Bulletin of the National Research Centre

LETTER TO THE EDITOR

Open Access

Concerns regarding SARS-CoV-2 JN.1 mutations should be raised

Miah Roney[1,2], A. K. M. Moyeenul Huq[3] and Mohd Fadhlizil Fasihi Mohd Aluwi[1,2*]

Abstract

JN.1 is a new variant of SARS-CoV-2 which is a subvariant of Omicron (BA.2.86) was first discovered in the USA in September 2023. The virus's capacity to spread and elude the immune system may be impacted by a single alteration in the spike protein, which serves as its distinguishing feature. JN.1 has been classified as an interesting variety by the World Health Organisation. JN.1 might lead to a rise in infections, or its possible influence on public health is yet premature. Current immunisations, examinations, and therapies are still anticipated to combat JN.1.

Keywords SARS-CoV-2, COVID-19, Variants, JN.1

Dear Editor,

The COVID-19 (SARS-CoV-2) pandemic claimed 7.01 million lives worldwide by 13 April 2024 (https://www.worldometers.info/coronavirus/). This pandemic was a major health and socioeconomic disaster akin to the Spanish flu of 1918 (Otolorin et al. 2022). The pandemic strained healthcare systems worldwide and posed challenges for both low-income and developed countries, leading to economic collapse, job losses, and social insecurity. Despite these challenges, collaborative efforts among health organizations, governments, medical professionals, and scientists resulted in the development of effective vaccines. The global response involved comprehensive preventative measures, including quick identification and diagnosis, mass vaccination, and the rapid expansion of intensive care units in hospitals. This multipronged strategy was essential in managing the COVID-19 issue on a worldwide scale, contributing to a high recovery rate and a decline in mortality cases since February 2022. In March 2020, the global case fatality rate rose to 39%, but by July–August 2022, it dropped to below 0.3%, reflecting a significant improvement (Horita and Fukumoto 2023). This positive trend aligns with a World Health Organization (WHO) report indicating a 16.06-fold reduction in COVID-19-related fatalities from 2021 to 2023 (WHO 2023c). As a result of these advancements, governments began lifting epidemic restrictions, people resumed their normal lives, and the WHO announced that COVID-19 is no longer global health concern that requires attention in 2023 (WHO 2023b). However, several newly developing SARS-CoV-2 mutations and variations posed significant health risks in the recent past (Dhama et al. 2023). The primary goal of this letter is to raise the consciousness of the COVID-19's new variant called JN.1, which is the Omicron subvariant (BA.2.86).

Four categories include the unique SARS-CoV-2 variations: variants of interest (VOI), variants of high consequence (VOHC), variants of concern (VOC), and variants being monitored (VBM) (Table 1). This categorization is based on factors such as the virus's virulence, transmissibility, capacity to cause serious illness, and fluctuating viral variations (Telenti et al. 2022). Thus, these groups

*Correspondence:
Mohd Fadhlizil Fasihi Mohd Aluwi
fasihi@umpsa.edu.my
[1] Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Persiaran Tun Khalil Yaakob, Kuantan, Pahang, Malaysia
[2] Centre for Bio-aromatic Research, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Persiaran Tun Khalil Yaakob, Kuantan, Pahang, Malaysia
[3] Centre for Drug and Herbal Research, Faculty of Pharmacy, Universiti Kebangsaan Malaysia, Jalan Raja Muda Abdul Aziz, 5300 Kuala Lumpur, Malaysia

Springer Open

© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

Table 1 VOC, VOI and VBM of SARS-CoV-2

Variant groups	Name of Variants	Linease	1st Isolated	Outbreak/ Country of sampling	Mutations	References
VOC	Alpha	B.1.1.7	20 Sep 2020	UK	69–70del, N501Y, P681H	Tao et al. (2021)
	Beta	B.1.351	May 2020	South Africa	K417N, E484K, N501Y	Tao et al. (2021)
	Gamma	B.1.1.28.1	Nov 2020	Brazil	K417T, E484K, N501Y	Tao et al. (2021)
	Delta	B.1.617.2	Oct 2020	India	L452R, T478K, P681R	Tao et al. (2021)
	Epsilon	B.1.429, B.1.427, CAL.20C	July 2020	USA	I4205V and D1183Y in the ORF1ab gene, and S13I, W152C, L452R in the spike protein's S-gene	Tao et al. (2021)
	Omicron	B.1.1.529	9 Nov 2021	South Africa	S371L, G446S, G496S, G399D, S373P, S375F, K417N, N440K, S477N, T478K, E484A, Q4963R, Q498R, N501Y, Y505H, S371F, R408S, T376A, D405N	Fan et al. (2022)
VOI	Theta	P.3	18 February 2021	Philippines	–	Tao et al. (2021)
	Zeta	P2 or B.1.1.28	July 2021	Brazil	–	Tao et al. (2021)
	Lambda	C.37	August 2020	Peru	–	Tao et al. (2021)
	Mu	B.1.621	January 2021	Colombia	–	WHO (2021)
	JN.1	BA.2.86	August 2023	Luxembourg	L455S	WHO (2023b)
VBM	Kappa	B.1.617.1	October 2020	India	–	Tao et al. (2021)
	Lotta	B.1.526	November 2020	USA	–	Tao et al. (2021)
	Eta	B.1.525	December 2020	UK	–	Tao et al. (2021)
	IHU	B.1.640	October 2021	Republic of Congo	–	Colson et al. (2022)

may also have an effect on the effectiveness and diagnostic potential of immunotherapies and immunisations (Sharun et al. 2021). Because of the introduction of new variations, spontaneous sickness, and extensive vaccination, the patterns of SARS-CoV-2 transmission have evolved during the pandemic. Even while the initial pandemic was marked by outbreaks in highly vulnerable people, SARS-CoV-2 major infections in vaccinated people as well as reinfections in previously infected individuals are now becoming more prevalent (Tan et al. 2023).

The WHO designated the Omicron version of COVID-19 as VOC on 26 November 2021, after it was initially found in November 2021 in Botswana, Gauteng, and South Africa (Gao et al. 2022; Silva et al. 2023). It outperformed the delta version and soon became the main lineage worldwide. The variation originated in western Europe, was recognised in the USA on 1 December 2021, and expanded to more than 150 nations, including the USA, UK, Australia, France, Germany, Denmark, Japan, Netherlands, and India (Janssen et al. 2021; Dhama et al. 2023). It is thought to be the most transmissible, most mutated, and partially resistant to COVID-19 vaccination or immunotherapy treatments now in use. The Omicron variant has many lineages, including BA.1, BA.1.1, BA.2, BA.3, BA.4, and BA.5. The WHO identified BA.2.86 as a variation under surveillance on 17 August 2023, after its discovery in a sample on 24 July 2023 (Chen et al. 2022; Desingu and Nagarajan 2022; Lambrou 2023).

By December, a new COVID-19 variety known as JN.1 (Pirola), which is the subvariant of Omicron (BA.2.86), had spread to 12 countries; among them, the USA, UK, China, and Singapore are notable. It was first identified in August in Luxembourg. Furthermore, it was found in Karakulam and Thiruvananthapuram district of Kerala, India, on December 8, 2023 (Reuters 2023). The discovery of this new variant has piqued attention and raised concerns throughout the world, and the WHO has announced as VOI on December 19, 2023 (WHO 2023a). The spike protein's lone mutation is what causes the JN.1 variation. It has an extra L455S mutation in the spike protein, giving it more capacity for immune evasion (Kaku et al. 2024). The spike protein (L455S) mutation found in JN.1 was absent from earlier versions of concern and Omicron sub-variants. Based on preliminary studies, it appears that these variations lessen the capacity of antibodies produced by vaccinations to neutralise them, which is important for JN.1. This is concerning since a number of COVID-19 vaccinations that are currently

being used are based on the spike protein of the SARS-CoV-2 ancestral Wuhan strain (Sohail et al. 2024). Over 60% of COVID-19 cases in the USA are attributed to JN.1, which is mostly due to its fast expansion and domination. Furthermore, there are some symptoms that people should be aware of as they could not be as mild as those of previous Omicron variants, even if its high transmissibility and mild symptoms are like those of earlier Omicron variants (Idris and Adesola 2024). Remember that at this point in time, there is no proof that this variation is more severe or deadly than other variants.

JN.1 continues to cause major illness and mortality; hence, the WHO has classified JN.1 as VOI. The IDSA report on 17 April 2024, JN.1 is anticipated to represent 95% of all SARS-CoV-2 variations in the USA, making it the most extensively circulating variant (IDSA 2024). So far, it has spread in the UK at an 84% weekly pace; JN.1 was associated with 3600 cases worldwide. Travel restrictions were implemented by Singapore and Indonesia in December 2023, since JN.1 was responsible for over 60% of cases in Singapore (The Star 2023). Health experts have cautioned the public to exercise caution considering the increase of COVID-19 cases in Malaysia caused by the JN.1 variation (The Star 2023).

Vaccination has traditionally been recognized as the major method of protecting against viral diseases. Vaccine hesitancy is considered an imminent risk to public health by the WHO (Miyachi et al. 2020). While different factors impacting vaccine acceptance or refusal have been thoroughly stated in previous investigations (Fisher et al. 2020), the same worries persist with COVID-19 vaccines, limiting their effectiveness (Lazarus et al. 2023). The causes for vaccination non-acceptance are many and nuanced, differing not just between countries but also within parts of the same state, and they can change over time. COVID-19 vaccine adoption challenges include distribution, price, accessibility, and acceptability at the national and individual levels (Yarlagadda et al. 2022). Low vaccination rates continue to be a concern in low-income countries, with just 17.4% of persons receiving a first dose (Mathieu et al. 2020). Recent study on vaccination acceptability found that nearly one in every eight vaccinated respondents is apprehensive about booster doses. According to Lazarus et al. (2023), over two-fifths of respondents claimed they were paying less attention to new COVID-19 content. Furthermore, according to the John Hopkins University Coronavirus Resource Centre (latest updated data on 3 October 2023), less than half of the population in 65 nations received only one dose of COVID-19 vaccination (https://coronavirus.jhu.edu/vaccines/international). From Fig. 1, we can easily observe a clear declining trend of COVID-19 vaccination over the world which is reflection of the above scenario.

The reference to viruses like the COVID-19-causing SARS-CoV-2 virus, immune pressure can influence the genetic diversity of the virus. Interestingly, heavy immunological pressure forced the rapid development of BA.2.86 variant to JN.1, giving it enhanced immune evasion capabilities which evade convalescent plasma substantially (Yang et al. 2024). This is consistent with the virus's tendency to change in order to evade the host's humoral immune reaction (Forni et al. 2021). Under high immunological pressure, the virus can exploit mutations to evade the action of antibodies (Andreano et al. 2021). This event lends support

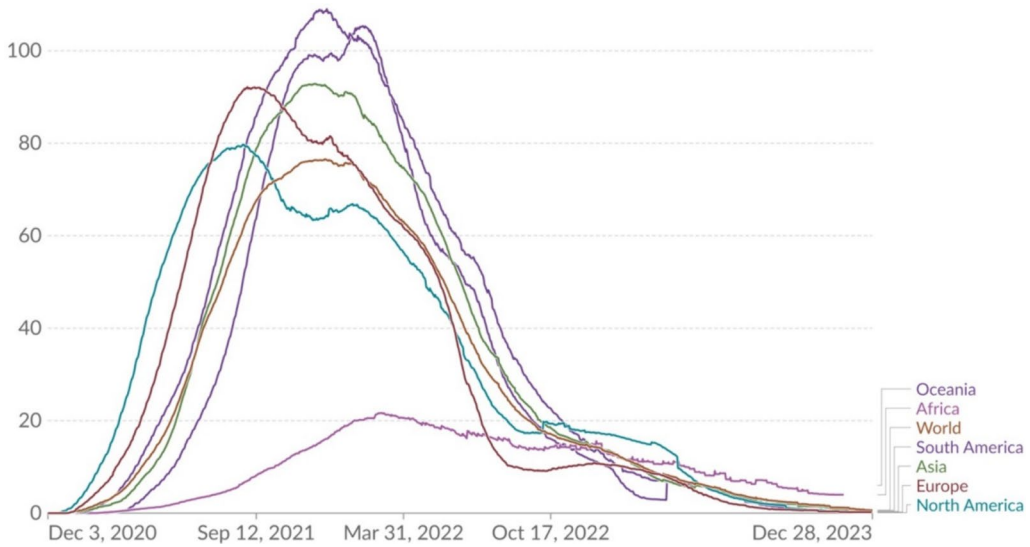

Fig. 1 Data visualisation for COVID-19 vaccine doses administered per 100 people (Mathieu et al. 2020)

to the idea that immunological pressure drives viral evolution (Yang et al. 2024).

In summary, despite the WHO's assurance that the JN.1 variant should not be a major concern, monitoring individuals affected by JN.1 and assessing their vaccination profiles can provide valuable insights into the efficacy of existing vaccinations against newly developing variations. Investigating immune pressure in the context of vaccine development and disease management demands extensive research efforts, enabling researchers and healthcare professionals to anticipate pathogen changes and adapt strategies to uphold or enhance vaccine and treatment effectiveness. Moreover, the creation of vaccinations that target mutants or variations specifically may provide enhanced defence against new strains. Public health guidelines, however, continue to be followed in terms of improving primary healthcare systems and raising awareness of maintaining good personal cleanliness and the key strategy for stopping the spread of new variants.

Abbreviations

COVID-19	Coronavirus disease 2019
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
VBM	Variants being monitored
VOC	Variants of concern
VOHC	Variants of high consequence
VOI	Variants of interest
WHO	World Health Organization

Acknowledgements
Thanks to the Faculty of Industrial Sciences and Technology, Universiti Malaysia Pahang Al-Sultan Abdullah, Lebuhraya Persiaran Tun Khalil Yaakob, Kuantan, Pahang, Malaysia.

Author contributions
MR conceptualized, performed the data curation, analysis, wrote the original draft. AMH and MFFMA reviewed and edited. All authors have read and approved the manuscript.

Funding
No funding was obtained for this study.

Availability of data and materials
Not relevant.

Declarations

Ethics approval and consent to participate
Not relevant.

Consent for publication
Not relevant.

Competing interests
The author claims that their interests are not at odds with one another.

Received: 18 March 2024 Accepted: 28 April 2024
Published online: 14 May 2024

References

Andreano E, Piccini G, Licastro D, Casalino L, Johnson NV, Paciello I, Rappuoli R (2021) SARS-CoV-2 escape from a highly neutralizing COVID-19 convalescent plasma. Proc Nat Aca Sci 118(36):e2103154118
Chen J, Wang R, Gilby NB, Wei GW (2022) Omicron variant (B. 1.1. 529): infectivity, vaccine breakthrough, and antibody resistance. J Chem Inform Mod 62(2):412–422
Colson P, Delerce J, Burel E, Dahan J, Jouffret A, Fenollar F, Raoult D (2022) Emergence in southern France of a new SARS-CoV-2 variant harbouring both N501Y and E484K substitutions in the spike protein. Arch Virol 167(4):1185–1190
Desingu PA, Nagarajan K (2022) Omicron BA. 2 lineage spreads in clusters and is concentrated in Denmark. J Med Virol 94(6):2360
Dhama K, Nainu F, Frediansyah A, Yatoo MI, Mohapatra RK, Chakraborty S, Harapan H (2023) Global emerging Omicron variant of SARS-CoV-2: Impacts, challenges and strategies. J Infec Public Health 16(1):4–14
Fan Y, Li X, Zhang L, Wan S, Zhang L, Zhou F (2022) SARS-CoV-2 Omicron variant: recent progress and future perspectives. Sign Transduct TargetTher 7(1):1–11
Fisher KA, Bloomstone SJ, Walder J, Crawford S, Fouayzi H, Mazor KM (2020) Attitudes toward a potential SARS-CoV-2 vaccine: a survey of US adults. Annal Int Med 173(12):964–973
Forni D, Cagliani R, Pontremoli C, Mozzi A, Pozzoli U, Clerici M, Sironi M (2021) Antigenic variation of SARS-CoV-2 in response to immune pressure. Mol Ecol 30(14):3548–3559
Gao SJ, Guo H, Luo G (2022) Omicron variant (B. 1. 1. 529) of SARS-CoV-2, a global urgent public health alert! J Med Virol 94(4):1255
Horita N, Fukumoto T (2023) Global case fatality rate from COVID-19 has decreased by 96.8% during 2.5 years of the pandemic. J Med Virol. https://doi.org/10.1002/jmv.28231
https://coronavirus.jhu.edu/vaccines/international
https://www.idsociety.org/covid-19-real-time-learning-network/diagnostics/covid-19-variant-update/#/+/0/publishedDate_na_dt/desc/
https://www.reuters.com/business/healthcare-pharmaceuticals/who-classifies-jn1-covid-19-variant-interest-2023-12-19/
https://www.thestar.com.my/news/nation/2023/12/25/be-wary-of-the-more-transmissible-jn1
https://www.worldometers.info/coronavirus/
Idris I, Adesola RO (2024) Emergence and spread of JN. 1 COVID-19 variant. Bullet Nat Res Centre 48(1):1–3
Jansen L, Tegomoh B, Lange K, Showalter K, Figliomeni J, Abdalhamid B, Donahue M (2021) Investigation of a SARS-CoV-2 B. 1. 1. 529 (omicron) variant cluster: Nebraska, November–December 2021. Morb Mortal Week Rep 70(51–52):1782
Kaku Y, Okumura K, Padilla-Blanco M, Kosugi Y, Uriu K, Hinay AA, Sato K (2024) Virological characteristics of the SARS-CoV-2 JN. 1 variant. Lancet Infect Dis 24(2):e82
Lambrou AS (2023) Early detection and surveillance of the SARS-CoV-2 variant BA. 2.86—worldwide, July–October 2023. MMWR Morb Mortal Week Rep 72:1162–1167
Lazarus JV, Wyka K, White TM, Picchio CA, Gostin LO, Larson HJ, El-Mohandes A (2023) A survey of COVID-19 vaccine acceptance across 23 countries in 2022. Nat Med 29(2):366–375
Mathieu E, Ritchie H, Rodés-Guirao L, Appel C, Giattino C, Hasell J, Macdonald B, Dattani S, Beltekian D, Ortiz-Ospina E, Roser M (2020) "Coronavirus Pandemic (COVID-19)". Published online at OurWorldInData.org. https://ourworldindata.org/explorers/coronavirus-dataexplorer?facet=none&country=OWID_WRL~OWID_AFR~OWID_ASI~OWID_EUR~OWID_NAM~WID_SAM~OWID_OCE&pickerSort=desc&pickerMetric=population&Interval=6-month+rolling+total&Relative+to+Population=true&Color+by+test+positivity=false&Metric=Vaccine+doses. Accessed Dec 30 2023
Miyachi T, Takita M, Senoo Y, Yamamoto K (2020) Lower trust in national government links to no history of vaccination. The Lancet 395(10217):31–32
Otolorin GR, Oluwatobi AI, Olufemi OT, Esonu DO, Dunka HI, Adanu WA, Mshelbwala PP (2022) COVID-19 pandemic and its impacts on the environment: a global perspective. Narra J. https://doi.org/10.52225/narra.v2i1.72
Our World in Data. Coronavirus (COVID-19) immunizations. https://ourworldindata.org/covid-vaccinations

Sharun K, Tiwari R, Dhama K, Emran TB, Rabaan AA, Al Mutair A (2021) Emerging SARS-CoV-2 variants: impact on vaccine efficacy and neutralizing antibodies. Human Vaccin Immunother 17(10):3491–3494
Silva SJRD, Kohl A, Pena L, Pardee K (2023) Recent insights into SARS-CoV-2 omicron variant. Rev Med Virol 33(1):e2373
Sohail MS, Ahmed SF, Quadeer AA, McKay MR (2024) Cross-reactivity assessment of vaccine-derived SARS-CoV-2 T cell responses against BA. 2.86 and JN. 1. Viruses 16(3):473
Tan ST, Kwan AT, Rodríguez-Barraquer I, Singer BJ, Park HJ, Lewnard JA, Lo NC (2023) Infectiousness of SARS-CoV-2 breakthrough infections and reinfections during the Omicron wave. Nat Med 29(2):358–365
Tao K, Tzou PL, Nouhin J, Gupta RK, de Oliveira T, Kosakovsky Pond SL, Shafer RW (2021) The biological and clinical significance of emerging SARS-CoV-2 variants. Nat Rev Gene 22(12):757–773
Telenti A, Hodcroft EB, Robertson DL (2022) The evolution and biology of SARS-CoV-2 variants. Cold Spring Harbor Perspect Med 12(5):a041390
WHO (2021) https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/
WHO (2023a) https://www.who.int/news/item/13-12-2023-statement-on-the-antigen-composition-of-covid-19-vaccines
WHO (2023b) World Health Organization. Statement on the Fifteenth Meeting of the International Health Regulations (2005) Emergency committee regarding the coronavirus disease (COVID-19) pandemic (2023). https://www.who.int/news/item/05-05-2023-statement-on-thefifteenth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic?adgroupsurvey=%7Badgroupsurvey%7D&gclid=EAIaIQobChMI4Ojtsdbe_gIVjQRyCh07igt4EAAYASACEgJ9pfD_BwE&fbclid=IwAR2M8EAyiSrAodhK9p-X582nHkP2AigpSX8pYIsLsPwqYh4SG26RGokGe7E
WHO (2023c) WHO Coronavirus (COVID-19) Dashboard. World Health Organization. https://covid19.who.int/
Yang S, Yu Y, Xu Y, Jian F, Song W, Yisimayi A, Cao Y (2024) Fast evolution of SARS-CoV-2 BA. 2.86 to JN 1 under heavy immune pressure. Lancet Infec Dis 24(2):e70–e72
Yarlagadda H, Patel MA, Gupta V, Bansal T, Upadhyay S, Shaheen N, Bansal TK (2022) COVID-19 vaccine challenges in developing and developed countries. Cure. https://doi.org/10.7759/cureus.23951

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.