India has recorded more than 89 million cases of coronavirus disease-2019 (COVID-19) so far with nearly 131,000 patients dying. The number of new cases showing resurgences in some areas as we approach winter and the festive season. This is going to be compounded by easing containment measures, across the country. Efforts of Herculean proportion are continuing worldwide to understand the epidemiology, pathogenesis, and treatments. Various labs across the globe are also racing to develop a vaccine. However, at the moment treatment remains supportive with oxygen therapy, steroids, repurposed antivirals, and prevention of multiple organ dysfunction by using immunomodulators. COVID-19 remains challenging since the disease spectrum varies from asymptomatic infection to severe acute respiratory distress syndrome (ARDS) with high fatality rates. It is thus necessary to predict clinical outcomes and risk-stratify patients for ensuring early intensive care unit (ICU) admissions. An important aspect is building surge capacity, managing and optimizing therapeutic and operational resources. So far, data have been scarce, particularly from India, to identify predictors of poor outcomes and mortality early in the course of the disease. Risk models need to be developed in larger patient cohorts and the models need to be simple and easy to employ at the onset of the disease process to predict the risk of severe disease, need for mechanical ventilation, ICU length of stay (LOS), and mortality.

**Keywords:** COVID-19, Predictors of mortality, Risk factors.

**Abstract**

Efforts are continuing worldwide to understand the epidemiology, pathogenesis, and treatments for coronavirus disease-2019 (COVID-19). However, at the moment treatment remains supportive with oxygen therapy, steroids, repurposed antivirals, and prevention of multiple organ dysfunction by using immunomodulators. COVID-19 remains challenging since the disease spectrum varies from asymptomatic infection to severe acute respiratory distress syndrome (ARDS) with high fatality rates. It is thus necessary to predict clinical outcomes and risk-stratify patients for ensuring early intensive care unit (ICU) admissions. An important aspect is building surge capacity, managing and optimizing therapeutic and operational resources. So far, data have been scarce, particularly from India, to identify predictors of poor outcomes and mortality early in the course of the disease.

In the current issue, of IJCCM, Chawla-Jain et al. reported retrospective data of 425 COVID-19 cases, where they tried to identify the risk factors predicting poor outcome. They had a predominantly male (73.4%) population with a median age of 49 (IQR: 21–77) years. Twenty-two (5.17%) patients died in the hospital. They found that the clinical variables age (>47 years (OR 4.52, 95% CI 1.5–13.6)), respiratory rate (>24 (OR 5.31, 95% CI 2.1–13.5)), oxygen saturation (<93% (OR 9.32, 95% CI 3.5–24.6)), diabetes (OR 2.70, 95% CI 1.14–6.4), and laboratory parameters, such as, lymphopenia (<12%) (OR 8.74, 95% CI 3.6–21.4), C-reactive protein (CRP) (OR 1.99, 95% CI 0.81–4.90), ferritin (OR 3.18, 95% CI 1.3–7.9), and lactate dehydrogenase (OR 3.37, 95% CI 1.4–8.2), were independent predictors of mortality. They then used 16 variables for constructing a training module and then tested it in subsequent patients. Using this logistic regression model, the module had an AUROC of 0.86 while the test module had an area under the receiver operating characteristics (AUROC) of 0.75. In this study, however, they do not mention other important variables, such as, the ICU length of stay (LOS), mechanical ventilation, and other ICU interventions.

Previous studies in different cohorts have shown that demographic data can predict higher mortality, such as, ethnicity, old age, gender, and comorbid conditions, such as, diabetes, hypertension, and obesity. Other admission characteristics, such, as, low oxygen saturation, tachypnea, renal and hepatic dysfunction, elevated procalcitonin, and lactate are now known risk factors for mortality.

COVID-19 infection may exhibit complex pathology with direct cellular injury along with abnormal host innate immune responses toward tissue and vascular endothelial injuries. This
can be consistently seen in various laboratory indices, such as, lymphopenia, i.e., exhaustion of the cytotoxic lymphocytes, eosinopenia, or neutrophil-to-lymphocyte ratio (NLR) which are strongly predictive of mortality.\textsuperscript{5-11}

The vasculitis and resulting thrombotic inflammatory syndrome manifesting as microthrombi in the pulmonary vasculature may also be pathognomonic. Elevated ferritin, troponin, CRP levels, and elevated D-dimer levels may also be useful in defining the problem and target therapeutic interventions, and assessing the response to treatment.\textsuperscript{12}

The persistent severe inflammatory state classically described as a “cytokine storm” with elevated IL-6 levels suggest poor outcomes. Patients who develop severe pneumonia with extrapulmonary manifestations, such as, myocardial injury, stroke, or acute kidney injury frequently have poor outcomes.

Various studies have looked at these variables and data sets and analyzed them with regression models to fit into survival models and have been able to predict mortality; however, they have not been extensively validated.

Future risk models need to be developed in larger patient cohorts and the models need to be simple and easy to employ at the onset of the disease process to predict the risk of severe disease, need for mechanical ventilation, ICU LOS, and mortality. However, it is also important to note that poorly validated or calibrated models may cause more harm than benefit. The current predictive models are more optimistic as they overfit the data and are mostly biased and non-transparent.\textsuperscript{13}

Objective scoring systems, such as, CT severity score or radiographic assessment of lung edema score and pleural effusions at the onset of disease process have shown to be early predictors of mortality. Although chest CT in high-risk patients to assess treatment response may not always be logistically possible.\textsuperscript{14}

These early predictors can significantly impact outcomes by shortening the time to hospitalization or early referral to the ICU for high-risk populations or predicting organ dysfunction which has shown to be associated with mortality.

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