


# Predictive Value of Systemic Immune-Inflammation index and Neutrophil-to-Lymphocyte Ratio in Patients with Severe COVID-19

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## Abstract

**Objective:** It was initially reported that a novel coronavirus (COVID-19) had been identified in Wuhan, China, in December 2019. To date, COVID-19 is still threatening all humanity and has affected the public healthcare system and the world economic situation. Neutrophil-to-lymphocyte ratio (NLR) has also been demonstrated that associated with severity of COVID-19, but little is known about systemic immune-inflammation index (SII) relation with COVID-19. **Methods:** One hundred and twenty-five patients with diagnosed COVID-19 including non-severe cases ( $n = 77$ ) and severe cases ( $n = 48$ ) were enrolled in this study. Each patient of clinical characteristic information, blood routine parameters, and the haemogram-derived ratios were collected, calculated, and retrospectively analyzed. Receiver operating characteristics (ROC) was performed to investigate whether these parameters could be used to the predictive value of patients with severe COVID-19. **Results:** White blood cell count (WBC), neutrophil count (NEU), red cell volume distribution width (RDW), NLR, Platelet to lymphocyte ratio (PLR), neutrophil-to-platelet ratio (NPR), and SII were significantly higher in the severe groups than in the non-severe group ( $p < 0.01$ ). Conversely, the severe group had a markedly decreased lymphocyte count, basophil (Baso#) count, red blood cell count (RBC), Hemoglobin (HGB), hematocrit (HCT), and lymphocyte-to-monocyte ratio (LMR) ( $P < 0.01$ ). ROC curve analysis showed the AUC, optimal cut-off value, sensitivity, specificity of NLR and SII to early predict severe-patients with COVID-19 were 0.867, 7.25, 70.83%, 92.21% and 0.860, 887.20, 81.25%, 81.82%, respectively. **Conclusion** The results suggest that the SII and NLR is a potential new diagnosed biomarker in severe-patients with COVID-19.

## Keywords

neutrophil lymphocyte ratio (NLR), systemic immune-inflammation index (SII), severity, novel coronavirus (COVID-19)

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## Introduction

In December 2019, firstly reported in China, Wuhan, outbreaks of pneumonia with an unknown cause occurred. Subsequently, the researchers identified that pathogens of unknown pneumonia belong to the novel Coronavirus,<sup>1</sup> which is unlike the Atypical Pneumonia Virus (SARS-CoV) and the Middle East Respiratory Syndrome Virus (MERS-CoV). According to the ICTV (International Committee on Taxonomy of Viruses), this novel coronavirus causes unknown pneumonia, and the disease was called "COVID-19" by the WHO (World Health Organization).<sup>2</sup> The COVID-19 infection has rapidly spread across many domestic regions along with abroad, since the

outbreak of the epidemic.<sup>3</sup> As of 11 June 2022, the WHO reported a total of 532,201,219 COVID-19 confirmed cases,

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including 6,305,358 deaths, with an average mortality of 1.18%, resulting in a negative effect on stability of medical healthcare and the world economy. Unfortunately, what's the number of confirmed cases is still increasing. Real-time polymerase chain reaction (RT-PCR) is the irreplaceable method for diagnosing COVID-19, according to the National Health Commission of the People's Republic of China's Novel Coronavirus Pneumonia Diagnosis and Treatment Plan (Provisional seventh Edition). COVID-19 patients are defined as mild, moderate, severe, or critical according to their clinical manifestations, and there is a high mortality rate, especially among elderly patients or those with underlying diseases.<sup>4,5</sup> Furthermore, the clinical progression of COVID-19 infection can be asymptomatic as well as progressing from mild to severe, and it usually begins with flu-like symptoms, indicating that the early symptoms of the disease lack specificity.<sup>6,7</sup> Meanwhile, there are no specific drugs for COVID-19. Accordingly, it is crucial to explore higher sensibility and specificity potential markers for distinguishing between severe and non-severe COVID-19. By accurately assessing the severity of the disease, we can administer appropriate treatment and maximize the use of limited medical resources, decreasing mortality risks.<sup>8</sup> In this context, it's necessary to identify efficient, convenient biomarkers to distinguish between severe and non-severe COVID-19.<sup>9</sup>

Blood routine examination parameters are one of the most commonly performed laboratory tests in clinical practice because its rapid, simple, and economical to reflect the state of inflammation *in vivo*. It is vital in the early diagnosis of COVID-19 and assessing the disease's prognosis.<sup>10</sup> Several studies have confirmed that RDW, PLR, LMR, and NPR are considered novel inflammatory markers for the diagnosis and prognosis of COVID-19 infection.<sup>11–14</sup> Of note, SII is novel hematological biomarker that may be derived from the platelet count  $\times$  neutrophil count/lymphocyte count. Multiple studies have shown that SII is used as a prognostic indicator to determine the prognosis of sepsis and different types of malignancy. This is because it is an indicator to assess the instability of the inflammatory response.<sup>15–17</sup> In addition, NLR is a novel inflammatory marker and its predictive role was established in various diseases including, ulcerative colitis,<sup>18</sup> diabetes mellitus,<sup>19</sup> cardiovascular diseases,<sup>20</sup> thyroiditis,<sup>21</sup> and functional bowel disorders.<sup>22</sup> More importantly, recent studies have confirmed that the NLR is an important predictor of the diagnosis of COVID-19 and the clinical progression of severe patients.<sup>23</sup> Platelet to lymphocyte ratio (PLR) as a noninvasive inflammatory marker has been widely investigated in inflammatory diseases, including thyroid conditions and type 2 diabetes.<sup>24,25</sup> Previous study validated that the high expression levels of PLR in severe COVID-19 patients with well predictive value, which is consistent with our findings.<sup>26</sup> Additionally, our data showed that the AUC, specificity, and sensitivity of PLR to identify severe COVID-19 patients were inferior to those of NLR and SII, therefore they were not the focus of this study.

Hitherto, few studies have been published that investigate the relationship between the hematological parameter and its

derived hematological profiles and COVID-19 disease severity, particularly NLR and SII. Therefore, this study aims to investigate the predictive value of blood routine examination parameters and haemogram-derived ratios, such as PLR, LMR, NPR, especially SII and NLR, to distinguish between patients with severe and non-severe COVID-19. The predicted findings can assist in clinicians identifying individuals who are more likely to progress to severe cases after being first admitted to the hospital.

## Materials and Methods

### Study Subjects

From January 21, 2020, to March 9, 2020, 125 patients diagnosed with COVID-19 were hospitalized at the Jingzhou Hospital Affiliated to Yangtze University for present study. The study participants were divided into two groups: 77 cases in the non-severe group (including mild or moderate), and 48 cases in the severe group (including 28 severe cases and 20 critical cases) According to the National Health Commission of the People's Republic of China's Guidelines for the Diagnostic and Treatment of COVID-19 (Seventh Edition), all patients met the clinical diagnostic and disease severity criteria. Patients who satisfied any of the following criteria were classified as having severe cases:

- (I) Severe patients have a respiratory rate  $\geq$  30 times/min, oxygen saturation greater than 93% at rest, partial pressure of oxygen with a partial pressure of inhaled oxygen  $\leq$  300 mm Hg, and progression of  $>$  50% of the patient's lung CT lesion extent within 24–48 h.
- (II) Critically ill patients with respiratory failure who meet the requirements for mechanical ventilation, infectious shock, and multi-organ failure are treated in the ICU. The exclusion criteria: Patients with other types of pneumonia, individuals suffering from severe hematological diseases, and those without complete clinical data were also excluded.

### Ethics Statement

The Ethics Committee approved this study at Jingzhou Hospital, affiliated to Yangtze University. Participants in this retrospective study were not required to provide written informed consent in accordance with the Declaration of Helsinki (revised in 2013).

### Data Collection

Patient available data, including clinical characteristics such as age, gender, comorbidities, signs and symptoms, epidemiological history, length of hospitalization, hematological findings, and severity assessment were obtained from the hospital's digital medical records.

**Table 1.** Baseline Characteristics of Patients with COVID-19.<sup>a</sup>

Variables	Total (n = 125)	non-severe (n = 77)	severe (n = 48)	P- value
Age, mean (SD), years	49.0 (15.7)	44.7 (14.4)	56.0 (15.2)	<b>&lt;0.001</b>
Gender, N (%)				0.785
Female	54 (43.2)	34 (44.2)	20 (41.7)	
Male	71 (56.8)	43 (55.8)	28 (58.3)	
Comorbidities, N (%)				
Hypertension	31 (24.8)	10 (13)	21 (43.8)	<b>&lt;0.001</b>
Diabetes mellitus	17 (13.6)	4 (5.2)	13 (27)	<b>0.001</b>
Coronary heart disease	5 (4)	2 (2.6)	3 (6.3)	0.311
COPD	2 (1.6)	1 (1.3)	1 (2.1)	0.734
Cerebral infarction	5 (4)	2 (2.6)	3 (6.3)	0.311
Hyperlipidemia	2 (1.6)	1 (1.3)	1 (2.1)	0.734
Chronic renal disease	7 (5.6)	3 (3.9)	4 (8.3)	0.294
Malignancies	4 (3.2)	1 (1.3)	3 (6.3)	0.126
Signs and symptoms, N (%)				
Fever	92 (73.6)	57 (74)	35 (72.9)	0.891
Dry cough	42 (33.6)	25 (32.5)	17 (35.4)	0.734
Chilly	32 (25.6)	22 (28.6)	10 (20.8)	0.335
Cough	32 (25.6)	18 (23.4)	14 (29.2)	0.471
Myalgia	15 (12)	9 (11.7)	6 (12.5)	0.892
Fatigue	42 (33.6)	26 (33.8)	16 (33.3)	0.960
Sore throat	14 (11.2)	11 (14.3)	3 (6.3)	0.166
Headache	10 (8)	9 (11.7)	1 (2.1)	0.054
Dyspnea	7 (5.6)	3 (3.9)	4 (8.3)	0.294
Shortness of breath	17 (13.6)	7 (9.1)	10 (20.8)	0.063
Chest distress	6 (4.8)	3 (3.9)	3 (6.3)	0.549
Diarrhea	10 (8)	7 (9.1)	3 (6.3)	0.569
Nausea and vomiting	3 (2.4)	2 (2.6)	1 (2.1)	0.855
Anorexia	9 (7.2)	5 (6.5)	4 (8.3)	0.699
Epidemiological history, N (%)				
History of residence or work in Wuhan	41 (32.8)	27 (35.1)	14 (29.2)	0.495
Close contact with confirmed patients	24 (19.2)	18 (23.4)	6 (12.5)	0.133
Close contact with suspected patients	30 (24)	16 (20.8)	14 (29.2)	0.286
No clear epidemic history	30 (24)	16 (20.8)	14 (29.2)	0.286
LOS, mean (SD), days	19.44 (9.7)	16.06 (7)	24.85 (11.1)	<b>&lt;0.001</b>

<sup>a</sup>Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19: 2019-coronavirus disease; LOS, length of hospitalization.

Note: Data are presented as mean (standard deviation [SD]) or as n (%).

### Detection of Hematological Parameters

A blood routine examination analyzer (BC-6900, Mindray, China) was used for routine blood tests. The white blood cell (WBC) count, neutrophil (NEU) count, lymphocyte (LYM) count, monocyte (MON) count, red blood cell count (RBC), and other hematological parameters were recorded. To avoid the drug's effects on hematological parameters, if a patient was already on glucocorticoid therapy before sample collection, the individuals were not included in our study statistics. Additionally, derived hematological profiles such as the NLR were calculated by dividing the absolute number of neutrophils by the absolute number of lymphocytes, the PLR by dividing the absolute number of platelets by the absolute number of lymphocytes, and the LMR by dividing the absolute number of lymphocytes by the absolute number of monocytes. The neutrophil-platelet ratio (NPR) was computed by dividing the total number of neutrophils by the number of platelets.  $SII = \text{platelet count} \times \text{neutrophil count} / \text{lymphocyte count}$ . The test

results for hematological parameters were divided into two groups for retrospective and comparative analysis based on non-severe and severe disease severity.

### Statistical Analyses

The Kolmogorov-Smirnov test was applied to determine whether the data in this study conformed to a normal distribution; normally distributed variables are expressed as mean  $\pm$  standard deviation (SD), and statistical significance was confirmed using the independent sample t-test. Furthermore, non-normally distributed variables are expressed as the median and interquartile range (IQR), and their statistical significance was determined using the Mann-Whitney U test. The frequency (%) of the categorical variables was used to represent them, and the  $\chi^2$  test was used. The predictive value of hematological parameters for COVID-19 severity assessment was determined using the receiver-operating curve (ROC). Finally, the predictive value of SII and NLR for COVID-19 that was severe was

**Table 2.** Hematological Profiles of Patients with COVID-19.<sup>a</sup>

Variables	Total (n = 125)	non-severe (n = 77)	severe (n = 48)	P value
<b>Hematological profiles</b>				
WBC, × 10 <sup>9</sup> /L	6.37 (4.34–8.54)	5.06 (3.91–6.60)	9.02 (6.68–14.06)	<b>&lt;0.001</b>
NEU, × 10 <sup>9</sup> /L	4.33 (2.96–7.55)	3.20 (2.20–4.74)	8.12 (4.70–12.46)	<b>&lt;0.001</b>
LYM, × 10 <sup>9</sup> /L	0.93 (0.61–1.36)	1.14 (0.82–1.58)	0.64 (0.42–0.85)	<b>&lt;0.001</b>
Mon, × 10 <sup>9</sup> /L	0.42 (0.31–0.57)	0.42 (0.33–0.57)	0.43 (0.30–0.66)	0.909
Eos, × 10 <sup>9</sup> /L	0.01 (0.00–0.08)	0.02 (0.00–0.09)	0.00 (0.00–0.07)	0.122
Baso, × 10 <sup>9</sup> /L	0.01 (0.01–0.02)	0.01 (0.01–0.02)	0.02 (0.01–0.03)	<b>0.019</b>
RBC, × 10 <sup>12</sup> /L	4.29(3.90–4.66)	4.38 (4.08–4.78)	4.06 (3.57–4.52)	<b>0.003</b>
HGB, g/L	132.0 (119.00–146.5)	134.0 (125.50–149.50)	124.0 (112.25–141.75)	<b>0.012</b>
HCT, %	0.40 (0.36–0.43)	0.41 (0.38–0.44)	0.38 (0.33–0.41)	<b>0.004</b>
MCV, fl	92.70 (90.50–95.20)	92.70 (90.50–94.70)	92.80 (90.05–97.30)	0.504
MCH, pg	31.10 (30.10–31.90)	31.00 (30.05–31.85)	31.30 (30.10–32.00)	0.455
MCHC, g/L	333.00 (326.0–341.0)	332.00 (327.00–339.00)	335.50 (326.00–342.00)	0.659
RDW-CV, %	12.30 (11.90–12.95)	12.20 (11.90–12.85)	12.50 (11.95–13.20)	<b>0.046</b>
PLT, × 10 <sup>9</sup> /L	186.00 (149.00–239.0)	181.00 (148.00–229.00)	210.00 (150.50–268.75)	0.162
MPV, fl	10.20 (9.50–10.90)	10.10 (9.30–11.05)	10.20 (9.70–10.90)	0.414
PCT, %	0.19 (0.16–0.24)	0.18 (0.16–0.21)	0.21 (0.15–0.26)	0.085
PDW, %	16.00 (12.30–16.40)	16.00 (12.70–16.30)	16.15 (11.83–16.58)	0.212
<b>Derived hematological profiles</b>				
NLR	4.18 (2.39–12.84)	2.70 (1.87–4.54)	14.91 (5.43–26.03)	<b>&lt;0.001</b>
PLR	190.32 (139.36–311.85)	167.31 (125.09–200.52)	316.00 (238.43–454.73)	<b>&lt;0.001</b>
LMR	2.30 (1.27–3.18)	2.70 (1.76–3.66)	1.24 (0.91–2.29)	<b>&lt;0.001</b>
NPR	0.02 (0.01–0.04)	0.02 (0.01–0.02)	0.05 (0.02–0.06)	<b>&lt;0.001</b>
SII	785.76 (438.41–2491.04)	518.59 (347.14–831.49)	2685.54 (983.45–5301.98)	<b>&lt;0.001</b>

<sup>a</sup>Abbreviations: White blood cell count, WBC; Neutrophil count, NEU; Lymphocyte count, LYM; Monocyte count, Mon; Eosinophil count, Eos; Basophil count, Bas; Red blood cell count, RBC; Hemoglobin, HGB; Hematocrit, HCT; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; RDW-CV, red cell volume distribution width-coefficient of variation; PLT, platelet count; MPV, mean platelet volume; PCT, platelet hematocrit; PDW, platelet distribution width; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; LMR, lymphocyte-to-monocyte ratio; NPR, neutrophil-to-platelet ratio; SII, systemic immune-inflammation index.

Note: Data are presented as median (interquartile range [IQR]).

determined, with an area under the curve (AUC) of more than 0.80 being a strong indicator. This study used SPSS statistics software (version 26.0) to analyze the data for quantitative variables and categorical variables. MedCalc software (version 19.1) was used for mapping. P-values <0.05 were considered statistically significant.

## Results

### Baseline Characteristics of 125 COVID-19 Patients

As shown in Table 1, demographics, clinical characteristics, and epidemiological history data for 125 patients admitted to the JingZhou Central Hospital group due to COVID-19 infection from January to March 2020 were enrolled. These diagnosed COVID-19 patients were grouped by non-severe (77 cases, 61.6%) and severe (48 cases, 38.4%) in the research cohort (Table 1). Of all the 125 patients, the mean age of 56 ± 15.2 years in the severe cases and 44.7 ± 14.4 years in the non-severe cases; Age was significantly different between the patients with COVID-19 severe and non-severe (P < 0.05). Of these patients, 71 were male (56.8%) and 54 were female (43.2%). Unfortunately, there was no statistical significance in the difference between the two groups of patients (P > 0.05). The overwhelming majority of patients had underlying

comorbidities (58.4%), including hypertension (24.8%), diabetes mellitus (13.6%), coronary heart disease (4%), chronic obstructive pulmonary disease (1.6%), cerebral infarction (4%), hyperlipidemia (1.6%), chronic kidney disease (5.6%), and malignancies (3.2%). The comorbidities proportion of hypertension and diabetes mellitus were in severe patients higher than non-severe patients (P < 0.05). Additionally, most of patients had fever (92 [73.6%]), dry cough (42 [33.6%]), and Fatigue (42 [33.6%]). Less common signs and symptoms were nausea and vomiting (3 [2.4%]), chest distress (6 [4.8%]), and dyspnea (7 [5.6%]). The signs and symptoms and epidemiological history were not significantly different between the two groups of patients. These patients of average length of hospitalization were 19.44 ± 9.7 days; The length of hospitalization (LOS) was longer in the severe group than in the non-severe group (P < 0.05).

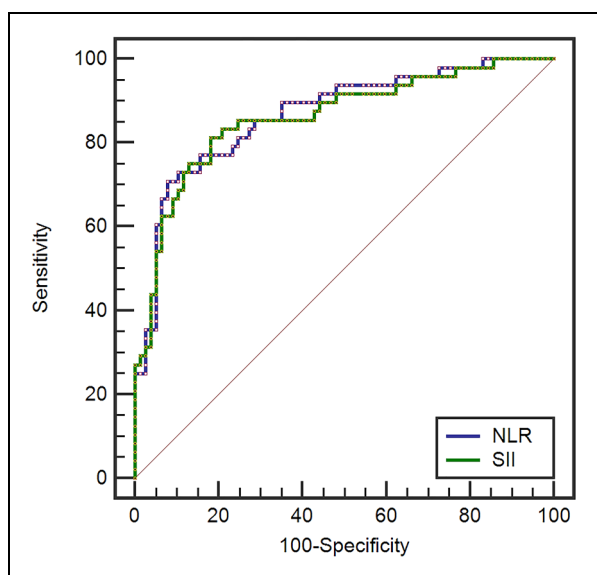
### Hematological and Derived Hematological Profiles of COVID-19 Patients

As shown in Table 2, hematological and derived hematological profiles in different severity of COVID-19 patients were analyzed. With disease aggravation, comparison of hematological profiles showed that WBC, NEU#, Baso#, RDW-CV, NLR, PLR, NPR and SII parameters remarkably increased in severe

**Table 3.** The Predictive Value of Hematological Profiles for Predicting Severely Patients with COVID-19.<sup>a</sup>

Variables	AUC	95% CI	Sensitivity (%)	Specificity (%)	Optimal cut-off value	P value
WBC	0.839	0.762–0.898	77.08	79.22	6.65	<0.001
NEU	0.866	0.793–0.920	72.91	85.71	5.14	<0.001
LYM	0.779	0.696–0.848	77.08	74.03	0.85	<0.001
RBC	0.657	0.566–0.739	50.00	80.52	4.03	0.002
HGB	0.634	0.543–0.718	50.00	81.82	123	0.011
HCT	0.653	0.562–0.736	50.00	80.52	0.369	0.003
RDW	0.606	0.515–0.692	68.78	54.55	12.20	0.043
NLR	0.867	0.795–0.924	70.83	92.21	7.25	<0.001
PLR	0.797	0.716–0.864	79.12	81.82	230.44	<0.001
LMR	0.768	0.678–0.858	60.42	85.71	1.46	<0.001
NPR	0.831	0.755–0.908	79.17	77.92	0.02	<0.001
SII	0.860	0.790–0.931	81.25	81.82	887.20	<0.001

<sup>a</sup>Abbreviations: AUC, area under curve.



**Figure 1.** Diagnostic values of SII and NLR for distinguishing severe-patients with COVID-19.

COVID-19 patients ( $P < 0.05$ ), conversely, the lymphocyte count (LYM#), RBC, HGB, HCT, LMR parameters obviously decreased in the severe cases ( $P < 0.05$ ).

### the Value of Hematological Profiles for Predicting Severely Patients with COVID-19

Receiver-operating characteristic (ROC) curves further were used to assess the blood cell parameters and hemogram-derived ratios, which were markedly different, between the patients with COVID-19 severe and non-severe ( $P < 0.001$ ). The findings revealed that the AUC values for WBC, NEU, LYM, RBC, HGB, HCT, RDW, NLR, PLR, LMR, NPR, SII were 0.839, 0.866, 0.779, 0.657, 0.634, 0.653, 0.606, 0.867, 0.797, 0.768, 0.831, and 0.860 respectively; and the optimal cutoff value respectively was 6.65 ( $10^9/L$ ), 5.14 ( $10^9/L$ ), 0.85 ( $10^9/L$ ), 4.03 ( $10^{12}/L$ ), 123 (g/L), 0.369(%), 12.20(%), 7.25, 230.44,

1.46, 0.02, 887.20, which represents the best of sensitivity and specificity. As shown in Table 3, Although SII had a lower AUC than other hematological parameters, the higher sensitivity and specificity of SII were still conducive for distinguishing severe- patients with COVID-19. Therefore, NLR and SII were considered as the better optimal parameters for early predicting the severity of COVID-19 patients. (Figure 1).

### Discussion

During the COVID-19 pandemic, worldwide, it is fairly difficult to early predict of an individual's risk of developing severe states for clinicians.<sup>27</sup> Therefore, distinguishing the severity of COVID-19 is vital to providing reasonable allocation of medical resources to reduce severe patient mortality. However, few comprehensive studies have revealed the relationships between blood cell parameters and hemogram-derived ratios and COVID-19 of severity.

Current study population consisted of 125 confirmed COVID-19-patients, the severe group ( $n = 48$ ) mean was 56 years, non-severe group ( $n = 77$ ) mean was 44.7 years, and there was a statistical difference in age between the severe and non-severe groups ( $P < 0.001$ ), suggesting that elderly patients are more likely to develop severe. Multicenter studies have shown that severe COVID-19 patients of median age were 52 years, and nonsevere patients of median age were 45 years, similar to our finding.<sup>28</sup> In severe cases, the numbers of patients with hypertension and diabetes mellitus were relatively high ( $P < 0.05$ ), implying that elderly patients with underlying diseases are more prone to be affected by the original disease during a viral infection. Most would develop severe symptoms that would require clinical intervention timely. Results of this study are in agreement with previous numerous studies where comorbidities were shown to be more frequently encountered in severe cases.<sup>29,30</sup>

Our results showed no statistically significant differences in signs and symptoms between patients in the severe and non-severe groups ( $P > 0.05$ ), Interestingly, contrary to the results of other studies.<sup>31,32</sup> We speculate that this is because most of

the clinical information for most of the patients in this study was recorded at the time of admission, when most of the patients were in the less symptomatic stages of the disease. In addition, most cases have epidemiological history in Wuhan, which are mainly divided into four categories: History of residence or work in Wuhan, close contact with confirmed patients, close contact with suspected patients, and no clear epidemic history, there was no significant difference in epidemiological history between severe group and the non-severe group ( $P > 0.05$ ). This may be due to these infected patients derived from the same region of infection.

Because of the advantage of blood cell parameters with economical, accessible, and rapid, several studies have reported characteristics of hematological profiles in COVID-19 individuals, such as, the expression levels of RDW, NLR, NPR, and PLR were higher in the severe cases compared to the non-severe cases. Conversely, the number of lymphocytes and hemoglobin levels were lower,<sup>33–36</sup> which is consistent with the present study. This study emphasises clinical application of haematological routine parameters, as well as the severity and predictive value of haemogram-derived ratios in the early stages of patients with COVID-19.

As far as we know, this is the firstly study that comprehensive investigates the role of hematological profiles and haemogram-derived ratios as inflammatory biomarkers for differentiating COVID-19 patients with a severe and the non-severe.

Previous study demonstrated that the NLR measured at admission and in isolation can be used to effectively predict the subsequent presence of disease deterioration and serious clinical outcomes in patients with COVID-19.<sup>37</sup> Another recent report showed that higher NLR is one of the independent predictors of hospitalized mortality of COVID-19.<sup>38</sup> This study of ROC curve observed that among the blood routine parameters, NLR and SII of AUC, sensitivity and specificity respectively were 0.867, 70.83%, 92.21%; 0.860, 81.25%, 92.21%. Therefore, considering the diagnostic specificity, sensitivity and AUC, our data concluded that NLR and SII are the best parameters for predicting severe COVID-19.

This study had some unavoidable limitations. Firstly, this was a single-center study involving a small number of cases with no multi-factor correction to assess the severity of the disease. Secondly, other hematological parameter data were missing and should be included. Lastly, the study data were mainly collected from the clinical data of patients at admission, the lack of dynamic monitored in two groups. To sum up, in order to solve these limitations, large-sample, multi-center and systematic prospective studies are the focus of our future study.

## Conclusion

In summary, this retrospective study aims at investigating the predictive value of blood routine examination parameters and hemogram-derived ratios, such as PLR, LMR, NPR, NLR, and SII, to distinguish between patients with severe and non-

severe COVID-19. Our findings indicate that the blood routine examination parameters both and hemogram-derived ratios are the statistical difference between patients with severe and non-severe COVID-19. Furthermore, The ROC curve of these hematological parameters analyses further that elevated NLR and SII levels were the best predictors in this study, NLR with optimal specificity of 92.21%, and SII with optimal sensitivity of 81.25%, to predict the occurrence of severe-patients with COVID-19, improving reasonable allocation of medical resources to reduce severe patient mortality for clinicians.

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## Author Contributions

Wei Xia and Yafeng Tan was involved in the paper drafting, responsible for data collection and data analysis; Shengmei Hu contributed to the critical revision of the manuscript for important linguistic content; Chengbin Li contributed to the data acquisition; Tao jiang was responsible for the research design and critical revision of the manuscript. All authors approved the final version of the manuscript for publication.

## Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

## Declaration of Conflicting Interests

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