A review on COVID-19 for medical students

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INTRODUCTION

Coronaviruses (CoVs), primarily of zoonotic origin, made their presence felt among humans through the SARS-CoV and MERS-CoV infections not so long ago. COVID-19, a new strain of the coronavirus, is currently a pandemic, with 1,780,356 reported cases and 108,828 reported fatalities worldwide.

ABSTRACT

It has not been very long since the SARS-CoV-2002 and MERS-CoV 2012 epidemics. Yet again, nature has introduced SARS-CoV-2, also known as COVID-19, a highly virulent strain of the coronavirus that has its origin in the city of Wuhan, Hubei Province, China. Primarily, a zoonotic infection, the virus probably found its way to humans through infected wild bats sold in the Wuhan local market. What makes the virus virulent, is its ability to infect multiple people at once through single index case. This has led to inability to contain the virus with ease posing a significant threat to national and international health-care resources and economies. The objective of this review is to highlight the key features of the novel CoV-19 infection as per existing data for better understanding of the disease.

Keywords: Novel Coronavirus, Infection, Health, Transmission

EPIDEMIOLOGY

It is hypothesized that wild bats are the reservoir of SARS-CoV-2. Theory says that infected wild bats were being traded along with livestock in the Huanan Seafood Market in Wuhan from where
nCoV-19 infected the index cases. Among humans, the virus is transmitted through nasopharyngeal droplets and fomites.\cite{5-7}

On December 12, 2019, a case of pneumonia not caused by influenza or other known CoV was first reported in Wuhan. By December 31, 2019, 27 similar cases were diagnosed in the same province.\cite{8,9} All cases reported a history of animal contact in the above-mentioned market.

On January 7, 2020, the Government of China announced that nCoV-19 was isolated from all the above cases.\cite{10,11}

Like other coronavirus outbreaks, COVID-19 seems to exhibit high incidence in the spring season across the globe. Being the season of celebrations and gatherings, high population densities in smaller areas assist in the easy transmission of the virus among humans. Compounded by the increase in international travel, the above-mentioned factors pose significant difficulties for countries to contain the spread of the virus.\cite{12}

**GENETICS**

According to research, SARS-CoV-2 is like SARS-CoV in 70% of its genome and to MERS-CoV in 50% of its genome. It has approximately 89% similarity with two bat-derived SARS-like CoVs.\cite{13-15} Metagenomic next-generation sequencing revealed the entire 29,881 base pair genome of the virus with 6–11 open reading frames (ORFs).\cite{16} Evolutionary analysis based on ORF1a/1b, S, and N genes suggests that SARS-CoV-2 was independently introduced from animals to humans.\cite{17,18}

Two-thirds of the viral RNA, located in the first ORF (ORF1a/b), translates to two polyproteins, PP1a and PP1ab and encodes 16 non-structural proteins (NSP). One-third of the viral genome encodes four essential structural proteins and several accessory proteins that interfere with the host innate immune response:\cite{19}

1. Spike (S) glycoprotein
2. Small envelope (E) protein
3. Matrix (M) protein
4. Nucleocapsid (N) protein

SARS-CoV-2 possesses the S-glycoprotein gene and receptor-binding domain (RBD) which confer the ability to be transmitted between two humans by direct contact.

When comparing SARS-CoV-2 with other known CoVs, no difference was found in the amino acid sequences of NSP7, NSP13, envelope, matrix, or accessory proteins p6 and 8b. A few differences were found in the NSP2, NSP3, spike protein, and underpinning subdomain (RBD).\cite{20} Mutations in NSP2 and NSP3 play a role in the infectious potential and differentiation mechanism of the virus.\cite{21}

Zhang et al.\cite{22} found that as the virus spread across different provinces in China, its genotype exhibited several mutations.\cite{23}

**PATHOGENESIS**
CLINICAL FEATURES

Viral load at the time of infection determines the clinical features in a host. The incubation period is approximately 14 days.

The most common clinical presentation is fever, headache, sore throat, productive wet cough, myalgia, diarrhea, and dyspnea. The spectrum of clinical cases includes asymptomatic carriers and mild respiratory infection that recover within a week, severe progressive respiratory distress and death. In severe respiratory distress, respiratory system examination reveals reduced tactile fremitus, dullness to percussion, and reduced air entry associated with rales.

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Majority of the case fatalities have been reported among the middle-aged and elderly population associated with multiple comorbidities such as diabetes mellitus, hypertension, coronary artery disease, liver cirrhosis, and cancer.

INVESTIGATIONS

Investigations can be divided into two classes:

1. Tests to confirm the diagnosis of COVID-19 – a positive RT-PCR test.
2. Tests to monitor and assess the severity of the disease and its progression – performed in critically ill-hospitalized patients.

A patient is declared as recovered from the infection if two samples taken on different days give a negative RT-PCR result.

Routine blood tests include the following:

1. Complete blood count: It shows decrease in lymphocytes and white blood cells with specific reduction in CD4 and CD8 T-cells.
2. Arterial blood gas analysis.
3. Lipid profile.
4. Renal function tests.
5. Liver function tests.
6. Myocardial enzymes.
7. Urine analysis.
8. Inflammatory factors – interleukin 6 (IL-6), IL-10, and TNF-α.
9. ESR and CRP.
10. Coagulation profile with D-dimer

IMAGING

Chest X-rays are the initial imaging modality followed by CT thorax without contrast.

Clues to the diagnosis of COVID-19 on a chest X-ray are as follows:

- Bilateral lung infiltrates along the subpleural plane and bronchial vascular bundles, singular or multiple patchy, nodular, and honeycomb- or cord-like infiltrates, particularly involving the middle and lower lobes of the lung.
- Typical bilateral subsegmental ground-glass appearance
- Interlobular thickening
- Consolidation and thickening of bronchial walls

Atypical findings on imaging include:

- Pleural effusion
- Enlargement of mediastinal lymph nodes
• Single or multiple solid nodules or consolidated nodules in the center of lobule surrounded by ground-glass opacities.

CT STAGING\[^{38}\]

| Stages | Type of patients | Radiological features |
|--------|------------------|-----------------------|
| 1 (No clinical symptoms) | Ultra-early stage Laboratory tests negative Positive throat swab | Single, double, or scattered focal ground-glass opacity Nodules located in central lobule surrounded by patchy ground-glass opacities Patchy consolidation and air bronchogram the middle and lower lobes |
| 2 Early stage (1–3 days after onset of symptoms) | Fever cough with/without sputum | Single or multiple scattered patchy or agglomerated ground-glass opacities, separated by honeycomb-like or grid-like thickened of interlobular septa |
| 3 Rapid progression stage | (3–7 days after the onset of symptoms) | Fused and large-scale light consolidation with air bronchogram |
| 4 Consolidation stage. | (7–14 days after onset of symptoms) | Multiple patchy consolidations with less density as compared to rapid progression stage |
| 5 (2–3 weeks after onset of symptoms) | Dissipation stage | Patchy consolidation or strip-like opacity evolving into grid-like thickening of interlobular septum, thickening and strip-like twist of bronchial wall and scattered patchy consolidation |

Differential diagnosis

1. Common cold caused by rhinoviruses
2. Viral pneumonia caused by influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, and human metapneumovirus
3. Atypical pneumonia caused by mycoplasma and chlamydia
4. Bacterial pneumonia
5. Pulmonary involvement in vasculitis, dermatomyositis, and organizing pneumonia

Management

General guidelines include:

• Supportive therapy: Rest and symptomatic treatment with antipyretics, nutritional supplements, and proton-pump inhibitors/ranitidine to prevent stress ulcers.
• Self-quarantine either at home or in the hospital to break the chain of infection.
• Isolation of all suspected and confirmed cases.
• ICU care for critical cases: Mechanical ventilation and extracorporeal membrane oxygenation (ECMO).
• VTE prophylaxis: Low-molecular-weight heparin. Contraindicated in a history of recent surgery, bleeding disorders, suspected hemorrhage, active ulcers, and allergy to heparin.

Medical therapy

Antivirals:

• These drugs are not specific for treatment of SARS-CoV-2 but may help to improve the patient's overall condition.
• Example: Lopinavir, ritonavir, and interferon-alpha
• Remdesivir is a 1-cyano-substituted adenosine nucleotide analog prodrug with broad-spectrum antiviral activity against several RNA viruses. The first reported case of COVID-19 in the USA was successfully treated by remdesivir\[^{38}\].

Antimalarials:

• Chloroquine\[^{40}\] shows great potential in the treatment of COVID-19 according to in vitro studies through the following mechanisms:
• Inhibiting pH-dependent steps of viral replication\[^{41}\]
• Immunomodulatory effects through suppression of TNF and IL-6 production\[^{42}\]
• Impaired glycosylation of host cell receptors for SARS-CoV-2\[^{43-46}\]
• Antibiotics to prevent secondary bacterial infections
• Corticosteroids in rapid progressive disease: Its impact on length of hospital stay is yet to be determined.

Complications of covid-19

The following complications have been reported to date\[^{33,47}\]:

• ARDS
• Arrhythmia
• Shock – circulatory and septic
• Acute kidney injury
• Liver dysfunction

Prevention of COVID-19

According to the WHO, by practicing the following five steps, we can successfully prevent the spread of nCoV-19 to others and avoid being infected by it ourselves:\[^{47}\]

• Frequent handwashing with soap and water or an alcohol-based hand rub for at least 20 s.
• Social distancing by at least 1 m or 3 ft with people who are unwell.
• Covering the nose and mouth with a disposable tissue or a flexed elbow when coughing or sneezing. Dispose the used tissue immediately. Avoid touching your face repeatedly, especially if your hands are dirty.
• Self-isolation (#StayHome) – especially if you feel unwell.
• Seek medical attention immediately if the following symptoms develop: Fever, cough, and difficulty breathing.
At a global level, countries across the world have imposed nationwide lockdowns and public health protocols to contain the spread of COVID-19 and protect the health of their residents. Some of the measures include:

- Temporary closure of international travel
- Surveillance and screening of suspected individuals
- Isolation of infected individuals with quarantine of their close contacts
- Nationwide sterilization drives.

**CONCLUSION**

From the time, SARS-CoV-2 made its appearance among humankind, several researchers and health-care professionals have been risking their lives to understand the properties of the virus and aid in the recovery of infected individuals while preventing its spread among communities. By implementing lessons learned from the previous coronavirus epidemics, we can design an effective vaccine and antiviral drug that will help combat the virus. A lot more knowledge is yet to be obtained regarding the virus and the disease which will better enable us to manage patients and reduce mortality rates.

**Declaration of patient consent**

Patient’s consent not required as there are no patients in this study.

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**Conflicts of interest**

There are no conflicts of interest.

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