EDITORIAL

COVID-19: Epidemiology, Case Fatalities and the Adversaries within

Arun Kumar

Indian Journal of Critical Care Medicine (2021): 10.5005/jp-journals-10071-23869

The epidemiological dynamics of coronavirus disease-2019 (COVID-19) have changed ominously over the course of months. The current pandemic has unfolded with increasing illness, unpredictable outcomes, and devastating socioeconomic disruptions. The contagion has exposed the fallible nature of the human race and resulted in unprecedented surge in worldwide deaths.

As per the WHO COVID-19 Dashboard, dated May 1, 2021, there have been more than 150 million globally confirmed cases of COVID-19, including over 3 million deaths. India currently has the second-highest number of cases (nearly 18 million) after the United States and the fourth highest tally (>2 lakh) of cumulative deaths.[1]

The mortality statistics have varied across the borders, alienated by the timeline of the infection, demographic patterns, testing strategies, disaster response vis-à-vis containment and lockdowns, and healthcare system reserves and preparedness. The actual death toll may thus be way higher than currently being reported. As on April 27, 2021, the case fatality rate (CFR) for world has been reported to be 2.11%; whereas, Italy tops the list with 3.01% India has a reported CFR of 1.12%.[2]

A PubMed search at the time of writing this editorial, using Me SH terms "COVID-19 & Mortality" displayed more than 15,000 articles. The majority of these studies have been based on the hospital/ICU admissions, while few others have included local population[3] or the entire population.[4] Most of these studies have been designed to ascertain factors associated with adverse COVID-19 outcomes.

An earliest peek into the damaging impact of the current pandemic is the retrospective, multicenter cohort study from Wuhan, China published in Lancet during the near commencement of the pandemic (December 2019–January 2020). The potential risk factors for poor prognosis were interpreted as old age, high SOFA score, and d-dimer greater than 1 µg/ml. Sepsis was observed to be the most frequently complication, followed by respiratory failure, heart failure, and septic shock. The in-hospital mortality was reported as around 28%. A large proportion (97%) of the patient who required mechanical ventilation did not survive.[5]

The research paper from Lombardy region of Italy offered further insight into the pattern of these case fatalities. This retrospective, observational cohort study evaluated the risk factors associated with mortality. In a subset of first 1,715 patients, the ICU and hospital mortalities were 48.8 and 53.4%, respectively. The findings established lower survival for older men requiring invasive ventilation and those with pre-existing diseases. Hypertension was noted to be the most frequent comorbidity and was associated with reduced survival. A subsequent multivariable analysis, however, did not reveal hypertension as an independent factor associated with death. A history of chronic obstructive pulmonary disease, hypercholesterolemia, and diabetes was independently associated with mortality.[6]

In this issue of the journal, Richa et al., the authors of the study "*Clinicoepidemiological features and mortality analysis of deceased patients with COVID-19 in a tertiary care center*," have evaluated the patient demography and mortality risk among the SARS-CoV-2 infected patients, who required ICU admissions during the early phase (April 4, 2020–July 24, 2020) of the pandemic in India.[7] The criteria for ICU admission included; "severe disease," defined as tachypnoea (RR >30/m), or saturation <90% on room air, and/or patients with hemodynamic instability and/or encephalopathy, or patients with moderate disease with risk factors for severe disease. The authors have explored the age and gender distribution, presenting symptoms, the impact of comorbidities, median duration of ICU stay and possible causes of COVID-19 related deaths. A separate subgroup analysis of the pediatric admissions and cause of death is also presented. The retrospective study reports an ICU mortality of 37.7% among adult patients admitted to ICU with highest mortality among the age-group of 18 to 50 years (42.1%) followed by 35% in the 51 to 64 years group and 23% in above 65 years group. A higher mortality was found among males (65%). Most of the deceased were found to have hypertension followed by diabetes and chronic kidney disease. The median SOFA score at admission was reported as 9.3. The most common cause of death in their analysis was sepsis with multi-organ dysfunction (55.1%) followed by severe ARDS (25.5%). The ICU mortality among the pediatric population has been reported to be 13% with most common cause of death being ARDS followed by sepsis with multi-organ dysfunction.[7]

Department of Intensive Care, Medical Intensive Care Unit, Fortis Healthcare Ltd, Mohali, Punjab, India

Corresponding Author: Arun Kumar, Department of Intensive Care, Medical Intensive Care Unit, Fortis Healthcare Ltd, Mohali, Punjab, India, Phone: +91 9872828779, e-mail: arun.udhv@gmail.com

How to cite this article: Kumar A. COVID-19: Epidemiology, Case Fatalities and the Adversaries within. Indian J Crit Care Med 2021;25(6):603–605.

Source of support: Nil

Conflict of interest: None

A systemic review and meta-analysis by Tian et al., further establishes the presence of comorbidities including coronary artery disease, hypertension, or diabetes with significantly higher risk of death among COVID-19 patients.[8]

In another study by Keller et al., the underlying conditions including cardiovascular disease, obesity, and diabetes have been reported as being associated with higher risk of COVID-19 infection and ICU admission.[9]

The European Centre for Disease Prevention and Control (ECDC) reports cardiac disorder, diabetes, and cancer as the leading conditions among COVID-19 related fatalities.[10]

A more recent research paper published in THE LANCET *Regional Health* provides a population based, nationally representative perspective of COVID-19 confirmed cases across all settings in Ireland. The study also suggests that male gender and the presence of chronic underlying condition specifically chronic heart disease, asthma requiring hospitalization, and a BMI >40 kg/m^2 were associated with increased risk of mortality and hospitalization.[11]

The present-day figures across the countries evidently suggest and link the presence of an underlying condition with worse COVID-19 infection related outcome. The elderly are most vulnerable due to higher prevalence of pre-existing cardiovascular or respiratory conditions. The gender predisposition to adverse outcomes among males has been attributed to behavioral/ lifestyle risk factors, immunological and hormonal differences, including the variable expression of angiotensin-converting enzyme 2. There are data to suggest that men with COVID-19 display greater upregulation of inflammatory cytokines, thus becoming susceptible to fierce cytokine storm and higher case fatality.[12,13]

India, currently, is home to about 80 million diabetics-2 and nearly 53 million patients with cardiovascular diseases. This is a sizeable pool of people who fall in the category of high risk patients with predisposition for severe COVID-19 disease.[14,15]

The epidemiological parameters pronouncing the probability of death due to COVID-19 are relevant to us for understanding the risk factors and to respond appropriately by directing our resources toward the most vulnerable sections of the society. The CFR, which is the ratio of confirmed death to confirmed cases, is a frequently reported parameter to measure the mortality risk associated with the current pandemic. The CFR, however, has been reported to have significant limitations especially during the evolving phase of any pandemic. It is known to vary by location, characteristics of population, and evolving standard of care over a period of time. Fallacies (over/ underestimation) may be noted based upon the scale of testing, and unpredictable outcome (recovery or death) of significantly large number of cases at a given point in time. The CFR may thus not be a true reflection of risk of death and should be carefully interpreted.[2]

The pattern of COVID-19 disease is changing and the resurgence is effecting the younger population more than seen with the first wave. The healthcare systems are currently overwhelmed with the spate of new cases requiring medical attention. A serious public awareness is warranted to contain the spread of the disease and to reduce the fatalities, especially among those at high risk. Judicious infection control practices are warranted to prevent secondary infections and resultant mortality in hospitalized critically ill patients with COVID-19.

A review of the disease pattern in last few months of resurgence and comparative studies highlighting the differences in the presentation of the disease and clinical outcomes would be worth the effort. Furthermore, larger studies representative of the total population are required to evaluate the true infection fatality rate and to provide further insights into the pathogenesis of the disease. The new knowledge assimilated by such studies would assist us to further refine our knowledge and understanding of this disease.

Orcid

Arun Kumar https://orcid.org/0000-0001-6522-007X

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