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# Review Article COVID-19 an update

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### ABSTRACT

In the month of December 2019 a bunch of unidentified viral pneumonia was reported in china. One month after the first appearance of this deadly virus WHO declared it as a Public Health Emergency of International Concern. Finally, a new coronavirus, putatively named 2019-nCoV was establishes as the causative pathogen of this outbreak by the World Health Organization (WHO) on January 12, 2020.

In spite of stringent universal containment and quarantine efforts, the prevalence of COVID-19 continues to grow. In response to this universal outbreak, we analyze the present state of awareness surrounding COVID-19.

In this study we reviewed, the causative agent, transmission, risk among health care workers, sign and symptoms, diagnosis, treatment and management of the disease are all reviewed.

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## 1. Introduction

In December 2019, a bunch of cases of anonymous viral pneumonia were reported in China.<sup>1–3</sup>The proved cases were related with the Huanan seafood merchandise in Wuhan, where various forms of live wild animals are sold, including poultry, bats, groundhogs, and snakes. Many investigations were conducted, aiming at the standing of the etiological factor. Several etiological agents that may lead to identical symptoms were proposed, including the severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), avian influenza virus, and other familiar respiratory pathogens. Finally, a new coronavirus, putatively named 2019-nCoV was established as the causative pathogen of this outbreak by the World Health Organization (WHO) on January 12, 2020.<sup>1,4</sup>

Although the disease started from a zoonotic origin, later on human-to-human transmission has taken place being The elderly patients with/without debilitating diseases, and the very young patients have a higher risk of getting infected compared to the young healthy individuals. Mounting evidence confirmed higher mortality among older individuals with COVID-19.<sup>2</sup>

This mini review provides concentrated and updated information on many aspects of COVID-19.

## 2. Structure of COVID-19

Coronaviruses are representatives of the subfamily Coronavirinae in the family Coronaviridae and the order Nidovirales. On the basis of its phylogenetic link and genomic structures, 2019-nCoV fits into the genera Betacoronavirus. Its genetic makeup is very close to that of (SARSr-CoV).<sup>8</sup>

\* Corresponding author. E-mail address: amitbyatnal@gmail.com (A. Byatnal). 2019-nCoV is a spherical or pleomorphic enveloped particles. It consists of a single stranded RNA with

responsible of the outbreak  $^2$  prompting the World Health Organization to declare it a pandemic on March 11th 2020.  $^{\rm 4-7}$ 

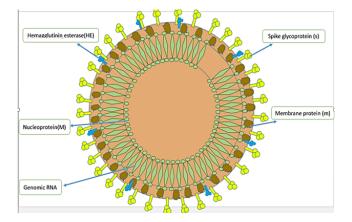


Fig. 1: Probable structure of COVID-19

a diameter of 80–120 nm, which is linked with a nucleoprotein within a capsid encompassing matrix protein. The enclosure carry club shaped glycoprotein projections.<sup>8</sup>

Coronaviruses contains the largest genomes (26.4-31.7 kb) amid all established RNA viruses, with G + C contents varying from 32% to 43%. Fluctuating sum of small open reading frame (ORFs) are present between the different conserved genes (ORF1ab, spike, envelope, membrane and nucleocapsid) and, downstream to the nucleocapsid gene in different coronavirus lineages. The viral genome consists peculiar features, including an exclusive N-terminal fragment within the spike protein.<sup>8</sup>

Corona viruses primarily use S protein on their surface to attach to the corresponding receptors on target cells to eventually enter into the cells. A structured model study displayed that 2019-nCoV binds to ACE2 receptors with more than 10-fold greater affinity than SARS-CoV, and at a level higher than the threshold recommended for virus infection, suggesting a swift transmission efficiency of SARS-CoV-2 in humans compared with SARS-CoV, a matter that explains the larger number of proved cases of COVID-19 compared with SARS-CoV infection. Given the superior affinity of SARS-CoV-2 binding to ACE2, soluble ACE2 may be a possible contender for the cure of COVID-19.<sup>9</sup>

#### 3. Transmission

Recognizing the routes of SARS-CoV-2 spread remains essential for anticipating the course of the pandemic and the possibility of continuous transmission. The spread of a given virus is represented by its reproduction number, R which means the average number of recent infections developed by each infected person, the initial constant of R is called the basic reproduction number, R0: the greater the R0 the more frequent the transmission potential. The RO of SARS-COV-2 as predicted by various research groups is ranging from 2.2 to 3.11, which is undoubtedly higher related to that of H1N1 (1.25), and very close to that of SARS (2.2–3.6), suggesting that SARS-CoV-2 has a greater spreading potential.<sup>1</sup>

Although patients with symptomatic COVID-19 have remained the major cause of transmission, latest information advocate that asymptomatic patients and patients in their incubation period are also carriers of the disease.<sup>3,5</sup> Due to this fighting COVID-19 is immensely challenging, as it is not easy to find and quarantine these patients in time, which eventually leads to build up of the disease in the society. Furthermore, it is early to exempt whether patients in the recovering phase are a potential source of disease spread.<sup>5</sup>

All ages are prone to develop infection. Person-to-person spread is speculated to arise amid close contacts chiefly by virtue of giant respiratory droplets produced during coughing and sneezing by patients who are symptomatic, asymptomatic and can also occur even before the onset of symptoms.<sup>3,6</sup> The viral overload is similar among symptomatic and asymptomatic people with higher loads in the nasal cavity as compared to the throat. These infected droplets can spread till 1-2 m and drop on surfaces. The virus can continue to be viable on surfaces for days in supportive climate but it can be eradicated by simple disinfectants like sodium hypochlorite, hydrogen peroxide etc. The virus is acquired both by inhalation of these droplets or touching surfaces contaminated by them and then touching the nose, mouth and eyes. It has been hypothesized that the virus can be acquired through feco oral route as virus has been identified in the stool. As stated by the joint WHO-China report the fecal-oral spread did not emerge to be an important aspect in the transmission of this infection.<sup>10</sup> However it has not been described that COVID-19 can be acquired through pregnant women to the fetus through placenta. The incubation period varies from 2 to 14 d. <sup>3,6</sup>

#### 4. Risk of Infection among Health Care Worker

Health care employee on the front lines of the fight against COVID-19 bear a greater possibility of getting infected and are encountered with the risk of not only getting sick and dying, but also of carrying the infection home to their families and contributing to spread in their communities. In a study carried out at Massachusetts General Hospital, King's College London revealed that frontline health care providers had approximately 12-times greater risk of testing positive for COVID-19 in comparison with the people in the general community, and in particular the workers who lack access to personal protective equipment (PPE) had an even greater risk.<sup>11</sup>

In China, more than 3000 health care providers have been infected with the virus, and at least 22 have died. Some reports even proposed that spread has resulted when the healthcare provider were asymptomatic.<sup>12</sup> It is predicted that they constitue in between 4% and 19% of all reported COVID-19 cases in Europe and China.<sup>10</sup>

The standard preventive measure according to CDC for covid-19 are as follows:

- 1. Wash your hands regularly with soap and water, or clean them with alcohol-based hand rub.
- 2. Maintain at least 1 metre distance between you and people coughing or sneezing.
- 3. Avoid touching your face.
- 4. Cover your mouth and nose when coughing or sneezing.
- 5. Stay home if you feel unwell.
- 6. Refrain from smoking and other activities that weaken the lungs.
- 7. Practice physical distancing by avoiding unnecessary travel and staying away from large groups of people.<sup>13</sup>

## 5. Clinical Manifestation

The COVID-19 presents with complex and varied symptoms.<sup>14</sup> It can differ among individuals from being mild(i.e. non-pneumonia and mild pneumonia), severe(i.e. dyspnea, respiratory frequency  $\geq$ 30/min, blood oxygen saturation  $\leq$ 93%, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, and/or lung infiltrates >50% within 24 to 48 hours), to critical (i.e. respiratory failure, septic shock, and/or multiple organ dysfunction or failure).<sup>15</sup>

The most prevelent symptoms of COVID-19 are fever, cough and fatigue; occasionaly patient might have diarrhea and vomiting. Most of the patients develop acute respiratory distress syndrome after 9 days from the time of symptom outbreak.<sup>6,9,14</sup> Cases resulting in death were primarily middle-aged and elderly patients with pre-existing diseases (tumor surgery, cirrhosis, hypertension, coronary heart disease, diabetes, and Parkinson's disease).<sup>6</sup>

## 6. Diagnosis

According to the protocol released by WHO on case vigilance of COVID-19 on 31<sup>st</sup> January 2020, which states that if an individual match certain criteria, WHO advocate to initially screen for other frequent sources of respiratory ailment given the season and region. If a negative outcome is established, the sample should be sent to standard lab for SARS-CoV-2 recognation.<sup>6</sup> A suspect case of COVID-19 is an individual who has fever, sore throat and cough and who has history of tour to China or other field of repeated regional spread or contact with patients with identical tour history or those with proved COVID-19 infection.<sup>3</sup>

Real time-polymerase chain reaction (RT-PCR) has served as the initial clinical laboratory diagnostic test during COVID-19 spread. It is frequently utilized to identify causative viruses from sputum, throat swabs, and secretions of the lower respiratory tract samples. Numerous specific and sensitive assays addressing RdRP, N, and E genes of the SARS-CoV-2 genome were created to identify viral RNA in clinical samples. Lower respiratory tract specimens contribute the higher viral loads.<sup>16</sup>

#### 7. Radiologic Findings

Radiology finding may vary with patients age, disease progression, immunity status, comorbidity, and initial medical intervention.<sup>6</sup>

Since the disease present itself as pneumonia, X-ray imaging plays a significant role in the diagnostic process, treatment, and follow-up. Basic radiographic examination (X-ray) of the chest has a low sensitivity in finding initial lung variations and in the early phase of the disease. However in the advanced phase of infection, the chest X-ray examination commonly display bilateral multifocal alveolar opacities, which tend to confluence up to the complete opacity of the lung.<sup>16,17</sup>

Computed tomography (CT) plays a crucial part in the diagnosis and evaluation of COVID-19. CT imaging typically display infiltrates, multiple patchy ground glass opacities and sub segmental consolidation with peripheral distribution.<sup>1,6,16,18,19</sup> Although a positive contact history, systemic symptoms, and radiographic changes of pneumonia make the diagnosis likely, the laboratory diagnosis is more reliable.

Various studies were done to evaluate the efficacy of chest CT and RC-PCR for the diagnosis of COVID-19 infection and they concluded that the sensitivity of chest CT was higher than that of RC-PCR.<sup>16</sup> In suspicious patients it was 97% based on positive RT-PCR result and 75% based on negative RT-PCR results. These data suggest that chest CT is a sensitive method to identify SARS-CoV-2 infection.<sup>1,20</sup>

#### 8. Treatment

At this stage, there is no definitive antiviral therapy approved for COVID-19, neither there is any specific vaccine available.<sup>1,16,21</sup> Hence the management is mainly essentially supportive and symptomatic.<sup>5,6,9,16,18,20-22</sup> The initial step is to assure sufficient confinement to avoid spread to other contacts, patients and healthcare workers.<sup>6,15,18,21</sup>

Effective symptomatic backing remains the key for management of mild to moderately ill patients, like managing hydration and nutrition and controlling fever and cough. <sup>1,9,16,18</sup>

As far as the management of severe or patients with respiratory failure is concerned, oxygen inhalation through a mask, high nasal oxygen flow inhalation, non-invasive ventilation, mechanical ventilation and even extra corporeal membrane oxygen support may be required. <sup>1,6,15,16,18</sup>

## 9. Antiviral Theraphy

Antivirals are leading medications under research for the management of COVID-19.<sup>4</sup> In a patient where viral infection has been previously established, antiviral therapy can be initiated.<sup>23</sup> Current guidelines suggest IFNalpha, lopinavir/ritonavir, ribavirin, chloroquine phosphate, and arbidol as antiviral therapies.<sup>1,18</sup> A combination of Oseltamivir an antiviral drug with empirical antibiotic has been utilized to treat COVID-19 patients.<sup>6</sup> A broad spectrum antiviral drug Ramsedivir, has established in vitro and in vivo effectiveness against SARS-CoV-2 and has also started its clinical trial.<sup>4,6,15,16,20,23,24</sup>

In a statement released in late February 2020 by the assistant director-general of the World Health Organization Mr Bruce Aylward thinks that remdesivir is the sole antiviral drug which has real efficacy.<sup>16</sup> The outcome from a randomized trial for the management of COVID-19 with a triple drug combination remedy for 14 days that comprised of interferon beta-1b, lopinavir-ritonavir and ribavirin, has demonstrated the combination is safe and useful at diminishing the span of viral shedding than lopinavir-ritonavir alone in mild to moderately ill patients. However severe cases were not included in this trial. They further stressed that it should be confirmed in a larger 3 phase trial.<sup>25–27</sup>

## 10. Chloroquine

Chloroquine (500 mg every 12 hours), and hydroxychloroquine (200 mg every 12 hours) were suggested as immunomodulatory therapy.<sup>15,16</sup> Multicenter clinical trials supervised in China indicated that chloroquine phosphate, might possess certain potency against COVID-19 related pneumonia, with respectable safety.<sup>1,16</sup>

While contradicting the above study other researcher observe that the usage of chloroquine or hydroxyl-chloroquine doesn't have any benefit and it is associated with increased hazard of mortality and heart arrhythmias amid hospital patients with COVID-19. The authors advocate that the above mentioned drug regime should not be adopted to manage COVID-19 outside of clinical trials.<sup>28,29</sup>

The Executive Group of the Solidarity Trial decided to implement a temporary pause of the hydroxychloroquine arm of the trial, because of concerns raised about the safety of the drug, later on 3hrd of June 2020 the group endorsed the continuation of all arms of the Solidarity Trial, including hydroxychloroquine.<sup>2</sup>

#### 11. NSAIDs and Corticosteroids

Numerous research in humans recognized that corticosteroids emerged useful in diminishing immunopathological harm, but concerns focused over the backing of viral rebound and association with adverse incident.<sup>30</sup> Initial clinical trial in critically ill patients with COVID-19 in UK shows that dexamethasone, a corticosteroid, can be lifesaving. For patients on ventilators, the treatment was shown to reduce mortality by about one

third, and for patients requiring only oxygen, mortality was cut by about one fifth.<sup>31</sup> Elevated ACE2 expression was noted while using ibuprofen in diabetic and those patients treated with angiotensin II type-I receptor blocker. Therefore it was proposed that this elevated expression in these patients could aid infection with COVID-19.<sup>32</sup> On 16<sup>th</sup> march 2020 Belgian Federal Agency for Medicines and Health Products stated that NSAIDs and corticosteroids can induce severe complications. Another report by French Authorities recommended that the usage of ibuprofen in COVID-19 patients was unfavourable to patient status and recovery.<sup>30</sup>

## 12. Convalescent Plasma

Maximum patients after recovery from COVID-19 will produce immunoglobulin antibodies in the plasma which can curb viremia and their serum could be of use to avoid re-infection.<sup>9</sup> Certain studies claimed that after plasma transfusion development in clinical conditions were noted including normalization of body temperature within three days and decline in sequential organ failure assessment score, resolution of ARDS, an accomplishment of veining off from mechanical ventilation and decrease in viral loads and increase in SARS-COV-2 specific ELISA and neutralizing antibody.<sup>32</sup>

Standard CDC guidelines for the treatment of COVID-19 patients are as follows:

## 12.1. Mild illness

Patients with fever, cough, malaise without shortness of breath dyspnea on exertion, or abnormal imaging. Most mildly ill patients can be managed in an ambulatory setting or at home through telemedicine or remote visits. All patients with symptomatic COVID-19 and risk factors for severe disease should be closely monitored. In some patients, the clinical course may rapidly progress. No specific laboratory evaluations are indicated in otherwise healthy patients with mild COVID-19 disease.

## 12.2. Moderate illness

Moderately ill COVID-19 patients who have evidence of lower respiratory disease by clinical assessment or imaging with SpO2  $\geq$ 94% on room air at sea level. Close monitoring of patients with moderate disease is recommended. If bacterial pneumonia or sepsis is strongly suspected, administer empiric antibiotic treatment for community-acquired pneumonia, re-evaluate daily, and if there is no evidence of bacterial infection, de-escalate or stop antibiotics.

## 12.3. Severe illness

Patients with COVID-19 are considered to have severe illness if they have SpO2 less than 94% on room air at sea level, respiratory rate less than 30, PaO2/FiO2, less than 300mmHg or lung infiltrate more than 50%. These patients may experience rapid clinical deterioration and will likely need to undergo aerosol-generating procedures. They should be placed in AIIRs, if available. Administer oxygen therapy immediately using nasal cannula or high-flow oxygen.

If secondary bacterial pneumonia or sepsis is suspected, administer empiric antibiotics, re-evaluate daily, and, if there is no evidence of bacterial infection, de-escalate or stop antibiotics.

Evaluation should include pulmonary imagining (chest x-ray, ultrasound, or, if indicated, CT) and ECG, if indicated. Laboratory evaluation includes a CBC with differential and a metabolic profile, including liver and renal function tests. Measurements of inflammatory markers such as CRP, D-dimer, and ferritin, while not part of standard care, may have prognostic value.

## 12.4. Critical illness

Severe cases of COVID-19 may be associated with acute respiratory distress syndrome, septic shock that may represent virus-induced distributive shock, cardiac dysfunction, elevations in multiple inflammatory cytokines that provoke a cytokine storm, and/or exacerbation of underlying comorbidities. In addition to pulmonary disease, patients with COVID-19 may also experience cardiac, hepatic, renal, and central nervous system disease. Because patients with critical illness are likely to undergo aerosolgenerating procedures, they should be placed in AIIRs when available. Most of the recommendations for the management of critically ill patients with COVID-19 are extrapolated from experience with other life-threatening infections. Currently, there is limited information to suggest that the critical care management of patients with COVID-19 should differ substantially from the management of other critically ill patients, although special precautions to prevent environmental contamination by SARS-CoV-2 are warranted.

As with any patient in the intensive care unit (ICU), successful clinical management of a patient with COVID-19 depends on attention to the primary process leading to the ICU admission, but also to other comorbidities and nosocomial complications. They further advise to refer Antiviral and Immune based therapy to review the available clinical data regarding drugs being evaluated for treatment of COVID-19.<sup>33</sup>

#### 13. Source of Funding

None.

## 14. Conflict of Interest

None.

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