Recent Development of COVID-19 Vaccines In Pandemic Condition

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ABSTRACT
Covid-19, a disease caused by SARS-COV2 found highly contagious. In December 2019 first patient with symptoms like pneumonia of unknown cause was found in Wuhan, China. During investigation Chinese health care found viral infection analogous to SARS-COV named as novel corona virus, COVID-19 corona virus disease 2019. They found that the disease spread by bats to human. Thailand, Japan, South Korea, Malaysia, Singapore, and the USA has report the patients with similar symptoms. With time disease spread worldwide. Soon WHO declared COVID-19 is pandemic disease and declared the ongoing outbreak to be global public health emergency. Currently various researches of SARS-COV2 in its primary stages at various research institutes. This review summarizes pathogenesis, symptoms, prevention, and treatment of disease. It hopes the review helps people to deal with SARS-COV2.

Keywords: Covid-19, Hydroxychloroquine, Remdesivir, ritonavir, vaccines

INTRODUCTION
Viruses are obligate intracellular parasites containing either DNA or RNA enveloped in protein coat known as capsid. Some of the viruses may contain lipid coat containing antigenic glycoprotein. Basically viruses are nonliving thing which replicate in host body. Corona virus are family various types of corona viruses, It causes mild to severe respiratory disorders. It consists various corona virus such as Severe Acute Respiratory Syndrome corona virus (SARS-COV)2003, Middle East Respiratory Syndrome corona virus (MERS-COV) 2012, Swine Acute Diarrhea Syndrome corona virus (SADS-COV) 2016, recently developed (SARS-COV 2) dec2019 novel corona virus also known as COVID-19 which means Corona Virus Disease 2019. Among all of these corona virus family COVID-19 found...
to be highly pathogenic to human and animals.

**Morphology of COVID-19**

COVID-19 caused by SARS-COV2, corona name is generates by its crown like structure. It consists single stranded positive sense RNA enveloped under lipid bilayer and various proteins named spike proteins (s proteins), membrane (M) proteins,(N) nucleocapsid proteins, envelop (E) proteins. Focus of pathogenesis is on S proteins.

![SARS-CoV 2 Structure](image)

**PATHOGENESIS**

**Stage 1: Asymptomatic stage**

This is initial stage 1-2 days of infection. Inhaled SARS-COV 2 likely bind to the epithelial cell in nasal cavity and start to replicate. After inhalation SARS-COV 2 bind to ACE 2 receptors. SARS-COV 2 propagates locally with low innate immune response. At this stage nasal swab can detect the virus by RT-PCR. Sample collection procedure should be standardized. Nasal swab is effective than throat swab.

**Stage 2: Upper airway and conducting airway response (next few days)**

At this stage virus propagate and migrate down the respiratory tract, most of immune response trigger severe at this stage. Beta and lambda interferon are major secretion by infected cell.CXCL10 is useful as disease marker. For most of patients disease will mild and restricted to upper airway.
Stage 3: Hypoxia, ground glass infiltrates, and progression to ARDS

Unfortunately few of patients progressed towards stage 3 and develop pulmonary infiltration and some patients may develop severe disease. Fatality rate varies according to age of patients. At this stage virus infect alveolar type II cells. Due to large infection apoptosis takes place and cell die. Most of alveolar type II cells are loses. Pathology leads to severe fibrosis. Wound healing and recovery requires great innate and acquire immune response and regeneration of epithelial cells requires. In this condition viral load may increases due to more ACE2 expression. Old age patients are at risk because their immunity is decreased and ability to repair damage also reduced.

Further detail study is going on to study other mechanisms of viral attack and pathogenicity of COVID-19.

DIAGNOSIS

Diagnosis is made by quantitative RT-PCR assay. If above mention symptoms are develop then refer to family doctor or physician, nasal or throat swab are taken and the detection of SARS-COV2 to be carried out by real time polymerase chain reaction.

TRANSMISSION

1. Zoonotic: transmission of COVID-19 by animal to human is known as Zoonotic
2. Person to person: transmission of disease by infected person to the others persons by sneezing, coughing, touching contaminated hands to each other
3. Contact with infected surfaces: touching to non-living infected surfaces and then to nose, eye, mouth may spread disease.

SYMPTOMS:

- Fever
- Difficulty in breathing
- Cough
- Headache
- Shortness in breath
- Shortness in breath.
COMPLICATIONS IN COVID-19

Cytokine
Cytokines are no of proteins secreted by cell in immune system which act as chemical messenger to activate and regulate immune cell against antigen. Cytokines are mainly acting by binding with receptor present at other immune cells. This protein mainly includes interleukins, interferons, lymphokines and TNF (Tumor necrosis factor). Lymphocytes, Macrophages and other immune cells secret cytokines. Main function of cytokines is to regulate immune system locally or systemically.

Cytokines storm
In viral infections large amount of cytokines are secreted which result in worsening of patients condition and may cause multi-organ failure, which may fatal to patient. In simple way cytokine storm is uncontrollable flood of cytokines which may worsens respiratory function with multi-organ failure. Cardinal feature of cytokine storm include fever, high rate of erythrocyte sedimentation, Adult Respiratory Distress Syndrome, massive increased ferritin. It was found that IL-2 and IL-7 levels were increased during SARS-COV2 infection. Thrombocytopenia also occurs, cytokines storm occurs after few days of infection.

TREATMENT
There is no specific treatment for the COVID-19 treatment given to patients for reducing their symptoms

Drugs:
1. Hydorxychloroquine and chloroquine
   It is belong to antimalarial drug approved by US FDA for emergency use. It is a drug recommended as chemoprophylaxis to COVID-19 dose recommended is 400 mg twice at day 1 and then weekly 400 mg. It is mostly used by healthcare workers, asymptomatic person contacted in infected patient. It act by increasing intracellular PH and prevent the lipid envelop degradation of virus which found effective to avoid replication of COVID-19.
2. Lopinavir and ritonavir:
   These are HIV protease inhibitors which are under trial for treatment of SARS-COV19.
3. Remdesivir:
   This drug is under randomized trial.
4. Ashwagandha:
SARS-COV2 infection is related to immune system of person. Ashwagandha may use as prophylaxis. Ashwagandha may effective in management of COVID-19 by modulating th1/th2 of host cell. It has immunomodulatory properties which boost host immunity and health.

Managing cytokine storm:
Randomized trial of anakinra (IL-1 inhibitor) proved effective in many patients with hyper inflammation. In randomized trial of tocilizumab (IL-6 inhibitor) proved effective at multicentre. Tacrolimus and mycophenolate (IL-2 inhibitor) are suggested in addition to above drugs. Corticosteroids not recommended daily.

Convalescent plasma therapy
Convalescent plasma therapy used in India is effective to treat COVID-19 patients. Patient recovering from COVID-19 are developing neutralizing antibodies in blood. Plasma obtained by separating and removing blood cells from blood which contains neutralizing antibodies which kills SARS-COV2 are used for treatment of COVID-19 in infected person.

Monoclonal antibody
Monoclonal antibodies are effective to target S (spike) proteins present on envelop of SARS-COV2 and inhibit viral entry in host cell. Spike proteins bind to angiotensin converting enzyme 2 (ACE2) proteins as host cell. This S protein bind to human and bat ACE2 enzyme. MAB may prove effective in treatment of COVID-19.

PREVENTION of COVID-19
1) Vaccine development
Development of virus vaccine have numerous challenges nowadays, virus vaccine must be immunogenic, safe, can induce long-lasting immunity in body, safe to use. To meet all these requirements, it is important to understand the role of B and T cell mediated protective immune response, Virus molecular biology and pathogenesis, complexity of viral antigen. There are various types of vaccines like live attenuated vaccine, whole inactivated vaccine, vectored vaccines with their own advantages and limitations. Live attenuated vaccine is generally most efficacious than inactivated non-living vaccine, but in terms of safety non-living vaccine is most safe than live attenuated vaccine. Currently there is numerous research institutes are studying virus for preparation of vaccines.
Some institutes studying vaccines in clinical trials.

2) Wash hands regularly with soap for 20sec or alcohol based hand sanitizer.
3) Clean and disinfect surface regularly.
4) Use mask and hand gloves.
5) Put a tissue while sneezing and coughing, throw the tissue in dustbin.
6) Avoid touching surfaces having chance of infection.
7) Wash fruits vegetables neatly before use.
8) Avoid frequent touching to mouth, eye, nose.
9) Take a bath after coming home from public places.
10) Maintain 3feet distance while talking with anyone.
11) If any symptoms are seen, self-quarantine must prefer.
12) Sick peoples must stay at home.

AYUSH Guidelines:
As we know there are no specific drugs or vaccines are not available for treatment or prevention of corona virus, AYUSH ministry suggest to improve immunity of body. Enhancing body’s natural immunity by various ways may found effective against fight with corona virus. We better know that prevention is better than cure.

General Measures
- AYUSH suggest drinking warm water daily.
- Practice Yoga, Pranayam, Exercise, and Meditation daily for at least 30min.
- Include Haldi (Turmeric), Lahsun (Garlic), Jeera(cumin), Dhaniya(coriander) indaily food.

Ayurvedic Immunity Boosting Measures
- Take 10 gm of chavanprash in morning or twice a day. Diabetics must prefer sugar free.
- Drink herbal tea containing sunthi (dry ginger), Dalchini (Cinnamon), kalimirch (Black pepper).
- Milk containing turmeric.

Simple Ayurvedic Procedure
- Apply coconut oil/ sesame oil / ghee in both nostrils in morning
- Take 1 tb spoon of coconut oil or sesame oil, do not drink Swish the mouth 2-3min and spit.

During dry cough/sore throat
- Steam inhalation with ajwain (caraway seed) once a day.
- Lavang powder in honey once or twice a day.

CONCLUSION:
The COVID pandemic is great challenge to peoples with no specific treatment option. Several researches are going on for development of vaccine and drugs for treatment of COVID-19.

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