ISSN: 2456-8090 (online)
DOI: https://doi.org/10.26440/IHRJ/0605.08556

REVIEW

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A Detailed Study of Covid-19 (Emphasizing its Genomic Variants, Pathogenicity, Phylogenetic Analysis, Epidemiology, and Clinical Measures)

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ABSTRACT

Covid-19 (Coronavirus) had spread all over the world. Around 213 countries were affected by the deadly virus and encountered a mob of dead. After analyzing the genome, we can say that the Coronavirus originates in bats and gets transmitted to humans. Although the intermediate source of origin and transmission to humans is unknown, rapid human-to-human transmission has been evinced. SARS-CoV-2 is phylogenetically related to a group of bat viruses known to cause severe acute respiratory syndrome (SARS-CoV). Both viruses (SARS-CoV and SARS-CoV2) belong to the same family of beta coronaviruses. The first case of SARS-CoV2 infection was reported from Wuhan, China. Till now, there have been 577,018,226 confirmed cases of Covid-19 worldwide. More than 6 million people have succumbed to this deadly disease worldwide. Presently, the urgent need to develop a drug and vaccine that could cure this disease is fulfilled. This current review summarizes the origin of SARS-CoV2, its genome structure, pathogenicity and phylogenetic analysis of the virus, and its epidemiology. We have also discussed the existing drugs and approved vaccines that are presently treating humanity. This review aims to compact every possible information regarding Covid-19.

KEYWORDS: SARS-CoV2, Variants, Outbreak, Antiviral Therapies

INTRODUCTION

Viruses are microscopic organisms that can cause infections to almost all kinds of life forms like humans, animals, plants, fungi, and even bacteria. They vary in complexity and consist of genetic material, RNA or DNA, surrounded by a coat of protein, lipid(fat), or glycoprotein. They cannot replicate in the absence of a host. They are the most abundant biological form on the planet.

Several novel diseases have emerged in various geographic areas over the past few decades, including pathogens such as Ebola, Zika, Nipah, and coronaviruses (CoVs).

Coronaviruses are enormous in numbers and common among many animals, even in human bodies. Respiratory and gastrointestinal illnesses are the two most common symptoms of Coronavirus in humans and animals. Various Coronavirus has large peplomers, and it almost looks like a crown under the electron microscope. The name corona denotes “crown” or “halo”.[1,2] A new type of viral infection has been discovered in Wuhan, China, and preliminary genomic sequencing data suggests that this virus is a novel strain of CoV (2019-nCoV), identified as severe acute respiratory syndrome CoV-2 (SARS-CoV-2). Although coronavirus disease 2019 (COVID-19) is thought to have originated in an animal host (zoonotic origin) and then spread from person to person, other routes should not be ruled out. Covid-19 was not considered a deadly virus before 2003. These are almost round in shape, and were causing minor symptoms in immunocompetent people. Runny nose, sore throat, cough, headache, and fever are the main symptoms of Covid-19. The symptoms can last for numerous days. Immunocompromised patients have a chance that the virus could cause a lower respiratory illness like bronchitis and pneumonia.[1-3]

In 2003 the world experienced the first pandemic of the 21st century. Severe Acute Respiratory Syndrome Coronavirus (2003) appeared in Guangdong, China, and it was the cause of 774 deaths and the illness of more than 8000 patients.[1,4,5] After nine years, the strains of Coronavirus immersed in Saudi Arabia, with 2500 cases and 861 deaths with a deadly case-fatality rate of 34.4%, were the terrible result of Middle East Respiratory Syndrome Coronavirus (MERS-CoV).[5]

COVID-19 infection symptoms were first seen in Wuhan's people, and then it gradually began to take on a larger size. In December 2020, many Covid-19 cases were found in the South China seafood markets. Twenty-seven patients of the South China seafood city were found in worse condition. The rest of the cases were in control. On January 9th, 2020, after examining

Submitted on: 11-Jun-2022; **Accepted on:** 29-Aug-2022

Wuhan city, the China government had found shocking reports; on that day, China government published a report about Covid-19. A piece of information on the CDC disclosed Coronavirus (COVID-19) had been found at the main reasonable specialist for 15 to 59 pneumonia cases. On January 10, 2020, the genome of covid-19 became accessible.[6] Then it was kept in the GenBank database (accession number- MN908947). Then Global Researchers took the data and called it influenza (GISAID). In the primary examination of this virus, it was told that the novel Coronavirus (SARS CoV-2) is affected by the SARS-related CoV clade and differs from the inside genome of known bat CoVs.[7] After the COVID-19 discovery, more than 577,018,226 patients were greatly affected, and about 6,401,046 died due to Covid-19 till August 3, 2022, 04:22 GMT. COVID-19 can spread quickly and cause significant illness in older adults and those in poorer health condition.[8,9] The Coronavirus is capable of mutation and recombination, and the genome sequence has already been muted. Some scientists have found that there are two circulating strains in the virus, the deadly strain "L" and the less virulent strain "S".[10,11]

THE ERA OF CORONAVIRUS

Coronavirus is not a new type of virus as it belongs to the subfamily Coronavirinae and with the family Coronaviridae and the order Nidovirales. The members of Coronavirinae subfamily are classified into four types based on their protein sequences and phylogenetic relationship as Alphacoronaviruses, Beta coronaviruses, Gamma coronaviruses, and Delta coronaviruses. Gamma coronavirus and Delta coronavirus are unable to affect humans. However, it can affect birds and might affect mammals[12,13] but Alpha coronaviruses and Beta coronaviruses can cause respiratory illness in human bodies and gastrointestinal disease in animals. Six common coronaviruses (members of Alphacoronaviruses and Betacoronaviruses) can affect humans significantly, as reported in December 2019. HCoV-229E, and HCoV-NL63 belong to the group of Alpha coronaviruses, and the linage A of Beta coronaviruses consists of HCoV-OC43 and HCoV-HKU1 and the deadliest SARS-CoV and MERS-CoV linages to B and C of Betacoronavirus respectively.[12] CoVs are zoonotic pathogens that arise in animal bodies and are later transmitted directly to humans. All Coronaviruses that affect massively in human life originated in bats and are the hosts of many Coronaviruses[3,14]but there is an animal hosts in between bats and humans. Market civets' cats and dromedary camels are the intermediate animal host of SARS-CoV and MERS-CoV, respectively.[14] Primarily in the seafood market in Wuhan city, China, Covid-19 is suspected, so the Chinese authority decided to close the market.[6,12] According to the analysis, the Coviid-19 is similar to SARS, which was named SARS-CoV-2.

ALPHA VARIANT (B.1.1.7)

The variant alpha or B.1.1.7 was first detected in the United Kingdom in September 2020 and emerged with a large number of unusual mutations across the world. As the dominant strain delta came, it started fading the alpha variant case. Compared with the strain that showed up in Wuhan, it has 23 more mutations, according to the American Society for Microbiology. Among these, eight mutations are linked to spike proteins. The N501y mutation in the receptor binding domain enhances its affinity for the human ACE2 receptor, while the P681H mutation can affect the cell's infectivity and replication of the virus. The variant has shown to be nearly 50% more transmissible than other dispersed lineages, according to the Centers for Disease Control and Prevention (CDC). Vaccines producing companies like Pfizer, Moderna vaccines, Johnson & Johnson vaccine have confirmed that the vaccine shots stimulate neutralizing antibodies against the alpha variant.

BETA VARIANT (B.1.351)

The strain was first detected in South Africa, spread faster than earlier variants, and derived from the second wave of pandemics. The variant was also designated as Variant of Concern (VOC). It carried eight distinct mutations, out of which notable mutations included N501Y, K417N, and E484K, which aides bind more tightly to the human receptors. K417N changes the shape of viral proteins, and E484K helps the variant escape from the immune system. The variant has shown to be nearly 50% more transmissible than other variants, and vaccines have less efficacy than other previous strains. The 501Y.V2 variant showed complete escape from neutralizing antibodies in 48% of patients treated with convalescent serum obtained from patients who had previously had Covid-19. Pfizer had 75% efficacy against the variant.

GAMMA VARIANT (P.1)

The gamma variant samples were first collected from Brazil in November 2020 and were designated as a variant of concern on January 11, 2021. The variant was also labeled as "previously circulating VOC" in March 2022. The gamma is closely related to the beta variant

and nearly has the same spike protein mutations. Unlike beta, it carries eight additional sequence changes in its spike: L18F, T20N, P26S, D138Y, R190S, D614G, H655Y, and T1027I. The gamma infection has a higher viral load and is more transmissible than other variants. The variant is relatively resistant to neutralization by convalescent plasma and vaccine (Moderna or Pfizer vaccination). According to the CDC, it showed less susceptibility to monoclonal antibody treatments, including bamlanivimab and etesevimab.

DELTA VARIANT (B.1.617.2)

The variant was first reported in India and classified as a variant of concern according to the WHO in May 2021. Rapidly it became the dominant variant in the US but was replaced by omicron in December 2021. The Delta variant has a faster growth rate than the alpha variant. The variant is identified by T19R, del157/158, L452R, T478K, D614G, P681R, D950N mutations L452R and D614G mutation aids if firm attachment to human receptors. In contrast, P681R mutation is caused by changing an amino acid beside the furin cleavage site enabling the virus to infect human cells. The variant emerged as the most transmissible variant, nearly 60% more contagious than the alpha. Vaccines like Pfizer showed 88% efficacy against the delta variant.

OMICRON (B.1.1.529)

First detected in South Africa and was assigned as a variant of concern (VOC) on November 24, 2021. The variant is highly mutated and showed more than 30 mutations in spike proteins, of which ten mutations are present in the receptor-binding domain (RBD). It also showed similarities between the beta and lambda variants. The omicron variant has two sub-variants denoted as BA.1 and BA.2, sharing 32 mutations but having 28 mutations differing between them. BA.1 is nearly four times more transmissible than the delta variant. Unlike BA.2, BA.1 has a deletion in the S protein.[15]

PHYLOGENETICS ANALYSIS OF SARS COV2

During the early stages of an outbreak, identifying a developing pathogen's sources was crucial since was enabling focused containment measures. Until December 2019, four betacoronavirus strains—HKU1, MERS-CoV, OC43, and SARS-CoV—were linked to severe human illnesses. In Wuhan, central China, researchers first characterized the fifth strain, a new beta coronavirus called SARS-CoV-2, which causes pneumonia in humans. Bats serve as both a natural host and a place where coronaviruses grow. It has been suggested that the bat reservoir is where most of the human coronaviruses come from to achieve this.

This novel beta coronavirus called SARS-CoV-2 causes human pneumonia. The fifth strain was initially reported in Wuhan, Central China. Bats, serving as a natural host, promote the outspread of coronaviruses. To do this, it has been proposed that the bat reservoir is the source of the bulk of human coronaviruses. Several researchers have recently recognized the genetic similarity between SARS-CoV-2 and the betacoronavirus of the subgenus Sarbecovirus. The novel virus' genomic sequence shares 96.2 % of its sequence with the bat. As illustrated in Fig.1, the SARS-related Coronavirus was discovered in Wuhan, China; however, it differs from the SARS-CoV (about 79%) or MERS-CoV (about 50%) genomes. Here the phylogenetic tree has been constructed by emphasizing the genomic variations within the different emerging mutant strains, where we find the beta variant to be the closes neighbor of initial SARS CoV2 strains.[16,17]

SARS-CoV-2

SARS-CoV-2 Coronaviruses belong to members of the Coronavirinae subfamily of the Coronaviridae family, which includes four genera: Alphacoronavirus, Beta coronavirus, Gamma coronavirus, and Delta coronavirus. SARS-CoV's genome (27–32 kb) is a single-stranded positive-sense RNA (+ssRNA) more significant than any other RNA virus. The nucleocapsid protein (N) produces the virus's capsid outside the genome. The viral genome is packed by an envelope that is associated with three structural proteins: membrane protein (M), spike protein (S), and envelope protein (E). The genome size of SARS-CoV-2, which was recently sequenced as a member of the coronavirus family, is around 29.9 kb. The genome of SARS-CoV-2 include four structural proteins (S, E, M, and N) and sixteen non-structural proteins (nsp1-16).[8]

Spike Protein: Coronavirus's S protein or spike protein is located on the virion surface in a looming out form. This is a class I viral transmembrane protein with multifunctional ability and higher transmembrane abundancy. The size of this protein varies from 1,160 amino acids to 1,400 amino acid residues. Apart from playing a significant role in the infection by virion entry, it also acts as a critical factor for host range determination and tissue tropism. This is a trimer protein, and its ectodomains (in all CoVs) have similar

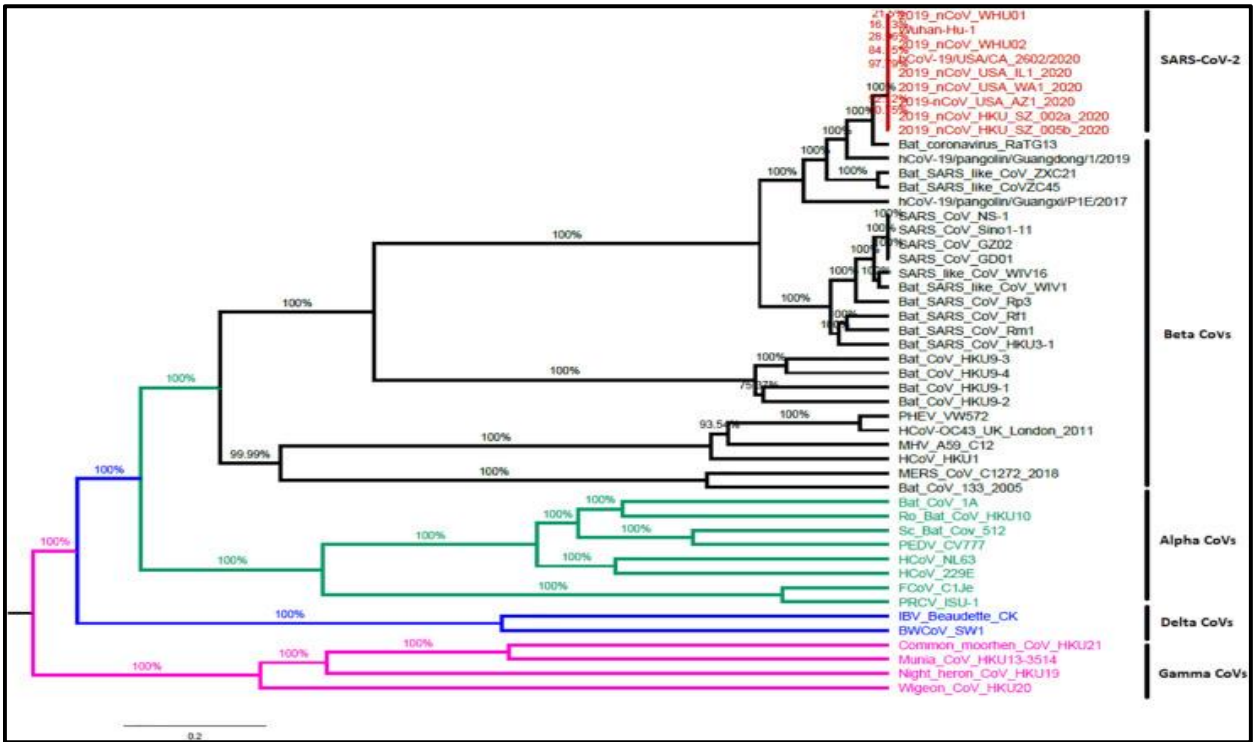

Figure 1. Whole genome-based phylogenetic tree of CoVs constructed with the maximum-likelihood method (Junejo et al. 2020)

domain organization. This organization involves two subunits, S1 and S2, among which the first is concerned with receptor binding while the other one is concerned with fusion. The C-terminal domain of the S1 subunit consists of the Receptor Binding motif (RBM).

Membrane Protein: M protein is concerned with defining the shape of the viral envelope as it exists in the maximum number among the viral protein. Binding to the nucleocapsid serves as the central organizer of the coronavirus assembly. Coronavirus's M protein contains varying amino acid contents, yet an overall structural similarity within the different genera is maintained. It comprises three transmembrane domains, flanked by a long carboxy-terminus inside the virion and a short amino acid terminus outside of it. The viral scaffold is generally maintained by M-M interaction.

Envelope Protein: E proteins of Coronavirus are the smallest and most mysterious of the significant structural proteins. This is an integral membrane polypeptide acting as a virion and possesses multifunctional capability in pathogenesis, assembly, and virion release. The alteration of virulence of Coronavirus is dependent on the action of this protein. It has three domains: an effective C-terminal, a large

Nucleocapsid Protein: The N protein of Coronavirus serves the versatile function. It includes a role in complex formation with the viral genome, and also it facilitates M protein interaction at the time of virion assembly, followed by enhancement of the transcription efficiency of the virus. It has three highly distinct and conserved domains: a CTD, an NTD, and an RNA-binding domain or a linker region (LKR). The NTD binds with the 3" end of the viral genome, probably via electrostatic interactions, and is highly diverged in length and sequence.[18]

GENOMIC STRUCTURE & REPLICATION

The world is aware of the trending novel zoonotic Coronavirus (SARS-COV-2), popularly called Covid-19, whose infection started in Wuhan in December 2019.[19] The Coronavirus family contains many contagious viruses- IBV-Beaudette, BCoVENT, hCoV-229E, MHV-A59, TGEV-Purdue 115, PEDV-CV777, etc. The range of their lengths is 27,317 to 31,357 nucleotides making the Coronavirus genome the largest one among all the RNA viruses. The members of this family have been known to contaminate humans and other vertebrates, causing respiratory and GIT-related issues. The organization of this genome is somewhat similar to older Nidovirus.[20] Before the pandemic spread, there were only two

viruses that were common in causing human infections, hCoV-229E, and hCoV-OC43. After the contamination started, the discovery of more strains was observed- SARS-CoV, hCoV-NL63, hCoV-HKU1 and MERS-CoV. Out of these, SARS-Cov and MERS-Cov are highly virulent and have the highest mortality rate. Interestingly, both of them have been derived from bats. At the 5' terminal end, the two-thirds portion of the genome codes for replication and transcription, while the leftover one-third codes for structural and accessory proteins of the virus. The research on these one-third proteins is compulsory to determine the drug treatments and develop vaccines against the virus.[21] SARS-CoV and MERS-CoV both are highly pathogenic and derived from the bat. But some phylogenetic research has revealed that though Coronavirus can enter the cell through human receptors, it doesn't transmit directly. Rather, it needs an animal host that stays close to humans to spread it. So, for SARS-CoV, it is raccoon dogs; for MERS-CoV, it is domestic riding camels. SARS CoV-2, the reason for the pandemic is 96% identical to bat SARS-like coronavirus gnomically. The virus is spherical in shape, with single-stranded positive-sense RNA 26 to 32 kb in size. The structural features show that it is crownlike, possessing clover leaf-shaped projections (made up of glycosylated proteins) from the viral envelope known as spike proteins. Except for spike proteins, they have 3 other proteins present: the membrane, envelope, and nucleocapsid ones (Figure-2).[22]

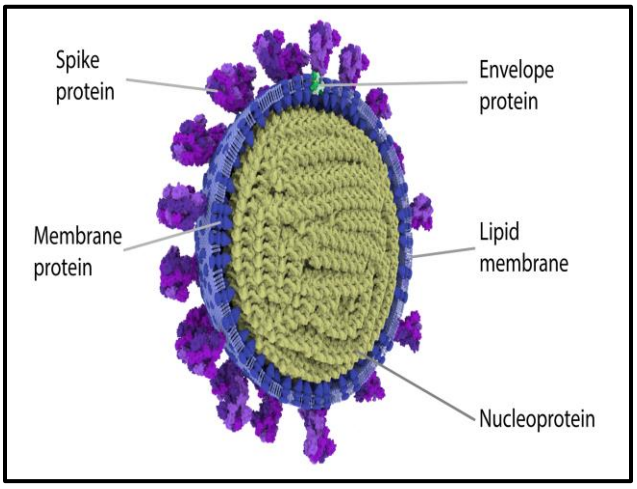

Figure 2. Structure of Coronavirus (David et al. 2020)

Almost 66% of the genome consists of two open reading frames overlapping code for 16 non-structural proteins, which involve RNA-dependent RNA polymerase, proteases, primase, helicase, etc. Jointly forming a viral replication system.

These irregular proteins are the main therapeutic targets to find a cure for the disease. The remaining one-third of the genome contains the proteins not involved in replication but cause suppression of the immune system and enhance pathogenesis.[23] A unique feature own by this virus is that it can also outspread by people showing no symptoms at all. Reports have disclosed that this virus can spread among cats but meager chances among dogs. Whether this can spread from domestic animals to humans is still untold.

EPIDEMIOLOGY

In the past two decades, China has experienced three major respiratory virus outbreaks that have escalated into epidemics: the H5N1 avian flu in 1997, SARS-CoV in 2003, and the ongoing SARS-CoV-2 (since 2019). The first infections of SARS-CoV-2 have direct links to the Hunan seafood market; later sources of infection were diseased people. Presently, human-to-human transmission is the primary mode of disease transmission worldwide. The intermediate host thought to have caused the outbreak is believed to be snakes or pangolins, although this has yet to be validated. Travel and importation were crucial in bringing SARS-CoV-2 to Korea, Japan, the Middle East, Europe, and especially India. SARS-CoV-2, which is of international concern, was labeled as a public health crisis by the World Health Organization (WHO) on January 30, 2020, and a controlled pandemic on March 11, 2020. According to the Chinese Centre for Disease Control and Prevention (CCDC), person to person transmission via respiratory droplets and contact are the most common routes of infection for humans. There has been no reliable evidence of vertical (intrauterine) transmission described in the literature thus far.[24]

As of June 10, there have been 532,201,219 cases and 6,305,358 deaths globally and 43,205,106 cases and 524,747 deaths in India.[25]

PATHOPHYSIOLOGY OF SARS COV-2

SARS-CoV-2 has a diameter of 60 nm to 140 nm with discrete spikes ranging in size from 9 nm to 12 nm, giving the virus the appearance of a solar corona. Coronaviruses can adapt to and infect new hosts via genetic recombination and variation. Although bats are assumed to be a natural reservoir for SARS-CoV-2, it

has been proposed that humans acquired the infection via an intermediary host, such as the pangolin.

The current state of knowledge on the human immune response elicited by severe acute respiratory syndrome coronavirus (SARS-CoV-2) is described. SARS-CoV-2 infects cells by binding to the angiotensin converting enzyme 2 receptor (ACE2) via the viral structural spike (S) protein. The host cell's serine protease type 2 transmembrane serine protease (TMPRSS2) increases viral uptake by cleaving ACE2 and activating the SARS-CoV-2 S protein. In the early stages, viral copy levels in the lower respiratory tract can be high.

Infected cells and alveolar macrophages, as well as recruited T lymphocytes, monocytes, and neutrophils emit inflammatory signalling molecules. Late-stage pulmonary edema can cause hyaline membrane development in the alveolar gaps, which is consistent with early-phase acute respiratory distress syndrome.[26]

REPORTED DRUGS AND VACCINES

Till now there are few antiviral treatments or vaccines of Coronavirus. Scientists are mainly focusing on the symptoms of the respiratory system as per the protocol issued by the health authority in each country, following WHO protocol.[8,9]

The Coronavirus leads to such epidemic in our world for the third times. As we have already fought with the two epidemics, formerly we can use the experience to create treatment plans against this. At this time scientists are using different types of drugs and medication to the positive patients and get a promising result. Also, vaccines are being developed to restrict the viral propagation from one host to another by elevating the immune system.

COVID-19 Treatment Guidelines external symbols are provided by the National Institutes of Health (NIH) to assist healthcare providers in working with their patients and determining the appropriate treatment options. COVID-19 can be treated at home or in an outpatient environment in a variety of ways. They are as follows.

Nirmatrelvir with ritonavir (Paxlovid) is an experimental antiviral therapy for adults and children aged 12 and up. It is eaten orally at home. It should be started as soon as possible, and no later than five days after the onset of your symptoms.

Remdesivir (Veklury) is an antiviral drug that can be used by both adults and children. Treatment involves intravenous (IV) fluids at a medical facility for three days. It should start as soon as possible and within seven days of the onset of your symptoms.

Bebtelovimab external icon is an experimental monoclonal antibody therapy for adults and children aged 12 and above. A single IV injection of bebtelovimab is administered by a healthcare practitioner. It should begin as soon as feasible and no later than seven days after your symptoms begin.

Molnupiravir (Lagevrio) is an antiviral medication for individuals aged 18 and up. It is taken orally at home (orally). It should begin as soon as feasible and no later than seven days after your symptoms begin.[27]

REPORTED VACCINES

Grouping into categories of vaccine construction, the reported vaccines are enlisted below.

RNA vaccines and DNA vaccines: Pfizer–BioNTech is a mRNA vaccine developed by the American corporation Pfizer and the German company BioNTech, COVID-19 is marketed under the trade name Comirnaty. Fosun Pharma distributes Comirnaty in Taiwan, Macau, and Hong Kong.

Moderna is created by the collaboration of Coalition for Epidemic Preparedness Innovations, the National Institute of Allergy and Infectious Diseases, the United States Biomedical Advanced Research and Development Authority, and the American corporation Moderna. It is also known as Spikevax. Men under the age of 30 in Finland are not eligible for the Moderna vaccine as a preventative measure to reduce a very low risk of myocarditis.

ZyCoV-D is a COVID-19 vaccine based on a DNA plasmid produced by the Indian pharmaceutical business Cadila Healthcare with funding from the Biotechnology Industry Research Assistance Council.

Adenovirus vector vaccines: Oxford-AstraZeneca COVID-19 vaccine, marketed as Vaxzevria and Covishield, is a viral vector vaccine developed by the British University of Oxford, the British-Swedish firm AstraZeneca, and the Coalition for Epidemic Preparedness Innovations. Because of a few isolated reports of a rare blood clot disease, Finland, Denmark,

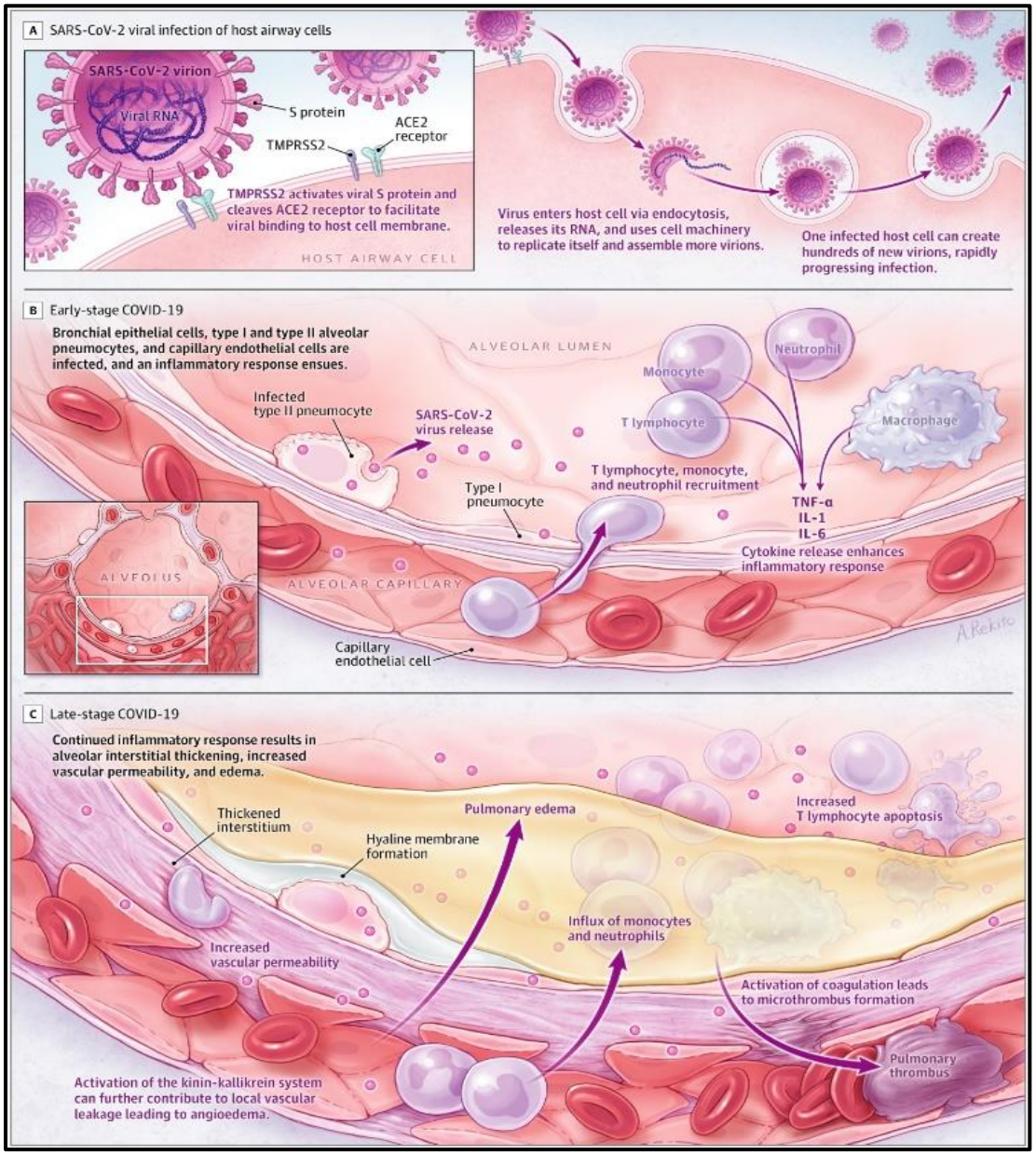

Figure 3. Mechanism of interaction of the SARS CoV-2 virus with human ACE-2 receptor (Wiersinga et al. 2020).

and Norway have stopped using the Oxford-AstraZeneca vaccine. Following the demise of a susceptible recipient, Slovakia discontinued its use. In August 2021, Japan began offering the vaccination to those 40 years of age or older to slow the spread of the Delta form. Over 1.3 billion people have received the AstraZeneca vaccination, making it the most well-liked and broadly accepted vaccine on a global scale. In comparison to other vaccines, the AstraZeneca vaccine is given in the most nations.

Janssen COVID-19 is collaboratively designed by The Beth Israel Deaconess Medical Center and Janssen Pharmaceutica. This is a viral vector vaccine in nature and it is also referred to as COVID-19 Vaccine Johnson & Johnson and COVID-19 Vaccine Janssen. Due to a potential connection between the Janssen vaccination and a rare blood clot disorder, Denmark, Finland, and Norway stopped using the vaccine in favour of other options. Finland started using the Janssen adenovirus vector vaccine in October 2021. Due to the extremely low risk of thrombosis in younger age groups, it is only made accessible to people who are 65 and older.

Sputnik V COVID-19 vaccine belongs to the viral vector vaccine type, which is manufactured by the Russian

Gamaleya Research Institute of Epidemiology and Microbiology. Sputnik Light is a reformed type of the prior, which consists of the first dose of the Sputnik V vaccine, and is based on the Ad26 vector.

Convidecia is a viral vector vaccine created by the Beijing Institute of Biotechnology of the Academy of Military Medical Sciences and the CanSino Biologics firm in China.

Inactivated virus vaccines: Sinopharm BIBP vaccine belongs to inactivated virus vaccine manufactured by the China National Pharmaceutical Group (Sinopharm) and its Beijing Institute of Biological Products.

CoronaVac vaccine is an inactivated viral vaccine for COVID 19 manufactured by Sinovac Biotech in China.

Covaxin was developed by the Indian company Bharat Biotech in cooperation with the Indian Council of Medical Research–National Institute of Virology. It is an inactivated virus vaccine. As with the inactivated polio vaccine, Covaxin makes use of an older, less sophisticated method of manufacturing.

Valneva vaccine comprises inactivated (killed) particles of the original strain of SARS-CoV-2 (the virus that causes COVID-19).

Sinopharm WIBP vaccine is developed by the collaboration of the China National Pharmaceutical Group (Sinopharm) and its Wuhan Institute of Biological Products.

Subunit vaccines: NVX-CoV2373 is a subunit COVID-19 vaccine candidate developed by Novavax and the Coalition for Epidemic Preparedness Innovations (CEPI) that is now being tested in India under the brand name Covovax.

Although the manufacturers refer to NVX-CoV2373 as a "recombinant nanoparticle vaccine," it has been called both a protein subunit vaccine and a vaccine against virus-like particles.

Abdala is a subunit vaccine was created by the Cuban Center for Genetic Engineering and Biotechnology.

EpiVacCorona is manufactured by the Russian State Research Center of Virology and Biotechnology VECTOR. To make the vaccine, a big carrier protein is linked to three chemically produced peptides (short fragments of a viral spike protein). An MBP and a viral nucleocapsid protein have been fused together to produce this protein.

Zifivax, also known as ZF2001 or ZF-UZ-VAC-2001, is an adjuvanted protein subunit COVID-19 vaccine that was developed by Anhui Zhifei Longcom in partnership with the Institute of Microbiology at the Chinese Academy of Sciences. ZF2001 was given the marketing name Zifivax. At this time, there are 29,000 people taking part in clinical trials for the vaccine candidate in countries like China, Ecuador, Malaysia, Pakistan, and Uzbekistan.

Soberana 02 or Soberana 2, also known by its technical designation FINLAY-FR-2, is a COVID-19 vaccine manufactured by the Finlay Organization, a Cuban institute for epidemiological research. It was created in conjunction with Iran's Pasteur Institute of Iran and is known as PastoCovac.[27]

CONCLUSION

The COVID-19 pandemic created a significant risk to the global public health systems. The consecutive two to three years of the pandemic by the rising numbers of infections and deaths have caused the international community to undergo a severe phase by the tireless struggle of the researchers and medical practitioner, along with other first-line workers has retrieved the health scenario of the world. Our review paper has inculcated information regarding genomic variants, pathogenicity, phylogenetic analysis, epidemiology, and clinical measures. We have cultivated the best to provide a void less details of every possible head. The different proteins involved in this disease and the drugs or vaccines reported for the control have been in prime focus along with its genomic variations. This study is done to sum up the complete documentation of the COVID 19 diseases from its onset till today.

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Cite this article as:
Dutta S, Ghosh R, Ghosh D, Santra P, Daw S. A Detailed Study of Covid 19 (Emphasizing its Genomic Variants, Pathogenicity, Phylogenetic Analysis, Epidemiology, and Clinical Measures). Int Healthc Res J. 2022;6(5):RV1-RVxx. https://doi.org/10.26440/IHRJ/0605.08556

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Source of support: Nil, **Conflict of interest:** None declared

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