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Review article

Severe acute respiratory syndrome coronavirus 2: Mutations and variants of concern – the Indian scenario

H. S. Darling[1], Purvish Parikh[2], Radhika Vaishnav[3], Amit Verma[4], Ashish Gulia[5], Akhil Kapoor[6], Randeep Singh[7]

[1]Department of Medical Oncology and Hemato-Oncology, Command Hospital Air Force, Bengaluru, Karnataka, [2]Department of Precision Oncology and Research, Shalby Hospital, Mumbai, Maharashtra, [3]Department of Anatomy and Physiology, College of Arts, Science and Education, IvyTech Community College, USA, [4]Department of Molecular Oncology and Cancer Genetics, Max Hospital, New Delhi, [5]Bone and Soft Tissue, Tata Memorial Hospital, Mumbai, Maharashtra, [6]Department of Medical Oncology, TMH Varanasi, Varanasi, Uttar Pradesh, [7]Department of Medical Oncology, Narayana Superspeciality Hospital, Gurugram, Dharamshila, India

***Corresponding author:**
Randeep Singh,
Department of Medical and Hemato oncology, Narayana Super speciality Hospital Gurugram, Dharamshila Narayana Hospital, New Delhi, India.

drrandeep@yahoo.co.in\

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ABSTRACT

When India did well to contain the first wave of coronavirus disease 2019 (COVID-19) pandemic, none of us had an inkling of the magnitude that the second wave was going to take. One of the main reasons for the resurgence is several new mutants of this virus – the important ones for our country being UK Variant, Indian Double mutant, South African, and Brazil variants. Questions regarding their impact on virulence, pathogenicity, transmissibility, detection, clinical symptomatology, morbidity, mortality, potential curability, and possibly decreased therapeutic/vaccine efficacy are being ascertained. We hereby summarize the importance of these variants with respect to Indian scenario, with emphasis on implications regarding COVID-19 diagnosis and efficacy of current vaccines.

Keywords: Vaccination, Coronavirus disease 2019, Pandemic, Double mutant, UK variant, South African variant

INTRODUCTION

It is not unusual for viruses to undergo mutations. For decades, we have seen the influenza virus change its genomic characteristics – with the vaccine manufacturers scrambling to guess the sequence that should be their target for the next year. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is no different, especially since it is a single-stranded ribonucleic acid (RNA) virus. The world is focusing on these genetic changes in the background of the second wave of the coronavirus disease 2019 (COVID-19) pandemic spreading across several countries. In India, the SARS-CoV-2 Consortium on Genomics was formed in December 2020 with 10 laboratories. From the initial 10,000+ samples tested, variants of concern (the UK, South African, and Brazilian mutations) were identified in 771 cases. The Indian double mutation (B1.617 E484Q and L452R) is also considered as variant of concern, having been identified in 206 samples from Maharashtra, especially those from Nagpur.[1] Interestingly, the E484Q is very similar to the E484K mutation – seen in the B.1.351 (South African) and P.1 (Brazilian) variants. Similarly, the L452R mutation is also part of the B.1.427/B.1.429 "Californian" variant first seen in the USA.

Do these mutations correlate with clinical scenario? Are they somehow responsible for increased virulence, infectivity, a different clinical presentation of the infection (gastrointestinal symptoms instead of lung related), lesser benefit from vaccination, and a relapse? These are questions that

affect how the COVID-19 pandemic shall play out and need to be addressed urgently. Our effort is to compile available data on the SARS-CoV-2 mutations with special focus on variants of concern and their clinical relevance in Indian context.[2-4]

TESTING FOR VARIANTS

The terminology used for viral variation is often confusing and various terms such as variant, strain, and lineage are being used interchangeably. This reflects the inherent replication biology of RNA viruses which eventually results in mutations. A variant is formed when specific mutations happen through numerous rounds of viral replication. A strain is termed when a distinctly different phenotype emerges due to sequences of variation and if a new variant is detected as a distinct branch on a phylogenetic tree, a new lineage is identified.

There are two ways to detect COVID-19 infection – reverse transcription polymerase chain reaction (RT-PCR) and antigen tests. RT-PCR is designed to detect specific sequences of the genome, particularly the S (spike) and N (nucleocapsid) genes. If mutations appear in these "target" sequences, the tests may no longer be able to detect the virus, yielding false negatives. As the pandemic progresses, the SARS-CoV-2 virus mutates, resulting in several new variants such as B.1.1.7, B.1.351, and P.1. These three variants have emerged in late 2020. The majority of mutations are common in the S gene.[5-8]

Various global authorities such as the Food and Drug Administration (FDA) and WHO have been evaluating the impact of these emerging new variants on a test's accuracy to detect COVID-19 infection. The sensitivity and specificity of a test may be impacted by various factors such as test design, sequence of the variant, and the prevalence of the variant in the geographical population. If a variant of SARS-CoV-2 evades detection, it will have serious consequences not only for individual patients, who will not receive appropriate treatment but will also affect the quarantine of individuals, contact tracing, and public health. Therefore, it is important to know whether the available tests can correctly identify all variants of SARS-CoV-2. Apart from the general population, this issue complicates care of the immunocompromised patients further, who *per se* are bound to have frequent hospital visits. For example, cancer patients need to be tested every time they come with any significant symptoms.[9,10]

Most of the tests available in India or globally target more stable regions of the genome (N gene), which are less likely to mutate, or have multiple target sequences (3–4 regions in S gene), hence can detect all the above variants which have become prevalent since late 2020. It is recommended that the tests designed to detect multiple genetic targets, should be preferred. Antigen tests detect specific proteins (N or S protein) on the outside of the virus. These tests are less sensitive than molecular tests, but they are cheaper and faster and are being used widely in coronavirus screening programs.[11]

FDA has analyzed various test kits available in the USA like using the TaqPath COVID-19 Combo Kit and the Linea COVID-19 Assay Kit. It is observed that in kits that are designed to detect multiple genetic targets, the overall test sensitivity is not impacted by the emergence of new variants. As a clinician, one should be aware that COVID-19 variants will keep emerging regularly during the pandemic and this may lead to some increase in the false negativity rate of detection. Repeat testing with a different molecular diagnostic test (preferably which target different genetic sequence) may be considered if COVID-19 is still suspected based on clinical behavior.[12]

UK VARIANT

The UK variant of SARS-CoV-2 is popularly known as B.1.1.7 (or VOC 202012/01) and is direct descendent of the D614G lineage.[13] It was first identified in the UK in September 2020. In a few months, it gained notoriety, because it spread across the country and became the dominant viral strain – responsible for the second wave's higher incidence, increased virulence, and hospital admissions.[14] At one point (a few months ago), it was responsible for almost all (98%) of COVID-19 infections in the UK.[15] B.1.1.7 also led to similar picture in other countries, especially Switzerland, Denmark, and the USA.[16] It has now been documented to have spread to more than 114 nations across the globe, including India.[17]

B.1.1.7 has 17 mutations (14 point mutations plus 3 deletions).[18] Of these, as many as eight are in the spike protein, and three of them have the potential to directly benefit the virus, (i) mutation N501Y enhances the binding affinity of the virus to human angiotensin-converting enzyme 2 (ACE2), (ii) mutation P681H is in close proximity to the spike region, augmenting infectivity, and transmissibility, and (iii) deletion ΔH69/ΔV70 is in the S region and is associated with immune escape in immunocompromised patients. It also increases infectivity. No wonder, it led to population growth rate of this VOC 202012/01 in its first 31 days being more than that of all the other 307 lineages put together.[19]

One community study of the outpatient department patients in the UK included samples from 54,906 matching pairs from October 2020 to January 2021. Primary end point was death within 28 days of the COVID-19-positive test. Clearly these were low-risk patients. Yet their data showed a higher risk of death (4.1/1000 positive cases) from the UK B.1.1.7 variant as opposed to the non-UK variant cases (death risk 2.5/1000 positive cases). This translated into a hazard ratio

of 1.64 (with 95% CI of 1.32–2.04).[20] This is in spite of the fact that the deletion ΔH69/ΔV70 has been documented to result in false-negative COVID-19 detection (some commercial testing kits commonly used in the UK failed to detect the spike glycoprotein gene – also called the S gene target failure).[18] Thus, the UK variant of concern was predicted to increase COVID-19-associated cases, infection severity, hospitalization, and deaths – all of which came true, especially in the population that was yet to be vaccinated.[14]

The final question is whether B.1.1.7 will change the protective effect of current COVID-19 vaccines being used. Preliminary data suggest that the vaccine efficacy will be influenced both by the type of vaccine used and the nature of the mutation prevalent in the concerned population overtime.[21] The ongoing second wave of the COVID-19 pandemic bathing most of the globe still has many surprises up its sleeve. While we see the light at the end of the pandemic tunnel, it seems to be flickering, casting shadows of doubt everywhere.[22]

INDIAN DOUBLE MUTATION VARIANT

Double mutation is said to occur when two mutated variants of a virus come together to form a third variant. The one reported in India is a combination of E484Q and L452R variants, and is known by the technical name of B.1.617.[23] E484Q and L452R are escape mutations in the spike proteins of the virus which help the virus to evade the immune system of humans. The B.1.617 coronavirus variant was identified for the 1st time in India on October 5, 2020. The lineage has so far been detected in 10 states in India, including Maharashtra, Delhi, West Bengal, Gujarat, Karnataka, Madhya Pradesh, and Jharkhand, as well as in 16 other countries such as Australia, Belgium, Germany, Ireland, Namibia, New Zealand, Singapore, the UK, and the US.[24]

Due to enhanced viral replication, B.1.617 variant is expected to be far more transmissible than the original one. This is attributed to its spike protein having more binding power to attack and infect human cells by biding itself to ACE2 entry receptors faster. In an analysis of the samples collected from Maharashtra, an increase in the fraction of samples with the E484Q and L452R mutations was found as compared with December last year.[25] Furthermore, since these are escape mutations, the double mutant also possesses the immune escape mechanism, theoretically, it may escape the antibodies in the human body developed from vaccination or previous infection.[23]

Besides, it is being implicated to evade the RT-PCR test as well. The conventional SARS-CoV-2 strain usually colonizes the nasopharyngeal region where the body's immune system counters it and stops it from directly accessing the lungs. However, the double mutant variant was believed to evade the nasopharyngeal region and colonize the lungs directly. This might be the reason why the sample drawn from the nasopharyngeal region might not have the viral load, resulting in the patient being recorded negative.[24] The Indian Council of Medical Research has commented that Covaxin neutralizes against multiple variants of SARS-CoV-2 and effectively neutralizes the double mutant strain as well.[25] However, there are inadequate data presently to support or refute the statement, and it is recommended to continue the vaccination drive with the available vaccines.

BRAZILIAN VARIANT

The Brazilian Ministry of Health reported the first case of reinfection by SARS-CoV2 on December 9, 2020.[26] This case was of a health care worker, aged 37 years, who had been infected with the virus in June and again in October 2020, as confirmed by RT-PCR. The genome of both viral samples was sequenced and the second infection was attributed to B.1.1.28 (E484K) strain variant, or P.2. In Manaus, Brazil, 78% of the population was determined to be seropositive for SARS-CoV-2 antibodies in October 2020, suggesting herd immunity.[27] Despite this, a rapid and alarming "second wave" of infections ensued in January 2021.[28,29] Such a second wave could have been due to variants that were successful at evading immune detection. Of particular concern is P.1, which has 17 acquired mutations, including 10 amino acid changes in the spike protein, is also known as 20J/501Y.V3, and is an offshoot of the B.1.1.28 lineage.[30] Although it originated in South America, it was first reported in Japan, in four samples from people who had traveled from Brazil.[31] The three amino acid substitutions of most concern in P.1 lineage were K417T, E484K, and N501Y, as these were in the receptor-binding domain (RBD) of the spike protein and are involved in binding to the ACE2 protein. K417T substitution occurs at the same site as the K417N mutation in the B.1.351 lineage. E484K appears to be involved in vaccine escape and is at the same site as one of the mutations seen in the Indian double mutant. N501Y is seen in several lineages of the SARS-CoV-2 virus which includes the UK, South African, and Brazilian variant strains. Both K417T and N501Y appear to increase transmission by enabling stronger binding to human cells.[32]

SOUTH AFRICAN VARIANT

One of the several SARS-CoV-2 variants believed to be of particular importance, South African variant (20H/501Y.V2, B.1.351 lineage) was first detected in the Nelson Mandela Bay metropolitan area of the Eastern Cape province of South Africa in October 2020, from where it has rapidly become the predominant strain in many countries such as the USA/UK/Norway/India.[33] This variant is characterized by eight mutations in the spike protein-coding sequences, including three in the RBD of the S protein, K417N, E484K, and N501Y.

The last mutation is also present in the UK VUI-202,012/01 variant and it helps the virus to attach easily to human cells and also evades immune system.[34] B.1.351 strains are less effectively neutralized by convalescent plasma from patients with COVID-19 and by sera from those vaccinated with several vaccines in development.[8,35] However, a recent small study examining the impact of the N501Y mutation on the recently licensed Pfizer-BioNTech vaccine did not show any loss of antibody neutralization efficacy.[36]

A more troubling new variant and its close relative have been identified in South Africa/Brazil, the N501Y.V2 variant. It has many more sequence changes located close to RBD and can affect neutralizing antibody (NAbs) National Institute of Health study now shows that NAbs induced by the Moderna mRNA vaccine are about 6-fold less active against the N501Y.V2 (B1.351) strain.[37] The study undertaken jointly by South Africa's and Oxford University demonstrated reduced efficacy of the AstraZeneca COVID-19 vaccine against the 501.V2 variant. The study found that in a sample size of 2000, the AZD1222 vaccine afforded only "minimal protection," although all the cases of disease post-vaccine were mild or moderate. In the meantime, the US drug company Moderna has announced the development of a booster vaccine candidate called mRNA-1273.351 against the emerging South African variant and has initiated Phase I studies to see whether this modified vaccine with variant-specific proteins would increase the immunological effect.[38,39]

VACCINE TYPES AND RECOMMENDATIONS IN VIEW OF VARIANTS

"Are first-generation vaccines good enough for new COVID-19 Variants"? SARS-CoV-2 has inflicted approximately 150 million known cases of COVID-19 till date.[40] Vaccines and antibody therapies have given us lot of hope to control this pandemic thus controlling the death. The current vaccine strategies are directed at the viral "spike protein or S gene," but newer viral variants, particularly the S gene variants, weaken this strategy. Thus, vaccine resistance has emerged as a new challenge.

CURRENTLY, APPROVED, AND RECOMMENDED VACCINES ARE MAINLY OF THREE TYPES

mRNA vaccine: Examples – Pfizer-BioNTech, Moderna

Laboratory data on the messenger RNA (mRNA) vaccines' efficacy against SARS-CoV-2 variants have been generated using genetically engineered versions of concerning variants and measuring NAbs titers. Research studies have shown that these vaccines elicit lower levels of NAbs against SARS-CoV-2 variants than against older common strain. Testing serum samples from individuals immunized with two doses of the Pfizer-BioNTech vaccine against recombinant viruses containing some or all of the spike protein mutations found in the B.1.351 variant, the NAbs titer against B.1.351 was approximately two-thirds lower than that of USA-WA1/2020, an early SARS-CoV-2 isolate.[41] The NAbs may be low but may provide protection against infection to some extent and severe complication. Modifying the RNA sequence, incorporating the mutant sequence while vaccine preparation is feasible. Thus, newer version of tailor-made vaccine or cocktail can be easily manufactured and given as booster dose.

Vector vaccine: Examples – CoviShield (Oxford-AstraZeneca), Johnson and Johnson/Janssen vaccine

Phase II trial with Oxford-AstraZeneca vaccine in South Africa was not encouraging. The trial data suggest that the vaccine did not protect against mild-to-moderate COVID-19 caused by the B.1.351 variant.[42] The genetic material used is large enough to represent majority portion of the viral genetic make-up, thus covers more possibilities of generating polyclonal immune responses targeting multiple virus protein/peptide sequence. In Scotland, researchers showed that Oxford-AstraZeneca's vaccine up to 94% effective compared to mRNA vaccine Pfizer-BioNTech's vaccine up to 85% effective in preventing COVID-19-related hospitalizations 28–34 days after a single dose.[43] The NAbs titer may be low albeit the immunity generated is polyclonal covering larger sequences and may provide better protection against infection including severe complication.

Protein subunit vaccine: Examples – Covaxin (Bharat Biotech International Ltd.) and Novavax

This is the most established and proven method of vaccination such as seasonal influenza, rabies, polio, Pertussis, and Japanese encephalitis. Data suggest that Novavax clinical efficacy is against both COVID-19 and both the UK and South African variants. Strong efficacy has been observed in Phase 3 UK trial where over 50% of cases are attributed to the now predominant UK variant and the remainder attributable to COVID-19 virus. Similarly, in Phase 2b South Africa trial, clinical efficacy has been demonstrated, with over 90% of sequenced cases attributable to prevalent South Africa escape variant.[43]

CONCLUSION

It is a fact that COVID-19 virus and its different variants are now established and will coexist with the human species for a long time. Despite tons of articles published in various scientific journals every month, we still have been able to discover only the tip of the iceberg. Clinical features along

with sensitive microbiological test and specific radiological features will be a key to the diagnosis of these new variants. The current vaccines have proven to be efficacious partially or completely to the original as well as variants of SARS-CoV-2 and should be promoted and continued for mass immunization. We do require newer version/generation of vaccines and these newer generation may be given as booster dose in future. As the human race joins hand and learn to fight with SARS-COV-2, personal protective measures, masking, hand washing is the best protective gear.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

Nil.

REFERENCES

1. Available from: https://www.timesofindia.indiatimes.com/life-style/health-fitness/health-news/india-coronavirus-variant-what-makes-indias-double-mutant-covid-variant-b-1-617-so-concerning/articleshow/82029148.cms. [Last accessed on Apr 20]
2. Available from: https://www.path.org/articles/virus-variants-and-vaccine-efficacy/?gclid=EAIaIQobChMIlqq50Jf_7wIVsoNLBR2JXQiFEAAYAyAAEgIiDfD_BwE. [Last accessed on Apr 20]
3. Available from: https://www.who.int/news-room/feature-stories/detail/the-effects-of-virus-variants-on-covid-19-vaccines?gclid=EAIaIQobChMI6L-g7pf_7wIVwgRyCh2SwwHwEAAYAiAAEgKSnvD_BwE. [Last accessed on Apr 20]
4. Mehta P, Parikh P, Aggarwal S, Batra A, Patel A, Kulkarni P, *et al*. Has India met this enemy before? From an eternal optimist's perspective: SARS-CoV-2. Indian J Med Sci 2020;72:8-12.
5. World Health Organization. SARS-CoV-2 Variants. Geneva: World Health Organization; 2021. Available from: https://www.who.int/csr/don/31-december-2020-sars-cov2-variants/en. [Last accessed on 2021 Apr 23].
6. Kemp SA, Datir RP, Collier DA, Ferreira I, Carabelli A, Harvey W, *et al*. Recurrent emergence and transmission of a SARS-CoV-2 Spike deletion ΔH69/ΔV70. bioRxiv 2020;2020:422555.
7. Santos JC, Passos GA. The high infectivity of SARS-CoV-2 B.1.1.7 is associated with increased interaction force between Spike-ACE2 caused by the viral N501Y mutation. bioRxiv 2021;2021:424708.
8. Wu K, Werner AP, Moliva JI, Koch M, Choi A, Stewart-Jones GB, *et al*. mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants. bioRxiv 2021;2021:427948.
9. Gundavda MK, Gundavda KK. Cancer or COVID-19? A review of guidelines for safe cancer care in the wake of the pandemic. SN Compr Clin Med 2020;2020:1-11.
10. Raja T, Parikh PM, Ghafur A, Krishna MV, Agarwal A, Singh R. South Asian declaration consensus guidelines for COVID-19 vaccination in cancer patients. South Asian J Cancer 2021. In Press.
11. Parikh PM, Bapna A, Krishna MV, Mehta P, Aggarwal S, Gulia A. COVID-19 testing in India in comparison to the rest of the world. If Indian testing strategy was replicated in the other top 15 COVID-19 affected countries in the world, the status would be startlingly different. Indian J Med Sci 2020;72:107-9.
12. Parikh P, Mehta P, Bansal S, Aggarwal S, Patel A, Batra A, *et al*. Protecting health-care professionals and workers (other than COVID-19 management facilities) from contamination during COVID-19 pandemic. Indian J Med Sci 2020;72:3-4.
13. Davies NG, Abbott S, Barnard RC, Jarvis CI, Kucharski AJ, Munday JD, *et al*. Estimated transmissibility and impact of SARS-CoV-2 lineage B.1.1.7 in England. Science 2021;372:6538.
14. Public Health England. Investigation of Novel SARS-COV-2 Variant: Variant of Concern 202012/01; 2020. http://www.gov.uk/government/publications/investigation-of-novel-sars-cov-2-variant-variant-of-concern-20201201.[Last accessed on Apr 28]
15. New and Emerging Respiratory Virus Threats Advisory Group. NERVTAG Meeting on SARS-CoV-2 Variant under Investigation VUI-202012/01; 2020. Available from: https://www.khub.net/documents/135939561/338928724/SARS-CoV-2+variant+under+investigation%2C+meeting+minutes.pdf/962e866b-161f-2fd5-1030-32b6ab467896.[Last accessed on Apr 28]
16. Washington NL, Gangavarapu K, Zeller M, Bolze A, Cirulli ET, Barrett KM, *et al*. Emergence and rapid transmission of SARS-CoV-2 B.1.1.7 in the United States. Cell 2021;
17. Available from: https://www.theprint.in/india/india-successfully-cultured-uk-variant-of-coronavirus-strain-says-icmr/578381. [Last accessed on 2021 Apr 20].
18. Public Health England. Investigation of novel SARS-CoV-2 variant Variant of Concern 202012/01: Technical Briefing 3; 2021. Available from: https://www.assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/950823/Variant_of_Concern_VOC_202012_01_Technical_Briefing_3_-_England.pdf.[Last accessed on Apr 28]
19. Kissler S, Fauver JR, Mack C, Tai CG, Breban MI, Watkins AE, *et al*. Densely sampled viral trajectories suggest longer duration of acute infection with B.1.1.7 variant relative to non-B.1.1.7 SARS-CoV-2. medRxiv 2021;2021:21251535.
20. Challen R, Brooks-Pollock E, Read JM, Dyson L, Tsaneva-Atanasova K, Danon L. Risk of mortality in patients infected with SARS-CoV-2 variant of concern 202012/1: Matched cohort study. BMJ 2021;372:n579.
21. Mahase E. Covid-19: Novavax vaccine efficacy is 86% against UK variant and 60% against South African variant. BMJ 2021;372:n296.
22. Parikh P, Singh R. Hot race for COVID-19 vaccines light at the

end of the tunnel just got brighter. Int J Mol Immunol Oncol 2021;6:1-3.
23. "Double Mutant" Covid Variant: Here's what we know as Israel Reports Vaccine Efficacy against Variant First Detected in India. Available from: https://www.forbes.com/sites/siladityaray/2021/04/20/double-mutant-covid-variant-heres-what-we-know-as-israel-reports-vaccine-efficacy-against-variant-first-detected-in-india/?sh=595266252fb3. [Last accessed on 2021 Apr 23].
24. B.1.617: The Curious Case of the Deadly Double Mutant Coronavirus Strain. Available from: https://www.in.news.yahoo.com/b-1-617-curious-case-125400557.html. [Last accessed on 2021 Apr 23].
25. Coronavirus: What makes India's double mutant COVID variant, B.1.617 so Concerning? Available from: https://www.timesofindia.indiatimes.com/life-style/health-fitness/health-news/india-coronavirus-variant-what-makes-indias-double-mutant-covid-variant-b-1-617-so-concerning. [Last accessed on 2021 Apr 23].
26. Available from: https://www.virological.org/t/spike-e484k-mutation-in-the-first-sars-cov-2-reinfection-case-confirmed-in-brazil-2020/584. [Last accessed on 2021 Apr 21].
27. Buss LF, Prete CA Jr., Abrahim CM, Mendrone A Jr., Salomon T, de Almeida-Neto C, *et al*. Three-quarters attack rate of SARS-CoV-2 in the Brazilian Amazon during a largely unmitigated epidemic. Science 2021;371:288-92.
28. Taylor L. Covid-19: Is Manaus the final nail in the coffin for natural herd immunity? BMJ 2021;372:n394.
29. Sabino EC, Buss LF, Carvalho MP, Prete CA, Crispim MA, Fraiji NA, *et al*. Resurgence of COVID-19 in Manaus, Brazil, despite high seroprevalence. Lancet 2021;397:452-5.
30. Faria NR, Mellan TA, Whittaker C, Claro IM, da Candido DS, Mishra S, *et al*. Genomics and epidemiology of a novel SARS-CoV-2 lineage in Manaus, Brazil. medRxiv 2021;2021:21252554.
31. Fujino T, Nomoto H, Kutsuna S, Ujiie M, Suzuki T, Sato R, *et al*. Novel SARS-CoV-2 variant in travelers from Brazil to Japan. Emerg Infect Dis 2021;27:1243-5.
32. Available from: https://www.nytimes.com/interactive/2021/health/coronavirus-variant-tracker.html. [Last accessed on 2021 Apr 21].
33. BBC News Online. South Africa Coronavirus Variant: What is the Risk? BBC News. Available from: https://www.bbc.com/news/health-55534727. [Last accessed on 2021 Apr 18].
34. Tang JW, Tambyah PA, Hui DS. Emergence of a new SARS-CoV-2 variant in the UK. J Infect 2021;82:e27-8.
35. Wibmer CK, Ayres F, Hermanus T, Madzivhandila M, Kgagudi P, Oosthuysen B, *et al*. SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma. Nat Med 2021;27:622-5.
36. Xie X, Zou J, Fontes-Garfias CR, Xia H, Swanson KA, Cutler M, *et al*. Neutralization of N501Y mutant SARS-CoV-2 by BNT162b2 vaccine-elicited sera. bioRxiv 2021;2021:425740.
37. Moore JP, Offit PA. SARS-CoV-2 vaccines and the growing threat of viral variants. JAMA 2021;325:821-2.
38. Booth W, Johnson CY. South Africa Suspends Oxford-AstraZeneca Vaccine Rollout after Researchers Report "Minimal" Protection against Coronavirus Variant. London: The Washington Post; 2021.
39. Tanne JH. Covid-19: Moderna plans booster doses to counter variants. BMJ 2021;372:n232.
40. Available from: https://www.worldometers.info/coronavirus.
41. Liu Y, Liu J, Xia H, Zhang X, Fontes-Garfias CR, Swanson KA, *et al*. Neutralizing activity of BNT162b2-elicited serum. N Engl J Med 2021;384:1466-8.
42. Rubin R. COVID-19 Vaccines vs variants determining how much immunity is enough. JAMA 2021;325:1241-3.
43. Available from: https://www.ir.novavax.com/node/15506/pdf.

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