Review Article

Management of SARS- CoV-2 (COVID-19) infection with special focus on Use of Hydroxychloroquine and Lopinavir/ritonavir

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Editor's comment -

A. The covid-19 pandemic is the greatest challenge for the current generation of physicians, scientists and health administrators
B. Strict use of PPE, face masks, isolation and quarantine are the most effective methods of prevention of this infection
C. The immunomodulator hydroxychloroquine is approved for prophylactic use in asymptomatic health care workers and household contacts. It is also approved as compassionate use for treatment of active covid-19 cases in the USA
D. Lopinavir/ritonavir and remdesivir are used in some countries, but efficacy is doubtful
E. Treatment with convalescent plasma may be considered in emergency situations.

Keywords: Coronavirus; Covid-19; Hydroxychloroquine; Isolation

The SARS- CoV-2 has spread to more than 160 countries in less than 100 days and infected more than a million humans worldwide, once human transmission started in the wet meat markets of Wuhan, China. On 11 March 2020, the WHO declared this global outbreak a pandemic. With no signs of its growing trajectory stabilising and an accompanying threat of a second wave of infection, by secondary transmission from asymptomatics and presymptomatics to the uninfected and unexposed, it is estimated thata third of the seven billion people in the world are at-risk of developing SARS-CoV-2 infection.

The SARS-CoV-2 as the novel COVID-19 is formally known, belongs to the family of coronavirus closely resembling SARS- CoV-1, which was responsible for the Severe Acute Respiratory Syndrome (SARS) outbreak in 2002-03 starting in Guangdong province of China, infecting around 8000 people and claiming around 700 lives globally.

COVID- 19, is a non segmented positive sense ssRNA virus. Originally zoonotic, it has skipped the species barrier following an animal-to-human transmission and subsequent human- to- human transmission[1]. The viral genome encodes four major proteins: spike, envelope, nucleocapsid and membrane proteins[2]. The spike proteins are responsible for facilitating the entry of virus into the target cells, via the specific ACE2 receptor found at various sites in the body. The ones involved in COVID-19 are present on the type 2 alveolar cells and the intestinal epithelial cells (villous cells)[3]. The envelope proteins are responsible for the positive serology.

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Transmission

COVID-19 is transmitted by large droplets (aerosols) and contact routes (fomites)[4]. In order to manage the COVID-19 pandemic, the transmission of the virus has to be contained. Aerosol or droplet transmission can be prevented by following the WHO guidelines for droplet precautions. Different surfaces harbour the virus particles for varying durations extending from few hours to days. Regular disinfection of surfaces with 70% alcohol or 0.5% sodium hypochlorite, regular washing of hands with soap and water for 20 seconds and avoidance or reduced touching of face, eyes, nose is recommended for limiting the spread of the virus[5]. More importantly, self isolation or physical (social) distancing of individuals needs to be practiced by the general population to limit the spread and contain the infection.

Another important factor contributing to the pandemic nature of COVID-19 is its Replication of virus R0 (naught); current estimates place the value around 2.5-2.9 which is higher than that of seasonal influenza6. A value greater than 1 signifies that the infection will increase exponentially in the population. However, the R0 is a modifiable factor and is the reflection of the virus and human behaviour. R0 onboard the Diamond Princess cruise ship was 15, emphasising the importance of social distancing, improved hygiene and isolation in containing the spread of this pandemic[7]. Incubation period is around 4 days (2-7) and may even extend up to 14 day[4].

Prevention

Role of facial masks at all times in community : It is essential that all persons minimize the innoculum through aerosol acquisition through a simple mouth and nostril cover with a home- made triple layer cloth face mask, which can be anything from a handkerchief, dupatta, turban or a bandana that can be easily disinfected (washed in soap water and dried in sunlight both of which are effective virucidal agents) and worn daily when they foray into open areas away from homes (when isolation) or national lockdown is lifted. Wearing the mask properly or even two such masks (for

better filtration of virus - free air) at the same time may impact ease of breathing and lessen compliance of its usage due to a closer fit around the face.

In hospitals, as a HCW, thoroughly effective personal protective equipment (PPE) is required as they need to care for patients for longer hours with large viral loads. Currently in triage areas, they would require N95 masks and bio protective items such as goggles or face protection, head cover, gowns, shoe covers and nitrile gloves. Among the individuals who are tested positive for COVID-19 requiring quarantine or isolation, require a triple layered face mask to be worn at all times during their hospital stay. However, N-95 masks are to be reserved for performing aerosol inducing procedures like intubation and tracheal aspiration. HCWs involved in house-keeping functions should wear rubber boots, longer gloves and should be trained to follow certain protective behaviour which is essential to maintain their own good health as well as the well being of the society. These include regular decontamination of surfaces regularly contacted such as mobile phones, keys, pens, etc. Avoid physical examination unless it is definitely indicated. Advice patients regarding limitation to visit clinics during these times. Thorough sanitation at home, of clothes to limit the spread to the family. It is best that we are prepared to have such PPE at all times and testing as many people as possible. Donning protective gears whenever available and complete adherence to social distancing protocols is mandated.

Infection with COVID-19, typically produces no symptoms (asymptomatic) to mild symptoms like mild fever, cough and occasionally diarrhoea. The disease however may progress to potentially fatal Acute respiratory distress syndrome (ARDS) and Severe Acute Respiratory Infection (SARI) .The development of ARDS follows destruction of the alveolar cells and hyaline membranes. This is secondary to the cytopathic effects of the virus and the immune response of the body. Fatality of the disease occurs due to hyperinflammation, a response by the adaptive immunity that progresses to immunopathological dysregulated cytokine storm, macrophage blockade representing a virus induced Haemophagocytic lymphohistiocytosis and effect on coagulation cascade in the pulmonary vessels impacting oxygenation[8]. Besides a virus induced effect on the haemoglobin chain moiety affects the oxygen delivery to tissues and inducing other organ failure.

Diagnosis:

Performance of Detection Methods Over Time (Sensitivity Scores, Days Post-Symptom Onset)

Current update of Covid-19 (April 21,2020)
Total cases globally: 2314621
Total death globally: 157847
India total cases: 18601
India total deaths: 590

Table 1: gives the information regarding the various serological tests that can be performed and their sensitivity scores over the timeline of COVID-19 infection[10].

	Days after Symptom Onset		
SARS-CoV-2 Test	1–7	8–14	15–39
RNA by RT-PCR	67%	54%	45%
Total Antibody	38%	90%	100%
IgM	29%	73%	94%
IgG	19%	54%	80%

The diagnosing criteria includes clinical as well as laboratory and radiological findings. Any patient following clinical suspicion must be isolated and thoroughly investigated.

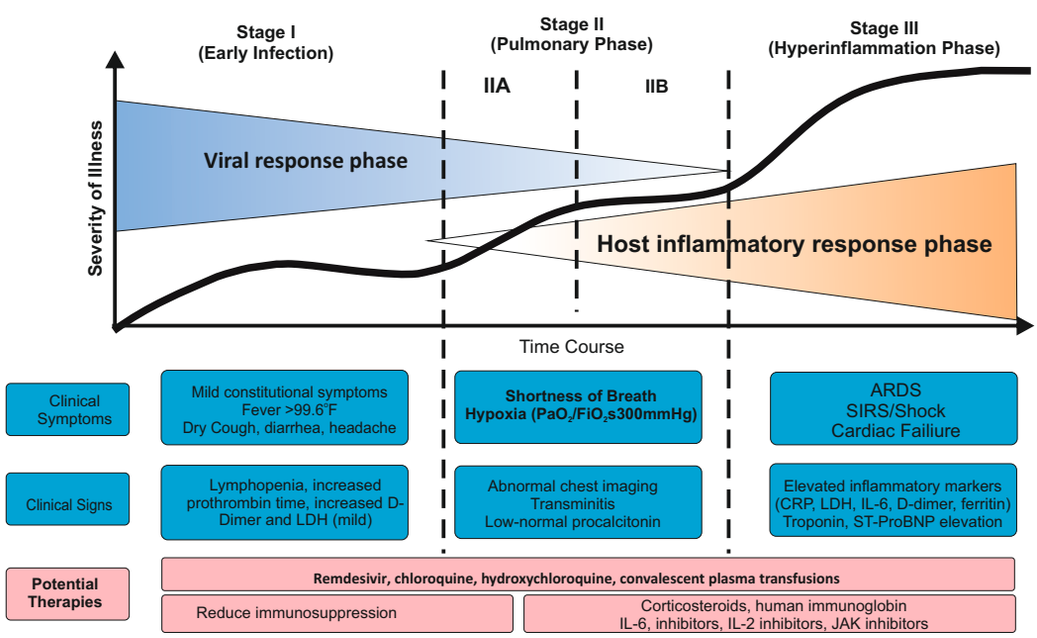

Figure 1: Covid-19: Stages, severity of illness, clinical signs, symptoms and potential therapies