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Short communication

Neutrophil-to-Lymphocyte ratio as a potential biomarker for disease severity in COVID-19 patients

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Sir,

The global spread of novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a threat to the world on a pandemic scale. Without an available effective vaccine and specific treatment, finding the best solutions for patient management is urgently needed. Looking for differences between vulnerable patients who are severely affected and those with non-severe symptoms is necessary for risk-stratified care management, especially during an emergency, and for forecasting intensive care unit (ICU) requirement. For example, it has been proposed that patients with neutrophil-to-lymphocyte ratio (NLR) of <3 may have a better clinical outcome, whereas NLR > 4 is a predictor of ICU admission [1].

In the search for a reliable prognostic marker of disease severity, we have also investigated the clinical features and laboratory findings of COVID-19 patients with confirmed positive reverse transcription PCR (RT-PCR) from affiliated hospitals of Isfahan University of Medical Sciences, Isfahan, Iran. Isfahan Province, with a population of ca. 5 million, has become one of the worst infected parts of Iran [2]. A total of 508 COVID-19 patients (59% male) were included in this study, among which 9.7% were in severe status with a partial pressure of oxygen (pO_2) of <93% and receiving mechanical ventilation. The mean age of severe patients (67.7 ± 15.1 years) was significantly higher than non-severe patients (56.8 ± 17.1 years) ($P < 0.0001$). Approximately 39% of patients had at least one underlying disease or disorder. Coronary vascular disease and diabetes mellitus were more common in severe patients, although this was not significantly different from mild cases ($P > 0.05$). The death rate in severe patients was significantly higher than the other cases (60% vs. 4.1%; $P < 0.0001$).

The average white blood cell (WBC) count in severe patients (9205 cells/mm^3) was significantly higher than in non-severe cases (5963 cells/mm^3) ($P < 0.0001$). The WBC count was >10 000 cells/mm^3 in 29.5% of severe cases and 8.6% of non-severe cases ($P < 0.0001$), whilst the rate of WBC count <4000 cells/mm^3 among moderate patients was 23% in contrast to zero in severe patients. The average lymphocyte count did not differ between severe patients (1409 cells/mm^3) and non-severe patients ($P = 0.4093$). In 7.3% of severe patients the lymphocyte count was >4000 cells/mm^3 compared with 1.1% in non-severe patients ($P = 0.003$). The percentage of lymphocyte counts <1000 cells/mm^3 was not different between the two groups ($P = 0.286$). In 26.8% of severe patients the neutrophil count was >8000/mm^3 compared with 8.4% in non-severe patients ($P = 0.003$). However, the percentage of neutrophil count <2500/mm^3 in non-severe patients was 21.4% in contrast to zero in severe patients. The percentage of NLR > 6.5 differed significantly between the two groups (56.1% in severe vs.

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Table 1
Factors associated with disease severity of COVID-19.

Factor	Odds ratio (severe vs. non-severe)			
	Univariate OR (95% CI)	*P*-value	Adjusted for age and sex OR (95% CI)	*P*-value
Age (≥70 years vs. <70 years)	2.17 (1.45–5.02)	0.002		
Male sex (vs. female)	0.78 (0.42–1.44)	0.431		
WBC count > 10000 cell/mm^3	4.43 (2.14–9.14)	<0.0001	3.98 (1.89–8.37)	<0.0001
Lymphocyte count >4000 cells/mm^3	6.91 (1.51–30.1)	0.010	5.85 (1.29–26.3)	0.021
Neutrophil count >8000/mm^3	3.99 (1.85–8.61)	<0.0001	3.66 (1.66–8.03)	0.001
NLR > 6.5	5.11 (2.64–9.88)	<0.0001	4.99 (2.47–10.7)	<0.0001

CO, confidence interval; WBC, white blood cell; NLR, neutrophil-to-lymphocyte ratio.

20.0% in non-severe patients; $P < 0.0001$), however patients with NLR in the range 3.5–6.5 did not differ ($P = 0.362$). C-reactive protein was ≥10 mg/L in 84.9% all of patients, with no significant difference between groups ($P = 0.552$). The odds of NLR > 6.5 associated with the severity of disease in patients aged ≥70 years was almost twice that of others, whilst patient sex had no significant effect. The odds of NLR > 6.5 associated with death was 1.44 [95% confidence interval (CI) 1.82–2.07] ($P < 0.0001$). Regarding adjustment for age and sex, the odds of disease severity in patients with WBC count >10 000 cells/mm^3 and lymphocyte count >4000 cells/mm^3 were 4 and 6 times more than other patients, respectively. NLR > 6.5 increased the odds of severity by 5 times and the odds of death were 1.76 (95% CI 1.02–2.46) after adjustment for age and sex ($P < 0.0001$) (Table 1).

In line with our results, increased NLR at admission is common in patients with COVID-19 and an independent risk factor for in-hospital mortality [3]. It could be speculated that the progress phase of the disease is the result of direct virus attack and injury caused by the cytokine storm. Liu et al. have reported that loss of T-cells in severe COVID-19 cases is associated with the magnitude of the cytokine storm [4]. Another favoured hypothesis for lymphopenia in COVID-19 patients could be infiltration of lymphocytes into the pulmonary tissue induced by local inflammation and pyroptosis of infected cells [5]. It seems that NLR monitoring is helpful both for early screening of severe COVID-19 cases as well as tracking therapeutic interventions.

In conclusion, the current study supports that NLR may be a rapid, easy and therefore favoured point-of-care test for patient stratification and an efficient tool for prioritisation of healthcare system resources.

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Competing interests

None declared.

Ethical approval

Not required.

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