

The Pandemic of 21st Century - COVID-19

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ABSTRACT

BACKGROUND

The global pandemic of novel coronavirus disease is mainly caused by the infection of Coronavirus 'SARS-CoV-2'. It is infecting persons of all ethnicity, race and community. Corona viruses are enveloped RNA viruses which range from 60 to 140 nm in diameter with spike like projections on their top. Coronavirus is affecting 199 countries, territories and international transport systems. Covid-19 is a recent pandemic, which started in Wuhan, China, at the end of 2019 and now it is affecting the whole world. WHO declared this outbreak as a pandemic on March 11, 2020. COVID-19 infection is transmitted by inhalation or contact with infected droplets or aerosols of infected persons, and the incubation period ranges from 5 to 14 days. Viral aerosols remain active for 3 hours in the air, 24 hours on cardboards, and 2 to 3 days on stainless steel and plastic. Symptoms are usually fever, cough, breathlessness, sore throat, malaise and fatigue. In some people, it may progress to pneumonia, multiple organ dysfunction, and acute respiratory distress syndrome. People with heart diseases, lung diseases, cancer, old age, diabetics, Immunosuppressed, and pregnant women are at higher risk for COVID-19 infection. To date, there are now more than 2,732,701 cases of COVID 19 globally with more than 191,150 deaths. In India, total cases are 23,502 with 722 deaths. First case of coronavirus was seen on 29 January 2020. On 24 March 2020, the government of India under Prime Minister Shri Narendra Modi ordered a nationwide lockdown for 21 days, after a 14-hour voluntary public curfew on 22nd March. India is one of the most populous countries of the world. India has the second largest population in the world. Due to the lack of vaccines, ventilators, targeted therapies, mass gatherings, the Indian government started lockdown, the largest exercise in the world with the second largest population. To reduce public movement, section 144 was implemented in many states. A full lockdown will help the collapse of the whole national health system.

KEY WORDS

Corona Virus, Pandemic, SARS, Transmission, Pandemic

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BACKGROUND

Coronaviruses are pathogenic agents that cause serious diseases in a variety of animal species including infections in humans. The virus causes illnesses such as common cold, severe acute respiratory syndrome and middle east respiratory syndrome, but then it started showing a cluster of different diseases^[1], by the end of 2002. Coronavirus leads to the development of "Severe Acute Respiratory Syndrome (SARS-CoV)" which emerged in China by the end of 2019 and it spread rapidly all over the world, resulting in around 8,000 deaths in 10 percent of the population. ^[2-4] In Saudi Arabia, the "Middle East Respiratory Disease Coronavirus (MERS-CoV)" arose in 2012 as a novel coronavirus that infected humans and had spread to nine additional countries.^[5,6] 182 "MERS-CoV" cases have been reported till date, resulting in 79 fatalities.

Medical presentation of infected patients have shown acute pneumonia, frequently involving kidney diseases.^[7] CoVs are similar to the SARS-CoV and MERS-CoV which were mainly isolated from the bats and spread worldwide,^[8-9] providing a possible reservoir for novice outbreaks of novel zoonoses into humans. There are total 6 species of Coronavirus, from which 1 species is divided into 2 strains making up 7 human coronavirus strains. Four of these, that mainly produce mild symptoms are, "Human Coronavirus OC43", "Human Coronavirus HKU1", "Human coronavirus 229E", "Human Coronavirus NL63". Three human coronaviruses primarily cause extreme symptoms, Middle East Respiratory Syndrome-Related Coronavirus (MERS-CoV), Severe Acute Respiratory Syndrome (SARS-CoV) and Severe Acute Respiratory Syndrome 2 (SARS-CoV-2). The COVID-19 causing pathogen were first identified in late January 2020, called SARS-CoV-2 and it is also known as 2019-nCoV,^[10,11] a novel virus not previously experienced in humans; coronavirus has caused a global outbreak which has triggered the World Health Organization (WHO) to declare an emergency of international concern for public health.^[12] COVID-19 is a zoonotic disease that is introduced into the human population by bats.^[13-14] The SARS-CoV-2, a transitional animal host between a plausible bat reservoir and humans is still unknown.^[15] The first array of cases detected at the end of 2019 were linked to marked seafood in Wuhan, China.^[13]

The first imported case of COVID-19 was registered in Thailand on 13 January. A second case imported into Japan was found two days later. South Korea was the third country to report an Imported COVID-19 case.^[16] Coronaviruses are a highly diverse group of enveloped, single-stranded, positive sense RNA viruses,^[17] causing various diseases affecting respiratory system, enteric, hepatic and neurological systems with varying severity among humans and animals.^[17,18] Corona viruses have envelope spike protein which is very necessary for its morphology.^[19] The S protein promotes the binding of receptors and helps in membrane fusion, and it is essential to confirm host tropism and transmission capacity.^[20-22] In general, the S protein is divided functionally into 2 domains mainly the receptor-binding domain S1, and the S2 domain, which is responsible for the cell membrane fusion.^[23] Further the analysis of structure has shown that the receptor-binding domain consisted of a core and an external sub domain. The enzyme-converting angiotensin II was

known as the SARS-CoV cell receptor.^[24-26] In the biophysical and the structural research, it is suggested that the SARS-CoV-2 gets bound to ACE2 with approximately 10- to 20-fold higher affinity than the SARS-CoV protein.^[27] The high affinity of S protein to human ACE2 can facilitate SARS-CoV-2 spread among the human population. While, SARS-CoV-2 doesn't use the other coronavirus receptors for entering cells, such as aminopeptidase N and Dipeptidyl peptidase 4. Common clinical results in the laboratory cover leucopenia and lymphopenia. The main fascinating feature of COVID-19 is lymphopenia, and the levels of Lactate dehydrogenase are elevated with an increase in creatinine kinase. Half of the patients are having elevated alanine aminotransferase or aspartate aminotransferase (SGOT,SGPT) that have impaired liver function. Most of the patients had shown abnormal myocardial zymogram that also shows increase levels of creatine kinase and lactate dehydrogenase. Many of the patients displayed normal procalcitonin serum levels but the c-reactive protein was above normal range, one third of patients had increased D-dimer.^[28-31] On study analysis, the changes for serum cytokines in COVID-19 patients which indicates triggering of immune response, would lead in the development of chemokines and cytokines and at the end it harms normal host lung.^[31]

Protective measures suggested by the world health organization in relation to Covid-19 awareness and information through media include:

1. Hands should be washed frequently with an alcohol based hand rub or soap.
2. Maintain a distance of at least 1 meter from the person coughing or sneezing.
3. Prevent rubbing of the head, nose and mouth by dirty hands.
4. Exercise respiratory hygiene by covering the mouth and nose with a bent elbow while coughing or sneezing and use masks or tissue.
5. Early medical attention should be taken when fever, cough, and breathing problems are present.
6. Minimal traffic in busy areas such as pilgrimage sites, gardens, markets and tourist sites.
7. Closure of nurseries, companies, local and foreign travel, schools and colleges, etc.
8. If you have a fever, cough and breathing difficulty, seek medical attention.^[32]

THE VIRION

Corona viruses are infectious pathogenic enveloped viruses between 80 and 120 nm in diameter, round or sometimes pleiomorphic virions, recording the largest genome (about 30 kb) of RNA till date.^[33,34] The RNA genome is functionalized to construct a helical capsid with the base nucleocapsid (N) protein located inside the viral membrane. Both of these coronavirus membranes consist of minimum 3 viral proteins, all were spike protein (S), the type 1 glycoprotein that builds the peplomers on the virion surface, by giving the virus its corona or crown-like morphology in electron microscope, the membrane protein or M protein, that intersects the membrane three times and also has a short N-terminal ectodomain and even having a cytoplasmic tail and a highly hydrophobic protein, small membrane protein (E).^[35] The

protein IBV E is composed of a short ectodomain, a transmembrane domain and a cytoplasmic tail.^[36] MHV's E protein is stated to stretch out the membrane twice, so both N and C termini are within the virion.^[37] Some coronaviruses in group II have an extra membrane protein called hemagglutinin esterase (HE).^[38]

Coronavirus is a large, approximately spherical particle with bulbous surface projection.^[39] The viral envelope is mainly consisted of lipid bilayer in which the structural proteins Membrane (M), Envelope (E) and Spike (S) are intercalate^[40] and the ratio of E:S:M in lipid bilayer is approximately 1:20:300^[41] coronavirus has approximately 74 surface spikes.^[42] The surface spikes of coronavirus are homotrimeric to S. protein and consist of S1 and S2 subunits. S1 protein is indeed a class I fusion protein that helps in receptor binding and membrane fusion between the host cell and the virus and the S1 subunit forms the spike's head and has a receptor-binding domain, while the S2 subunit forms the spike's stem and allows protease activation to be fused and the E and M proteins are critical in viral envelope formation and help to maintain shape and structure.^[43] Within the envelope, Nucleoprotein is present that gets bound to the positive-sense single stranded RNA genome in beads on a string like conformation.^[44] The ssRNA genome varies from 26.4 to 31.7 kilobases, which is the largest among all the RNA viruses and the genome has 5'Methylated cap and 3'polyadenylated tail.^[43]

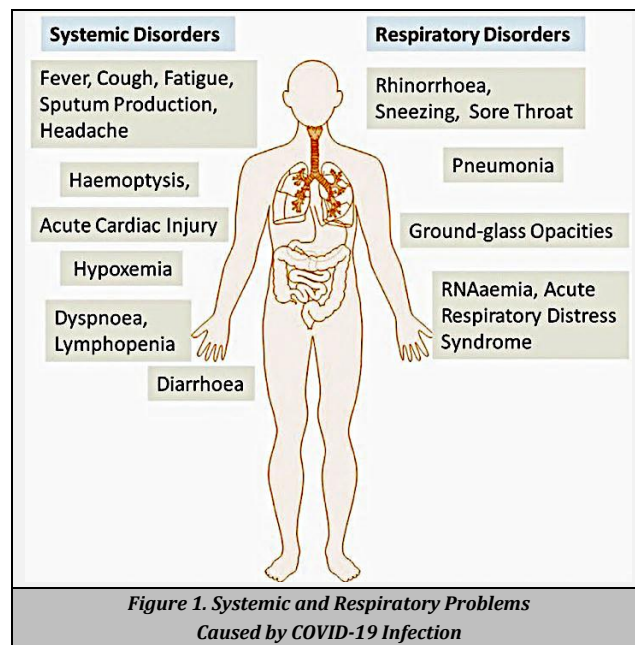
Transmission

The first step of viral infection is binding of receptor expressed by the host cells leading to the cell membrane by fusion. It is suspected that the primary or main target of the virus is the lung epithelial cells. Therefore, it was seen that human to human transmissions of SARS-CoV occur by linking the receptor-binding domain of virus spikes with the identified cellular receptor Known as the angiotensin-converting enzyme 2 receptor. Importantly, the COVID-19 sequences spike the receptor-binding domain parallel to the one of SARS-CoV. This evidence indicates strongly that the viruses most likely enter into the host cells via ACE2 receptors.^[44-46]

The incubation period ranges from 1 to 12.5 days, but can be as long as 14 days. The signs between the preceding beta coronavirus and COVID-19 are generally similar. COVID-19, however, displayed some unusual clinical features including targeting the lower airways as evident from symptoms of the upper respiratory tract such as rhinorrhoea, sneezing and sore throats. In addition, only a small percentage of MERS-CoV or SARS-CoV shows intestinal symptoms such as diarrhoeain patients diagnosed with COVID-19.

Bats seem to be the source of a wide variety of coronaviruses including "Severe Acute Coronavirus Respiratory Syndrome (SARS-CoV)" like viruses. SARS-CoV -2 may emerge from bats or unknown intermediate hosts, and may cross human boundaries of the species. Interactions with host-viruses affect the input and replication of viruses. SARS-CoV-2 is a two-thirds enveloped single stranded positive RNA (ssRNA), predominantly located within the first open reading frame (ORF 1A/B), which codes 16 non-structural proteins (NSPs). The remaining of the genome codes for viruses are

four basic structural proteins, including spike, envelope, matrix and nucleocapsid (N) protein, and several accessory proteins. SARS-CoV-2 glycoprotein binds 2 (ACE2) angiotensin-converting enzyme to host cell receptors, a crucial step in virus entry. Many virus-bearing proteins may contribute to pathogenesis. Infection tolerance and disease progression can also be affected by host factors.



After receptor interactions and the fusion of viral and plasma membrane, the virus-specific RNA and Proteins are synthesized, perhaps entirely within the cytoplasm. Coronaviral activation begins with the translation into the proteins that make up the replicase complex of two polyproteins, pp1a and pp1ab, that undergo cotranslational proteolytic processing. The entire complex is used for transcribing a3-coterminal series of recursive subgenomic mRNAs as well as genomic RNA, which has a common 5-leader series obtained from the 5-end genome. Proteins are translated at the 5-end of a mRNA. New viruses are brought together by budding through intracellular membrane and emitted by vesicles through the cell secretory mechanism. The principal protein of replicase-transcriptase is polymerase RNA-dependent.^[47]

CONCLUSIONS

People need to be aware of the severity of COVID-19 and take measures to ensure themselves, such as remaining at home, limiting social contacts, avoiding public gatherings, maintaining distance, and wearing appropriate masks in public. The authorities should encourage peoples to stay at home; should stop mass gathering; should postpone or cancel public activities and should close public institutions. Such preventive steps will help the countries infected with COVID-19 Pandemic. We conclude masks alone do not protect against COVID-19, it should be combined with physical distancing, hand hygiene and follow the advice provided by your local health authority.

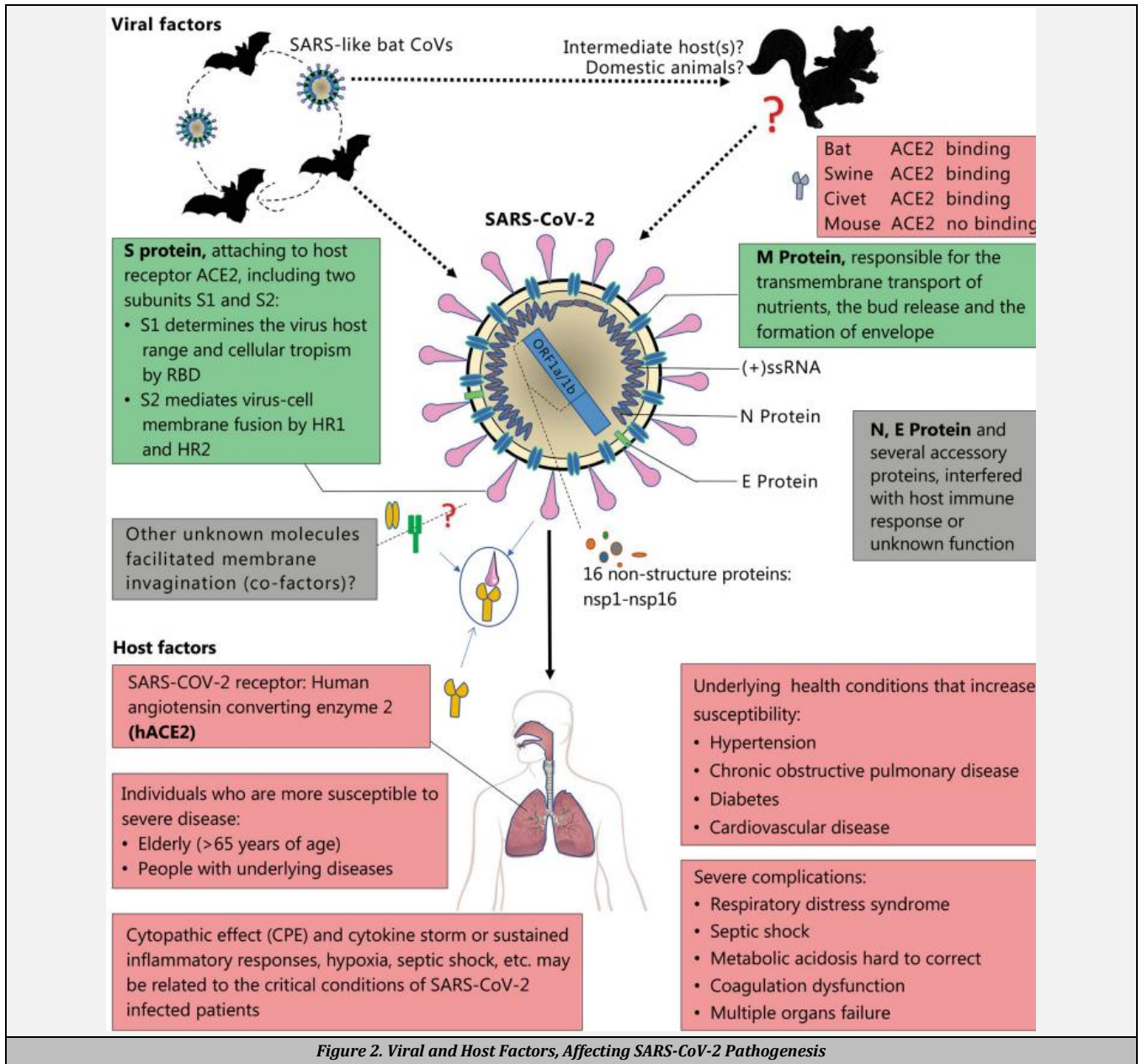


Figure 2. Viral and Host Factors, Affecting SARS-CoV-2 Pathogenesis

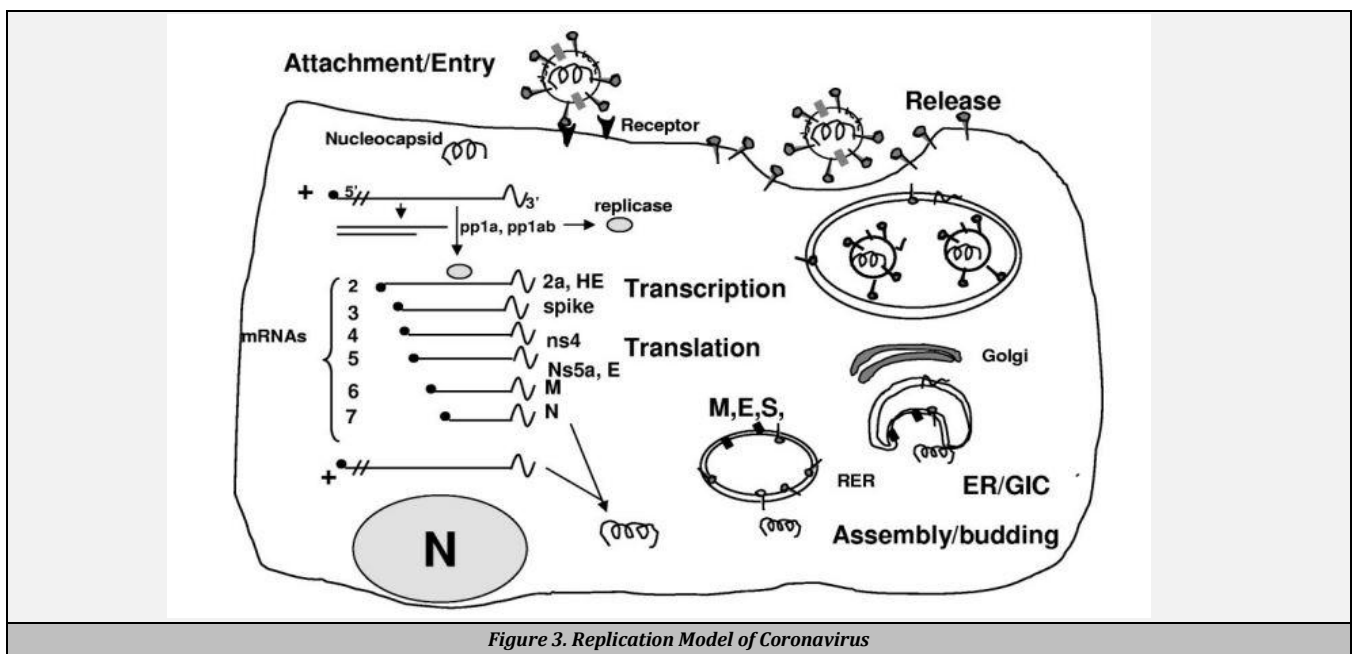


Figure 3. Replication Model of Coronavirus

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