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Original Article

Systemic Immune-Inflammation Index as a Potential Indicator of COVID-19 Severity in a Tertiary Hospital in Indonesia

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Abstract

Background: The progression of coronavirus disease 2019 (COVID-19) to severe stages is strongly influenced by host immunity and inflammatory. The systemic immune-inflammation index (SII) is a novel biomarker reflecting both immunity and inflammation. This study aimed to analyze differences in SII according to COVID-19 severity.

Methods: A cross-sectional study was conducted using medical records of COVID-19 patients hospitalized at Dr. Hasan Sadikin General Hospital, Bandung, Indonesia, between March 2020 and August 2021. SII was calculated as the absolute neutrophil count and platelet count divided by the absolute lymphocyte count obtained from peripheral blood samples. COVID-19 severity was classified based on oxygen saturation (SpO_2). Receiver operating characteristic (ROC) curve and the area under the curve (AUC) were used to evaluate the discriminatory ability of SII.

Results: Of the 1,192 patients included, 410 (34.3%) had severe symptoms and 782 (65.7%) had mild to moderate symptoms. The median SII at admission was significantly higher in severe symptoms [1779 x 109 /L (IQR 46–40416)] compared with mild to moderate symptoms [880 x 109 /L (IQR 14.5–23280)]; p<0.001. ROC analysis showed an SII cut-off of 1244 with an AUC of 0.695 (95% CI 0.668–0.721), sensitivity 65.9%, and specificity 66.2%.

Conclusion: SII may serve as a potential biomarker for predicting COVID 19 severity. Its simplicity and availability from routine blood counts make it particularly valuable for early risk stratification, especially in resource-limited settings. Moreover, early recognition of elevated SII could support timely interventions, prevent disease progression, and improve clinical outcomes.

Keywords: COVID-19, hematologic parameter, severity, systemic immune-inflammation index

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Introduction

Coronavirus disease 2019 (COVID-19) has posed a global health challenge due to its highly transmissibility and wide spectrum of clinical manifestations. The World Health Organization (WHO) classifies COVID-19 into five severity levels, ranging from asymptomatic to critical. A better understanding of clinical factors and disease prognostic is essential to assist healthcare professionals in managing COVID-19.[1–3] Most patients present with asymptomatic to moderate symptoms; however, progression to severe or critical stages is associated with markedly increased mortality.[4,5] In resource-limited settings, there is an urgent need for simple, affordable biomarkers that can aid in early identification of patients at risk of severe disease.[6]

Severe and critical COVID-19 cases characterized by distinct hematological abnormalities, including leukopenia and thrombocytopenia which are associated with poorer outcomes.[3,7] Several hematologic indices have been investigated as predictors of COVID-19 severity, including the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR).[6,8] Recently, the

systemic immune-inflammation index (SII), which integrates neutrophil, lymphocyte, and platelet counts, has emerged as a promising biomarker with stronger prognostic value than NLR and PLR.[9,10]

The (SII) reflects the balance between host immunity and inflammation and can be easily calculated from routine blood counts and has been used in previous research.[11,12] Early recognition of elevated SII could facilitate better triage, optimize treatment allocation, and improve outcomes. This study aimed to analyze differences in the SII values based on COVID-19 severity, as indicated by oxygen saturation (SpO_2), among hospitalized patients in a tertiary hospital in Indonesia.

Methods

This comparative observational cross-sectional study was conducted in 2022 using medical records of patients with confirmed COVID-19 admitted to the internal medicine ward of Dr. Hasan Sadikin General Hospital, Bandung, Indonesia between March 2020 and August 2021. Patient data were retrospectively extracted from the hospital database using SQL Server Report Builder and the "HCLAB" application. All patient information was anonymized. This study obtained approval from the institutional ethics committee of Dr. Hasan Sadikin General Hospital (Approval number: LB.02.01/X.6.5/172/2022, dated June 7, 2022).

Inclusion criteria were patients aged ≥18 years with confirmed COVID-19 who were admitted during the study period. Patients were excluded if they had incomplete blood test results, a diagnosis of cancer, autoimmune disease, human immunodeficiency virus-acquired immunodeficiency syndrome (HIV-AIDS), or pregnancy.

COVID-19 severity was classified according to the National Institute of Health (NIH) guidelines into five categories: asymptomatic, mild symptoms without complications, moderate, severe, and critical. Severe illness was defined as SpO_2 <94% on room air, arterial partial pressure of oxygen to fraction of inspired oxygen (PaO_2/FiO_2) <300 mmHg, respiratory rate >30 breaths/min, or lung infiltrates >50%. Critical illness included respiratory failure, septic shock, and/or multiple organ dysfunction.[2] The SII was calculated by dividing the absolute number of neutrophils and thrombocytes by the absolute number of lymphocytes from a peripheral blood sample at admission.[11]

For analysis, patients were categorize into two groups: mild-moderate and severe-critical. Patient characteristics were summarized as frequencies and percentages for categorical variables. Continuous data were tested for normality using the Shapiro–Wilk test. Normally distributed variables were presented as mean±standard deviation (SD), while non-normally distributed data were presented as median (IQR) . Group differences were analyzed using the independent t-test or Mann–Whitney U test for continuous variables, and the chi-square test for categorical variables. ROC curve analysis was performed to determine the predictive value of SII for severe COVID-19. A p-value <0.05 was considered statistically significant. Analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA).

Results

Of the 1,521 patients initially screened, 329 were excluded due to incomplete hematology data. The final analysis included 1,192 patients consisting of 410 (34.3%) with severe COVID-19 and 782 (65.7%) with mild to moderate symptoms.

Patients with severe COVID-19 were generally older [median age 58 years (IQR 49–66)] compared with those with mild to moderate disease [median age 49 years (IQR 36–59); p<0.001]. The proportion of males was slightly higher in the severe group (55.1%) than in the mild to moderate group (49.4%), although the difference was not statistically significant (p=0.059).

Comorbidities were more frequent in the severe group, particularly hypertension (38.3% vs 26.0%, p<0.001), type 2 diabetes mellitus (26.6% vs 14.7%, p<0.001), and cardiovascular disease (11.7% vs 7.2%, p=0.008). Chronic kidney disease was also more common among severe cases (9.0% vs 4.3%, p=0.001). Conversely, the absence of comorbidities was more frequent in the mild to moderate group (51.7% vs 33.7%, p<0.001).

Vital signs differed significantly between groups. Severe patients had a higher respiratory rate [28 breaths/min (IQR 24–30) vs 22 breaths/min (IQR 20–24), p<0.001] and lower oxygen saturation [92% (IQR 84.8–96) vs 97% (IQR 95–98), p<0.001].

Laboratory findings showed higher leukocyte and neutrophil counts but lower lymphocyte and monocyte percentages in severe cases compared with mild to moderate cases (all p<0.001). Mortality was significantly

Table 1 Baseline Characteristics of COVID-19 Patients at Dr. Hasan Sadikin General Hospital, Bandung, from March 2020 to August 2021 (n=1,192)

Variable	Classification of COVID-19		p-value
	Severe n=410	Mild to Moderate n=782	
Age (year), median (IQR)	58 (49–66)	49 (36–59)	<0.001[b]
Gender, n (%)			
Female (%)	184 (44.9)	396 (50.6)	0.059[c]
Male (%)	226 (55.1)	386 (49.4)	
Comorbidities, n (%)			
Hypertension	157 (38.3)	203 (26)	<0.001[c]
Diabetes mellitus	109 (26.6)	115 (14.7)	<0.001[c]
Cardiovascular disease	48 (11.7)	56 (7.2)	0.008[c]
Liver disease	3 (0.7)	5 (0.6)	1.0[c]
Chronic obstructive pulmonary disease	13 (3.2)	14 (1.8)	0.128[c]
Chronic kidney disease	37 (9)	34 (4.3)	0.001[c]
No comorbidities	138 (33.7)	404 (51.7)	<0.001[c]
Vital signs, median (min-max)			
Respiratory rate (breaths/min)	28 (24–30)	22 (20–24)	<0.001[b]
Body temperature (OC)	36.8 (36.5–37)	36.7 (36.5–37)	0.914[a]
Peripheral oxygen saturation (SpO_2)(%)	92 (84.8–96)	97 (95–98)	<0.001[b]
Laboratory values, median (IQR)			
Hemoglobin (g/dL)	13.6 (3.3–19.8)	13.7 (3.3–18.4)	0.957[a]
Hematocrit (%)	396 (9.4–59.7)	40 (9–52.5)	0.495[a]
Leukocyte ($\times 10^3/mm^3$)	9320(1070–43200)	7350 (730–63220)	0.000[a]*
Platelets ($\times 10^3/mm^3$)	258.5 (7–769)	260.5 (12–920)	0.171[a]
Neutrophils (%)	81 (25–98)	70 (3–97)	0.000[a]*
Lymphocytes (%)	12 (1–65)	20 (1–68)	0.000[a]*
Monocyte (%)	6 (1–19)	8 (0–28)	0.000[a]*
Treatment outcome, n (%)			
Death	180 (44.6)	37 (4.7)	<0.001[b]

Note: Values are presented as median (IQR) or n (%). [a] Independent T-test; [b]Mann Whitney; [c]Chi square

higher in the severe group (44.6% vs 4.7%, p<0.001) (Table 1).

The median SII on admission was significantly higher in patients with severe symptoms compared with those with mild to moderate [1779 × 10^9/L (IQR 46–40,416) vs 880 × 10^9/L (IQR 14.5–23,280); p<0.001]. Patients who died also had higher SII compared to survivors [2250 × 10^9/L (IQR 1124–3905) vs 970 × 10^9/L (IQR 534–1813); p<0.001] (Table 2).

The ROC curve analysis showed that an SII cut-off value of 1244 yielded an area under the curve (AUC) of 0.695 (95% CI 0.668–0.721; p<0.05). At this threshold, SII had a sensitivity of 65.9% and a specificity of 66.2% for identifying severe COVID-19 cases. These findings indicate that SII has moderate diagnostic accuracy in predicting disease severity at admission (Figure 1).

Discussion

This study demonstrated that the SII was significantly higher in patients with severe COVID-19 compared with those with mild to moderate disease. Elevated SII values reflects neutrophilia and thrombocytosis in

Table 2 Systemic Immune-Inflammation Index (SII) among COVID-19 Patients

Classification of COVID-19	Median (Min–Max) × 10^9/L	IQR	p-value
Severe (n=410)	1779 (930–3127)	46–40,416	<0.001[a]
Mild–moderate (n = 782)	880 (500–1683)	14.5–23,280	

Note: [a] Mann–Whitney U test.

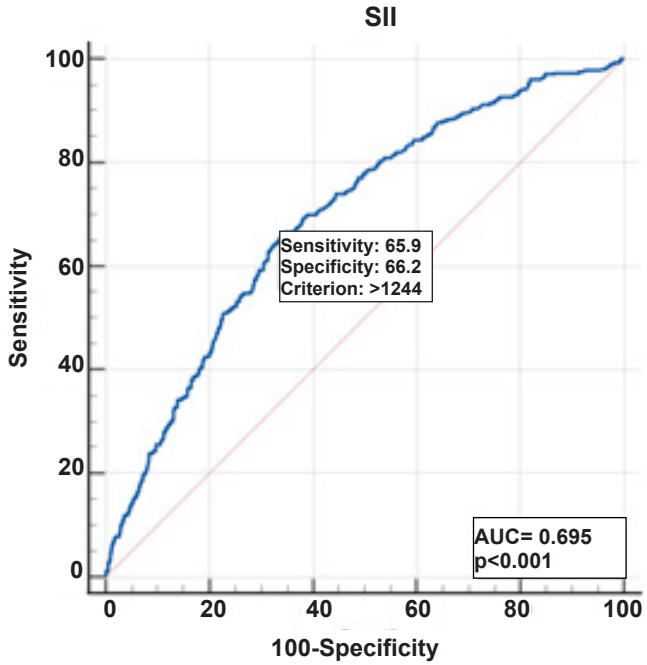

Figure 1 ROC Curve Analysis of the Systemic Immune-Inflammation Index (SII) on Admission of COVID-19 Patients

response to systemic inflammation, coupled with lymphopenia driven by catecholamine release, apoptosis, and cytokine-mediated suppression.[13–15] Clinically, elevated SII at admission may serve as an early warning indicator for severe disease requiring closer monitoring and intensified care.

The diagnostic performance of SII in this study (AUC=0.695) indicates moderate accuracy, with sensitivity and specificity comparable to chest X-ray findings and slightly lower than oximetry.[16,17] However, unlike radiological tools, SII requires no specialized equipment and can be derived from routine blood counts, making it particularly advantageous in resource-limited settings. Similar studies have linked SII to intubation requirements and mortality.[18,19] supporting its prognostic role across different populations.

The role of individual hematological markers during infection is well established.[20] However, our study demonstrates that their ratios can also be applied to the early detection of inflammation. Circulating leukocyte responses, such as increased neutrophils and reduced lymphocytes, become more informative when considered alongside thrombocyte responses. This combined approach offers broader insight into inflammatory processes beyond individual markers.

By integrating multiple hematologic markers, SII provides a more comprehensive reflection of the immune-inflammatory balance than individual parameters. Excessive neutrophil activation and neutrophil extracellular traps (NETs) formation,[21] platelet-driven coagulopathy,[22] and cytokine-induced lymphocyte apoptosis,[23–25] are central to COVID-19 pathogenesis. SII captures these processes in a single metric, reinforcing its potential as a practical biomarker for severity stratification. Thus, SII represents a simple, inexpensive, and widely applicable tool for predicting COVID-19 severity. Its use could improve triage, guide treatment allocation, and support clinical decision-making, especially during surges and in settings with limited resources.

This study has several limitations. First, it was retrospective and cross-sectional, restricting causal inference. Second, SII was only measured at admission; whereas changes during hospitalization were not assessed. Third, comorbidities were not analyzed in relation to SII, although they may influence inflammatory responses. Future multicenter prospective studies with serial SII measurements are warranted to validate these findings.

In conclusion, the SII is a practical

biomarker for predicting COVID-19 severity. Its accessibility through routine blood counts makes it valuable for early risk stratification, particularly in resource-limited environments. Elevated SII at admission should prompt physicians to consider intensified monitoring and tailored interventions to prevent disease progression and improve outcomes.

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