

A Brief Introduction and Treatment Protocol of COVID-19: A Review

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Abstract

There was the emergence of a new public health crisis known as COVID-19 or SARS-CoV-2. It is thought to be originated from a microbiology research lab of Wuhan, China. This was found to be similar as of SARS [Severe Acute Respiratory Syndrome] that was there in year 2003. The symptoms of COVID-19 that were reported are headache, pyrexia, cough, sore throat, breathlessness, fatigue, malaise etc. There were a lots of different treatment protocols in practice during that time because no one knew the exact treatment of this disease. Physicians were trying to treat it symptomatically. The primary symptoms in non-serious patients were loss of smell and taste. Various antivirals have been used in this but the most effective was found to be favipiravir. There were very serious complications of COVID-19 which cannot be treated properly. In this review article author have tried to give a treatment protocol which showed good results in patients with COVID-19 and also some of the drugs are there to overcome the Side effects of some drugs used in COVID-19. The major target organ of SARS virus is lungs and an attempt is made to prevent excess damage to the lungs but in some cases, it was not achieved so the last attempt is to transplant lungs is tried in some patients and a good result is obtained.

Keywords: Treatment protocol; Lungs; COVID-19; SARS; Pyrexia; Transplant

Introduction

Recently the world faced a serious bio war against a virus named SARS-CoV-2 broadly termed as severe acute respiratory syndrome corona virus 2, also known as n-CoV or novel coronavirus [1]. This was first released by a lab of Wuhan, Hubei province, china in December 2019. It was found to be spread via nasal route in the form of droplets.

As per record cases reported till date [23/05/21] are 16,63,46,635 and total deaths reported till [23/05/21] are 34,49,117 [2].

Its symptoms are similar to that of SARS which affected humans before 16 years [2003] which are fever, sore throat, headache, dry cough, dyspnea, acute respiratory distress syndrome (Table 1). This virus got spread too fast that who was compelled to declare it as 'Pandemic' on March 11, 2020 [3].

Corona is a self-mutating virus. It's different strains which are found till now are [4]:

Table 1: Classification of human corona virus.

Classification of Human Corona Virus	
HCOV-229E	Human Corona Virus 229E
HCOV-NL63	Human Corona Virus NL63
HCOV-HKUI	Human Corona Virus HKUI
HCOV-OC43	Human Corona Virus OC43
MERS-CoV	Middle East Respiratory Syndrome Corona Virus
SARS-CoV	Severe Acute Respiratory Syndrome Corona Virus
SARS-CoV-2	Severe Acute Respiratory Syndrome Corona Virus2

SARS-CoV-2 is the third corona virus that has caused severe respiratory disease in humans, originated from Wuhan, China which is spread globally in the past two decades. The first

corona virus that caused severe disease was SARS which was thought to be originated from Foshan, China and resulted in the pandemic of 2002-03. The second was the Middle East

Respiratory Syndrome Corona Virus [MERS] which was originated from Arabian Peninsula in 2012 [6].

SARS-CoV-2 has diameter of 60 nm to 140 nm and distinctive spikes which ranges from 9 nm to 12 nm giving the virions, the appearance of Solar Corona.

Variants of SARS-CoV-2 are [5]:

B.1.1.7 [Alpha]: This variant was first detected in the United States in December 2020. It was initially detected in the United Kingdom.

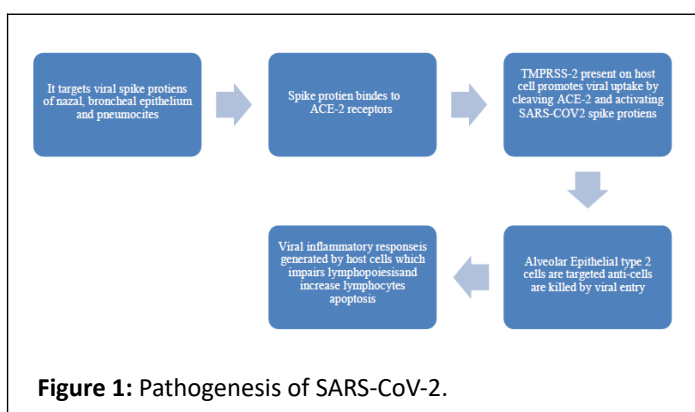
B.1.351 [Beta]: This variant was first detected in the United States at the end of January 2021. It was initially detected in South Africa in December 2020.

P.1 [Gamma]: This variant was first detected in the United States in January 2021. It was initially identified in travelers from Brazil who were tested during routine screening at an airport in Japan, in early January.

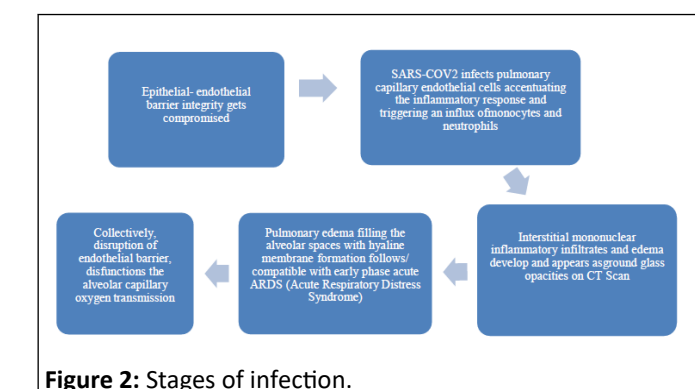
B.1.617.2 [Delta]: This variant was first detected in the United States in March 2021. It was initially identified in India in December 2020.

These variants were seen to be mutating and spreading very rapidly, which may lead to more cases of COVID-19. This rapid increase led to increase in number of patients and resources and healthcare facilities were being shorthanded day by day which led to more casualties and death rate. There was a huge demand of oxygen cylinders and medicines used for the treatment of symptoms [6].

Pathogenesis of SARS-CoV-2



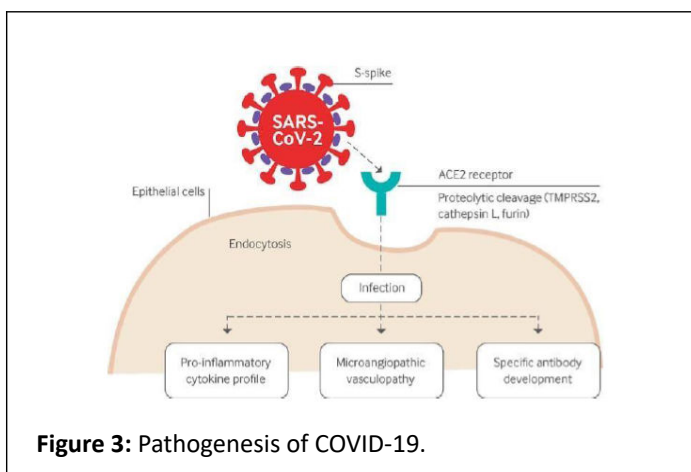
In later stages of infection



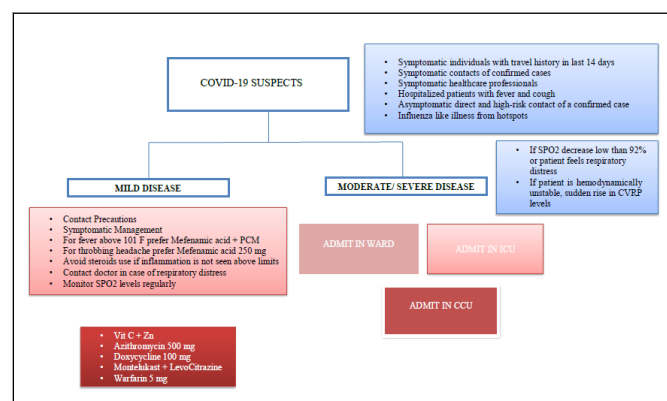
In severe COVID-19

- Fulminant activation of coagulation cascade and consumption of clotting factors occur which can lead to DIC [Disseminated Intravascular Coagulopathy]
- Inflamed lung tissues and pulmonary endothelial cells may result in micro thrombi formation and contribute to high-incidence of thrombotic complications such as DVT, pulmonary embolism, thrombotic arterial complications, ischemia, strokes, and myocardial infarction in critically ill patients.
- The end result may be sepsis by viral infection which can be defined by multi-organ failure which is a result of dysregulations of host response to infection.

Pathogenesis of COVID-19



Treatment protocol for management of COVID-19



Admit in ward

- Consider HCQS 400 mg Bd for 1st day & 400 mg Od for 4 days
- Take patient on oxygen support target [92%-96%]
- Prefer non re-breathing oxygen mask
- Closely monitor serology, blood parameters & ABG [Arterial Blood Gases]
- Prefer anti-viral like: Lopinavir, Ritonavir, Favipiravir
- Steroid's therapy should be administered in accordance with CRP, IL-6 and other inflammatory parameters
- Start methyl prednisolone from 0.5 mg per kg to 1 mg per kg

- Low molecular weight heparin/enoxaparin should be considered in accordance with D-dimer levels
- Antibiotics like clarithromycin, clindamycin, augmenting, doxycycline should be considered
- Systemic alkalosis or acidosis should be monitored and agents like sodium citrate or phosphoric acid derivatives should be administered as per requirement of patient
- Vit B complex and Vit C should be administered for prophylaxis
- Nebulization with budesonide +levosalbutamol+ipratropium bromide
- Mucolytics can be used if patient complaints of mucus or wheezing is heard
- A janus-kinase inhibitor like: baricitinib can be used with remdesivir for better cytokine storm controlling
- Admit In ICU [SpO2 below 75%]
- Give full O2 support
- Give mechanical ventilation
- IV methyl prednisolone 1- 2 mg/kg
- Dexamethasone 6 mg bd
- Antibiotics like Feropenem/Meropenem/Vancomycin should be considered in addition to broad spectrum antibiotic like Piperacillin+Tazobactam
- IL-6 inhibitor therapy can be given in severe patients which include Ramdesivir- if SpO2 => 75% & IL- 6 is 1.85 pg/ml
- Baricitinib+Ramdesivir- for IL-6 above 1.85 pg/ml or patient with severe respiratory depression
- Immunomodulatory therapy can be administered. Example: Methotrexate, cyclosporine etc.
- C-pap or bi-pap can be used for patients with poor ventilation
- Iron exchange therapy can be given with deferoxamine, revofer and darbepoetin
- Adjunct therapy of thiamine 200 mg and Vit C 100 mg can be given
- Prophylaxis if D-dimer is high then use NTG with LMWH with close monitoring of blood pressure
- Cardiac leads should be placed permanently till the time being in ICU for cardiac monitoring
- Lactate levels should be closely monitored in order to prevent septic shock
- If lactate level does not control by single antibiotic use colistin
- For increase in IL-6 above 15 pg/ml use tocilizumab 400 mg/ itolizumab /bevacizumab

Admit in CCU

- Take patient on full life support ventilation
- Broad spectrum antibiotics and colistin can be administered
- For patients who are not responding to IL-6 inhibitors well, prefer Anakinra 100 mg
- Take patient on ECMO-ventilation [Extracorporeal Membrane Oxygenation]
- IV steroids therapy like methyl prednisolone 2 mg/kg, hydrocortisone etc. can be used

- Mucus extraction can be done by mucus extractor
- For control of blood sugar levels, administer SC insulin
- If condition of patient is not improving, try for lungs transplant

Additional therapies targeted to specific components of the inflammatory cascades' macrophage activation and cytokine modulation by inhibition of:

- IL-1 inhibitor- Anakinra [11], Canakinumab [12], Rinolacept [13]
- IL-6 inhibitors [14] - Tocilizumab, Itolizumab, Sarilumab
- Janus Kinase inhibitor [15]- Baricitinib, Tofacitinib, Ruxolitinib
- IL-5 inhibitor for asthmatic COVID-19 patients, example: Mepolizumab [16]
- TNF alpha inhibitor- Adalimumab [17], Etanercept [18], Infliximab [19]
- Inflammasome- Colchicine [20]
- IL-17 inhibitor- Brodalumab [21]
- Steroids- Prednisolone, Methylprednisolone, dexamethasone [22]
- Anticoagulants – Rivaroxaban, low molecular weight Heparin, Apixaban, Warfarin, Clopidogrel [23]

Major side effects of interleukin inhibitors

- Bone marrow depression
- Oedema
- Gi irritation
- Nausea
- Vomiting
- Loss of apatite
- Mouth ulcers [Apathoes ulcer]
- Secondary infection
- Itching
- Respiratory difficulty

Treatment for controlling possible side effects of drugs

- Furosemide: edema
- Azacytidine [25]: bone marrow depression
- Iron replacement therapy by deferoxamine and darbepoetin [26,27]
- Idaruzimab: can be used to reverse the effect of dabigatran if there is overuse of dabigatran or bleeding due to any drug side effects [28]
- IV Ig can be used to reverse the adverse effect of COVID-19 induced autoimmune disease [29]
- Amphotericin b, Caspofungin, Posaconazole can be used for mucormycosis [30]

Laboratory Tests

Table 2: Details of laboratory tests.

LFT	KFT
CBC	CRP
D-dimer	Ferritin
LDH lactate	IL-6
IL-1	Blood glucose
Bacterial culture	Lipid profile
Troponin T	Troponin I
ANA	HR-CT
Chest X-Ray	CT-scan
MRI	CECT

Complications of COVID-19

- It triggers autoimmune disorders like GBS [31], RA [32]
- CHF [Congestive Heart Failure] [33]
- Mucormycosis [34]
- Pneumonia [35]
- Sepsis [36]
- Kidney injury [37]
- Clotting disorders [38]
- DIC [39]

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