

*Editorial*

# Omicron in Delta dominant India: Implications and outcome

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Every virus mutates and so does SARS-COV-2, as we have seen it move from the original Wuhan strain to Delta. The ancestral strain was responsible for India's first wave and the rapidly spreading Delta for India's second wave of the COVID-19 pandemic. The Delta then went on to become the most dominant strain on earth and currently is the primary strain driving the current pandemic. Alpha originally came in September 2020 in the United Kingdom, Beta around a similar time in South Africa, Gamma in Brazil came a little later but it was the Delta that is now swept across the globe. Delta has a RO around 9 like chickenpox compared to 3.5 of the ancestral strain, making it fast-spreading, but it also has a faster recovery.<sup>[1]</sup> Due to larger numbers, Delta leads to exponentially high numbers stretching healthcare systems across the world. B.1.1 lineage in the virus phylogenetic tree possibly evolved in 2020 but suddenly in November 2021, we saw in Botswana, South Africa, and Hongkong report cases of B.1.1.529 lineage which got red-flagged as a potential new variant. Genomic scientists suddenly saw more than 30 mutations on the spike protein, 10 mutations on the entry receptor the ACE2 as well as a cluster of mutations at the cleavage sites, nucleocapsid protein, etc., which all totaled above 50, this constellation of mutations made B.1.1.529 look sinister and deadly.<sup>[2]</sup> The large constellation of mutations conferred this new strain the potential to spread ultra rapidly in some provinces of South Africa like Gauteng and a span of 2 weeks replaced the dominant Delta strain completely which leads the WHO to take note of the strain to consider it as a variant of concern and label it as "Omicron" after Delta. The WHO team skipped the Greek alphabets "Nu" and "Xi" due to taxonomy rules which do not allow common terms or relationships with common ethnic surnames and labeled it as "Omicron." The origin of the strain biologically as well as its country of origin is still unknown. The geography of its origin is likely from a low exposure one where the surveillance system is weak and only time will tell us if Botswana or other neighborhood places around South Africa were the places where original Omicron was born or it was

also there in Europe. The evolution of the strain is also an enigma as it is speculated that possibly the virus mutated in an immunocompromised host where it stayed longer in the body in a chronic state from where it spilled over.

Omicron is rapidly spreading, clinically appears to be similar to Beta strain as per early reports from South African clinicians who claim most cases have mild symptoms of fatigue, sore throat, cough, and fever but an absence of lack of smell or taste and rarely deteriorates. Omicron is now driving the fourth wave of South African pandemic after first from ancestral strain, second from Beta, and third from Delta. The rationale why the WHO labeled it as the variant of concern was as Omicron displaced the dominant Delta strain in South Africa in <2 weeks and now has led to an explosion of cases across the whole of South Africa with community spread.<sup>[3]</sup> The explosive rise in the number of cases as well as the increasing number of hospital admission is worrisome. The only current silver lining is the lack of rising of critical cases as well as death but it is too early to comment on the current wave.

Omicron is born in a time world in vaccination mode with different platforms. South African Beta strain had shown a very clear immune escape to adenovector vaccine from AstraZeneca, namely, the Oxford Chad-ox one, and they adopted mRNA platform with Pfizer-BioNTech as well as Jansen Adenovector platform in their vaccine program. At present, only one-third of South Africa is vaccinated and it is unknown if Omicron will have immune escape both to natural infection leading to reinfection or even to vaccination. Early virological plausibility of reinfection is likely from Omicron as well as the threat of immune escape. The current COVID-19 pandemic now clearly is ravaging in Europe and the USA is driven by the Delta strain predominantly in the partially or unvaccinated population. Omicron in less than a month has rapidly spread to more than 30 countries though many have unfairly targeted South Africa with travel bans. Omicron tells us the COVID-19 pandemic which was heading for an endemic state is not over and till we do not vaccinate every

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**Received:** 06 December 2021 **Accepted:** 06 December 2021 **Published:** 23 December 2021 **DOI** 10.25259/IJMS\_561\_2021

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geography, every human on planet earth we will not be able to make the world safe from the SARS-CoV-2 virus. Vaccine equality is the key to ending the COVID-19 pandemic.

Omicron relies on genomic testing for which a sophisticated laboratory network is needed which South Africa had but is not universally available across the globe. However, South Africa showed us that a full RT-PCR test when done for *s*, *n*, *e*, or other genes shows an S gene deletion in the system which can be used to red flag the presence of Omicron as a screening tool for further testing. Genome testing of Omicron is unraveling many speculations which need validation in human host clinical behavior of Omicron in the human host will be the key to the outcomes which will only be known in next few months. Thus, the virulence, severity of disease, mortality, immune escape, or response to drugs or vaccines of Omicron are all currently in the realm of speculations without evidence till proper data emerges.

India in early December is seeing the thinning of the small tail of its second wave in scattered geographies of Kerala, South West India, and North East with <10,000 cases being reported per day. Due to large exposure to Delta strain, various sero surveys across metropolitan cities such as Mumbai and Delhi as well as urban-rural India and adult and pediatric populations have revealed seropositivity rates ranging from 70% to 90% which indicate some form of herd immunity threshold.<sup>[1]</sup> Furthermore, India has currently vaccinated fully 40% of its population and more than 126 crores have received at least one dose. Thus, the large Indian population now has exposure both naturally or vaccine-induced hybrid immunity, and the third wave appears most unlikely except if a new variant of concern like Omicron now displaces the dominant Delta strain. The present Indian genomic surveillance reveals Delta derivatives with a lot of diversity but clinical and mortality outcomes are driven essentially by age, comorbidities, and immunocompromised states. Mortality in India is driven by an unvaccinated population or comorbidities or delayed seeking of medical care and the aim is toward zero COVID-19 mortality.<sup>[1]</sup> The use of a monoclonal cocktail of antibodies such as casirivimab plus imdevimab (half dose) has altered clinical outcomes of severe disease if used early though the cost is the rate-limiting step of routine use in high-risk vulnerable groups. The role of prophylaxis of these cocktail antibodies is also being investigated. Better early age antivirals such as molnupiravir are undergoing combined Phase 2–3 trials in India which are awaiting regulatory approval. There is a clear need for extra vaccine dose either called additional or booster dose is medically indicated cohorts such as moderate to severe immunocompromised states, comorbidities, the elderly, and people who are working in health care as well as frontline who have high exposure to

the circulating virus. The need to generate India-specific data on mix and match, additional dose, as well booster dose is necessary. Indian COVID-19 vaccine innovations of DNA vaccine from Zydus, nasal vaccine from Bharat Biotech, and mRNA vaccines from Emcure as well as India being a hub to make global vaccines such as CoviShield or subunit vaccines from Serum Institute will be the ones to look out for in 2022. Indian manufacturers have an alliance with Merck (MSD) to make molnupiravir and many manufacturers such as Biocon now make their monoclonals such as CD 6 itolizumab or Adagio in early space as therapeutic antibodies which will generate Indian evidence in near future. India is the vaccine and generic pharmacy of the world and Indian Science agencies have an opportunity to generate a high-impact evidence base to counter the future outbreaks of COVID-19. Pandemic preparedness plans both of center and states are in place with lessons learned from the second wave. The unique lessons from Mumbai's Dharavi model as well as the decentralized approach of the Mumbai model in the second wave are innovations in public health which are case studies by themselves now globally.

Omicron threatens to disrupt the global pandemic predictions and will need a strong global will to counter it. India like many countries is seeing now travel-related sporadic cases with microclusters that will need tight containment. Inbound global travel will need super vigilance, voluntary participation of travelers, and behavior change of people. A combined strategy of people participation with regulatory compliance only can make us counter the inbound threat of Omicron. At present, only responsible behavior, double masking, and vaccination seem to be the only answer to Omicron which threatens to disrupt the world and displace Delta strain on the earth. Omicron is an airborne droplet and will clear allow us to refocus on air ventilation apart from COVID appropriate behavior. Vaccination will still hold the key across as new variants emerge like Omicron.

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**How to cite this article:** Joshi S. Omicron in Delta dominant India: Implications and outcome. *Indian J Med Sci* 2021;73:287-88.