

## A Brief Review on Novel Coronavirus 2019 for Future Point Based on the Facts

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### ABSTRACT

Recently, a novel coronavirus disease 2019 (COVID-19) emerged in the city of Wuhan, China, in December 2019, is a highly contagious disease. This virus is spreading rapidly to all regions of China and multiple countries. The World Health Organization (WHO) has declared this outbreak as the sixth public health emergency of international concern. As of 0:00 am March 26, 2020, a total of 416,686 cases have been reported throughout the world, 18,589 deaths and 197 countries, areas, or territories with COVID-19 cases (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019>). At present, research is going on for the development of medication against COVID-19. We systematically summarize the symptoms, routes of transmission of virus, and diagnosis and treatment for COVID-19, based on the current published data. This review focused on helping the public to understand and deal effectively with COVID-19 and also provide a reference for future studies.

**Key words:** Coronavirus disease 2019, Coronavirus, Severe acute respiratory syndrome coronavirus, Middle East respiratory syndrome coronavirus.

### 1. INTRODUCTION

Recently, a novel unidentified epidemic coronavirus (CoV), namely, severe acute respiratory syndrome CoV 2 (SARS-CoV-2) that emerged in city of Wuhan, China, in December 2019, and rapidly spreading throughout the country within 1 month. However, on February 11, 2020, the WHO announced a new name as coronavirus disease 2019 (COVID-19). CoV is a single positive-stranded RNA virus, belongs to the family of Coronaviridae, and may cause respiratory and neurological diseases. It is divided into four types:  $\alpha$ -CoV,  $\beta$ -CoV,  $\delta$ -CoV, and  $\gamma$ -CoV. Previously, six CoVs were identified, namely, 229E (human CoV [HCoV]-229E) ( $\alpha$ -CoV), HCoV-OC43 ( $\beta$ -CoV), SARS-CoV-1 ( $\beta$ -CoV), HCoV-NL63 ( $\alpha$ -CoV), HCoV-HKU1 ( $\beta$ -CoV), and Middle East respiratory syndrome CoV [MERS-CoV] ( $\beta$ -CoV) [1,2]. The novel seventh HCoV, namely, SARS-CoV-2 is responsible for respiratory infection. SARS-CoV-2 belongs to  $\beta$ -CoV (Figure 1), it has many potential natural hosts, intermediate hosts, and final hosts. Compare to other viruses such as SARS-CoV and MERS-CoV, this virus has high transmissibility and infectivity, despite low mortality rate [3-5].

#### 1.1. Status of CoV in India

The first case of the COVID-19 CoV in India was reported on January 30, 2020, in Kerala state. As of April 9, 2020, at 8:00 am, the Indian Council of Medical Research (ICMR) and Ministry of Health and Family Welfare were reported in the country a total of 5095 cases, 472 recoveries, 1 migration, and 166 death cases (<https://www.mohfw.gov.in/>).

Janata curfew is an attempt to counter the spread of CoV, initiated by India's Prime Minister, Narendra Modi, in the wake of the 2020 CoV pandemic in India. The prime minister advised all Indian people to observe a self-imposed "curfew" on March 22, 2020, from 7 am to 9 pm Indian Standard Time, which reduce the communal spreading of CoV disease in India ([https://en.wikipedia.org/wiki/Janata\\_Curfew](https://en.wikipedia.org/wiki/Janata_Curfew)).

### 2. SYMPTOMS

As of February 20, 2020, and based on 55,924 laboratory confirmed cases, patients infected by COVID-19 showed a range of symptoms including, fever (87.9%), dry cough (67.7%), fatigue (38.1%), sputum production (33.4%), shortness of breath (18.6%), sore throat (13.9%), headache (13.6%), myalgia or arthralgia (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), and hemoptysis (0.9%), and conjunctival congestion (0.8%) (<https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf>).

### 3. ROUTES OF TRANSMISSION OF VIRUS

CoVs can be transmitted across species barriers. Initially, the patients infected with COVID-19 were suspected in Wuhan wholesale seafood market in the early stages, suggesting that animal-to-person spread. However, huge number of cases are reported who are not exposed to markets, suggesting that COVID-19 also spreads through person-to-person contact [6,7].

The previous epidemiological studies have shown that there are three major factors for the spread of virus, i.e., person-to-person contact, aerosol transmission, and transmission by touch [8,9]. The

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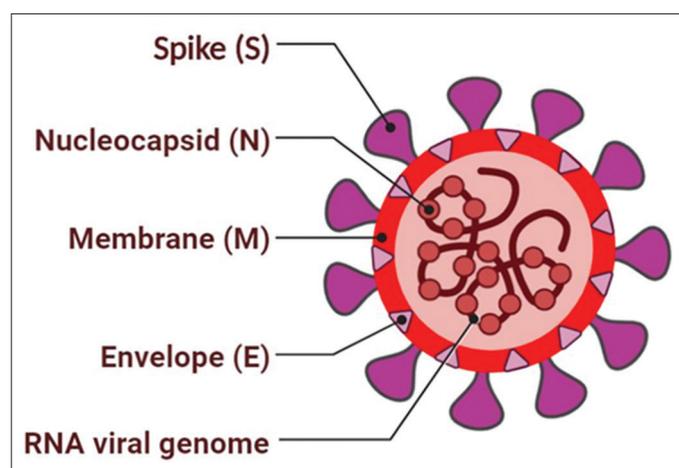
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**Figure 1:** Structure of coronavirus disease 2019.

virus is thought to spread mainly from person to person who are in close contact with each another (within about 6 feet). Through respiratory droplets that are formed when an infected individual coughs or sneezes, such droplets may land in people's mouths or noses nearby or probably inhaled into the lungs. An individual might be able to get COVID-19 by touching a surface or an object that has the virus on it and then touching their own mouth, nose, or probably eyes, but this is not thought to be the primary way the virus spreads. The rapid and early detection of COVID-19 is more useful in controlling the sources of infection and also helps the patients to avoid progression of the disease, subsequently reduces the transmission of CoV [10].

#### 4. DIAGNOSIS OF SARS-COV-2

Nucleic acid detection methods have developed rapidly with developments in molecular biology technology to identify viruses.

##### 4.1. Nucleic Acid Amplification Test (NAAT)

NAAT is used to detect specific nucleic acid sequence of COVID-19 virus using reverse transcription polymerase chain reaction for amplification purpose because of its advantages such as specific and simple quantitative assay. And also, rRT-PCR detects early infection compared to RT-PCR assay [11]. Therefore, the real-time RT-PCR assay is still a prevalent tool to be used to detect all types of CoVs [12,13], including SARS-CoV-2 [14].

##### 4.2. Serology Test

Serology testing is used in people who may have been exposed to the virus to detect past infection (antibodies to MERS-CoV). Antibodies are the proteins that origin from the body's immune system to target and destroy viruses, bacteria, and other microbes during infection. The presence of MERS-CoV antibodies indicates that a person was previously infected with the virus and developed an immune response.

Serological surveys may assist with an ongoing outbreak investigation and a retrospective evaluation of the attack rate or severity of an outbreak. In cases, where NAAT assays are negative and there is a clear epidemiological link to the infection with COVID-19, paired serum samples (in the acute and convalescent phase) could support diagnosis once validated serology tests are available. For this reason, serum samples can be stored. Cross reactivity to other CoVs can be challenging [15], but commercial and non-commercial serological tests are currently under development. A few studies have been published on clinical samples with COVID-19 serological data [16,17].

#### 4.3. Viral Sequencing

Standardized serological tests have been developed to detect anti-MERS CoV antibodies in human sera and validated to assist in the diagnosis and monitoring of the disease. These studies are based on indirect immunofluorescence assay (IFA) and enzyme-linked immunosorbent assay (ELISA) technology.

Standardized serological assays for the detection of anti-MERS CoV antibodies in human sera have been rapidly developed and validated to aid diagnosis and surveillance of the disease. The assays are based on IFA and ELISA technology. In collaboration with leading virology institutes in Germany, namely, the Institute of Virology at the University of Bonn Medical Center and the Robert Koch Institute, serological tests were developed to detect anti-MERS-CoV antibodies in human sera [15].

In addition, MIT professor, Zhang F, developed a test paper with SHERLOCK technology for rapid detection of SARS-CoV-2 in 1 h. While clinical testing has not yet been carried out, once confirmed, this technology may be favorable to the rapid diagnosis of the disease [18]. A research group at the University of Peking, China, reported to have developed a new method for the rapid construction of transcriptome sequencing library of SHERRY, which helps to quickly sequenced SARS-CoV-2 [19].

#### 5. VACCINATION FOR COVID-19 (UNDER TRIALS)

At Kaiser Permanente Washington Health Research Institute in Seattle, the first US clinical trial of a COVID-19 vaccine has started, which is Moderna's mRNA-1273. The mRNA vaccine is intended to act against the encoding of SARS-CoV-2 for a pre-fusion stabilized form of the spike (S) protein, which was selected by Vaccine Research Center (VRC) in collaboration with researchers. The VRC is part of the National Institutes of Health (NIH) and National Institute of Allergy and Infectious Diseases, a part of NIH (<https://www.pharmaceutical-business-review.com/news/moderna-mrna-1273-coronavirus-trial/>).

During the Phase I trial, a total of 45 healthy adults aged 18–55 years have chosen to evaluate the safety and immunogenicity of 25 µg, 100 µg, and 250 µg dose levels of mRNA-1273 given on a two-dose vaccination schedule 28 days apart. The research includes a 12-month follow-up after the second vaccination. The primary goal is the safety and reactogenicity of a two-dose vaccination schedule while the secondary goal is immunogenicity of the SARS-CoV-2 S protein (<https://www.clinicaltrialsarena.com/news/first-us-covid-19-vaccine-trial-moderna/>).

#### 6. TREATMENT FOR COVID-19

##### 6.1. Convalescent Plasma (CP) Therapy

Over the past decades, CP therapy has proved and successfully used for the treatment of MERS [20], SARS [21], H1N1 [22], and H5N1 [23]. At present, there are no specific antiviral drugs for the treatment of novel SARS-CoV-2, some drugs are still under investigation. Therefore, CP is also one of the best treatments for the treatment of SARS-CoV-2, CP involves the transfusing of antibodies into a person suffering with virus, the antibodies collected from the blood of a person who has recovered from a virus, which improve the person's immune system.

Recently, a Chinese team published an article in Proceedings of the National Academy of Sciences, the article is a pilot study on CP therapy, the results of that study show a potential therapeutic effect and low risk in the treatment of severe COVID-19 patients [24]. According to case report in the Journal of Korean Medical Science, doctors gave CP therapy treatment two patients suffered with SARS-CoV-2. The results showed that the two patients were fully recovered from COVID-19 [25].

### 6.2. Medicinal Plant Extracts

In recent years, Chinese medicinal herbal extracts are used for the treatment of SARS and MERS [26-28]. 3-chymotrypsin-like cysteine protease (3CLpro) is vital for CoV replication and is essential for its life cycle. Therefore, 3CLpro is a proven drug discovery target in the case of SARS-CoV, MERS, and SARS-CoV-2. The following Chinese medicinal herbal extracts had the capacity to inhibit the enzymatic activity of SARS 3CLpro: Chinese Rhubarb extracts, water extract of *Houttuynia cordata*, flavonoid extracted from *Litchi* seeds, and beta-sitosterol extracted from the root extract of *Isatis indigotica*. Further, the following herb-derived compounds, including sinigrin, indigo, aloe-emodin, hesperetin, quercetin, epigallocatechin gallate, gallic acid, herbacetin, rhoifolin, and pectolinarin, were able to inhibit the SARS 3CLpro activity [29].

### 6.3. Remdesivir 20

Remdesivir (development code GS-5734) is a novel antiviral drug in the class of nucleotide analogs that show broad-spectrum antiviral activity against several RNA viruses [30]. It was developed by Gilead, used for the treatment of Ebola and related viruses, which inhibits the replication enzyme RNA-dependent RNA polymerase, subsequently prevents the replication process [31]. According to the case report in the New England Journal of Medicine (NEJM), a young man belonging to Snohomish County, Washington, was diagnosed against with remdesivir COVID-19 when his condition worsened, the next day he improved [32].

Prof. Jiang Shibo, Fudan University in Shanghai, China, who has been working on CoV therapy for a long time, says that such an individual case data do not prove that drug is safe and reliable. Still, from the drugs in the SOLIDARITY trial, "remdesivir has the greatest potential to be used in hospitals [33]."

### 6.4. Chloroquine and Hydroxychloroquine

On February 17, 2020, the Chinese State Council held a news conference reporting that chloroquine phosphate, an old medication used to treat malaria, had demonstrated significant effectiveness and acceptable safety in the treatment of COVID-19, multicenter clinical trials conducted in China [34,35].

A Chinese team recently published an article, the paper reports that chloroquine and hydroxychloroquine are used for the treatment of SARS-CoV-2, among that hydroxychloroquine ( $EC_{50}=0.72\% \mu\text{M}$ ) found to be more effective than chloroquine ( $EC_{50}=5.47\% \mu\text{M}$ ) [36]. Gautret reported that COVID-19 patients were treated with hydroxychloroquine and azithromycin to cure their infection and restrict the transmission of the virus to others to control the spread of COVID-19 globally [37].

### 6.5. Ritonavir/Lopinavir

According to the case report in the NEJM, doctors in Wuhan, China, gave 199 patients two pills of lopinavir/ritonavir twice a day plus standard care or standard care alone. However, no benefit was observed with lopinavir-ritonavir treatment beyond standard care. Future trials in patients with severe illness may help to confirm or exclude the possibility of a treatment benefit [38].

The ICMR has suggested that combination therapy of lopinavir/ritonavir used for the treatment of COVID-19 patients based on the observational studies of clinical benefit among patients with SARS-CoV and MERS CoV19-21, as well as the docking studies carried out by the National Institute of Virology, Pune [39].

A man belongs to British nation, who as administered in Ernakulam Medical College Hospital in Kochi, India, for treating his CoV

infection. The person was diagnosed against COVID-19 with HIV antiretroviral drugs (ritonavir and lopinavir), the results showed that he has tested negative for the virus (<https://www.indiatoday.in/india/story/coronavirus-pandemic-foreigner-treated-hiv-drugs-covid-19-tests-negative-1659761-2020-03-26> dated: 26-03-2020).

## 7. CONCLUSION

Novel CoV, namely, COVID-19 is a severe epidemic viral disease emerged in Wuhan, China, in December 2019. Its symptoms are similar to that of SARS such as fever, dry cough, fatigue, sputum production, shortness of breath, sore throat, and headache. This virus is highly dangerous and easily spreads to others through person-to-person contact, aerosol transmission, and transmission by touch. This disease has severe threat to global health and safety; therefore, we should control the virus as early as possible. At present, there are no effective vaccine and drugs for this virus. The research has been going on for the development of vaccine and drugs for COVID-19. Therefore, it is important to cut off the transmission of virus and use the existing drugs to control the progress of the disease and maintaining a distance of 1 m between person to person.

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