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2019 Coronavirus Disease (COVID-19) Outbreak: A Review Article

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ABSTRACT

 In December 2019, an outbreak of severe acute respiratory syndrome coronavirus 2 infections occurred in Wuhan, Hubei Province, China and spread across China and beyond. On February 12, 2020, WHO officially named the disease caused by the novel coronavirus as Coronavirus Disease 2019(COVID-19). The COVID-19
is a respiratory illness caused by a coronavirus and pandemic is now a major global health threat. Coronaviruses (CoV) belong to the genus Coronavirus with its high mutation rate in the Corona viridae. This review focuses to have a preliminary opinion about the disease, the ways of treatment, and prevention in this early stage of COVID-19 outbreak.

Keywords: Global emerging disease outbreak, Clinical Symptom Spectrum, Diagnosis of COVID-19 Infection, Treatment and Protection

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Introduction

On January 7th, 2020, a novel coronavirus was isolated and named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV) in the wake of an outbreak of pneumonia of unknown cause in Wuhan city, China (1,2). The COVID-19 pandemic is now a major global health threat. As of 23th March 2020, there have been 341,329 cases and 14,746 deaths confirmed worldwide. Global spread has been rapid, with 192 countries now having reported at least one case. The objective of this review article was to have a prelimi-nary opinion about the disease, the ways of treatment, and prevention in this early stage of this outbreak.

Methods

A review based on the current literature direct.

Global emerging disease outbreak and possible strategies

The last time the world responded to a global emerging disease epidemic of the scale of the current COVID-19 pandemic with no access to vaccines was the 1918-19 H1N1 influenza pandemic. In that pandemic, some communities, notably in the United States (US), responded with a variety of non-pharmaceutical interventions (NPIs) - measures intended to reduce transmission by reducing contact rates in the general population (3). Examples of the measures adopted during this time included closing schools, churches, bars and other social venues. Cities in which these interventions were implemented early in the epidemic were successful at reducing case numbers while the interventions remained in place and experienced lower mortality overall (3).

Whilst our understanding of infectious diseases and their prevention is now very different compared to in 1918, most of the countries across the world face the same challenge today with COVID-19, a virus with comparable lethality to H1N1 influenza in 1918. Two fundamental strategies are possible (4):

(a)   Suppression. Here the aim is to reduce the reproduction number (the average number of secondary cases each case generates), R, to below 1 and hence to reduce case numbers to low levels eliminate human-to-human transmission. The main challenge of this approach is that NPIs (and drugs, if available) need to be maintained – at least intermittently - for as long as the virus is circulating in the human population, or until a vaccine becomes available. In the case of COVID-19, it will be at least a 12-18 months before a vaccine is available (5). Furthermore, there is no guarantee that initial vaccines will have high efficacy.

(b) Mitigation. Here the aim is to use NPIs (and vaccines or drugs, if available) not to interrupt transmission completely, but to reduce the health impact of an epidemic, akin to the strategy adopted by some US cities in 1918, and by the world more generally in the 1957, 1968 and 2009 influenza pandemics. In the 2009 pandemic, for instance, early supplies of vaccine were targeted at individuals with pre-existing medical conditions which put them at risk of more severe disease (6). In this scenario, population immunity builds up through the epidemic, leading to an eventual rapid decline in case numbers and transmission dropping to low levels.

Clinical Symptom Spectrum

Understanding the clinical symptoms of COVID-19 is important, although the clinical symptoms are indicated nonspecific. Common symptoms include fever, cough and myalgia or fatigue. Patients may initially present with diarrhea and nausea a few days prior to fever, suggesting fever is dominant but not the premier symptom of infection. A small number of patients can have headache or hemoptysis (7, 8) and even relatively asymptomatic (9). Affected older men with comorbidities are more likely to have respiratory failure due to severe alveolar damage (10). Disease onset may show rapid progression to organ dysfunction (e.g., shock, acute respiratory distress syndrome [ARDS], acute cardiac injury, and acute kidney injury) and

even death in severe cases (8, 11). Meanwhile, patients might show normal or lower white blood cell counts, lymphopenia, or thrombocytopenia, with extended activated thromboplastin time and increased C-reactive protein level (7,8-10,11). In short, a patient having fever and upper respiratory tract symptoms with lymphopenia or leukopenia should be suspected, especially for patients with especially for patients with Wuhan exposure or close contact history.

Diagnosis of COVID-19 Infection

The first task for the clinical diagnostic workflow is to confirm Wuhan exposure history or close contact with people from Wuhan or confirmed patients during the past two weeks. However, the number of the patients with unknown exposure history is increasing due to the rapid and wide spread of the disease. The National Health Commission of China (12,13) formulated the Diagnosis and Treatment Program of 2019 New Coronavirus Pneumonia (trial sixth version) (Table 1) based on the recommendations of the World Health Organization (WHO) on severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) (14-16). A patient with one exposure history and two clinical conditions is considered as suspected case. If there is no clear exposure history, suspected patients should meet 3 clinical conditions (Table 1). Based on the fifth trial edition (17), chest CT findings of viral pneumonia are regarded as evidence of clinical diagnosis of COVID-19 infection. However, the WHO did not accept CT without RT-PCR confirmation until February, 17, 2020 (18) and the most recently published Diagnosis and Treatment Program of 2019 New Coronavirus Pneumonia (trial sixth version) has deleted the term of clinical diagnosis (13). The final etiology diagnosis of COVID-19 is necessary, which can be further confirmed by positive real-time RT-PCR assay for COVID-19 using respiratory or blood samples or by viral gene sequencing of respiratory or blood samples that are highly homologous with COVID-19. According to the clinical manifestations, confirmed patients are divided into mild, moderate, severe, and critical types (Table 2) (17,13, 19).

Table 1: Case Definition for Surveillance of Coronavirus Disease 2019 (COVID-19) by Chinese Health Commission

Suspected case
Present at least two of the following conditions of
i. Fever and/or respiratory symptoms (eg, cough, myalgia, fatigue)
ii. Imaging features of viral pneumonia
iii. Normal or low white blood cell count or reduced lymphocyte in early onset
AND
One or more of the following exposures during the 14 days prior to onset of symptoms
1)   Travel or residence history in Wuhan, other areas with recent local transmission of COVID- 19, or the local community with confirmed patient
2)   Close contact* with patient with laboratory-confirmed COVID-19 (positive for nucleic acid test)
3)   Close contact with people from Wuhan or surrounding areas or local communities with fever or respiratory symptoms case report
4)   Cluster onset
Patients without exposure history should meet all of conditions i, ii and iii.
Clinically diagnosed case (added in the trial fifth edition but deleted in the trial sixth edition)
The suspected case with typical imaging findings of pneumonia (only for Hubei)
Confirmed case
Suspected cases have at least one of the following etiological evidence
i. Positive real-time fluorescence polymerase chain reaction of the patient's respiratory or blood specimen for COVID-19 nucleic acid
ii. Viral gene sequences in respiratory or blood specimen are highly homologous to COVID-19

Data from Refs.[17, 12-13] *Close contact is defined as healthcare-related exposures, including direct care for patients with confirmed COVID-19, collaboration with healthcare workers with confirmed COVID-19, Visiting or staying in the same closed environment with patients with confirmed COVID-19, or Members who live in the same family environment with patients with confirmed COVID-19.

Table 2: Criteria for Clinical Severity of Confirmed Coronavirus Disease 2019 (COVID19) Pneumonia

Types	Findings
Mild	Mild clinical symptoms [fever <38℃ (quelled without treatment), with or without cough, no dyspnea, no gasping, no chronic disease] No imaging findings of pneumonia Moderate Fever, respiratory symptoms, imaging findings of pneumonia
Moderate	Fever, respiratory symptoms, imaging finding of pneumonia
Severe	Meet any of the followings: a. Respiratory distress, RR ≥30 times/min b. SpO2 <93% at rest c. PaO2/FiO2 ≤ 300 mmHg * Patients showing a rapid progression (>50%) on CT imaging within 2448 hours should be managed as severe (added in the trial sixth edition)
Critical	Meet any of the followings: a. Respiratory failure, need mechanical assistance b. Shock c. "Extra pulmonary" organ failure, intensive care unit is needed Data from Refs.13,34-39

Data from Refs. [13-19] Abbreviations: RR: respiratory rate; SpO2: oxygen saturation; PaO2: partial pressure of oxygen; FiO2: fraction of inspired oxygen

Treatment & Protection

In general, there are few or no treatment options for viral diseases that occur suddenly (20). In parallel with this knowledge, today there is no vaccine or effective treatment to prevent COVID-19 infection. Molecules are being tested for COVID-19 in in-vitro and human-based SARS-CoV and MERS-Cov trials. Studies evaluating the antiviral activity of types I and II interferons have reported, interferon-beta (IFNb), as the most potent interferon, was reducing in- vitro MERS-CoV replication (21). According to a human MERSCoV case report from South Korea, the use of the combination of Lopinavir/Ritonavir (LPV/RTV) (Anti-HIV drugs), pegylated interferon and ribavirin provided a successful viral clearance (22). For this purpose, a randomized control trial (MIRACLE Trial), that aimed to determine whether LPV/RTV-IFNb improved clinical results in MERS-CoV patients, was initiated in 2016 and 76 patients were enrolled (23). Although another antiviral drug, remdesivir was used in the first case reported from the United States of America, seemed successful, controlled studies with more cases are needed (24). In-vitro studies have shown that viral RNA transcription was terminated with remdesivir in early stage (25, 26). There are publications demonstrating that remdesivir has a strong antiviral activity in epithelial cell cultures against SARS-CoV, MERS-CoV and related zoonotic bat CoVs (27, 28).

 Many measures should be taken, such as timely publication of epidemic information for elimination of the source of infection, early diagnosis, reporting, isolation, supportive treatments and for avoiding unnecessary panic. CDC reminds basic measures such as hand washing, using disinfectant solutions, avoiding contact with patients in order to prevent the spread of viruses by droplets. Precautionary actions including the provision of medicines supply chains, personal protective equipment, and hospital supplies should be made in a short time for the protection of the Chinese people and global health, especially in the places with close travel ports to major Chinese ports (29).

Based on the 2003 SARS-CoV epidemic experience, the Chinese government takes many effective measures including closing public transport, reducing migration and promoting personal protection with masks in Wuhan and other provinces. Hence, there are reported cases of infected hospital personnel, healthcare staff should be informed about taking personal protective measures such as the use of gloves, eye masks and N95 masks during the examination of patients with a suspected history of COVID-19 contact or travel to China (11, 33).

Conclusion

Coronaviruses belong to the genus Coronavirus in the Coronaviridae. All Coronaviruses are pleomorphic RNA viruses characteristically containing crown-shape peplomers with 80-160 nM in size and 27-32 kb positive polarity [30]. In conclusion, Wuhan exposure or close contact history, highly suggest COVID-19 pneumonia, although RT-PCR remains the reference standard. Reduce transmission by reducing contact rates in the general population and isolation in case of severity detected.

Conflict of Interest: None declared.

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