**Review Article**

# Novel Coronavirus Disease 2019 (COVID-19): A Focused Clinic Overview

## Xinhang Tu[1] and Miao Cui[2]*

[1]*Department of Internal Medicine, Medstar Health Internal Medicine Residency Program, USA*

[2]*Department of Pathology, Mount Sinai St. Luke's Roosevelt Hospital Center, USA*

**\*Corresponding author:** Miao Cui, Department of Pathology, Mount Sinai St. Luke's Roosevelt Hospital Center, USA.

## Abstract

At the end of 2019, a series of COVID-19 related respiratory infections were initially identified in China. After a few months of spreading via human-to-human transmission, it has been rapidly outbreak over 200 countries worldwide, becoming an emergency of primary international concern and posing a severe threat to public health globally. COVID-19 infection can cause clusters of symptoms from mild influenza-like illness to the severe acute respiratory syndrome. A better understanding of clinical symptoms, risk factors, and clinic progression will benefit disease control. This literature review demonstrates the clinical course of COVID-19, including risk factors, clinical presentation, progression and complication.

**Keywords:** COVID-19; SARS-CoV-2; Pandemic; Respiratory Tract Infections; Clinical Presentation

**Abbreviation:** COVID-19: Coronavirus Disease 2019; WHO: World health organization; CDC: Centers for Disease Control and Prevention; SD: Standard deviation; COPD: Chronic Obstructive Lung Disease; ARDS: Acute Respiratory Distress Syndrome; DIC: Disseminated Intravascular Coagulation; URT: Upper Respiratory Tract ; CXR: Chest X-ray; CT: Computed Tomography; PaO2: Partial Pressure of Oxygen; FiO2: Fraction of Inspired Oxygen; ICU: Intensive Care Unit; AST : Aspartate Transaminase; ALT: Alanine Transaminase; LDH: Lactate Dehydrogenase; α-HBDH: α-Hydroxybutyrate Dehydrogenase; SARS: Severe Acute Respiratory Syndrome; MERS: Middle East Respiratory Syndrome Coronavirus; RT-PCR: Reverse Transcriptase Polymerase Chain Reaction

## Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a novel coronavirus in one of the members of the family Coronaviridae and the disease caused by this virus, termed coronavirus disease 2019 (COVID-19) by the world health organization (WHO) [1,2]. An outbreak of a COVID-19 infection has been identified since December 2019 in Hubei, Wuhan, China, firstly [3]. Subsequently, it has rapidly spread throughout the world as a global health emergency, drawn attention from the WHO, and declared a pandemic on March 11, 2020. COVID-19 is a human airborne disease, and its transmission is a potential impact as and the infection rate is rapid [4]. Because of no effective target therapy for COVID-19 currently [5], the clinical treatment mainly focused on reducing clinical symptoms [6]. On the other hand, due to the lack of available diagnostic assays, early screening in populations relies on clinical symptoms [7], especially during the incubation period.

Therefore, a comprehensive summary of clinical symptoms and course is essential for early diagnosis and preventive quarantine in communities and supportive management in clinics.

## Risk Factors

Many clinical studies indicated that patients with certain characteristics are at higher risk of infection with COVID-19 compared with the control group, including elder age, male gender, and chronic comorbidities [2, 8]. For instance, a report from the Chinese Center for Disease Control and Prevention (CDC) showed 77.8% of patients are between 30 to 69 years old in 44,672 confirmed infections. Among them, 31.2% are aged above 60 years old and the fatality rate of the population above 60 years is significantly higher than other age groups. Furthermore, the portion of male patients is slightly higher (51.4%) [9]. Similarly, a report from the Centers for Disease Control and Prevention (CDC) in the United

States (US) (https://www.cdc.gov/coronavirus/2019-ncov/covid-data/covidview/index.html) revealed the hospitalization rates in people of 65 years and older are the highest among all age groups. However, the median age of the susceptible population and gender ratio vary with locations. In a study of 1591 infected patients in Italy, the median age of infected patients was 63 years, with 82% were male [10]. In contrast, the cases of Korea between January, 2020 and April 2020 showed the median age of patient was 45 and male patients accounted for 39.9% [11].

According to US CDC [12], there is a trend towards an increasingly younger population in the US from May, 2020 to July, 2020. The incidence is increased in the <80 years group overall, among which the largest increases are the group of <30 years. Furthermore, the median age of COVID-19 cases decreased from 46 years to 37 years from May, 2020 to July, 2020. Similarly, the median age of COVID-19 patients in the Europe decreased from 54 years to 39 years from January-May, 2020 to June-July, 2020. Especially, young people (20s age group) account for the largest proportion (19.5%). Patients with underlying comorbidities are prone to a higher risk for infection (Table 1). Based on a study with 1099 patients diagnosed with COVID-19 in China [13], about 24% of patients had at least one coexisting illnesses, including cardiovascular disease, diabetes mellitus, hypertension, chronic lung disease, cancer, chronic kidney disease, obesity, smoking. Patients with chronic comorbidities are found to have a higher case fatality rate. A meta-analysis of 1527 patients [20] showed the proportions of hypertension, cardia-cerebrovascular diseases, and diabetes in patients with COVID-19 were 17.1%, 16.4%, and 9.7%, respectively, and incidences were about two folds, three folds, and two folds, respectively, higher in the ICU/severe cases than in their non-ICU/non-severe counterparts. In addition, China CDC Weekly [9] demonstrated patients with comorbid conditions had higher case fatality rates-10.5% for those with cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6.0% for hypertension, and 5.6% for patients with cancer. In comparison, patients with no comorbidities only had a case fatality rate of 0.9%.

## Clinical Presentation

A study of 1099 patients [13] showed the median incubation period was four days with an interquartile range of 2 to 7 days. Whereas data from the US CDC (https://www.coronavirus.gov/) showed the incubation period varies from 2 to 14 days after exposure to the virus. The initial presentation of infected patients can be either symptomatic or asymptomatic. Asymptomatic infections refer to patients diagnosed with positive detection of the nucleic acid of SARS-CoV-2 by reverse transcriptase-polymerase chain reaction (RT-PCR), with no typical clinical symptoms or signs, and no apparent abnormalities in images, such as pulmonary computed tomography (CT). Although the percentage of asymptomatic population varies among different locations and

settings, it seems to be more prevalent in areas outside of China and on certain cruises [21]. The clinical presentation spectrum ranges from mild to critical among those who are symptomatic. Data from China CDC [22] revealed that 81% of 44,415 COVID-19 positive patients presented mild pneumonia or non-pneumonia, 14% patients had severe disease with symptoms of dyspnea, respiratory frequency ≥30/minute, blood oxygen saturation ≤93%, $PaO_2/FiO_2$ ratio <300, and/or lung infiltrates >50% within 24-48 hours, and 5% developed critical disease with presentations of respiratory failure, septic shock, and/or multiple organ dysfunction/failure.

The early stage of its clinical course is similar to common viral respiratory infections, presenting with fever, sore throat, fatigue and cough coupled with recent exposure [23], but compared with others, it can rapidly progress to dyspnea within several days after the initial infection. Based on the current published studies (Table 2), the most common typical symptom is fever overall. 43.8% of all patients reported fever on admission, and 88.7% developed fever during hospitalization. The following most common symptoms are dry cough [13] and shortness of breath [14]. Besides, gastrointestinal symptoms were not a common finding in the early stage according to clinical observation in China, but they were sometimes found to be the only presenting symptoms based on later reports [24]. Furthermore, anosmia and dysgeusia were more common in Europe and North America than in Asia.

## Imaging Findings

Chest X-rays (CXR) and chest CT are well-known standard diagnostic tools for pulmonary diseases and upper respiratory tract (URT) infections in the clinic. A clinical study involving 1014 cases in the Wuhan [25] showed 97% of COVID-19 positive patients confirmed by RT-PCR have abnormal chest CT findings. The most common patterns of COVID-19 pneumonia are bilateral patchy shadowing on CXR, with ground-glass opacity (56.4%) and bilateral patchy shadowing (51.8%) on the chest CT. However, both CXR and chest CTs can be negative initially or in mild disease [13,26].

## Progression

The clinical course is mainly progress of resolving COVID-19 related infections and secondary systemic inflammatory response [13]. The median time from illness onset to hospital admission is seven days, the median length of hospitalization ranges between 11-12 days, and the ICU admission rate is about 5-26% [16]. The median time from illness onset to ICU admission is 12 days, from symptom onset to acute respiratory distress syndrome ARDS varies from 7.5 to 12 days, and from illness onset to death or discharge is about 21 days [15]. Furthermore, certain patients can progress to refractory patients who do not reach obvious clinical and radiological remission within 10 days of hospitalization. Aging and male patients and those with comorbidities were more prone to progress to refractory cases [17]. The mortality rate varies in

different groups and locations [27]. Generally, it is higher in elderly. Heretofore, case fatality rate is 1.9% in United States and 5.0% in China from the mortality analyses by the Coronavirus Resource Center, Johns Hopkins University of Medicine on 12/12/2020 (https://coronavirus.jhu.edu/data/mortality) Complications [28] due to severe inflammatory reaction can impact multiple organs, including septic shock, coagulopathy, acute respiratory distress syndrome (ARDS), and end-organ injury (Table 3). Among them, ARDS is one of the most common complications, which can be developed rapidly over a short period. Notably, liver injuries tend to be more prevalent in COVID-19 patients, especially in patients with severe disease, compared with non-COVID-19 pneumonia [29]. Liver injury secondary to COVID-19 infection usually manifests with abnormal hepatic panel results, including increased lactate dehydrogenase (LDH), bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), and α-Hydroxybutyrate dehydrogenase(α-HBDH). The abnormal laboratory tests could help to differentiate and evaluate the progress of Covid-19 pneumonia [24].

## Conclusion

The outbreak of emerging severe acute respiratory infections in humans caused by COVID-19 has spread to a global pandemic and become a global health concern [29, 30]. Although the initial symptoms and complications are similar to severe acute respiratory syndrome (SARS) in 2003 and middle east respiratory syndrome coronavirus (MERS) in 2012, the presentation of COVID-19 is less severe with a lower fatality rate overall but a stronger ability to spread in communities than MERS and SARS [31]. However, COVID-19 patients with chronic comorbidities are found to have a higher case fatality rate. Liver injuries are more prevalent in severe COVID-19 cases, varying from transient mild abnormal blood tests to severe liver damage. Since the COVID-19 outbreak is still a significant challenge for clinicians, we urge clinicians to continue reporting their data to understand and control this novel virus better.

## Conflicts of Interest

All authors declare that there is no conflict of interest regarding the publication of this article.

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