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Review Article

Global Pandemic of a Century: A Review on the Coronavirus (COVID-19)

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ABSTRACT

Coronavirus disease 2019 (COVID-19) emerged in December 2019 in Wuhan, the capital of Hubei province, China. While the outbreak in China is almost over, this highly contagious disease is currently spreading across the world with a daily increase in the number of affected countries, confirmed cases, and infection-related deaths. In January, the World Health Organization (WHO) declared that the outbreak of COVID-19 constituted a Public Health Emergency of International Concern (PHEIC). Based on the high levels of global spread and the severity of COVID-19, on 11 March 2020, the Director-General of the WHO declared the COVID-19 outbreak a pandemic.

COVID-19 is an acute respiratory disease caused by a newly emerged zoonotic coronavirus. A positive-sense enveloped single-stranded RNA virus, named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), has been isolated from a patient with pneumonia and connected to the cluster of acute respiratory illness cases from Wuhan. The virus is transmitted from human to human via droplets coughed or exhaled by infected persons and by touching droplet-contaminated surfaces or objects and then touching the eyes, nose, or mouth.

Population groups that have been more frequently reported as having severe disease and a higher mortality rate include people aged over 60 years, males, people with underlying conditions such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease, and cancer. Current estimates suggest a median incubation period of five to six days for COVID-19, with a range of one to 14 days. Disease-specific pharmaceuticals and vaccines are still under research and development. The therapeutic use of convalescent plasma donated by patients recovered from COVID-19 might play a role in the efforts to find a possible treatment for COVID-19.

Keywords: *Coronavirus, COVID-19, WHO, SARS-Cov-2, Zoonotic.*

INTRODUCTION

Coronaviruses are a family of viruses that cause illness ranging from fever to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV) (Zhou et al., 2020).

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These groups of viruses are mainly found in mammals and birds, and very few cases have been reported to affect humans. It is mainly referred to as zoonotic means transferring from animals to human beings. It usually causes respiratory, gastrointestinal, and central nervous system diseases in animals and humans lead to the upper and lower respiratory tract infections which are more threatening to human life (Li, 2016).

One of the main characteristics of coronaviruses is its ability to adapt to the new environment through mutation and recombination easily (Li, 2016). In late December 2019, a new strain of coronavirus has been found which affects the lower respiratory tract of patients with symptoms of pneumonia in the province of Wuhan, China. The World Health Organization (WHO) named this strain as 2019 novel coronavirus (2019-nCoV), later it renamed it to a clinical identification as Coronavirus Disease 19 commonly referred to as COVID-19 disease (WHO, 2020). The virus that causes COVID-19 is also nominated as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) (Gulyaeva et al., 2020).

Due to its nature of easy mutation and recombination, this virus is already mutated to two different strains after its original transmission from the animal host to human beings. Genetic analysis of at least 103 SARS-CoV-2 (COVID-19) genomes indicates that the two major types evolved from this virus is designated as L & S type. It has been reported that the L type (~70%) is more prevalent than the S type (~30%), the S type was found to be an ancestral version Both the types have a role in this outbreak however, L type is found as more virulent than the S type (Xiolu Tang, 2020).

This review article emphasizes the nature of this pandemic disease (COVID-19) including its status, epidemiology, structure, and clinical manifestations in briefly.

EPIDEMIOLOGY

The outbreak of COVID-19 was first reported from the local seafood market located in Wuhan, Hubei Province, China in December 2019 (Song et al., 2020). The cluster of patients tested for pneumonia and other symptoms were linked to this wet market. Primary examinations of some of the environmental specimens for the COVID-19 test shows positive results in Huanan Seafood Market, Wuhan, China (Gralinski & Menachery, 2020). However, according to the WHO report, the market place was deemed positive for COVID-19, but there is no confirmation of any specific association with animals yet (WHO, 2020). Many researchers speculated that these viruses have a wide range of animal and bird reservoirs (CDC, 2020), and they are still working to establish a possible animal reservoir for COVID-19 (Guo et al., 2020).

Initially, it has been found that patients with this disease had activities related to the market, but there are some positive cases of patients who did not visit the suspected market. This disease is now transmitted worldwide and, affects most of the countries. The health care professionals in various countries are always at high risk and are most affected by infected patients, which indicates that human to human transmission of COVID-19 is highly possible (Riou & Althaus, 2020; Chen et al., 2020; Wu et al., 2020). World Health Organization (WHO) has declared COVID-19 as a Public Health Emergency of International Concern (WHO, 2020).

VIRAL STRUCTURE

Coronaviruses are enveloped, pleomorphic, ranging from 150 to 160 nm in size. The viral structure comprises a positive single-stranded RNA, unsegmented, nucleoprotein, capsid, matrix, and S-protein (Fig 1). Nucleocapsid Protein (N), Membrane Glycoprotein (M), and Spike Glycoprotein (S) are the important proteins of Coronavirus (Perlman, 2020). COVID-19 encodes an additional glycoprotein which makes it different from other classes of coronaviruses. This additional glycoprotein of COVID-19 has the properties of acetyl esterase and hemagglutination (HE) (Wu et al., 2020).

It has been suggested that the heterophilic antibodies generated against the N-protein of SARS-CoV may cross-react with the COVID-19 and does not provide any cross-protection to it (Gralinski & Menachery, 2020). One of the important mechanisms of the N-protein of SARS-CoV is to act as a Viral Suppressor Protein of RNA*i* (VSR) to counter the host immune response (Cui et al., 2015). These Viral Suppressor Proteins suppress the RNAi at the pre-dicer or post dicer level to overcome the host defense for the establishment of infection (Ding, 2010; Sullivan & Ganem, 2005; Maillard et al., 2013; Ali et al., 2015).

The first step of the viral infection is the binding of a receptor expressed by the host cells followed by the fusion with the cell membrane. It has been found that the epithelial cells of the lung are the primary target of this virus. Therefore, it has been reported that human to human transmission of SARS-CoV is mainly occurred by the binding between the receptor-binding domain of virus spikes and the cellular receptor identified as angiotensin-converting enzyme 2 (ACE2) receptor (Wan Y et al., 2020; Jaimes JA et al., 2020). Recent studies suggest that the sequence of the receptor-binding domain of COVID-19 spikes is similar to that of SARS-CoV which strongly confirmed that the entry into the host cell is most likely via the ACE2 receptor (Wan et al., 2020).

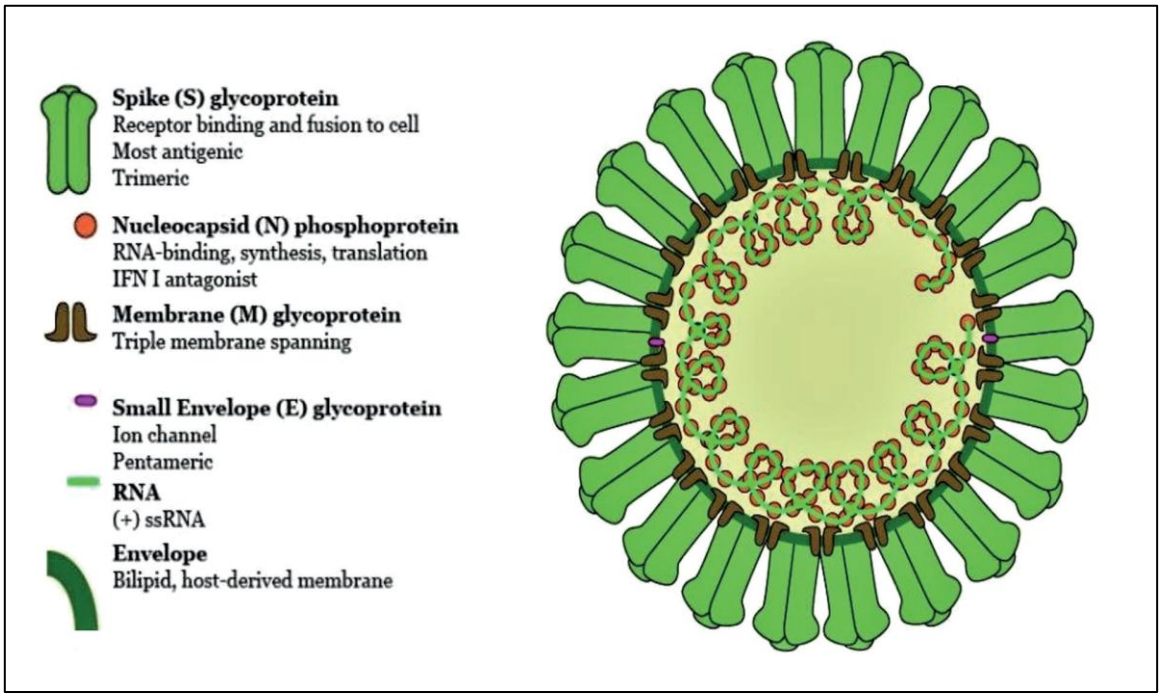

Fig. 1: Schematic Diagram of Coronavirus 2006

SYMPTOMS OF COVID-19

The actual symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days (Li Q et al., 2020). It has been observed that the period from the first onset of symptoms of COVID-19 to death ranged from 6 to 41 days with a median of 14 days (Wang, W., Tang, J., & Wei, F., 2020). However, this period is mainly depending on the age and the status of the immune system of the infected patients. It was shorter among the patients above the age of 70 as compared with those under the age of 70 (Wang, W., Tang, J., & Wei, F., 2020).

The illness reported from the confirmed cases of COVID-19 has ranged from people with little or asymptomatic to people being severely ill and dying. Some of the common symptoms include (Nanshan Chen, 2020):

- Fever
- Cough
- Shortness of breath
- Muscle ache

This disease may also occur with mild symptoms only including low-grade fever, cough, sore throat, malaise, shortness or difficulty in breathing, increased respiratory secretions (i.e. Sputum), gastrointestinal symptoms such as vomiting, nausea, diarrhea (Fig. 2) (WHO, 2020).

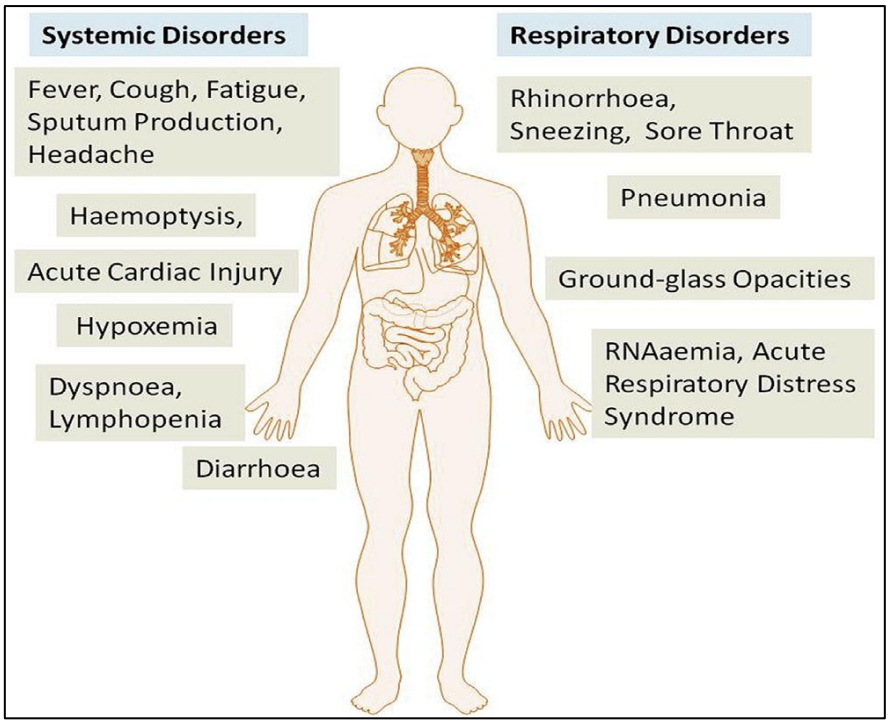

Fig. 2: The systemic and respiratory disorders caused by COVID-19 infection

The risk factors for severe illness are still not clear, although older patients or patients with underlying medical comorbidities such as (diabetes, cancer, cardiovascular disease, hypertension) are at higher risk. In most severe cases, the infection caused by COVID-19 may lead to pneumonia, kidney failure, severe acute respiratory syndrome, and even death (WHO, 2020).

MODE OF TRANSMISSION

It has been reported that the domestic and wild animals are the main host for the coronaviruses (National Health Commission of People's Republic of China, 2020), and it is considered that animal coronaviruses do not spread among humans (CDC, 2020). However, there are exceptions, such as SARS and MERS, which are mainly spread from an infected person to a healthy person via respiratory droplets from cough or sneezing.

World Health Organization (WHO) describes 3 main transmission routes for the SARS-CoV-2 (COVID-19) which are as follows (National Health Commission of People's Republic of China, 2020):

1. **Droplets Transmission:** Most often from one person to another via respiratory droplets produced during coughing or sneezing by an infected person. The close contact person may inhale these droplets via mouths, noses, or eyes.
2. **Contact Transmission:** It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes.
3. **Aerosol Transmission:** When respiratory droplets mix into the air, forming aerosols and may cause infection when inhaled high doses of aerosols into the lungs in a relatively closed environment.

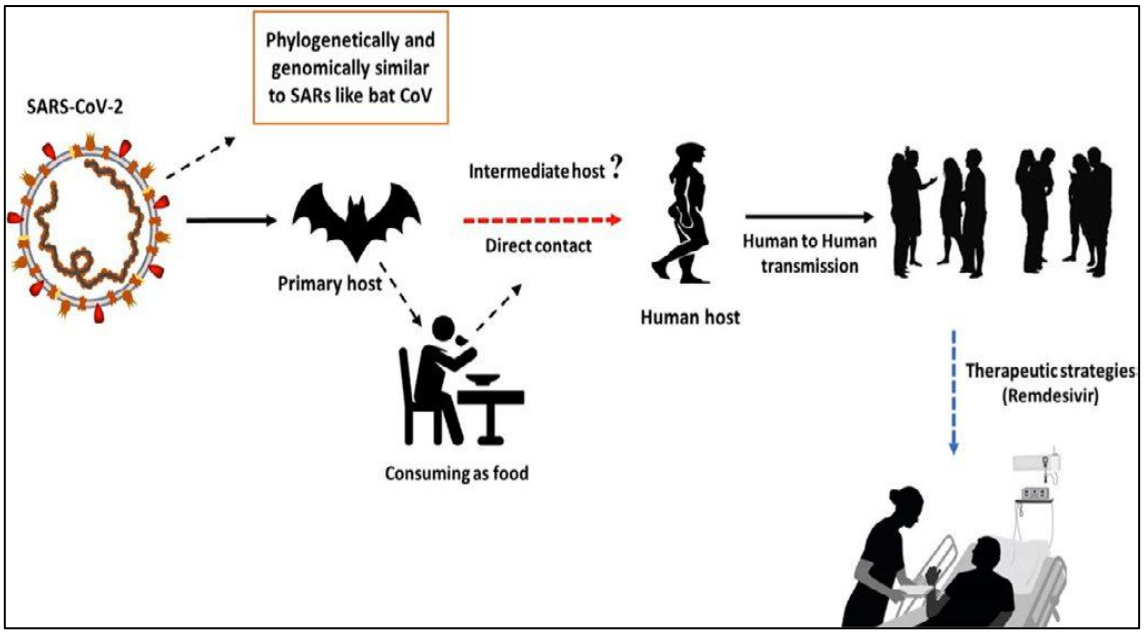

Fig. 3: Transmission of COVID-19 to a human host

In most of the cases of respiratory viruses, it has been found that people are thought to be most contagious when they are most symptomatic, but with COVID-19, there have been reports of spread from an asymptomatic infected patient to a close contact (CDC, 2020; Rothe, 2020). This leads to a widespread expansion of the disease through asymptomatic persons (Ruiyun, 2020).

Very limited information regarding COVID-19 during pregnancy is available. The intrauterine or perinatal transmission has not been identified. The limited studies on women infected with COVID-19, SARS-CoV, and another coronavirus infection suggest that the virus has not been detected in the breast milk, but whether mothers with COVID-19 can transmit the virus via breast milk is still unknown. The CDC has no specific guidance for breastfeeding during infection with similar viruses like MERS-CoV or SARS-CoV or also both coronaviruses. In a similar situation to COVID-19, the CDC recommends that a mother with flu continue breastfeeding or feeding expressed breast milk to her infant while taking precautions to avoid spreading the virus to her infant. Given low rates of transmission of respiratory viruses through breast milk, the World Health Organization presently states that mothers with COVID-19 can breastfeed (Academy of Breastfeeding Medicine, 2020).

PREVENTION OF COVID-19

One of the main focal points to control the spread of the virus within the community is to isolate the peoples who are suspected or confirmed to have the disease from other healthy people. Confirmed cases of infected patients should be treated by health workers using strict infection control precautions. There is a need to identify the social contacts with symptomatic individuals and kept them in isolation for at least 14 days for the monitoring of the onset of any symptoms (FIP Health Advisory, 2020).

There are some standard recommendations issued by WHO for the general public to reduce exposure to and transmission of this disease are as follows, which include hand and respiratory hygiene, and safe food practices (WHO, 2020):

1. Always clean the hands by using soap and water by following safe hand cleaning procedures at a regular interval.
2. Try to rub hands with alcohol-based sanitizer frequently.
3. Always cover the mouth and nose with a flexed elbow or tissue during coughing and sneezing. Through the tissue away immediately and wash the hands.

4. Always wear mask and gloves while going to markets or crowded places.
5. Avoid close contact with anyone who has a fever and cough.
6. If you have a fever, cough, and difficulty breathing seek medical care early and share previous travel history with your healthcare provider.
7. When visiting live markets in areas currently experiencing cases of a novel coronavirus, avoid direct unprotected contact with live animals and surfaces in contact with animals.
8. The consumption of raw or undercooked animal products should be avoided. Raw meat, milk, or animal organs should be handled with care, to avoid cross-contamination with uncooked foods, as per good food safety practices.

Self-isolation by persons with symptoms and/or persons who may have been in contact with infected persons:

Self-isolation means avoiding situations where you could infect other people. This means all situations where you may come in contact with others, such as social gatherings, workplaces, schools, child care/pre-school centers, universities, faith-based gatherings, aged care, and health care facilities, prisons, sports gatherings, supermarkets, restaurants, shopping malls, and all public gatherings. (Ministry of Health of New Zealand, 2020).

TREATMENT OF COVID-19

The treatment of COVID-19 disease is supportive and symptomatic. The first step is the isolation of positive cases of patients to stop the spread of transmission. Currently, there are no specific antiviral drugs or vaccines for COVID-19 infection. At present, drugs like nucleoside analogues and also HIV-protease inhibitors which could attenuate virus infection has been available as an option for use (Lu H, 2020).

Antiviral therapy is mainly used for both symptomatic and supportive treatment based on the clinical condition of the infected patients. However, supportive treatments include oxygen therapy, fever/pain control, hydration, and antibiotics in the presence of bacterial co-infection (FIP Health Advisory, 2020).

Currently, the antiviral drugs that can be tested for the treatment include α-Interferon, ribavirin, lopinavir-ritonavir, chloroquine phosphate, umifenovir, etc. However, further evaluation is required to know the efficacy of the currently recommended trial drugs in clinical applications (FIP Health Advisory, 2020). Most of these antiviral drugs have been tried to depend on the anecdotal knowledge with HIV, SARS and MERS infection therapies (Shen et al., 2020; Dong et al., 2020).

One of the immunotherapy drug tocilizumab can be tried in patients with extensive lung disease and severe disease. The use of three or more antiviral drugs at the same time is not recommended. Relevant diagnosis and treatment guidelines emphasize the avoidance of the blind or unreasonable application of antibacterial drugs or glucocorticoids (NHM, China, 2020).

Convalescent Plasma Therapy (CPT): Convalescent plasma therapy was first successfully used in the treatment of SARS & H1N1 influenza (Chen L, 2020). This method is very effective against these diseases which encourages health professionals to use this method for the treatment of COVID-19 infected patients. This therapy can be used for those COVID-19 infected patients who have rapid disease progression, severe and critical illness. (NHM, China, 2020). CPT utilizes a certain titre of virus-specific antibodies in the plasma of the convalescent individual to enable the patient to receive the infusion to obtain passive immunity and remove pathogens from the blood circulation.

The use of CPT treatment can follow the following principles (NHM, China, 2020):

1. In principle, the course of disease does not exceed three weeks. Also, the patient should have a positive viral nucleic acid test or viraemia certified by clinical experts.
2. Patients with severe disease with rapid disease progression, or critically ill early-

stage patients, or patients comprehensively evaluated by clinical experts as requiring plasma therapy. The infusion dose is determined according to the clinical situation and the weight of the patient, usually the infusion dose is 200-500 ml (4-5 ml/kg).

Advances in Vaccine Developments: Vaccine development is a very long time-taking process. It involves procedures such as virus strain isolation and selection, in vitro experiments, animal experiments, clinical trials, and administrative approvals. At present, some recognition sites for SARS-CoV-2 have been found and can be used for vaccine development (Ahmed SF, 2020; Ramaiah A, 2020).

CONCLUSION

The COVID-19 outbreak is proving to be an unprecedented disaster for the whole world. It affects the countries in all aspects especially health, social, and economic. Developing countries seem to face a catastrophic perspective than the developed countries. Extensive measures are required to control the current outbreak. Special efforts need to be put in place to protect or reduce transmission within the community including children, health care professionals, and elderly people. The COVID-19 infections should be mostly thought in the cases with fever, cough, and sore throat that have had contact with a suspected/verified cases. There is a lot of curiosity among the peoples about the COVID-19. Therefore, a guideline has been published for healthcare professionals, public health individuals, and researchers interested in the COVID-19 (Jin et al., 2020).

The early death case of the COVID-19 outbreak was occurred primarily in elderly people due to their weak immune system that permits faster progression of the infection. To decrease the danger of spread in society, people should be advised to wash hands assiduously, carry out respiratory hygiene, and keep away from crowds and close contact with sick individuals. Facemasks are not regularly suggested for asymptomatic cases, but social distancing is advised in every place that has society spread. Regular monitoring of any epidemiological changes in COVID-19 infection should be carried out by taking into the consideration of route of transmission and sub-clinical infections, including the adaptation, evolution, and virus spread among the humans and possible reservoirs.

There is no specific vaccine or medicine that has been fully tested for efficacy and safety against COVID-19 yet. Various clinical trials are going on worldwide to develop an effective vaccine for COVID-19. The most clinical trials of antiviral medicines are anti-HIV medicine such as ritonavir-lopinavir, azivudine, darunavir-cobistastat, followed by anti-influenza viruses medicine such as umifenovir, fapilavir and some clinical trials of remdesivir, which are considered to be very effective against COVID-19 infection.

Since the outbreak of COVID-19, it becomes a rapidly growing body of literature for researchers and health professionals all over the world. Everyone is putting all efforts into finding an effective vaccine and the best practices for the management and treatment of the symptomatic as well as asymptomatic cases. Once this pandemic ends, one will be able to assess the health, social, and economic impact that occurs worldwide due to this disease outbreak. This outbreak of COVID-19, allows us to learn a lesson especially in terms of public and global health for any future pandemics.

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