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Corona Virus SMS



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ABSTRACT

COVID – 19, the disease caused by SARS-COV-2 (Severe Accurate Respiratory Syndrome – Corona Virus -2) a novel coronavirus, initiated and outbreak of pneumonia, cold, sneezing & coughing while in animals it causes diarrhea and upper respiratory diseases. Coronavirus transmitted humans to humans or animals to humans via airborne droplets. The epicenter of infection was linked to seafood and exotic animal wholesale markets in the city. SARS-COV-2 is highly contagious and has resulted in rapid pandemic COVID -19. This review will introduced general overview of coronavirus and described the clinical features, evaluation and treatment of covid-19 patients. It will also provide a means to raise awareness among primary and secondary health care providers during the current pandemic. Furthermore, our review focuses on the most up-to-date information of covid-19, its prevention, diagnosis, treatment and counselling of patient worldwide.

INTRODUCTION:-

Coronavirus (CoV) is a large family of sense, single stranded RNA viruses that belong to the Nidovirales order. The order includes Roniviridae, Arteriviridae and coronviridae families. The coronviridae family is subdivided into Torovirinae and coronvirinae subfamilies. Coronaviridae which is further sub classified into α -, β -, γ -, and δ - CoV. Their viral RNA genome ranges from 26 to 32 kilo bases in length (1). They can be isolated from different animal species. These include birds, livestock, and mammals such as bats, mice, dogs and cats. Human pathogenic subtypes of CoV are associated with mild clinical symptoms. Highly pathogenic coronaviruses that have resulted in regional and global outbreaks. Among them SARS-COV and Middle East Respiratory Syndrome Corona Virus (MERS-CoV). The virus is spherical or pleomorphic with 80-120 nm size. The spikes are made of hemagglutinin esterase. The patients with pneumonia of unknown etiology and had a history to seafood market, indicating a possible human-to-human transmission. The (SARS- COV-2) retains the classic CoV structure like the presence of spike protein expression of other nucleoproteins, polyproteins, and membrane proteins such as RNA polymerase, 3-chymotrypsin-like protease, papain-like protease, helicase, glycoprotein and accessory protein(2). The structure of CoV was shown in the following figure -1.

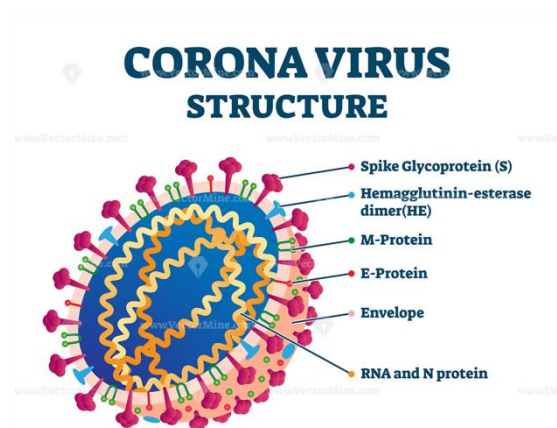


Figure No. 1: Structure of coronavirus

HISTORY

In Dec 2019, a cluster of pneumonia cases caused by newly identified β - CoV which is occurred in China and Wuhan, which was initially named as the (2019-nCoV). On 12th Jan 2020 officially named it is named COVID-19 by the WHO. Given the SARS-CoV outbreak

in 2002 and the MERS-CoV outbreak in 2019, 2019-nCoV is the third CoV to emerge in the human population in the past 2 decades. An emergence that has put GPH institutes on high alert. China responded quickly after informing WHO (3). Mild symptoms of nCoV-2019 travelers from Wuhan in the United States are screening travelers. Thailand, China, Japan, Korea updates indicate that the disease associated with 2019-nCoV appears to be relatively mild as compared with SARS and MERS. Coronavirus makes up a large family of virus that can infect birds and mammals including humans according to WHO (MERS) outbreaks in South Korea in 2015. Coronavirus is a trending virus now through all over the world. Coronavirus a group of enveloped genome virus with non segmented single stranded and positive sense RNA. Apart from infecting a variety of economical vertebrates (such as like pigs and chickens), six CoV have been known to infect human host. Now currently doctors recognized 7 types of CoVs that can infect human host. From those types of viruses a zoonotic (i.e. which is caused by germs that spread by animals and people) disease and highly pathogenic coronavirus that have resulted in regional and global out breaks. Among them severe are SARS-CoV and MERS-CoV which belongs to the members of the family is coronviridae cause a broad spectrum of human and animal diseases. In the last 15yrs have witnessed the emergence of two zoonotic, highly pathogenic HCoVs they are (SARS-CoV) and (MERS-CoV), where (SARS-CoV) was identified in 2002 and (MERS-CoV) in 2012 the third intro has been marked highly pathogenic and large-scale epidemic coronavirus into the human population in the 21st century (4). As of 1st march 2020 SARS-CoV-2 belongs to the β -Coronavirus, with highly identical genome to bat CoV pointing to bat as natural host. The novel CoV uses the same receptor (ACE2) Angiotensin-Converting Enzyme 2 as that for SARS-CoV, mainly spreads to respiratory tract (5). Due to covid-19 pandemic the brain changes linked to pandemic which causes COVID infection according to covid infection addition to mood disorder there are common symptoms includes fatigue, headache, memory loss, and problems with attention. The virus may gain access to the brain *via* the forebrains olfactory bulb which is the most important for the processing of smell (i.e., loss of smell)(6). Due to this virus people have suffered from increased anxiety and depression. Along with many exported cases across the globe increasingly evidence showed human to human transmission(7),(8).

Replication of HCOV is regulated by a diversity of host factors and induces drastic alterations in cellular structure and physiology(9,10). The disease is being cured through general treatment, symptomatic treatment by using antiviral drugs, oxygen therapy and by the

immune system and by using the plasma therapy is necessary to identify the potential cases as soon as possible and isolate the suspected people from the confirmed cases of COVID-19, prevent the potential transmission of infection to other patients and health care staff(11,12).

TYPES

Corona belongs to the subfamily coronavirinae in the family coronaviridae. Types vary in how severe the resulting disease becomes and how far they can spread. Now currently doctors recognize 7 types of coronavirus that can infect humans(13).

Common types:- 1) 229E (α -CoV)

2) NL63 (α -CoV)

3) OC43 (β -CoV)

4) HKUL (β CoV)

ORIGIN AND TRANSMISSION OF SAR- COV:-

The SARS-CoV-2 is a β - CoVs, which is enveloped non-segmented positive-sense RNA virus (subgenus sarbeco irus, Orthocoronavirinae subfamily)(14). CoV are divided into 4 genera by which including α -/ β -/ γ -/ δ -CoV. α and β -CoV are able to infect mammals, while γ - and δ -CoV tend to infect birds (15). Previously 6 CoVs have been identified as human-susceptible virus, among which α -CoVs HCoV-229E and HCoV-NL63, and β -CoVs HCoV-HKU1 and HCoV-OC43 with low pathogenicity, cause mild respiratory symptoms similar to a common cold(16). The other two known β - CoVs, SARS-CoV and MERS-CoV lead to severe and potentially fatal respiratory tract infection(17). Genome sequence of SAR-CoV-2 is 96.2% identical to a bat CoV RaTG₁₃, where it shares 79.5% identify to SARS- CoV(18). It is clear now that SARS-CoV could use (ACE2) Angiotensin converting enzyme 2 the same receptor as SARS-CoV(19). Based on virus genome sequencing results and evolutionary analysis, bat has been suspected as natural host of virus origin, and SARS-CoV-2 might be transmitted from bats via unknown intermediate hosts to infect humans(20). It is clear now that SARS-CoV-2 could use ACE - 2, the same receptor as SARS-CoV, to infect humans(21,22). The Simplified Representation of SARS-CoV-2 Viral Lifecycle and Potential Drug Targets was shown in the following figure-2.

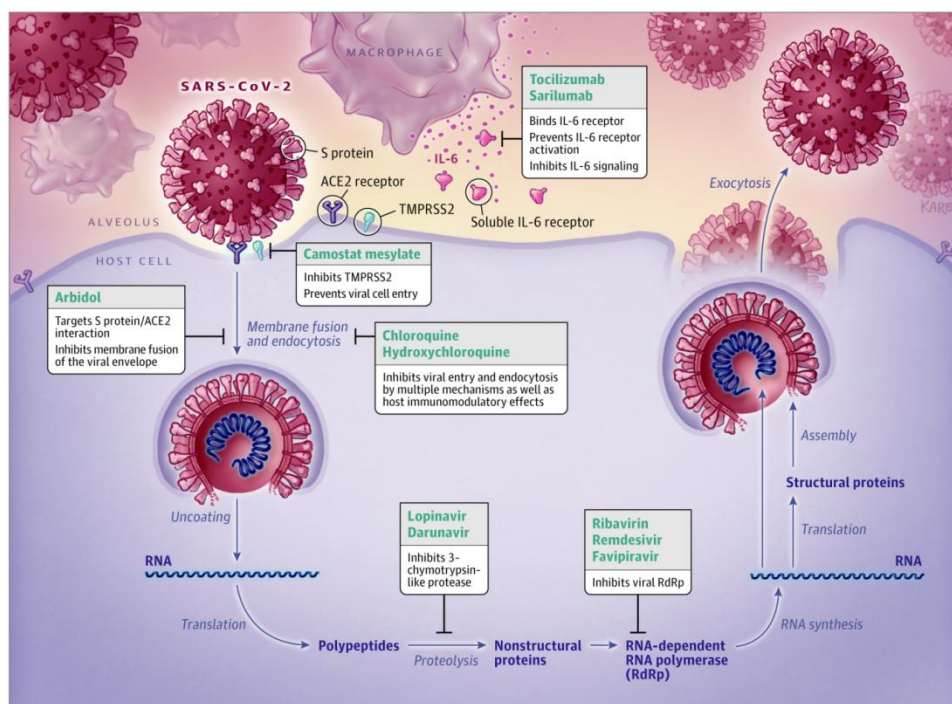


Figure No. 2: Simplified Representation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Viral Lifecycle and Potential Drug Targets

CORONAVIRUS CAN SPREAD IN SUCH A FOLLOWING WAYS

Coughing and sneezing without covering the mouth can disperse droplets into the air(23). Shaking hands with a person (or) touching a person, touching face, nose, eyes can easily pass the virus into the body(24). Some animal CoV such as Fetrine CoV (FCoV) may spread through contact with feces. The National Institute of Health (NIH) suggests that several groups of people have the highest risk of developing complications due to COVID-19.

These groups include:

1. Young children
2. People aged 65 years or older
3. Who are pregnant.

CoV will infect most people at some time during lifetime(25). CoV can mutate effectively, which makes them so contagious. To prevent transmission, people should stay at home and rest while symptoms active. They should also avoid close contact with other people. They

should cover their mouth and nose with a tissue or handkerchief while coughing and sneezing(26).

SYMPTOMS

Include headache, fever, fatigue, breathlessness, cough, sputum production, sore throat, congestion, and diarrhea(27,28). Gastrointestinal symptoms with vomiting and lesser known symptoms include headache, loss of sense and smell or taste, confusion, breathing difficulty, dizziness, eye flu, blue lips, intestine lips, muscle pains, tiredness. It may take 2-14 days for a person to notice symptoms after infection(29).

EPIDEMIOLOGY

As of March 3, 2020, WHO has confirmed 87,317 cases worldwide. Of these confirmed cases, 2,977 (3.42%) patients have succumbed to the virus. The majority of cases and deaths have been reported in China of the total number of cases 79,968 (92%) patients have been identified in China. Likewise, the majority of fatalities have also been reported in China. It is important that confirmed cases have emerged in 59 countries(30). Due to the ongoing nature of the pandemic, the number of cases and involved countries are expected to vary(31). The first case of COVID-19 in India was reported on January 30th, 2020 with the origin from China(32). As of April 29th, 2020 there are 22,629 active cases in India 1007 deaths(34). Upon virus genome sequencing, the covid-19 was analyzed throughout the genome to bat COV RaTG13 and showed 96.2% overall genome sequence identify suggesting that bat CoV and human SARS-COV-2 might share the same ancestor, although bats are not available for sale in this seafood market. Besides, protein sequences alignment and phylogenetic analysis showed that similar residues of receptor were observed in many species, which provided more possibility of alternative intermediate hosts such as pangolins snakes, and turtles(33). The transmission of SARS-COV and MERS-COV is reported to occur mainly through nosocomial transmission. Infections of healthcare workers 33-42% of SARS cases and transmission between patients (62-79%) was the most common route of infection in MERS-CoV cases(34).

GENOME STRUCTURE AND ITS KEY VIRAL FACTORS

Isolated from a COVID-19 pneumonia patient, a worker in the Wuhan seafood market, the complete genome of Wuhan-Hu-1 CoV (WHCV), one strain of SARS-CoV-2, is 29.9 kb(35).

While SARS-CoV and MERS-CoV have positive-sense RNA genomes of 27.9 kb and 30.1 kb. It has been shown that the genome of CoVs contains a variable number (6–11) of Open Reading Frames (ORFs). Two-thirds of viral RNA, mainly located in the first ORF (ORF1a/b) translates two polyproteins, pp1a and pp1ab, and encodes 16 non-Structural Proteins (NSP), while the remaining ORFs encode accessory and structural proteins. The rest part of virus genome encodes four essential structural proteins, including spike (S) glycoprotein, small envelope (E) protein, matrix (M) protein, and nucleocapsid (N) protein, and also several accessory proteins, that interfere with the host immune response(36). A deep meta-transcriptomic sequencing on WHCV was performed, which contained 16 predicted NSP. WHCV exhibits some genomic and phylogenetic similarity to SARS-CoV, particularly in the S-glycoprotein gene and receptor-binding domain (RBD), indicating the capability of direct human transmission. Compared with the known SARS-CoV and MERS-CoV genome, SARS-CoV-2 is closer to the SARS-like bat CoVs in terms of the whole genome sequence. Most genomic encoded proteins of SARS-CoV-2 are similar to SARS-CoVs, as well as exist certain differences(37). At the protein level, there are no amino acid substitutions that occurred in NSP7, NSP13, envelope, matrix, or accessory proteins p6 and 8b, except in NSP2, NSP3, spike protein, underpinning subdomain, i.e., RBD(38). Another recent research suggested that the mutation in NSP2 and NSP3 play a role in infectious capability and differentiation mechanism of SARS-CoV-2(42). This provokes people to explore the difference of the host tropism and transmission between SARS-CoV-2 and SARS-CoV or conduct further investigations on the potential therapeutic targets. The genotypes of COVID-19 was analyzed in different patients from several provinces and found that SARS-CoV-2 had been mutated in different patients in China. Although the degree of diversification of SARS-CoV-2 is smaller than the mutation of H7N9 avian influenza. A population genetic analysis of 103 SARS-CoV-2 genomes was conducted and classified out two prevalent evolvement types of SARS-CoV-2, L type (~ 70%) and S type (~ 30%). The strains in L type, derived from S type, are evolutionarily more aggressive and contagious. Thus, virologists and epidemiologists need to closely monitor the novel coronavirus, in order to inspect the virulence and epidemic(39).

COVID REPLICATION AND PATHOGENESIS

ACE2 found in the lower respiratory tract of humans is known as cell receptor for SARS-CoV and regulates both the cross species and human- human transmission. The SARs-CoV-2

uses the same cellular entry receptor ACE₂ as SARS-CoV which was confirmed in the isolated from the Bronchoalveolar Larger Fluid (BALF) of a covid-19 patient. The virion s-glycoprotein on the surface of CoV can attach to the receptor i.e., (ACE₂) surface of human cell where these s-glycoprotein's includes two subunits s1 and s2, where s1 determines the virus host range and cellular tropism with the key function domain. While s₂ mediates virus cell membrane fusion by two tandem domains heptad repeats 1(HR₁) and HR₂. After fusion of the membrane, the viral genome RNA is released into the cytoplasm, and the uncoated RNA translates 2 polyproteins PPl_a and PPl_b. Encode with non structural proteins and form (RTC) replication transmission complex in double membrane vesicle. Continuously RTC replicates and synthesize a nested set of sub genomic RNAs which encode accessory proteins and structural proteins and envelope glycoprotein's assemble and form viral with the plasma membrane to release the virus. Because the binding of SARS-CoV-2 spike glycoprotein and ACE₂ receptor is a critical step for virus entry, systematic detection of β-CoV receptors showed that human cells expressing ACE₂, but not human (DPP₄) Dipeptidyl peptidase-4 (or) Aminopeptidase N where enhanced entry of SARS-CoV-2. The currently analyzed mortality of covid-19 is 34% lower than the death rate of SARs(9.6%). Thus the potential mechanisms for humans-humans transmission and pathogenic of the SARs-CoV-2 are studied under extensively(40).

TREATMENT

The first step is to ensure adequate isolation (discussed later) to prevent transmission to other contacts, patients and healthcare workers. Mild illness should be managed at home with counseling about danger signs. The usual principles are maintaining hydration and nutrition and controlling fever and cough.

Routine use of antibiotics and antivirals such as oseltamivir should be avoided in confirmed cases. In hypoxic patients, provision of oxygen through nasal prongs, face mask, High Flow Nasal Cannula (HFNC) or non-invasive ventilation is indicated. Mechanical ventilation and even extracorporeal membrane oxygen support may be needed. Renal replacement therapy may be needed in some cases. Antibiotics and antifungal are required if co-infections are suspected or proven. The role of corticosteroids is unproven, while current international consensus and WHO advocate against their use. Chinese guidelines recommend short term therapy with low to moderate dose corticosteroids in COVID-19 ARDS. At present the treatment of patients with covid-19 is mainly symptomatic. Remdesivir has been reported as a

promising antiviral drug against a wide array of RNA viruses. The treatment of a patient with COVID-19 with Remdesivir achieved good results. Remdesivir was effective in the control of covid-19 in vitro. Meanwhile, chloroquine has been found to have immune modulatory activity and could effectively inhibit SARS-CoV *in vitro*. Clinical controlled trails have shown that chloroquine was effective in the treatment of patients with COVID-19(41).

DIAGNOSIS

A suspect case is defined as one with fever, sore throat and cough who has history of travel to China or other areas of persistent local transmission or contact with the patients with similar travel history or those with confirmed COVID-19 infection. However, cases may be asymptomatic or even without fever. A confirmed case is suspect case with a positive molecular test. Specific diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/sputum/endotracheal aspirates and bronco alveolar lavage). Virus may also be detected in the stool and in severe cases, the blood. The detection of the viral nucleic acid is the standard for non-invasive diagnosis of covid-19. However, the detection of SARS-CoV-2 nucleic acid has high specificity and low sensitivity, so there may be false-negative results and the testing time could be relatively long. The novel coronavirus pneumonia diagnosis and treatment plan (5th trial version) includes suspected cases with pneumonia imaging features as the clinical diagnostic criteria in Hubei province. The novel coronavirus pneumonia diagnosis and treatment plan (6th trial version) eliminated the distinction between Hubei province and other provinces.

PREVENTION

Prevention must focus on optimizing infection control protocols, self isolation, and patient isolation during the provision of clinical care. The WHO has advised against close contact with patients, farm animals. Patients and the general public must cover coughs and sneezes to help prevent aerosol transmission. Frequent handwashing with soap and water is also required. As an alternative measures sanitizers can also be used. SMS (social distancing, mask, sanitizer) procedure should be followed. Only limited options are available to prevent coronavirus infection vaccines have only been approved for IBV, TGEV and canine CoV, but these vaccines are not always used because they are either not very effective. Emergency medicine departments must apply strict hygiene measures for the control of infections. Healthcare personal must use personal protective equipment as N95 masks, FFP3 masks,

gowns, eye protection and gloves. 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. Avoid visiting markets and places where live or dead animals are handled (42).

CONCLUSION

The COVID-19 pandemic is spreading across the globe at an alarming rate. It has caused more infections and deaths as compared with SARS or MERS. Based on R_0 values, it is deemed that SARS-CoV-2 is more infectious than SARS or MERS. Elderly and immune compromised patients are at greatest risk of family. The rapid spread of disease warrants intense surveillance and isolation protocols to prevent further transmission. Prophylactic vaccination is required for the future prevention of COV-related epidemic or pandemic.

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