



COVID-19: A Threat to Mankind

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Abstract

An outbreak of pneumonia of unknown cause detected in Wuhan, China was first reported to the WHO Country Office in China on 31 December 2019. The outbreak was declared a Public Health Emergency of International Concern on 30 January 2020. Thousands of people died in China, and more than a million of people infected as 2019-nCoV continues to spread around the world. This novel virus spread mainly through respiratory droplets and close contact. As disease progressed, a series of complications tend to develop, especially in critically ill patients.

Keywords: COVID-19, Origin and spread, Transmission, Clinical features, therapeutic agents

Introduction

Currently, corona virus disease 2019 (COVID-19) poses a significant threat to global health. Within the first two months of the outbreak, the epidemic spread rapidly around the country and the world. The COVID-19 is an emerging disease, has unique biological characteristics, clinical symptoms, and imaging manifestations, though considerable progress has been made on the clinical management.

The Virus

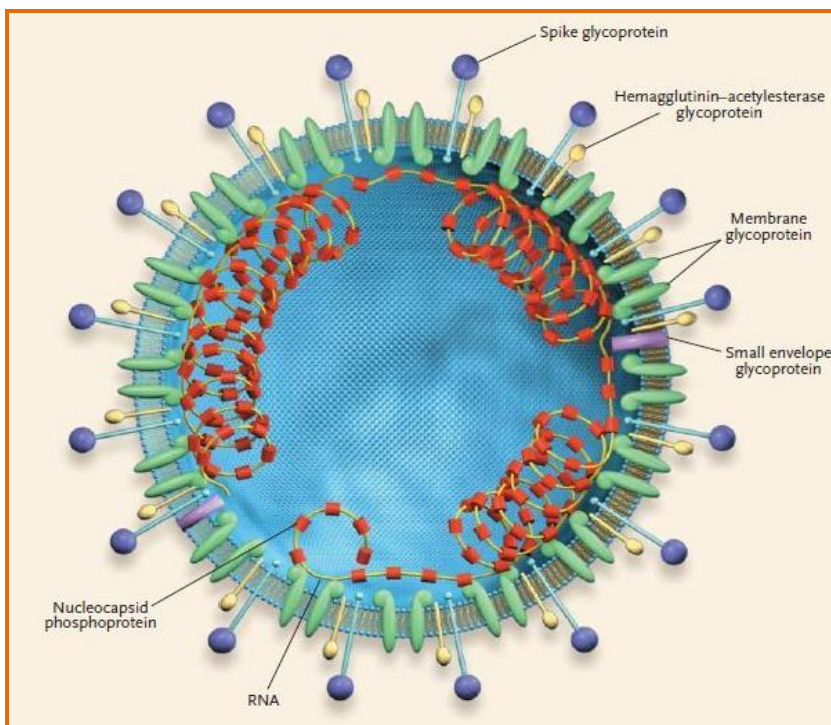
The Corona virus is an enveloped positive-sense RNA virus, which is characterized by club-like spikes projecting from its surface of S-glycoprotein. Although corona virus is commonly associated with acute respiratory infections in humans, its ability to infect multiple host species and a variety of diseases makes it a complex pathogen. The frequent interactions of wild animals with humans make them a

common source of zoonotic infections. The 2019-nCoV is the new member of the genus *Betacoronavirus*.

Currently, there is only one complete 2019-nCoV genome (29870-bp, excluding the poly(A) tail) in GenBank (accession number MN908947). Five typical ORFs on the same coding strand were identified, including ORF1ab polyprotein (7096-aa), spike glycoprotein (1273-aa), envelope protein (75-aa), membrane protein (222-aa), and nucleocapsid protein (419-aa). Our pair-wise sequence analysis demonstrated that bat SARS-like corona virus (Genbank accession number MG772933) was the closest relative to 2019-nCoV, sharing 88% nucleotide similarity. The rapid spread of 2019-nCoV appears to have resulted from human-to-human transmission.

As an RNA virus, 2019-nCoV still has the inherent feature of a high mutation rate, although like other corona viruses the mutation rate might be somewhat lower than other RNA viruses because of its genome-encoded exonuclease². This aspect provides the

possibility for this newly introduced zoonotic viral pathogen to adapt and become more efficiently transmitted from person to person and possibly become more virulent.



Structure of the Coronavirus Virion

Source: Internet

Origin and spread

In December 2019, adults in Wuhan, capital city of Hubei province and a major transportation hub of China started presenting to local hospitals with severe pneumonia of unknown cause. Many of the initial cases had a common exposure to the Huanan wholesale seafood market that also traded live animals. The surveillance system (put into place after the SARS outbreak) was activated and respiratory samples of patients were sent to reference labs for etiologic investigations. On December 31st 2019, China notified the outbreak to the World Health Organization and on 1st January the Huanan sea food market was closed. On 7th January the virus was identified as a corona virus that had >95% homology with the bat corona virus and > 70% similarity with the SARS- CoV. Environmental samples from the Huanan sea food market also tested positive, signifying that the virus originated from there². The number of cases started increasing exponentially, some of which did

not have exposure to the live animal market, suggestive of the fact that human-to-human transmission was occurring. The first fatal case was reported on 11th Jan 2020. The massive migration of Chinese during the Chinese New Year fuelled the epidemic. Cases in other provinces of China, other countries (Thailand, Japan and South Korea in quick succession) were reported in people who have travel history from Wuhan. Transmission to healthcare workers caring for patients was described on 20th Jan, 2020. By 23rd January, the 11 million population of Wuhan was placed under lock down with restrictions of entry and exit from the region. Soon this lock down was extended to other cities of Hubei province. Cases of COVID-19 in countries outside China were reported in those with no history of travel to China suggesting that local human-to-human transmission was occurring in these countries. Airports in different countries put in screening mechanisms to detect symptomatic people returning from China and placed them in isolation and testing them for COVID-19.

Soon it was apparent that the infection could be transmitted from asymptomatic people and also before onset of symptoms.

Therefore, countries evacuated their citizens from Wuhan through special flights or had travelers returning from China, placed all people symptomatic or otherwise in isolation for 14 days and screened them for the virus.

Transmission

Human-to-human transmission of SARS-CoV-2 occurs mainly between family members, including relatives and friends who intimately contacted with patients or incubation carriers. The transmission of SARS-CoV and MERS-CoV is also reported to occur mainly through nosocomial transmission. Infections have occurred in healthcare workers in 33–42% of cases and transmission between patients (62–79%) has become the most common route of infection in COVID-19 cases. Direct contact with intermediate host animals or consumption of wild animals was suspected to be the one of the main route of SARS-CoV-2 transmission. However, the various sources and transmission routines of SARS-CoV-2 remain elusive.

Based on the large number of infected people that were exposed to the wet animal market in Wuhan City where live animals are routinely sold, it is suggested that this is the likely zoonotic origin of the COVID-19. Efforts have been made to search for a reservoir host or intermediate carriers from which the infection may have spread to humans. Initial reports identified two species of snakes that could be a possible reservoir of the COVID-19. However, to date, there has been no consistent evidence of corona virus reservoirs other than mammals and birds. Genomic sequence analysis of COVID-19 showed 88% identity with two bat-derived severe acute respiratory syndromes (SARS)-like corona viruses, indicating that mammals are the most likely link between COVID-19 and humans. Person-to-person transmission seems to be a most likely route for spreading COVID-19 infection. This is supported by cases that occurred within families and among people who did not visit the wet animal market in Wuhan. Person-to-person transmission occurs primarily via direct contact or through droplets spread by coughing or sneezing from an infected individual.

Relation with other corona viruses

The COVID-19 represents the seventh member of the corona virus family that infects humans and has been classified under the Orthocoronavirinae subfamily. The COVID-19 forms a clade within the subgenus Sarbecovirus. Based on the genetic sequence identity and the phylogenetic reports, COVID-19 is sufficiently different from SARS-CoV and it can thus be considered as a new Betacoronavirus that infects humans. The COVID-19 most likely developed from animal origin due to high degree of homology of the ACE2 receptor from a diversity of animal species, thus implicating these animal species as possible intermediate hosts or animal models for COVID-19 infections. Moreover, these viruses have a single intact open reading frame on gene 8, which is a further indicator of animal origin Corona Virus. However, the amino acid sequence of the tentative receptor-binding domain resembles that of SARS-CoV, indicating that these viruses might use the same receptor

Clinical features

The COVID-19 is now classified as four levels based on the severity of symptoms: mild, moderate, severe, and critical. Mild patients only present mild symptoms without radiographic features. Moderate patients present with fever, respiratory symptoms, and radiographic features. Severe patients meet one of three criteria: (a) dyspnea, RR greater than 30 times/min, (b) oxygen saturation less than 93% in ambient air, and (c) $\text{PaO}_2/\text{FiO}_2$ less than 300 mm Hg³. Critical patients meet one of three criteria: (a) respiratory failure, (b) septic shock, and (c) multiple organ failure.

Clinical symptoms of severe and critical patients with COVID-19 resembled most of SARS and MERS, including fever, dry cough, myalgia, fatigue, dyspnea, anorexia, diarrhea, arrhythmia, acute kidney injury, various degrees of liver damage, and septic shock. Common symptoms of hospitalized patients with COVID-19 included fever (98.6%), fatigue (69.6%), dry cough, and diarrhea. Less common symptoms included muscle ache, confusion, headache, sore throat, rhinorrhoea, chest pain, sputum production, and nausea and vomiting. Severe complications included anemia, acute cardiac injury and multiple organ failure. The median time from first symptom to dyspnea was 5.0 days, to hospital admission was 7.0 days, and to multiple organ failure was 8.0 days.

A few patients had symptoms, such as nasal congestion, runny nose, sore throat, myalgia, and diarrhea. Most patients had a good prognosis according to the guidelines for diagnosis and treatments for COVID-19.

Gastrointestinal manifestations and fecal–oral transmission

Detection of extra-pulmonary viral RNA suggests presence of infectious virus; further positive viral culture suggests the possibility of salivary gland infection and possible transmission. Successful isolation of live 2019-nCoV from the stool of patients has also been attempted¹. Taken together, a growing number of clinical evidence reminds us that digestive system other than respiratory system may serve as an alternative route of infection when people are in contact with other family members along with pets and also with infected wild animals.

Difference from other pneumonia

However, the caused symptoms of the virus are similar to those of and the outbreak is occurring during endemic presence of respiratory illnesses from influenza, respiratory syncytial virus, and other respiratory viruses. The CT scan is a useful tool to screen the suspected cases of 2019-nCoV infection as most NCOVID-19 patients but NON-NCOVID-19 had bilateral pneumonia with the feature of a multiple mottling and ground-glass opacity in CT images. The ratio mean of neutrophils is slightly higher in NCOVID-19 than in NON-NCOVID-19 although no statistic difference observed.

Host range

The corona virus infections have also been reported in cattle, swine, horses, camels, rodents, cats, dogs, bats, palm civets, ferrets, mink, rabbits, snake, and several other wild animals and avian species³. Though human corona virus have been identified for the first time in the year 1960 from respiratory infections in adults as well as children, the major scientific interest in corona virus research grew only after the emergence of Severe Acute Respiratory Syndrome corona virus (SARS-CoV) in the year 2002-2003. Following SARS-corona virus incidence in 2003, a similar corona virus named HKU3-1 to HKU3-3 was identified in the horseshoe bats in 2005 from Hong Kong. Since then, bats are considered to be the natural host and potential reservoir⁵.

Relation with climate

The Corona virus Disease 2019 (COVID-19), caused by SARS-CoV-2, has established significant community spread in cities and regions along a narrow east west distribution roughly along the 30-50° N' corridor at consistently similar weather patterns consisting of average temperatures of 5-11°C, combined with low specific (3-6 g/kg) and absolute humidity (4-7 g/m³). Through March 10, 2020, significant community transmission has occurred in a consistent east and west pattern. Initially, the new epicenters of disease were all roughly along the 30-50° N' zone; to South Korea, Japan, Iran, and Northern Italy. COVID-19 failed to spread significantly to countries immediately north (such as Russia and Mongolia) and south of China. The number of patients and reported deaths in Southeast Asia is much less when compared to more temperate regions noted above. The association between temperature and humidity in the cities affected with COVID-19 deserves special attention. There is a similarity in the measures of average temperature (5-11°C) and RH (44-84%) in the affected cities and known laboratory conditions that are conducive to corona virus survival (4°C and 20-80% RH)⁴. It is important to note that even colder areas in the more northern latitudes have been relatively free of COVID-19 pointing to a potential minimum range for the temperature, which could be due to avoidance of freeze-thaw cycles.

Potential therapeutic agents against COVID-19

The outbreak of corona virus caused by the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is spreading very fast all over the world. Agents or vaccines of proven efficacy to treat or prevent human corona virus infection are in urgent need and are being investigated vigorously. There are evidence of potential therapeutic agents, such as lopinavir/ritonavir, remdesivir, favipiravir, chloroquine, hydroxychloroquine, interferon, ribavirin, tocilizumab, ivermectin and sarilumab. More clinical trials are being conducted for further confirmation of the efficacy and safety of these agents in treating COVID-19.

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Access this Article in Online	
	Website: www.ijarbs.com
	Subject: Virology
Quick Response Code	
DOI: 10.22192/ijarbs.2020.07.04.013	

How to cite this article:

Sanower, A. K. Upadhyay, Ansari Iram, Singh N.K. and Maansi. (2020). COVID-19: A Threat to Mankind. *Int. J. Adv. Res. Biol. Sci.* 7(4): 126-130.
DOI: <http://dx.doi.org/10.22192/ijarbs.2020.07.04.013>