



## Review Article

## COVID-19 and Various Comorbidities: A Review

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## ABSTRACT

Coronavirus currently known as COVID-19, originating from China in December 2019 had caused several severe unusual respiratory illnesses. This virus had spreads among individuals and had now developed into a great pandemic worldwide. More than 50% of COVID-19 patients have at least one comorbidity. Among the people suffering from COVID-19, hypertension is ought to be the most prevalent disease followed by diabetes, cardiovascular diseases, respiratory diseases, liver, and kidney diseases. Furthermore, older individuals (>60 years) are more likely to possess multi-morbidities, therefore, are more prone to the infection caused by the COVID-19. The underlying mechanism of this virus in the still contradictory. The health care sector can manage the symptoms of COVID-19 and comorbidities associated with it with help of management and treatment strategies underlined by the WHO. As it is of utmost need to identify the risk factors and critical clinical outcomes linked with COVID-19 so that the proper steps could be adopted in the future This review extensively elaborates the relationship between COVID-19 and various comorbidities based on up-to-date data extracted from reputed journals and official websites.

## INTRODUCTION

Severe acute respiratory disorder caused by the SARS-CoV2 virus is major source of the global pandemic. These are enveloped positive sense RNA viruses belongs to family Coronaviridae, that ranges of about 60 nm to 140 nm in the diameter. Coronavirus's name is Latin. In the ancient language, corona means crown. The structure of virus consists majorly of a core of genetic material that is enclosed by an envelope by means of protein spikes. It provides the shape like a crown. This disease is spread by contact or inhalation of the infected droplets and the incubation time varies from about 2 to 14 days. In December 2019, Wuhan, China, suffered from the first outbreak of

COVID-19, from which it gradually spread to the rest of the world. On 30th January 2020, a public health emergency was announced by World Health Organization (WHO), and by March 2020, the pandemic had quickly turned into an epidemic that had affected millions of people globally. It is known by now that COVID-19 has a greater influence on certain populations resulting in adverse clinical outcomes [1]. Case fatality rates (CFR) for this disease vary significantly among countries and is typically changing over time. By 27th January 2021, the virus has affected almost every country with 100 million confirmed cases across the globe and the cumulative death toll surpassed

2.16 million, raising serious global concern [2]. This review aims to highlight the relationship among primary medical conditions or comorbidities that place people of any age at higher jeopardy for getting infected by COVID-19 with clinical complications built on the most current literature report since the outbreak.

**Clinical manifestation of COVID-19 symptoms**

This infection of COVID-19 had a very wide-ranging spectrum of severity that ranges from an asymptomatic form to a very severe acute respiratory disease [3]. Asymptomatic patients are those in which corona virus test is positive but they don't have any symptoms and their chest image testing is also normal. Some people develop moderate to mild symptoms as well as got well without any hospitalization as shown in Table 1. Within 5-7 days from the beginning, these mild to moderate symptoms of approximately 1 out of 6 infected individuals, eventually develop into more severe respiratory problems including chest pain, shortness of breath as well as loss of speech [4,5].

Type of severity of symptoms	Clinical manifestation
Mild	Fever, cough, sneezing, runny nose, nausea, vomiting, abdomen pain
Moderate	Cough, fever, pneumonia with no less oxygen level, chest imaging shows lesions
Severe	Pneumonia with low oxygen level
Critical	Kidney damage, heart failure, acute respiratory distress syndrome

**Table 1:** Severity of COVID-19 in patients and their clinical representation

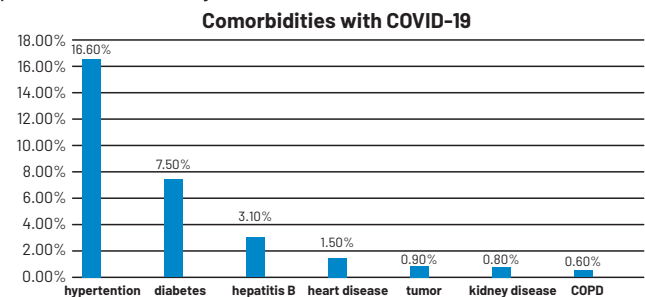
**Comorbidities with COVID-19**

The concept of comorbidity is defined as the presence of a medical condition existing simultaneously but independently with another condition in a patient. COVID-19 has a greater influence on populations resulting in adverse clinical outcomes, especially on the patients with comorbidity and the older patients (>60)[6-9]. The number of comorbidities also affects the progression of the patient's infection. The more the number of diseases, the more severe will be the infection [10-12].

**Hypertension and COVID-19**

Multiple types of research on COVID-19 analyse that out of all the comorbidities, hypertension is the most prevalent with more than 50% of cases in all types of studies [13]. It is reported that initial research on the prevalence of comorbidities showed a 21% to 30% occurrence of hypertension in the patients suffering from Covid-19 which elevated successively to more than 36% with the increasing age [14-17]. It had been estimated that the novel virus had used angiotensin-converting enzyme 2 (ACE2) to target human cells as these exists on the epithelial cells of intestine, lung, blood vessels and kidney. A retrospective study concluded that out of 856 patients, approx. 242

(28.3%) were older and having comorbidities, that includes hypertension 142 (16.6%) as the most common underlying health condition, followed by diabetes 64 (7.5%). Figure 1 presents this study.



**Figure 1:** Prevalence of comorbidities according to a retrospective study

**Diabetes and COVID-19**

Previous statistical research reported diabetes as the second most commonly found comorbidity in COVID-19 patients with a mortality risk of 2.85- to 3.21-fold. Recent studies from the USA stated that, in over a third of hospitalized patients, diabetes mellitus was presented as major comorbidity along with COVID-19 infection [18]. A study from Italy shows that comorbid diabetes along with COVID-19 causes deaths in two-thirds of hospitalized patients [19]. Moreover, developing COVID-19 infection is also associated with impaired T-cell function and elevated levels of interleukin-6 (IL-6) [5]. Other possible reasons include chronic immune system imbalances, metabolic syndrome, or excess nutrition caused by obesity [20].

**COPD and COVID-19**

Chronic obstructive pulmonary disease has been declared the 3rd leading cause of death by WHO. The clinical presentation of COPD and COVID-19 is difficult to differentiate which leads to delayed recognition of coronavirus disease or inappropriate medical intervention [21]. It has been observed from research studies that COVID-19 in patients can exacerbate the pre-existing COPD resulting in respiratory failure. It is of great importance to highlight the issue as most of the older patients living with COPD. Over 174 million people suffer from COPD worldwide [22] with a case fatality rate of 6.3% [23]. Since it is known from different research studies that SARS-CoV-2 primarily invades the pulmonary alveolar epithelial cells which may result in respiratory distress syndrome and that is a major concern for patients who are already suffering from pulmonary diseases such as COPD [16]. It has been suggested that COVID-19 patients with comorbid COPD require advanced medical support such as a mechanical ventilator.

**Renal disease and COVID-19**

It has been confirmed to date, there is not only a single risk factor for COVID-19 but according to recent clinical

research, the major risk factor for severe COVID-19 is chronic kidney disease (CKD) with 16% CFR [24, 25]. Another study estimated the prevalence to be 3% [26]. Research studies show a decrease in the estimated glomerular filtration rate (eGFR) and an increase in the urea in CKD patients suffering from COVID-19 leading to adverse clinical outcomes [27]. COVID-19 in patients with CKD is of utmost concern, especially if associated with hypertension as it can negatively impact the deteriorating kidney function. Therefore, people with greater potential to develop severe disease need meticulously monitoring and intervention.

#### **Asthma and COVID-19**

Recent data from the Centres for Disease Control and Prevention (CDC) indicate asthma as a risk factor for COVID-19. Since coronavirus affects the respiratory tract, it can also trigger asthma exacerbations, leading to an asthma attack and acute respiratory disorder [28]. The symptoms for asthmatic patients with COVID-19 include chest tightness, shortness of breath and cough more commonly compared to non-asthmatic patients suffering from COVID-19 [29]. The mechanism of asthma in COVID-19 is uncertain, yet multiple hypotheses are presented suggesting the mechanism, delayed secretion of IFN- $\lambda$ , and delayed innate antiviral immune response could be the target for SARS-CoV-2 [5]. One of the studies quite surprisingly hypothesized that in asthmatic patients type II inflammatory response cytokines (IL-4, -5, and -13) and accumulation of eosinophils in the respiratory tract act as a defensive factor against COVID-19 [30]. Moreover, it is hypothesized that asthmatic patients had reduced gene expression for the ACE2 protein in their respiratory epithelial cells and therefore it may also play a protective role against COVID-19 [31, 32].

#### **Liver disease and COVID-19**

The liver is a vital organ that comes up with extreme clinical challenges if associated with COVID-19. The hypothesis of elevated ACE2 expression that may act as a target protein for SARS-CoV also implies here compared with severe COVID-19 cases [41]. Liver test markers such as gamma-glutamyl transferase (GGT), alanine transaminase (ALT), serum aspartate aminotransferase (AST) as well as total bilirubin (TB) were increased in the patients that were suffering with severe COVID-19 when linked to those with non-severe COVID-19 disease [41]. Another possibility seen in different research studies is that the virus could also be the reason for the damage in the liver, but a pathological analysis of the liver confirmed that virus inclusions were not observed in the liver of an old man who died of COVID-19 [33, 34]. A histological study stated that hepatotoxicity can only develop after the long-term usage of drugs so it cannot be said that the hepatic impairment in COVID-19 patients is

due to anti-viral therapy until it is used for a long period [35].

#### **Cardiovascular disease (CVD) and COVID-19**

CVD can be a comorbid disease, or it may develop in healthy subjects during the course of COVID-19. CVD was found in about 40% of hospitalized COVID-19 patients and 14.5% from 138 hospitalized COVID-19 patients in China, indicating it as one of the commonly found comorbidities [19]. According to the Chinese Centre for Disease Control and Prevention, case fatality rate of the patients with comorbid CVD was found to be 10.5% [23] which is significantly 10-fold higher than other comorbidities [36]. Meta-analysis indicates occurrence of CVD to be 8.4% [37]. The underlying mechanism is found to be elevated levels of angiotensin-converting enzyme (ACE2) as in diabetes as well as hypertension. A retrospective study of 1906 laboratory-confirmed COVID-19 patients concluded that individuals with pre-existing CVD are at greater risk of developing severe COVID-19 than those without CVD [38].

#### **Cancer and COVID-19**

Cancer is rare comorbidity. Due to compromised immunity due to the malignancy and anticancer treatments, cancer patients are more expected to get infected by COVID-19 [39, 40] with an elevated risk (~3.5-fold) of requiring ICU admission and mechanical ventilation compared with patients without cancer [41, 42]. A nationwide analysis in China revealed that out of all the types of cancer, lung cancer was the most frequently observed 5 (28%) of 18 patients and 10 (19.2%) of 52 patients. Large scale findings in China established the case fatality rate of cancer as 5.6% compared with 2.3% in the general population [43]. This suggests that despite the adverse clinical outcomes of COVID-19, cancer patients should continue receiving curative cancer therapy. COVID-19 with comorbid cancer brings great challenges for oncologists to manage both diseases without deteriorating the clinical outcomes. It is suggested that immunosuppressive treatment should be avoided or have dosages decreased in cancer patients suffering from COVID-19 to suppress the severity of the infection.

#### **Older patients with comorbidities**

Of the numerous possible risk factors of COVID-19, older age is one of them [8-10]. Reduction of estimated 10-year survival has been observed in older people of age 50 years [11]. Similarly, comorbidities have a critical impact on COVID-19 patients as different research studies declared that elderly people are more prone to get infected by this novel virus especially those with coexisting health problems. It is known that elderly people have poor immunity and are more likely to have other abnormalities or adverse health conditions compared with younger patients. This makes them more susceptible to infectious

virus. A retrospective study was conducted specifically on older patients with COVID-19 showed a significantly higher mortality rate of 34.5% (19/55) for patients of age 65 or more, compared with younger patients at 4.7% (7/148)[7]. A

meta-analysis was conducted, concluded that there is a significant association of older age with the disease severity [12]. Some comorbidities impacted by COVID-19 are discussed in Table 2.

Sr. No.	Disease	Prevalence	CFR	SARS-CoV-2 targets	Symptoms	Severity	References
1.	Hypertension	21-36%	6.0%	Upregulated ACE-2 expression	High blood pressure with pneumonia like symptoms	Moderate severity	[16, 42]
2.	Diabetes mellitus	11-17.4%	7.3%	impaired phagocytic cell activity, elevated levels of interleukin-6 (IL-6) and ACE2 expression	Pneumonia like symptoms	High severity	[16, 42]
3.	COPD	2.0-7.5%	6.3%	Suppressed respiratory system, Upregulate ACE-2 expression	Exaggerated respiratory suppression, hypoxemia	Moderate severity	[44]
4.	CKD	2.6-3.6%	16%	Upregulation of ACE2 enzyme	Impaired kidney function	High severity	[45]
5.	Asthma	>3%	6%	delayed secretion of IFN-λ, delayed innate antiviral immune response	Chronic respiratory diseases along with symptoms of pneumonia	Less severity	[45]
6.	Liver disease	2.9%	16%	elevated ACE2 expression in liver cells	lobular inflammation and apoptosis, elevated levels of liver test markers	Moderate severity	[45]
7.	CVD	5.8-8.9%	10.5%	Suppressed immunity	acute myocardial injury as well as chronic impairment to the cardiovascular system	High severity	[45]
8.	Cancer	2.7-3.5%	5.6%	compromised immunity	anaemia, hypoproteinaemia, lymphopenia and high levels of highly sensitive C-reactive protein	Mild severity	[45]

**Table 2:** Impact of COVID-19 on comorbidities based on recent research data

## CONCLUSIONS

Comorbid patients are more susceptible to COVID-19 with adverse clinical manifestations and high mortality rate compared with those without underlying health conditions. Hypertension is the most prevalent disease followed by diabetes, CKD as the second common and cancer as the rarest disease among COVID-19 patients. Due to multiple diseases and low resistance, older patients (>60 years) are more vulnerable to get infected with COVID-19 requiring ICU, ventilator, and other supportive measures. Medications such as ACE inhibitors, ARBs and other comorbidity related medicines are recommended to be continued in ongoing pandemic. Hence, this review shows that patients with comorbidities are more likely to get infected from SARS-CoV2 with exacerbation of poor clinical outcomes than those without any comorbidity and how some comorbidities like hypertension, asthma and cancer shows less severity of clinical outcomes in patients with COVID-19, compared to cardiovascular diseases, diabetes, and CKD. Future research will further elaborate the link between COVID-19 and comorbidities as it is of utmost need to highlight the relation between COVID-19 and comorbidities to contain the infection.

## Conflicts of Interest

The authors declare no conflict of interest.

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