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**SR Zaheen**  
PMCoE, Govt. Jatashankar  
Trivedi College, Balaghat,  
Madhya Pradesh, India

**HR Silhare**  
PMCoE, Govt. Jatashankar  
Trivedi College, Balaghat,  
Madhya Pradesh, India

**NB Dhurve**  
PMCoE, Govt. Jatashankar  
Trivedi College, Balaghat,  
Madhya Pradesh, India

**RM Faye**  
PMCoE, Govt. Jatashankar  
Trivedi College, Balaghat,  
Madhya Pradesh, India

**DM Agase**  
PMCoE, Govt. Jatashankar  
Trivedi College, Balaghat,  
Madhya Pradesh, India

## **COVID-19 pandemic: Origin, transmission, impact, and preventive approaches and future perspective**

**SR Zaheen, HR Silhare, NB Dhurve, RM Faye and DM Agase**

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### **Abstract**

In December 2019, Wuhan, China, was the emerging site of the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which subsequently spread globally during the COVID-19 pandemic. SARS-CoV-2 is a contagious virus belonging to the Betacoronavirus genus and possesses single-stranded RNA as its genetic material. Variants of SARS-CoV-2, such as P.1, contain mutations in the virus' spike protein, which may result in a decreased effectiveness of treatments that use vaccines or monoclonal antibodies.

The pandemic has negatively impacted not only the virology of SARS-CoV-2, but also the psychological health of individuals, with increased levels of anxiety, depression, and post-traumatic stress disorder in people with pre-existing conditions. The education system encountered many challenges as a result of the pandemic; therefore, there was an urgent need to transition from traditional methods of learning to having online learning platforms. New vaccine types that have been developed due to the COVID-19 pandemic have been classified into five categories: Whole Virus, Protein based (Subunit), Viral Vector, and Nucleic Acid (DNA/AIDS) vaccines. While all vaccines have an acceptable level of safety, the most commonly encountered adverse events associated with these vaccines are fatigue; muscle pain; headache; fever; and injection site reactions. Less frequently, potentially life threatening or serious adverse effects can occur such as anaphylactic reactions or thrombocytopenia.

This review lists recent advancements in the understanding of SARS-CoV-2 virology, how variants occur, how the pandemic has affected the mental and societal health of people worldwide, the impact on education, and the safety profile of the new COVID-19 vaccines. The importance of an integrated approach to the response to the COVID-19 pandemic is emphasized in this review. The new vaccine technology has allowed for an unprecedented amount of development in a very short period and should allow for a greater responsiveness to future outbreaks.

**Keywords:** Diagnosis, future perspective, impact, origin, preventions, symptoms, transmission, treatment, vaccination

### **Introduction**

In December 2019 in Wuhan, Hubei Province, China, a cluster of cases of pneumonia of an unknown origin was detected. As a result of epidemiological correlation with the Huanan Seafood Wholesale Market, respiratory samples grown in cultured human airway epithelial cells and Vero E6 and Huh7 cell lines were discovered to contain a new type of respiratory virus; genotyping led to identification of a novel coronavirus called "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2).

The virus is a  $\beta$ -coronavirus that has been positioned in the subgenus "Sarbecovirus." As with past pandemics, the exact pathway for penetration into humans remains unclear; however, as a result of much epidemiological, veterinary, virological and ecological information, the route of origin is assumed to be via a  $\beta$ -coronavirus in the sarbecovirus group, which infects pangolins and bats that are native to countries across Asia and South-Eastern Asia (Morens *et al.*, 2020)<sup>[1]</sup>.

Furthermore, the term "pandemic" refers to a situation in which a worldwide epidemic has extended beyond national borders and/or continental boundaries affecting a large segment of the population at a time. The COVID-19 pandemic is currently having a large impact on the countries that comprise Europe, as such efforts have proven very challenging due to the complete disregard for safety measures demonstrated by many of the members of society; many refuse vaccination and/or safety due to their complete lack of understanding of the seriousness of the problem (Suryasa *et al.*, 2021)<sup>[3]</sup>.

**Corresponding Author:**  
**SR Zaheen**  
PMCoE, Govt. Jatashankar  
Trivedi College, Balaghat,  
Madhya Pradesh, India

To elucidate the phylogeny of SARS-CoV-2, a comparative analysis of genomic sequences from different coronavirus strains was performed, and the resulting phylogenetic tree highlights their evolutionary relationships.

The analytical framework followed the approach previously described by Zaheen *et al.* (2025) [55] in their comparative phylogenetic study of COX1 and Cyt b markers in teleosts. In the present work, this methodology was adapted to viral genomes by retrieving representative SARS-CoV-2 and related coronavirus sequences, performing multiple sequence alignment, and constructing a phylogenetic tree using standard evolutionary models. This allowed clear visualization of the genetic proximity of SARS-CoV-2. The selected genomes include SARS-CoV-2 Wuhan-Hu-1, SARS-CoV Tor2, MERS-CoV HCoV-EMC/2012, HCoV-HKU1, HCoV-NL63, BCoV-ENT, Rousettus bat coronavirus HKU9, and HCoV-OC43 VR-759. These

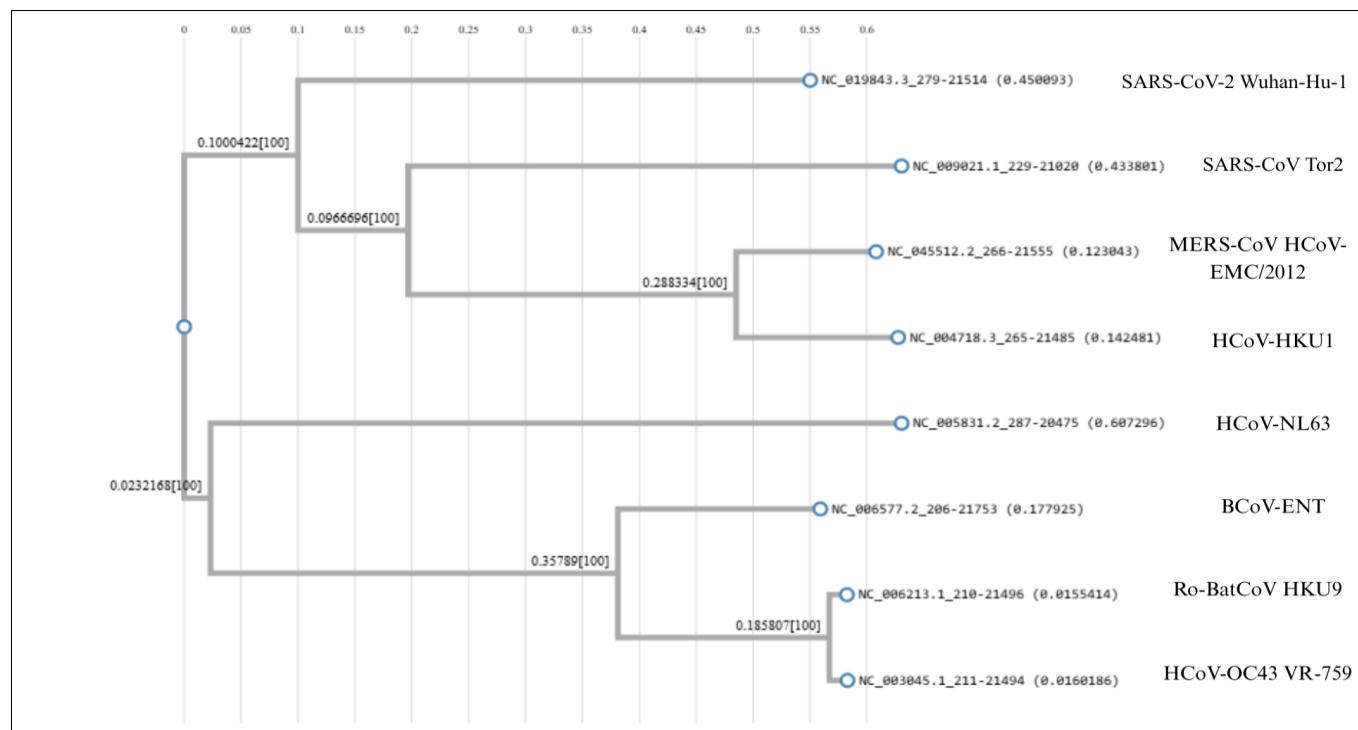
strains were chosen to reflect both human-infecting coronaviruses and their closely related zoonotic counterparts. The ORF1ab region, one of the most conserved and informative genetic markers among coronaviruses, was used to construct the phylogenetic tree, as it provides high-resolution insights into evolutionary divergence and ancestral relationships.

Most published phylogenetic studies use the ORF1ab gene for robust tree construction due to its size and evolutionary signal, but spike protein sequences are also frequently used for insights into host range and receptor interactions. Hence we did the same.

This phylogenetic illustration helps demonstrate the placement of SARS-CoV-2 within the broader coronavirus family, highlighting its genetic proximity to other betacoronaviruses and supporting current understanding of its zoonotic origin.

**Table 1:** Genomic Accession Numbers and Taxonomic Classification of Selected Coronaviruses.

S.No	Species Name	Family	Accession number
1.	SARS-CoV-2 Wuhan-Hu-1	Coronaviridae	NC_045512.2
2.	SARS-CoV Tor2	Coronaviridae	NC_004718.3
3.	MERS-CoV HCoV-EMC/2012	Coronaviridae	NC_019843.3
4.	HCoV-HKU1	Coronaviridae	NC_006577.2
5.	HCoV-NL63	Coronaviridae	NC_005831.2
6.	BCoV-ENT	Coronaviridae	NC_003045.1
7.	Ro-BatCoV HKU9	Coronaviridae	NC_009021.1
8.	HCoV-OC43 VR-759	Coronaviridae	NC_006213.1



**Fig 1:** Phylogenetic Relationships Among Selected Human and Animal Coronaviruses Based on ORF1ab Sequences.

## Transmission

As the COVID-19 pandemic marked a turning point at the start of 2020, the zoonotic illness followed suit. The way COVID-19 spreads and how sick it can make you are both unique features for COVID-19, however it also shares many similarities with previous zoonotic diseases such as SARS-CoV and MERS, including causing severe flu-like symptoms and acute respiratory symptoms. In addition, the molecular structure of SARS-CoV and COVID-19 are very

similar that COVID-19 was named SARS-CoV-2.

The similarities between SARS and COVID-19 allowed for the use of some of the same treatment regimens that worked for the SARS patients, treating the COVID-19 patients with the same medications used to treat SARS patients. Furthermore, by having the same pathways of entry to human hosts, replicating and progressing through their respective diseases, led to the opportunity to utilize some of the same medications developed to treat SARS-CoV to treat

individuals who have been infected with COVID-19. Kumar and Chaudhury, 2021 first compared the origins of COVID-19 with other zoonotic diseases, especially SARS and MERS. It then examined the properties of droplets and aerosols released by infected individuals and their role in spreading the virus. The molecular processes that allow SARS-CoV-2 to infect hosts and surpass other betacoronaviruses like SARS-CoV in transmissibility were also analyzed. Additionally, it reviewed current diagnostic and symptomatic treatment methods for COVID-19, explored vaccine development efforts, and summarized the use of drug repurposing and novel therapeutic approaches (Kumar & Choudhury, 2021)<sup>[4]</sup>.

### Symptoms

Most individual symptoms of COVID-19, are not very reliable for diagnosis. Simply having or not having symptoms is not enough to confirm or rule out the disease. However, loss of smell or taste (anosmia or ageusia) can serve as important warning signs, while the presence of cough may also justify further testing. At the same time, there is no current evidence to suggest that people showing only mild upper respiratory symptoms like sore throat, runny nose, or nasal congestion should automatically undergo PCR testing.

A more accurate approach may involve combining symptoms with other factors such as travel or contact history and local infection rates, which could be useful in primary care or hospital outpatient settings. Overall, the ability of symptoms alone to correctly identify COVID-19 cases is only moderate to low. Any testing system based only on symptoms will miss many cases while also requiring many people to be tested unnecessarily. The balance depends on the main aim of testing: if the goal is to control the spread, then even minimal symptoms should be used as criteria; but if the aim is to detect cases with more serious illness, then testing could be focused on specific symptoms such as fever and loss of smell (Struyf *et al.*, 2022)<sup>[5]</sup>.

### Diagnosis

Additionally, though the genetic and structural features of the SARS-CoV-2 virus were initially unknown, research laboratories and biomedical companies frequently studied the virus's important characteristics, which helped researchers worldwide develop a wide range of diagnostic solutions for a reliable diagnosis of COVID-19. Rapid antigen or antibody analysis, immunoenzymatic serological tests, and RT-PCR-based molecular tests are the most common and trustworthy approaches among these alternatives. These three categories of diagnostic tests can all be used at the exact time of infection. Furthermore, only diagnostic kits, reagents, and molecular probes that have been validated by the World Health Organisation (WHO) and the Centres for Disease Control and Prevention (CDC) and that have been approved by the FDA and the EMA in the United States and Europe are permitted for use. A proper diagnosis of the COVID-19 virus is possible only by taking careful consideration of the test to be used, the variety of sample to be examined, and the timing of the test itself, even with the availability of all these diagnostic techniques. As a result, a proper test must be run in the proper biological sample at the correct moment in time (Falzone *et al.*, 2021)<sup>[6]</sup>.

### 1. Nucleic acid amplification test

Infection with viruses is typically observed early in the course of an outbreak; nucleic acid amplification tests (NAAT) are the most sensitive assays and frequently the test of choice for detecting early viral infections. For the quick and precise diagnosis of COVID-19, several NAAT assay types have been developed, such as reverse transcriptase real-time PCR (RT-qPCR), loop-mediated isothermal amplification-based assay (RT-LAMP), microarray, and high-throughput sequencing. However, high-quality SARS-CoV-2 RNA is required by NAAT (Rai *et al.*, 2021)<sup>[7]</sup>.

#### Real-time reverse transcriptase-PCR

The "gold standard" to recognise some viruses is the polymerase chain reaction (PCR) technology, which has been defined by its quick detection, high sensitivity, and specificity. Because of its advantages as a fast and specific qualitative test, real-time reverse transcriptase PCR (RT-PCR) is presently of great interest for the identification of SARS-CoV-2. In addition, the sensitivity of real-time RT-PCR is good enough to provide significant help in the early diagnosis of infection. Thus, the "criterion-referenced" real-time The RT-PCR test can be seen as a primary technique to be used in order to identify the SARS-CoV-2 infectious agent of COVID-19 (Tahamtan & Ardebili, 2020)<sup>[8]</sup>. With great sensitivity and specificity, this analysis finds viral nucleic acids in nasopharyngeal swab samples. (Thompson & Lei, 2020)<sup>[9]</sup>.

This method amplified brief DNA segments in vitro using an enzyme-driven procedure. In order to generate oligonucleotide primers that selectively hybridise to the target sequences, this approach requires knowledge of at least partial sequences of the target DNA. Real-time RT-qPCR is a major development in clinical settings that allows for simultaneous amplification and analysis in a closed system, allowing for real-time gene(s) detection and expression analysis while the PCR reaction proceeds. Additionally, this closed system reduces false-positive results brought on by amplification product contamination (Dutta *et al.*, 2022)<sup>[10]</sup>.

#### RT-LAMP

Notomi T. discovered loop-mediated isothermal amplification (LAMP) in 2000. Since then, LAMP has been widely employed for recognizing a broad spectrum of diseases, including Zika, influenza, dengue, salmonella, malaria, and chikungunya viruses (Huang *et al.*, 2021)<sup>[12]</sup>.

With the exception that nucleic acid amplification takes place at the same temperature, the loop-mediated isothermal amplification (LAMP) technique is comparable to traditional PCR testing. As a result, some essential PCR equipment, like a thermal cycler, is no longer needed. In the case of diagnosis, the LAMP-enabled viral RNA/DNA assay is faster, simpler to use, and more cost-effective than the qRT-PCR assays due to the fact of its special nucleic acid amplification technique. Additional benefits of the LAMP approach include its broad range of acceptable pH and temperature, its capacity to handle fresh samples, and the adaptability of its readout techniques, all while maintaining sensitivity and specificity that are about in line with PCR assays. (Thompson & Lei, 2020)<sup>[9]</sup>.

In accordance with the manufacturer's instructions, assays were carried out using a Loopamp TM SARS-CoV-2 Detection Kit (Eiken Chemical, Tokyo, Japan), focused on

genes encoding the SARS-CoV-2 nucleocapsid (N) and RNA-dependent RNA polymerase (RdRp). The response RNA sample (10  $\mu$ L) and the given master mix, which included a set of primers (15  $\mu$ L), made up the mixture. A real-time Loopamp EXIA turbidity meter (Eiken Chemical) was used to monitor the mixture's turbidity every 6 seconds while it was incubated at 62.5°C for 35 minutes. When the differential value got close to 0.05, the assays were considered positive, and the threshold time (T<sub>t</sub>) was measured. We reconsidered RT-LAMP responses using this visual endpoint detection since LAMP positive reactions may also be visually identified by fluorescence using calcein staining (Kitajima *et al.*, 2021)<sup>[11]</sup>.

### Next-generating sequencing (NGS)

An interesting amplicon-based technique for amplifying highly conserved SARS-CoV-2 genome segments and employing NGS sequencing to uniquely identify them. Our NGS technique was tested using the following RNA extraction methods: (1) a traditional kit extraction using the MagMAX Viral/Pathogen II Nucleic Acid Isolation Kit (MVP II; Thermo Fisher) and (2) an easily performed one-step RNA extraction using QuickExtract (Lucigen, WI, USA) (de Mello Malta *et al.*, 2021)<sup>[13]</sup>.

Although some individuals think that SARS-CoV-2 might be man-made, there is most likely no reason to believe that SARS-CoV-2 is manufactured. SARS-CoV-2 is not a lab-created virus or one that has been purposefully altered, as demonstrated by Kristian G. Andersen *et al.* Additionally, NGS revealed two noteworthy genetic characteristics of SARS-CoV-2. The two subunits of the spike protein, S1 and S2, are located at amino acid sequences 685 and 686. The receptor binding domain (RBD), which is mostly found in S1, is in charge of cell receptor recognition. The fundamental components needed for membrane fusion are present in S2. The most changeable component of the coronavirus genome is the RBD in the spike protein.

Additionally, the spike protein of SARS-CoV-2 inserts 12 nucleotides with a functional multibase (furin) cleavage site (RRAR) at the S1-S2 boundary, which also results in the expected three O-linked glycans surrounding the site. It has been demonstrated that six RBD amino acids are essential for binding to ACE2 receptors and for defining the host range of SARS-CoV-like viruses. (Chen *et al.*, 2021)<sup>[14]</sup>.

### CRISPR

Combining its easy and productive approach of accurately modifying the genome of practically any growing creature, the CRISPR (clustered regularly interspaced short palindromic repeat) Cas9 (CRISPR-associated nuclease 9) technique has the potential to revolutionize developmental biology. This method, which is based on RNA-guided nuclease (RGN), has already shown success in producing endogenously tagged proteins, conditional alleles, and targeted mutations in many genes at once. The effective modification of the genomes of over 20 distinct plant and animal species, as well as several cell lines and primary cells, demonstrates the versatility of RGNs (Harrison *et al.*, 2014)<sup>[15]</sup>.

For a fast detection of recently discovered COVID-19, the SHERLOCK DETECTOR protocols based on CRISPR/type II (Cas9), V (Cas12), and VI (Cas13) are compared (Hillary *et al.*, 2021)<sup>[16]</sup>.

Recently developed CRISPR-based diagnostics have taken

advantage of the concept of "collateral cleavage activity." To create a novel nucleic acid-based diagnostic tool, the developers created fluorescently labeled ssDNA/RNA reporter probes to detect the visible bands through the lateral flow assay in a paper strip. The most widely used Cas effectors are those with collateral action, such as Cas12a or Cas13 nuclease (explained in more detail in the following section on therapies). Of them, Cas12 effectors are more successful at detecting tumor-associated viral markers like HPV, while Cas13 effectors are more adept at detecting RNA from viruses like dengue and Zika. Utilizing this technology, various Cas proteins are utilized to create very effective COVID-19 diagnostic procedures (Deol *et al.*, 2022)<sup>[17]</sup>.

### ddPCR

Based on traditional digital PCR, Hindson developed the droplet digital PCR (ddPCR) technology in 2011. Compared to RT-PCR, ddPCR has a substantially lower limit of detection. With absolute quantification at its core, digital PCR is founded on the ideas of restricted dilution, end-point PCR, and Poisson statistics. The sample is divided into distinct partitions (thousands of droplets) at random; some of these partitions have no template, while others have one or more templates.

The concentration is estimated by modelling as a Poisson distribution after the partitions are amplified to the endpoint and the number of positive partitions is tallied by a droplet reader. Consequently, low amplification efficiency and amplification inhibitors that might be present in samples have less of an impact on quantification. By decreasing competition between various targets for amplification reagents in the reaction mixture, sample partitioning also efficiently concentrates template molecules within the micro-reactions, increasing analytical sensitivity for uncommon species (Suo *et al.*, 2020)<sup>[18]</sup>.

### 2. Antigen/Antibody detection assays

Immunological tests might be a useful addition in this context. But when it comes to diagnosis, immunoassays differ from molecular assays because they require some understanding of the protein and the antibody response produced against it. Immunoassays can therefore be used to identify certain viral proteins, or antigens, or the antibodies that the host B cells produce in reaction to those antigens (Ejazi *et al.*, 2020)<sup>[19]</sup>.

### ELISA (enzyme-linked immunosorbent assay)

The Euroimmun IgA and IgG ELISA, the first ELISA, received approval from CE at the end of March 2020. While being a well-established technique for antibody detection, ELISA has limitations such as a longer turnaround time, the requirement for a laboratory setting, and higher manpower expenses to generate a result (Van Elslande *et al.*, 2020)<sup>[20]</sup>. In general, proteins, glycoproteins, hormones, antibodies, and antigens can all be detected and quantified using ELISA, the gold standard of immunoassay. A known capture antigen is immobile on a plate, and the patient's antibodies in a sample bind to the immobilised capture antigen to identify patient antibodies. The captured patient antibodies then combine with an enzyme-labelled detection antibody that is specific to any antibody isotype (i.e., IgG, IgM, etc.) to form a complex. Next, an enzyme (often horseradish peroxidase, or HRP) and its substrate interact to

produce a colorimetric change that can be measured and linked to the antibody's presence and/or concentration. In order to get the best sensitivity and specificity, the majority of ELISA validation studies compared many antigens and antibody isotypes. This method is laborious and susceptible to contamination. Infrastructure and skilled workers are also required (Mohit *et al.*, 2021)<sup>[21]</sup>.

### Lateral flow immunoassay

Self-testing and decentralised diagnosis are made possible by LFTs' ability to quickly read out analytes from a wide range of samples. The COVID-19 epidemic has demonstrated the capacity and appropriateness of large-scale testing using lateral flow tests (LFT) for use in clinical and public health settings. LFTs can detect different types of analytes, such as SARS-CoV-2 nucleoproteins or antibodies (IgG and IgM), and, in certain instances, can also detect nucleic acid. Currently, LFTs for the purpose of detecting nucleic acids are available through only one US company and in China. There are differences in sample collection protocols (buffer solution and incubation period) between the different conditions for which LFTs are used, namely, the disease and the type of sample matrix. Throughout the course of testing, samples containing analytes detected by LFTs may include blood, urine, saliva, or vaginal swabs (Budd *et al.*, 2023)<sup>[22]</sup>.

### Chemiluminescent immunoassay

The Chemiluminescence Assay (CLIA) is a fast, accurate, and reproducible method of measuring the amounts of IgG and IgM antibodies by combining the chemiluminescence technique with immunochemical reactions (Yin *et al.*, 2021)<sup>[23]</sup>.

### 3. Chest CT

According to some specialists, a chest CT scan might be considered a standard for diagnosing COVID-19. Chest CT was suggested as an efficient way to screen worrisome patients in the China government's Diagnosis and Treatment of Pneumonitis Caused by 2019-nCoV (trial sixth version) guidelines. Tens of thousands of COVID-19 cases were clinically diagnosed in China as a result of the addition of chest CT for diagnosis, which significantly helped to contain the country's epidemic. As a result, a thorough and prompt assessment of chest CT's efficacy in diagnosing COVID-19 is still vital and required. In the current study, they used a thorough meta-analysis to validate the efficacy of chest CT for COVID-19 diagnosis (Xu *et al.*, 2020)<sup>[24]</sup>.

### Complications

SARS-CoV-2 has infected hundreds of millions of people worldwide and spread quickly throughout the world. Our knowledge of the immediate and long-term consequences of contracting SARS-CoV-2 is expanding along with our experience with this virus. (Desai *et al.*, 2021)<sup>[25]</sup>.

### Neurologic complications

Cases of neurological problems in people infected with COVID-19 are scarce. Individuals with COVID-19 infections may also exhibit acute encephalopathy and altered consciousness because older individuals with chronic illnesses are more likely to experience altered mental status in the context of acute infections (Filatov *et al.*, 2020)<sup>[26]</sup>.

### Acute cerebrovascular

One of the more common serious neurologic side effects observed in COVID-19 patients is acute cerebrovascular condition. This last common indication, however, has a complex aetiology. Increased D-dimers, a prolonged prothrombin time, and disseminated intravascular coagulation are signs of a hypercoagulable state brought on by SARS-CoV-2, which also produces a worldwide inflammatory response (Bridwell *et al.*, 2020)<sup>[27]</sup>.

### Encephalitis and encephalopathy

Another serious neurological side effect of COVID-19 has been identified as encephalitis, an inflammatory disease of the brain. Encephalitis associated with COVID-19 infection has not been clearly identified, despite a growing percentage of cases being recorded (Siow *et al.*, 2021)<sup>[28]</sup>.

Acute or subacute impairment of consciousness is a symptom of encephalopathy, a temporary brain malfunctioning condition. People who are older, have previous signs of cognitive memory loss, have vascular risk factors (hypertension), or have a history of comorbidities are more likely to experience an altered mental state linked to COVID-19. Individuals who have experienced acute respiratory symptoms and neurological impairment in the past are more likely to get encephalopathy as a first symptom of COVID-19. It has been noticed that a patient with COVID-19 developed an encephalopathic condition and was unable to respond to verbal instructions (Carod-Artal, 2020)<sup>[29]</sup>.

### Guillain-Barré syndrome (GBS)

Guillain-Barré syndrome (GBS), an immune-mediated inflammatory polyradiculoneuropathy, can result in significant neurological impairment. The association of GBS with SARS-CoV-2 infection and COVID-19 vaccines has raised many concerns, especially following the worldwide outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The purpose of the review is to investigate the characteristics of GBS associated with COVID-19. It was found that patients with GBS associated with COVID-19 had electrophysiological evidence of acute inflammatory demyelinating polyneuropathy (AIDP) (Zheng *et al.*, 2023)<sup>[30]</sup>.

### Haemophagocytic lymphohistiocytosis (HLH)

Common clinical findings associated with Hemophagocytic Syndrome (HPS), or Hemophagocytic Lymphohistiocytosis (HLH), include: Acute Unremitting Fever; Lymphadenopathy; Hepatosplenomegaly; and Multiorgan Failure. HPS is a rapidly progressive systemic inflammatory disorder characterized by Cytopenia, Excessive Cytokines, and Hyperferritinemia. The excess production of Cytokines has earned HLH the designation "Cytokine Storm Syndrome". HLH can be challenging to diagnose because there are two types of HLH. The first is Secondary HLH (triggered by infections, autoimmune/autoinflammatory diseases, and exposure to toxins) and the second is Primary HLH (caused by Genetic Abnormalities) (Soy *et al.*, 2021)<sup>[31]</sup>.

### Cardiovascular complication

An individual's quality of life and health outcomes are impacted by the frequent cardiovascular problems linked to SARS-CoV-2 infection, which cause high acute mortality and high chronic morbidity. A higher risk of myocarditis,

dysrhythmia, pericarditis, ischaemic heart disease, heart failure, and thromboembolism is seen in patients with COVID-19 infection. (Terzic & Medina-Inojosa, 2023)<sup>[32]</sup>.

### Myocardial injury and myocarditis

Myocardial injury and myocarditis with troponin elevation have been linked to previous viral diseases, such as Middle East respiratory syndrome coronavirus (MERS-CoV). These conditions are believed to be caused by direct myocardial injury, hypoxia, or increased cardiac physiologic stress.

In the COVID-19 era, acute myocarditis is a major diagnostic problem that manifests in a wide spectrum of clinical severity. Acute left ventricular failure, dyspnoea, dysrhythmia, and chest discomfort are all possible symptoms in COVID-19 patients (Long *et al.*, 2020)<sup>[33]</sup>.

### Venous thromboembolic events

Hypercoagulability has been linked to an elevated risk of blood clot formation in SARS and MERS cases. In a similar vein, COVID-19 has been linked to hypercoagulability. Excess thrombin production and fibrinolysis shutdown are the outcomes of endothelial cell dysfunction brought on by infection. Because severe COVID-19 causes hypoxia, this can also increase blood viscosity, which can promote thrombosis. A transcription is necessary for a signalling pathway. When treating thromboembolism in COVID-19 infections, direct-acting oral anticoagulants (DOACs) may potentially be an option. However, before prescribing these medications, it is necessary to take into account drug interactions between DOAC and antiviral therapies as well as dosage issues in the context of altering renal function. One factor and is induced by hypoxia also contributes to the blood's increased coagulability (Bandyopadhyay *et al.*, 2020)<sup>[24]</sup>.

### Heart failure

Myocardial damage may result in pump failure, and COVID-19 infection may exacerbate chronic stable heart failure. Mild heart failure with intact ejection fraction in the early stages of the illness to severe end-stage heart failure and cardiogenic shock with significant death rates are all possible outcomes for people with COVID-19. Patients with underlying heart failure also have a higher risk of death and morbidity (Talasaz *et al.*, 2021)<sup>[35]</sup>.

### Cardiac arrest

Carers face complications when malignant tachyarrhythmias cause cardiac arrest. During the initial weeks of the COVID-19 pandemic in the United States, both regions with high and low case-fatality rates showed worse outcomes for out-of-hospital cardiac arrest incidents (Lo *et al.*, 2022)<sup>[36]</sup>.

### Dysrhythmias

According to meta-analyses, the incidence of cardiac dysrhythmias, which range from 10.11% to 15.3%, and atrial arrhythmias, which have been reported to be 9.2% (95% CI: 6.5-12.7%), may be the first clinical indication of cardiovascular manifestation of COVID-19 after acute SARS-CoV-2 infection. Furthermore, patients who experienced arrhythmias for the first time were more likely to require ICU admission or develop severe illness (RR = 13.09, 95% CI: 7.00-24.47,  $P<0.001$ ). In patients with COVID-19, atrioventricular (AV) block may be the cause of up to 12% of arrhythmias. Additionally, 44.4% of patients

brought to the intensive care unit had cardiac arrhythmias. Atrial fibrillation, significant bradycardias, non-sustained ventricular tachycardia (NSVT), and cardiac arrest were common findings in both hospitalised and intensive care unit (ICU) patients. Atrial arrhythmia was more common in patients with poor outcomes. Additionally, ventricular tachycardia, fibrillation, and malignant arrhythmias were linked to patients with high troponin T (TnT) levels (Kole *et al.*, 2024)<sup>[37]</sup>.

### Pulmonary complications

Systemic inflammatory response syndrome, which is characterised by increased levels of pro-inflammatory cytokines, develops excessively during COVID-19. The body reacts by creating compensatory anti-inflammatory response syndrome in order to restore equilibrium. Prolonged immunosuppression, also known as prolonged inflammation, immunosuppression, and catabolism syndrome, occurs if the reaction is insufficiently robust. In addition to being more susceptible to bacterial and fungal infections, these patients are also more likely to develop chronic pulmonary fibrosis (Jakubec *et al.*, 2022).

Acute respiratory distress syndrome (ARDS) and associated consequences might occur in some patients, particularly in the elderly and in those with comorbidities. According to a number of studies, COVID-19 may make people more susceptible to thrombotic conditions such as pulmonary embolism (PE) and deep vein thrombosis (DVT). Because of severe inflammation, platelet activation, endothelial dysfunction, and stasis, infection and sepsis result in a hypercoagulable state. In addition, other factors, such as changes in coagulation parameters among those diagnosed with COVID-19 pneumonia, are highly predictive of increased mortality in these patients. Early diagnosis is important for improving the overall prognosis for patients diagnosed with COVID-19 pneumonia, which is made by obtaining CTPA when there is clinical suspicion of PE or worsening clinical status with the development of hypo- or a-coma and/or hemodynamic instability.

### Endocrine complications

Once SARS-CoV-2 passes through the Lung it then infects the lung and infects the host cell. This happens because the virus attaches or "binds" to the host cell via receptors called angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2). SARS-CoV-2 has been detected in the blood, stool, and urine of COVID-19 positive individuals. The presence of the virus in these specimens suggests that SARS-CoV-2 may also target other tissues besides the lung. As well, these specimens suggest that the virus uses ACE2 and TMPRSS2 for infection in other parts of the body. ACE2 and TMPRSS2 have been identified to be expressed by endocrine glands, including the pituitary, thyroid, adrenal glands, testes, ovaries, and the pancreas. The concentration of these glands is highest in the testes, followed by the thyroid, and lowest in the hypothalamus. Since the pandemic, research has focused on whether COVID-19 exacerbates pre-existing endocrine disorders or whether patients with endocrine histories, such as those with obesity and diabetes mellitus (DM), have a worse prognosis (Kazakou *et al.*, 2021)<sup>[10]</sup>.

### Preventions, Treatment and vaccination

According to the World Health Organization (WHO),

effectively managing the spread of contagious diseases like COVID-19 requires a multifaceted approach that includes public education, patient isolation, infection prevention, controlling transmission, and appropriate treatment of infected individuals. Reducing transmission can be achieved by implementing several key recommendations.

People who are at a low risk of getting COVID-19 can help to reduce the chances of transmitting the virus by following a number of recommended practices.

If possible, remaining at home, particularly if one has been in close contact with someone who has tested positive for COVID-19, and not to have physical contact with either symptomatic or asymptomatic individuals (this is sometimes referred to as shielding).

Limit non-essential travel, adhere to social distancing (maintain a distance of at least two metres from individuals), refrain from any physical greetings (e.g. handshake) and avoid congregating in large groups.

Maintain good hand hygiene, wash your hands regularly using soap and warm water for a minimum of 20 seconds (or hand sanitiser containing at least 60% alcohol) after touching areas where others have been, using the washroom and making physical contact with another person.

Do not touch your face, particularly the area surrounding your eyes, your nose, and mouth, with unwashed hands, and disinfect any frequently touched surfaces using household cleaning products (Lotfi *et al.*, 2020)<sup>[41]</sup>.

It is advised that healthcare professionals wear medical masks when providing care to suspected or confirmed cases and utilise particulate respirators, such as those certified N95 or FFP2, when undertaking aerosol-generating procedures. This recommendation states that people with respiratory symptoms should adhere to infection prevention recommendations when using medical masks in both healthcare and home care settings. Masks must be used and disposed of properly to prevent any rise in the risk of transmission. A guideline was released by the China CDC to increase public knowledge of COVID-19 prevention and control, in addition to scientific journal articles. Causes, how to select and wear face masks, appropriate handwashing practices, preventive measures at various locations (e.g., at home, on public transit, and in public spaces), disinfection techniques, and medical surveillance at home are among the principal messages of the guideline. The recommendation offers strategies to end public fear in addition to scientific understanding of how to manage the COVID-19 pandemic (Adhikari *et al.*, 2020)<sup>[42]</sup>.

The development of new drugs and vaccines, along with advances in drug repurposing, in vitro and in silico screening platforms, novel technologies, and innovative diagnostic tools, has opened fresh directions for scientific

research. Among these, artificial intelligence (AI) stands out as one of the most promising areas, offering new opportunities for drug discovery and development. AI supports early detection and diagnosis of infections through methods such as CT scans, X-rays, laboratory testing, and genome sequencing. It shows strong potential in both discovering new therapeutic options and repurposing existing drugs for the treatment of COVID-19.

During the COVID-19 pandemic, clinicians, scientists, and pharmacists faced urgent challenges in selecting effective treatment options. Since the development of new vaccines and drugs is expensive, time-intensive, and historically has a very low success rate of just 2.01%, drug repurposing quickly became a practical and necessary alternative. Approaches to repurposing are generally divided into computational and experimental methods. Drugs investigated for different stages of COVID-19 treatment include lopinavir, hydroxychloroquine, atazanavir, nintedanib, tocilizumab, and remdesivir.

Remdesivir was the first drug to receive approval for COVID-19 treatment. Acting as a nucleoside analog of ATP, it inhibits RNA polymerase and prevents viral replication. It also demonstrates a broad antiviral spectrum, with activity against RNA viruses such as Ebola, MERS-CoV, and SARS-CoV-2. Most evidence of its effectiveness comes from in vitro and in vivo studies, but promising results against coronaviruses supported its emergency use during the pandemic (Chavda *et al.*, 2022)<sup>[43]</sup>.

Immunization is crucial for preventing and controlling the spread of diseases, and to overcome the pandemic, a significant portion of the global population must be vaccinated. Current data indicates that 66.8% of people worldwide have received at least one dose of a COVID-19 vaccine, with a total of 12.15 billion doses administered globally. Several types of vaccines have been developed, including mRNA vaccines that deliver genetic instructions for producing disease-specific antigens. In addition, DNA-based, attenuated, and vector-based vaccines are being used, as they represent faster, more cost-effective, and promising alternatives to traditional vaccine methods. Attenuated vaccines consist of live pathogens that have been weakened or altered through attenuation, allowing them to replicate in the body and trigger a prolonged immune response. Subunit vaccines, on the other hand, use only specific components of an antigen to stimulate immunity. Additional categories of vaccines include toxoid vaccines, conjugate vaccines, and nucleic acid-based vaccines such as RNA and DNA vaccines, which introduce genetic material to produce antigenic proteins similar to those generated by disease-causing organisms (Chavda *et al.*, 2022)<sup>[43]</sup>.

**Table 2:** Types of Vaccines according to its Variants.

Variants	Discovered in	Types of vaccine
1. Alpha (B.1.1.7)	UK in late 2020	Human Cov-229E(human) Human Cov-NL63(human) PRCV/ISU-1(pig) TGEV/PUR46-MAD(pig) PEDV/ZJU-G1-2013(pig) SeACo-CH/GD-01(pig) Canine CoV/TU336/F/20089(dog) Camel alphacoronavirus isolate camel/Riyadh(camel) Feline infectious peritonitis virus(cat)
2. Beta (B.1.351)	South Africa in May 2020	Human CoV-HKU1(human) Human CoV-OC43(human)

		SARS-CoV(human) MERS-CoV(human) Covid 19(human) Bovine CoV/ENT(cow) Equine CoV/Obihiro12-1(horse) MHV-A59(mouse)
3. Delta (B.1.617.2)	India in 2021	Bulbul coronavirus HKU11(bulbul) Sparrow coronavirus HKU17(sparrow)
4. Gamma (P.1)	Brazil in January 2021	Beluga Whale Cov/SW1(whale) IBV(hen)

(Pourhatami *et al.*, 2021)<sup>[44]</sup>.

### Social and Economic Impacts

This study explores the socio-economic effects of the COVID-19 pandemic across global industries. Beyond its impact on healthcare, the crisis disrupted markets such as IoT, where devices and sensors could instead play a role in tracking movement and supporting contact tracing through geomaps. These technologies may help curb virus spread and accelerate economic recovery. The article also outlines strategies, guidelines, and sector-specific insights to support policy and decision-making in both government and private sectors. A comprehensive socio-economic development framework, encompassing sector-specific initiatives and robust infrastructure, is vital for supporting businesses with sustainable and reliable models. Insights from existing literature and practical observations indicate that IoT, sensors, wearable technologies, and computational systems play a critical role in maintaining economic stability by mitigating the spread of COVID-19 (Kumar *et al.*, 2020).

COVID-19 has emerged as one of the largest global pandemics, infecting millions and causing widespread deaths. By November 2020, despite many recoveries, the virus continued to affect over 220 countries, with lockdowns and shutdowns serving as the main preventive measures. The pandemic has disrupted social, economic, educational, and religious spheres worldwide, with some religious events even accelerating its spread. In the absence of a specific cure or vaccine, these adverse effects were expected to continue (Das *et al.*, 2022)<sup>[46]</sup>.

By mid-July 2020, India had recorded over one million COVID-19 cases and more than 25,000 deaths, making it the third most affected country after the U.S. and Russia. Daily new cases averaged 28,000-30,000, though recovery rates were steadily improving. The government imposed a nationwide lockdown starting March 25, 2020 the largest of its kind worldwide, shutting down all non-essential activities, transport, schools, and businesses. Restrictions were gradually relaxed in June, but rising cases led to extensions, particularly in high-risk states like Delhi, Maharashtra, and Tamil Nadu.

The lockdown aimed to strengthen India's underfunded health system by expanding testing, quarantine centers, and temporary hospitals, though facilities still struggled under pressure. Economically, the shutdown caused widespread job losses, mass migration of workers, severe supply chain disruptions, and a collapse in consumer demand. These combined effects highlighted the difficult balance between controlling the pandemic and sustaining economic stability (Dev & Sengupta, 2020)<sup>[47]</sup>.

### Current Status / Ongoing Challenges

The global pandemic crisis caused by the recent emergence and rapid global spread of the SARS-CoV-2 virus as a causal agent of the disease COVID-19 is unprecedented. On

11 March 2020, the World Health Organization declared this outbreak as a global pandemic. The first identification of the SARS-CoV-2 virus occurred in Wuhan, Hubei province, China. An outbreak of viral pneumonia cases occurred in Wuhan, which had been linked to the Huanan Seafood Wholesale Market. The Chinese authorities submitted notification of the outbreak to the WHO on 31 December 2019. After conducting laboratory studies of viral genetic material from patients in Wuhan, it became evident that SARS-CoV-2 belonged to a sub-family of coronaviruses that is genetically similar to coronaviruses isolated from bats and was entering human cells predominantly through interaction with the angiotensin converting enzyme 2 (ACE2) receptor (Lu *et al.*, 2020; Wan *et al.*, 2020)<sup>[48, 49]</sup>. Thus, it is believed that SARS-CoV-2 was a zoonotic virus that initially spread to humans but subsequently was confirmed to be transmitted from human-to-human through respiratory droplets and close contacts. Severity of disease from SARS-CoV-2 varied widely with some individuals being asymptomatic and others having mild clinical manifestations (fever, cough, shortness of breath) and in severe disease cases, developing heightened immune responses causing cytokine storm, respiratory failure, and death. The genetic similarities of SARS-CoV-2 with SARS-CoV-1 (causative agent of the SARS outbreak in 2003), and MERS-CoV (causative agent of the Middle East Respiratory Syndrome outbreak of 2012) have been described (De Wit *et al.* 2016)<sup>[50]</sup>. SARS-CoV-2 causes significantly fewer deaths than its predecessors SARS-CoV-1 and MERS-CoV (Fauci *et al.* 2020)<sup>[51]</sup>, but the rampant spread of SARS-CoV-2 is placing an extreme strain on healthcare systems globally.

Numerous COVID-19 preprints have been generated by scientists to help with identification of the disease's mechanism of action to discover ways to minimize its effects. The Icahn School of Medicine at Mount Sinai created an institutional organization named the Precision Immunology Institute (PrIISM), which integrates all institutional efforts in coordinating a systematic review of both published and unpublished literature (Vabret *et al.*, 2020)<sup>[52]</sup>. In addition to summarizing what is currently known about how SARS-CoV-2 causes disease by activating the innate and adaptive immune response and what laboratory and clinical prognostic markers are available to predict how patients will respond to treatment, PrIISM provides information about clinical studies currently underway to identify various therapies, and about a variety of strategies for developing effective vaccines.

### Future Perspective

The COVID-19 pandemic has emerged as an unprecedented global crisis, severely affecting countries such as China, Italy, Iran, and the USA across health, social, and economic

dimensions. Although it is too early to predict precise outcomes, the pandemic is expected to have widespread consequences. High-income nations already impacted by COVID-19 may face severe challenges, while low-income countries could experience one of two scenarios. In a worst-case scenario, many low-resource countries would be unprepared for the outbreak, leading to catastrophic consequences. Conversely, in a best-case scenario, similar to the 2003 SARS-CoV outbreak, COVID-19 might not extensively affect regions like Africa or South America, as respiratory viruses tend to spread more efficiently during winter, potentially delaying or reducing the impact in the southern hemisphere. Contributing factors could include climate-related cultural practices (such as spending more time outdoors), UV light reducing viral survival on surfaces, innate immune differences, prior coronavirus exposure, and higher temperatures. This perspective is indirectly supported by studies from Chin and colleagues, who examined viral survival under different environmental conditions. Moreover, effective prevention measures could also lead to a reduction in hygiene-related diseases, which continue to be major causes of mortality (Di Gennaro *et al.*, 2020) [53].

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