We Know the Prognosis but can We Change It?

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Coronavirus pandemic has been ravaging the world for quite sometime. There had been similar outbreaks of viral pneumonia previously. Outbreaks of the severe acute respiratory syndrome and Middle East respiratory syndrome had much higher case fatality rates than this present outbreak. However, in the case of coronavirus disease-2019 (COVID), the sheer number of total cases has increased the number of deaths to millions.[1] Hence a system is needed that could identify the potential serious patients and if possible start an effective treatment, before their condition turns more serious.[2]

COVID-19 has some unique patterns. Mostly the older population has serious disease—86% of the hospitalized patients are above the age of 50 years. However, up to 12% of the intensive care unit patients are less than 40 years of age. The mortality varies widely from less than 5% in individuals with no comorbidities to more than 90% in patients with critical illness, advanced age, and comorbidities. The average mortality in hospitalized cohorts varies from 16 to 29%.[1,3] A report from the Chinese Center for Disease Control and Prevention, which studied about 70,000 patients, has put the mortality in all the patients at 2.3%, which rises to 8% when the patients' age crosses 70 years and touches 49% in critical patients.[4]

A host of risk factors from age, sex, obesity, several comorbidities, clinical presentations, laboratory to radiological parameters have been associated with poor outcomes in the COVID-19 patients. The center for disease control and prevention and the American College of Cardiology (in a bulletin) have identified obesity, cardiovascular disease, hypertension, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, and cancer (hematological and pulmonary) as serious risk factors. On the contrary, patients without any risk factor have mortality of less than 1%.[2]

Among the laboratory and radiological values, high neutrophil counts, low lymphocyte count, high C-reactive protein, serum aspartate transaminase, lactate dehydrogenase level, serum ferritin level, and D-dimer level have all been related to the risk of developing ARDS and the risk of death.[5] Interestingly, cardiometabolic risk factors foretell worse outcomes than respiratory risk factors, this is contrary to other viral pneumonias.[6]

In this backdrop, Singh Y, et al. has published a prospective observational study comparing neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as parameters to predict the severity of the disease in COVID-19 patients.[7] Two hundred one patients of diagnosed COVID-19 pneumonia were divided into severe and nonsevere groups, based on mostly respiratory symptoms, signs, and support levels. The cell counts and their ratios were recorded on the first and the third day of the presentation. There were statistically significant differences in the NLR of the two groups on days 1 and 3. The authors conclude that the NLR was a better predictor of outcome than PLR. The mortality in the nonsevere group remained much lower (25.9%) than in the severe group (67.7%). The sensitivity and the specificity of the

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NLR could be enhanced when they were combined with other parameters, like the age, comorbidities, and initial respiratory support.

Even in the early reports of COVID-19, it was noted that the patients had lower lymphocyte counts. Studies reported that more than 80% of COVID-19 patients had lymphopenia.[8,9] In fact, it was shown that in the critically ill COVID-19 patients, 96.1% showed lymphopenia with a count below 1.0×10^9/L. This was attributed to the destruction of the T cells by the virus and also to the destruction of lymphoid tissues. There was also a relative increase in neutrophil counts as a result of inflammation. This resulted in the increased NLR values. It is to be noted that this ratio remains a dynamic value, which may change with time, disease state, and age of the patient.[10]

Several studies have also associated the NLR with the severity of the disease and its outcome. Wang et al. found significantly high NLR (13.87) in nonsurvivors vs low NLR (1.95) in survivors.[11] A meta-analysis that included a total of 828 patients corroborated such findings.[12] In line with our present article, a novel score based on hypertension, neutrophil count, C-reactive protein level, lymphocyte count, and lactate dehydrogenase level (HNC-LL score) enhanced the predictive power and proved itself to be better than the usual CURB 65 in predicting the outcome in the COVID-19 patients.[13]

The present study makes a case for itself. NLR is a simple and cheap test, which proves itself to be a useful tool to predict the outcome in COVID-19 patients. The accuracy increases substantially when combined with a few parameters, like age and comorbidities.

However, a few questions remain unanswered. In our present study in the nonsevere group, the mortality still remained at an uncomfortable 25.9%. The authors remain silent whether there was any significant difference between the NLR values of the survivors and nonsurvivors of this nonsevere group. Almost all the studies of therapies, which have made tangible differences in the outcome, have singularly used hypoxemia as the marker for intervention. The RECOVERY trial has demonstrated that the use of glucocorticoids before the development of hypoxemia will increase mortality.[14]

Can we use the NLR level to defy the RECOVERY protocol and use glucocorticoids earlier? Possibly not. One significant intervention in recent months has been the monoclonal antibodies. They have been shown to improve the mortality when given very early in the disease. However, they use a different list to pick out the high-risk patients, who are suitable for treatment.[15] Can we use NLR to pick out the high-risk patients for using the monoclonal antibodies?

NLR along with some clinical parameters prognosticate the COVID-19 patients well, but will they help us to change the prognosis?

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