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## Implications of the second wave of COVID-19 in India

The second wave of COVID-19 in India has had severe consequences in the form of spiralling cases, reduced supplies of essential treatments, and increased deaths particularly in the young population. Understanding why the second wave has been more dangerous than the first could help to identify the potential areas of diagnostics to target with future control strategies.

Studies have identified various circulating double-mutant and triple-mutant strains of SARS-CoV-2 across different regions of India, which are more pathogenic than the initial strains. Such altered transmissibility and pathogenicity indicates evolution of the virus. The larger the population density, the higher are the chances of viral replication, mutation, and evolution, as suggested by Moya and colleagues.<sup>1</sup> India's overpopulation and poor execution of a coherent containment strategy and policies have allowed a substantial number of viral mutations to persist in the environment. The earlier discovered variants in other countries, such as B.1.351, B.1.1.7, and P.1, as reported by Boehm and colleagues,<sup>2</sup> are also circulating within India along with the new variants. The SARS-CoV-2 double-mutant strain B.1.617, possessing the key structural mutations Glu484Gln and Leu452Arg in the spike protein, is highly infectious and less affected by current vaccine responses, and is a central cause of the COVID-19 surge in India.<sup>3</sup> Similarly, Sahoo and colleagues<sup>4</sup> reported the presence of a triple-mutant strain, B.1.618, carrying the potent mutations Glu154Lys, Pro681Arg, and Gln1071His in addition to others, that is also strongly associated with India's deteriorating COVID-19 situation.

During the second wave in India, many cases of mucormycosis, also

known as the black fungus, have been reported in patients with diabetes and patients with COVID-19, as well as patients who were recovering from infection. The excessive use of steroids in the treatment of COVID-19 and immunosuppression by the virus led to the emergence of this opportunistic fungal infection.<sup>5</sup> Although cases of black fungus were reported during the first wave, cases during the second wave have become more prominent in many cities of India, leading state governments to declare this too as an epidemic. As of June 7, 2021, the Indian Ministry of Health had recorded 28 252 cases of black fungus. The risk of the white fungus *Aspergillosis*—assumed to be even more fatal than the black fungus—is also on the rise with some cases reported in parts of India.<sup>6</sup>

Patients in the first wave infected with SARS-CoV-2 were predominantly older than 60 years and those with comorbid conditions were at increased risk of death. However, surprisingly, younger adults appear to be prone to infection during this latest cycle and many patients have died at a young age, including patients aged between 25 and 50 years.<sup>7</sup>

The reason why the younger population is now more vulnerable to SARS-CoV-2 is not apparent and beyond current scientific explanations. However, an important observation as the situation develops is that every individual appeared to have equal risk of being infected with the virus, but the ability to sustain and overcome infection was variable among individuals. Some people with presumed suboptimal immune responses could survive, and some individuals, despite having presumed stronger immunity, could not overcome the rapid infection. A further observation in the peak of the second wave was the sudden decrease in the oxygen saturation of some patients, even when they were recovering well, giving less time for the proper ventilation support. This situation

created fear and panic among patients and family members as there was uncertainty around whether the patients would survive the viral infection even when showing signs of recovery. No answers are available as to why individuals respond differently to SARS-CoV-2 infection. Many reasons could be behind this observation. One explanation could be the presence of different strains of the SARS-CoV-2 that infect individuals simultaneously, with some variants more pathogenic than others. India's poor air quality index could be a potential factor as to why spread of the infection has been severe across the country. Comunian and colleagues reported that an increase in fine particulate matter (<2.5 µm) is associated with increased risk of COVID-19 infection.<sup>8</sup> Given that nine of the 15 most polluted cities globally are in India, it could be postulated that the ability of the Indian population to fight against COVID-19 is impaired because people's lungs are severely affected by the air pollution. A further reason could be the presence of different immune responses among individuals; and someone who appears healthy might not have a strong or potent enough response with regard to immunity. However, absence of scientific studies



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on individual immune responses limits our reasoning for this hypothesis.

A crucial reason for increasing deaths among individuals who appear healthy enough to overcome SARS-CoV-2 infection could be that these individuals are prone to the effects of cytokine storms. Therefore, we propose that, in addition to focusing research on drugs and vaccines to fight against the current pandemic situation, prediction models will be essential to our understanding of why specific individuals are more vulnerable to developing a cytokine storm. By monitoring probable outcomes that are based on recovery possibilities among individuals, we could help to

save millions of COVID-19 patients worldwide by providing better-prioritised treatment. Identification of immune-based markers (eg, numbers of T-cells and their subsets, B-cells, and natural killer cells, or protein markers such as interleukins 6 and 10, ferritin, C-reactive protein, and procalcitonin) to pre-empt the possibility of recovery among COVID-19 patients will also help in the focused treatment of patients. These markers might be linked to severe and mild forms of COVID-19 infection. As such, assessing individuals for variations in protein expression levels as indicators of disease prognosis and severity could provide a robust method to protect individuals based on personalised diagnostics.

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