

## COMMENTARY

# Twin combination of Omicron and Delta variants triggering a tsunami wave of ever high surges in COVID-19 cases: A challenging global threat with a special focus on the Indian subcontinent

Ranjan K. Mohapatra<sup>1</sup>  | Ruchi Tiwari<sup>2</sup>  | Ashish K. Sarangi<sup>3</sup>  |  
Sanjay K. Sharma<sup>4</sup> | Rekha Khandia<sup>5</sup>  | G. Saikumar<sup>6</sup>  | Kuldeep Dhama<sup>6</sup> 

<sup>1</sup>Department of Chemistry, Government College of Engineering, Keonjhar, Odisha, India

<sup>2</sup>Department of Veterinary Microbiology and Immunology, College of Veterinary Sciences, Uttar Pradesh Pandit Deen Dayal Upadhyaya Pashu Chikitsa Vigyan Vishwavidyalaya Evam Go Anusandhan Sansthan (DUVASU), Mathura, Uttar Pradesh, India

<sup>3</sup>Department of Chemistry, School of Applied Sciences, Centurion University of Technology and Management, Bhubaneswar, Odisha, India

<sup>4</sup>Department of Chemistry, JECRC University, Jaipur, Rajasthan, India

<sup>5</sup>Department of Biochemistry and Genetics, Barkatullah University, Bhopal, Madhya Pradesh, India

<sup>6</sup>Division of Pathology, ICAR-Indian Veterinary Research Institute, Bareilly, Uttar Pradesh, India

## Correspondence

Ranjan K. Mohapatra, Department of Chemistry, Government College of Engineering, Keonjhar 758002, Odisha, India.  
Email: [ranjank\\_mohapatra@yahoo.com](mailto:ranjank_mohapatra@yahoo.com)

Kuldeep Dhama, Division of Pathology, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly 243 122, Uttar Pradesh, India.  
Email: [kdhama@rediffmail.com](mailto:kdhama@rediffmail.com)

## Abstract

The emergence of Omicron (B.1.1.529) variant of SARS-CoV-2 has resulted into a very massive surge in COVID-19 cases worldwide. Due to continuous emergence of multiple variants of SARS-CoV-2, the ongoing pandemic has caused severe morbidity and mortality in last two years. The rate of infectivity of Omicron variant is much higher than Delta variant and in a very quick time Omicron has displaced the Delta variant and now become a dominant variant across the globe. The twin combination of Omicron and Delta variant is triggering a Tsunami wave of ever high surges in COVID-19 cases worldwide. This article highlights the global threats and challenges posed by Omicron, and strategies to counter it with a particular focus on Indian sub-continent.

## KEYWORDS

COVID-19, Omicron & Delta, SARS-CoV-2 VoCs, winter

Due to the continuous emergence of multiple variants of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the coronavirus disease 2019 (COVID-19) pandemic has caused severe morbidity and mortality worldwide in the last 2 years amidst waves of the pandemic within the ongoing pandemic, resulting in high global health concerns and adverse socioeconomics impacts.<sup>1-4</sup> Omicron, the recent highly mutated SARS-CoV-2 variant (B.1.1.529), classified as a variant of concern (VoC) by the World Health Organization on November 26, 2021, is now becoming a dominant strain in several

countries and a very massive surge in COVID-19 cases is being faced presently with nearly 300 million cumulative cases and 5.5 million deaths reported as of January 5, 2022.<sup>3,5-9</sup> This variant exhibits multiple mutations in viral spike (S) protein's receptor-binding domain (RBD) and N-terminal domain region, hence associated with more efficient cell entry, immune evasion, and greater infectivity.<sup>10</sup> The effective reproduction number of Omicron has been reported to be 3.19 (95% confidence interval 2.82–3.61) times higher as compared to the Delta variant; therefore, a rapid increase in Omicron cases may

be seen as soon as it is introduced and established itself in the population of a country.<sup>11</sup> Omicron has been found to be partially resistant to COVID-19 vaccine-induced immunity and overpowering key antibody-based immunotherapies.<sup>12–14</sup> As the mutations help the virus to partially evade the immune responses, the present COVID-19 vaccines are less effective to prevent infection with Omicron; thus, a large number of breakthrough infections are being reported in vaccinated individuals worldwide.<sup>15,16</sup> The Pfizer-BioNTech has suggested a booster dose after two existing vaccine doses, which may potentially provide protection of up to 25% against the Omicron variant. Moderna also pointed to a third vaccine dose, which may increase protective antibody levels of the body to fight against infection with Omicron. The Omicron variant is observed to replicate more than 70 times in human bronchus, but less efficiently in the lung tissue as compared to the Delta variant.<sup>17</sup> As per the report, the Omicron RBD binds to human angiotensin-converting enzyme 2 receptors with enhanced affinity.<sup>18</sup> The lower replication ability in human lung suggests less disease severity of Omicron as compared to the Delta variant. The immunity induced from the COVID-19 vaccines, booster doses, and previous SARS-CoV-2 infections may be the possible reasons for lower hospitalization and mortality in Omicron cases, and lastly, the newer variant being of mild nature as compared to other variants such as Delta.<sup>19,20</sup>

The previous variants (Alpha, Beta, and Delta) have caused consecutive waves of COVID-19 across the entire world,<sup>4,21,22</sup> so the researchers are now speculating a new wave of the ongoing pandemic due to the Omicron variant owing to its very high transmissibility with the doubling time to be 1.5 to 3 days.<sup>23–25</sup> The world has witnessed the devastating effects of the third wave of COVID-19 pandemic a few months back, wherein particularly the delta variant lead to a high surge in cases owing to its high transmission rates, ability to cause severe disease, reinfection, causing severe breakthrough infections in vaccinated individuals, and especially affecting nonvaccinated and vulnerable persons severely, altogether adding to the massive rise in the number of deaths worldwide.<sup>22,26–28</sup> As per the studies, Omicron cases may not be posing severe illness, especially for vaccinated people and those who have received a booster shot.<sup>29–31</sup> Although, until now, the Omicron variant is considered as milder as compared to previous SARS-CoV-2 VoCs such as Delta, however, much is yet to be known about this newly emerged variant; infected individuals can transmit it potentially to the vulnerable population and to those who are immunocompromised, elderly, suffering from comorbid diseases, and coinfections, and even if such persons may be vaccinated, omicron infection might result into complicated illness or deaths as has been observed earlier with infection from SARS-CoV-2 and its variants in such highly susceptible population.<sup>32–34</sup> It should also be kept in mind that despite the current assumption on Omicron causing low-to-mild disease severity with lesser requirements of hospital admittance, the chances of acquiring Omicron infection in the household and community settings are much higher than that of the Delta variant due to its very high transmission rates, and the scenario of the vulnerable population getting infected more and more may lead to alarming health concerns

worldwide as the number of cumulative deaths will increase globally.<sup>11,20</sup> Omicron and Delta variants, both possessing higher transmissibility, posing threats on the efficacy of vaccines and causing breakthrough infections in vaccinated individuals, may together bring a tsunami of COVID-19 cases in the coming weeks, and then hospitalizations and death rates might also rise significantly.<sup>22,27</sup>

Omicron was first identified in India on November 25 and is now detected in most of the states in a very quick time and may soon dominate over the Delta variant.<sup>5</sup> As on January 5, 2022, India reported nearly 2200 Omicron cases, and most importantly, Omicron-infected persons are already vaccinated. So, we are afraid that whether two doses of COVID-19 vaccines is enough to counter this new variant.<sup>29</sup> In this context, several countries such as the United States and the United Kingdom have provided booster doses to their people to mitigate the spread of the Omicron variant. Israel also declared to provide the fourth dose of vaccine to their citizens. In the meantime, Bharat Biotech sought approval from the Drug Controller General of India to conduct the Phase-III trial of intranasal booster dose of its vaccine for COVID-19. The government has also approved Corbevax and Covovax vaccines to be included in the vaccination program in India. The Indian scenario is unique as only 44.0% of the people are fully vaccinated, while 61.4% of the people have received the first dose in India as on January 1, 2022 ([https://www.google.com/search?q=covid+vaccination+graph+india&ei=Ce7FYa-pDr6G4-EpJbyT8A0&oq=covid-10+vaccination+graph+india&gs\\_lcp=Cgdnd3Mtd2l6EAEYADIFCAAQzQl6BwgAEEcQsAM6CggAEEcQsAMQyQNKBAhBGABKBAhGGABQnQlY2RZgu0loAXAcECAAaY-CiAGXCpIBAZItNzgBAKABAcgBCMABAQ&scit= gws-wiz](https://www.google.com/search?q=covid+vaccination+graph+india&ei=Ce7FYa-pDr6G4-EpJbyT8A0&oq=covid-10+vaccination+graph+india&gs_lcp=Cgdnd3Mtd2l6EAEYADIFCAAQzQl6BwgAEEcQsAM6CggAEEcQsAMQyQNKBAhBGABKBAhGGABQnQlY2RZgu0loAXAcECAAaY-CiAGXCpIBAZItNzgBAKABAcgBCMABAQ&scit= gws-wiz)). Very recently, the vaccine booster programme is being initiated in India from January 10, 2022, especially for medical doctors, health care and frontline workers, and the elderly people over 60 years of age (<https://www.reuters.com/world/india/india-give-covid-19-booster-shots-healthcare-workers-jan-10-2021-12-25/>; <https://timesofindia.indiatimes.com/life-style/health-fitness/health-news/india-to-roll-out-precaution-booster-dose-for-60-above-what-is-the-required-gap-between-the-second-and-the-third-shot/photostory/88545838.cms?picid=88545852>). India is the second most populated country and the people need to certainly obey the recommended COVID-19 safety measures and guidelines to limit the spread of the Omicron variant. Due to the evolution of the Delta variant of SARS-CoV-2, the second wave of COVID-19 pandemic was initiated in India, while the third wave is being faced in several countries; the second wave in India during the first half of this year caused a massive surge in COVID-19 cases and associated deaths and created a very high panic and fear.<sup>9,22,35</sup> The rate of infectivity of Omicron is much higher than the Delta variant. So, Omicron may likely displace Delta as the dominant variant in the coming weeks in India. The new variant (Omicron) spread very rapidly to almost all the continents of our planet with 140 countries and territories reporting nearly 0.5 million cases and 111 deaths due to Omicron, and the global tally of cumulative COVID-19 cases has crossed an ever high mark of 2 million cases per day and has broken all the previous records during this week as of January 5, 2022.<sup>8,9</sup> Genomic sequencing is being

performed on only a small number of COVID-19 cases, hence the actual number of Omicron cases might be significantly higher, and this variant is spreading more and more continuously into the population.<sup>8</sup> India's tally of COVID-19 cases has very recently seen a rise of nearly eight times, from around 7000 to over 58,000 cases in the past few days as of January 5, 2022 with a rapid surge in Omicron cases (<https://www.mygov.in/covid-19/>, accessed on January 5, 2022).<sup>9</sup> The United States, Canada, and the European countries (Britain, Denmark, France, Italy, Spain, and Switzerland) are facing serious surges in COVID-19 cases this time. As per the provided data, the Omicron variant is found in 58.6% of all new infections in the United States in the last week of December, 2021. In India and other countries winter season has started, which may predispose to rising cases of Omicron,<sup>10</sup> so the most dangerous phase is knocking in the coming weeks, which will bring a triple respiratory virus threat; Delta, Omicron with seasonal flu. During the previous year, a high surge of COVID-19 cases was observed may be due to Delta and the winter season. Hence, the government, physicians, and the public must be careful and robust efforts are needed to mitigate the present challenges of Omicron and surges in COVID-19 cases in India. It is highly recommended to enhance the surveillance and gene sequencing efforts to understand the circulation of the new variants. India confirmed the first Omicron-associated death in a person having a travel history to Nigeria, who was a 52-year-old man (had diabetes for the last 13 years) and had died of a heart attack. During the last week, the global COVID-19 cases have risen by 11% and the WHO warns of a very high Omicron risk worldwide. Moreover, only 5.8% of booster doses are given globally as on December 21, 2021.

The children and younger students are not vaccinated yet in India as only very recently COVID-19 vaccination has been announced to be started for 15–18 years age group from January 3, 2022, so as to avoid Omicron infection to this category of the younger population in India. After the second wave, Indian schools and colleges were reopened and regular classes are going on with COVID-19 guidelines. However, a significant number of COVID-19 cases is regularly reported in several Indian schools and colleges. In this context, 53 girl students of St. Marys Girls High School, 54 medical students of Veer Surendra Sai Institute of Medical Sciences and Research (VIMSAR), and 16 students of Maha school were infected with COVID-19 recently.<sup>5</sup> As Indian school settings are different, it is really challenging to obey COVID-19 guidelines fully by students in schools and colleges.<sup>36</sup> The Omicron variant is now potentially circulating throughout the country and may be responsible for another fresh wave (the so-called third wave) in the coming weeks. Moreover, the current vaccines are reported to be less effective but still provide some protection against Omicron, and adding up of booster doses will increase the protection level to avoid breakthrough infections and disease severity. A massive awareness programme for the general public for convincing them to take up a full course of vaccination along with booster dose as well as strict implementation of adequate COVID-19 safety measures, prevention, and control strategies should be the immediate priority before the Omicron causes a very high surge in cases.<sup>37</sup> Vaccination is not only the ultimate way, and as per the given global data, India is yet to vaccinate half of its population to achieve as fully vaccinated people ([\[bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/\]\(https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/\)\);](https://www.</a></p></div><div data-bbox=)

thus, we should emphasize on the alternative measures of prevention and control to mitigate the spread of the novel variants. The government should announce wearing of face masks to be compulsory in outdoor areas such as in public places, transport, offices, shops, and schools. Moreover, the general public should obey the appropriate COVID-19 measures (physical distancing, hand hygiene, wearing well-fitting face masks, avoiding crowded spaces and mass gathering events of religious and social ceremonies and functions, etc.) to reduce the risks of catching COVID-19 with such variants as like Omicron, which can be transmitted with a faster speed within the community and the household.

Normally, SARS-CoV-2 infections generally involve a single mutant strain, however two strains may strike simultaneously though this is considered as an extremely rare event. More recently, some news have come up with regards to a newly identified Delmicron double variant, though these need thorough investigations to reach any conclusion. The new super-variant would be created if both the variants (Omicron and Delta) infect someone at the same time and the immunocompromised people can harbour both strains. The Delmicron (considered to be highly transmissible), possibly suspected to be generated as a combination of the most deadly Delta and most mutated Omicron variant of SARS-CoV-2, is now being blamed in making a fresh surge of COVID-19 cases in North America, Europe and may be in other countries, however such assumptions require further explorative studies and authentication by the WHO if in case are proven, and presently are not confirmed. Delmicron is not a new variant like Alpha, Beta, Gamma, Delta, Lambda, Omicron, Mu and others, rather it seems to be having a simple combination of twin spikes and the name is created arbitrarily by merging the existing Delta and Omicron variants, but yet not confirmed. Delta plus Omicron variants are both supposed to be implicated for driving COVID-19 surges, and has raised concerns over the possibility of magnifying the fourth wave of COVID-19 pandemic across the globe.<sup>38</sup> In the mean time, Israel has reported a simultaneous coronavirus and flu infection in an unvaccinated young woman and named 'flurona', however giving any such common name to a co-infection still requires authentic nomenclature and confirmation by designated health agencies. The world is again shivering with high surge in COVID-19 cases and any feasibility of such combinations of viruses and their variants might trigger a more dangerous variant and lead to an aggravated COVID-19 pandemic. Of note, genomic sequencing is used to confirm the variant, which is generally carried out on only a small proportion of COVID-19 cases, hence the real numbers of Omicron as well as Delta cases are supposed to be considerably higher than the number of confirmed cases reported till now.

In conclusion, rapid detection, genomic surveillance, and evolutionary dynamics studies should be carried out at an enhanced pace along with contact tracing of variants, gaining more knowledge on this variant (Omicron) along with updating the current COVID-19 vaccines, developing second-generation vaccines, ramping up of vaccination drives with incorporating booster shots, finding out treatable options from a drug developer's perspective as well as strengthening and strict implementation of adequate mitigation and

proactive and targeted control measures to counter this newer variant having the substantial advantage of speedy transmission, and also the Delta variant needs to be given the top priority at the global level amid the ongoing pandemic.<sup>11,26,33,39–49</sup>

## ACKNOWLEDGMENTS

All the authors acknowledge and thank their respective institutes and universities of affiliation.

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

## AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript. Ranjan K. Mohapatra, Ruchi Tiwari, Ashish K. Sarang, and Kuldeep Dhama conceptualized the manuscript. Ranjan K. Mohapatra wrote the first draft with input from Ashish K. Sarang, Ruchi Tiwari, Sanjay K. Sharma, and G Saikumar. All Authors updated the manuscript. Kuldeep Dhama updated, reviewed, and edited the manuscript. All authors contributed to revisions and approved the final manuscript.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

## ORCID

Ranjan K. Mohapatra  <http://orcid.org/0000-0001-7623-3343>

Ruchi Tiwari  <http://orcid.org/0000-0001-7763-5547>

Ashish K. Sarangi  <http://orcid.org/0000-0002-5602-4736>

Rekha Khandia  <http://orcid.org/0000-0002-9961-3127>

G. Saikumar  <http://orcid.org/0000-0001-6492-4673>

Kuldeep Dhama  <http://orcid.org/0000-0001-7469-4752>

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**How to cite this article:** Mohapatra RK, Tiwari R, Sarangi AK, et al. Twin combination of Omicron and Delta variants triggering a tsunami wave of ever high surges in COVID-19 cases: A challenging global threat with a special focus on the Indian subcontinent. *J Med Virol*. 2022;94:1761-1765. doi:10.1002/jmv.27585