GSC Advanced Research and Reviews

eISSN: 2582-4597 CODEN (USA): GARRC2

Cross Ref DOI: 10.30574/gscarr

Journal homepage: https://gsconlinepress.com/journals/gscarr/

(REVIEW ARTICLE)

Check for updates

Structure, mutations and variants of Coronavirus 2 (SARS-CoV): A brief report

Mohammad Farhan Qureshi [1,*], and Shoeb Qureshi [2]

[1] *Prince Sultan Military Medical City, Division of Neonatology, Department of Pediatrics, Saudi Arabia.*

[2] *Department of Research, King Saud Bin Abdulaziz University for Health Sciences, National Guards, Saudi Arabia.*

GSC Advanced Research and Reviews, 2022, 10(03), 001–006

Publication history: Received on 06 January 2022; revised on 27 February 2022; accepted on 01 March 2022

Article DOI: https://doi.org/10.30574/gscarr.2022.10.3.0050

Abstract

The COVID-19, also known as the coronavirus pandemic, is an ongoing global pandemic of coronavirus disease 2019 caused by severe acute respiratory syndrome SARS-CoV-2. The novel virus was first identified from an outbreak in the Chinese city of Wuhan in December 2019, and attempts to contain it there failed, allowing it to spread across the globe. The ongoing pandemic is resulting from extreme acute breathing syndrome. The World Health Organization declared a Public Health Emergency of International Concern on 30 January 2020 and later declared a pandemic on eleven March 2020. As of eight July 2021, greater than 185 million instances had been showed, with greater than four million deaths attributed to COVID-19. Over two hundred twenty-eight million cases of COVID-19 in the world have been reported until the 21st of September 2021 after the first rise in December 2019. The virus caused the disease called severe acute respiratory syndrome. The structure of SARC-CoV-2 shows the presence of Spike S protein, Membrane M protein, Envelop protein and Nucleocapsid. Currently, four SARS-CoV-2 variants, these are Alpha, Beta, Gamma, Delta and Omicron variants originated from United Kingdom, South Africa, Brazil/Japan, and India, respectively. The classification of SARS-CoV-2 variants is based on the mutations in the structure, based inclusions. Mutations in covid-2 create variants which are helpful in making stable vaccine and/or anti-viral drug design. In view of the significance of the structure, mutations and variants of Covid-19, it was found necessary to emphasize the whole problem into a brief review.

Keywords: SARS-CoV-2 genomes; 149 mutations; Variants – Alpha; Beta; Gamma; Delta and Omicron; Stable vaccine or anti-viral drug design

1. Introduction

Coronaviruses (CoVs), enveloped positive-sense RNA viruses, are characterized by club-like spikes that project from their surface. Coronaviruses are a group of RNA viruses that cause diseases in mammals and birds. In humans they cause respiratory tract infections (1). COVID-19 infections occur faster in patients of respiratory distress who have comorbidities such as cardiovascular diseases, hepatic disorders, pulmonary diseases, renal insufficiency, gastrointestinal and neurological complications, in addition to certain risk factors, such age, sex, race and genetics (2, 3). With the recent emergence of severe acute respiratory syndrome (SARS-CoV-2), responsible for the current coronavirus disease pandemic, there are now seven coronaviruses known to infect humans (4). The novel human coronavirus disease has become the fifth documented epidemic since the 1918 flu pandemic. COVID-19 was first reported in Wuhan, China, and has since spread rapidly around the globe with over 210 countries and territories reporting infections. The global new COVID-19 cases and deaths are soaring. Increasing number of cases and deaths are being reported weekly since early October 2020. The numbers peaked in the second week of November 2020 with almost 4 million new cases and 60,000 new deaths recorded. As of 13 December 2020, SARS-CoV-2 is known to have infected over 70.4 million individuals with more than 1.5 million associated deaths reported (5). Fortunately, through

* Corresponding author: Dr. Mohammed Farhan Qureshi

Consultant, Prince Sultan Military Medical City, Division of Neonatology, Department of Pediatrics, Riyadh, Saudi Arabia..

a global effort, COVID-19 vaccines are now entering the market to slow the spread of COVID-19, with the vaccines developed by Pfizer-BioNTech and Moderna both reporting greater than 94% efficacy in clinical trials (5). The Pfizer-BioNTech COVID-19 vaccine has been approved for use in the United States, Canada, and United Kingdom, and priority is being given to people over 80 years of age and health care workers (6). On 18 December 2020, the U.S. Food and Drug Administration issued an emergency use authorization for Moderna's vaccine (5, 7). However, caution is still warranted, as it is still unknown whether these vaccines will provide long-term protection.

Multiple clinical risk factors for severe COVID-19 have been identified, including older age, male sex, African American race, smoking, and comorbidities. Patients with these comorbidities and risk factors have severe responses to the coronavirus infection (3, 8, 9) Studies have shown that a higher incidence of severe and fatal COVID-19 in male sex and is observed with increasing age (3, 10), and it is speculated that this phenomenon is partly attributed to preexisting comorbid conditions (11, 12). To date, there are several systematic reviews being published regarding the effect of comorbidities on prognosis of COVID-19 patients. However, much of the previous data analysis is limited by factors such as incomplete prevalence reporting due to the use of non-peer reviewed data and only using data from China (13, 14, 15). This limits the conclusions that can be drawn from these early studies, particularly given the global reach of the SARS-CoV-2 pandemic.

As the pandemic has progressed, an increasing amount of clinical data has been made available from around the world. Here we analyze the most recent data available in the literature to gain better insights into the development of COVID-19 and severe forms of the disease resulting in death to aid the development of strategies to better manage SARS-CoV-2-infected patients.

2. Structure of SARS-CoV-2

SARS-CoV-2 has typical features among the CoV family, belongs to the beta-CoV 2b group and is an enveloped +ssRNA virus (12). SARS-CoV-2 encodes the basic structural proteins of Spike S protein (S), Membrane M protein (M), Envelop E protein (E) and Nucleocapsid (N), as seen in the Figure (1, 2).

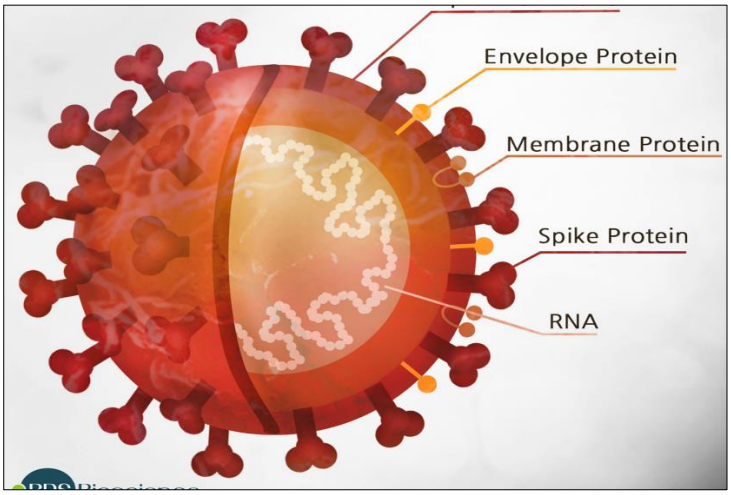

Figure 1 Structure of SARS-CoV-2

+ssRNA viruses, a large group that includes human pathogens such as SARS-CoV-2, replicate in the cytoplasm of the infected host cells. Replication complexes are generally associated with modified host cell membranes (14). The SARS-CoV-2 replication is driven by the membrane-bound viral enzyme complex. This complex is often linked to modified intracellular membranes. CoVs and other members of the Nidovirus family have a polycistronic genome, and use a variety of transcriptional and (post-) translational mechanisms to regulate their expression (15, 16). Post translational modifications or PTMs are involved in modifying the protein structure after they have been translated by ribosomes. It identifies new functional groups such as phosphate and carbohydrates, expands the chemical repertoire of 20 standard amino acids through post-translational modifications, and plays important roles in regulating the folding, stability, enzymatic activity, subcellular localization and interaction of a protein with other proteins (17). Viruses that maintain compulsory cell life receive support from the protein synthesis mechanisms of the host cells after respiration. For this reason, after the polypeptides are synthesized, they modify protein functions by creating covalent modifications (18). The gene encoding the replicase/transcriptase contains nearly two-thirds of the CoV genome, the largest known RNA

genome to date. The replicase gene consists of open reading frames (ORFs) 1a and 1b. ORF1b is expressed by a ribosomal frameshift near the 3′-terminal of the ORF1a. Thus, the SARS-CoV genome translation yields two polyproteins (pp1a and pp1ab) (19, 20).

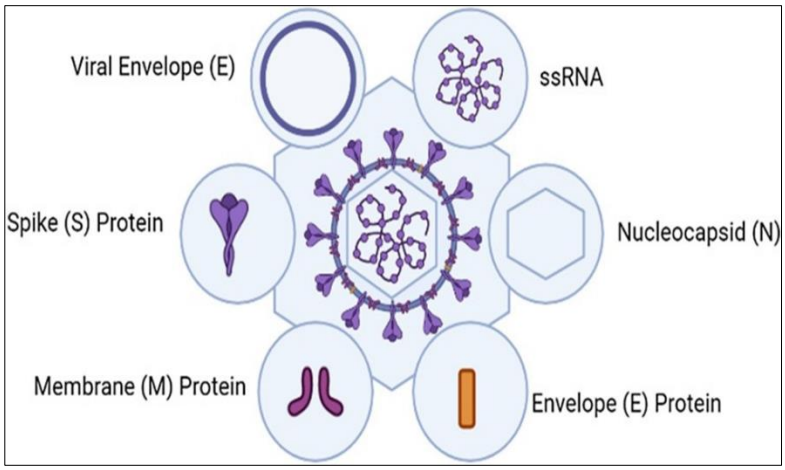

Figure 2 Structure of SARS-CoV-2

3. Mutations and Variants of SARS-CoV-2

A mutation is just a genetic change. Mutations include point changes that are simply changes of one base to another (e.g., an "A" to a C, G, or T/U), insertions or deletions of single bases, or larger changes like insertion or duplication of a whole chunk of DNA/RNA. Many mutations are neutral. But some benefit the virus, allowing it to spread faster in humans, such as by becoming more transmissible or better at evading the COVID vaccines. Currently, there are some “variants of concern” out of which 10 “variants are being monitored” by the U.S. government SARS-CoV-2 Interagency Group. As these mutations take place, new versions of a virus develop and begin infecting more people. These new versions of the virus are called variants. The main difference between mutation and variation is that mutation is an alteration in the nucleotide sequence of a gene whereas variation is any difference between individuals of a particular species (21).

Aim of this study is to present an updated systematic review on the influence of comorbidities on the exacerbation of COVID-19. In our review, we conducted a literature survey under the scope of the exponentially increasing SARS-CoV-2 mutations and the numerous viral variations as the outcome. In the light of current knowledge, we aim to elaborate SARS-CoV-2′s ever changing disguises into novel mutant forms in various locations around the world, to analyze what features of such upcoming mutants differ from its original manifestation, and to emphasize the apparent discrepancies, which may be able to, in return, possibly aid in finding solutions for developing novel therapeutic approaches. Thus, the benefit of mutations in covid-2 is to form many variants and they will do benefit for the treatment of the disease (22).

The commonly known severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus disease 2019 (COVID-19) that initially appeared by public reports in December 2019 in China and then spread worldwide, causing a pandemic outbreak throughout 2020 and 2021. As of 24th September 2021, COVID-19 has led to approximately 230 million confirmed cases and caused over 4.7 million deaths worldwide. In the United States, there have been around 42 million confirmed cases of COVID-19, with 677,323 deaths (21, 22).

Viral variants result from mutations during viral replication. A mutation is described as any change, such as a substitution, deletion, or addition, in a genetic sequence of a virus compared to the normal sequence. Coronaviruses are positive, single-stranded RNA viruses resembling a crown appearance under a microscope (23). The mutation rate is slow compared to other common viruses, such as influenza (24). This means SARS-CoV-2 is less likely to experience mutational changes, such as antigenic drift and antigenic shift responsible for altering the virus composition that leads to differences in infectivity, transmission, and disease severity. As COVID-19 spreads across the world, the virus naturally mutates to form new variants that can either be more or less infectious than the previous form depending on the altered composition. Some of the mutations, especially those occurring at the Spike (S) protein, could affect the entry of the virus into the target cells and the efficacy of the antibody protection. Specifically, mutations occurring in the Receptor-Binding Domain (RBD) of the S protein are of high significance as most vaccines and neutralizing antibodies target the RBD (25). Other mutations in the S protein, such as one occurring at the N-terminal Domain (NTD), could

impair the capability of the neutralizing antibodies as well (26). With more studies, the impact of mutations occurring in other regions of the genome will be determined.

The D614G mutation in the S protein documented in the early part of the pandemic is found in almost every sequence worldwide. This mutation is characterized by the replacement of aspartic acid with glycine at position 614 of the S protein and influences viral infectivity (27). Higher levels of viral RNA were noted in the patients, indicating high viral load and potential for higher infectivity (28). As the transmission of the virus continued, several new variants with multiple mutations have emerged globally (29). The Center for Disease Control, in collaboration with SARS-CoV-2 Interagency Group (SIG), classify SARS-CoV-2 variants into variants of concern (VOC), variant of interest (VOI), and variants of high consequence depending on the threat level they pose to the public's health, as described in the following sections (30).

In this review, the various prevalent SARS-CoV-2 variants are identified to determine their impact on altering the current disease pathology. The focus is on the variants of concern, its multiple mutations, and their consequences. Furthermore, we compare the different COVID-19 variants to understand the underlying changes and how they could impact the current pandemic, at-risk patient populations, and healthcare professionals and facilities if certain variants become more emergent than the original strain.

The naming of the SARS-CoV-2 variants is based on Phylogenetic Assignment of Named Global Outbreak Lineages (PANGOLIN) or interchangeably referred to as Pango lineage nomenclature (31). According to the nomenclature, there are two major lineages, namely, A and B, at the root of the phylogeny of SARS-CoV-2. Lineage A viruses, for instance, the Wuhan/WHO4/2020 sequence sampled in January 2020, share two nucleotides (positions 8782 in ORF1ab and 28144 in ORF8) with the closest known bat viruses (RaTG13 and RmYN02). In comparison, lineage B, such as the Wuhan-Hu-1 strain sampled in December 2019, display different nucleotides at the above-mentioned sites. The additional SAR-CoV-2 genomes, which descend from either lineage A or lineage B, are designated a numerical value, for example, lineage A.1 or lineage B.2. Furthermore, these lineages (A.1 or lineage B.2) can act as predecessors for virus lineages that emerge in other geographical areas or at different time points, and these are designated with two sublevels, for instance, A.1.1. These designations can proceed for a maximum of three sublevels (e.g., A.1.1.1), after which new descendent lineages are given a letter (in English alphabetical sequence from C, so A.1.1.1.1 would become C.1 and A.1.1.1.2 would become C.2). These descendent lineages should show phylogenetic evidence of emergence from an ancestral lineage into another geographically distinct population, implying substantial forward transmission in that population.

As of September 2021, lineage B and its sub-lineage B.1 appears to be the most prevalent worldwide. In the United States, there are four circulating variants, with B.1.1.7 being the most common. The other variants include B.1.351, P.1 (B.1.1.28.1), and B.1.617.2 (the B.1.427 and B.1.429 variants have been de-escalated due to low prevalence). These variants appear to spread more easily and quickly than other variants, leading to more cases of COVID-19. The Centers for Disease Control and Prevention categorizes SARS-CoV-2 variants into different groups regarding the potential for causing severe disease leading to morbidity and/or mortality, significant infectivity rate, or decreased response to SARS-CoV-2 antibodies generated from a previous infection or vaccination (32). The different variants have been categorized into variants of interest (VOI), variants of concern (VOC), or variants of high consequence (VOHC) in the United States. Conversely, the European Centre for Disease Prevention and Control categorizes them into variants of interest (VOI), variants of concern (VOC), or variants under monitoring (VOM) (33).

The World Health Organization (WHO) revised the naming system for SARS-CoV-2 (both VOC and VOI) based on the Greek alphabet, such as "Alpha", "Beta" or "Gamma". This system has the advantage of referring to the variants more quickly in a simplified scientific language, especially for non-scientists, national authorities, media, and others. Additionally, it avoids identifying them by the countries where they were identified first; thereby, preventing stigmatization of a country for detecting and reporting variants (34).

4. Conclusion

The viruses have a mutation rate that is much higher than even humans or other animals, and they replicate at a rate that is very fast. Among the 103 SARS-CoV-2 genomes, a total of 149 mutations are identified. The number of variants in SARS-CoV-2 are Alpha, Beta, Gamma, Delta and Omicron. SARS-CoV-2 mutate and create divergent variants by altering the composition of essential constituent proteins. Pharmacologically, it is crucial to understand the diverse mechanism of mutations for stable vaccine or anti-viral drug design. The study may easily be extended to the samples across the globe.

Compliance with ethical standards

Disclosure of conflict of interest

There is no conflict of interest among the authors.

References

[1] Yang D, Leibowitz JL. The structure and functions of coronavirus genomic 3′ and 5′ ends. *Virus Res.* 2015; 206: 120–133.

[2] Weiss SR, Leibowitz JL. Coronavirus pathogenesis. *Adv Virus Res.* 2011; 81: 85–164.

[3] Mohammad FQ, Hania F, Shoeb Q. A brief report on comorbidities and risk factors of Covid-19 (SARS-CoV-2). Submitted (Unpublished). 2022.

[4] Drosten C, Günther S, Preiser W, van der Werf S, Brodt H-R, Becker S, Rabenau H, Panning M, Kolesnikova L, Fouchier RAM, Berger A, Burguière A-M, Cinatl J, Eickmann M, Escriou N, Grywna K, Kramme S, Manuguerra J-C, Müller S, Rickerts V, Stürmer M, Vieth S, Klenk H-D, Osterhaus ADME, Schmitz H, Doerr HW. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med.* 2003; 348: 1967–1976.

[5] World Health Organization. Coronavirus disease (COVID-2019) situation reports. World Health Organization, Geneva, Switzerland. 2020.

[6] Li X, Wang W, Zhao X, Zai J, Zhao Q, Li Y, Chaillon A. Transmission dynamics and evolutionary history of. 2019-nCoV. *J. Med. Virol.* 2020; 92: 501–511.

[7] Chen J, Wang R, Wang M, Wei G.W. Mutations strengthened SARS-CoV-2 infectivity. *J. Mol. Biol.* 2020; 432: 5212–5226.

[8] Collier DA, De Marco A, Ferreira IATM, Meng B, Datir R, Walls A.C, Kemp SA, Bassi J, Pinto D, Fregni CS, Bianchi S, Tortorici MA, Bowen J, Culap K, Jaconi S, Cameroni E, Snell G, Pizzuto MS, Pellanda AF, Garzoni C, Riva A, Elmer A, Kingston N, Graves B, Mccoy LE, Smith KG, Bradley JR, Thaventhiran J, Ceron-Gutierrez L, Barcenas-Morales G, Virgin H.W, Lanzavecchia A, Piccoli L, Doffinger R, Wills M, Veesler D, Corti D, Gupta R.K. SARS-CoV-2 B.1.1.7 escape from mRNA vaccine-elicited neutralizing antibodies The CITIID-NIHR BioResource COVID-19 Collaboration. *MedRxiv.* 2021.

[9] Finkel Y, Mizrahi O, Nachshon A, Weingarten-Gabbay S, Morgenstern D, Yahalom-Ronen Y, Tamir H, Achdout H, Stein D, Israeli O, Beth-Din A, Melamed S, Weiss S, Israely T, Paran N, Schwartz M, Stern-Ginossar N. The coding capacity of SARS-CoV-2. *Nature.* 2021; 589: 125–130.

[10] Kim D, Lee J.Y, Yang J.S, Kim J.W, Kim V.N, Chang H. The architecture of SARS-CoV-2 transcriptome. *Cell.* 2020; 181: 914–921.

[11] Chen L, Zhong L. Genomics functional analysis and drug screening of SARS-CoV-2. *Genes Dis.* 2020.

[12] Mittal A, Manjunath K, Ranjan R.K, Kaushik S, Kumar S, Verma V. COVID-19 pandemic: insights into structure, function, and hACE2 receptor recognition by SARS-CoV-2. *PLoS Pathog.* 2020; 16.

[13] Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: origin, transmission, and characteristics of human coronaviruses. *J. Adv. Res.* 2020; 24: 91–98.

[14] Corman VM, Muth D, Niemeyer D, Drosten C. *Adv. Virus Res.* Academic Press Inc. Hosts and sources of endemic human coronaviruses. 2018; 163–188.

[15] Knoops K, Kikkert M, Van Den Worm S.H.E, Zevenhoven-Dobbe J.C, Van Der Meer Y, Koster A.J, Mommaas A.M, Snijder E.J. SARS-coronavirus replication is supported by a reticulovesicular network of modified endoplasmic reticulum. *PLoS Biol.* 2008; 6: 1957–1974.

[16] Ziebuhr J. Molecular biology of severe acute respiratory syndrome coronavirus. *Curr. Opin. Microbiol.* 2004; 7: 412–419.

[17] Gorbalenya A.E, Enjuanes L, Ziebuhr J, Snijder E.J. Nidovirales: Evolving the largest RNA virus genome. *Virus Res.* 2006; 117: 17–37.

[18] Fung T.S, Liu D.X. Post-translational modifications of coronavirus proteins: roles and function. *Future Virol.* 2018; 13: 405–430.

[19] Kumar R, Mehta D, Mishra N, Nayak D, Sunil S. Role of host-mediated post-translational modifications (PTMS) in RNA virus pathogenesis. *Int. J. Mol. Sci.* 2021; 22: 1–26.

[20] Thiel V, Ivanov K.A, Putics Á, Hertzig T, Schelle B, Bayer S, Weißbrich B, Snijder E.J, Rabenau H, Doerr H.W, Gorbalenya A.E, Ziebuhr J. Mechanisms and enzymes involved in SARS coronavirus genome expression. *J. Gen. Virol.* 2003; 84: 2305–2315.

[21] Harcourt BH, Jukneliene D, Kanjanahaluethai A, Bechill J, Severson KM, Smith CM, Rota PA, Baker SC. Identification of severe acute respiratory syndrome coronavirus replicase products and characterization of papain-like protease activity. *J. Virol.* 2004; 78: 13600–13612.

[22] WHO Coronavirus Disease (COVID-19) Dashboard with Vaccination Data. [(Accessed on 24 September 2021)].

[23] Cascella M, Rajnik M, Aleem A, Dulebohn SC, Di Napoli R. *StatPearls.* StatPearls Publishing LLC; Treasure Island, FL, USA: 2021. Features, Evaluation, and Treatment of Coronavirus (COVID-19).

[24] Astrezeneca. The Natural Evolution of SARS-CoV-2: How Science Responds to These Challenges. [(Accessed on 24 September 2021)].

[25] Ju B, Zhang Q, Ge J, Wang R, Sun J, Ge X, Yu J, Shan S, Zhou B, Song S, et al. Human neutralizing antibodies.

[26] McCallum M, De Marco A, Lempp F.A, Tortorici M.A, Pinto D, Walls A.C, Beltramello M, Chen A, Liu Z, Zatta F, et al. N-terminal domain antigenic mapping reveals a site of vulnerability for SARS-CoV-2. *Cell.* 2021; 184: 2332–2347.e16.

[27] Zhang L, Jackson C.B, Mou H, Ojha A, Peng H, Quinlan B.D, Rangarajan ES, Pan A, Vanderheiden A, Suthar MS, et al. SARS-CoV-2 spike-protein D614G mutation increases virion spike density and infectivity. *Nat. Commun.* 2020; 11: 6013.

[28] Korber B, Fischer WM, Gnanakaran S, Yoon H, Theiler J, Abfalterer W, Hengartner N, Giorgi EE, Bhattacharya T, Foley B, et al. Tracking Changes in SARS-CoV-2 Spike: Evidence that D614G Increases Infectivity of the COVID-19 Virus. *Cell.* 2020; 182: 812–827.e19.

[29] Burki T. Understanding variants of SARS-CoV-2. *Lancet.* 2021; 397: 462.

[30] 30. CDC SARS-CoV-2 Variant Classifications and Definitions. [(Accessed on 24 September 2021)].

[31] Rambaut A, Holmes E.C, O'Toole Á, Hill V, McCrone JT, Ruis C, du Plessis L, Pybus OG. A dynamic nomenclature proposal for SARS-CoV-2 lineages to assist genomic epidemiology. *Nat. Microbiol.* 2020; 5: 1403–1407.

[32] CDC About Variants of the Virus that Causes COVID-19. [(accessed on 24 September 2021)].

[33] Sandhu R, Manoj G, Rachel SP, Logan N, Tharanath S et al. Emerging SARS-CoV-2 Variants: A Review of Its Mutations, Its Implications and Vaccine Efficacy. Vaccines (Basel). Oct 2021; 9(10): 1195.

[34] Das JK, Antara S, Pabitra PC, Swarup R. Characterizing genomic variants and mutations in SARS-CoV-2 proteins from Indian isolates. Gene Rep. Dec 2021; 25: 101044.