Review Article

SARS-CoV-2: A Systematic Review

Abstract

Viruses, which are incredibly tiny particles, are what give humans pandemic and epidemic diseases. Many viral infections have impacted human health throughout history, and epidemic and pandemic diseases have claimed many lives. Many viral infections, such as SARS, the Middle East respiratory syndrome corona virus, Ebola, H1N1, and the current COVID-19, have affected people in this decade. Positive sense single-stranded RNA is present in SARS Cov-2. The virus's structure is reminiscent of the Corona virus found in bats. SARS-CoV-2, which has its genesis in Wuhan, China's primary transportation hub, is the cause of COVID-19. SARS-CoV-2 spread globally from China. In 213 countries, 1.5 crore people have been diagnosed with COVID-19, and 6.3 lakh of them have died. The primary symptoms include headache, dry cough, myalgia, difficulty breathing, and fever. Serological testing, RT-PCR, and CT-Scan imaging are used to diagnose this condition. Like SARS virus, SARS-CoV-2 virus binds to ACE2 receptors. The same medications used to treat SARS are also utilised to treat COVID-19 patients. Drugs like Remdesivir, ritonavir-lopinavir, and umifenovir work well to lower viral loads in patients. The vaccine is being prepared in numerous nations. The COVID-19 disease vaccines are being made by Oxford University (AZD1222), the USA (MRNA-1273), India (COVAXIN), and China (INO-4800). Since the vaccinations are still in the clinical trial stage, we are still waiting for an effective vaccine.

Comment [a1]: There are also vaccines in other countries. (Türkiye)

Key words: ACE2 receptors, CT-image, COVID-19, COVAXIN, RT-PCR, SARS-CoV-2.

Introduction

A pandemic illness called COVID-19 has been detected in China. It was initially detected in Wuhan in December 2019 and quickly spread over the entire planet[1-4]. Hubei province's Wuhan is a significant transportation hub in China. In Wuhan, the sickness first appeared in the seafood market. This city is renowned for its live animal trading. In Wuhan, there were numerous pneumonia cases as well as unidentified cases. Corona viruses are the cause of the covid-19. The coronavirus is the seventh member of the coronaviridae family[5]. The corona viruses, often known as SARS-COV-19, are a significant group of viruses that are largely responsible for zoonotic transmission of diseases to humans. After SARS (severe acute respiratory syndrome)

and MERS (Middle East respiratory syndrome), it is a serious respiratory condition[6, 7]. The disease's primary cause, intermediate hosts, diagnosis, and effective treatments are all unclear[8]. During China's Spring Festival, the illness went from being an epidemic to becoming pandemic. This infectious disease has been deemed a pandemic by the WHO.

Comment [a2]: (World H.....)

10 lakh deaths occurred worldwide due to the corona virus, which affects 3.7 crore individuals. More than 2.7 billion people have recovered from Corona illness to date. There are roughly seven different types of corona viruses[9]. Important viruses are among the four. Alpha Corona Virus, Alpha Corona Virus NL63, Beta Corona Virus OC43, and HKU1 are the four viruses (beta corona virus). Other corona viruses include SARS-CoV, COVID-19[10], MERS-CoV, and SARS-CoV-2. MERS-CoV is the beta corona virus that causes Middle East Respiratory Syndrome (MERS). SARS-CoV is the beta corona virus that causes severe acute respiratory syndrome (SARS).Upper and lower respiratory tract illnesses are brought on by human corona viruses. The respiratory infections caused by HCoVs and other human corona viruses are widespread worldwide, but the species differ by region[11].

Symptoms

140 people with corona were recognised by Wuhan University's Zhongnan Hospital as having a variety of issues. 50% of patients reported feeling tired and having a dry cough, and 99% of patients had a fever with an exceedingly high temperature[12]. 33% of patients had a dry cough and had trouble breathing. A few of the patients show no symptoms. Patients with Corona frequently experienced colds and flu. 80% of patients with corona illness exhibit just minor symptoms. Adults are spreading the disease because they are more immune than children[13]. The condition also causes body aches, headaches, runny or stuffy noses, and diarrhoea. The percentages of common symptoms are as follows: 99% fever, 70% fatigue, 60% dry cough, and 44% myalgia[14,15,16.].

Elderly people who already have conditions like diabetes, hypertension, cardiovascular disease, or cerebrovascular illness are more likely to experience negative effects from covid-19. Acute respiratory distress syndrome, arrhythmias, acute cardiac injury, shock, and acute renal injury are the most frequent consequences of illness [(17–19)]. 40% of transmissions occur in hospitals, and 4% of deaths occur there. There is a need for planned construction for interdisciplinary treatment in hospitals to lower the death rate. Corona patient mortality can be reduced by designing and constructing isolation wards[20].

Cov-2 single stranded RNA virus from SARS. The genome resembles the structure of the bat corona virus. The disease COVID-19 is caused by the SARS-CoV-2 virus. It has four structural proteins known as spike(S), spike have RBD(receptor -binding domain), spike have envelope(E), spike have membrane(M), and nuleocapsid. It has positive sense, enveloped, single stranded RNA genome (N). Nucleoplasm contains other genes as well. Additional genes that code for proteins, including RNA-dependent RNA polymerase [21,22], include ORF1a/b, ORF3a, ORF6,

ORF7a/b, ORF8, and ORF10.The alveolar type 2 cells of the lung (AT2), as well as lymphocytes and cells of the kidney, heart, and gastrointestinal system, as well as angiotensin converting enzyme 2(ACE2), are among the many organs and tissueswhere S protein naturally binds to ACE2[23-25]. S protein priming, which is performed by transmembrane serine protease 2 (TMPRSS2)[26,] promotes SARS-Cov-2 binding to ACE2.

Diagnosis of COVID-19:

For the initial COVID-19 test, ambulatory patients must provide a nasopharyngeal and/or oropharyngeal swab or wash. To test the covid-19, sputum, endotracheal aspirate, or bronchoalveolar lavage are also taken. To diagnose the COVID-19[27,28], biological samples such blood, urine, stool, and saliva were also examined.

Table 1: Detection of SARS-CoV-2 Using Various Biological Materials

S.No	Biological source	Detection Rate
1	Blood	~15-30%
2	Throat washing	~30%
3	Stool	~30%
4	Pharyngeal swabs	~30%
5	Nasal swabs	~60%
6	Nasopharyngeal and oropharyngeal swabs	~70%
7	Sputum	~70%
8	Saliva	~90%
9	Bronchoalveolar fluid	>90%

The SARS-Cov-2 virus can be diagnosed utilising biological sources such upper and lower respiratory tissues by applying molecular diagnosis techniques, which have the support of the WHO and CDC (Centers for Disease Control and Prevention). The SARS-CoV-2 genome was targeted by real-time reverse transcription polymerase chain reaction (rRT-PCR) assays, which were chosen by the WHO. The reverse transcription to cDNA, cDNA amplification using RT-PCR equipment, and (fluorescent) signal detection are all steps in the RT-PCR method[29]. According to the WHO, RT-PCR must be performed in a BSL-2 laboratory and virus culture must be performed in a BSL-3 laboratory [30,31].SARS-CoV-2 can be isolated in cell lines and verified by RT-PCR. German scientist Charite Berlin is credited with creating RT-PCR and standardising the procedure[32]. Three genes, E, RdRp, and N, are found by the RT-PCR test. The

three genes will only be examined in order if the one before it is positive. This is a step-by-step procedure. The simultaneous amplification and analysis in a closed system of real-time RT-PCR assays helps to reduce false-positive results brought on by amplification contamination. The E gene test and RdRp gene assay are the first-line screening methods that are advised by the WHO[33].

Serological research on COVID-19 disease has focused on finding antibodies to the S proteins found in the spike[34] of the Corona virus. Corona virus spikes are in charge of causing receptor binding. The hosttropism and transmission capacity of spikes are determined by their binding and fusion[35,36]. The S protein is produced by the S gene. This S protein is divided into two functional subunits (S1 and S2). S1 domain of these two subunits is in charge of receptor binding, and S2 domain is in charge of fusion. Human renal, gastrointestinal, and respiratory cells all contain angiotensin-converting enzyme 2. Angiotensin-Converting Enzyme 2 is where these SARS-Cov-2 and SARS-COV interact [37,38,39].For the creation of serological assays to find the Covid 19, the reaming N protein looks to be a key antigenic location. The helical nucleocapsid structure, or N protein, is crucial for viral pathogenicity, replication, and RNA packing. Patients with COVID-19 have antibodies because of the N protein[40,41]. One of the immunodominant antigens in the early diagnosis of COVID-1942 may be N protein. Although not for screening[42-43], the serology is helpful in confirming the diagnosis of COVID-19.

During the serological testing, there were anti-SARS-Cov-2 IgA and IgM antibodies in the patient's serum. Patients with fevers or respiratory illnesses have antibodies in their serum for one to two weeks[44.]According to Chunqin Long, 36 people with COVID-19 clinical symptoms have lesions in the lung lobes as seen on CT scans. Covid-19 pneumonea was identified in a total of 36 individuals. 35 patients were present with aberrant CT findings. Thoracic CT [45] results were only normal in one patient. Our study demonstrates that CT imaging can also confirm the diagnosis of COVID-19, but only if the patient additionally has lung infections, as is the case in this report. This approach requires a careful diagnostic to identify COVID-19 disease[46].

Therapy:The sites of attachment for SARS and SARS-Cov-246 are ACE2 receptors. Therefore, the SARS medications also work to lower the viral load in the body of the afflicted patient. Remdesivir[47,48], ritonavir-lopinavir combination[49], vitamin C infusion[50], darunavir and cobinastat[51,] hydroxychloroquine for neumonia[52], umifenovir[53], and conventional medicines[54] are the medications used to treat covid-19 infection. Chinese employed alpha interferon along with the lopinavir/ritonavir combo as treatment for hospitalised patients[55]. Remdesivir was administered to the first American patient, who showed a positive clinical response in animal models [56]. The course of treatment may call for non-invasive ventilation, mechanical ventilation, and extracorporeal membrane oxygenation to address respiratory failure. The additional intensive care therapies used to treat SARS-Cov-2 infections include vasopressors and renal replacement therapy.

Precautions:In every county, a number of precautionary precautions are being taken. The primary preventative measure to stop the corona virus from spreading is lockdown. Wearing N-95 masks, avoiding social situations, and eating immune-boosting foods are some preventative measures used globally. Indians consume a soup made with a variety of spices. The ingredients of the soup are zinger, garlic, mint, coriander, and jiggery [57].

Clinical trial status: SARS-Cov-2 is being developed in a number of nations. Innovating the SARS-Cov-2 vaccine is a goal of several nations and their research facilities.

Chinese clinical trial: INO-4800 is a well-known vaccine type created by Beijing Advaccine Biotechnology and INVIO Pharmaceuticals based on a DNA plasmid vaccine electroporation device. Phase 1 clinical trials for Inovio are planned to start simultaneously in China and the US[58]. A trimetric S protein-based recombinant subunit vaccination is also being developed by Clover Biopharmaceutical Company[59].

Oxford University Clinical Trial: Oxford University's Vaccinology Department, under the leadership of Professor Sarah Gilbert, is developing the COVID-19 vaccines. ChAdOx1 Ncov-19 is the name of the developed vaccine (AZD1222). The ChAdOx1 virus, a weaker and non-replicating variant of the common cold virus, is used to create the vaccine. The SARS-COV-2 spike protein is expressed in the vaccine thanks to genetic engineering. In the Phase III clinical trial, 8000 participants are from the United Kingdom. Brazilians also took part in these clinical trials. The number of patients receiving this vaccine in Brazil could rise to 5000. The Oxford research team also plans to trial this vaccine in South Africa with 2000 people. AstraZeneca has a licence to sell the vaccine AZD1222.

This SARS-Cov-2 vaccine, AZD1222, elicits an immunological response. Even in those with weakened immune systems, this vaccine is safe. The ChAdOx1 virus[60] was modified to incorporate genetic material known as spike glycoprotein, which is expressed on the surface of the SARS-CoV.

India's clinical trial: India is the country that created the COVAXIN vaccine. Bharath Biotech and the Indian Council of Medical Sciences (ICMR) worked together to create the vaccine. The COVAXIN vaccine was developed by the government's National Institute of Virology (NIV, Pune)[61]. 12 institutes were chosen by ICMR to carry out the clinical trials. Different parts of India are starting human clinical studies. Two volunteers received the initial dose from NIMS, Hyderabad. After 14 days of observation, they will be released and administer the second dose.

US clinical trial for vaccination (MRNA-1273) from US companyModerna: It was created in the USA. Moderna and researchers at the NIAID Vaccine Research Center collaborated to choose mRNA-1273 as a potential mRNA vaccine against the new corona virus SARS-CoV-2, which codes for a prefusionstabilised form of the Spike (S) protein. This vaccine is undergoing a third-stage clinical study. This research trial will involve 30,000 volunteers and a dosage of 100ug. There are 600 healthy participants in Phase II.There are 300 adults (ages 18 to 54) and 300

seniors (ages 55 and older) among them. At both vaccinations, the participant will either receive a placebo, a dose of 50 or 100 mg, or both. Twelve months after the second immunisation, participants will continue to be monitored. The prevention of symptomatic Covid-19 disease is the Phase III trial's primary aim, while the prevention of severe Covid-19 disease and SARS-CoV-2 infection are important secondary endpoints[62.]

Conclusion: The COVID-19 sickness is brought on by SARS-CoV-2 and is disseminated all over the world. Clinical signs of COVID-19 disease include fever, a dry cough, respiratory infections, and myalgia. The infection was confirmed by the diagnostic techniques. The conformation test for COVID-19 is the RT-PCR Test, and this test provides reliable results. When compared to CT-Scan Imagining, the accuracy rate of RT-PCR is low. Although serological antibodies are present one to two weeks after infection, serological tests are still able to detect COVID-19. The Covid-19 was confirmed by an RT-PCR test, a CT scan, and serological assays. Remdesivir, lopinavir, and combination therapies are more effective at lowering the patient's body's viral load.With this medication, the recovery rate is quite great. All of the drugs combined produced positive outcomes. Therefore, it is preferable to treat Corona patients with SARS virus medications, Vitamin C, hydroxychloroquine, and multivitamins. Clinical studies are being conducted to create the corona vaccine in China (INO-4800), Britain (AZD1222), the United States (MRNA-1273), and India (COVAXIN). All of these nations have finished their animal testing and are now engaged in phase I, phase II, and phase III human investigations. The only option up until the vaccine is approved is to take precautions in accordance with international, national, and governmental health organisation and government norms.

Comment [a3]: Most countries have passed this stage.

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