



COVID19 Surge in India - What we Know so Far

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India is now facing a daunting task of battling the raging COVID-19 surge. It is second wave of infection that has rapidly surpassed its first wave in 2020 in terms of the number of new cases and deaths per day. Rates in India trended down significantly during fall and winter with a complete drop in January. However, March and April had some large public gatherings of thousands of people due to religious activities and political rallies in several states probably leading to dissemination of virus. The country has been recording more than 300,000 cases of COVID-19 per day since April 21, up from 100,000 per day on April 4. These numbers eclipse India's previous highest number of new cases reported in a single day, at 97,860 cases on Sept 16, 2020. Fully opening up with unrestrained crowding, mass gatherings, large scale travel, and lack of personal protective measures such as masks, lack of a concrete national containment, surge and vaccination strategy have all contributed to this very preventable situation. Shortages of Medical oxygen, beds, pharmaceuticals like Remdesivir and Tocilizumab has made the situation even more challenging. Lack of preexisting vaccine procurement contracts are leading to shortages of life saving vaccines at a critical time.

Variant of concern B.1.617.2

B.1.617, a COVID19 virus variant first detected in India and is now one of the dominant strains in the country along with B.1.17(the variant first identified in UK). B.1.617 has also been detected in 60 other countries, including the United States. The virus is also called the double mutant by mass media due to following two concerning mutations appear together for the first time:

- **L452R:** A mutation also found on CAL.20C (variant first detected in California). Research has shown that L452R is about 20% more transmissible.

- **E484Q:** This is very close to the E484K mutation on the B.1.351 (S. Africa) and P.1 (Brazil) variants. We know that E484K is an escape mutation. This means it reduces the number of neutralizing antibodies from vaccinated and unvaccinated people.

By December 2020, 271 million people in India were already considered naturally infected from the first wave. Once B.1.1.7. and B.1.617 spread rapidly due to several reasons as detailed above, India was devastatingly hit with its biggest surge yet. This happened in Brazil too. Hence, natural immunity from infection is short lived and is all the more reason to get our patients vaccinated.

The obvious question would be "does vaccine induced immunity protect us against the B.1.617 variant?". Data is limited given this is a novel strain. The bench studies so far for certain vaccines like Covaxin and Astra Zeneca/COVI Shield indicate that even though there is a decrease in neutralizing antibody titers for the variant virus compared to the wild virus, the vaccines are still able to stand ground with reasonable immunogenicity. Real world data regarding vaccine efficacy coming in from India and several countries seem to reaffirm this finding from bench studies. There is also limited data indicating efficacy of the mRNA vaccines with the variant too. However, knowing what we know with other variants, vaccine induced immunity against variants is definitely successful in preventing hospitalization and deaths which are the endpoints which matter the most.

Current situation in India

As of May 23, 2021, there have been about 26 million cases and 300000 deaths reported in India so far. The country is reporting 4000 deaths per day. The positivity rate had declined to 14.2%.

Only 3% of the population is fully vaccinated and vaccine shortages have led to decline in the rates of vaccination. Most large Indian states are under strict lockdown.

New emerging and concerning infections disease condition is the uptrend in incidence of a very rare, rapidly progressive, life threatening aggressive fungal infection- rhino cerebral and ocular mucormycosis in patients recovering from COVID-19. India has reported more than 9000 cases in the last 2 weeks and has now been made a notifiable disease. Indiscriminate use of steroids has been implicated as one of the reasons for the same. However, these cases are being seen in patients who have never been treated with steroids. These previously non-diabetic patients were found to have severe hyperglycemia during the diagnosis. The condition being endemic and limited to COVID19 patients in the Indian sub-continent makes it even more puzzling. This is an evolving situation and now being studied by various groups.

What can be done by the rest of the world?

We live in a global world and the fight against this invisible enemy is a global one. The PAN in the pandemic itself implies that we are not safe until all of us are safe from the virus. The Indian government needs to step it up on several fronts with a national strategy to combat the current crisis. The urgent need is to save as many lives as possible. India needs donations of oxygen concentrators, ventilators, medications, vaccines, high-quality personal protective equipment (PPE), and SARS-CoV-2 diagnostic tests. The international community can help support the public and private sectors with the scale-up of oxygen production and transport of oxygen and medical supplies over large geographical areas. PAMed has a considerable membership of physicians of Indian origin and many of them are involved in these efforts. Many of them have family and friends impacted by this virus and some have lost loved ones.

Global partners must support expanded access to COVID-19 vaccines in India and other countries. India's shortage in vaccine supply is projected to last until July, 2021. The Serum Institute of India (the world's largest vaccine manufacturer) is a major contributor to COVAX, the global alliance for COVID19 vaccination. India's current crisis has forced the country to prioritize vaccinating Indian citizens over supplying COVAX with vaccines. This shift will likely delay vaccines reaching other low-income and middle-income countries. The international community should release its surplus

COVID-19 vaccine stockpiles to India and other countries that are facing COVID-19 surges. The Biden Administration has pledged to release the unused AZ vaccine doses to Low and Middle income countries which is a welcome step. High-income countries (HICs) must waive intellectual property rights on COVID-19 vaccines, lift road blocks to raw materials needed for vaccine manufacture, and support technology transfer to increase global vaccine manufacturing. It is also imperative to support India and other LMICs in efforts with genomic sequencing and surveillance to quickly identify concerning trends. Several of our physicians in the US have provided informal advice to their counterparts from India to help manage challenging cases.

Vaccination is our only sure path out of this pandemic and to avoid the current Indian scenario happening elsewhere. We need to continue educating our patients and try to convince the reluctant ones to pursue the vaccine to safeguard themselves, their families and their communities. Meeting patients where they are goes a long way in this venture.

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