A Detailed Essay on the Pandemic COVID-19

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Abstract

The name "coronavirus" comes from the crown-like projections on their surfaces. "Corona" in Latin means "halo" or "crown". Coronavirus is causing an outbreak that was first identified in Wuhan City, Hubei Province, China. Since then, the virus has spread to nearly every country, leading the World Health Organization (WHO) to declare this as a pandemic. According to WHO, common signs include fever, cough, and respiratory difficulties. Serious cases can lead to pneumonia, kidney failure, and even death. Researchers believe that the viruses transmit via fluids in the respiratory system. Centre for Diseaase control and Prevention(CDC) recommends that all people wear masks in public places where it is difficult to maintain a 6-foot (2-meter) distance from others. Social distancing is advised as currently there are no drugs or other therapeutics approved by the US Food and Drug Administration(FDA) to prevent or treat COVID-19. Current clinical management includes infection prevention, control measures, and supportive care, including supplemental oxygen and mechanical ventilator support when indicated. However, hydroxychloroquine and chloroquine are under investigation in clinical trials for pre-exposure or post-exposure prophylaxis infection, and treatment of patients with COVID-19. Also, FDA has issued guidance for administering and studying the use of convalescent plasma therapy which aims at using antibodies from the blood of a recovered COVID-19 patient to treat those critically affected by the virus. People can take steps to prevent the spread of coronavirus and help protect themselves and others.

Key Words: *Coronavirus, COVID-19, SARS-CoV 2, Viral Infection, Pandemic.*

Introduction

At the beginning of December 2019, a novel coronavirus has caused an international outbreak of respiratory illness termed as COVID-19.(1) The pathogen has been identified as a peculiarly enveloped RNA β-coronavirus that has presently been named as Severe acute respiratory syndrome coronavirus 2(SARS-CoV 2).(2) Phylogenetic data implies a zoonotic origin and the rapid widespread suggests an ongoing person to person transmission.(3) It emerged from Wuhan, China, and spread to other countries both in and outside china leading WHO to declared coronavirus disease 2019(COVID-19) a public health emergency of international concern.(2)

Coronaviruses (CoVs) are the largest group of viruses affiliated to the *Nidovirales*order, which incorporates *Coronaviridae, Arteriviridae, Mesoniviridae*, and *Roniviridae* families. The *Coronavirinae* consists of one of two subfamilies in the Coronaviridae family, with the other being the *Torovirinae*. In *Nidovirales* order the viruses are enveloped by non- segmented positive-sense RNA viruses.(4)

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The *Coronavirinae* are further separated into four genera, the alpha, beta, gamma, and delta coronaviruses. The viruses were initially categorized into these genera based on serology and later separated by phylogenetic clustering.[4]

Seven types of coronavirus that can infect humans are identified by the doctors. Common types include[5] :

229E (alpha coronavirus)

NL63 (alpha coronavirus)

OC43 (beta coronavirus)

HKU1 (beta coronavirus)

Since the beginning of the 21st century two β-coronaviruses have induced the plague of deadly pneumonia in humans. In humans the severe acute respiratory syndrome coronavirus (SARS CoV) arise and was liable for an epidemic that circulated to five continents with a fatality rate of 10% before being contained in 2003. In the Arabian Peninsula in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV) emerged and induced recurrent outbreaks in humans with a fatality rate of 35%. SARS-CoV and MERS-CoV are zoonotic viruses that navigated across the species barrier using bats/palm civets and dromedary camels' respectively.[6]

Structure

The virions are spherical with a diameter of roughly 125nm. The most distinguishable feature of coronaviruses is the club-shaped spike projections emanating from the surface of the virion. These spikes are defining features and give the appearance of a solar corona, suggesting the name, coronaviruses. Coronavirus particles contain four main structural proteins. These are the spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins, all of these are encoded within the 3′ end of the viral genome. The S protein utilizes an N-terminal signal sequence to gain access to the endoplasmic reticulum and is heavily N-linked glycosylated. Homotrimers of the virus-encoded S protein make up the distinctive spike structure on the surface. The M protein is the most abundant structural protein and is thought to give the virion its shape. The nucleocapsid constitutes of N protein and is helically symmetrical composed of two separate domains, an N-terminal domain, and a C-terminal domain, both capable of binding RNA in vitro. A fifth structural protein, the hemagglutinin-esterase (HE), acts as a hemagglutinin, binds sialic acids on surface glycoproteins, and contains acetyl-esterase activity.[4]

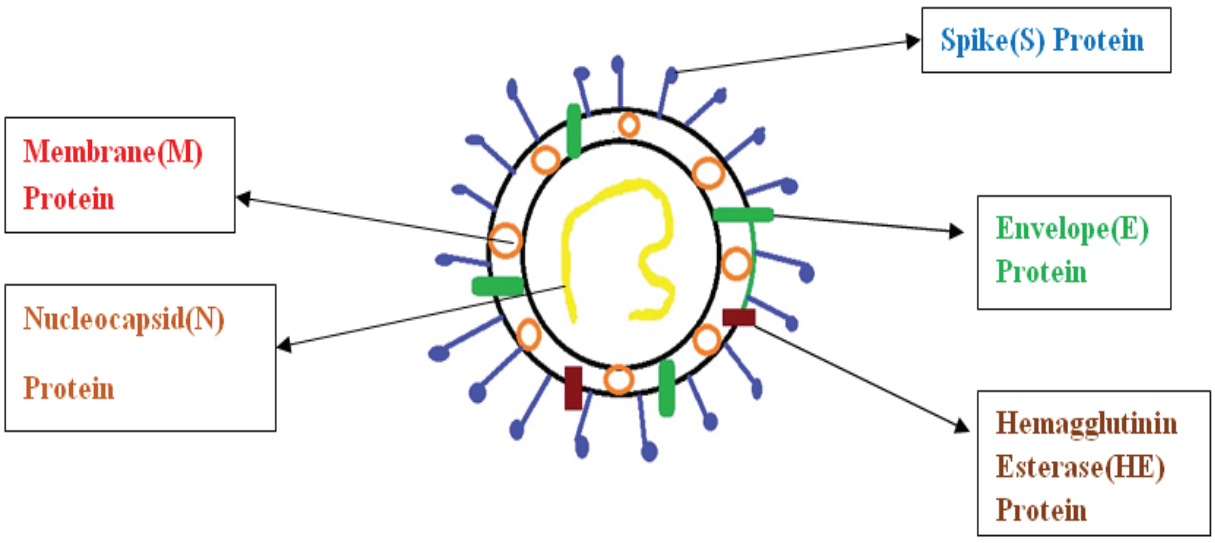

Figure 1: Structure

**This Image is just for better understanding and may differ from original viral structure.*

Life Cycle

Attachment and Entry

The initial attachment to the host cell by the virion is initiated by interactions between S protein and its receptor. Virus acquires entry into host cell cytosol which is attained by acid-dependent proteolytic cleavage of S protein. This is accompanied by the fusion of virus and cellular membrane.

Replicase Protein Expression

Further there is a transfer of the replicate gene from virion genomic RNA. This is accompanied by the replicated gene that encodes two large open reading frames (ORFs), rep1a, and rep1b, which express two co-terminal polyprotein pp1a and pp 1b. This causes ribosomal frameshifting from the rep1a reading frame into rep1b ORF. The pseudoknot is unwound by the ribosome and this continues till it reaches stop codon.

Replication and Transcription

After the translation is done the viral RNA synthesis occurs which produces both RNA and subgenomic RNA which are further formed by negative intermediates. After viral RNA synthesis, viral replicase complexes are formed.

Assembly and release

Viral structural proteins S, E, and M are translated and inserted into the Endoplasmic Reticulum. These proteins move along the secretory pathway into ERGIC (Endoplasmic Reticulum-Golgi Intermediate Compartment). Viral genomes encapsulated by N-protein bud into membranes of ERGIC which contains viral structural proteins. And form mature virion.[4]

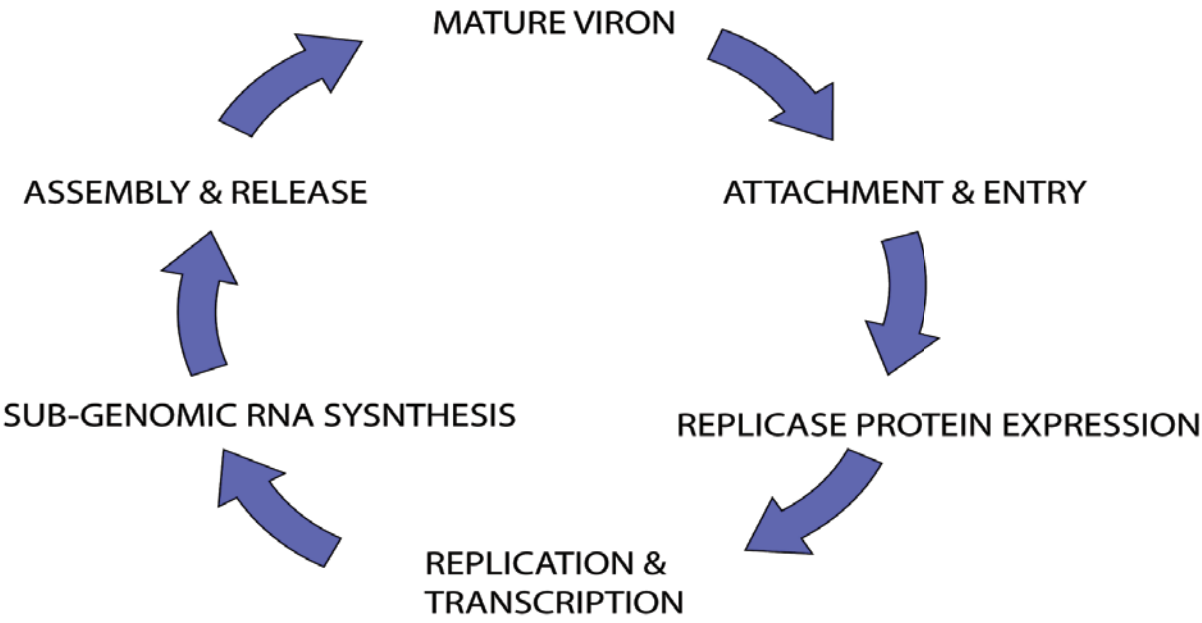

Figure 2: Life Cycle

Epidemiology

According to WHO dashboard, the worldwide reports are as follows[7] :

Weeks	Date	No. of infected patients worldwide	No. of Deaths
1st	26/1/2020	2014	56
2nd	2/2/2020	14557	305
3rd	9/2/2020	37558	813
4th	16/2/2020	51857	1669
5th	23/2/2020	78811	2461
6th	1/3/2020	87137	2977
7th	8/3/2020	105836	3584
8th	15/3/2020	153517	5735
9th	29/3/2020	634813	29891
10th	5/4/2020	1133758	62784
11th	12/4/2020	1696588	105952
12th	19/4/2020	2241778	152551

Transmission

The first cases of the COVID-19 disease were linked to direct exposure to the Huanan Seafood Wholesale Market of Wuhan, the animal-to-human transmission was presumed as the main mechanism. However, subsequent cases were not associated with this exposure mechanism. Hence, it was concluded that the virus could also be transmitted from human-to-human.[8]

Due to the limited research it is not clear as to how the human coronavirus spreads and further studies are needed to understand the mechanisms of transmission, incubation times and clinical course, and the duration of infectivity. However, researchers believe that the viruses transmit via fluids in the respiratory system, such as mucus.[9] Coronaviruses can spread in the following ways[9] :

While coughing and sneezing, not covering mouth by tissues or masks can scatter droplets.

Touching or shaking hands with the patient who has the virus can infect other individuals.

Making contact with a surface or object with the virus and later touching the nose, eyes, or mouth.

Some animal coronaviruses, such as feline coronavirus, may spread through contact with feces. However, it is unclear whether this also applies to human coronaviruses.

Symptoms

It may take 2–14 days for a person to notice symptoms after infection.

According to the CDC, children are not at higher risk of COVID-19. Although there are currently no published scientific reports about the susceptibility of pregnant women, the CDC notes that**:**"Pregnant [women] have had a higher risk of severe illness when infected with viruses."The CDC also recommends that infants born to mothers with suspected or confirmed COVID-19 go into isolation. Also people aged 65 years or older, living in nursing home or care facilities and people of any age who have serious underlying medical conditions, including chronic lung disease, serious heart conditions, severe obesity, a compromised immune system, or diabetes are at higher risk.

Cold or flu-like symptoms usually set in from 2–4 days after a coronavirus infection and are typically mild. However, symptoms vary from person-to-person, and some forms of the virus can be fatal.[9]

Symptoms may include [10] :

Sneezing

Runny nose

Fatigue

Cough

Breathlessness

Fever

Sore throat

The potential loss of taste or smell

Exacerbated asthma

Diagnosis can be done by suggested procedures: performing real-time fluorescence reverse transcriptase-polymerase chain reaction (RT-PCR) to detect the positive nucleic acid of SARS- CoV-2 in sputum, throat swabs and secretions of lower respiratory tract samples and also by taking a sample of respiratory fluids, such as mucus from the nose, or blood.[9]

Concerning laboratory examinations, in the early stage of the disease, a normal or decreased total white blood cell count and a decreased lymphocyte count can be demonstrated. Increased values of liver enzymes, lactate dehydrogenase, muscle enzymes, and C-reactive protein can be found. In critical patients, D-dimer value is increased, blood lymphocytes decreased persistently, and laboratory alterations of multiorgan imbalance (high amylase, coagulation disorders, etc.) are found.[5]

Treatment

There is no cure for coronaviruses that cause symptoms resembling the common cold. Treatments include self-care and over-the-counter medication. [9] Currently there are no drugs or other therapeutics approved by the US FDA to prevent or treat COVID-19. Current clinical management includes infection prevention and control measures and supportive care, including supplemental oxygen and mechanical ventilatory support when indicated. Interim guidelines for the medical management of COVID-19 will be provided soon by the Department of Health and Human Services COVID-19 Treatment Guidelines Panel.

Remdesivir:

Remdesivir is an investigational intravenous drug with the broad antiviral activity that inhibits viral replication through premature termination of RNA transcription and has in-vitro activity against SARS-CoV-2 and in-vitro and in-vivo activity against related β-coronaviruses.

Hydroxychloroquine and Chloroquine:

Hydroxychloroquine and chloroquine are oral prescription drugs that have been used for the treatment of malaria and certain inflammatory conditions. Hydroxychloroquine and chloroquine are under investigation in clinical trials for pre-exposure or post-exposure prophylaxis of SARS-CoV-2 infection, and treatment of patients with mild, moderate, and severe COVID-19. FDA issued an Emergency Use Authorization (EUA) to authorize the use of chloroquine and hydroxychloroquine external icon from the Strategic National Stockpile for treatment of hospitalized adults and adolescents (weight ≥50 kg) with COVID-19 for whom a clinical trial is not available or participation is not feasible.

Other Drugs:

Several other drugs (e.g., investigational antivirals, immunotherapeutic, host-directed therapies) are under

investigation in clinical trials or are being considered for clinical trials of pre-exposure prophylaxis, post-exposure prophylaxis, or treatment of COVID-19 in the United States and worldwide. FDA has issued guidance for administering or studying the use of convalescent plasma therapy.[11]

Plasma Therapy:

Amongst the myriad clinical trials for vaccines to prevent COVID-19 and drugs to treat infections, doctors are looking to survivors' plasma for a possible therapy. The US FDA released a statement stating that investigators can request to use plasma from COVID-19 survivors to deliver antibodies to seriously ill patients, under an emergency investigational new drug (IND) protocol. It is based on the premise that because antibodies were developed in the survivor were throughout the course of their infection, donating blood to those who became recently ill would give the recipients' immune systems a leg up. To bring the treatment up to modern standards, plasma donations would be processed and purified, creating a serum to transfuse into critically ill patients. While an eventual vaccine would ideally provide long-lasting immunity by spurring the recipient to create their own antibodies, receiving antibodies via the convalescent treatment would only form a temporary immunity, so multiple treatments would be required over the course of illness.

There are still certain details that needs to be figured out in using convalescent plasma for COVID-19 treatment, which also includes determining an effective dosing size. In its statement announcing the emergency IND access protocols, the FDA outlined standards for donor and recipient eligibility.

Plasma transfusions are commonplace nowadays, but are not without risks. Severe lung injury or allergic reactions can occur after receiving donor plasma which is contradicted in COVID-19.[12]

Ineffective Therapies:

Many patients were administered with lopinavir and ritonavir. It wasn't much effective because even highly active antibacterial agents have limited efficacy in advanced bacterial pneumonia. Secondly, lopinavir isn't particularly potent against SARS-CoV-2. The concentration necessary to inhibit viral replication is relatively high as compared with the serum levels found in patients treated with lopinavir-ritonavir. We currently know little about drug concentrations in the tissues.[3]

Preventive Measures:

COVID-19, a contact-transmissible infectious disease, is thought to spread through a population via direct contact between individuals. Outbreak control measures aimed at reducing the amount of mixing in the population have the potential to delay the peak and reduce the final size of the epidemic. To evaluate the effect of location-specific physical distancing measures such as extended school closures and interventions in workplaces are advised.[13]

The virus is contagious because of its ability to mutate effectively. To prevent transmission, people should maintain social distancing,stay at safe place and isolate themselves if symptoms are active. Covering the mouth and nose at public places with a mask can also help prevent transmission. Also, washing hands regularly and the use of sanitizers and disinfectants are vital. It is important to dispose of any tissues after use and maintain hygiene.[14]

The CDC recommends that everyone wear cloth face masks in public places where it is difficult to maintain a 6-foot (2-meter) distance from others. This will help slow the spread of the virus from asymptomatic people. People should wear cloth face masks while continuing to practice physical distancing. **Note:**Surgical masks and N95 respirators must be reserved for healthcare workers.[9]

The disadvantaged socio-economic positioned individuals are more likely to be affected by the virus because of occupation, income, and education. We rely on quarantine, isolation, and infection-control measures to prevent disease spread and on supportive care for those who become ill.[15] The proposal should converge on four fundamental values: maximizing the benefits produced by scarce resources, treating people equally, promoting and rewarding instrumental value, and giving priority to the worst off. These procedures must be transparent to ensure public trust in their fairness.[14]

Conclusion

Non-pharmaceutical interventions based on sustained physical distancing have a strong potential to reduce the magnitude of the epidemic peak of COVID-19 and lead to a lesser number of overall cases. Lowering and flattening of the epidemic peak is particularly important, as this reduces the acute pressure on the health-care system. The premature and sudden lifting of interventions could lead to an earlier secondary peak, which could be flattened by relaxing the interventions gradually.Governments and policymakers must do all they can to prevent the scarcity of medical resources. Maximization of benefits can be understood as saving the most individual lives or as saving the most life-years by giving priority to patients likely to survive the longest after the treatment.

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Ethical Clearance: This is a research article so no ethical clearance is required for it.

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