# Severe acute respiratory syndrome-coronavirus 2 and novel coronavirus disease 2019: An extraordinary pandemic

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## ABSTRACT

COVID-19 has emerged as one of the most significant illnesses of the current century. It is caused by severe acute respiratory syndrome coronavirus 2. The world was initially viewing it as a localized outbreak in Wuhan city of China; however, it started spreading quickly to other parts of the world. Globally, half-hearted containment measures and a false sense of safety against this novel coronavirus led to the dissemination of disease. Currently, no effective therapy or vaccine is available to manage this illness. After learning a huge lesson, global efforts would hopefully lead to effective control of this pandemic.

**KEY WORDS:** COVID-19, pandemic, severe acute respiratory syndrome coronavirus 2

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## INTRODUCTION

The World Health Organization (WHO) was notified of a pneumonia of unknown cause in Wuhan city, China on December 31, 2019, in people visiting the Huanan seafood market which was subsequently shut down.[1] The pneumonia was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and is called as the novel coronavirus disease 2019 (COVID-19). The disease spreads across China and subsequently the world. As of March 22, 2020, there have been 318,662 confirmed cases and 13,672 deaths in 169 countries across the world with an increasing number reported daily.[2] On March 12, 2020, the WHO declared COVID as a pandemic.

## CORONAVIRUS 2

Coronaviruses infect mammals and birds, primarily involving the respiratory and gastrointestinal tract.[3] However, they have been involved in three epidemics so far: SARS-CoV-1 leading to SARS pandemic in 2003, Middle East respiratory syndrome (MERS) in 2013, and the novel coronavirus outbreak in 2019. The coronaviruses primarily reside in the bats then infect the civets, followed by camels and then human beings. However, now human-to-human transmission has been documented. They are extremely pathogenic, and the SARS-CoV-2 has 380 amino acids different from the SARS-CoV-1.[3]

The spread of infection is through droplets from respiratory tract secretions and possibly a fecal–oral route. Once the pandemic subsides, it needs to be seen whether the disease would become an endemic or vanishes rapidly. The reproductive number ($R_o$) for SARS-CoV-2 is around 3, which means each case infects three new cases.[4,5] This is much higher than H1N1 influenza which is 1.4–1.6.

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Although the virus has been isolated from conjunctival secretions, tears, and stools, it is unclear whether these may be a source of infection.[6] The CoV-2 is apparently quite sturdy with a recent study reporting that the virus can survive on steel and plastic for up to 4 days similar to the CoV-1.[7] SARS-CoV-1 epidemic also had previously reported in patients, family members, and hospital staff indicating a nosocomial spread.[8] The incubation period varies but is usually within 14 days.[9-11] The case fatality rate is 2%–4%, compared to 10% and 35% for SARS-CoV-1 and MERS, respectively.

## RISK FACTORS

Population at risk for severe infection are elderly (>60 years), those having comorbid conditions such as diabetes, hypertension, coronary artery disease, chronic pulmonary diseases, and cancer. More recently, it has been found to affect the younger population as per the Centers for Disease Control and Prevention data from the USA. Health-care workers are another susceptible group with longer duty hours, poor hand hygiene, and high-risk settings as the possible causes.[12]

## CLINICAL FEATURES

Reports have suggested that around 80% of CoV-2 illness manifest mild, 15% moderate, and 5% severe symptoms requiring intensive care unit care. There is a group of patients who do not manifest symptoms and are thereby asymptomatic carriers. These make the case count much higher and case fatality rate lower. Clinical manifestations comprise fever, cough, and fatigue. Dyspnea is reported in patients who develop lower respiratory tract involvement. Hemoptysis has also been reported.[13] Nausea, vomiting, and diarrhea are uncommon.[14] Computed tomography reveals ground-glass haziness or patchy areas of consolidation or crazy-paving pattern with or without subpleural predominance.[5] Unilateral and bilateral lung involvement has been noted. However, cavitation, tree in bud, and pleural effusion are less likely in COVID. Postpneumonia fibrosis has also been documented, and it is unclear about the prognosis of this fibrosis.[15] Laboratory abnormalities include lymphocytopenia, thrombocytopenia, leukopenia, and elevated C-reactive protein and serum ferritin levels. Derangement of liver function tests, renal function tests, and raised d-dimer has also been reported. A throat swab for reverse transcriptase polymerase chain reaction for novel-CoV-2019 is diagnostic for the virus. The strategies for testing of suspects have been evolving with current recommendations to test symptomatic people who have a history of travel outside the country, symptomatic contacts of confirmed COVID cases, symptomatic health-care workers, and patients admitted with acute severe respiratory illness. In addition, asymptomatic individuals or health-care workers who have had direct contact with a positive case without adequate personal protective equipment need to be tested.[16]

## MANAGEMENT STRATEGIES:

It seems that this virus has a unique capability to affect a large population cohort within a very short span of time due to rapid and sustained person-to-person transmission and can disrupt the health-care system of even highly sophisticated nature. Indirect economic impact of the illness on a particular political region may be enormous.

So far, the most effective strategy against this virus is containment measures. The importance of adequate respiratory droplet precautions, hand hygiene, and disinfection of frequently touched surfaces can never be overemphasized. Half-hearted travel restrictions, unmonitored containment, and meager screening at entry points seem to be counterproductive. Quarantine, social isolation, and lockdown have been tried successfully by China and some other countries, but unless we develop a concrete therapeutic strategy, we are going to see recurrent emergence of the illness in areas cleared of illness in large proportions.

Since the COVID-19 is due to a novel virus, the therapeutic strategies against it have been evolving rapidly after its first outbreak in China. No vaccine or specific treatment for COVID-19 can be recommended till this writing, and the care is mainly supportive.

In case of no lower respiratory tract involvement, isolation is advised. Once patient develops lower respiratory tract infection, supplemental oxygen, high-flow nasal cannula, or noninvasive ventilation (NIV) may be attempted. A full face mask or helmet mask may be tried. However, close watch should be kept on the patient's condition; in case of deterioration or NIV failure, prompt intubation should be done. Mechanical ventilation should be initiated as per the acute respiratory distress syndrome net protocol. Extracorporeal membrane oxygenation may be needed in severe cases. Elderly patients, comorbid conditions, high d-dimer levels, or higher sequential organ failure assessment score have been associated with worse survival.[17]

The therapeutic measures are mainly based on weak level of evidence due to a lack of high-quality randomized controlled trials. Some regulatory authorities have suggested restricted protocols for compassionate use of some drugs or combinations for epidemic setting based on the effectiveness of these drugs in other indications. Most of the antiviral agents have been used in moderate-to-severe COVID-19 disease. It has been postulated that the use of these agents earlier in the course of illness may prove to be a better option in halting disease progression. Herein, we will try to briefly enumerate some of the most promising therapeutic options that are likely to emerge in the near future.

### 4-aminoquinolines

Both chloroquine and hydroxychloroquine have been demonstrated to inhibit CoV-2 *in vitro*.

Hydroxychloroquine acts by increasing the pH of endosomes and lysosomes which make the epithelial cell resistant to viral replication. It reduces the transcription of pro-inflammatory genes, therefore cytokine storm. It interferes with glycosylation of angiotensin-converting enzyme 2 (ACE2) and reduces the binding efficiency between ACE2 on the host cells and the spike protein on the surface of the coronavirus. As per Chinese experience, the use of chloroquine has been associated with decreased duration of symptoms and reduced progression of the disease.[18]

In the French study, hydroxychloroquine was associated with increased effectiveness in combination with azithromycin.[19]

However, this study has serious methodological limitations and was based on improper rationale. Chloroquine and hydroxychloroquine are also being seen as promising agents for prophylaxis against COVID-19 in the high-risk groups including health-care workers.[20]

### Lopinavir-ritonavir

Which is primarily used in HIV has shown *in vitro* activity in CoV-1. The experience on the clinical use of this combination in CoV-2 is mainly limited to case reports. A controlled trial from China on 99 patients with COVID-19 has failed to show its significant effect on mortality or time to clinical improvement.[21]

### Remdesivir

Remdesivir is a nucleotide analog having *in vitro* activity against CoV-2. It has been tested in CoV-1 and MERS CoV. It has been recently tried on the first case of COVID-19 in the USA.[22]

A phase 3 randomized, double-blind, placebo-controlled trial is evaluating the efficacy and safety of remdesivir in patients hospitalized with mild-to-moderate COVID-19 respiratory disease.[23] Remdesivir is given as 200 mg of loading dose IV on day 1, followed by 100 mg IV once daily as a maintenance dose for 9 days. The trial is expected to complete by the end of April 2020.

### Tocilizumab

An interleukin (IL)-6 inhibitor has been tried in severe COVID-19 disease with raised IL-6 levels.[24] A variety of other investigational molecules including ribavirin, immunoglobulins, washed microbiota transplant, combination of darunavir cobicistat, arbidol hydrochloride, sofosbuvir, favipiravir, and interferon are under the study for COVID-19.[25,26]

The use of corticosteroids has been discouraged in COVID-19 unless indicated for other associated conditions such as exacerbation of the chronic obstructive pulmonary disease or advanced respiratory illness. This is based on observed association of their use with worsening of other viral illnesses. The use of ascorbic acid in COVID-19 disease is not supported with solid scientific database. Irrational drug combinations are to be avoided.

## CONCLUSION

COVID-19 has emerged as a global health problem of a large magnitude. Containment measures at population level are currently suggested as the best strategy to curtail the epidemic spurt of disease. As of today, no effective vaccine or a drug is available. However, a variety of evidence-based prevention and treatment modalities are expected to come out in the near future. In the period of crisis, media may play a role of public educator in order to calm down emotional responses associated with sense of helplessness due to acute surge of this pandemic. The global leaderships should join hands in devising effective management policies to combat this disease.

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### Conflicts of interest

There are no conflicts of interest.

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