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SARS-COV-2 and the emerging variants: A Review

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Abstract:*Numerous novel diseases have emerged in various geographical areas over the last few decades, with pathogens such as coronaviruses (CoVs). A new viral infection has recently emerged in Wuhan City, China, and preliminary genomic sequencing data of this virus do not match with previously sequenced CoVs, implying the presence of a novel CoV strain (2019-nCoV), which has now been termed severe acute respiratory syndrome CoV-2 (SARS-CoV-2). In comparison to diseases caused by previously known human CoVs, COVID-19 has a less severe pathogenesis but a higher transmission competence, a significant number of mutations have accumulated in the spike (S) protein, particularly in the amino terminal domain (NTD) and the receptor binding domain (RBD), and it is quickly becoming dominant among populations. Through increased affinity of S RBD for the cellular angiotensin-converting enzyme-2 (ACE-2) receptor, these alterations have a direct impact on virus infection rates. ACE2 is found in various degrees in almost all of the human organs. Type 2 alveolar epithelial cells, the principal site of ACE2 expression, indicating that the lungs are the primary target of SARS-CoV-2, also affecting organs that have high ACE2 expression, such as myocardial cells, kidney proximal tubular cells etc. In this review, we explain about the classification and nomenclature of the SARS-CoV-2, describing the mutation patterns, incidence rate, transmissibility, and the severity of the disease in terms of symptoms, mortality and morbidity caused by the variants of concern of SARS-CoV-2.*

Key Words:*CoV, SARS-CoV-2, variant of concern, WHO, Covid-19.*

1. INTRODUCTION:

In December 2019, the Coronavirus Disease 2019 (COVID-19) was detected in Wuhan, China. The causative virus was named novel coronavirus (nCov) by the World Health Organization (WHO) on January 12, 2020; the virus was renamed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Virus Classification Commission on February 11, 2020 [1]. Several new diseases have emerged in various geographical areas over the last few decades, with pathogens such as Ebola virus, Zika virus, Nipah virus, and coronaviruses (CoVs). A new viral infection has recently emerged in Wuhan City, China, and preliminary genomic sequencing data of this virus do not match with previously sequenced CoVs, implying the presence of a novel CoV strain (2019-nCoV), which has now been termed Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2). In comparison to diseases caused by previously known human CoVs, COVID-19 has a less severe pathogenesis but a higher transmission competence, as evidenced by the continuously increasing number of confirmed cases globally [2]. SARS-CoV-2 belongs to the family of corona viruses with the Nidovirus superfamily [3], These are the positive-sense RNA viruses with the ability to survive in multiple hosts and affect multiple organs. Like other coronaviruses, SARS-CoV-2 can cause clinical disease in humans that may extend from common cold to severe respiratory distress. According to current research, the most prevalent symptoms of COVID-19 are respiratory symptoms such as fever, dry cough, and even dyspnea. Sepsis, secondary infections, and organ failure have all been described in severe cases. SARS-CoV-2 is primarily transmitted through respiratory droplets, either directly from the air when an infected patient coughs or sneezes, or as fomites on surfaces. Recently, researchers discovered indications of COVID-19 gastrointestinal symptoms and probable fecal-oral transmission [4]. The most striking characteristic of COVID-19 is the spike glycoprotein on the surface of this single-stranded RNA molecule. This spike protein mediates the entry of virus into the host cells. Spike protein contain three receptor binding S1 heads sitting on top of a trimeric membrane fusion S2 stalk. The receptor binding domain (RBD) on S1 recognizes the two-lobed N-terminal peptidase domain of

ACE-2 protein. The RBD alternates between a standing-up and a lying-down state for receptor binding and immune evasion respectively. Furthermore, entry-activating proteases such as cell surface protease TMPRSS2 and lysosomal proteases cathepsins are required for the SARS-CoV-2 spike to fuse membranes. these enzymes activate spike protein at S1/S2 boundary, such that S1 dissociates and S2 undergoes a structural change. Following the membrane fusion, RNA accesses the cells' cytoplasm, resulting in infection [5]. When compared to the RBD of SARS-CoV-2, the SARS-CoV-2 spike RBD displaces more amino acids, resulting in a four-fold greater binding affinity[6]. The remarkable infectivity and global spread of COVID-19 may be due to the strong binding affinity between SARS-CoV-2 RBD and its receptor ACE2 [7]. ACE2 is found in various degrees in almost all of the human organs. Recent research has identified type 2 alveolar epithelial cells as the principal site of ACE2 expression, indicating that the lungs are SARS-primary CoV-2's target. The virus could migrate from the lungs to other organs that have high ACE2 expression, such as myocardial cells, kidney proximal tubular cells, bladder urothelial cells, and small intestine enterocytes. This explains why critically ill patients develop multiple organ damage [8].

2. CLASSIFICATION AND NAMING OF COVID-19 VARIANTS :

Classifications are extremely useful for identifying shared characteristics and properties among populations. Viruses are now primarily identified by phenotypic characteristics such as morphology, nucleic acid type, mode of replication, host organisms, and disease type. The World Health Organization proposed general guidelines for naming newly recognized human infectious diseases in 2015. According to their statement, "a disease name should consist of generic descriptive terms...and more specific descriptive terms," if such information is available. The pathogen's name could also be included. More importantly, no references to geographical locations, specific cultures or populations, occupations, or people's names should be included in the disease name. The WHO statement notes that these best practices "minimize unnecessary negative effects on nations, economies, and people [9]. To aid in the development of diagnostic tests, vaccines, and medicines, viruses are named based on their genetic structure. This work is done by virologists and the larger scientific community, so viruses are named by the International Committee on Taxonomy of Viruses (ICTV) [2]. WHO Director Tedros Adhanom Ghebreyesus stated that they needed to find a name that did not refer to any animal, geographical location, person, or group of people [1]. The World Health Organization (WHO) nomenclatures coronaviruses in collaboration with the World Organization for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) based on a variety of factors, including :- 1) Generic descriptive (respiratory disease), 2) Specific descriptive terms: Age group or population of patients (not very specific in coronavirus as it affects all age groups), Time course, epidemiology, origin: Acute respiratory Severity- severe, moderate, mild. Seasonality- Winter, summer, seasonal. Causal pathogen and associated descriptors- Coronavirus and Novel and Subtype, serotype. Year/ month first detected- 2019, Arbitrary identifier- Alpha, beta etc. The term "novel" can be used to describe a new pathogen of a previously known type, with the understanding that this term will become obsolete if other new pathogens of that type are discovered. When distinguishing between similar events that occurred in different years, a date (year, or month and year) may be used. SARS-CoV-2 in 2003 and SARS CoV-2 in 2019(COVID-19). On 11 February 2020, ICTV named the new virus "Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)." This name was chosen because the virus is genetically related to the coronavirus responsible for the 2003 SARS outbreak. While the two viruses are related, they are not the same, and the name covid-19 is announced by WHO in collaboration with World Organization for Animal health (OIE) and Food and Agriculture Organization of the United nations (FAO) to indicate a new pathogen of previously known diseases (Novel approach) [2]. Corona Virus Disease (COVID-19) refers to symptoms and its year of discovery while attempting to disassociate from the public fear and stigma associated with the SARS-CoV-2 outbreak in Asia in 2003 [10]. The classification of RNA viruses must take into account their inherent genetic variability, which frequently results in two or more viruses with non-identical but similar genome sequences being considered variants of the same virus [11]. In May 2021, WHO announced a new naming system for COVID-19 variants based on the Greek alphabet and their detection order. According to The Guardian and other news outlets, this decision was made after months of deliberation among WHO experts on the best ways to reduce stigma and misinformation [10].

3. VARIANTS OF CONCERN :

Alpha - Alpha, novel SARS-Cov-2 variant of concern also known as B.1.1.7 or GRY: earliest variant of concern identified during end of December 2020 in the United kingdom, depending on whole-genome sequencing of patient samples who screened positive for SARS-CoV-2 [12], There are 17 mutations that make up an alpha variation, 14 of which are from changes in the amino acids. The spike protein gene has several variants, three of which are deletions and aid viral entry into human cells; Spike Mutations-HV69-70del, Y144del, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H; Nucleocapsid Mutations : D3L, R203K, G204R, S235F [13]. One is a mutation

called N501Y that increases the spike protein's ability to connect to cellular receptors and makes the virus more infectious. Additionally, it has the D614G mutation, which is thought to promote viral replication [14]. Epidemiological studies have provided strong evidence that the B.1.1.7 variant is more contagious than other variants [15]. Comparing Alpha to the initial Wuhan strain, transmission is thought to increase by about 50% [14]. In Switzerland, Denmark, and the United States, this variant's transmission rate has been observed to be similar [15]. The Alpha variation is linked to higher disease intensity in terms of hospitalizations and fatality rates. Alpha variant symptoms of SARS-Cov-2 include a prolonged cough, fever, diarrhoea, delirium, hoarseness, headache, strange muscle pains, loss of smell or taste, skipping meals, severe shortness of breath, sore throat, chest discomfort, stomach pain, noted in a study conducted on the population of the United Kingdom [15], while anosmia, dysgeusia, and hearing impairment were less frequent with the Alpha strain, myalgia, sleeplessness, brain fog, anxiety, and depression dramatically increased [16]. Vaccines and monoclonal antibodies work efficiently against the alpha strain of SARS-Cov-2, According to research, the Pfizer-BioNTech vaccine had a 93.7 percent vaccine efficacy rate against the alpha version after two doses, compared to 74.5 percent for the Oxford-AstraZeneca vaccine , where Novavax vaccine has 85.6% efficacy rate [17] and 100 % with Moderna [18], The Sputnik V vaccine research revealed some diminished neutralizing activity against the alpha variant [19], while according to the Public Health Ministry of Thailand, the Sinovac vaccine is 71–91% efficient against alpha variant [20].

Beta - A novel SARS-CoV-2 variant of B.1.351 lineage commonly known as the "Beta variant," "GH501Y.V2," or "South African variant," with various spike mutations, responsible for the second wave of covid19, emerging from Nelson Mandela Bay in South Africa in October 2020. The spike protein of the B.1.351 variation has nine mutations (L18F, D80A, D215G, R246I, K417N, E484K, N501Y, D614G, and A701V), three of which are found in the receptor binding domain and improve the binding affinity for ACE receptors (K417N, E484K, and N501Y) [12]. Both Public Health England and the World Health Organization (WHO) have designated the variant as a variant of [21]. Around the world, different SARS-CoV-2 variants have been found that are more contagious, might evade natural and vaccine-induced immunity and could increase SARS-CoV-2 infection which was discovered for the first time in October 2020. Now it has been identified in 115 different countries, making it the most common lineage in South Africa [22]. Including its widespread prevalence, Clinical samples from South African visitors revealed the presence of the Beta strain in India in late December 2020 [23]. According to a study, the Beta variation of SARS-CoV-2 may be much more contagious than earlier variants that were in circulation. It has been noted that the beta variation caused roughly 40% of new SARS-CoV-2 infections, comparing to the alpha variant's 20%; Decreased efficiency against Beta was seen in an in vitro investigation using convalescent plasma samples and monoclonal antibodies from COVID-19 cases [24]. The Beta variant's symptoms do not appear to be any distinctive from those of other Covid variants, Although, the Wuhan virus variant is considered to be more contagious than the original, it is not considered to produce more severe illness [21]. According to the results of the NVX-CoV2373 clinical trial, the post-hoc vaccine efficacy in South Africa, where the Beta variation was common, was ‘51%’, Additionally, it’s been suggested that the beta variant is less vulnerable to the current vaccines, including ChAdOx1 nCoV-19, mRNA-1273, BNT162b2, and NVX-CoV2373 [22], Besides that, studies on the Pfizer and Moderna vaccines revealed that both were successful in preventing the beta variant [21].

Gamma - The Gamma variant, also known as the P.1 Variant or GR/501Y.V3, is the third variant of concern that was discovered in Brazil in December 2020 [25]. Beginning in January 2021, the Gamma variation began to be seen more often throughout Brazil, and it eventually became the main lineage linked to the second wave of Covid infection. Brazil became the core of the coronavirus disease 2019 (COVID-19) pandemic after the incidence rates accelerated in 2021, with more than 13 million patients diagnosed and 350 000 fatalities. According to the WHO epidemiological analysis, 45 nations now have this variant [25]. Gamma may induce more severe illness, particularly in children, as evidenced by the fact that patients hospitalized for COVID-19 during the second wave in Brazil that was dominated by Gamma, proved to be younger and more likely to die [26]. Gamma has 21 lineage-defining mutations, 10 of which are in the spike protein and three of which (K417T, E484K, and N501Y) are in the receptor binding domain, demonstrating an unexpected convergence with the receptor binding domain of B.1.351. It has been demonstrated that these three mutations in the receptor binding domain work together to raise receptor binding affinity, the mutations discovered in Gamma have been linked to SARS-CoV-2 reinfection, enhanced transmissibility, a greater viral load, and a tendency to evade the immune system [27]. According to a study, COVID-19 induced by the Gamma variant manifests differently from non-VoC infections. Given a drop in the incidence of hyposmia/anosmia and dysgeusia, the rise in Gamma variant cases should alert medical professionals to the possibility that COVID-19 may more frequently present with cold-like symptoms [28]. The Gamma form might be less neutralized by monoclonal antibody treatments, recovering sera, and post-vaccination sera [25]. In Manaus, which served as the epicenter for the evolution of the P.1 variant, a study involved over 70,000 healthcare professionals. 14 days following

the first dose of its two-dose regimen, CoronaVac (an inactivated vaccine) was proven to be 50% effective in preventing disease [29].

Delta - The 4th variant of concern, B.1.617.2, also known as the Delta variant, was first discovered in India's state of Maharashtra in December 2020 and was the cause of the fatal second wave of COVID-19 infections in India in April 2021, Rapid global proliferation of the Delta variant led to the WHO classifying it as a VOC in May 2021, Ten mutations in the spike protein (T19R, (G142D*), 156del, 157del, R158G, L452R, T478K, D614G, P681R, and D950N) are present in the B.1.617.2 variant [12]. The delta variant spreads twice as quickly as the alpha variant, as per the CDC [30]. Although it took place over a significantly shorter period of time, it is clear on a substantial level that the disease and fatality rates increased far more quickly [31]. Quantitatively, the delta variant has been demonstrated to have a 133 percent greater chance of fatality than the original variant and a 108 percent greater risk of hospitalization and ICU admission [32]. The delta variant frequently causes symptoms like fever, coughing, shortness of breath, nausea, diarrhoea, sore throats, and headaches, Myalgias, loss of taste, loss of smell, tiredness, and rhinorrhea are other symptoms. Studies conducted in the UK have revealed that the delta variant is specifically responsible for hearing loss and gangrene due to worse blood clots, while less frequently causing cough and olfactory loss [33]. In the delta variant, greater transmission rates can result in high mutation rates and the emergence of new strains, for that Moderna and Pfizer provide booster doses for their vaccines due to the emergence of new coronavirus strains. According to a UK study, vaccine recipients exhibit comparable protection against the delta variation as they do with the alpha variant when it comes to developing COVID-19 infections, A single dosage of either the BNT162b2 or ChAdOx1 nCoV-19 will have equal effectiveness against the delta and alpha, respectively, of 30.7% and 48.7%, respectively, BNT162b2 was shown to be 93.7 percent efficient against the alpha variant and 88 percent effective against the delta variant after administering two doses, The effectiveness of ChAdOx1 nCoV-19 was determined to be 74.5 percent against the alpha and 67 percent against the delta, Up to 88 percent of the population were protected by the Pfizer/BioNTech vaccination, however not as well as they were against the alpha variant [34]. In addition to the vaccinations' decreased effectiveness in preventing infection, the characteristics of affected people make it harder to stop the spread. According to a study, people who are fully vaccinated and develop breakthrough infections exhibit an equal viral load with those who are unvaccinated [35].

Omicron - After an increase in COVID-19 cases in South Africa on 23 November 2021, World Health Organization (WHO) initially detected the 5th variant of concern B.1.1.529, also known as the Omicron variant [36]. Omicron exhibits over 30 mutations and a few deletions, several of which overlap with those in the alpha, beta, gamma, or delta VoCs (e.g., 69-70del, T95I, G142D/143-145del, K417N, T478K, N501Y, N655Y, N679K, and P681H) [37], these mutations and deletions are believed to enhance antibody escape, viral binding affinity, and risk of transmission [38]. An upsurge in the probability of reinfection following a first infection may be linked to the Omicron variant, according to a retrospective study of data from regular epidemiological surveillance[39]. The SARS-CoV-2 Omicron variant, following the D614G, Beta/Gamma, and Delta VOCs, may serve as the impetus for the fourth wave of the COVID-19 pandemic to spread over the world, Omicron VOC spreads more quickly than any preceding variants and is very contagious [40], 80 nations had already reported seeing the Omicron variant since around December 15, 2021[38]. Hospitalization rates were rising in South Africa, and majority of the outbreak infections with Omicron had milder symptoms than prior variants. Less people required oxygen support during that Covid19 outbreak [41]. Cough, drowsiness, and congestion or a runny nose were the most often recorded symptoms [42]. The Omicron variant has the highest mutations out of all the VOCs up to this point, making it more transmissible and somewhat resistant to the immunity induced on by COVID-19 vaccines [43], the COVID-19 vaccine from Pfizer-BioNTech has become less effective due to the Omicron variation, but it can still minimize the likelihood of hospitalization [42], As according to BioNTech and Pfizer, two doses of the vaccine should indeed provide protection against serious illness because the Omicron's mutations do not alter the T-cells, which generally develop after vaccination, that targets the surface structures on the Omicron's spike protein [42].

4. CONCLUSION:

In addition to increasing transmissibility, severity, and fatality, the new variants also demonstrate lower susceptibility to antivirals and monoclonal antibodies, These variants can induce reinfection in Covid-19 recovered and vaccinated populations and can remain undetected by diagnostic methods. In this article, we have explored how variant of concern evade natural and vaccine-induced immunity, are more transmissible and virulent, and create new global healthcare problems. The probability of a virus mutating increases with exposure. Since vaccine breakthrough incidents are frequently underreported, vaccinated populations also should always take precautions in order to avoid the viral mutation and spread.

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