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Review Article

Corona Virus: A Review on Covid-19

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ABSTRACT

The COVID-19 pandemic caused by SARS-CoV-2 remains a significant issue for global health, ecomomy and society. SARS-Cov-2 (sever acute respiratory syndrome Coronavirus 2) epidemic has spread to virtually every continents in the world. These viruses get spread through airbone droplets from human to human or human to animal. Coronavirus cause respiratory infections in human and diarrhoea, Upper Respiratory disease in animals, person to person transmission of virus is occurred by contact with disease individual and droplet inhalation of injected person. This virus enters in human cell through membrane. ACE-2 expo peptidase receptor. The advice from WHO and ECDC to avoid public places and close contact with infected persons and animals.

Key words: Corona virus, WHO, Emergency, Pandemic, Covid 19

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INTRODUCTION

Corona virus was first identified and isolated from pneumonia patient belongs to Wuhan, china. Corona virus is also names as CAVID 19, in that CO stand for corona VI stand for virus D stand for disease, this disease referred to as 2019 novel corona virus or also known as human corona virus 2019. Severe acute respiratory syndrome corona virus 2 is the strain of corona virus that causes corona virus disease 2019.

The world health organization declared the outbreak a public health emergency of international concern on 30th January 2020, and a pandemic on 11th march 2020. Coronavirus are large family of viruses that usually cause mild to moderate upper respiratory tract illness like common cold. However, three new corona viruses have emerged from animal reservoirs over the past two decades to cause serious and widespread illness and death. It spread from pigs, camels, bats, and cats, sometimes those virus jumps to humans that's called as spillover event and can cause disease. This virus are inactive form in environment and that show activity when goes into the human metabolic pathway. Coronaviruses are a group of spherical swirled particles containing nonsegmented, single-stranded (positivesense) RNA genomes depicted in Figure 1.

Corona viruses which are known to contaminate human host counts six while economically important vertebtrates like pigs and chicken are infected by other type of COVID. Among those six assortments, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic (animal disease) and highly pathogenic coronaviruses are resulted in local and universal outbreak. Coronaviruses is classified under the order Nidovirales, family Coronaviridae, subfamily Coronavirinae, as per the International committee on Taxonomy of viruses. [1-3]

Fig.1 Structure of Coronavirus

How it spreads

SARS-CoV-2 spreads from person to person through close communities. When people with COVID-19 breathe out or cough, they expel tiny droplets that contain the virus. These droplets can enter the mouth or nose of someone without the virus, causing an infection to occur.

The most common way that this illness spreads is through close contact with someone who has the infection. Close contact is within around 6 feet.
The disease is most contagious when a person's symptoms are at their peak. However it is possible for someone without symptoms to spread the virus. A new study suggests that 10% of infections are from people exhibiting no symptoms.

Droplets containing the virus can also land on nearby surfaces or objects. Other people can pick up the virus by touching these surfaces or objects. Infection is likely if the person then touches their nose, eyes, or mouth. It is important to note that COVID-19 is new, and research is still ongoing. There may also be other ways that the new coronavirus can spread.

LIFE CYCLE

Life cycle coronavirus virion (a virus particle that infects a host) goes through a replication life cycle within a host cell, thereby creating more copies of itself that can eventually infect more cells. SARS-CoV is the causative agent responsible for the 2003 SARS epidemic and an example of such a coronavirus infecting a human cell. The virion responsible for the new coronavirus outbreak in 2019 (COVID-19) is called SARS-CoV-2 and is closely related to SARS-CoV. Its life cycle, and how the disease develops, have yet to be fully resolved. The key stages of a general coronavirus replication life cycle include binding to a host cell surface receptor, cell entry, virion uncoating, translation of replicase proteins, RNA transcription, RNA synthesis, virion assembly, and release of mature virions into the extracellular space, where the cycle can begin again.

The virion is an enveloped particle surrounded by a protein shell. This shell, called a capsid, is made up of spike (S), envelope (E), membrane (M), and nucleocapsid (N) proteins, containing the single-stranded RNA genome. This RNA molecule is 28 to 32 kilobases (kb) in length and a "plus-strand RNA" with positive polarity, which means that it can be translated directly into protein. The S, E, M, and N proteins are all structural proteins. The spike proteins on the capsid give coronaviruses their distinctive "crown" or "solar corona" appearance under electron microscopy. They are crucial in determining cell tropism (which type of host tissue can be infected) and host species specificity (which

host species can be infected). For virion replication to begin, the spike proteins first bind to specific host cell surface receptors that are embedded in the host cell membrane - a process called host cell recognition (Step 1). In the case of SARS-CoV, this receptor is angiotensin-converting enzyme 2 (ACE2). ACE2 is a regular cellular protein that happens to be used by the virus to gain entry to the cell. It has been been confirmed that the new coronavirus SARS-CoV-2 also binds to ACE-2 and structurally resembles SARS-CoV.

Once the binding between the spike protein and the receptor is complete, the virion enters the cell through one of two processes. Step 2a: membrane fusion from without where viral and cellular membranes fuse and the RNA genome of the virus gets access to the cytosol. Step 2b: endocytosis where the receptor-bound virus is enveloped by the cell membrane and enters the cytosol within a vesicle. Following either route of cell entry, the viral RNA genome is released into the cytoplasm (Step 3), which is followed by uncoating of the RNA (Step 4).

Once in the host cytoplasm, a replicase gene on the RNA strand is translated into two replicase polyproteins (Step 5). Translation is the production of proteins from RNA, and a polyprotein is a large protein that can be cleaved into smaller proteins. The polyproteins are further processed by viral proteinases (enzymes that break down proteins) to yield individual replicase proteins (Step 6).

These replicases mediate the production of full-length negative-strand RNA, which later serves as a template for positive-strand virion genomic RNA (Step 7). In contrast to plus-strand RNA, negative-strand RNA is complementary to the mRNA and cannot be translated directly. It needs to be converted to plus-strand RNA by RNA polymerase first. The full-length negative-strand RNA is transcribed to produce shorter mRNAs (Step 8). These shorter mRNAs code for the structural proteins (e.g., S, E, M, and N) and nonstructural accessory proteins, including the viral proteinases, during translation (Step 9).

The newly produced plus-strand viral genomic RNA as well as nonstructural and structural proteins are translocated (Step 10) to assembly sites at a transitional zone between the endoplasmic reticulum (ER) and the Golgi apparatus. The Golgi apparatus and the ER are both organelles involved in protein synthesis, post-translational modification of proteins, protein packaging into membrane-bound vesicles, and protein transport. Here the new virions assemble (Step 11), start maturing, and bud off from the Golgi membranes as vesicles (Step 12). These vesicles are translocated to the host cell membrane (Step 13) where they fuse with the host cell membrane and are released into extracellular space (Step 14). This release process does not rupture the host cell and is called nonlytic exocytosis.

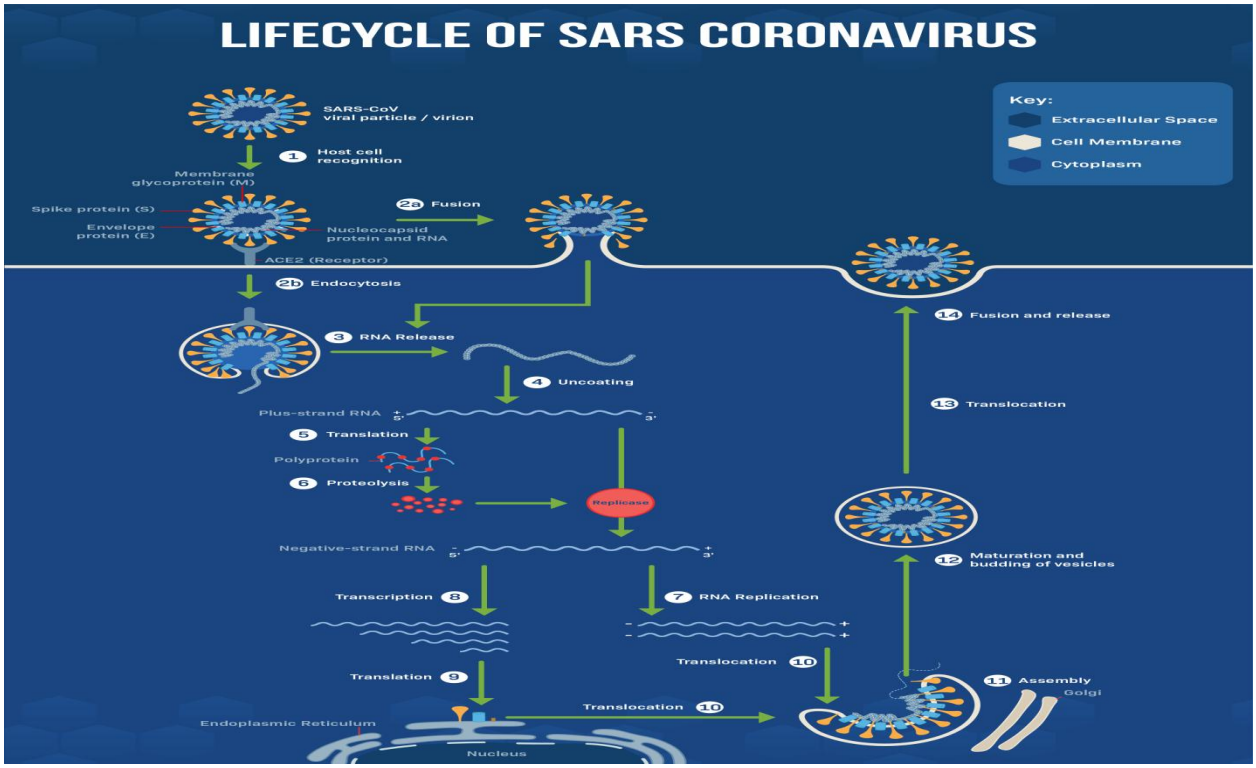

Fig.2 Life cycle of SARS Coronavirus

Pathophysiology & Clinical Manifestation

Coronavirus is one of the major pathogens that primarily target the human respiratory system. Previous outbreaks of coronaviruses (CoVs) include the severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV which have been previously characterized as agents that are a great public health threat. The symptoms of COVID-19 infection appear after an incubation period of approximately 5.2 days. The period from the onset ofCOVID-19 symptoms to death ranged from 6 to 41 days with a median of 14 days.

This period is dependent on the age of the patient and status of the patient's immune system. It was shorter among patients > 70-years old compared with those under the age of 70. The most common symptoms at onset of COVID19 illness are fever, cough, and fatigue, while other symptoms include sputum production, head-ache, haemoptysis, diarrhoea, dyspnoea, and lymphopenia. It is important to note that there are similarities in the symptoms between COVID-19 and earlier betacoronavirus such as fever, drycough, dyspnea, and bilateral ground-glass opacities on chest CT scans. However, COVID-19 showed some unique clinical features that include the targeting of the lower airway as evident by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat.

In addition, based on results from chest radiographs upon admission, some of the cases show an infiltrate in the upper lobe of the lung that is associated with increasing dyspnea with hypoxemia. World Health Organisation (WHO) has classified COVID-19 as aβCoV of group 2B. Ten genome sequences of COVID-19 obtained from a total of nine patients exhibited 99.98% sequence identity .Another study showed there was 99.8–99.9% nucleotide identity in isolates from five patients and the sequence results revealed the presence of a new beta-CoV strain. The name "coronavirus," coined in 1968, is derived from the "corona"-like or crown-like morphology observed for these viruses in the electron microscope (318).

The Patients infected with COVID-19 showed higher leukocyte numbers, abnormal respiratory findings, and increased levels of plasma pro inflammatory cytokines. Causes fever, sneezing, cough, and difficulty in breathing. One of the COVID-19 case reports showed a patient at 5 days of fever presented with a cough, coarse breathing sounds of both lungs, and a body temperature of 39.0 °C. COVID-19 represents the seventh member of the coronavirus family that infects humans and has been classified under the orthocoronavirus 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 COVID19 most likely developed from bat origin coronaviruses. Another piece of evidence that supports the COVID-19 is of bat origin is the existence of a high degree of homology of the ACE2 receptor from a diversity of animal species.

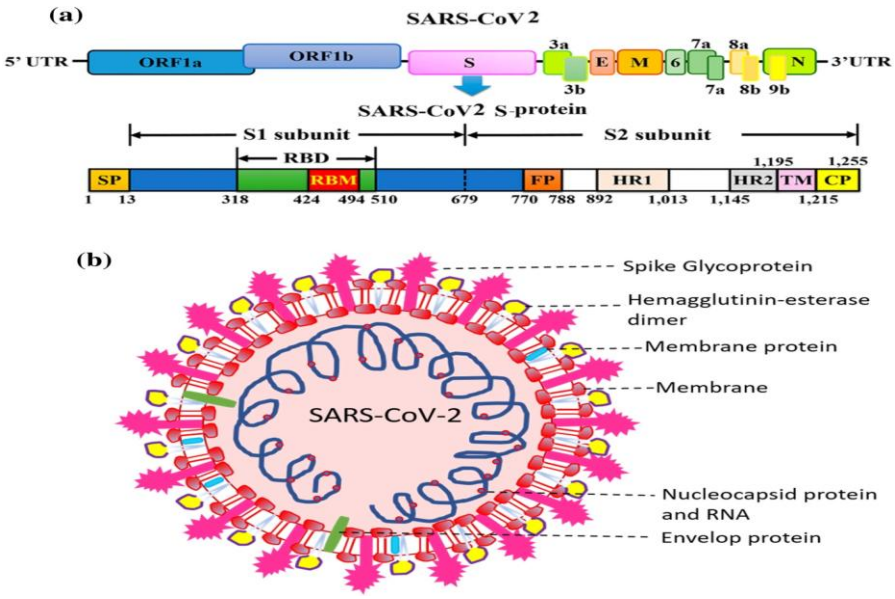

Fig.3 Pathophysiology & Clinical Manifestation

Mechanism

The mechanism of viral entry and replication and RNA packing in the human cell is mapped in Figure 2. The coronavirus spike (S) protein attaches to angiotensin converting enzyme 2 (ACE2) receptors that is found on the surface of many human cells, including those in the lungs allowing virus entry. The coronavirus S protein is subjected to proteolytic cleavages by host proteases (i.e. trypsin and furin), in two sites located at the boundary between the S1 and S2 subunits (S1/S2 site). In a later stage happens the cleavage of the S2 domain (S2′ site) in order to release the fusion peptide. This event will trigger the activation of the membrane fusion mechanism. Searching for antibodies can find support on molecular targeting which can utilize the structural information (aa sequence) of the binding region which is found in angiotensin-converting enzyme 2 receptor. In this way this protocol could device a treatment to block the viral entry. Typically, human cell ingests the virus in a process called endocytosis. Once entered the cytoplasm, it has been suggested most likely that COVID-19 employs a unique three-step method for membrane fusion, involving receptor-binding and induced conformational changes in Spike (S) glycoprotein followed by cathepsin L proteolysis through intracellular proteases and further activation of membrane fusion mechanism within endosomes (Simmons et al., 2005). Then, the endosome opens to release virus to the cytoplasm, and uncoating of viral nucleocapsid (N) is started via proteasomes which typically can hydrolyse endogenous proteins, but they are also capable of degrading exogenous proteins such as the SARS nucleocapsid protein. A different two-step mechanism has been suggested and in this case the virion binds to a receptor on the target host cell surface through its S1 subunit and the Spike is cleaved by host proteases (Hasan et al., 2020) and then it is expected the fusion at low pH between viral and host target membranes via S2 subunit. Finally, the viral genetic material a single stranded RNA is fully released into the cytoplasm. There takes place the replication and transcription processes which are mediated by the so-called replication/transcription complex (RTC). Such complex is encoded in the viral genome and it is made of non-structural proteins (nsp). The RTC is believed to induced double-membrane structures in the cytoplasm of the infected cell (Van Hemert et al., 2008). Following the positive RNA genome is translated to generate replicase proteins from open reading frame 1a/b (ORF 1a/b) (see Figure 1). These proteins use the genome as a template to generated full-length negative sense RNAs, which subsequently serve as templates in generating addition full-length genomes. Structural viral proteins, M, S and E are synthesized in the cytoplasm and then inserted into the endoplasmic reticulum, and transfer to endoplasmic reticulum-Golgi intermediate compartment (ERGIC) (Masters, 2006; Song et al., 2004). Also, in the cytoplasm nucleocapsids are formed from the encapsidation of replicated genomes by N protein, and as a result they coalesce within the ERGIC membrane in order to self-assembly into new virions. Finally, novel virions are exported from infected cells by transport to the cell membrane in smooth-walled vesicles and then secreted via a process called exocytosis, so that can infect other cells. In the meantime, the stress of viral production on the endoplasmic reticulum eventually leads to cell death. However, the mechanism of action for novel COVID-19 is still unknown.[9-15]

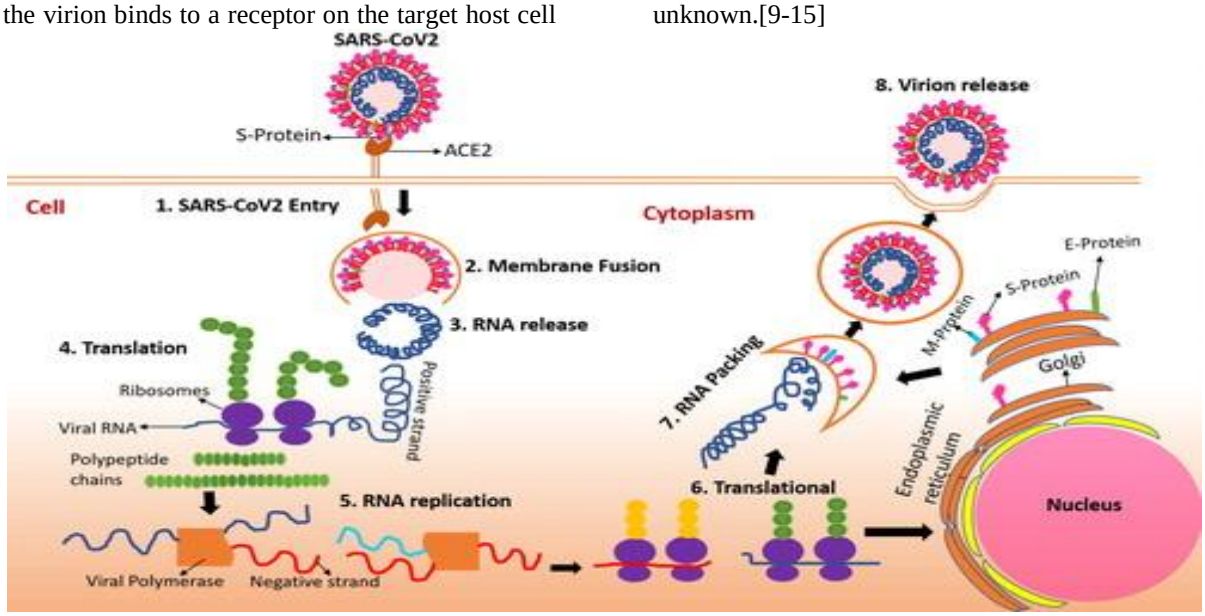

Fig.4 mechanism of COVID-19

Prevention

There is nothing to provide complete guidance to prevent from corona virus but some guidelines was presented by WHO and ECDC. Basically these guidelines are for health profession to set during the caring of infected patient. Because many evidence was presented by studies about human to human transmission of corona from Wuhan, china. Another study reported about airborne transmission of virus while no one was presents the solid evidence. As the lack of transmission evidence health professionals were not able to present prevention guidelines. According to WHO, some general guidelines were published such as separate the infected patient from other family member to single room, implementation of contact and droplet precaution, airborne precaution etc. European Centre for Disease Prevention and Control (ECDC) also published the information leaflet to peoples i.e. Avoid contact with sick people, in particular those with a cough. Avoid visiting markets and places where live or dead animals are handled, Wash your hands with soap and water or use an alcohol based disinfectant solution before eating, after using the toilet and after any contact with animals, Avoid contact with animals, their excretions or droppings.[13]

Trial test of the FDA-approved drugs for COVID-19 patients

- Hydroxychloroquine
- Azithromycin+vitaminD+Paracetamol+le ocitrizine+Oral rehydration salt

CONCLUSION

Corona virus was spreading human to human to transmission by close contact via airborne droplets generating by coughing, sneezing, kissing and smooching. So avert these activities with infected partners and family members. Corona virus may be transmit through pet animals such as dog, cat, pig, cow, turkeys. So avoid contact and seprate them if observed any infection activities like diarrhea, cold, fever. According to WHO, the only possible way to parry the virus is to avoid contact with infected person. It also known that Vaccines are not available in market, it is individual responsibility to take care a avoidance is better than cure, and also avoid the market or public place as per possible. There are no anti corona virus vaccine to avoid or treatment but some supporting therapy work. Future research needed to fight with corona virus. Till only 'Distance is rescue'.

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