful swallowing			p = 0.601 [a]
Yes	129 (82.7%)	37 (86.0%)	
No	27 (17.3%)	6 (14.0%)	
Comorbidities			p = 0.601 [a]
Yes	127 (81.4%)	39 (90.7%)	
Hypertension (HT)	46 (29.5%)	6 (14.0%)	
Diabetes Mellitus (DM)	40 (25.6%)	13 (30.2%)	
HT and DM	27 (17.3%)	9 (20.9%)	
Asthma	1 (1.6%)	1 (2.3%)	
Others (Kidney, heart)	13 (8.3%)	10 (23.3%)	
None	29 (18.6%)	4 (9.3%)	
Radiology results			p = 0.003 [a]
Bronchopneumonia	128 (82.1%)	43 (100%)	
Not Bronchopneumonia	28 (17.9%)	-	
Hb (gr/dL)	13.42 ± 2.13	13.31± 2.29	p = 0.644 [b]
Ht (%)	39.60 ± 5.89	38.96 ± 6.49	p = 0.365 [b]
Erythrocytes (/µL)	4.79 ± 0.76	4.83 ± 0.81	p = 0.635 [b]
Leukocytes (x10^3/µL)	8.72 ± 5.17	9.72 ± 4.76	p = 0.051 [b]
Eosinophils (%)	0.53 ± 1.32	0.28 ± 0.60	p = 0.200 [b]
Basophils (%)	0.23 ± 0.15	0.16 ± 0.14	p = 0.004 [b]
Neutrophils (%)	71.32 ± 12.70	80.60 ± 7.69	p < 0.001 [b]
Lymphocytes (%)	19.28 ± 10.52	11.66 ± 6.68	p < 0.001 [b]
Monocytes (%)	7.55 ± 3.59	5.58 ± 2.52	p = 0.001 [b]
Platelets (x10^3/µL)	243.90 ± 114.92	251.23 ± 147.18	p = 0.416 [b]
NLR	5.57 ± 4.85	11.24 ± 17.61	p < 0.001 [b]
MLR	0.47 ± 0.29	0.61 ± 0.42	p = 0.031 [b]
ELR	0.02 ± 0.06	0.03 ± 0.07	p = 0.552 [b]

Characteristics	Recovered (n = 156)	Deceased (n = 43)	P value
PLR	204.09 ± 131.91	308.99 ± 244.88	p = 0.001 [b]
ALC (/µL)	1,491.53 ± 1,445.48	996.27 ± 470.86	p < 0.001 [b]
D-dimer (mg/L)	2.46 ± 4.85	13.56 ± 35.39	p < 0.001 [b]
CRP (mg/L)	68.74 ± 88.50	107.54 ± 82.29	p < 0.001 [b]
CT-Value	23.38 ± 5.17	17.25 ± 4.33	p < 0.001 [b]

[a] = chi-square, [b] Mann Whitney, Ht= Haematocrit, NLR= Neutrophils Lymphocyte Ratio, PLR= Platelets Lymphocyte Ratio, MLR= Monocyte Lymphocyte Ratio, ELR= Eosinophil Lymphocyte Ratio, ALC= Absolute Lymphocyte Count, CRP= C-Reactive Protein, CT-Value= Cycle Threshold Value
Source: Primary Data, 2021

TABLE 2. Cut-off Point for Hematology-Biochemistry Parameter Test Results

Markers	Cut Off Point	Sensitivity	Specificity	AUC	p-value	95% ci*
Hb (gr/dL)*	13.75	58.10%	53.20%	0.523	0.644	0.425 – 0.621
Ht (%)*	39.85	55.80%	56.40%	0.545	0.365	0.448 – 0.643
Erythrocytes (x10^6/µL)**	4.85	55.80%	52.60%	0.524	0.635	0.427 – 0.621
Leukocytes (x10^3/µL)**	7.52	60.50%	53.80%	0.597	0.051	0.507 – 0.688
Eosinophils (%)*	0.05	58.10%	50.60%	0.559	0.234	0.466 – 0.653
Basophils (%)*	0.15	53.50%	73.10%	0.642	0.004	0.549 – 0.734
Neutrophils (%)**	77.90	69.80%	66.70%	0.728	<0.001	0.648 – 0.808
Lymphocytes (%)*	15.35	76.75%	60.30%	0.736	<0.001	0.657 – 0.816
Monocytes (%)*	6.05	62.80%	60.30%	0.660	0.001	0.572 – 0.747
Platelets (x10^3/µL)*	201.50	51.20%	60.30%	0.541	0.416	0.440 – 0.641
NLR**	4.85	76.70%	58.30%	0.730	<0.001	0.651 – 0.808
MLR**	0.42	58.10%	53.80%	0.607	0.031	0.510 – 0.705
ELR*	0.0029	60.50%	50.60%	0.528	0.580	0.427 – 0.628
PLR**	177.03	69.80%	55.10%	0.671	0.001	0.576 – 0.765
ALC (/µL)*	1145	72.10%	60.30%	0.702	<0.001	0.614 – 0.791
D-dimer (mg/L)**	0.995	74.40%	55.10%	0.680	<0.001	0.594 – 0.766
CRP (mg/L)**	40.55	81.40%	50.60%	0.687	<0.001	0.602 – 0.772
CT-Value*	21.96	76.70%	54.50%	0.837	<0.001	0.754 – 0.920

*= positive if the value is less than or equal to
**= positive if the value is more than or equal to
Ht= haematocrit, NLR= neutrophils lymphocyte ratio, PLR= platelets lymphocyte ratio, MLRr= monocyte lymphocyte ratio, ELR= eosinophil lymphocyte ratio, ALC= absolute lymphocyte count, CRP= c-reactive protein, CT-Value= cycle threshold value

(13.56 ± 35.39 µg/mL) compared to recovered patients, whose corresponding values were 71.32 ± 12.70%, 5.57 ± 4.85, 0.47 ± 0.29, 204.09 ± 131.91, 23.38 ± 5.17, 68.74 ± 88.50 mg/L, and 2.46 ± 4.85 µg/mL, respectively. Conversely, basophil, lymphocyte, monocyte percentages, and absolute lymphocyte count (ALC) were notably lower in deceased patients ($p < 0.05$) (TABLE 1).

Elevated levels of erythrocytes, leukocytes, neutrophils, NLR, MLR, PLR, CRP, and D-dimer were correlated to increased mortality risk, whereas lower levels of hemoglobin, hematocrit, eosinophils, basophils, lymphocytes, monocytes, platelets, ELR, ALC, and CT values were also indicative of higher risk. Among these, basophils, neutrophils, monocytes, lymphocytes, NLR, MLR, PLR, ALC, D-dimer, CRP, and CT values emerged as potential predictors of mortality (TABLE 2).

Multivariate logistic regression identified lymphocytes, CT value, basophils, platelets, and D-dimer as independent predictors of mortality. Adjusted odds ratios (aOR) were 4.263 (95% CI: 1.661–10.945, $p = 0.003$) for lymphocytes, 3.913 (95% CI: 1.666–9.193, $p = 0.002$) for CT value, 3.058 (95% CI: 1.368–6.837, $p = 0.006$) for basophils, 3.030 (95% CI: 1.269–7.235, $p = 0.013$) for platelets, and 2.816 (95% CI: 1.147–6.910, $p = 0.024$) for D-dimer. Lymphocyte count was the most significant determinant of mortality (TABLE 3). Kaplan–Meier analysis found the mean survival time was 24.92 days for recovered and 19.75 days for deceased patients (FIGURE 2).

COVID-19 remains a global health emergency, as the virus mutates and produces new variants, thereby maintaining its potential

TABLE 3. Multivariate Test on Selected Variables

Variables	aOR	95% CI	P value
Lymphocyte (%)	4.263	1.661 – 10.945	p = 0.003 [a]
CT-Value	3.913	1.666 – 9.193	p = 0.002 [a]
Basophil (%)	3.058	1.368 – 6.837	p = 0.006 [a]
Platelets ($X10^3$/ML)	3.030	1.269 – 7.235	p = 0.013 [a]
D-dimer (mg/L)	2.816	1.147 – 6.910	p = 0.024 [a]

[a]= binary logistic regression test, CT-Value= Cycle Threshold Value

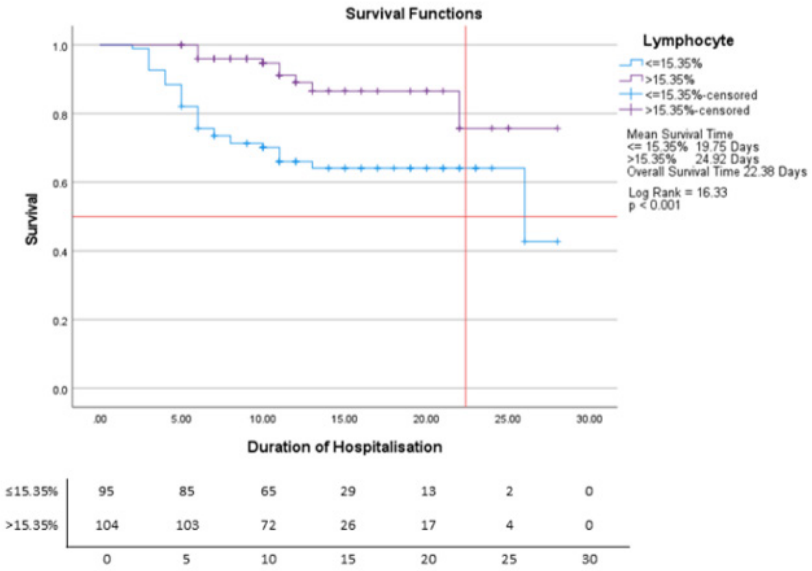

FIGURE 2. Kaplan–Meier survival curves of COVID-19 patients categorized by clinical outcomes.

for high transmissibility and severe disease. This study, involving 199 hospitalized patients at RSI Sultan Agung, Semarang, evaluated hematological, molecular, and biochemical parameters measured at admission, and identified several independent predictors of in-hospital mortality. The findings offer a pragmatic basis for early prognostic assessment and may inform guidelines tailored to resource-limited settings.

One of the most consistent findings in this study is that low lymphocyte count (lymphopenia) was independently associated with mortality (Michels *et al*., 2024). Patients who died had significantly lower lymphocyte counts than survivors. This result aligns with broader evidence: a comprehensive meta-analysis concluded that lymphopenia is significantly more common in severe or fatal COVID-19 cases (risk ratio. SARS–CoV–2–induced immune dysregulation may trigger a cascade of inflammatory cytokines, which result in apoptosis of Tlymphocytes (Araya *et al*., 2021; I. Huang & Pranata, 2020). This immunologic collapse may facilitate persistent viral replication, excessive inflammation, and organ damage (Shen *et al*., 2021). As lymphocytes play a central role in cellular immunity, their depletion compromises immunological defenses and may predispose patients to severe disease and death (Delshad *et al*., 2021). Several biological mechanisms may explain this association. SARS-CoV-2 infection can induce profound immune dysregulation characterized by excessive production of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and other mediators involved in cytokine storm syndrome. This hyperinflammatory response contributes to apoptosis and functional exhaustion of T lymphocytes, resulting in a marked reduction in circulating lymphocyte counts. In addition, lymphoid organ damage, impaired lymphopoiesis, and redistribution of lymphocytes from peripheral blood to infected tissues have also been proposed as contributing factors to COVID-19-associated lymphopenia. Our analysis supports the role of lymphopenia as a robust prognostic indicator, especially in settings lacking access to advanced immunophenotyping or cytokine assays (Diao *et al*., 2020). These findings also have important public health implications, as routine lymphocyte assessment may serve as a practical tool for identifying high-risk patients and optimizing healthcare resources in low- and middle-income settings, supporting evidence-based strategies for reducing COVID-19 mortality (Wu *et al*., 2024).

In this cohort, low RTPCR cycle threshold (CT) values targeting the RdRp gene were independently associated with increased mortality (Fajnzylber *et al*., 2020). Deceased patients had significantly lower CT values compared to survivors. Lower CT values commonly show greater viral loads, which may correlate with more aggressive viral replication, greater cellular injury, and a stronger inflammatory response (Abbasi *et al*., 2022). CT value is influenced by pre-analytical factors (sampling quality, timing, swab type), and interpretation must consider the clinical context (Aluru *et al*., 2021). Nevertheless, in combination with hematological and biochemical markers, the CT value can enhance prognostic assessment. In resource-limited settings where quantitative viral load testing or repeated viral kinetics are not feasible, the CT value readily available from standard RTPCR may function as a useful early marker to identify at-risk patients for severe disease or death (Aluru *et al*., 2021). Furthermore, the use of CT value as part of routine admission assessment may support early risk stratification and timely clinical decision-making, particularly in healthcare settings with limited resources, where rapid identification of high-risk patients is essential(Pertiwi *et al*., 2023).

Although this study identified total neutrophil percentage, NLR, MLR, and PLR differences between survivors and non-survivors, the multivariate analysis did not retain all of them as independent predictors. Still, their elevation in the deceased group reflects underlying inflammation and immune imbalance. Consistently observed in individuals with progressive COVID-19, the combination of neutrophilia and lymphopenia is recognized as a hallmark of immunopathology. Increased NLR reflects a shift toward innate immune activation and has been linked to poor outcomes (Jafarzadeh *et*

al., 2020). A retrospective observational study found that high NLR combined with elevated D-dimer significantly increased death risk in severe cases of COVID-19 (Murdaca *et al*., 2021). Based on data, elevated neutrophils (or NLR) with lymphopenia indicate immune dysregulation, leading to hyperinflammation, coagulopathy, and multi-organ failure (Chen *et al*., 2020; Sun *et al*., 2021). While NLR or neutrophil percentage alone may not always emerge as independent predictors, their evaluation alongside lymphocyte count, platelet count, D-dimer, and other markers strengthens the overall prognostic profile, especially to anticipate inflammatory or thrombotic complications (Song *et al*., 2021). These findings have important public health implications, as readily available laboratory markers may help identify patients at higher risk of death, support early intervention, and improve the use of healthcare resources, particularly in resource-limited settings (Wu *et al*., 2024).

This study found thrombocytopenia (low platelet count) to be significantly associated with mortality (aOR = 3.030; p = 0.013), consistent with the lower platelet counts observed in deceased patients. This aligns with aggregated data: a recent systematic review and meta-analysis demonstrated that non-survivors had significantly lower platelet counts than survivors, along with higher D-dimer and abnormal coagulation parameters (INR). In COVID-19, thrombocytopenia may result from multiple mechanisms: Platelet consumption due to widespread endothelial injury and microthrombus formation. Bone marrow suppression or direct viral effects on megakaryocytes (Boccatonda *et al*., 2022; Gheiasi *et al*., 2024). Immune-mediated destruction of platelets, or increased clearance due to disseminated intravascular coagulation (DIC) or platelet aggregation in microthrombi. Reduced platelet count may thus reflect ongoing coagulopathy, endothelial dysfunction, and systemic inflammation, all factors contributing to poor prognosis. Platelet count, readily available via routine CBC, offers a practical prognostic tool(Rossaint *et al*., 2018; Zhao *et al*., 2020). In conjunction with D-dimer and other markers, thrombocytopenia at admission should prompt careful monitoring for thrombotic or bleeding complications, early anticoagulation examination, and prioritization for supportive care. Therefore, routine platelet count assessment may serve as a simple and cost-effective tool for early identification of patients at higher risk of adverse outcomes, particularly in healthcare settings with limited resources (Boccatonda *et al*., 2022).

D-dimer levels were elevated and independently associated with mortality in this cohort; mean values were significantly higher among deceased patients compared to survivors. This result echoes findings from multiple studies and meta-analyses: increased Ddimer and other coagulation abnormalities (elevated PT/INR, prolonged aPTT) are common in severe or fatal COVID-19 (Tang *et al*., 2020; Zhou *et al*., 2020). Pathophysiological rationale: SARS-CoV-2 infection can induce endothelial injury, systemic inflammation, and activation of coagulation pathways, resulting in micro- and macro-thrombosis, disseminated intravascular coagulation (DIC), and organ hypoxia. The degradation of fibrin during thrombosis can increase circulating D-dimer levels, serving as a surrogate marker for thrombotic risk and coagulopathy (Klok *et al*., 2020; Milenkovic *et al*., 2022). Elevated D-dimer at admission may thus signal ongoing or impending thrombotic complications, higher disease severity, and mortality risk. D-dimer measurement is widely available, inexpensive, and can be integrated into routine admission labs. Elevated Ddimer should prompt early consideration of anticoagulation, close monitoring, and more intensive management, especially when combined with other risk markers (Creel-Bulos *et al*., 2020; Naymagon *et al*., 2020). D-dimer testing is widely available in hospital settings; it may provide a practical tool for early risk assessment and prioritization of clinical care, particularly during periods of high healthcare demand (Oblitas *et al*., 2024).

Our findings support previous evidence from Indonesia showing that routine laboratory biomarkers can help predict mortality in hospitalized COVID-19 patients. These tests are widely available and relatively inexpensive; they may serve as practical tools for early risk stratification, patient triage, and efficient use of healthcare resources, particularly in

resource-limited settings (Pertiwi *et al*., 2023). An important finding of this study is that several routine laboratory parameters can be used together to identify COVID-19 patients at higher risk of death. Instead of depending on a single biomarker, the combination of lymphocyte count, Ct value, platelet count, and D-dimer level provides a broader picture of a patient's condition during hospital admission. This approach may be particularly useful in hospitals with limited resources, where early recognition of high-risk patients is needed to support triage decisions, prioritize clinical monitoring, and make better use of available healthcare resources. The implications of these findings extend beyond the COVID-19 pandemic. Routine laboratory tests are relatively affordable and widely available, making them practical tools for supporting patient assessment during future infectious disease outbreaks. The use of these indicators may help strengthen hospital preparedness, improve early identification of patients at risk of poor outcomes, and support more effective healthcare planning in resource-constrained settings. In addition, incorporating routinely collected clinical data into risk assessment strategies could contribute to more efficient healthcare delivery and enhance the ability of health systems to respond to future public health emergencies.

Conclusion

This study demonstrated that routine laboratory biomarkers obtained at hospital admission, particularly lymphocyte count, Ct value, platelet count, and D-dimer level, were associated with mortality among hospitalized COVID-19 patients. Lymphopenia emerged as the strongest independent predictor of death, indicating the important role of immune dysregulation in disease progression. These findings suggest that simple and widely available laboratory tests can support early identification of high-risk patients, especially in resource-limited healthcare settings. From a public health perspective, the use of routine biomarkers for risk stratification may assist hospitals in improving triage systems, prioritizing clinical monitoring, and allocating limited healthcare resources more efficiently during infectious disease outbreaks. Integrating these laboratory indicators into hospital admission assessments may contribute to more timely clinical decision-making and strengthen preparedness for future public health emergencies. Further multicenter studies involving larger and more diverse populations are needed to validate these findings and develop practical risk prediction models for use in Indonesian healthcare facilities.

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