

CORONAVIRUS DISEASE - 19 – A SERIOUS THREAT TO PUBLIC HEALTH

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ABSTRACT

The year 2020 is a public health emergency period declared globally by the WHO when on March 11, 2020, the deadly novel coronavirus-2019 causing severe acute respiratory syndrome (SARS) extended its stride in almost 150 countries commenced from Wuhan wet market, China led to declare globally as pandemic disease. Till date, more than 3 million are worldwide infected and the number is still in progression and nearly 200,000 people have succumbed, nearly 50,000 people only in United State died of this virus. Hence, this virus has brought global disaster. Therefore, this review is attempting to present a picture on coronavirus disease (COVID)-19 in terms of epidemiology, pathophysiology, and diagnosis, treatment, on the basis of available literature after search from the renowned database, especially focusing on public health impact. Treatment strategy is most essential part to focus for public health management and to save more life from this pandemic. As of date, there are no specific drugs for its treatment only repurpose drugs are employed for the hospitalized patient in present scenario, for example, Remdesivir made for Ebola is being use now in Covid-19 which inhibit replicase enzyme and reduced viral load, chloroquine and hydroxychloroquine an antimalarial drugs which prevent binding of S1 domain of Spike protein of SARS coronavirus 2 with Angiotensin Converting Enzyme-2 receptor and prevent fusion by S2 subunit thus overall prevent entering into the human susceptible cells along with it increases endosomal instability by increasing pH. In addition, supportive care management such as supplemental oxygen and mechanical ventilation procedure is highly supportive to the critical patient. There infected more than 10 million people with more than 0.5 million death, the observation of July 7, 2020.

Keywords: Corona virus disease-19, Pandemic, Public Health.

INTRODUCTION

Date was December 31, 2019, world was excited to welcome new year 2020 with glory and enthusiasm but China was encountering etiologically unknown pneumonia was reported in patient in Wuhan Central hospital complaining of dry cough, high fever, and difficulty in breathing since 1st week of December. This case was shared electronically public by Li Wenliang a Chinese ophthalmologist and reported as SARS like pathogens [1,2].

This mystery of outbreak was notified by China to World Health Organization on December 31, 2019, but the WHO only declared this contagious disease pandemic on March 11, 2020. The hypothesis came up the origin of virus is spread from bat as the isolated virus genome matches 96% bat coronavirus (Cov) and 70% homology with SARS Cov; hence, it is Zoonotic virus transmitted from bats to human. Initially, just seven cases were encountered, but later, the number of cases started to hike exponentially, even the patient who is not concerned or not have exposed to the live animal market was positive for the virus, guiding the fact that there exists human-to-human transmission [3,4].

CORONAVIRUS FAMILY

It is not surprising to say that Cov infection is not new to human being. In 1937, the first Cov was extracted and isolated from chicken, whereas the first Human Cov (HCoV) was known in mid-1960. Cov fall in corona viridae family, this is a family of enveloped single stranded positive sense RNA virus with 30 Kb genome size, with s, e, m, and n coding region which encode spike, membrane, envelope, and nucleocapsid protein, respectively. The structural protein S is the responsible spike protein that interact with host receptor and invade into the host, the M and E play role in forming virus envelope while that N protein is involved in viral component assembly. Furthermore, the genome structure and phylogenetic analysis showed that Coronaviridae family can be divided into phylogenetic analysis showed that Coronaviridae family can be divided into α , β , γ , and δ genera [4-6].

The coronaviruses of the α and β genera are infectious for human and mammals while the coronaviruses of the γ and δ genera are of avian

type. SARS-CoV-2 belongs to β genus; it is round or oval with a diameter of approximately 60-140 nm exhibiting crown shape under electron microscope. Besides SARS-CoV-2, six other coronaviruses can infect humans, including HCoV-229E, OC43 (HCoV-OC43), NL63 (HCoV-NL63), HKU1 (HCoV- HKU1), SARS-CoV, and MERS-CoV. Coronaviruses are sensitive to heat and ultraviolet rays. They can be stored for several years at -80° C and can be inactivated at 56° C for 30 min as shown by its laboratory used method. Moreover, SARS-CoV-2 could be inactivated by 75% ethanol, peracetic acid and by chlorine containing disinfectant in less than a minute (Fig. 1) [7-9].

EPIDEMIOLOGY

Virus does not select gender, race or ethnicity, every human residing in this earth is non-immune till date to this novel Cov. It could transmit with great ease from one individual to another through aerosol droplets and therefore study suggest at person should remain in 2 m of social distancing. Both symptomatic and asymptomatic patient could transmit the virus but asymptomatic is more dangerous as it is unknown to the one who get transmitted. Studies have reported that higher viral loads in the nasal cavity as compared to the throat with no difference in viral burden between symptomatic and asymptomatic people [10-12].

The super spreader event is also become evident in this pandemic; a person from UK participated in a conference in Singapore that transmitted the infection to other 11 people during his stay in resort in the French alps and on return to the UK. The droplet from infected patients spread to more people that are in the distance less than six feet that is approximately 2 m, deposit the virus on the surfaces where it settles and could remain viable there for days to weeks depending on the surface [13-15]. However, get annihilated in less than a minutes by common disinfectant such as sodium hypochlorite, and hydrogen peroxide. Healthy person acquire virus either by inhalation of the droplets or by touching the surface of virus remain or contaminated by it and later touching own hand to nose, mouth and eyes. Virus is also reported infecting through stool, urine, and water subsequent transmission through aerosolization fecal-oral route [16,17].

Till this, date April 28, 2020, one good side is that, yet trans-placental transmission is not reported, pregnant women on delivery gave birth of non-infected neonate providing evidence that this novel coronavirus is unable to cross placenta unit but neonatal infection is described immediate after postnatal transmission with incubation period varies from 2 to 14 days with median 5 days [18,19].

PATHOPHYSIOLOGY

The pathophysiology of coronavirus disease (Covid)-19 is much less known till date being the new virus its pathobiology will be concerned of quest to the scientist molecularly in coming times. We have very less understanding of cellular biology and whatever probable pathology is presented and is on the basis of past studied results of SARS Cov. To understand its course of infection to susceptible host cells, here it is divided into three phases [20].

STAGE #1: ASYMPTOMATIC PHASE OR YELLOW GROUP

As the virus get to enter nasal or by oral or conjunctiva route, the virus prefers to bind to epithelial cells considerably to Angiotensin Converting Enzyme-2 (ACE2) receptor by its S spike protein, endocytosis by clathrin mediated endocytosis and then replication, proceeding to propagation using host machinery preceding it has to encounter limited innate immune response of the host. In this condition, where the viral load being propagating it could be detected by nasal swab and person infected with viral load reach optimum number and thus this increased viral load combat the innate immune response easily, thus symptoms appears [21-23].

- Expression of two mucosa-specific serine proteases, TMPRSS2 facilitates SARS-CoV-2 spike fusogenic activity and promoted virus entry into host cells
- ACE2 receptor of viruses S proteins (Fig. 2).

STAGE #2 SYMPTOMATIC PHASE OR ORANGE GROUP

This phase could arise as virus propagates and move down the respiratory tract along the conducting airways here some more robust innate immunity by leukocyte is seen where they produce interleukin (IL) profusely specifically IL-6, sometime labeled as "Cytokines storm" which could aggravate the condition [24]. Possibly by M2 macrophages of alveoli causing death of the cell forming debris to encounter the virus attack and acts on enormous of its own cells and tissues damages thus causing pulmonary fibrosis, help in differentiation of B lymphocytes, promotes the growth of some and inhibits other categories of cells, temperature regulation that result into fever possibly played by the cytokines, in addition to, it also stimulates the production of acute phase proteins. Furthermore, it is implicated in the pathogenesis of the cytokines release syndrome that is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunction of the host attack by the virus. As the cytokines storm deluge (IL-6) if its activity could dampen by any means than patient hospitalized could emerge out from critical condition of pneumonia, fibrosis thus by keeping this principle on, tocilizumab a monoclonal antibody that block the IL-6 would be one important agent to be evaluated in clinical trial [25,26].

For about 80% of the infected patients, the disease will be either asymptomatic as reported in India or paucisymptomatic with mild fever and cough, and if the virus has followed oral route to course into gastrointestinal tract than diarrhea.

STAGE #3 CRITICAL PHASE OR RED GROUP

Unfortunately, about 20% patients progress to severe symptomatic infiltration that encompasses pulmonary infiltrates and develop serious conditions with initial recorded fatality rate 2% but varies with old age and immunity deficit population in that specific country. The route of virus is now reaching to alveoli the gas exchange region and invade alveolar type 2 cells through ACE2 receptor; propagate within the cell the result is enormous viral particle that burst out in the course host

cell undergo apoptosis and die, the released virus from infected type 2 alveolar cells than infect adjacent many other type 2 cells in adjacent unit, it seems as if pulmonary toxin is released to ravage more other type 2 cells. The resultant will be diffused type 2 alveolar cell damage and subsequently the regenerating pathway begins as type II cells are the precursor cells for type I cells [27,28].

The pathologic result of both SARS and COVID-19 is diffuse alveolar damage with fibrin rich hyaline membranes and a few multinucleated giant cells. The aberrant wound healing may lead to more severe scarring and fibrosis than other forms of acute respiratory distress syndrome (ARDS). Recovery will require a vigorous innate and acquired immune response and epithelial cell regeneration [29].

From the mentioned understood pathophysiology elderly population are at high risk to Covid-19, because of their lessened immune response due to old age and diminished ability to repair their damaged epithelium. Further, elderly also do have lessened mucociliary clearance and this let the virus to easily move towards the gas exchange units of the lungs [30].

CLINICAL FEATURES

The symptoms of the Covid-19 are rarely observed at the moment of infection, it takes an incubation period of 1-14 days. The patients symptoms varies on different stages as study reported that 43.8% had a fever on admission, 88.7% during hospitalization, and 67.8% were seen with cough. The mortality and case fatality rate increased with increasing ages; the case fatality rate was 8% in patients aged between 70 and 79 years while it was 15% in those aged 80 years or more but children as they with Covid-19 showed mild symptoms and 100% recovery. A study with ten children enrollment revealed of symptoms fever in 80% while 60% were with cough but recovered; however, they are more dangerous to society as the patient had prolonged virus shedding nature even in convalescent stage keep on outpouring virus in feces or in respiratory droplets. Most commonly children remain asymptomatic, but they keep on carrying the virus and if took test, will be tested positive, one study recruiting infected infants of age 1-11 months did not ask for mechanical ventilation or had to be admitted in intensive care [31].

Thus, Covid-19 clinical spectrum ranges from asymptomatic to paucisymptomatic form or in serious condition pneumonia led ARDS and needs mechanical ventilation in intensive care unit (ICU) support. The serious clinical manifestation appears to be pneumonia manifested by bilateral infiltrates in chest imaging with cough, high fever dyspnea, the less common symptoms reported includes headaches, sore throat, and rhinorrhea. Extra-respiratory symptoms are also common in elderly such as nausea and diarrhea.

The likelihood of Covid-19 symptoms made to suspect if the patient.

1. Was arrived from the Hotspot of SARS-CoV-2 within the prior 14 days
2. Has had come to engaged or not followed social distancing with suspected or Covid-19 patient prior 14 days or not wearing personal protective equipment in hospital setting [10].

DIAGNOSIS

The diagnosis is made on the basis of reverse transcriptase-polymerase chain reaction (RT-PCR) reference of virus RNA to find the positive nucleic acid of SARS Cov-2 in nasal, sputum, throat swab, and secretion of lower respiratory tract samples. The test could be false negative, the WHO guideline suggest that in that case of false-negative resampling and collection of sample from multiple respiratory sites are recommended as this testing have systematically evaluated. WBC counting might be another tool of diagnosis but it is uncertain whether the patient leukocytosis or leucopenia or lymphopenia but most commonly found is lymphopenia. Third tool for diagnosis is enzyme detection such as lactate dehydrogenase, aminotransferase, and ferritin level elevated.

Procalcitonin level soar up go when shifted to ICU but before it was normal, severe lymphopenia is associated in the patient with high mortality.

Computed tomography of chest demonstrates ground glass opacification without consolidated abnormalities with viral pneumonia in COVID-19 patient. However, others study have suggested that chest computed tomography abnormalities are more likely to be bilateral, have a peripheral distribution, and involve the lower lobes. Less common findings include pleural thickening, pleural effusion, and lymphadenopathy [32,33].

TREATMENT OF COVID-19

Till date, April 28, 2020, there is no specific medicine or vaccine for the treatment of the Covid-19, all the management is done on the basis of symptomatic and supportive therapy.

The first thing necessary to keep in mind is to prevent transmission if a person is found corona positive go to isolation, for mild symptoms, as done by the UK Prime Minister Boris Johnson when got infected of Cov and tested RT-PCR positive went on to isolate himself on his own apartment. While in early days milder symptoms were seen but later after 10 days, when symptoms become worsened than taken to hospital. Therefore, with this example one could easily understand that initial mild symptoms can be managed by staying at home remembering the danger sign to come if immune response of the host failed to combat the virus. Furthermore, maintenance of hydration, nutrition and controlling the cough and fever is the first basic principle of treatment [34].

There is, as of now, no approved treatment for COVID-19. Antiviral drugs such as ribavirin and lopinavir-ritonavir have been used based on the experience with SARS and MERS. In a historical control study in patients with SARS, treated with lopinavir-ritonavir with ribavirin had better outcomes.

Other therapeutics such as remdesivir seems to slows the progression of virus activity by block and mislead the virus to read the human machinery and prevent from the synthesis of its protein.

These drugs do not have large scale study but do contain compassionate therapy reports and need clinical trials. In this pandemic, most famous and globally demanded medicine to treat Covid-19 is chloroquine and hydroxychloroquine that showed antiviral and anti-inflammatory activity *in vitro*, the mechanism of action suggested is they interfere the binding of virus spikes with ACE2 receptor by S1 domain, prevent the fusion by S2 domain and packaging of the virus by altering impairment of acidification of endosome as well cover the effect of pro-inflammatory cytokines such as IL-1 and other setting provided additional benefits if used along with Azithromycin but the valid methodological concern of the control study and biologic basis of using azithromycin in this setting is still unclear given the relative safety of short-term use of hydroxychloroquine to intervene severe viral infection is practiced provided there is no other clinical trials [35]. However, individual more susceptible of having possibility of its toxicity QTc (prolongation of QT interval) and retinal toxicity, epilepsy, porphyria, myasthenia gravis, and retinal pathology – glucose-6-phosphate dehydrogenase deficiency should be considered before its use. As the “cytokines storm” deluge (IL-6) in severe Covid-19 patient, if its activity could dampen by any way then patient hospitalized could emerge out from critical condition of ARDS. Tocilizumab a monoclonal antibody that block the IL-6 is one agent need to be evaluated in clinical trial to patients with severe COVID-19.

The severity of illness result into the hypoxemic respiratory failure, in that case, patient is treated by supportive oxygen therapy like high flow nasal oxygen, the benefit of this is it reduces need of intubation, for critically ill COVID-19 patient main supportive treatment is mechanical ventilation. The COVID-19 hospitalized patient D-Dimer is found to be 4 times higher than normal limit; therefore, recommendation is

anticoagulant therapy if anticoagulant is not contraindication, and it is more caring decision to provide paracetamol than nonsteroidal anti-inflammatory drug.

PREVENTION

The basic principle is to get prevented from the infection by eliminating the source of infection, to cut the chain of transmission and to protect the susceptible population.

The main transmission occurs through respiratory droplets. Since, at this time, there are no approved treatments for this infection, prevention is only the management understood till date as Covid-19 virus properties is difficult to understand and being unclear over its infectivity, it is declared by the WHO that this virus is highly contagious, 10 times more than SARS and MERS, here, this virus is transmissible from asymptomatic cases, with long incubation period, transmission even after recovery clinically and viable in the surface area where it settles for long period.

The corona positive patient, therefore, must be placed in isolation for the virus containment and those who are in suspicious or traveller coming from Hotspot were kept under supervision of quarantine for at least 14 days and then tested for Covid-19 even if they are asymptomatic. The isolation room should be well ventilated and easy sunlight allowance for the destruction of virus. Surgical mask wearing to the patient and N95 mask for health worker with personal protective equipment, i.e., N95 respirators and protective suits and goggles to the health worker who are engaged to provide care to the patient and hand washing with soap in every 15–20 min strictly recommended. Health worker is highly in the zone of transmission; hence, their protection is the first priority of the government to combat this pandemic [36].

In isolation, patient room and surface should be cleansed regularly with sodium hypochlorite. Healthcare worker in the service should undergo self-quarantine for 14 days after handling the Covid-19 positive patient care for a week. From isolation patient is normally discharged only if they are afebrile for 3 days and have two consecutive negative RT-PCR test at 1 day sampling interval.

Wild animal that is the probable source of this virus, consumption and selling must be strictly prohibited in all part of the world especially China.

In summary, for protection and prevention, one must wear the mask in public or highly crowded area, should stay far away from the patient who are already infected, clean clothes or handkerchief must be used while coughing or sneezing to cover the mouth, should wash hand regularly for 20 s with soap and water to kill COVID-19, follow social

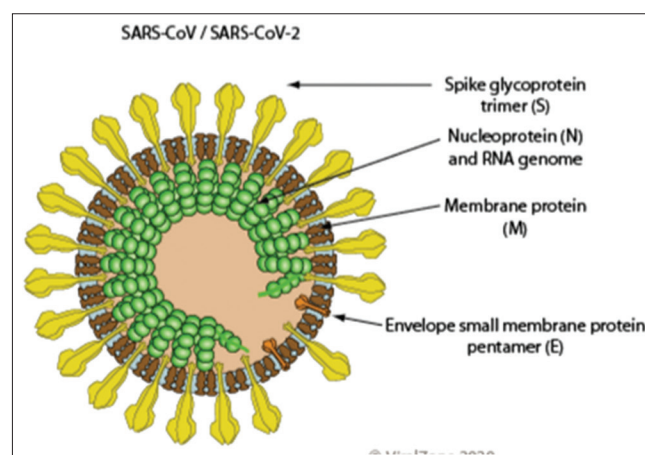


Fig. 1: Depicting severe acute respiratory syndrome-n CoV-2019 and its different proteins

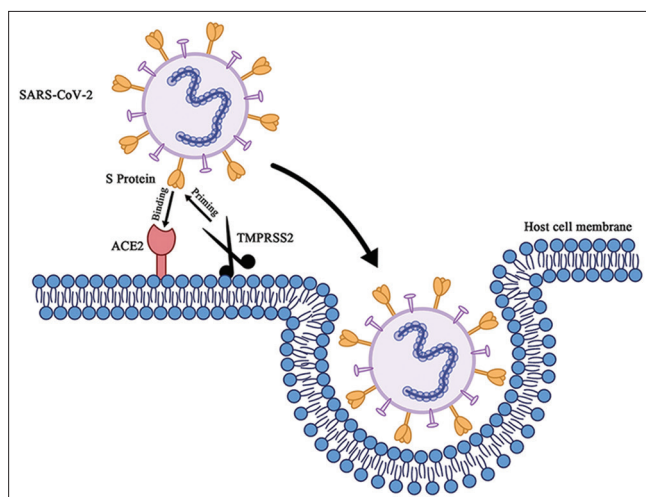


Fig. 2: Entry of virus into host cell

distancing by staying 2 m apart among and between one another, should abandon habit of touching hand to mouth, eyes and nose, for mild symptoms patient must follow isolation and for serious symptoms seek for hospitalization. At last but not the least, always follow the advice of doctors, nurse, or other health-care provider.

CONCLUSION

As no specific therapies are available for SARS-CoV-2, early containment and prevention of further spread will be crucial to stop the ongoing outbreak and to control this novel infectious threat. Therefore, properties, characteristics features of novel Cov 2019 understanding became quintessential to refrain from the viral infection and to know all the necessary precautionary step is mandatory for the survival of human being by this deadly disease. Hence, to vanquish this virus, a comprehensive strategy includes acute surveillance in diagnostic field boosting test and development of vaccines or drugs is urgently needed to win the battle against this COVID-19. It is very urgent to adopt social distancing, wearing mask and cleaning hand with soap for 20 s are only best way to remain safe until the vaccine be developed.

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