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Review Article

A Recent Epidemiological Condition of Covid-19 Pandemic: A Review

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Abstract

The ongoing Covid-19 pandemic has grappled the world with fear, infecting around 18.2 Cr people and resulting in the deaths of 39.5 L in the span of a mere eighteen months (until July 2021). First identified as the cause of a cluster of pneumonia cases in Wuhan, China in 2019, Covid-19 is now proving to be a complex and long-lasting challenge for everyone. Just as any other virus, SARS-CoV-2 also mutates all the time, it has been acquiring minor random mutations ever since it jumped from animal (bat) to humans. These constant mutations are creating new variants and are posing a challengeto scientific efforts all over the globe. The aftermath is especially felt in the United Kingdom (with the B.1.1.7 variant), India (B.1.617), and Brazil (P1). Despite the extraordinary speed of vaccination and other drug discoveries against the novel corona virus, these variants continue to threaten mass destruction. This article describes SARS-CoV-2, its dominant variants (α, β, γ), associated mortality rate, epidemic, and prevalence factor, how immune system reacted to different variants and the current treatment available.

Keywords: Epidemic; Immune Evasion; SARS-CoV-2; Dominant Variants; Spike Protein; and Variant of Concern

Introduction

The first Human corona virus was identified in the mid -1960s [1,2] and until now seven corona viruses directly infect humans (229E, NL63, OC43, HKU1) causing minor infections. The animal corona viruses (MERS-CoV, SARS-CoV, and SARS-CoV-2) are posing a major threat to human existence by causing fatal diseases. COVID-19 is caused by the RNA virus SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona virus 2). The genome of CoV-2 is a single-stranded positive-sense RNA (+ssRNA) which is larger than any other RNA viruses. The nucleocapsid protein (N) forms the capsid outside the genome and the genome is protected by a membrane protein (M), spike protein (S), and envelope protein (E) envelope made up of three structural proteins [3].

Among all these structural proteins, spike protein is the main component responsible for the entry of the virus into the host. It has two subunits, S1: which binds to a receptor on the surface of the host's cell; S2: which fuses with the cell membrane. The S1 subunit binds to the ACE-2 enzyme receptor on the target membrane. The spike protein gets activated by the host transmembrane serine protease, TMPRSS2. The virus then enters the host cell by endocytosis and there it replicates and translates to form more of the main cause infection [4].

SARS-CoV-2 variants of concern (VOCs)

Viruses constantly change and become more diverse by mutations. The first mutant of SARS-CoV-2 was the D614G strain which showed up in Australia and India in May 2020. Today, there are multiple variants of SARS-CoV-2 around the world among which the three most dangerous and rising variants are-The India or Delta variant (B.1.617.2), The UK, cantor Alpha variant (also known as B.1.1.7), and Brazil or Gamma variant (P.1).

The indian or delta variant (B.1.617.2) and delta plus variant (AY.1)

The World Health Organization has categorized this variant as a variant of concern (VOC) which implies that this variant is more transmissible and causes more severe illness and reduces the effectiveness of vaccines or treatments. The strain has been detected in at least 82 countries and 51 U.S. states. The Spike protein mutations in B.1.617.2: T19R, G142D, 156 del, 157 del, R158G, L452R, T478K, D614G, P681R, D950N, E484K. It lacks the E484Q mutation. The Delta plus mutant comes with an additional K417N mutation. Scientists have called this mutation a dangerous one as it has increased immune evading properties and can be transmitted more easily even in Covid recovered patients. These mutations also increase the virus's affinity to bind to ACE-2 receptors. Symptoms: Dry cough, tiredness, fever. The severe symptoms of this strain include shortness of breath, abdominal pain, and skin rashes, loss of smell and appetite, and runny nose [5]. The number of SARS-CoV-2 Delta variant cases worldwide as of February 07, 2022, by Statista 4,186,000 (SARS-CoV-2 delta variant cases worldwide 2021 | Statista). The mortality rate associated with Delta variant is +137% (50-230%) [5].

Public Health England reported on June 3, 2021, that twelve of the 42 deaths in England due to the Delta strain were among the fully vaccinated, and that it was spreading approximately twice as rapidly as the Alpha version [6]. Foothills Medical Centre in Calgary, Canada, reported on June 11 that half of their 22 Delta variant cases were among the completely vaccinated [7].

The UK, Kent, or alpha variant (B.1.1.7)

This variant has also been categorized as the Variant of concern (VOC) by WHO. The strain has been detected in at least 155 countries and 55 U.S. states. In India, 3,119 cases have been reported with this strain so far. The number of SARS-CoV-2 Alpha variant cases worldwide as of February 07, 2022, by Statista 1,162,427 (SARS-CoV-2 Alpha variant cases worldwide 2021 | Statista). The mortality rate associated with Alpha variant is +59% (44-74%) B.1.1.7 with E484K assumed to only differ from B.1.1.7 on neutralizing antibody activity [8-10].

The Spike protein mutations in B.1.1.7: N501Y, HV69/70, and P618H

The mutations in the spike protein cause the conformational change in the S1, S2 subunits, and the Receptor binding domain site. These changes make the variant more transmissible and also increase the chances of reinfection (by neutralizing the antibodies). Symptoms: Fever, cough, loss of appetite and smell, shortness of breath, runny nose. The number of SARS-CoV-2 Beta variant cases worldwide as of February 07, 2022, by Statista 38143 (SARS-CoV-2 Beta variant cases worldwide 2021 | Statista). The associated mortality rate with Beta variant has been possibly increased since last year (40,380 death recorded worldwide on February 07, 2022). Although the T cell response generated by the D614G virus is reduced, it is still effective [11,12].

Brazil or gamma variant (P.1)

It is categorized as the variant of Concern; the gamma variant has been detected in at least 62 countries and 52 U.S. states. So far no cases of this strain have been detected in India [4]. The Spike protein mutations in P.1: N501Y, E484K. The E484K mutation changes the structure of the Receptor binding motif of the spike protein and increases the interaction between the virus and the ACE-2 receptor which causes increased viral entry. However, this variant is not believed to be more deadly than others. Symptoms: Fever, cough, loss of appetite and smell, shortness of breath, runny nose. The number of SARS-CoV-2 Gamma variant cases worldwide as of February 07, 2022, by Statista 122,392 (SARS-CoV-2 Gamma variant cases worldwide 2021 | Statista). The associated mortality rate with Gamma variant is +50% (50% CrI, 20-90%). The reported confidence or credible interval has a low probability, so the estimated value can not only be understood as possible, not certain nor likely. As for the fatality ratio, infections by Gamma were also found to be 10-80% more lethal [13-15].

SARS-CoV-2 V501Y.V2 strain (B.1.351)

Since the outbreak of the pandemic (2020-21), the SARS-CoV-2 has been continually changing, transforming into a new variant

strain. Due to the introduction of new variant strains, the World Health Organization (WHO) has documented a recurrence of SARS-CoV-2 infection in a few countries. The Indian public health system has also followed the spread of the SARS-CoV-2 mutation across the country, recognizing the necessity of genomic monitoring. VUI- 202012/01 variation (lineage B.1.1.7) was recently detected and reported from India [16] as a result of this work. Before being detected, these tourists may have disseminated the virus to intimate contacts, resulting in the emergence of novel variations in India. The Indian Council of Medical Research (ICMR)-National Institute of Virology (NIV), Pune, has been screening overseas passengers for SARS-CoV-2 as part of ongoing surveillance measures, with a focus on Indian nationals returning from South Africa (Johannesburg) and Tanzania.

The presence of SARS-CoV-2 was discovered using the real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) technique in clinical samples (nasal/throat swabs) of four returnees from South Africa. Two of the men (ages 44 and 39) developed a low-grade fever and cold for five days and cough with dyspnea for eight days, respectively, while the other two were asymptomatic (age: 19 and 56 years). No new symptoms appeared in any of the instances, and they all fully recovered. The positive samples were utilized in a hybrid capture-based technique to identify the variations using next-generation sequencing to obtain the genome of SARS-CoV-2. Between 98.93 and 99.96 percent of the genome was recovered (in comparison to reference sequences) [17]. The discovery of the South African V501Y.V2 in travelers has alarmed the country, and a thorough search for these variations is currently underway during diagnosis and sequencing in cases where cases are rapidly increasing after a period of control in the country. Because genetic changes are a natural component of the life cycle of RNA viruses, limiting the spread of new variant strains of SARS-CoV-2 by implementing existing pandemic control measures should be the primary strategy for preventing future transmission. As the result, the virus's ability to evolve will be limited.

The Omicron (B.1.1.529 Covid variant)

Although the Omicron version has "concerning" alterations that might make it more transmissible and immune-evading, vaccinations are still an important tool, according to the researchers. The B.1.1.529 Covid variant, first detected in South Africa in last week of November'2021, was designated by the World Health Organization as a Variant of Concern (VOC). The Omicron virus possesses roughly 50 mutations, 32 of which are spike proteins, which the virus utilizes to enter human cells, and 10 of which are high-importance changes, such as the H655Y, P681H, and N679K mutations, which might boost the virus's transmissibility. Increased infectivity is thought to be connected to the mutations R203K and G204R. Deletions in NSP6 have the same ability to fool the immune system. Similarly, deletions at NSP6 have the potential to deceive the immune system. Weakness, lack of appetite, and Covid pneumonia are all common symptoms. No cough or fever, but joint pain has been detected in affected patients. The virus has returned, this time with more energy, tactics, and disguise, as well as a greater death rate and a shorter time to reach the extreme. Because the strain does not reside in the nasopharyngeal area, it immediately affects the lungs, resulting in shorter window durations. Fever symptom is absent in many patients, but an x-ray report shows moderate chest pneumonia. COVID19 is frequently found to be negative on a nasal swab.

Sub-lineages and BA.2 sub variant of Omicron

Three sub-lineages of Omicron have been discovered by scientists. The 'standard' sub-lineage is now known as BA.1/B.1.1.529.1, while the other two are known as BA.2/B.1.1.529.2 and BA.3/B.1.1.529.3 [18]. They have a lot of mutations in common, but they also have a lot of differences. BA.1 and BA.2 have 32 mutations in common but have 28 mutations in common [19]. This distinguishes them from certain other main variants [20], prompting the suggestion that BA.2 be given its own designation based on the Greek alphabet [19] (Table 1). According to 'The Economic Times' dated (12th January'2022), 115 deaths reported globally due to Omicron, one in India. The number of SARS-CoV-2 Omicron variant cases worldwide as of February 07, 2022, by Statista 1,018,274 (SARS-CoV-2 Omicron variant cases worldwide 2021 | Statista).

New spikes in Covid is experiencing two brand-new, quickly spreading sub variants that are spreading over the world. According to health experts and BBC news, BA.4 and BA.5, which were initially discovered in South Africa, may soon overtake other strains as the predominant ones in Europe and the US. Since it first manifested, Covid has undergone mutations or changed its appearance. Variants are the always developing genetic variations. Significant changes like alpha and delta have already caused large waves of infection. The most recent ones, BA.4 and BA.5, are the

ones that experts are most concerned about since they resemble the Omicron variant that produced the wave last winter pretty closely. They were included to the World Health Organization's monitoring list in March after being identified as variants of concern in Europe. They were first identified as being in use in South Africa at the beginning of the year, and they are currently spreading much more quickly than other varieties. They are now accessible in the majority of Europe, and they will soon exceed earlier Covid types. That has already occurred in Portugal - BA. There, 5 has taken over.US authorities claim that the two new sub variants are increasing infection rates. Covid infections are rising in the UK as well, driven by BA.4 and BA.5. Australian cases have also been documented. Experts don't know how badly certain nations will be hurt. None of the Covid variants, including BA.4 and BA.5, are thought to be more lethal than the others. Overall, the sickness is less serious since many individuals have some protection from earlier infections and immunizations. But it does seem as though the new sub variants are spreading more quickly. This is a result of the virus's modifications as well as the potential loss of protection.

The virus has more chances to spread because Covid restrictions have been lifted in several countries. Infections with BA.4 and BA.5 tend to be contagious, even in those who have recently had other Omicron kinds. More hospitalizations and a few more deaths could result from a wave of new infections. Similar to earlier Covid formulations, the risk of serious illness is still higher in the elderly or in people with serious underlying medical conditions. The best line of defense continues to be the current vaccines, even though they are not perfect. They have decreased the probability of a significant sickness in contrast to the other major Covid kinds, such as Delta, Alpha, Beta, and Gamma. Doctors advise getting the recommended number of dosages in order to maximize protection from current and future variations.

	Number of mutations onthe spike protein*	Increased transmissibility (%)**	Number of countries/territo-riesreported
Alpha (B.1.1.7, UK)	11	29	203
Beta (B.1.351, South Africa)	10	25	153
Gamma (P.1, Brazil)	12	38	113
Delta (B.1.617.2, India)	10	97	208
Omicron (B.1.1529, South Africa)	32	-	199

Table 1: Comparison of variants of concern of SARS-CoV-2 March 29, 2022 (Statista).

* No value means increased transmissibility is only suggested/unknown yet.

** Change relative to previously circulating variants at the time and place of appearance. No value means no reliable.

SARS-CoV-2 variants of interest (VOIs)

VOIs are characterised as genetic variants with particular genetic markers that have been linked to alterations that may result in changes that increase transmissibility or virulence, reduce the ability of antibodies acquired through natural infection or vaccination to neutralise the organism, allow the organism to evade detection, or reduce the efficacy of therapeutics or vaccinations. The WHO has so far identified eight variations of interest (VOIs) since the start of the pandemic, including Epsilon (B.1.427 and B.1.429), Zeta (P.2), Eta (B.1.525), Theta (P.3), Iota (B.1.526), Kappa (B.1.617.1), Lambda (C.37), and Mu (B.1.621).

Epsilon (B.1.427 and B.1.429) variants, also known as CAL.20C/L452R, first appeared in the US around June 2020 and increased from 0% to >50% of sequenced cases between September 1, 2020, and January 29, 2021. They showed an 18.6-24% increase in transmissibility compared to wild-type circulating strains. These variations contain particular mutations (B.1.427: L452R, D614G; B.1.429: S13I, W152C, L452R, D614G). This strain was identified by the CDC as a variation of concern in the US because of its heightened transmissibility.

Zeta (P.2) was discovered for the first time in Brazil in April 2020 and carries the important spike mutations L18F, T20N, P26S, F157L, E484K, D614G, S929I, and V1176F. As a result of its probable reduction in neutralisation by antibody therapies and vaccination sera, this variation is categorised as a VOI by the WHO and the CDC.

Eta (B.1.525) and Iota (B.1.526) variants were first discovered in New York in November 2020 and were deemed to be variants of interest by the CDC and the WHO due to their potential reduction in neutralisation by antibody treatments and vaccine sera (B.1.525: A67V, Δ69/70, Δ144, E484K, D614G, Q677H, F888L; B.1.526: (L5F*), T95I, D253G, (S477N*), (E484K*), D614G, (A701V*))

Theta (P.3) variety, also called GR/1092K. The WHO has identified V1 as a variant of interest because it carries important spike mutations (141-143 deletion E484K, N501Y, and P681H) and was first found in the Philippines and Japan in February 2021.

The Kappa (B.1.617.1) variant, which was originally identified in India in December 2021 and is categorised by the WHO and the CDC as a variant of interest, carries important mutations ((T95I), G142D, E154K, L452R, E484Q, D614G, P681R, and Q1071H).

The Lambda (C.37) variant was initially discovered in Peru, and the WHO identified it as a VOI in June2021 due to the variant's increased prevalence in the South American region.

The Mu (B.1.621) variant was found in Columbia, and the WHO classified it as a VOI in August 2021. The Epsilon (B.1.427 and B.1.429) variations have been classified by the CDC as a VOC, and Eta (B.1.525), Iota (B.1.526), Kappa (B.1.617.1), Zeta (P.2), Mu (B.1.621, B.1.621.1), and B.1.617.3 have been classified as VOIs.

Covid-19 as an endemic

COVID-19, the pandemic will not end once the virus has become endemic; instead, it is hoped that enough people will develop immunity to the virus through vaccination and natural infection, resulting in less transmission and far fewer COVID-19-related hospitalizations and deaths, regardless of whether the virus continues to circulate. In contrast to the first wave of SARS in 2003 and the Ebola virus outbreak in West Africa in 2014, when public health interventions eventually stemmed the transmission and brought both outbreaks to an end, SARS-CoV-2 is predicted to circulate indefinitely. While the viruses and circumstances differ significantly, this comparison highlights the crucial need to upgrade our global public health infrastructure and surveillance systems in order to monitor for and respond to the inevitable next possible pandemic virus. Because viruses only propagate when there are enough susceptible persons and enough interaction between them to maintain transmission, it's difficult to predict when COVID-19 will become endemic. It depends on a variety of circumstances, including the degree and length of immune protection provided by vaccination and natural infection, our patterns of interaction with one another, and the virus's transmissibility. Because of the diverse reactions to COVID-19 throughout the world—with some regions adopting "zero-COVID" policies, others with limited responses, and greatly varying vaccination availability and uptake—the patterns

Figure 1: The total number of Covid-19 cases, recoveries and deaths reported as of July 15, 2022.

Number and change of coronavirus (COVID-19) cases and deaths among the most impacted countriesworldwide as of July 15, 2022*

Country	Total number of infections	Average daily number of new cases in last 7 days	Total number of deaths	Change in average new deaths last 7 days vs. previous 7 days
United States	89.294.234	130,000	1.023.256	420
India	43.689.989	18,000	525.56	36
Brazil	33.142.158	55,000	674.78	240
France	32.881.645	100,000	151.45	67

Germany	29.569.943	92,000	142,399	92
Great Britain	23.280.957	28,000	182,262	120
Italy	19.887.543	100,000	169,601	110
South Korea	18.680.142	30,000	24,712	15
Russia	18.206.982	3,500	374,024	42
Turkey	15.297.539	-	99,088	-

Table 2: COVID-19 cases and deaths among hardest hit countries worldwide as of July 15, 2022.

(*Source Johns Hopkins University; Statista).

will likely diverge significantly from those seen with previous pandemics (For worldwide data see figure 1 and table 2).

A meta-analysis of mortality prevalence and associated risk factors in COVID 19 Patients

The mortality rate among hospitalized COVID-19 patients was high, according to one meta-analysis, and male gender, older age, and patients with comorbidities including hypertension, diabetes, and cardiovascular disease were all strongly linked to the risk of death [22].These findings will assist health-care professionals and physicians in detecting the danger of high mortality among COVID-19-infected patients and creating suitable health-care management measures to lower this high mortality rate and battle the COVID-19 pandemic in order to preserve human lives. As per data provided by WHO dated 19th July'2022, total active cases of Covid-19 around the globe are 559,469,605 and cumulative 6,361,157 deaths were reported.

How our immune system reacts to COVID-19 variants - A Research study

The virus that causes COVID-19, SARS-CoV-2, recognises and enters host cells using a protein called the spike protein. Changes, or mutations, have been found in recent SARS-CoV-2 variations at a crucial region on the spike protein called the receptor-binding site (RBS). Antibodies generated against previous virus strains are rendered less effective as a result of certain of these modifications. This enables the variations to evade the immunological response elicited by vaccination or prior infection. It raises fears that new variations will render current vaccinations ineffective, prolonging the epidemic. Proteins, such as the SARS- CoV-2 spike, are made up of long chains of amino acids that fold into a particular form. An amino acid can be replaced by a different type of amino acid due to a mutation in the viral genome. This can change the structure and function of the protein. The mutations in the RBS 417, 484, and 501 are shared by the variations discovered in South Africa and Brazil. Antibodies from COVID-19 patients were examined to see how strongly they bind to viruses with these mutations.

The majority of antibodies produced against SARS-CoV-2 fall into one of two categories. Antibodies from these classes were unable to bind due to mutations at locations 417 and 484. The virus's ability to connect to host cells was similarly harmed by the position 417 mutation. The mutation at position 501, on the other hand, counteracted this impact by increasing host cell binding. The scientists looked into why these alterations hinder antibodies from binding and neutralising. They looked at the molecular structures of over 50 human antibodies that had been linked to the SARS-CoV-2 spike protein. When antibodies from the two main classes attach to the RBS, they virtually invariably interact with the amino acid at position 417 or 484. Changing either amino acid would interfere with antibody binding by disrupting these interactions. This research explains why antibodies produced by COVID-19 vaccinations or spontaneous infection with the original pandemic strain are typically ineffective against these variations of concern [23]. Antibodies that bind to regions of the spike protein outside of the RBS were also examined. Even in the presence of the mutations of interest, these antibodies could still attach and neutralise the virus. These antibodies are very potent against a wide range of coronaviruses (Figure 2) [24,25].

Treatments

As soon as SARS-CoV-2 was discovered, research groups

Figure 2: Antivirals pathways for COVID-19 (Pathogenesis) {Source 1. Colin D. Funk. [24]; 2. Samudrala PK., *et al*. [25]}.

worldwide started examining its biology; they started developing diagnostic tests or investigated public-health measures to control it. So here are some of the available treatments for COVID-19.

Vaccines

World's first COVID-19 vaccine. The Pfizer-BioNTech vaccine was developed in Germany, 2020. At the same time, the Cambridge-developed Moderna vaccine was approved for emergency use in the United States. Bharat Biotech collaborated with the Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV) to create India's first COVID-19 vaccine, COVAXIN. Other vaccines like Sputnik V, Johnson and Johnson, and Covishield are also effective against different corona virus strains (Figure 3) [26].

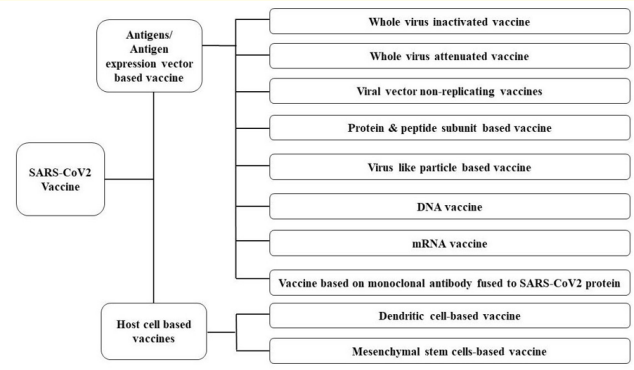

Figure 3: Schematic representation of various SARS-CoV-2 vaccines (Source 1. Ghosh PK. [26]).

Anti-Covid19Drug-2-deoxy-D-glucose

2-DG has been developed by the Institute of Nuclear Medicine and Allied Sciences, New Delhi, a lab of the Defense Research and Development Organization (DRDO), in collaboration with Hyderabad-based Pharma Company, Dr. Reddy's Laboratories. 2-deoxy-D-glucose (2-DG) is a powder that comes in sachets and must be taken orally by dissolving it in water. The medication builds up in virus-infected cells and stops viral manufacturing and energy generation, preventing the virus from spreading.

Antiviral therapy

Remdesivir an intravenous nucleotide prodrug of an adenosine analog. It binds to the viral RNA-dependent RNA polymerase and prevents viral replication by terminating RNA transcription prematurely [27]. Chloroquine or Hydroxychloroquine (with or without Azithromycin) Chloroquine is an anti-malarial drug and Hydroxychloroquine is an analog of chloroquine. They increase

the endosomal pH, inhibiting the fusion of severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) and the host cell membranes [28]. Chloroquine inhibits glycosylation of the cellular angiotensin-converting enzyme 2 receptors, which may interfere with the binding of severe acute respiratory syndrome-associated corona virus (SARS-CoV) to the cell receptor [29]. Both of them have strong immunomodulatory effects. Ivermectin. They have potent anti-inflammatory properties, which are beneficial in people with COVID-19 [30].

Other treatments like Plasma Therapy, Antibody cocktails, etc. are also available.

Discussion and Conclusion

In conclusion, SARS-COV-2 is a dangerous, highly transmissible, and fast-mutating virus. The mutations in SARS-COV-2 have led to continuous pandemics. However, the mutations are not always hazardous, sometimes they have little or no effect on the virus's ability to spread or cause disease. Today vaccines have a remarkable impression against the variants. But as the virus is mutating rapidly, there may be a chance that these vaccines would not be effective against the strains. So it's important for us to follow the safety protocols to the best of our abilities-sanitize regularly, wash our hands, wear masks, and maintain social distance.

We should consider increasing the focus on alternative susceptible locations on the virus that are not impacted by the mutations detected in variants of concern when creating next-generation vaccines and antibody treatments [31]. Vaccines and antibodies that target locations other than the RBS might thus provide protection against a variety of viral types. If SARS-CoV-2 is never totally eradicated, such widespread protection will be critical. SARS-CoV-2 genomic monitoring should be maintained to track the development and spread of novel variant strains. This will

Bibliography

1. Hamre D and Procknow JJ. "A new virus isolated from the human respiratory tract". *Proceedings of the Society for Experimental Biology and Medicine* 121 (1966): 190-193.

2. McIntosh K., *et al*. "Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease". *Proceedings of the National Academy of Sciences of the United States of America* 57 (1967): 933-940.

3. Van Der Most RG., *et al*. "Homologous RNA recombination allows efficient introduction of site- specific mutations into the genome of coronavirus mhv-a59 via synthetic co-replicating RNAs". *Nucleic Acids Research* 20 (1992): 3375-3381.

4. Ghosh PK. "Global efforts on vaccines development against SARS-CoV-2 and Indian endeavor". *MGM Journal of Medical Sciences* 8 (2021): 422-434.

5. Public Health England (2021): 16 and 22.

6. "SARS-CoV-2 variants of concern and variants under investigation in England, technical briefing 14". *Public Health England* (2021): GOV-8530.

7. Pearson H., *et al*. "AHS breaks down vaccination data of COVID-19 Delta variant outbreak at Calgary hospital". *Global News* (2021).

8. "SARS-CoV-2 variants of concern". ECDC.eu. European Centre for Disease Prevention and Control (2021).

9. "SARS-CoV-2 variants of concern and variants under investigation in England Technical Briefing 21". *Public Health England* (2021): 16-22.

10. Nyberg T., *et al*. "Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: Cohort Anal". *BMJ* 373 (2021): 1412.

11. "SARS-CoV-2 Variant Classifications and Definitions". CDC.gov. Centers for Disease Control and Prevention (2020).

12. World Health Organization (2021).

13. Faria NR., *et al*. "Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil". *Science* PMC (2021) 8139423.

14. Andreoni M., *et al*. "Brazil's Covid Crisis Is a Warning to the Whole World, Scientists Say - Brazil is seeing a record number of deaths, and the spread of a more contagious coronavirus variant that may cause reinfection". The New York Times (2021).

15. Zimmer C. "Virus Variant in Brazil Infected Many Who Had Already Recovered from Covid-19". The New York Times. (2021)

16. Yadav PD., *et al*. "Isolation and characterization of VUI-202012/01, a SARS-CoV-2 variant in travelers from the United Kingdom to India". *Journal of Travel Medicine* 28-2 (2021): 9-11.

17. Pragya DY. "Imported SARS-CoV-2 V501Y.V2 variant (B.1.351) detected in travelers from South Africa and Tanzania to India". *Travel Medicine and Infectious Disease* (2021): 102023.

18. "Lineage B.1.1.529". PANGOLIN (2021).

19. McGregor G. "What is stealth Omicron? The rise of the subvariant is alarming some scientists who say it needs its own Greek letter". *Fortune* (2022).

20. "A subvariant of Omicron, BA.2., now comprises almost half of all Danish Omicron cases". Statens Serum Institute (2022).

21. Aleem A., *et al*. "Emerging Variants of SARS-CoV-2 And Novel Therapeutics Against Coronavirus (COVID-19)". In: StatPearls. Treasure Island (FL) (2022).

22. V'kovski P., *et al*. "Coronavirus biology and replication: implications for SARS-CoV-2". *Nature Reviews* 020 (2021): 00468-6.

23. Brian Doctrow. "How COVID-19 variants evade immune response. NIH Research matters-Short Communication". U.S. Department of Health and Human Services National Institutes of Health- (NIH) research matters (2021).

24. Colin D Funk. "A Snapshot of the Global Race for Vaccines Targeting SARS-CoV-2 and the COVID-19 Pandemic". *Frontiers in Pharmacology* (2020): 11-937.

25. Samudrala PK., *et al*. "Virology, pathogenesis, diagnosis and in-line treatment of COVID-19". *European Journal of Pharmacology* 15.883 (2020): 173375.

26. Ghosh PK. "Global efforts on vaccines development against SARS-CoV-2 and Indian endeavor". *MGM Journal of Medical Sciences* 8 (2021): 422-434.

27. Eastman RT., *et al*. "Remdesivir: A Review of Its Discovery and Development Leading to Emergency Use Authorization for Treatment of COVID-19". *ACS Central Science* 6 (2020): 672-683.

28. Jia Liu., *et al*. "Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection *in vitro*". *Cell Discovery* 6 (2020): 16.

29. Vincent MJ, *et al*. "Chloroquine is a potent inhibitor of SARS coronavirus infection and spread". *Virology Journal* 2 (2005): 69.

30. Di Nicolantonio JJ., *et al*. B. "Ivermectin may be a clinically useful anti-inflammatory agent for late-stage COVID-19". *Open Heart* (2020): 001350.

31. Meng Y, *et al*. "Structural and functional ramifications of antigenic drift in recent SARS-CoV-2 variants". *Science* (2021).