



BATTLING A FRESH COVID-19 WAVE: IS NB.1.8.1 VARIANT A POTENTIAL CAUSE OF CONCERN?

Clinical Microbiology

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ABSTRACT

Just as the world had begun to breathe easier, a fresh reminder of the SARS-CoV-2 lingering presence has hit our faces. Cases have surged over Southeast Asian countries, Eastern Mediterranean, and Western Pacific Region in the past few weeks. Countries battling the fresh COVID-19 waves have reported the dominance of JN.1 variant which is a subvariant of Omicron that has evolved from BA.2.86, also known as Pirola variant. World Health Organization has classified it as a 'Variant of Interest' as of now. Of the several JN.1 sublineages under monitoring, NB.1.8.1 is presently under scrutiny for being the dominant circulating one. The overall risk evaluation of NB.1.8.1 is low as presently there are no reports to suggest that the associated disease severity is higher as compared to other circulating variants. Even though it is growing rapidly, it has only marginal additional immune evasion over LP.8.1. Furthermore, routine clinical surveillance data does not point towards increased COVID-related ICU admissions or deaths per hospitalizations. Continuous surveillance, enhanced laboratory testing, and booster doses of vaccine are the need of the hour.

KEYWORDS

COVID-19, JN.1 variant, NB.1.8.1 variant, SARS-CoV-2, Variant of interest, Variant under monitoring

INTRODUCTION

The World Health Organization (WHO) declared COVID-19 (Coronavirus disease 19) a pandemic in March 2020. It began as an outbreak in Wuhan, China, in December 2019 subsequently spreading to other parts of Asia and eventually around the world by early 2020¹. Caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pandemic caused a widespread social and economic disruption securing its rank among the deadliest pandemics in history². Even though it ceased to be a Public Health Emergency of International Concern on 5 May 2023, the virus continues to circulate after 2 years causing outbreaks and deaths among the vulnerable and immunocompromised³.

Current Situation

Just as the world had begun to breathe easier, a fresh reminder of the SARS-CoV-2 lingering presence has hit our faces. Cases have surged over Southeast Asian countries, Eastern Mediterranean, and Western Pacific Region in the past few weeks. As per the Global Influenza Surveillance and Response System from sentinel surveillance sites, there has been a test positivity of 11% as of 11 May 2025. This matches the peak level (12%) last observed in July 2024. Lower levels of test positivity of about 2-3% is being reported from European, American, and the African regions⁴. Countries or regions reporting increased number of cases include Thailand, Singapore, United Kingdom, Brazil, India, Hong Kong, Greece, and France⁵. Table 1 shows the number of COVID-19 cases and deaths reported to WHO by various countries as of 25 May 2025^{6,7}. Figure 1 shows the state wise status of cases and deaths in India as of June 12, 2025. Total active cases in the country stand at 7154 with 77 deaths recorded since January 2025. Most of the mortality has been attributed to old age, comorbid conditions, and immunocompromised status⁸.

Table 1: Showing country wise COVID-19 cases and deaths reported to WHO as of 25 May 2025

S.NO	Country	Total Cases*	Total Deaths*
	World	206000	1000
1	Thailand	181000	43
2	Brazil	8600	30
3	United Kingdom of Great Britain and Northern Ireland	5100	3
4	Greece	2600	6
5	India	495	2

*Data reported is from past 28 days to 25 May 2025

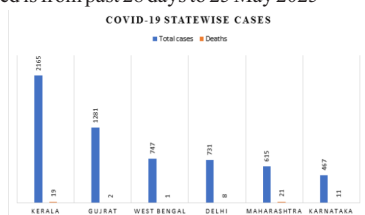


Figure 1: Showing Indian states with maximum COVID-19 cases and deaths as of June 12, 2025

Characteristics Of Circulating Strain

Countries battling the fresh COVID-19 waves have reported the dominance of JN.1 variant which is a subvariant of Omicron that has evolved from BA.2.86, also known as Pirola variant⁹. WHO has classified it as a 'Variant of Interest' and not a 'Variant of Concern' as of now. Variant of Interest has mutations that are suspected or known to cause significant changes from its original strain and is spreading widely in many places or many countries. Variant of Concern is known to have one or more of- tendency to spread rapidly, tendency to cause severe disease, changes in clinical presentation, immune escape, and/or decrease effectiveness to known public health measures, diagnostics, treatment, or vaccines. Variants under Monitoring (VUM) are SARS-CoV-2 variants that may require prioritized attention and monitoring¹⁰. Sublineages of JN.1 that are currently classified as VUM by WHO include KP.3, KP.3.1.1, LB.1, XEC, LP.8.1, and NB.1.8.1¹¹.

Symptoms of the present strain include mild fever, muscle weakness, runny nose, cough, headache, fatigue, gastrointestinal symptoms, exhaustion, loss of appetite, nausea, and sore throat. Some patients have been reporting extremely painful sore throats comparing the sensation to swallowing razor blades or glass coining the term 'razor blade throat' for this variant. Breathlessness may emerge as a critical symptom in immunocompromised and older adults indicating severe infection. Cases presenting with these upper respiratory tract symptoms are usually mild and resolve within a week. Loss of taste and smell are uncommon in this wave¹².

JN.1 variant was first reported in the United States in August 2023. John Hopkins Medicine has revealed that this variant has the ability to evade the immune system and rapidly spread due to unique mutations in spike and non-spike proteins contributing to its increased transmissibility¹³.

Emergence And Spread

The cause of concern in the present uprise of cases is its unusual timing- summers when respiratory viruses do not peak. The increase in numbers can be attributed to the fact that antibody or immunity levels have decreased over time. Most people have taken the last dose of vaccine or boosters a long time back leading to waning immunity. Hence, more individuals can catch and spread the infection¹⁴. This virus seems to never truly disappear and occasionally shows a reflection of its presence through localized or regional outbreaks. As the antibody levels decline, the virus finds an opportunity to spread especially among the immunocompromised and persons with comorbidities.

Of the several JN.1 sublineages, NB.1.8.1 is presently under scrutiny for being the dominant circulating variant. The WHO Technical Advisory Group on Virus Evolution has conducted an initial risk evaluation for NB.1.8.1 designated on 23 May 2025 revealing some

interesting facts¹⁵. It is derived from the recombinant variant XDV.1.5.1 and for which the first sample was collected on 22 January 2025. It has the following additional mutations: T22N, F59S, G184S, A435S, F456L, T478I, and Q493E. The spike protein mutations at position 445 have demonstrated enhanced binding affinity to hACE2, potentially increasing the variant's transmissibility. Additionally, mutations at position 435 have shown to reduce the neutralisation potency of class 1 and class 1/4 antibodies, and mutations at position 478 have revealed enhanced evasion of RBD-targeting neutralizing monoclonal Class 1/2 antibodies^{16, 17}. This strain has also depicted a 1.5–1.6-fold reduction in neutralization compared to LP.8.1.1¹⁷. As of 18 May 2025, 518 sequences of this strain have been submitted to Global Initiative on Sharing All Influenza Data from 22 countries and an increased prevalence in all WHO regions have been noticed. NB.1.8.1 antigenicity has only been examined in a single study using pseudoviruses utilizing serological data from two cohorts. Auxiliary laboratory studies employing sera from different cohorts and regions are required to further assess the risk of antibody escape¹⁵.

In comparison with XBB.1.16.1, EG.5.1.3 and BA.2.86.1 variants, the NB.1.8.1 does not contain any additional protease substitutions and therefore unlikely to exhibit increased resistance to Nirmatrelvir as compared to these variants. Also, NB.1.8.1 displays the Nsp12 (polymerase) substitution D284Y (Orf1b: D275Y) but, the potential impact of this substitution on antivirals like molnupiravir and remdesivir has not been examined presently¹⁸.

The overall risk evaluation of NB.1.8.1 is low as presently there are no reports to suggest that the associated disease severity of this strain is higher as compared to other circulating variants. Even though it is growing rapidly across all WHO regions in comparison to its co-circulating strains, it has only marginal additional immune evasion over LP.8.1. Furthermore, routine clinical surveillance data does not point towards increased COVID-related ICU admissions or deaths per hospitalizations. Hence, WHO does not consider additional public health risks relative to other circulating Omicron descendent lineages¹⁵.

Scaling Up Measures

India is witnessing a rise in COVID-19 testing and scaling up of laboratories with RT-PCR (Real Time Polymerase Chain Reaction) and rapid antigen testing. RT-PCR testing has spiked up by 70% as timely testing allows prompt intervention and isolation of affected cases. With learnings from past waves, laboratories have started streamlining workflows, reinforcing staff trainings, and extending working hours to reduce the turn-around time to 4-6 hours¹⁹.

WHO and its Technical Advisory Group on COVID-19 Vaccine Composition periodically assess the impact of new and emerging variants on the effectiveness of COVID-19 vaccines for informed decision making regarding updation of vaccine components. As per the latest recommendations published on 15 May 2025, it is advised that monovalent JN.1 or KP.2 remain appropriate COVID-19 vaccine antigens and monovalent LP.8.1 can be deemed as a suitable alternative vaccine antigen²⁰.

CONCLUSION

COVID-19 waves may come and go but prompt vigilance and timely attention to persistent symptoms are need of the hour. Preventive measures such as staying up to date with booster shots, avoiding overcrowded places, wearing N95 or surgical masks, and boosting up immunity through adequate diet and nutrition are essential to reduce disease transmission and safeguard public health.

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