

Omicron (B.1.1.529 variant of SARS-CoV-2); an emerging threat: Current global scenario

To the Editor,

The Coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and its various emerging variants, is posing very high health threats with its continued pandemic waves with 5.5 millions deaths out of 272 million confirmed cases reported worldwide as of December 17, 2021, and recently again a rapid surge of cases is being seen at global level.¹⁻⁴ After the Alpha, Beta, Gamma, and Delta SARS-CoV-2 variant of concerns (VOCs), the most recent B.1.1.529 variant (named as Omicron) is classified as VOC by WHO on November 26, 2021, is creating alarming situations worldwide. The first case of Omicron was documented from Botswana, South Africa in early November month, and within a very short time this variant has now spread rapidly to 108 countries with nearly 1.5 lakh reported cases and 26 deaths as on December 25, 2021.⁵⁻⁹ Various studies are being carried out to investigate the theories and hypothesis underlying the emergence of the Omicron variant such as several mutations might have accumulated in chronically infected persons, lesser-studied human population, in animal reservoirs, diverse evolutionary mechanisms, intra-host adaptation, various immune pressures, insufficient vaccination rates, larger population of immunocompromised persons, and other predisposing factors that could provide an ideal situation for the emergence of newer variants.¹⁰⁻¹⁴

Omicron is the most mutated SARS-CoV-2 variant possessing 50 mutations in its genome including 30 mutations in its spike (S) protein alone, owing to which it gained higher transmissibility and partial resistance to immunity induced by currently available COVID-19 vaccines and antibody-based therapies.¹⁵⁻²¹ The omicron variant is detected by RT-PCR,²² however genomic sequencing is required for confirmation. Preliminary evidence also suggests an increased risk of reinfection in COVID-19 recovered patients as well as vaccine breakthrough in vaccinated individuals with this variant. Altogether, the high genetic changes will affect virus characteristics such as of acquiring higher transmissibility, disease severity, immune escape from vaccine and immunotherapies based protection and impeding diagnostics. Therefore, it is highly recommended to enhance the global surveillance and sequencing efforts to understand circulating SARS-CoV-2 variants with a particular focus on Omicron. Until now, Omicron has been reported to cause asymptomatic infection or a milder disease with earliest common symptoms such as sore throat, headache, running nose, body ache, fever, and fatigue/weakness.²³ In South Africa, Omicron has 80% lower risk of hospitalization as per report. Cases of infections with Omicron are on rise but fewer

hospital admissions are observed as compared to delta variant in South Africa.²⁴ The increasing positive electric charge in the crucial regions of S protein of Omicron may facilitate viral infection of the host cell.²⁵ Moreover, this emerging variant does not raise significantly the risk of severity and death in vaccinated people,²⁶ however, it is too early to conclude.

As the Alpha, Beta, and Delta variants were associated with consecutive waves of SARS-CoV-2 infections across the entire world with high surge of COVID-19 cases and associated deaths seen during first half of this year, so it is expected that the world may face a new wave of pandemic due to Omicron in the coming time owing to its very rapid spread in many countries.²⁷ Now the COVID-19 cases are increasing rapidly in South Africa and the early doubling time is higher than that of the previous three waves of COVID-19 pandemic.^{8,28,29} As on December 24, the UK reported maximum Omicron cases (26,447) followed by the USA (4614), Denmark (2001), South Africa (1643), and Australia (859) while cases are also increasing on daily basis in other many countries.⁷ As per the Institute for Health Metrics and Evaluation (IHME, the USA), world will witness 300 crore Omicron cases globally in next 2 months however, the infection-fatality rate will be lower than the Delta variant.³⁰ Now, Omicron has become the dominant variant and found in more than 70% of the samples collected in the United States, and it may likely displace Delta as the dominant variant in the coming days.³¹ So, the international responses towards Omicron have been raised as compared to other previous variants. Due to the seasonal influenza (already been reported), the coming winter will be more challenging and will bring triple respiratory virus threat (Omicron, Delta, and influenza).³¹ As on today (December 25, 2021) the USA and UK reported more than lakhs of COVID-19 cases daily.

The COVID-19 vaccines are based on the SARS-CoV-2 spike receptor-binding domain (RBD). The Beta variant has three mutations and Delta variant has two mutations, however, Omicron has 10 to 15 mutations in this region. The COVID-19 vaccines were found less effective against Beta and Delta variants as the mutations facilitated the virus variants to partially evade immune responses.¹⁵ In case of this newer variant (Omicron), many such functions and impacts of higher mutations on efficacy of vaccines are yet to be analyzed. Researchers are trying to understand whether antibodies produced from vaccination can neutralize Omicron variant and upto what extent the currently available COVID-19 vaccines and immunotherapies will be efficacious,^{18,19,32} time will answer all these questions. Moreover, Zhang and coworkers have suggested that Omicron may

lead to more significant escape from immune protection.²⁰ In between this, the vaccine vendors have also announced their plans to make new versions of their COVID-19 vaccines tailored to Omicron.¹⁵ In this context, Moderna and Pfizer have declared to produce specific vaccines for omicron within 100 days.²⁶ Booster doses are being recommended to increase the protective potentials of COVID-19 vaccines and preventing health impacts of infection with Omicron variant as well as other variants.^{33,34} There is also a need to design and validate potent commercial immunoassays for detecting anti-SARS-CoV-2 spike and RBD antibodies against the newly emerging and highly mutated variants such as Omicron.³⁵ A recent study also suggests that the Omicron variant of SARS-CoV-2 encodes 37 amino acid substitutions in the spike protein, out of which 15 are in RBD region and the Omicron RBD binds to human ACE2 with increased affinity.³⁶ Still vaccine inequity and hesitancy are the influential factors for the emergence of such novel variants and their transmission.

Omicron variant was first identified in India from the specimen collected from a 37-year-old man who came from South Africa on November 25. Thereafter, 415 cases of Omicron have been detected from different states (mainly from Maharashtra, Delhi, Gujarat, and Telangana) as on December 25, 2021. It is important to note that most of the reported Omicron infected individuals are already vaccinated. The rate of infectivity of Omicron variant is five times more than Delta variant.¹⁵ Moreover, Omicron may be twice more likely to escape currently available COVID-19 vaccines as compared to the Delta variant.³⁷ So, vaccines are not only the sufficient way to control the transmission, we also need face mask, sanitizer, and surveillance to break the transmission.³⁸ It is uncertain that whether it will cause more disease severity or not. India is the second most populated country and the people are still not obeying the appropriate COVID-19 guidelines. The vaccine booster program is not started and only 41.8% people are fully vaccinated (taken two doses) while 60.7% people have received the first dose in India as on December 25, 2021.³⁹ The huge rapid surge of COVID-19 cases and deaths during second wave of pandemic in India owing to evolution and emergence of Delta variant of SARS-CoV-2, lesser vaccine coverage at time, mass gathering events happening in festivals and religious ceremonies, rushes in markets and crowding at other places while lowering down the COVID-19 appropriate behaviors of wearing masks and social distancing by the public during routine activities. The Delta variant is also responsible for surging multiple fresh waves throughout the world from time to time and hence the pandemic is still ongoing despite promoting massive vaccination drives at global level. Recently, schools and colleges have been reopened in offline mode as well as all other official and private organizations are functioning routinely. In this context, 53 girl students (of VIII, IX, X class) of St. Marys Girls High School were infected with SARS-CoV-2 recently.⁴⁰ Moreover, 54 medical students of Veer Surendra Sai Institute of Medical Sciences and Research (VIMSAR) were detected COVID-19 positive after attending college annual function.⁴¹ Recently, 16 students (of VIII, IX, X, XI class) of Maha school at Ghansoli in Mumbai have also tested positive.⁴² As the classes are started in offline mode,

so, COVID-19 cases are rising in several educational institutes.⁴³ So, obeying COVID-19 guidelines to the desired levels by students in schools and colleges are really challenging in Indian school settings.⁴⁴ Moreover, such students have not taken COVID-19 vaccines yet. Under these situations, the Omicron variant may infect younger populations. The government, authorities, and parents must be careful on this issue to protect students amid spread and rising cases of this newly emerged variant. This new variant (Omicron) has now started its game and may potentially circulate to larger population owing to its higher transmissibility and might be in future become responsible for another wave (the so-called third wave) of the COVID-19 pandemic. Amid such high threats of the micron variants, urgent and utmost priority need to be given for enhancing genomic surveillance, strictly implement the recommended prevention and control strategies including testing and isolation, wearing of face mask, hand hygiene, social distancing, speeding up vaccination programs and opting for booster doses for all, developing highly efficacious vaccines, attempting for designing multivalent (multiple antigen-based), and mutation-proof vaccines, and potent immunotherapies, so as to limit the dangers of Omicron and other variants well before facing the surge in COVID-19 cases as third wave in the country.

As per initial data, cases of Omicron infected patients in India are mainly males as compared to females. Indian government has implemented strict measures for the travelers from South Africa and risk countries, and imposed necessary bans on international flights. Due to this new variant, some countries quickly closed their borders for foreign travelers, while other countries enforced quarantine for the travellers coming from South Africa and neighboring countries.²⁹ After the death of an Omicron-infected patient confirmed by the UK Health Security Agency (UKHSA), the UK announced a third COVID-19 vaccine dose for their adults.²⁶ The UK government has also announced wearing of face masks again as compulsory on public transport and in shops and schools. People contacted with an Omicron infected patient will be required to be isolated for 14 days. The government has expanded vaccine booster program to people under 40 years of age.⁴⁵ The currently available COVID-19 vaccines may be less effective against the Omicron, however may provide some protection against Omicron. The general public has to take up full course of vaccination along with booster dose.⁴⁵ It is highly recommended to develop more efficacious and protective vaccines at global level. The vaccination drive programs must be strictly implemented towards obtaining herd immunity. World Health Organization also reminded the individuals to take measures (physical distancing, hand hygiene, wearing well-fitting masks, avoiding crowded spaces, getting vaccinated, etc.) to reduce the risk of COVID-19 with such variants. Any failure to timely tackle the Omicron would facilitate continued emergence of newer SARS-CoV-2 variants which could give rise to as scenario of never-ending pandemic, therefore implementation of recommended COVID-19 prevention and control measures, wisely translating the gained knowledge of SARS-CoV-2 and designing newer and modified strategies are the need of the hour to counter Omicron with a holistic approach amid the ongoing pandemic.⁴⁶⁻⁴⁹

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

Ranjan K. Mohapatra: Conceptualization, Writing- original draft. Ruchi Tiwari; Ashish K. Sarangi; Mohammad Azam: Data analysis and interpretation. Kuldeep Dhama; Venkataramana Kandi: Writing—review & editing.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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