Review Article

Diagnosis and Treatment Options for Coronavirus

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ABSTRACT:
Since December 2019, multiple cases of novel coronavirus pneumonia (NCP) have been identified in China. With the rapid spread of the epidemic, such cases have also been found in unusually high numbers in abroad as well. Most of the know-how about the physical and chemical properties of coronavirus comes from the research on SARS-CoV and MERS-CoV. Transmission of the virus happens mainly through respiratory droplets and close contact. The main clinical manifestations were respiratory symptoms and occasional gastrointestinal symptoms. it is a never been experienced respiratory disease before and with infection ability widely and quickly, it attracted the world's attention but without treatment and control manual. It is imperative in these cases to rapidly diagnose as well as to try and form a standardized protocol for the treatment of patients especially the critical cases.
Key words: 2019 novel coronavirus, 2019-nCoV, Respiratory disease, Pneumonia, Infectious diseases.

INTRODUCTION

Coronavirus (CoV) belongs to the Coronaviridae family, Nidovirales order. CoVs are divided into four genera: α-, β-, γ-, and δ-coronavirus. α- and β-coronaviruses only infect mammals, whereas γ- and δ-coronaviruses mostly infect birds, with a few infecting mammals. Human CoVs include α-coronaviruses (229E and NL63), β-coronaviruses (OC43 and HKU1), the Middle East respiratory syndrome related coronavirus (MERS-CoV), severe acute respiratory syndrome-related coronavirus (SARS-CoV), and 2019- nCoV. The 2019-nCoV belongs to the β-coronavirus genus,[1] which includes bat-SARS-like (SL)-CoVZC45, bat- SL-CoVZXC21, SARS-CoV, MERS-CoV, and 2019-nCoV. Current studies have revealed that 2019-nCoV may originate from wild animals, but the exact origin remains uncertain. In December, 2019, a cluster of pneumonia cases, who were later proven to be caused by a novel coronavirus (named as "2019-nCoV"), emerged in Wuhan City, Hubei Province, China.[2]

People of all ages are vulnerable to 2019-nCoV. They either have a travel history to affected areas or they appear to have contact with someone who is affected by this disease. Human -Human transmission has become communal and a matter of concern giving rise to the clusters of cases which can later progress to a larger population easily. The elderly and those with underlying chronic diseases are more likely to become severe cases. Based on the current epidemiological data, the incubation period of 2019-nCoV infections ranges from 1 to 14 days, mostly ranging from 3 to 7 days. Data from patients expose that severe cases often develop dyspnoea one week after disease onset.

Infected people might appear asymptomatic [3] or present with fever, dry cough, and fatigue, and few have upper respiratory symptoms including nasal congestion and running nose; some patients presented with gastrointestinal symptoms including abdominal discomfort, nausea, vomiting, abdominal pain, diarrhoea and anosmia. Severe cases may quickly progress to acute respiratory distress syndrome (ARDS), septic shock, refractory metabolic acidosis, and coagulation dysfunction.[4] In the initial phase of the disease, white blood cell count is normal or decreased, with decreased lymphocyte count; liver enzymes, muscle enzymes, and myo-haemoglobin levels are increased in some patients. Samples from throat swabs, sputum, lower respiratory tract secretions, stool and blood, etc. are tested positive for 2019-nCoV nucleic acids.[5] Real -Time Polymerase Chain Reaction (RT-PCR) is the gold standard as compared to rapid antibody test kits that can give false negatives which might hamper in identifying asymptomatic and /or susceptible cases. Those with one of the following pathogenic evidence is the confirmed case:

(1) positive for the 2019-nCoV by the real-time PCR test for nucleic acid in respiratory or blood samples.

(2) viral gene sequencing shows highly homogeneity to the known 2019-nCoV in respiratory or blood samples.[6]

Suspected cases should undertake chest X-ray examination as soon as possible. Chest CT scan is essential when necessary. In the initial stage of disease, chest images show numerous small plaques and interstitial changes, which are clear in the lung periphery, further depreciating to bilateral multiple ground-glass opacity and/or infiltrating shadows. Lung consolidation may occur in severe cases. Pleural effusion is rarely seen.[5] Cases can be classified as mild, moderate, severe and critical based on intensity of clinical symptoms. **(Table 1)** It should also be differentiated from other respiratory illnesses. **(Table 2)** The general treatment plans include bed rest and supportive treatment which safeguard sufficient calorie and water intake, along with maintaining water electrolyte balance and homeostasis as well as monitoring vital signs and oxygen saturation. Keeping respiratory tract unobstructed and inhaling oxygen when necessary, measuring blood routine, urine routine, C-reactive protein, and other blood biochemical indexes including liver and kidney function, myocardial enzyme spectrum, and coagulation function according to patient's conditions should also be observed. Blood gas analysis and timely re-examination of chest imaging should be performed when necessary.[2] The patients with high fever should be actively controlled. If patient's body temperature exceeds 38.5 °C then antipyretic drug treatment should be performed. Common orally given drugs includes ibuprofen and acetaminophen. When hypoxia appears, effective oxygen therapy should be given instantly including nasal catheter, mask oxygen. Nasal high-flow oxygen therapy, and non-invasive or invasive mechanical ventilation should be undertaken when necessary.[2] Antiviral therapy is also given although specific to 2019-nCoV hasn't been developed yet. Interferon-α can decrease viral load in the initial stage of infection which can help to ease symptoms and curtail the course of disease.[5] Remdesivir/ Lopinavir/Litonavir has also been tried for the treatment of patients with 2019-nCoV pneumonia, but its efficacy and safety remain to be determined.[7] The use of glucocorticoids should be based on the severity of systemic inflammatory response, degree of dyspnoea, with or without ARDS, and the progress status of chest imaging results. Immunoglobulin can be used in critical cases when indicated, but its efficacy needs further evaluation.[5] Arbidol is administrated for adults infected with 2019-nCoV; however, its efficacy and safety remain unclear.[8]

Table 1- 2019-nCoV severity status of patients

Case severity status	Description
Mild cases	The clinical symptoms were mild, and there was no sign of pneumonia on imaging.
Moderate cases	Showing fever and respiratory symptoms with radiological findings of pneumonia.
Severe cases	Cases meeting any of the following criteria: 3.1 Respiratory distress ($\geqq$30 breaths/ min); 3.2 Oxygen saturation$\leq$93% at rest; 3.3 Arterial partial pressure of oxygen (PaO2)/ fraction of inspired oxygen (FiO2) $\leqq$300mmHg (l mmHg=0.133kPa). Cases with chest imaging that showed obvious lesion progression within 24-48 hours >50% shall be managed as severe cases.
Critical cases	Cases meeting any of the following criteria: 4.1 Respiratory failure and requiring mechanical ventilation; 4.2 Shock; 4.3 With another organ failure that requires ICU care.

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Table 2- Differential Diagnosis of 2019-nCoV respiratory distress

1.	Mild manifestations of COVID-19 need to be distinguished from upper respiratory tract infections caused by other viruses.
2.	Influenza pneumonia
3.	Adenovirus pneumonia
4.	Respiratory syncytial virus pneumonia
5.	Vasculitis
6.	Dermatomyositis
7.	Other non-infectious organizing pneumonia

Oseltamivir and other anti-influenza agents can be applied for patients coinfected with other influenza virus. Supportive broad-spectrum antibiotics or antifungal drugs, can be administered in cases with other co-infections with bacteria or fungi. [5] On the basis of symptomatic treatment, active monitoring should be done to avert complications, underlying diseases, secondary infection, and provide organ function support as indicated. On the basis of full fluid resuscitation, improve microcirculation, use of vasoactive drugs, and monitoring of hemodynamics should be done, if necessary. The invasive mechanical ventilation should adopt low tidal volume "lung protective ventilation strategy" to reduce ventilator related lung injury. If essential, prone position ventilation, lung recruitment, or extracorporeal membrane oxygenation (ECMO) can be applied. [5]

DISCUSSION
Coronaviruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms extending from those similar to the common cold to more severe respiratory, enteric, hepatic and neurological symptoms. [9] Studies also stated that 2019-nCoV S-protein supported strong interaction with human Angiotensin converting enzyme -2 (ACE2) molecules despite the dissimilarity of its sequence with that of SARS-CoV. [10] Recent research shows it has more than 85% homology with SARSr-CoV (bat-SL CoVZC45). 2019-nCoV can be found in human respiratory epithelial cells 96 h after in vitro isolation and culture, while it takes about 6 days in VeroE6 or Huh-7 cell lines. [11] Suspected and confirmed cases need to be treated in designated hospitals with effective isolation and protection conditions. Suspected cases need to be treated separately in single room, confirmed cases are admitted to a same ward, and critical cases should be admitted to ICU as soon as possible. [5] There are other laboratory tests for the status of 2019-nCoV infection, including blood gas analysis, liver and kidney function, myocardial enzyme, myoglobin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Procalcitonin (PCT), lactate, D-dimer, coagulation image, urine routine test, inflammatory factors (interleukin(IL)-6, IL-10, TNF - α), 11 items of tuberculosis (TB) subgroup, complement, anti-acid staining, etc. Blood gas analysis is helpful to judge the oxygenation of moderately-ill and severe patients. Combining the increase of lactic acid, it is feasible to

screen the patients with high-risk of oxygenation disorder. Some infected patients have increased liver enzymes, muscle enzyme, ESR and myoglobin. The detection of CRP and PCT is of certain value to distinguish whether there was bacterial infection in the lung. D-dimer of most severe patients was significantly increased in this epidemic, with frequent clotting disorders and micro-thrombotic formation in peripheral blood vessels. Detection of other inflammatory factors may help to preliminarily evaluate the immune status of patients. [6] In some cases, the decreased Absolute Leukocyte count (ALC) and the percentage of CD3+, CD3+CD4+, and CD3+CD8+ cells have been detected before treatment. However, these cells gradually returned to normal levels after viral clearance. Chest CT examination and the detection of SARS-CoV-2 RNA also play a vital role. The improved lung lesions later have a good consistency with the recovery of the laboratory characteristics including C-reactive protein (CRP), arterial partial pressure of carbon dioxide (pCO2) and oxygen (pO2). This is helpful for rapid clinical assessment and taking effective segregating actions, while also contributing to the clinical diagnosis and specific drug therapy. [12] Conservative fluid management can be adopted for ARDS patients without tissue hypoperfusion. Use of vasoactive drugs should be done to improve microcirculation. Empirical antibiotics targeting the suspected potential infection should be used as soon as possible, blind or improper combination of broad-spectrum antibiotics should be avoided. Unless for special reasons, the routine use of corticosteroids should be avoided. [13] The patient should be discharged only if the body temperature returned to normal for more than 3 days; respiratory symptoms improved significantly; inflammation of the lungs showed obvious signs of absorption; and respiratory nucleic acid was negative for two consecutive times (one-day sampling time interval at least); and the patient can be released from isolation. [6]

CONCLUSION
Coronavirus has caused a huge public concern around the world. It is all the more imperative to avert the spread of this deadly disease. Since no specific treatment is available, it is vital that more testing and quarantining the susceptible cases as well as providing supportive care to those who are severely affected by this disease should be done.

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