

A COMPREHENSIVE FINDINGS ON SARS-COV-19 VIRUS

Kajal D. Chaudhari¹, Jagdish V. Manwar¹, Ravindra L. Bakal², Rahul D. Jawarkar², Chetan M. Jain²,
Snehal S. Manekar²

¹ IBSS's Dr. Rajendra Gode College of Pharmacy, Mardi Road, Amravati-444 602, MS, India.

² IBSS's Dr. Rajendra Gode Institute of Pharmacy, Mardi Road, Amravati-444 602, MS, India.

*Corresponding Author: Email: kajuchaudhari89@gmail.com

Received: 11 November 2021 / Revised: 28 November 2021 / Accepted: 21 February 2022 / Available online: 31 March 2022

ABSTRACT

SARS-CoV-2 is one amongst the various styles of coronavirus; these viruses are known to cause illnesses which range from a typical cold to a more severe respiratory disorder. The infection began to spread from the Human seafood wholesale market in Wuhan, China, while the precise infection route of the primary case remains unclear. As of September 4th 2020, the etiologic agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread all over the world, leading to around 26 million confirmed cases and around 865,000 deaths. The disease is transmitted by inhalation or contact with infected droplets and the incubation period ranges from 2 to 14 d. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, malaise among others. The antiviral drugs, including Oseltamivir, ribavirin, ganciclovir, lopinavir, and ritonavir have been used in attempts to reduce viral load and to prevent the likelihood of respiratory complications in several studies. Chloroquine and Remdesivir effectively controlled the COVID-19 infection in in-vitro cell culture. The University of Oxford developed a vaccine supported Chimpanzee Adenovirus Vector (ChAdOx1) which is immunogenic in mice. The vaccine candidate entered phase I/II (NCT04324606) trial in April 2020 to check its safety, tolerability, and immunogenicity in 510 volunteers. The protective efficacy and the short term and long-term side effects of vaccine are of major concern.

Keywords – SARS-CoV-2; droplet infection; Chloroquine; Remdesivir.

1. INTRODUCTION

The World Health Organization (WHO) announced in March 2020, that the outbreak of coronavirus diseases (COVID-19), which initially started in Asia, had become a pandemic. As of September 2020, the etiologic agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread all over the world, leading to around 26 million confirmed cases and around 865,000 deaths. The rapid availability of the genomic sequence of the viral RNA has been instrumental in the development of diagnostic tools and for the identification of experimental treatments. [1]

In this review, we will focus on the discovery of SARS-CoV-2, its virology features, and pathogenesis, as well as diagnostic tools. The Chinese Centre for Disease Control and Prevention (CCDC) identified this infection as a completely unique coronavirus infection on Jan 7, 2020, and on Feb 11, 2020, the WHO announced a replacement name for the infectious disease as 2019-new coronavirus disease (2019-nCoV and now called COVID-19) (Organization, W.H.O, 2020). Additionally, the International Committee on Taxonomy of Viruses named 2019-nCoV as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 has become a significant global health concern and therefore the WHO declared the coronavirus outbreak a worldwide pandemic in March 2020 (Whitworth, 2020). As of Pan American Day, 2020, COVID-19 has affected over 1,948,617 patients in 210 countries and territories around the world and two international conveyances and left around 121,846 deaths worldwide.

Coronavirus is the pandemic disease includes different kinds like flu and cold or some cause other disease. Latest coronavirus, SARS-CoV-2, has caused respiratory illness like shortness of breath or difficulty in breathing called COVID-19. [2]

First know about the overall structure of the coronavirus. The virus structure consists of an outer envelope, the core, nucleoprotein and a nucleocapsid. The virus's diameter is 120nm with a lipid bilayer and a core RNA genome. The envelope made up of lipid bilayer has a membrane, envelope and anchored spike proteins. The nucleocapsid protein is binded by RNA genome as shown in fig.1

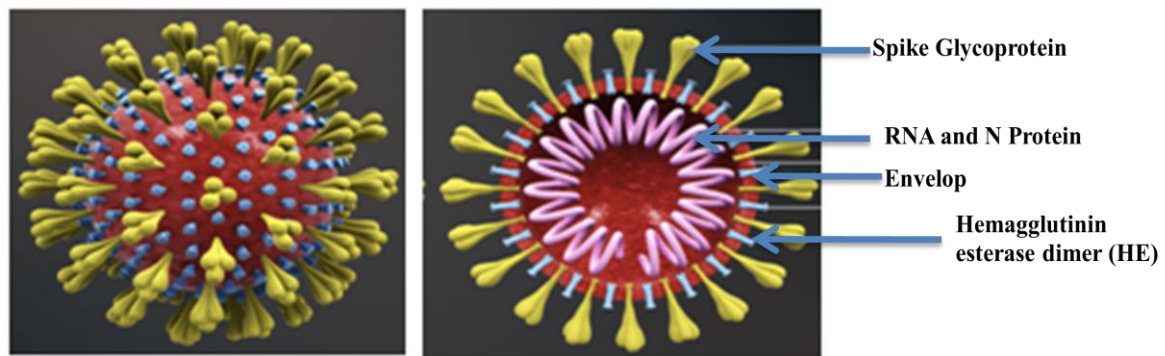


Fig 1: Structure of coronavirus

1.1 S-Protein

The S protein is the whole number of hormones present inside the structure with two subunits S1 and S2. The S1 subunit plays the role of a receptor-binding domain while the S2 makes the stalk of the spike. Both S1 and S2 protein helps in virion-host cell receptor binding. The protease present on a host cell cleaves the S protein into segments. The S protein is ~150KDa in size. The S protein is a kind of glycoprotein.

Another type of protein called He-hemagglutinin esterase is present in some strains of coronavirus like the beta coronavirus. It is believed that the present protein induces cell entry of S protein-mediated virions. [3, 4]

1.2 Spread or Transmission of Corona Virus

COVID-19 appeared in Wuhan, a city in China, in December 2019. Although health officials are still tracing the precise source of this new coronavirus, early hypotheses thought it's going to be linked to a seafood market in Wuhan, China. Some folks that visited the market developed a viral infection caused by the new coronavirus. A study that came out on Jan. 25, 2020, notes that the individual with the primary reported case became ill on Dec. 1, 2019, and had no link to the seafood market. Investigations are ongoing on how this virus originated and spread. [5]

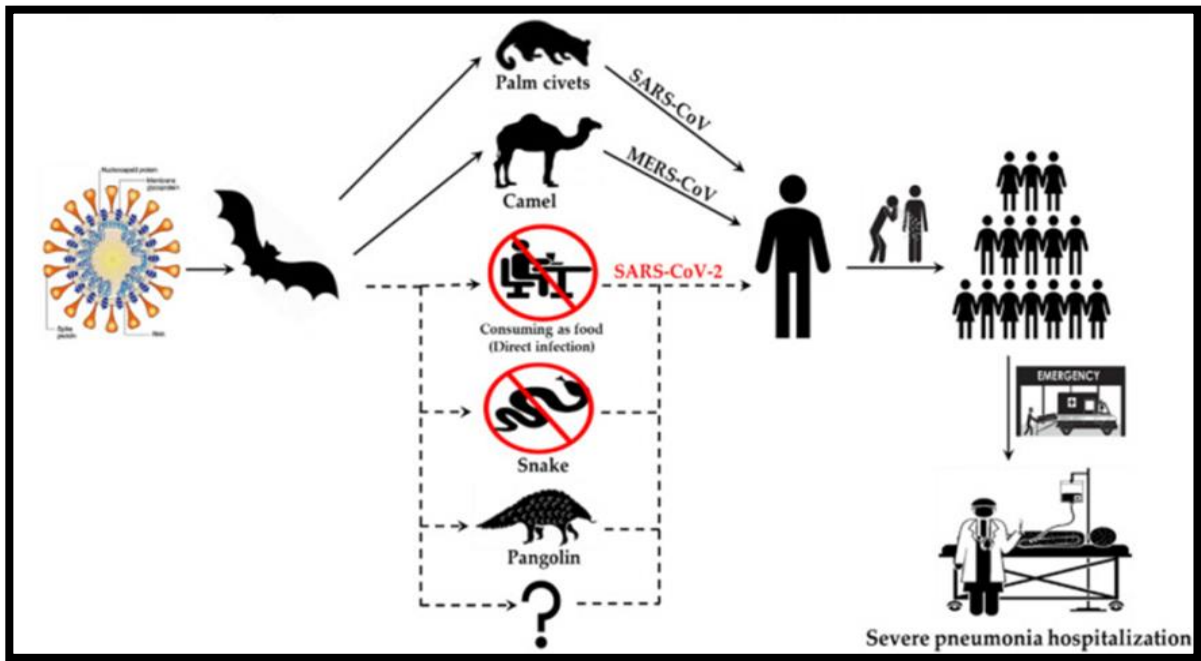


Fig 2: Transmission of Covid-19

The key reservoir and potential interspecies transmission routes of SARS-CoV, MERS-CoV, and SARS-CoV-2. The ingesting of the infected animal as a source of food is that the major reason for an animal to human transmission of the virus and thanks to close contact with an infected person, the virus is further transmitted to healthy persons. However, there are not many documented cases of direct bat-human transmission. The solid black arrow represents the confirmed transfer while the broken line denotes unknown host and suspected transmission. [6]

1.3 Replication of Coronavirus

The replication of coronavirus occurs in the host cell cytoplasm near the nuclear membrane once it enters into the host cell. This process is done by endocytosis. The virus enters into the host cell via binding of viral spikes to the cell receptor of a host cell. [7]

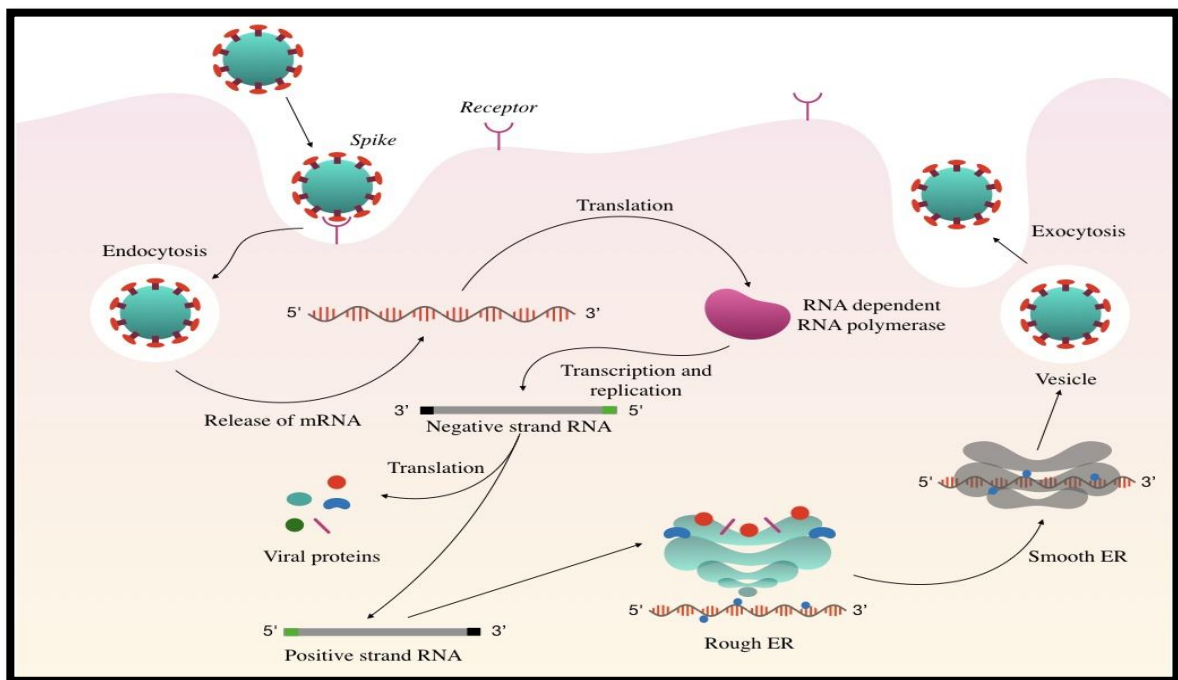


Fig 3: Replication of coronavirus

The deadly killer begins its action with its spike protein. The receptor-binding domain present on the S1 interacts with the receptor on the host cell surface.

It doesn't matter, where the RBD (Receptor binding domain) is found on S protein, either on NTD or CTD, its only function is to interact with the receptor. Notably, some species also interact with various peptidases present on a cell surface, however, the sort of peptidase varies from species to species.

By proteolytic cleavage, virus enters into the host cell cytoplasm. Dimeric cleaving by the protease digests spike protein into fragments and makes the protein non-functional. Proteases break the viral protein and release RNA into the cytoplasm and make it uncoated. [8-10]

2. CLINICAL MANIFESTATION

Coronavirus (Covid-19) symptoms usually appear after five to six days, according to the WHO reports. In some cases, rarely the incubation period of the virus at list up to 40 days with a median incubation period of 14 days. The incubation period for severe cases may be different compared to mild cases and depend on the age of the patient and their immune response. This period tended to be shorter among patients >70 years (11.5 days) than those aged <70 years (20 days). However, it is different for people suffering from underlying diseases such as diabetes, heart, lung and other diseases. In this case, the disease can take on critical forms that sometimes lead to death. Some people have no symptoms (mild pneumonia). The most common symptoms of COVID-19 according to a recent WHO report that was done on more than 70,000 cases in China are the following: fever (in 88% of cases), dry cough and sore throat (68%), fatigue (38%) and diarrhea (4%), which were similar to SARS-COV and MERS-COV. Furthermore, severe shortness of breath occurred in nearly 20% of cases and around 13% had a sore throat or severe headache.[11] Infected patients may have lymphopenia which is that the most typical laboratory manifestation, normal or lower white vegetative cell counts, or thrombocytopenia, with elevated C-reactive protein level.

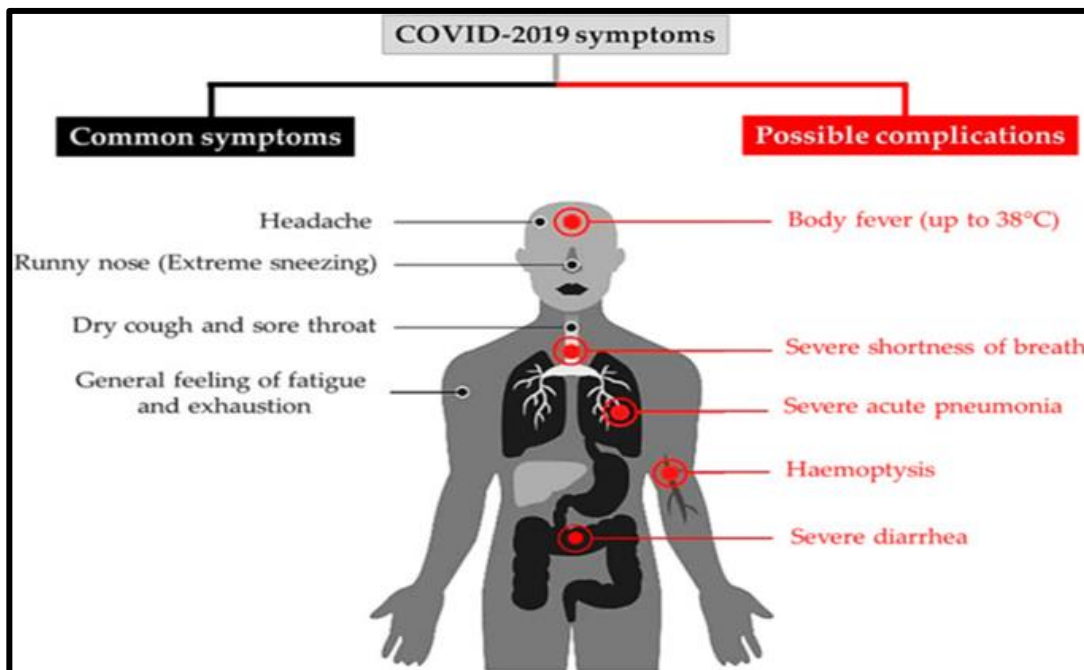


Fig 4: Covid-19 symptoms & their complications

Generally, CoV-19 is a member of the coronaviruses family that usually attacks the respiratory system. Some patients are disposed to various complications to include acute respiratory distress syndrome, acute heart injury, and secondary infection with bacteria.

The virus first infects the lining cells of the throat, trachea, and lung, transforming these cells into virus factories that produce huge amounts of viruses that infect more cells. The high temperature and feeling of general malaise are caused by the response of the immune system to the virus and sending signals to the body to release cytokines. However, the virus disturbs the immune response and the body gets more inflammation than needed. Inside the lungs, oxygen travels to the blood but in the case of severe pneumonia, the alveoli begin to fill with water and may cause shortness of breath. In some cases, this results in coughing with sputum, which is a thick mucus that contains lung cells killed by the 19. The problem may not be limited to the lungs, as 19-nCoV attacks other important organs in the body to include the kidneys, which may lead to organ failure. [12-15]

3. EPIDEMIOLOGY

The number of COVID-19 cases reported to the WHO has been growing since the primary report of COVID-19 in December 2019 from the WHO China Country Office. The infection began to spread from the Human seafood wholesale market in Wuhan, China, while the precise infection route of the primary case remains unclear. The number of confirmed cases in China grew until mid-February 2020. Then, the quantity of daily new cases in China began to decrease from late February 2020.

An outbreak of the cases in China on February 17 is due to the change in COVID-19 diagnostic criteria. At the time of writing (March 19, 2020), COVID-19 cases are still be reported globally from over 170 countries. As of March 15, 2020, 153,517 laboratory-confirmed COVID-19 cases with 5,735 deaths (approximately 3.8% mortality) are reported in keeping with WHO.[16]

In the early stages of the world COVID-19 spread, the cases identified outside of China were mostly traveling people that were infected in China and so travel outside areas of China. Countries outside of China that reported travel-associated COVID-19 cases were Singapore, Japan, the Republic of Korea, Malaysia, Vietnam, Australia, the US. of America, Germany, etc. Unfortunately, COVID-19 has begun to spread domestically in the Republic of Korea, Italy, Iran, and Japan from mid-February 2020.[17]

Particularly, within the Republic of Korea, the spread of COVID-19 had been well managed until mid-February. The number of confirmed cases in the Asian country was 31 on February 18, 2020, and most of those cases were traveled from. China or their close contacts. However, COVID-19 infections among a spiritual group within the Daegu metropolitan area and a close-by hospital triggered a sudden spread to other major domestic cities in the Republic of Korea in mid-February. As a result, every week later, the confirmed cases soared to 763 and 74.6% of these cases were tied to the event (as of February 24, 2020). On March 1, the full number of confirmed cases reached 3,526, among which 59.5% belonged to the religious group-related cases. The fatality rate of SARS-CoV-2 (3.8%) is less than that of SARS-CoV (10%) or MERS-CoV (37.1%), but the amount of relative infection cases is quite 10 times higher.[18]

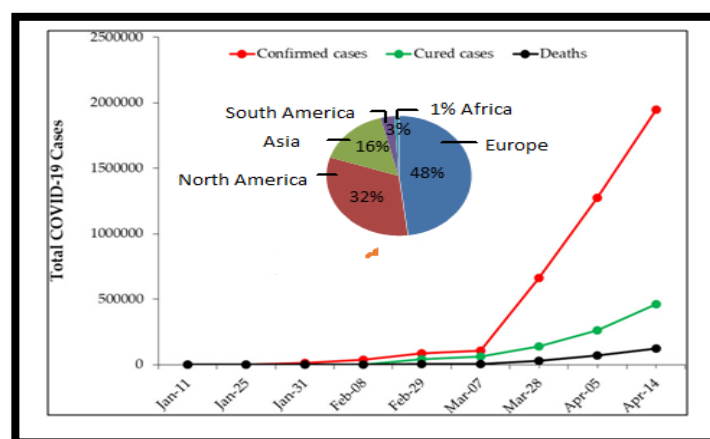


Fig 5: Total covid-19 cases

4. SCREENING AND DIAGNOSIS

In the present scenario, the lack of standardized screening and diagnosis methods is one of the serious complications. Notwithstanding, thermal screening is one of the most popular and trusted primary screening methods, accepted globally.

4.1 Thermal Scanning

You may have seen the railway and airport authorities scanning everyone with some variety of gun-like devices. This device is truly a thermal scanner, they aim it on the top a part of an individual to live the temperature. Every live organism emits infrared energy or heat. A thermal scanning device captures the warmth emitted from someone. After that, it creates a 2D type image of someone with different color patches as per heat emitted. As we knew, just in case of infection the bodily temperature of individual increases, the device captures 100F or above temperature as abnormal. The person is separated immediately and quarantined until tested for COVID-19. The Thermal screening method is barely trusted accustomed screen the infection of coronavirus (covid-19). [19]

4.2 Diagnosis Method

They are two types of testing that are now available to validate the infection of coronavirus (covid-19) viz, RT-PCR and Serological testing which comes under Molecular genetic testing.

Molecular genetic testing

Most laboratories across the US use the RT-PCR-based diagnosis method for the diagnosis of MERS-CoV-2 or COVID-19 (SARS-CoV-2) infection. However, the test isn't yet approved by the FDA. CDC approved it through the Emergency Use Authorization.

The viral RNA is amplified, measured, and/or sequenced to validate the active infection of COVID-19 within the patient. Two unique sequences of RARS-CoV-2 are amplified using the fluorescent label probes in real-time PCR. As the target viral cells are very few, first the supermolecule from the virus is amplified using the polymerase chain reaction. In that process, approximately 1 ml of the nasopharyngeal swab sample is collected first, followed by viral DNA extraction. Nasopharyngeal, oropharyngeal, or bronchoalveolar lavage is taken. sputum, serum, and stool samples are also considered for testing. Unique regions of viral RNA are amplified using two sets of probes and primers. For that first, the RNA is reverse transcribed into cDNA. Within the following step, the cDNA is measured from the sample. Also, for cross-validating results, RNA sequencing is performed. [20]

Serological testing

Our bodily cells produce antibodies against infectious pathogens. The antibody could be a kind of protein that protects our cells from microbial infection. The serological testing is practiced to seek out antibodies against SARS-CoV-2 previous infection. The conventional ELISA- enzyme-linked immunosorbent assay is employed to live the amount of antibodies present within the sample. Viral nucleocapsid and spike protein are the targets for this test. Antibodies secreted against any of the proteins or both proteins are determined in ELISA using the precise substrate. Scientists believe that the ELISA method is more a screening kind of technique instead of a diagnosis method. Thus, for confirming the results of either ELISA or RT-PCR another kind of test is employed, the microneutralization assay.[21]

5. SARS CORONAVIRUS REPLICASE POLY

Protein 1AB

The coronaviruses express the foremost important and most complex polyproteins of any RNA viruses. The polyproteins are translated from the genome RNA open reading frames 1a and 1b, and are called replicase, replicase/transcriptase, or polymerase polyproteins, in recognition of the expected and demonstrated roles in viral RNA synthesis. However, the appellation of

“replicase/transcriptase”, while appropriate, is an incomplete description of all probable ORF1ab protein functions. It has been predicted, furthermore as demonstrated in some cases, that the mature proteins within the polyprotein may serve roles distinct from or additionally to roles in viral RNA synthesis. More specifically, it's becoming clear that proteins or protein domains encoded in ORF1ab may serve specific roles in virulence, virus-cell interactions, and/or alterations of virus-host response.[22]

Two events within the history of coronavirus biology have dramatically accelerated the studies and discoveries in protein functions: the SARS epidemic and also the event of reverse genetic strategies for the study of coronavirus replication. The rapid identification and sequencing of SARS-CoV isolates led to bioinformatics analyses highlighting both conserved and divergent regions of the replicase genes, particularly in relationship with known group 2 coronaviruses like mouse hepatitis virus (MHV).[23] Additionally, the detailed analysis of animal and human isolates of SARS-CoV during the epidemic revealed evidence of adaptive mutations within the replicase to an extent that matched or exceeded that within the structural proteins.

Concurrently, the rapid establishment of a reverse genetic system for SARS-CoV, also because of the event of reverse genetic systems for other group 2 coronaviruses, allowed direct studies of conserved and divergent domains of the replicase in replication. Subsequently, it's become clear that the replicase gene proteins will likely demonstrate multiple functions, many of the novel, in viral pathogenesis. This review will summarize the organization, expression, processing, and putative replication functions of the nonstructural proteins (nsps 1–16) of SARS-CoV; describe studies of ORF1b nsps demonstrating interactions with host cells or host immune response; describe studies of SARS-CoV nsps that support functions for the proteins in pathogenesis and adaptation.[24]

The novel coronavirus (SARS-CoV-2) broke to go into November/December 2019 in Wuhan, situated within the Chinese province of Hubei. This virus created a worldwide pandemic that has affected most countries on the planet. As of 30th August 2020, there are 25,051,178 recorded cases of the virus and 843,641 recorded deaths as a result of the novel coronavirus. This is also a replacement Severe Acute Respiratory Syndrome virus and to keep with current research and evidence, SARS-CoV-2 is principally transmitted by respiratory droplets, contact pathways, and there is growing research to suggest that mechanism is additionally possible.[25]

SARS-CoV-2 is one of the various styles of coronaviruses; these viruses are known to cause illnesses that range from a typical cold to a more severe respiratory disorder. The novel coronavirus is kind of just like the MERS-CoV which could be a geographical region Respiratory Syndrome virus. Over the past twenty years, there has been a major number of coronavirus breakouts, each sort of virus has certain unique features however there are a variety of similarities likewise. The primary SARS virus outbreak was in 2002 and emerged within the Chinese province of Guangdong. This epidemic spread to about 26 countries and caused quite 8000 cases similarly to 774 deaths. All three of the Coronaviruses mentioned sharing the similarity of how they quickly spread to different countries and therefore the early phases of the viruses are similar. [26] SARS-CoV-2 could be a single-stranded, RNA beta coronavirus that's surrounded by a fatty outer layer called an envelope. It's a 'crown', otherwise called 'corona', of proteins around the RNA molecules. Coronaviruses are zoonotic and hence may be transmitted from animals to humans. There's research to believe that the virus originated from bats which then spread to humans in China. [27] Both SARS-CoV and SARS-CoV-2 are closely related in this sense because it is assumed that they both have originated from bats, this implies that these organisms are also a reservoir host for the virus. [28] Since the virus has been infecting humans for a comparatively short period of your time (the first case was recorded in December 2019), there's plenty of unknown information about SARS-Cov-2 and hence during this study, we aim to research the functions and properties of the various polyproteins present within the virus and to spot the protein chains to which the polyproteins are cleaved to. Coronaviruses (CoVs) are highly multiple families of enveloped positive-sense single-stranded RNA viruses. They infect humans, other mammals, and avian species, including livestock and companion animals,

and are therefore not only a challenge for public health but also a veterinary and economic concern. Within the order of Nidovirales and therefore the suborder of Coronavirineae lies the family Coronaviridae. The latter is further specified into the subfamily of Ortho coronavirinae, which consists of 4 genera: alpha coronavirus, beta coronavirus, gamma coronavirus and delta coronavirus. Alpha coronaviruses and beta coronaviruses exclusively infect mammalian species whereas gamma and delta coronaviruses have a wider host range that features avian species. Human and animal coronavirus infections mainly lead to respiratory and enteric diseases. [29-31]

Human coronaviruses, like HCoV-229E and HCoV-OC43, have long been known to circulate within the population and that they, along with the more recently identified HCoV-NL63 and HCoV-HKU1, cause seasonal and frequently mild tract infections related to symptoms of the 'common cold'. In strong contrast, severe acute respiratory syndrome coronavirus (SARS-CoV), Near East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2, which have emerged within the human population over the past 20 years, are highly pathogenic. By infecting bronchial epithelial cells, pneumocytes, and upper tract cells in humans, SARS-CoV, MERS-CoV, and SARS-CoV-2 infections can grow to be severe, life-threatening respiratory pathologies and lung injuries that no specific prophylactic or therapeutic treatment has been approved up to now. The initial steps of coronavirus infection involve the particular binding of the coronavirus spike (S) protein to the cellular entry receptors, which are identified for several coronaviruses and include human aminopeptidase N (APN; HCoV-229E), angiotensin-converting enzyme 2 (ACE2; HCoV-NL63, SARS-CoV and SARS-CoV-2) and dipeptidyl peptidase 4 (DPP4; MERS-CoV). Viral tropism and pathogenicity are affected by the appearance and tissue distribution of entry receptors. During the intracellular life cycle (Fig. 3), coronaviruses express and replicate their genomic RNA to provide full-length copies that are incorporated into newly produced viral particles. Coronaviruses possess remarkably large RNA genomes flanked by 5' and 3' untranslated regions that contain cis-acting secondary RNA structures essential for RNA synthesis. At the 5' end, the genomic RNA features (ORFs; ORF1a and ORF1b) hold two-thirds of the capped and polyadenylated genome. ORF1a and ORF1b encode [32] non-structural proteins (nsp), of which 15 compose the viral replication and transcription complex (RTC) that features, amongst others, RNA-processing and RNA-modifying enzymes and an RNA proofreading function necessary for maintaining the integrity of the >30 kb coronavirus genome.[33] ORFs that encode structural proteins and interspersed ORFs that encode accessory proteins are transcribed from the 3' one-third of the genome to make a nested set of subgenomic mRNAs (sg mRNAs). Coronavirus accessory proteins are denoted as virus-specific proteins that display limited conservation even within individual species but they're principally thought to contribute to modulating host responses to infection and are determinants of viral pathogenicity. Nevertheless, the molecular functions of the many accessory proteins remain largely unknown because of the shortage of homologies to accessory proteins of other coronaviruses or other known proteins. To detect genetic material from a specific organism RT-PCR is done. We established three individual real-time RT-PCR assays. [34]

Target sequences were chosen by using the next criteria:

The regions are distributed over the complete genome, including the nonstructural polyprotein 1a and 1ab genes therefore the spike glycoprotein gene.

The regions are highly conserved among the 89, 90, and 100 respective sequences available publicly sequence databases;

The regions are suitable for the planning of a real-time RT-PCR assay; and

The designed primers, 5'-nuclease probes, and amplicons displayed no considerable homology to other viruses, including human CoV OC43 and 229E in7LAST searches.

Coronaviruses are a various group of viruses infecting many different animals, which they'll cause mild to severe respiratory infections in humans. In 2002 and 2012, respectively, two highly pathogenic coronaviruses with zoonotic origin, severe acute respiratory syndrome coronavirus (SARS-CoV) and Mideast respiratory syndrome coronavirus (MERS-CoV), emerged in humans

and caused fatal respiratory disorder, making emerging coronaviruses a contemporary public health concern within the twenty-first century.[35]At the tip of 2019, a unique coronavirus designated as SARS-CoV-2 emerged within the town of Wuhan, China, and caused a virulent disease of bizarre pneumonia. Being highly transmissible, this novel coronavirus disease, also called coronavirus disease 2019 (COVID-19), has spread fast everywhere on the planet.[36] By metagenomic RNA sequencing and virus isolation from bronchoalveolar lavage fluid samples from patients with severe pneumonia, independent teams of Chinese scientists identified that the causative agent of this emerging disease is additionally a beta coronavirus that had never been seen before. within the first week of January 2020, the results of this etiological identification were publicly announced the first genome sequence of the novel coronavirus was published on the Virological website on 10 January, and more nearly complete genome sequences determined by different research institutes were then released via the GISAID database on 12 January 7. Later, more patients with no history of exposure to the Human Seafood Wholesale Market were identified. Several familial clusters of infection were reported, and nosocomial infection also occurred in healthcare facilities. of those cases provided clear evidence for human-to-human transmission of the new virus. Because the outbreak coincided with the approach of the year, travel between cities before the festival facilitated virus transmission in China. This novel coronavirus pneumonia soon spread to other cities in Hubei province and other parts of China. Within 1 month, it had spread massively to any or all or any or any 34 provinces of China. the number of confirmed cases suddenly increased, with thousands of recent cases diagnosed daily during late January 15. On 30 January, the WHO declared the novel coronavirus outbreak a public health emergency of international concern¹⁶. On 11 February, the International Committee on Taxonomy of Viruses named the novel coronavirus 'SARS-CoV-2', and thus the WHO named the disease 'COVID-19'. [37,38]

6. TREATMENT OF COVID-19

As per the most recent report of WHO, and CDC (Centre for Disease Control and Prevention), no appropriate therapy, medicine, or vaccine is developed and approved to date for the prevention and treatment of SARS-CoV-2 infection. However, the scientific fraternity throughout the world is aggressively working to search out a promising solution to the present epidemic outbreak that originated in China. Many preclinical and clinical investigations by different Institutions, Government bodies, research centers, and pharmaceutical industries focused on testing the efficiency of assorted existing drug moieties supported their previous history to treat viral infections.[39] During this sequence, Wang and the team in February 2020, estimated the antiviral efficacy of 5 different approved drugs, including chloroquine, ribavirin, nitazoxanide, penciclovir, nafamostat together with two commonly used wide spectrum antiviral agents favipiravir and remdesivir against COVID-19 infection. The drugs were trial in vitro on the clinically isolated sample of COVID-19 strain. They need to perform cytotoxicity assessment and evaluated the drug effect on yield of virus and rate of infection on the in vitro culture of COVID-19. The study divulges that chloroquine and remdesivir effectively controlled the COVID-19 infection in vitro cell culture. Supported their safety profile and efficacy in other viral infections, the author suggested the drug should be tried in human patients littered with COVID-19 infection. Currently, there are not any effective vaccines for the prevention of COVID-19. But few candidates moved into the run. CanSino Biologicals started Phase 2 trial in China (NCT04341389) for Ad5- nCoV which showed safe, tolerable, and immunogenic in phase 1 trial. Moderna Announces Positive Interim Phase 1 Data for the mRNA-1273 vaccine. The vaccine elicited virus-neutralizing antibodies at the amount displayed in convalescent sera and showed full protection against viral replication within the lungs during a mouse model. The vaccine candidate mRNA-1273 also showed safe and well-tolerated. Inovio Pharmaceutical developed INO-4800 which is in phase 1 trials showed safe and protective immunity. LV- SMENP- DC from Shenzhen Geno-Immune Medical Institute (phase1) may offer

promising vaccines against COVID-19. The University of Oxford developed a vaccine supported Chimpanzee Adenovirus Vector (ChAdOx1) which is immunogenic in mice. The vaccine candidate entered phase I/II (NCT04324606) trial in April 2020 to check its safety, tolerability, and immunogenicity in 510 volunteers. [40-42]

7. CONCLUSION

Over the past twenty years, there has been a major number of coronavirus breakouts, each sort of virus has certain unique features however there are a variety of similarities likewise. Generally, 19-nCoV is a member of the coronaviruses family that usually attacks the respiratory system. As of Pan American Day, 2020, COVID-19 has affected over 1,948,617 patients in 210 countries and territories around the world and two international conveyances and left around 121,846 deaths worldwide. Currently, supportive care measures such as ventilation oxygenation and fluid management remain the standard of care. Several clinical trials are currently trying to identify the most potent drug or combination against the disease, and it is strongly recommended to enroll patients into ongoing trials. Antivirals can be proven as safe and effective only in the context of randomized clinical trials.

8. ACKNOWLEDGMENTS

Authors are thankful to Shri. Yogendraji Gode (President) and Dr. Yogeshji Gode (Secretary), IBSS's Dr. Rajendra Gode College of Pharmacy, Amravati and Dr. Rajendra Gode Institute of Pharmacy, Amravati, Maharashtra (India) for providing necessary facility to undertake this work.

9. DISCLOSURE OF CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

1. Abd El-Aziz TM, Stockand JD. Recent progress and challenges in drug development against COVID-19 coronavirus (SARS-CoV-2)-an update on the status. *Infection, Genetics and Evolution*. 2020 Sep 1;83:104327.
2. Rello J, Belliato M, Dimopoulos MA, et al. Update in COVID-19 in the intensive care unit from the 2020 HELLENIC Athens International symposium. *Anaesth Crit Care Pain Med*. 2020;39(6):723-730. doi:10.1016/j.accpm.2020.10.008
3. Ahn JY, Sohn Y, Lee SH, et al. Use of Convalescent Plasma Therapy in Two COVID-19 Patients with Acute Respiratory Distress Syndrome in Korea. *J Korean Med Sci*. 2020;35(14):e149.
4. Brian D.A., Baric R.S. Coronavirus Genome Structure and Replication. In: Enjuanes L. (eds) *Coronavirus Replication and Reverse Genetics*. Current Topics in Microbiology and Immunology.2007; vol 287: 1-30 Springer, Berlin, Heidelberg.
5. Mian A, Khan S. Coronavirus: the spread of misinformation. *BMC medicine*. 2020 Dec;18(1):1-2.
6. Mallapaty S. Why does the coronavirus spread so easily between people?. *Nature*. 2020 Mar 1;579(7798):183-4.

7. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. *Methods Mol Biol.* 2015;1282:1-23.
8. 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. Published 2020 Mar 16. doi:10.1016/j.jare.2020.03.005
9. Anand K, Ziebuhr J, Wadhwani P, Mesters JR, Hilgenfeld R. Coronavirus main proteinase (3CLpro) structure: basis for design of anti-SARS drugs. *Science.* 2003;300(5626):1763-1767. doi:10.1126/science.1085658.
10. Baranov PV, Henderson CM, Anderson CB, Gesteland RF, Atkins JF, Howard MT. Programmed ribosomal frameshifting in decoding the SARS-CoV genome. *Virology.* 2005;332(2):498-510. doi:10.1016/j.virol.2004.11.038
11. Cyranoski D. Mystery deepens over animal source of coronavirus. *Nature.* 2020;579(7797):18-19. doi:10.1038/d41586-020-00548-w.
12. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China [published correction appears in *JAMA.* 2021 Mar 16;325(11):1113]. *JAMA.* 2020;323(11):1061-1069. doi:10.1001/jama.2020.1585.
13. Huang B, Ling R, Cheng Y, et al. Characteristics of the Coronavirus Disease 2019 and related Therapeutic Options. *Mol Ther Methods Clin Dev.* 2020;18:367-375. Published 2020 Jun 24. doi:10.1016/j.omtm.2020.06.013
14. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020;382(18):1708-1720. doi:10.1056/NEJMoa2002032
15. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020;395(10223):514-523. doi:10.1016/S0140-6736(20)30154-9
16. Alharbi NK, Padron-Regalado E, Thompson CP, et al. ChAdOx1 and MVA based vaccine candidates against MERS-CoV elicit neutralising antibodies and cellular immune responses in mice. *Vaccine.* 2017;35(30):3780-3788. doi:10.1016/j.vaccine.2017.05.032
17. Assiri A, Abedi GR, Al Masri M, Bin Saeed A, Gerber SI, Watson JT. Middle East Respiratory Syndrome Coronavirus Infection During Pregnancy: A Report of 5 Cases From Saudi Arabia. *Clin Infect Dis.* 2016;63(7):951-953. doi:10.1093/cid/ciw412
18. Bulut C, Kato Y. Epidemiology of COVID-19. *Turk J Med Sci.* 2020;50(SI-1):563-570. Published 2020 Apr 21. doi:10.3906/sag-2004-172
19. Baric RS, Yount B, Hensley L, Peel SA, Chen W. Episodic evolution mediates interspecies transfer of a murine coronavirus. *J Virol.* 1997;71(3):1946-1955. doi:10.1128/JVI.71.3.1946-1955.1997
20. Chen L, Xiong J, Bao L, Shi Y. Convalescent plasma as a potential therapy for COVID-19. *Lancet Infect Dis.* 2020;20(4):398-400. doi:10.1016/S1473-3099(20)30141-9

21. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507-513. doi:10.1016/S0140-6736(20)30211-7.
22. Barretto N, Jukneliene D, Ratia K, Chen Z, Mesecar AD, Baker SC. The papain-like protease of severe acute respiratory syndrome coronavirus has deubiquitinating activity. *J Virol*. 2005;79(24):15189-15198. doi:10.1128/JVI.79.24.15189-15198.2005
23. Bhardwaj K, Guarino L, Kao CC. The severe acute respiratory syndrome coronavirus Nsp15 protein is an endoribonuclease that prefers manganese as a cofactor. *J Virol*. 2004;78(22):12218-12224. doi:10.1128/JVI.78.22.12218-12224.2004.
24. Bhardwaj K, Sun J, Holzenburg A, Guarino LA, Kao CC. RNA recognition and cleavage by the SARS coronavirus endoribonuclease. *J Mol Biol*. 2006;361(2):243-256. doi:10.1016/j.jmb.2006.06.021
25. Graham RL, Sparks JS, Eckerle LD, Sims AC, Denison MR. SARS coronavirus replicase proteins in pathogenesis. *Virus Res*. 2008;133(1):88-100. doi:10.1016/j.virusres.2007.02.017
26. Bonilla PJ, Hughes SA, Piñón JD, Weiss SR. Characterization of the leader papain-like proteinase of MHV-A59: identification of a new in vitro cleavage site. *Virology*. 1995;209(2):489-497. doi:10.1006/viro.1995.1281.
27. Bonilla PJ, Hughes SA, Weiss SR. Characterization of a second cleavage site and demonstration of activity in trans by the papain-like proteinase of the murine coronavirus mouse hepatitis virus strain A59. *J Virol*. 1997;71(2):900-909. doi:10.1128/JVI.71.2.900-909.1997
28. Bost AG, Carnahan RH, Lu XT, Denison MR. Four proteins processed from the replicase gene polyprotein of mouse hepatitis virus colocalize in the cell periphery and adjacent to sites of virion assembly. *J Virol*. 2000;74(7):3379-3387. doi:10.1128/jvi.74.7.3379-3387.2000
29. Bost AG, Prentice E, Denison MR. Mouse hepatitis virus replicase protein complexes are translocated to sites of M protein accumulation in the ERGIC at late times of infection. *Virology*. 2001;285(1):21-29. doi:10.1006/viro.2001.0932.
30. Brockway SM, Denison MR. Mutagenesis of the murine hepatitis virus nsp1-coding region identifies residues important for protein processing, viral RNA synthesis, and viral replication. *Virology*. 2005;340(2):209-223. doi:10.1016/j.virol.2005.06.035.
31. Brockway SM, Lu XT, Peters TR, Dermody TS, Denison MR. Intracellular localization and protein interactions of the gene 1 protein p28 during mouse hepatitis virus replication. *J Virol*. 2004;78(21):11551-11562. doi:10.1128/JVI.78.21.11551-11562.2004.
32. V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. *Nat Rev Microbiol*. 2021;19(3):155-170. doi:10.1038/s41579-020-00468-6.
33. Xie M, Chen Q. Insight into 2019 novel coronavirus - An updated interim review and lessons from SARS-CoV and MERS-CoV. *Int J Infect Dis*. 2020;94:119-124. doi:10.1016/j.ijid.2020.03.071
34. Chinese SARS Molecular Epidemiology Consortium. Molecular evolution of the SARS coronavirus during the course of the SARS epidemic in China. *Science*. 2004;303(5664):1666-1669. doi:10.1126/science.1092002.

35. Chou CY, Chang HC, Hsu WC, Lin TZ, Lin CH, Chang GG. Quaternary structure of the severe acute respiratory syndrome (SARS) coronavirus main protease. *Biochemistry*. 2004;43(47):14958-14970. doi:10.1021/bi0490237.
36. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. *Nat Rev Microbiol*. 2021;19(3):141-154. doi:10.1038/s41579-020-00459-7
37. Nitsche A, Schweiger B, Ellerbrok H, Niedrig M, Pauli G. SARS coronavirus detection. *Emerg Infect Dis*. 2004;10(7):1300-1303. doi:10.3201/eid1007.030678
38. Jeddy N, Lakshmi SLJ. Coronavirus disease 2019 and its vaccines: An update. *J Oral Maxillofac Pathol*. 2021;25(1):5-11. doi:10.4103/jomfp.jomfp_90_21.
39. Chen W, Yan M, Yang L, et al. SARS-associated coronavirus transmitted from human to pig. *Emerg Infect Dis*. 2005;11(3):446-448. doi:10.3201/eid1103.040824.
40. Cheng Y, Wong R, Soo YO, et al. Use of convalescent plasma therapy in SARS patients in Hong Kong. *Eur J Clin Microbiol Infect Dis*. 2005;24(1):44-46. doi:10.1007/s10096-004-1271-9.
41. Stasi C, Fallani S, Voller F, Silvestri C. Treatment for COVID-19: An overview. *Eur J Pharmacol*. 2020;889:173644. doi:10.1016/j.ejphar.2020.173644.
42. Samudrala PK, Kumar P, Choudhary K, et al. Virology, pathogenesis, diagnosis and in-line treatment of COVID-19. *Eur J Pharmacol*. 2020;883:173375. doi:10.1016/j.ejphar.2020.173375.