Review Article

The Corona Virus Disease COVID-19: A Pulmonologist Perspective

Dr. Tarig Fadelelmoula, MD, FCCP

Corresponding Author: Dr. Tarig Fadelelmoula, MD, FCCP Associate Professor and Consultant Pulmonologist, Department of Respiratory Care, College of Applied Sciences, Almaarefa University, Riyadh, Saudi Arabia.

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Abstract

The current epidemic of the novel coronavirus in the city of Wuhan in China is a worldwide emergency that requires preparedness at all levels of healthcare provision. With the number of confirmed cases multiplying every day and fatality rate exceeding that of the SARS-CoV outbreak back in 2002 and 2003 in China, this threatening outbreak constitutes a challenge for all healthcare providers and decision-makers, especially with the limited data availability, and the uncovered clinical and epidemiological characteristics of this new virus. Clinical features are not specific and event, when cases are diagnosed by polymerase chain reaction (PCT) or chest, computed tomography (CT-Scan) still treatment, is mainly supportive and little evidence is present to support the use of emerging medications like chloroquine, remdesivir, and renin-angiotensin system inhibitor, in the treatment of pneumonia caused by COVID-19. Preventive measures, therefore, constitute the core of the global health response in an attempt to halt the spread of this catastrophic epidemic. In this review, the epidemiology, pathophysiology, and treatment of the recently discovered Novel COVID-19 are reviewed, with an emphasis on best practices and the public health consequences.

Keywords: *China; Coronavirus; COVID-19; Emerging Viruses; the Middle East Respiratory Syndrome Coronavirus; Novel Coronavirus; Outbreak; SARS Coronavirus; Wuhan.*

The Epidemic

As a result of this outbreak of COVID-19 in the Chinese city of Wuhan (Hubei province), **(**1**)** and its fast transmission of other countries across the world, **(**2**)** the World Health Organization (WHO) declared a global health emergency on 30 January 2020. **(**3**)** This fast change from epidemic to pandemic just occurred one month after the first reported case. **(**4**)** The pandemic presents a challenge for stakeholders, as limited data are available to allow planning and actions, and the epidemiological characteristics of this novel coronavirus are yet to be explained for better prevention, diagnosis, and treatment of cases.

Morbidity and Mortality Rate

The initial report on the first 41 cases of the COVID-19 outbreak showed that they were males [(73%], with less than 50% possessing underlying confounding diseases [32%] like diabetes, high blood pressure and cardiovascular-related illnesses, the median age of cases was 49.0 years (Inter Quartile Range 41.0–58.0). Of the first cohort of patients infected, 66% reported direct exposure to the seafood market and the case fatality rate (CFR) was nearly 2%. **(**5**)**

Virology

Coronaviruses are single-stranded RNA viruses that belong to the Coronaviridae family of viruses. These viruses are known to infect animals like birds and mammals more than humans. In humans, they are generally known to cause mild respiratory tract illnesses, mimicking those seen in the common flu. Unfortunately, some emerging human coronaviruses have resulted in fatal respiratory diseases, which include the SARS (Severe Acute Respiratory Syndrome) and MERS (Middle East Respiratory Syndrome) diseases. **(**6**)** Like other coronaviruses, COVID-19 is a single strand RNA virus from the subfamily Orthocoronavirinae. **(**7**)** This subfamily is divided into four genera: α, β, γ, and δ according to serotype and genome characteristics. **(**8**)** SARS-CoV, MERS-CoV, this COVID-19 are Betacoronavirus, **(**9**)** with a genome size of ~30 kilobases, that encodes their characteristic structural and non-structural proteins.

Genetic Diversity and Evolution of COVID-19

The genetic code of the virus was analyzed and many mutations were discovered, including deletions on coding and non-coding regions of the genome. These discoveries emphasized the genetic diversity and rapid evolution of this novel coronavirus. **(**10**)**

Genome Detective Coronavirus Typing Tool

Genome Detective is a web-based, user-friendly software application to quickly and accurately assemble all known virus genomes from next-generation sequencing datasets. The tool also allows tracking of new viral mutations as the outbreak expands globally, which may help to accelerate the development of novel diagnostics, drugs, and vaccines to stop the COVID-19 disease. **(**11**)**

Disease Transmission

Most of the initial cases had a history of exposure to the South China Seafood Market in Wuhan city, and some cases rendered a family clustering feature. The source of infection is still unknown, however, it is speculated that bats or vipers may have caused the infection. **(**12**)** The infection is mainly transmitted through respiratory droplets and the median time from onset to admission to the hospital is 9 days, and mostly affects patients between 40 and 60 years-old. **(**13**)**

Pathogenesis

In a similar manner to other viruses, SARS-CoV-2 adopts a mechanism to invade lung alveolar epithelial cells using receptor-mediated endocytosis via the angiotensin-converting enzyme II (ACE2) as an entry site and hence resulting in pneumonia and respiratory distress syndrome. **(**14**)**

Clinical Features

Symptoms and Signs

Patients with COVID-19 infection present with nonspecific symptoms. Common symptoms included fever, cough, and fatigue. Diarrhea and nausea may be the presenting features in some patients even a few days before the onset of fever, telling that fever is dominant but not always the first symptom of the infection. Headaches and hemoptysis may be seen in some patients while other patients might be relatively asymptomatic. **(**15-17**)** Elderly patients with chronic disease are more prone to respiratory insufficiency due to severe alveolar injury. **(**18**)** The patient's condition may progress rapidly to failure of end organs and even death in extreme cases. **(**5, 16**)**

Nonspecific laboratory tests

White cell count (WCC) may be normal in some patients while a low WCC, lymphopenia, or thrombocytopenia, with extended activated thromboplastin time and increased C-reactive protein level may occur in others. **(**19**)**

Polymerase chain reaction (PCR)

The confirmation of COVID-19 in suspected patients is through reverse transcription-polymerase chain reaction (RT-PCR) or gene sequencing from respiratory or blood specimens and this provides the key point for patient triage and hospitalization. However, with limitations of sample collection and transportation, and kit performance, the total positive rate of RT-PCR for throat swab samples was reported to be about 30% to 60% at initial presentation. **(**20**)**

Rapid COVID-19 Test

An IgG-IgM combined antibody test using advanced immunological detection techniques was recently launched to rapidly test patients for COVID-19, it's reported that it generates results in less than 15 minutes to determine whether there is recent COVID-19 infection. **(**21**)** The rapid test is easy to perform without the need for extra equipment. Study results demonstrated the sensitive and specific of this test, and that it has promising potential for the fast screening of COVID-19 infections, and it has already gained a lot of interest and increased clinical uses after a short time trial in Chinese hospitals. **(**22**)**

Chest imaging

Currently and due to the low sensitivity of RT-PCR, many COVID-19 patients may not be picked and consequently do not receive timely treatment and constitute a risk for infecting a larger population taking into consideration such highly contagious virus. **(**23**)** Thus, a chest computed tomography scanning (CT-Scan) plays an important diagnostic role. CT presentations are mostly bilateral patchy ground-glass opacities in the peripheral areas under the pleura with partial consolidation, which will be absorbed with the formation of fibrotic stripes if improved. **(**24**)** CT scanning provides important bases for early diagnosis and treatment of COVID-19 pneumonia. **(**25**)** Chest CT has a high sensitivity for the diagnosis of COVID-19 and may be considered as a primary tool for the current COVID-19 detection in epidemic areas. **(**26**)**

Case Definition

The National Health Commission of the People's Republic of China and the National Administration of Traditional Chinese Medicine adopted a set of clinical criteria for the diagnosis and classification of COVID-19 patients. **(**27**)**

Suspected Cases

An individual is considered a suspected case of COVID-19 disease if complies with any item of A and any two items of B, or with 3 items of B, where items A and B are defined as follows; items in A are based on the epidemiological history within two weeks before disease onset,

1. have a history of travel or residence in an area with case report;
2. have contacted confirmed patient;
3. have contacted with the patients with fever and respiratory symptoms from the district with case report;
4. disease onset in clustering, item B.

On the other hand, is based on the clinical manifestations:

1. Have fever and/or respiratory tract symptoms;
2. Have pneumonia with the image characteristics mentioned above;
3. In the early stage of the disease, have normal or decreased total number of leukocytes, or decreased lymphocyte count.

Confirmed Cases

Confirmed cases are the suspected cases testing positive on COVID-19 real-time RT-PCR or gene sequencing, from the sputum, throat swab, lower respiratory tract secretion, or other samples collected from patients.

Clinical Typing of the Confirmed Cases

Confirmed cases are further typed clinically into mild cases, common cases, severe cases, and critical cases to facilitate triaging and case management strategies.

Mild cases

This group of patients usually have mild symptoms, no pneumonia manifestation in chest image and usually have better prognoses and outcomes.

Common cases

These patients have a fever, respiratory symptoms, and pneumonia manifestation in radiological chest imaging.

Severe cases

Patients in any of the following items are considered severe cases.

(A) dyspnea, respiratory rate ≥30 times/min;

(B) finger oxygen saturation ≤ 93% at rest;

(C) PaO2/FiO2 ≤ 300 mmHg (1mmHg = 0.133 kPa).

Critical cases

Patients in any of the following items are considered critical cases.

(A) Show respiratory failure and mechanical ventilation is required;

(B) Present with shock;

(C) combine with other organ failure needing Intensive Care Unit (ICU) monitoring and treatment;

(D) Chest imaging shows multilobe lesions or progress of lesion focus within 48 h ≥ 50%;

(E) Combine with other clinical conditions requiring hospitalization.

Case management strategies

Up-to-date there are no specific vaccines or antimicrobials for COVID-19, nonetheless, there are ongoing efforts for vaccine development. **(**28**)** Both suspected and confirmed cases should be treated in isolation in healthcare settings where effective isolation and protective conditions are available. The suspected cases are isolated in a single room, and the confirmed cases can be accepted in the same room. Critical cases should be treated in an intensive therapy unit as soon as possible. **(**29**)** Support with oxygen, fluid, and administration of antibiotics to treat secondary bacterial infections for alleviating the symptoms and preventing end-organ dysfunction is the current WHO recommendation for hospitalized suspected and confirmed cases. **(**29**)**

Possible Pharmacotherapeutics

Remdesivir

The novel coronavirus currently isolated in China has been evaluated regarding its sensitivity to the already used drugs and the new antiviral drug remdesivir found to be effective in preventing viral replication. **(**30**)**

Interferon-a

A combination of Ribavirin and Interferon-α is recommended by the fifth edition National Health Commission's Regimen because of the effect on MERS (Middle East Respiratory Syndrome), and the effectiveness of Lopinavir, Ritonavir, and Remdisivir need to be confirmed by randomized controlled trial (RCT). **(**31**)**

Chloroquine

Chloroquine, which is an old antimalarial and disease-modifying drug was also found to be effective in preventing the replication of this virus in vitro if the biological results are clinically confirmed, the novel coronavirus-associated disease will have become one of the simplest and cheapest to treat and prevent infectious respiratory diseases. **(**32**)**

Inhibitors of RAS

Animal studies have shown that RAS inhibitors could effectively relieve symptoms of acute severe pneumonia and respiratory failure. Therefore, we speculate that ACEI and AT1R inhibitors could be used in patients with COVID-19 pneumonia under the condition of controlling blood pressure, and might reduce the pulmonary inflammatory response and mortality. **(**33**)**

Steroids in COVID-12 Pneumonia

Previous experiences of systemic steroids in the treatment of SARS and MERS showed disappointing results, so clinical use of glucocorticoids to control COVID-19 pneumonia and to regulate cytokine production to avoid lung injury should be avoided. **(**34**)** Although intravenous immunoglobulin and systemic steroids have been used in several reports, their efficacy and associated adverse effects remain to be understood. **(**5, 7, 18**)**

Global Preparedness and Response

Information sharing to fight COVID-19

Rapidly sharing scientific information is an effective way to reduce public panic about COVID-19, and doing so is the key to providing real-time guidance to epidemiologists working to contain the outbreak, clinicians managing patients, and modelers helping to understand future developments and the possible effects of various interventions. **(**35**)** Scientists are rapidly reviewing and publishing articles describing COVID-19, including the drug treatment options for SARS-CoV-2, its clinical characteristics, and therapies involving a combination of traditional Chinese and Western medicine, the efficacy of chloroquine phosphate in the treatment of COVID-

19 associated pneumonia according to clinical studies, and reflections on the system of reserve medical supplies for public health emergencies. **(**36**)**

Safety of Staff caring for COVID-10 patients

Medical professionals caring for patients with coronavirus disease 2019 (COVID-19) are at high risk of contracting the infection. **(**37**)** Aerosol-generating procedures, such as non-invasive ventilation (NIV), a high-flow nasal cannula (HFNC), bag-mask ventilation, and intubation are of particularly high risk. **(**37**)** As medical staff caring for COVID-19-patients are at high risk of contracting. All medical personnel involved in the management of patients with suspected COVID-19 must adhere to airborne precautions, hand hygiene, and donning of personal protective equipment. **(**38**)** All aerosol-generating procedures should be done in an airborne infection isolation room. Double- gloving, as a standard practice at our unit, might provide extra protection and minimize spreading via fomite contamination to the surrounding equipment after intubation. **(**39**)**

Prevention and Control

All continents reported confirmed cases of COVID-19. Several measures have already been implemented, to prevent and control possible case importations from China. **(**40**)** However, the ability to limit and control local transmission after importation depends on the application and execution of strict measures of detection, prevention, and control. These measures include heightened surveillance and rapid identification of suspected cases, followed by patient transfer and isolation, rapid diagnosis, tracing, and follow-up of potential contacts. **(**41**)** The application of such a vast technical and operational set of interventions depends on each country's public health and laboratory infrastructures and resources.

The CDC Guidelines

The American Centers for Disease Control and Prevention (CDC) has established transitional clinical protocols to guide the response to the COVID19 outbreak by implementing aggressive measures to slow the transmission of the disease in the US. **(**42**)** These measures include the identification of cases and their contacts in the country as well as appropriate check and care of travelers returning home from China. **(**42**)** All efforts are being made to slow the spread of the illness, provide time to better prepare healthcare systems and the public, to better characterize COVID-19 to guide public-health recommendations and to develop timely diagnostics, therapeutics, and vaccines. **(**43**)**

Conclusion

The novel coronavirus, which emerged from a known viral family that was considered rather benign before the turn of the century, has been involved in a public health catastrophe of a global concern according to the World Health Organization. Outbreaks like this necessitate the existence and adoption of effective public health strategies to respond to the never-ending threats created by such emerging viruses.

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Conflict of Interest

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