Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Neutrophil-to-lymphocyte ratio and clinical outcome in COVID-19: a report from the Italian front line

Dear Editor,

Since December 2019, cases of disease related severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), now known as COVID-19 (coronavirus disease 2019), have rapidly spread from Hubei Province in China to the whole world. The World Health Organization (WHO) has officially recognised COVID-19 as a pandemic and countries worldwide are now facing huge challenges trying to prevent its further spread as well as treating the growing number of COVID-19 patients. In fact, although the majority of cases are usually self-limiting with mild symptoms such as low-grade fever and cough, the disease can be fatal [1]. Serious COVID-19 cases can develop severe pneumonia, acute respiratory distress syndrome (ARDS) and multiple organ failure leading to death; the mortality rate is much higher in elder patients with pre-existing chronic diseases [1]. Clinicians are searching for a reliable prognostic marker that can distinguish patients at risk of developing more severe forms of the disease in order to better manage hospital resources. The neutrophil-to-lymphocyte ratio (NLR) in peripheral blood has been studied as a systemic inflammatory marker and various studies have shown that it is a valid prognostic factor in various solid tumours [2] and other chronic diseases such as lung, cardiovascular and kidney diseases. Here we describe the clinical characteristics of hospitalised patients with COVID-19 and aim to assess predictors of clinical outcome.

A group of 74 patients with confirmed COVID-19 hospitalised in our centre in March 2020 were retrospectively analysed. Patients' follow-up was censored on 28 March 2020. COVID-19 diagnosis was performed via molecular assay from nasopharyngeal and oropharyngeal swabs. For each patient, demographic data, clinical history, laboratory findings and treatment measures during hospitalisation were collected. According to signs, symptoms, co-morbidities and clinical parameters at admission and during hospitalisation, patients were divided into severe and non-severe COVID-19 cases in accordance with Italian guidelines [3]. Clinical improvement was defined as the resolution of fever for $\geq$48 h and the suspension of oxygen supplementation. Parametric and non-parametric tests were used, as appropriate, to compare changes, and logistic regression analyses were used to assess predictors.

Of the 74 patients analysed, 51 (68.9%) were male, the median age was 63 years [interquartile range (IQR) 52–73 years] and the median time between symptom onset and hospitalisation was 7 days (IQR 3–9 days). Regarding pre-existing co-morbidities, 24 patients (32.4%) had hypertension, 15 (20.3%) had a pre-existing heart condition and 8 (10.8%) had type 2 diabetes mellitus. At hospital admission, the median leukocyte count was 5900 cell/mm^3 (IQR 4412–7782 cell/mm^3), the median neutrophil count was 4240 cell/mm^3 (IQR 3122–5995 cell/mm^3) and the median lymphocyte count was 925 cell/mm^3 (IQR 700–1275 cell/mm^3). The median platelet-to-lymphocyte ratio (PLR) was 191.7 (IQR 133.3–311.0), whilst the median NLR was 4.5 (IQR 3.1–7.1). In addition, 41 patients (55.4%) had radiological signs of interstitial pneumonia at admission. In this case series, 19 patients (25.7%) required admission to the intensive care unit (ICU) during hospitalisation. At censor, 8 deaths (10.8% of the total population) were registered, 25 patients (33.8%) were discharged and 41 patients (55.4%) were still hospitalised. Among all patients, 46 cases of severe COVID-19 (62.2% of total cases) were recognised. Patients with severe disease were significantly older (median age 70 years vs. 56 years; $P = 0.007$) and had a significantly higher NLR (median 5.6 vs. 3.0; $P = 0.001$) compared with non-severe cases.

In the multivariate analysis, clinical improvement was predicted by younger age ($P = 0.040$) and a NLR of <3 ($P = 0.010$) after adjusting for sex, pre-existing hypertension and signs of interstitial pneumonia at admission. Admission to the ICU was instead predicted by a NLR of >4 ($P = 0.046$) after adjusting for age. Death was solely predicted by older age ($P = 0.047$) after adjusting for NLR, sex, pre-existing hypertension and signs of interstitial pneumonia at hospital admission.

COVID-19 is a rapidly spreading infectious disease caused by SARS-CoV-2, a novel coronavirus. In recent weeks, reports on the feasibility of either NLR or PLR in predicting prognosis in patients with SARS-CoV-2 infection have been published. In particular, Qu et al. suggested a possible prognostic role of PLR by analysing the data of a cohort of 30 patients with confirmed COVID-19 [4]. Meanwhile, a recent study by Qin et al. showed a significantly higher NLR in patients with severe forms of COVID-19 in a cohort of 452 hospitalised patients [5]. In the current study, a higher NLR at hospital admission was associated with a more severe outcome: in particular, a NLR of >4 was a predictor of admission to the ICU. Patients with severe disease presented a significantly higher NLR at admission compared with patients with a milder form of COVID-19, which is in agreement with the work of Qin et al. [5], reinforcing the theory of a close association between hyperinflammatory state and COVID-19 pathogenesis.

Although further studies with a larger sample size will be needed to properly assess this matter, the current study shows that NLR may be a rapid, widely available, useful prognostic factor in the early screening of critical illness in patients with confirmed COVID-19.

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