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Review Article

Revisiting Covid-19: The Novel Disease That Shattered the World

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ABSTRACT

COVID-19 is a highly contagious disease which is caused by SARS-CoV-2. The disease was initially originated from Wuhan in China. SARS-CoV-2 has a similarity with the SARS-CoV virus and MERS virus. However, the fatality rate in infection caused due to SARS-CoV-2 is less as compared to the infection caused by SARS-CoV and MERS virus. Initially, the WHO had declared the disease as Public Health Emergency of International Concern, and later the disease was categorized as pandemic disease. The disease had affected more than 200 countries. The USA tops the list with the highest number of infected patients. The ACE is the primary receptor of this virus, and the transmission is through both direct and indirect contact. The disease is diagnosed through the reverse-transcription polymerase chain reaction and complimented with a chest computed tomography scan. There is no specific treatment of COVID-19, and supportive management is recommended in severe cases.

Key words: COVID-19, Transmission, MERS virus, SARS-CoV

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INTRODUCTION

The world is struggling to manage the Corona virus disease (COVID-19). The disease is caused by SARS-CoV-2. It is a highly contagious disease and is spreading too fast.

In late 2019, a patient in Wuhan, Hubei Province, People's Republic of China (PRC), was suffering from the disease which had the symptoms similar to viral pneumonia. Later, it was analyzed that the disease was caused by a novel Corona virus.¹ On December 31st, 2019, China informed the World Health Organization about this disease. On the 7th of January, the comprehensive structure of the virus revealed that the virus has more than 70% similarity with the SARS-CoV and more than 95% similarity with bat corona virus. Environmental samples from the Wuhan food market were positive indicating that that is the originating place of the virus. The first fatality from this virus was reported on 7th January 2020.

There were a couple of incidences in the past where the Corona virus from the animals has resulted in serious disease in humans. The first instance was the spreading of

Severe Acute Respiratory Syndrome (SARS) and causes severe deaths in China and Hong Kong with a fatality rate of 11%.² This incidence occurred in 2002-2003 when the virus generally found in bat cross over to the humans via the palm civet cats as a carrier. The second incidence was the spreading of Middle East respiratory syndrome Corona virus (MERS-CoV) in 2012. It too affected several people and lead to several deaths with a fatality rate of 34% with 27 countries reported the cases of this deadly disease.³

In this review, we would summarize information about Corona virus, the WHO notifications on the pandemic, symptoms, diagnosis, and treatment measures to manage this highly contagious disease.

HISTORY

Corona viruses are enveloped RNA virus having the diameter 60 nm to 140 nm. The virus has spikes like projection on its surface and has a crown-like appearance, hence the name given Corona virus.⁴ SARS-CoV-2 is classified in family Coronaviridae and order Nidovirales. The virus classified under nidovirales has non-segmented positive-sense RNA. They have large RNA genomes and

have a conserved genomic organization. They have a large replicase gene and have the capability of ribosomal frame shifting.

It is under the subfamily Coronavirinae which is further subdivided into four genera: Alpha Corona virus which includes human Corona virus (HCoV)-229E and HCoV-NL63, the Beta Corona virus which have HCoV-HKU1, HCoV-OC43, Severe Acute Respiratory Syndrome human Corona virus (SARS-HCoV), and Middle Eastern respiratory syndrome Corona virus (MERS-CoV), the Gamma Corona virus which contains viruses of birds and whales, and Delta Corona virus which has viruses from birds and pigs.⁶ It is interesting to note that the novel Corona virus, SARS-CoV 2 has been classified into the beta Corona virus genera containing viruses that cause highly deadly diseases i.e. SARS and MERS.

Like the other viruses, the SARS-CoV 2 too has various hosts including the initial host, the intermediate, and the final host. Fortunately, compared with the Middle East Respiratory Syndrome Corona virus and Severe Acute Respiratory Syndrome Corona virus, the novel Corona virus has low mortality, high infectivity, and transmission.⁷

WHO STATUS OF CORONA VIRUS

Looking into the rapid spreading and highly contagious nature of the disease, the WHO in its meeting on January 30, 2020, it was declared as the Public Health Emergency of International Concern (PHEIC) as per the International Health Regulations (IHR, 2005). It was because at that time, the disease had spread to 18 countries, and the cases of human to human transmission were reported in 4 countries. Further, on February 26, 2020, the USA witnessed the first case of disease that was not related to China. Although the new virus was initially named as 2019-nCoV, due to its similarity with the SARS-CoV virus, the experts of the International Committee on Taxonomy of Viruses named the virus as SARS-CoV 2. Because of the progressively increasing number of cases, the WHO, on February 28, 2020, elevates the threat of viruses to a 'very high' level. On March 11, 2020, when the number of countries affected were 114 with around 1,18,000 cases and 4000 deaths, and the number of infected patients outside China were increased approximately 13 times, WHO declared the disease as pandemic.⁸

EPIDEMIOLOGY

People with Corona virus infections were not limited to the originating country i.e. in China. Within a month of infection cases initiated at Wuhan, the SARS-CoV-2 virus spread rapidly to many parts of China.⁹ As on 1st July 2020, the total number of Corona virus cases were 10,592,134, and there were 514,072 deaths. The number of patients recovered was 5,801,131 and the active cases were 4,276,931. Out of these active cases, approximately 99% of cases are with mild condition and 1% of patients are in serious condition. USA topped the list with several cases followed by Brazil, Russia, India, and the UK. It had affected more than 200 countries worldwide.¹⁰

The presence of underlying medical conditions such as hypertension, coronary artery disease, and diabetes also

considered as risk factors for COVID-19 infection. In a study on 85 patients, with a median age 65 years, who died due to COVID-19, concluded that majority of the patients died due to multiorgan failure as respiratory failure was seen in 94% of patients, the shock was seen in 81% of the patients and acute respiratory distress syndrome was seen in 74% of cases.¹¹

PATHOGENESIS

Although being the novel Corona virus, the pathogenesis of this particular virus is not fully understood, however, a lot of information can be retrieved by studying the previous virus i.e. SARS-CoV virus and MERS virus that belongs to the same class.

Like SARS-CoV and MERS virus, the angiotensin-converting enzyme 2 (ACE2) is the main receptor for SARS-CoV-2. The angiotensin-converting enzyme 2 (ACE2) is expressed in alveolar monocytes, respiratory epithelium, macrophages, and vascular endothelium.¹² The primary route of this virus for entering the body is indirect or direct exposure to the respiratory tract. SARS-CoV 2 has the potential to replicate in the upper respiratory tract.^{12;} ¹³This fact is indicated through the isolation of live virus from the respiratory tract and the presence of messenger RNA in upper respiratory tract cells.¹³

The five-step constitute the life cycle of the virus inside a host. In the first step i.e. attachment, the virus firmly binds to the host receptors. In the second step, which is called penetration, the virus enters into the host cells. The entry may either through membrane fusion or endocytosis. After entry into the host cells, the virus releases its content in the host cells along with the RNA genome. The viral RNA enters the nucleus and initiates replication. This results in the formation of new viral particles, a step is known as maturation. The newly formed viral particles are released from the infected host cells in the final step by fusing with the plasma membrane.^{14,15}

The other viruses such as SARS-CoV and MERS use various strategies to avoid the immune attack. These viruses initiate the formation of double-layered vesicles that do not have pattern recognition receptors (PRRs). These receptors are responsible for recognizing pathogen-associated molecular patterns. These viruses replicate in these vesicles thereby avoiding the detection from the immune system.¹⁶ The presentation of antigen is also affected due to Corona virus infection. MERS Corona virus down regulates the gene expression of the antigen.¹⁷ Thus, the immune system evasion of SARS-CoV 2 should be considered while managing the disease and developing the drug.¹⁸

SPREAD OF CORONA VIRUS INFECTION

The transmission of infection is both through indirect contact and direct contact. Indirect contact includes airborne contagion and contaminated objects while direct contact includes human-to-human transmission and droplets. The airborne infection may also be caused due to personal protective equipment.¹⁹ Human to human transmission of SARS-CoV-2 may occur in the form of droplets. The infection through droplet spread when the

person coughs, talks, sings, or sneezes. In general cases, the droplets do not remain suspended in the air for a long period. However, droplets containing SARS-CoV-2 may remain suspended in the air for up to three hours.²⁰ The sufficient washing of hands, multiple time a day have been recommended. This is to avoid indirect transmission. The spread of infection may occur if the person touches the contaminated surface and touches the mouth, nose, or eyes with the contaminated hands.²¹ Normal speaking and breathing also have the potential to form an aerosol. The aerosol formation is also affected by the volume of speech, thus impacting the capacity of individuals in viral transmission.²² It is also important to note the resuspension of the floor aerosol may also be possible due to various human activities and may form an important part of the overall aerosol in an occupied area.^{23,24}

Cases have been reported where the transmission of infection has been from the people who do not have any symptoms and without any radiological findings. These also include the people in incubation period.^{25,26,27}

SYMPTOMS OF COVID-19

There is a stage of adaptive immunity after the initial stages of replication in the initial days of infection. During the replications of the virus, the patient experiences the symptoms similar to that of influenza. However, when the immune system of the body fights against the virus, there is a decline in viral levels. However, the increase in the level of cytokines leads to tissue destruction and deterioration. It indicates that there should be the use of antiviral medications in the initial stages of replication and later there should be administered on immunosuppressive therapy.^{28,29} In an observation done on 44,500 confirmed cases of COVID-19, it was indicated that the disease has the varying spectrum of illness ranging from the mild cases with no mild pneumonia to severe cases where patient experiences hypoxia, dyspnoea or have more than 50% of lung involvement. In 5% of the cases, the critical symptoms were experienced like sepsis, septic shock or Acute Respiratory Distress Syndrome.³⁰ In a retrospective study, clinical data of nine children and their families were collected and analyzed. After the families have onset, all the children were infected, and their results came positive. Three children have fever or cough, while the six others were asymptomatic. Among the 14 adult patients of the children's family, major symptoms reported were fever, cough, chest pain and tightness, fatigue, and sore throat. 10 adults have abnormal imaging with pulmonary consolidation, ground-glass opacity, and nodular show. Around 70% of the patients have normal, and 28% had reduced white blood cell counts.³¹

DIAGNOSIS OF THE DISEASE

COVID-19 is a highly contagious disease, and the laboratory staff involved in the testing of COVID-19 should have the proper equipment to prevent any transmission of COVID-19. For accurate and early results related to COVID-19 diagnosis, the sample should be taken at the right time from the correct site.³² The present diagnostic tests for COVID-19 include reverse-transcription polymerase chain reaction (RT-PCR), reverse transcription

loop-mediated isothermal amplification (RT-LAMP), and real-time RT-PCR (rRT-PCR).^{33,34}

Various guidelines have been recommended by the World Health Organization (WHO), Centre for Disease Control and Prevention (CDC), and Indian Council of Medical Research (ICMR). The specimen should be collected by the BSL-3 laboratory. The WHO recommends that the specimen should be collected from the lower respiratory tract and upper respiratory tract. From the upper respiratory tract, the oropharyngeal or nasopharyngeal swab should be collected while the sputum, tracheal aspirate, and bronchoalveolar lavage should be collected from the lower respiratory tract. The current diagnostic methods are time-consuming, resulting in the delay of test results. Further, there is a shortage of testing kits because of the large number of individuals affected by this disease. It is to be noted that despite the negative RT-PCR test results in patients experiencing fatigue, fever, sore throat, or dyspnoea, the COVID-19 infection should be diagnosed with typical chest computerized tomography.³⁵

DISEASE MANAGEMENT

Although there is no particular treatment for COVID-19, the early diagnosis, preventive measures, and supporting healthcare may result in reducing the outbreak of this pandemic disease. In critical cases, intravenous fluid infusion and oxygen therapy along with a life support system should be provided. As the proteins of Corona virus for replication are comparable to that of HIV, the HIV protease inhibitors may be used to treat COVID-19.³⁶ Vinyl sulfone protease inhibitors, and an angiotensin-converting enzyme-2 bases peptides have also shown antiviral properties.³⁷

At Sawai Man Singh Hospital in Jaipur, Rajasthan, India, an Italian patient was treated with the combination of ritonavir (50mg) and lopinavir (200mg) twice daily. Oseltamivir and chloroquine were also administered to the patient. The patient was found negative for COVID-19 after the treatment.³⁸ The critical patients should be provided with aggressive treatment. 5% of the patients suffering from COVID-19 become seriously ill and out of this 5%, almost 30% of the patients require intensive treatment. Patients who are not responding to standard oxygen therapy should be given advanced oxygen therapy of ventilation.

In the initial reports, the use of non-invasive ventilation was not supported because of the increased risk of spreading COVID-19 as the methods used for non-invasive ventilation produces aerosols.³⁹ However, it has now been proposed that CPAP can be used during the pandemic.⁴⁰

CONCLUSION

SARS-CoV-2 is taking a toll on the healthcare system of many countries and is a serious public threat because of its rapid transmission. Most patients experience mild to moderate symptoms while some experience severe symptoms. An early and accurate diagnosis of the disease is required to prevent the spread of infection. Positive cases without any symptoms are also noticed. There is no specific drug available for COVID-19 and thus, it is important to prevent and manage the disease by various

supplementary and supportive interventions. Various antiviral drugs that are used to treat SARS-CoV are also used to treat the SARS-CoV-2 and also to prevent COVID-19 pneumonia.

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