Predictive value of neutrophil-to-lymphocyte ratio and other inflammatory indicators in estimating clinical severity of coronavirus disease

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Dear editor,

The recent outbreak of coronavirus disease (COVID-19) has become a major public health issue caused by 2019 novel coronavirus (2019-nCoV).[1] Severe COVID-19 patients may reveal a dysregulated immune response that allows the development of viral hyperinflammation.[2] In the fight against COVID-19, inflammatory parameters towards illness severity should be identified to improve the prognosis of patients. In this study, we aimed to assess the discriminative ability of several inflammation indicators in severe COVID-19 infection.

We conducted a comprehensive search through electronic databases until May 26, 2020: PubMed, the Cochrane Library, EMBASE, and Web of Science. Keywords included COVID-19, nCoV-2019, 2019-nCoV, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR). To be included, studies must provide mean and standard deviation (SD) values or median and interquartile range or adjusted odds ratio (OR) with corresponding 95% confidence interval (CI). The pooled weighted mean difference (WMD) and pooled OR were worked out by STATA 12.0.

After the application of selection criteria, there were 13 studies[2-14] with 2,140 patients included that provided data describing NLR, PLR, and MLR on COVID-19 cases and in-hospital mortality. The meta-analysis for the continuous outcome variables included ten studies,[2-11] and for the binary variables included six studies.[5,8,10,12-14] There were two studies reporting clear data on in-hospital mortality.[12,14]

Overall, more severe COVID-19 infection was associated with higher NLR (WMD=3.55, 95% CI 2.47–4.64, P<0.001) and higher MLR (WMD=0.39, 95% CI 0.19–0.59, P<0.001). There was no significant difference in PLR (WMD=81.48, 95% CI −93.44 to 256.40, P=0.361) between the severe group and the non-severe group. For COVID-19 patients, NLR with the pooled OR value could predict the severe infection (OR=1.40, 95% CI 1.02–1.93, P=0.038) and in-hospital mortality (OR=1.08, 95% CI 1.02–1.15, P=0.009).

As for blood parameters in severe COVID-19, seven studies described counts of white blood cell (WBC), neutrophil, and lymphocyte in the non-severe and severe groups. Patients with severe COVID-19 had higher WBC counts (WMD=1.48×10^9/L, 95% CI 0.90–2.05, P<0.001), higher neutrophil counts (WMD=1.80×10^9/L, 95% CI 1.25–2.35, P<0.001), and fewer lymphocyte counts (WMD=-0.35×10^9/L, 95% CI −0.48 to −0.22, P<0.001) than those in the non-severe group. Four studies compared platelet counts between the two groups, and severe cases demonstrated lower platelet counts (WMD=-26.39×10^9/L, 95% CI −46.50 to −6.27, P<0.010) compared with the non-severe group. Three studies reported the monocyte counts. However, no statistical difference was found between the two groups (WMD=0.00×10^9/L, 95% CI −0.02 to 0.03, P=0.731).

Table 1. Pooled outcomes of blood parameters in severe COVID-19

Indicators	Number of studies reporting variables	Number of patients analyzed	Pooled *WMD* with 95% *CI*	I^2	*P*-value
WBC[2-4,6-9]	7	1,514	$1.48×10^9$/L (0.90–2.05)	65.1%	<0.001
Neutrophil[2-4,6-9]	7	1,514	$1.80×10^9$/L (1.25–2.35)	61.4%	<0.001
Lymphocyte[2-4,6-9]	7	1,514	$-0.35×10^9$/L (–0.48 to –0.22)	81.7%	<0.001
Monocyte[2,4,6]	3	661	$0.00×10^9$/L (–0.02 to 0.03)	0.0%	0.731
Platelet[3,6,8,9]	4	894	$-26.39×10^9$/L (–46.50 to –6.27)	66.1%	<0.010
CRP[2,4,5,7-10]	7	1,539	41.23 mg/L (28.86–53.60)	72.2%	<0.001

WBC: white blood cell; CRP: C-reactive protein; *WMD*: weighted mean difference; *CI*: confidence interval.

Seven studies depicted C-reactive protein (CRP) levels, and severe cases also had higher CRP levels (*WMD*=41.23 mg/L, 95% *CI* 28.86–53.60, *P*<0.001). The pooled *WMD* for blood parameters of the included studies are presented in Table 1.

Meta-regression analysis showed that the increased NLR in severe COVID-19 patients was associated with WBC (*P*=0.007) and neutrophil (*P*=0.011) but not lymphocyte, CRP, age, or the study size of COVID-19. There was no evidence of publication bias according to the *WMD* of NLR. Sensitivity analysis showed no significant differences produced by excluding every single study.

In conclusion, during severe COVID-19 infection, NLR, MLR, WBC, neutrophil, and CRP were significantly increased, while lymphocyte and platelet were significantly decreased. Patients with a higher level of NLR experienced a higher risk of in-hospital mortality. The assessments of NLR and other inflammatory indicators may help physicians to identify severe patients with COVID-19 and predict the prognosis of this infection.

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