Insights into the NB.1.8.1 Variant of SARS-CoV-2

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the pathogenic virus which is responsible for coronavirus disease 2019 (COVID-19) pandemic has caused millions of deaths globally since its first identification in December 2019. Since then, several SARS-CoV-2 variants have been emerged leading to waves of SARS-CoV-2 infections and significantly impacted global health. Despite the availability of effective vaccines and preventive measures, new infections with emerging variants continue to occur with each passing year. The variants derived from the JN.1 are currently circulating worldwide. NB.1.8.1 is the newly identified variant which was classified as a variant under monitoring by the World Health Organization. The continuous emergence of new viral variants presents a significant challenge to public health and immunization efforts. Currently, there are no reported studies assessing the clinical impact of this variant. However, preliminary studies showed that, this variant exhibit enhanced evasion of neutralizing monoclonal antibodies. Further studies are necessary to evaluate the potential impact of this variant on public health. The development of effective public health strategies aimed at prevention, containment, and long-term management of the disease is critical for the disease control. The challenges posed by the variants like NB.1.8.1 can be addressed by combining updated vaccination strategies, non-pharmaceutical interventions, surveillance, and global coordination. Furthermore, continuous monitoring and understanding of the emerging viral variants is vital for keeping the virus under control.

Keywords: COVID-19; emerging viral variants; pandemic preparedness; SARS-CoV-2; virus evolution; vaccine

1. Context

Viruses pose an increasing threat to human and animal health. In recent years, the risk of the emergence and spread of reemerging and novel viruses has increased including coronaviruses, mpox, Oropouche virus, Zika and many more [1-3]. Among the recent outbreaks, coronavirus disease 2019 (COVID-19), an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a devastating impact worldwide and still continues to cause significant mortality and morbidity. Since its outbreak in Wuhan, Hubei province, China in late 2019, the pandemic has resulted in an excess of 778 million infections so far and over 7 million deaths worldwide (As of May 2025) [4]. High number of cases was reported in the United States of America (USA), China, India, France and Germany. The overall impact of the pandemic varied greatly across countries. During the pandemic, most of the countries implemented emergency measures such as travel restrictions, social distancing, school closures, quarantines and personal protective measures to control the virus transmission [5].

In response to the pandemic, researchers and pharmaceutical companies rapidly developed effective vaccines including inactivated, mRNA, protein subunit based vaccines, and viral-vector vaccines in a record time of less than a year. The vaccines from Pfizer-BioNTech (BNT162b2) [6], Moderna (mRNA-1273) [7], and Oxford-AstraZeneca (ChAdOx1 nCoV-19) [8, 9] received early regulatory approval. The availability of effective vaccines significantly reduced millions of hospitalizations, disease severity and mortality associated with COVID-19 [10-13]. So far, billions of total vaccine doses have been administered globally. However, cases were still reported in several countries. From May 05, 2025 to June 01, 2025, new cases were reported in 75 countries. The data from this period showed an increase in new cases and decrease in the death rate [4]. The co-circulation of different variants poses serious threats to the human health and economy. Therefore the newly emerging and circulating variants required close monitoring in order to quickly assess their impact on public health. Hence, in this review, we have summarized the recent available information of the emerging variant NB 1.8.1 of SARS-CoV-2 in order to provide a timely and relevant understanding of this emerging variant.

2. Data Acquisition

We conducted a review of relevant articles from Scopus, PubMed, and Google Scholar databases to collect and analyze existing literature on the SARS-CoV-2 and its emerging variants. The search terms included "SARS-CoV-2", "emerging variants", "COVID-19", "public health impact of NB 1.8.1" "new SARS-CoV-2 variants" and the relevant articles were identified. Research articles, review articles, perspectives and commentaries providing relevant information that fits with the aim of the study were included. The data from the collected articles were used to highlight the current state of knowledge on the NB.1.8.1 Variant of SARS-CoV-2.

3. Results

3.1. Emerging Variants

Similar to many other RNA viruses, SARS-CoV-2 continuously evolves resulting in genetic changes and giving rise to several new variants throughout the course of the pandemic that have quickly spreads across the globe [14, 15]. The emergence of multiple SARS-CoV-2 variants over the last five years badly impacted the health of people, health care systems, the global community, the economy, and development. Some variants emerge and disappear quickly, whereas some variants continue to spread and replaced previous variants. The emerging variants were characterized by their ability to evade immune responses, increased fitness, transmission rates, high pathogenicity, disease severity, susceptibility to vaccines and treatments and drives new waves of COVID-19. The mutations identified in the spike region and receptor binding domain (RBD) play a major role in affecting viral infectivity, pathogenic mechanism, and immune evasion [16-19]. Other than spike protein, mutations were also identified in other regions and contribute to the distinct characteristics of each variant.

World Health Organization (WHO) in collaboration with other researchers is assessing the risk of emerging variants and has implemented nomenclature for naming these variants using the greek alphabet. The WHO categorized SARS-CoV-2 variants into variant of concern (VOC), variant of interest (VOI), or variant under monitoring (VUM). VUM is a variant with genetic changes suspected to affect virus characteristics, but with unclear phenotypic or epidemiological impact which requires enhanced monitoring and assessment pending more evidence. VOI is a variant with genetic changes affecting virus characteristics and shows early signs of increased transmission and number of cases suggesting an emerging public health risk. The variant that meets the definition of VOI and proven to significantly impact transmissibility, disease severity, or effectiveness of vaccines, or treatments are designated as VOC [20, 21]. The previously circulating VOC such as Alpha, Beta, Gamma and Delta variants has caused major impact during 2020-2022. Subsequently, Omicron and its subvariants have spread widely leading to a huge spike in the number of daily cases and became the dominant variant. Omicron sublineages (BA.2.75, BA.4/5, BF.7, XBB, BA.2.86 and JN.1) are dominating worldwide till date and several variants continue to co-circulate even in 2025 [22, 23]. The vaccines developed based on the ancestral strains exhibited remarkable efficacy during the early stages of pandemic. However, these vaccines do not provide complete protective immunity and are less effective against the emerging variants. The variants particularly Delta and Omicron exhibit several mutations in the spike region, which makes them to escape from the neutralizing antibodies induced by the firstgeneration vaccines causing hurdles in the global vaccination efforts [24-29]. Hence, booster doses and variant specific vaccines were developed [30-33].

Currently, circulating variants did not meet the criteria for classification as VOC. The variants currently designated as VUM's include KP.3, KP.3.1.1, LB.1, XEC, LP.8.1 and NB.1.8.1 (Table 1) [34]. These variants carrying the spike protein substitutions are descendants of the JN.1 variant which was first identified on August 25, 2023 [35] and it has been gradually replaced by the JN.1 derived subvariants. Currently, JN.1 sublineages continue to pose a major risk to public health.

Table 1: Currently Circulating SARS-CoV-2 variants and their key mutations (As of September 2025) [20]

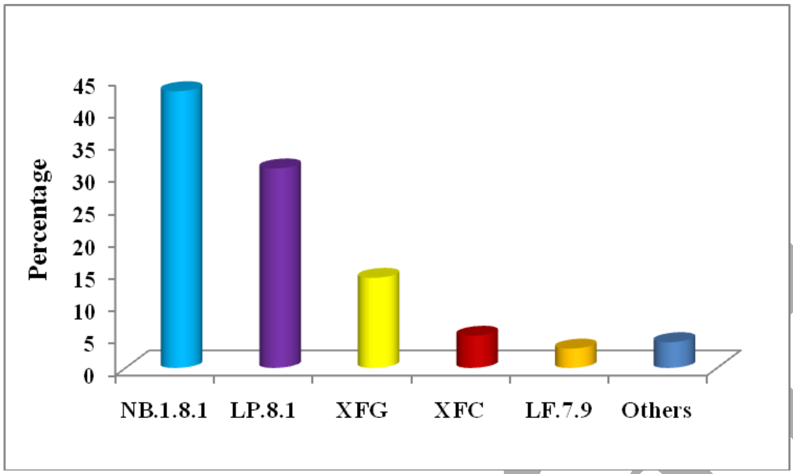
Classification	**Name of the variant**	**Key spike mutations**	**Date of designation**
VOI	JN.1	BA.2.86 + S:L455S	December 2023
VUM	KP.3	JN.1 + S:F456L, S:Q493E, S:V1104L	May 2024
	KP.3.1.1	KP.3 + S:S31–	July 2024
	XEC	JN.1 + T22N, F59S, F456L, Q493E, V1104L	September 2024
	LP.8.1	JN.1 + S31–, F186L, R190S, R346T, V445R, F456L, Q493E, K1086R, V1104L	January 2025
	NB.1.8.1	JN.1 + T22N, F59S, G184S, A435S, F456L, T478I, Q493E	May 2025
	XFG	JN.1 + T22N, S31P, K182R, R190S, R346T, K444R, V445R, F456L, N487D, Q493E, T572I	June 2025

3.2. NB.1.8.1

After the spread of SARS-CoV-2 variant BA 2.86 in 2023, JN.1 received global attention in 2024. The L455S mutation in the spike region of JN.1 enhanced its transmissibility and ability to evade the antibodies [22]. Lately, focus has been turned to its subvariants, such as KP.2, KP.3, KP.3.1.1, and XEC, LP.8.1 which rapidly spreads globally. NB.1.8.1 is the most recently identified variant derived from XDV.1.5.1 (recombinant lineage of XDE and JN.1) [36, 37]. It was classified as a VUM by the WHO on May 23, 2025. There has been an increase in the number of infections and hospitalizations associated with this variant in several countries during the past few weeks; however no significant increase in the severe COVID-19 cases or the number of deaths has been reported [38]. WHO reported that the test positivity for SARS-CoV-2 has been increasing since February 2025 in Eastern Mediterranean, South-East Asia, and Western Pacific regions [36].

The cases associated with the NB.1.8.1 infections have been reported in several countries including China, Hong Kong, Singapore, India and UK in recent weeks [39]. As per the data from U.S. Centers for Disease Control and Prevention (CDC), NB.1.8.1 accounted for approximately 43 % of newly sequenced cases as of June 26, 2025 (Figure 1). The prevalence of NB.1.8.1 in the USA has significantly increased in recent weeks, rising from 2% of cases in April to 5% in early May, 15% by late May, 24% in early June [40]. The Indian SARS-CoV-2 genomics consortium (INSACOG) has reported four cases of NB.1.8.1 in India as of June 26, 2025 [41]. As of June 19, 2025, a total of 2,831 genome sequences have been submitted from 33 countries in global initiative on sharing all influenza data (GISAID). The nations with the highest percentage of NB.1.8.1 sequences are China (1052 sequences), Singapore (366 sequences), USA (261 sequences), Australia (234 sequences) and Canada (186 sequences) (www.gisaid.org).

Figure 1: Prevalence of SARS-CoV-2 variants in the USA (Data as of June 26, 2025).



NB.1.8.1 shares several characteristics with other Omicron subvariants, including high transmissibility, immune escape, and similar clinical outcomes. However, it also exhibits differences in its mutational profile and transmission patterns which require continuous monitoring to assess its impact on public health. Compared with the JN.1, seven spike mutations (T22N, F59S, G184S, A435S, V445H, F456L, T478I, and Q493E) and 23 non-spike substitutions were reported in NB.1.8.1. Further this variant features four specific substitutions such as G184S, K478I, A435S, and L1104V compared with XEC spike protein [34]. The mutation at the 445 has been reported to enhance the binding affinity with human angiotensin-converting enzyme 2 (ACE2) which could further increase the variants transmissibility. Further, T478I and A435S mutations enhanced the evasion of class 1/2 antibodies and reduced antibody neutralization potency. The estimated relative effective reproduction number (R) of NB.1.8.1 was 1.17-fold higher than that of LP.8.1, suggesting a greater potential to outcompete other major SARS-CoV-2 lineages. The virological experiments using a lentivirus-based pseudovirus assay demonstrated that the NB.1.8.1 had higher infectivity (2.5-fold; $p<0.0001$) compared to LP.8.1. The K478I and L1104V substitutions in the NB.1.8.1 spike protein significantly decreased XEC pseudovirus infectivity. Further, the neutralization assays using XEC

convalescent sera and JN.1 mRNA vaccine–elicited sera demonstrated similar 50% neutralization titers across XEC, LP.8.1, and NB.1.8.1 variants. [37].

A recent study showed that the RBD of NB.1.8.1 binds strongly to human ACE2 receptors than LP.8.1. The pseudovirus infectivity assays confirmed that NB.1.8.1 maintains acceptable infectivity and displayed enhanced immune escape than LP.8.1.1, with a 1.5-1.6-fold reduction in 50% neutralization titre (NT50) in human plasma. NB.1.8.1 presents a balanced profile of ACE2 binding and immune escape, making it a variant with significant potential for sustained transmission and future prevalence [42]. As an emerging variant, further investigations are necessary to better understand its virulence over time.

COVID-19 symptoms tend to remain broadly similar across different variants with infected persons showing a range of symptoms from mild to severe and life-threatening. The symptoms include cough, runny nose, fever, congestion, fatigue and muscle weakness [43, 44]. The recently emerged variants including KP.2, KP.3, LP 8.1 and NB 1.8.1 are associated with milder clinical symptoms and lower mortality. However, in recent weeks, few variants have led to the increase in the daily hospitalization cases, although the number of daily ICU cases was significantly lower. Currently, there are no reports indicating that the disease severity of NB 1.8.1 is higher compared to other circulating variants [38, 45]. However, the transmissibility and effectiveness of the vaccines against this variant is not available and requires further investigation. At this stage, the public health impact is considered low on a global scale, as the currently available vaccines are expected to offer protection against this variant. In May 2025, the WHO technical advisory group on COVID-19 vaccine composition suggested that the monovalent JN.1 or KP.2 is the suitable vaccine antigen, while monovalent LP.8.1 is the suitable alternative [46]. The CDC recommended that the adults aged 18 and older can receive the 2024-

2025 updated COVID-19 vaccine, which was designed closely to target the JN.1 lineage of the Omicron variant, for optimal protection against the currently circulating strains. Currently, there are three updated COVID-19 vaccines (2024–2025) available in the USA from Pfizer, Moderna and Novavax [47]. The Pfizer and Moderna vaccines are mRNA-based targeting the KP.2 variant, whereas the Novavax vaccine is a protein subunit vaccine targeting the JN.1 variant.

4. Conclusion

The emergence of new variants over time is probably inevitable and represents a part of virus evolution. The potential of the emerging variants to evade immune response and the extent to which this occurs, remains a significant concern. The variants such as delta, omicron and JN.1 sublineages represent different chapters in the fight against SARS-CoV-2. Even after ending of the public health emergency of international concern in May 2023, both national and international authorities are adopting diverse approaches for the broader disease management. WHO is continuously monitoring the emerging variants and evaluating the risk of each variant with the support of technical advisory group of virus evolution and rapidly assessing the threat levels posed by new variants. The evolving nature of SARS-CoV-2 continues to pose a major public health challenge that demands for strengthened surveillance and continued virus monitoring. The regular surveillance of respiratory viruses through genome sequencing and waste water monitoring is critical throughout the year [48, 49]. Further, effective field surveillance coupled with laboratory infrastructure, reliable and rapid diagnostics and intersectoral coordination are vital to identify the early warning signs of emerging variants. The timely knowledge about the new virus variants will help in rapid contact tracing and disease containment. Further, monitoring its course will help to determine case trends and mortality rates, tracking changes in epidemiologic characteristics, understanding the nature of immune evasion, guiding the selection of suitable variants for vaccine development, and inform policy development and implementation. Vaccination is the most effective approach for protection against currently circulating variants and possibly against future variants [50].

The constant emergence of SARS-CoV-2 variants showcases the evolutionary dynamics of the virus and its threat to global health. These variants has the ability to evade immune responses, challenge the existing prevention and control measures highlighting the need for constant vigilance, genomic surveillance, ongoing vaccine development, and data based public health responses for the effective and targeted response. As we learn to live with SARS-CoV-2, it is important to update vaccines to stay ahead of its evolution and also reinforcing preventive measures when needed, for managing the virus spread. In the post-pandemic era, measures are still necessary to reduce the SARS-CoV-2 transmission.

Acknowledgements

The authors (BS, DY, GV) are thankful to Karpagam Academy of Higher Education and DST-FIST (SR/FST/LS-I/2018/187 dt 20.12.2018) for the support.

Author Contributions

Conceptualization, B.S.; literature review, B.S., D.Y., G.V., A.M., R.S; writing—original draft preparation, B.S., A.M; writing—review and editing, B.S., D.Y., G.V., A.M., R.S.; supervision, B.S., R.S. All authors have read and agreed to the published version of the manuscript.

Conflict of interests

None. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

None

Availability of data and material

The data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Clinical trial registration

Not applicable

Clinical trial number

Not applicable

Ethics approval and consent to participate

Not applicable.

Consent for publication

I hereby provide consent for the publication of this manuscript.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Not applicable.

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