Editorial

Covid-19 Epidemic: Preparing for the Next Wave

Rajeev Gupta
Editor, RUHS Journal of Health Sciences; Chair, Academic and Research Development Unit, Rajasthan University of Health Sciences, Jaipur, Rajasthan, India
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The COVID-19 epidemic has led to a massive worldwide health crisis.[1] From the initial spread of infection in high- and upper middle-income countries of Europe and the Americas, the disease has now homed onto lower middle-income and low-income countries of Asia and Africa, and led to major social, economic, and health related challenges.[2] The virus has led to more than 176 million cases and 3.8 million deaths in the last 18 months.[3] These numbers are likely to be underestimates as many countries across the globe, especially lower-middle and low-income countries, do not have robust disease and death surveillance systems.[1] In India, so far more than 30 million cases and 390,000 deaths have been reported.[3]

COVID-19 IN INDIA AND RAJASTHAN

Fluctuating course of COVID-19 epidemic in India,[4] especially the massive second wave of cases and deaths in almost all states of the country, has attracted worldwide attention.[5] Stringent lockdown along with strict public health mandates regarding universal masking and physical distancing at the beginning of the epidemic in March 2020 led to curtailment of disease spread.[6] The number of cases and deaths were low in early months of the epidemic but as the restrictions were eased, an increase was observed that peaked in September-October 2020.[6] Then, without any explicable reason or changes in the public health mandates, the number of cases and deaths started to decline and nadired by January 2020.[4] The infection then resurfaced with exponential increase in morbidity and mortality in the last few months.[4] Trends in COVID-19 cases and deaths per million population in India as well as Rajasthan from March 2020 to May 2021 are shown in the Figure. There is a bimodal distribution with two distinct peaks the first in September-October 2020 and the second in April-May 2021.

Apart from a number of medical and social factors, highlighted earlier,[5,6] biological factors could also be responsible. Biological changes in SARS-CoV-2 virus are due to ongoing mutation of the virus genome that has mutated to variants of concern (VOCs).[7] Evolutionary biology of viruses informs us that virus genomic structure changes due to either genetic drift or genetic shift. Genetic drift is usually a non-serious concern and involves changes in a few amino acid sequences that are helpful for taxonomic purposes with limited clinical significance. Genetic shift, on the other hand, may lead the virus to mutate into VOCs as has been reported for SARS-CoV-2.[2] These mutations have led to a number of clinically important variants (Table 1). A number of factors promote mutations. These are prolonged illness especially among the elderly and the immuno compromised, long-term use of immuno suppressants including injudicious use of steroids, anti-interleukin drugs, plasma and other immunosuppressant, and widespread use of empirical therapies.[5,6] Unfortunately in India, such patients and practices are widely prevalent.[5]

Genomic analyses data for India are available at GISAID (Global Influenza Surveillance and Response System) website,[8] and reported that the first peak correlated with surge in VOCs B.1.1.306, B.1.1.326, and B.1.36, and the second and larger peak with B.1.1.7 and B.1.617.2. These newer SARS-CoV-2 strains alpha (B.1.1.7), beta (B.135), and delta (B.1.617.2) are more transmissible (50-60% greater) than the previous ones (Table 1).[9,10] These mutants, especially the delta, have contributed to the massive second peak in India.[4,7] Detailed virus genomic data from Rajasthan are not yet available although preliminary analysis suggest importance of the delta virus in the second peak.[11] The reasons for rise and fall of the virus-related

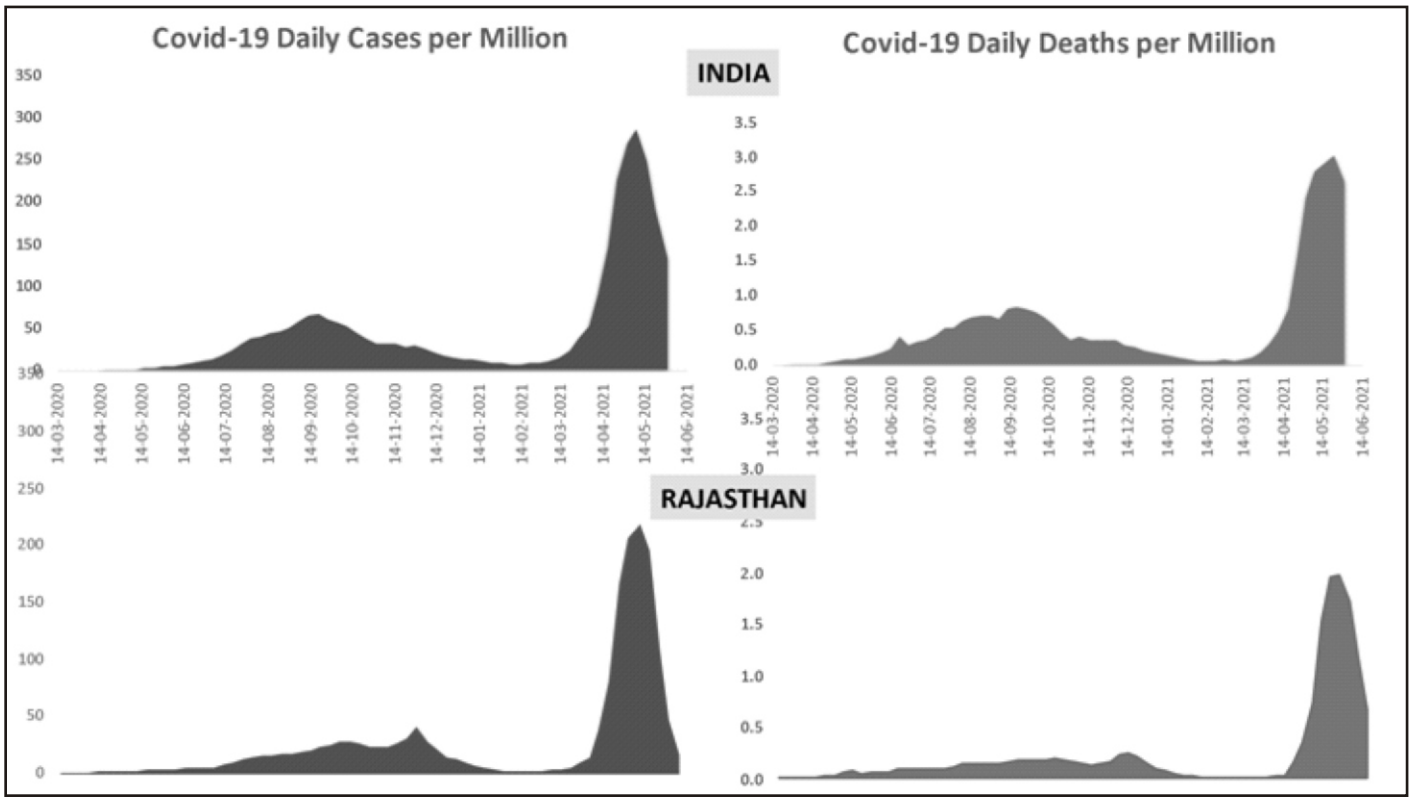

Figure: Trends in daily COVID-19 cases and deaths per million population in India and Rajasthan from March 2020 to May 2021.

Table 1: Characteristics of the important SARS-CoV-2 variants of concern

Variant	WHO Nomenclature	Transmissibility	Immune Evasiveness	Vaccine Effectiveness	Presence in India
Ancestral	--	--	--	++	√√
D614G	--	+	--	++	?
B.1.1.7	Alpha	+++	--	++	√√
B.1.351	Beta	+	++++	+	√
P.1	Gamma	++	++	+	?
B.1.429	Epsilon	+	+	++	√
B.1.526	Iota	+	+	++	√
B.1.617.2	Delta	++++	++++	++	√√

morbidity and mortality are still under investigation. More studies are needed on virus dynamics, host factors and public health responses.

IS A THIRD WAVE INEVITABLE?

The second wave of the epidemic has now largely subsided across India and in Rajasthan (Figure). Previous epidemics, whether small pox in the pre-historic era, plague pandemics in the first millennium, and influenza epidemic a century ago, have informed us of occurrence of multiple waves of any infectious disease epidemic.[1,12] These waves are due to changing individual behaviors, health care practices, disease management, availability of vaccines and social, economic and political factors. Populations and individuals tend to respond to the "burn-out" imposed by the epidemic in multiple ways and an important response is neglect of the effective non-pharmaceutical interventions.[13] Sociological studies in

India have also reported such behaviors.[6,13] It has been speculated that as soon as the mitigation measures are relaxed in India, the virus would recur.[6] It has also been debated that unless strict non-pharmacological interventions and other public health mitigation measures continue, the third wave is likely to occur in India. Moreover, we cannot predict emergence of VOCs. It has also been suggested that with the current pace of vaccination in the country, although very high by the global standards,[15] vaccination of many vulnerable populations (rural, poor, illiterate) and children shall not be achieved soon.[16] Thus, although a third wave is likely, it could not be as severe as the second wave as large swathes of older populations have been vaccinated in the country.[15] Low death rate in recent delta-strain infected UK populations is a pointer in this direction.[9]

Concurrent epidemiological studies in UK and USA have highlighted importance of public health measures including non-pharmacological interventions and rapid deployment of vaccination in control of the epidemic.[9,10] India is a large country with widespread poverty and mixed economy and although strict deployment of public health measures, importantly lockdowns, have helped, they have resulted in economic hardship and social disruption that is difficult to sustain.[6] Successful mitigation in European and North American countries have identified factors that could be implemented to prevent a third wave. Two important science-led policy interventions are important: (a) continued focus on non-pharmacological interventions; and (b) rapid deployment of vaccination. I believe that there are some more important factors for the prevention of the third wave (Table 2). Knowledge of VOCs is important in India to plan regional and state-level mitigation procedures and development of VOC specific vaccines as well as polyvalent vaccines.[17,18]

PREPARING FOR THE NEXT WAVES

It has been argued that waves of infection-related pandemic are inevitable, and if not COVID-19, there are other viruses and bacteria presently hidden from sight.[19] Therefore it is imperative for the politicians, bureaucrats, health administrators and healthcare professionals, to be prepared. The international non-governmental organization, *Vital Strategies*, lists seven key preparedness factors (Table 3). These are also important for India and include risk assessment and planning; emergency response operations; national laboratory system; disease surveillance; national legislation, policy and financing; human resources; and risk communication.[20] Many countries have demonstrated that the most important factors to control the present epidemic successfully are *strong preparedness* and *decisive response*.

In conclusion, although third wave of COVID-19 epidemic in India can occur, strong preparedness (Table 3) and decisive response can minimize the impact. The wave can be prevented by continuation of non-pharmacological

Table 2: Prevention of third wave of the epidemic

Focus	Interventions
Standard public health measures	• Deployment of non-pharmaceutical interventions • Mass vaccination programs to high risk and underserved populations • Rapid and widespread deployment of available vaccines
Clinical interventions	• Development of appropriate treatment guidance for prevention of emergence of virus mutations and VOCs • Widespread health professional and public education to limit demand/s for inappropriate therapies
Basic science-led interventions	• Real-time identification of VOCs and their clinical characteristics • Rapid development of vaccines against the new VOCs including strain-specific and polyvalent vaccines • Development and deployment of child-friendly vaccines

VOCs ; variants of concern

Table 3: COVID-19 epidemic preparedness factors[4]

Factors	Technical areas	Relevance to India
National laboratory system	Country has a national laboratory system to test disease specimens and confirm outbreaks.	Creation of better standardized local, district-level, and regional laboratories with central monitoring of quality.
Real time surveillance	Country can find disease outbreaks quickly.	Use of electronic health systems for disease surveillance at primary and secondary levels. Realtime data processing and outcomes assessment.
Workforce development	Country has a capable workforce to find, stop, and prevent outbreaks.	Clinician led interventions. Training and deployment of non-physician healthcare-worker based system. Appropriate salary and promotional avenues.
Risk assessment and planning	Country has done preparedness planning and risk assessment for public health emergencies	Better health information systems. Clinical orientation rather than management facing.
Emergency response operations	Country has emergency system to find and stop outbreaks.	Strengthening primary healthcare and district health systems.
Risk communication	Country can listen and exchange information between experts and the public effectively so that healthcare workers and the public can take protective measures.	Science-based public education.
National legislation, policy, and financing	Country has legislation, policy, and financing in place to support overall preparedness for prevention of epidemics.	Development and deployment of science-led policies for legislation, financing, and implementation.

interventions (masking, physical distancing) and rapid and widespread deployment of vaccination.[21] It is important to prevent development of SARS-CoV-2 variants of concern by science-led strategies (Table 2). Rapid development of vaccines and vaccine strategies to counter the VOCs are essential. Ultimately, science-based strategies are the only panacea that can deliver all of us from evils of this dreadful disease.

REFERENCES

1. Ferguson N. Doom: The Politics of Catastrophe. Penguin Random House Books. Allen Lane UK. 2021.
2. Clarke JM, Majeed A, Beaney T. Measuring the impact of COVID-19. *BMJ*. 2021; 373:n1239.
3. Anonymous. Coronavirus outbreak in India. Available at: www.COVID19india.org. Accessed 13 June 2021.
4. Vaidyanathan G. Coronavirus variants are spreading in India what scientists know so far. Nature.2021;593:321-22.
5. Editorial. India's COVID-19 emergency. *Lancet.* 2021; 397:1683.
6. Ghosh A. Billions under lockdown: The inside story of India's fight against COVID-19. New Delhi. Bloomsbury India. 2021.
7. Singh J, Rahman SA, Ehtesham NZ, Hira S, Hasnain SE. SARS-CoV-2 variants of concern are emerging in India. *Nature Med*. 2021;EPub. DOI: 10.1038/s41591-021-01397-4.
8. Global Influenza Surveillance and Response System (GISAID). Available at:www.gisaid.org. Accessed 13 June 2021.
9. Public Health England. COVID-19 Vaccine Surveillance Report-Week 21. May 2021. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/990096/Vaccine_surveillance_report_-_week_21.pdf. Accessed 29 May 2021.
10. Center for Disease Control and Prevention. Genomic surveillance for SARS-CoV-2. Available at: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-surveillance.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcases-updates

%2Fvariant-surveillance.html. Accessed 31 May 2021.

11. Ali SI. Virulent delta variant caused deadly second wave in Rajasthan. Available at: https://timesofindia.indiatimes.com/city/jaipur/virulent-delta-variant-causeddeadly-second-wave-in-state/articleshow/83415146.cms. Accessed 13 Jun 2021.
12. Tumbe C. The age of pandemics: How they shaped India and the World. Noida, India. Harper Collins Publishers. 2020.
13. Brauner JM, Mindermann S, Sharma M, Johnston D, Salvatier J, Gavenciak T et al. Inferring the effectiveness of government interventions against COVID-19. *Science*. 2021; 371:eabd9338.
14. Sinha A. Explained: what is a wave in a pandemic and will India see a third wave of COVID-19. The Indian Express. 2021. Available at: https://indianexpress.com/article/explained/india-coronavirus-third-wave-covid-vaccines-oxygen-supply-7322145/. Accessed 13 Jun 2021.
15. Subramanian SV. India faces challenge with its mass vaccination efforts. *Lancet Global Health*. 2021;EPub. DOI: 10.1016/S2214-109X(21)00260-6.
16. Kuppalli K, Gala P, Cherabuddi K, Kalantri SP, Mohanan M, Mukherjee B et al. India's COVID-19 crisis: A call for international action. *Lancet*. 2021; 397:2132-35.
17. Chakraborty D, Agrawal A, Maiti S. Rapid identification and tracking of SARS-CoV-2 variants of concern. *Lancet*. 2021; 397:1346-47.
18. Cohen J. Vaccines that can protect against many coronaviruses could prevent another pandemic. *Science*. 2021; 371:abi9939.
19. Neuzil KM. Interplay between emerging SARS-CoV-2 variants and pandemic control. *N Engl J Med*. 2021; 384:1952-54.
20. Vital Strategies. Epidemic preparedness. 2021. Available at: https://preventepidemics.org/preparedness/, Accessed 13 Jun 2021.
21. Mangal K, Gupta R. COVID-19 vaccines: Hope at last. *RUHS J Health Sciences*. 2020; 5:181-85.

Corresponding Author

Dr Rajeev Gupta, Department of Medicine, Eternal Heart Care Centre and Research Institute, Jagatpura Road, Jawahar Circle, Jaipur 301017 India.

email: rajeevgg@gmail.com