EDITORIAL

# Crystal Gazing: Myth or Reality for Critical Care for COVID-19 Patients?

Shilpushp J Bhosale[1], Atul P Kulkarni[2]

## 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. 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.

*Indian Journal of Critical Care Medicine* (2020): 10.5005/jp-journals-10071-23694

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.[1,2] The data of 5,700 COVID-19 patients from New York showed that 373 patients (14.2%) needed intensive care unit (ICU) admission. Of these patients, 320 (12.2%) were invasively ventilated and 553 (21%) patients died. The early data from Italy showed that 12% of all positive cases needed ICU care. This was much worse than seen in the Chinese population, where only 5% needed admission to the ICU, with 2.3% being ventilated and only 1.4% died.[3–5]

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 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.[6]

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.[7,8]

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

[1,2]Department of Anesthesia, Critical Care and Pain, Division of Critical Care Medicine, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India

**Corresponding Author:** Shilpushp J Bhosale, Department of Anesthesia, Critical Care and Pain, Division of Critical Care Medicine, Tata Memorial Hospital, Homi Bhabha National Institute, Mumbai, Maharashtra, India, Phone: +91 9619310657, e-mail: shilbhosale@gmail.com

**How to cite this article:** Bhosale SJ, Kulkarni AP. Crystal Gazing: Myth or Reality for Critical Care for COVID-19 Patients? Indian J Crit Care Med 2020;24(12):1161–1162.

**Source of support:** Nil

**Conflict of interest:** None

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.[9–11]

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.[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.[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.[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.

## References


1. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020;382(13):1199–1207. DOI: 10.1056/NEJMoa2001316.
2. Mastaglio S, Ruggeri A, Risitano AM, Angelillo P, Yancopoulou D, Mastellos DC, et al. The first case of COVID-19 treated with the complement C3 inhibitor AMY-101. Clin Immunol 2020;215:108450. DOI: 10.1016/j.clim.2020.108450.
3. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York city area. JAMA 2020;323(20):2052–2059. DOI: 10.1001/jama.2020.6775.
4. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: Early experience and forecast during an emergency response. JAMA. 2020;323(16):1545–1546.
5. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. China medical treatment expert group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020;382(18):1708–1720. DOI: 10.1056/NEJMoa2002032.
6. Jain AC, Kansal S, Sardana R, Bali RK, Kar S, Chawla R. A Retrospective Observational Study to Determine the Early Predictors of In-hospital Mortality at Admission with COVID-19. Indian J Crit Care Med 2020;24(12):1174–1179.
7. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, et al. Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York city. BMJ 2020;369:m1966. DOI: 10.1136/bmj.m1966.
8. Feng Y, Ling Y, Bai T, Xie Y, Huang J, Li J, et al. COVID-19 with different severity: a multi-center study of clinical features. Am J Respir Crit Care Med 2020;201(11):1380–1388. DOI: 10.1164/rccm.202002-0445OC.
9. Giamarellos-Bourboulis EJ, Netea MG, Rovina N, Akinosoglou K, Antoniadou A, Antonakos N, et al. Complex immune dysregulation in COVID-19 patients with severe respiratory failure. Cell Host Microbe 2020;27(6):992–1000.e3. DOI: 10.1016/j.chom.2020.04.009.
10. Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G. Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a metaanalysis. Clin Chem Lab Med 2020;58(7):1021–1028. DOI: 10.1515/cclm-2020-0369.
11. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 inWuhan, China: a retrospective cohort study. Lancet 2020;395(10229):1054–1062. DOI: 10.1016/S0140-6736(20)30566-3.
12. Ciceri F, Beretta L, Scandroglio AM, Colombo S, Landoni G, Ruggeri A, et al. Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis. Crit Care Resusc 2020;22(2):95–97.
13. Wynants L, Van Calster B, Collins GS, Riley RD, Heinze G, Schuit E, et al. Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal. BMJ 2020;369:m1328. DOI: 10.1136/bmj.m1328.
14. Warren MA, Zhao Z, Koyama T, Bastarache JA, Shaver CM, Semler MW, et al. Severity scoring of lung oedema on the chest radiograph is associated with clinical outcomes in ARDS. Thorax 2018;73(9):840–846. DOI: 10.1136/thoraxjnl-2017-211280.