THE SEVERITY OF COVID-19 SYMPTOMS AMONG PATIENTS WITH COMORBIDITY AND ITS PREVENTIVE BEHAVIORS: A NARRATIVE LITERATURE REVIEW

1Alfira Damayanti, 2Anida Laela Salma, 3Shalsabila Mutiara Asri, 4Intan Rosenanda Sofiany
1,4Faculty of Public Health, Universitas Muslim Indonesia Jakarta
K.H. Ahmad Dahlan St, Cireundeu, Ciputat, South Jakarta, 15419
Email: intanrosenanda31@gmail.com

ABSTRACT
In early 2020, the world was shocked by a new coronavirus variant called SARS-CoV-2 that caused COVID-19. The disease was first discovered in Wuhan, China, in November 2019. COVID-19 can infect both healthy people and those with comorbidity. An infected person might develop symptoms ranging from mild, such as cough and fever, to severe such as respiratory problems and decreased oxygen saturation. This study synthesizes the literature investigating the relationship between hypertension, diabetes mellitus, and pulmonary tuberculosis (TB) comorbidities with the severity of COVID-19 symptoms and the adherence of patients with comorbidity to COVID-19 preventive behaviors. This study used a narrative review method by retrieving existing literature obtained through Google Scholar and PubMed search engines. This study involved eight relevant articles published between January 2020 and March 2022. COVID-19 patients with hypertension, diabetes mellitus, or pulmonary tuberculosis (TB) comorbidity were more likely to suffer severe symptoms than those without comorbidity. Furthermore, COVID-19 patients with comorbidity also had a higher mortality risk. Due to their fear of contracting COVID-19, people with comorbidity tend to adhere to COVID-19 preventive behaviors. Individuals with comorbidity have to increase awareness and implement preventive behaviors because of their higher susceptibility to prevent COVID-19 infection and the severity of its symptoms.

Keywords: Comorbidity, COVID-19, Preventive Behaviors, Severity

ABSTRAK

Kata Kunci: COVID-19, Keparahan, Komorbiditas, Perilaku Pencegahan
INTRODUCTION

On December 21st, 2019, a new case of pneumonia with unknown etiology was detected from the animal market in Wuhan City, China. Since its first finding, similar cases have continued to increase daily until The National Health Commission and China CDC investigated the etiology and epidemiology of the disease. This disease became known as Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Moreover, COVID-19 has spread swiftly to other countries less than a month after its initial appearance. Indonesia has become one of the countries affected by COVID-19 since the first case was identified in Depok, West Java province, in March 2020. The disease, which the World Health Organization has declared a global pandemic, impacts public health conditions and has broader social, educational, and economic influences. Since COVID-19 is an emerging and understudied disease, various controversies have arisen about this disease, including those concerning the diagnosis, treatment, and prevention.

Initially, some people assumed that COVID-19 was a disease with common influenza-like symptoms. However, medical analysis and various studies reveal that COVID-19 can cause severe illness and even the risk of mortality which cannot be ignored. In addition, COVID-19 also has rapid transmission from person to person. In 2020, the development and transmission of COVID-19 were found to be very significant globally. COVID-19 can infect individuals through viruses that spread from direct contact with an infected patient, and droplets come out when coughing or spitting. A person who tests positive for COVID-19 might develop various symptoms, ranging from asymptomatic to severe. Patients with mild symptoms will generally suffer mild respiratory tract inflammation similar to influenza. However, in other cases, symptoms can include fever, cough, dyspnea, unexplained loss of taste or smell (anosmia), weakness, fatigue, headache, and diarrhea. A study shows that one out of six people infected with COVID-19 will become seriously ill and have difficulty breathing. These conditions are more common in the elderly with underlying health conditions or comorbidity than others.

Comorbidity is defined as the occurrence of two or more diseases (physiological or psychological) that coincide and are allied; however, they can affect an individual’s health condition. In the case of COVID-19 patients, significant comorbidities include hypertension, diabetes mellitus, and pulmonary tuberculosis (TB). According to previous studies, patients with those comorbidities had a greater chance of being infected with COVID-19 and developing more severe symptoms. The studies state that individuals with hypertension, diabetes mellitus, or pulmonary tuberculosis comorbidities are more susceptible to COVID-19 infection. In addition, several comorbidities can play an essential role in the quicker rate of COVID-19 disease progression. The existence of comorbidity in COVID-19 patients also correlates with an increased need for an Intensive Care Unit (ICU). Furthermore, a more significant number of comorbidities are associated with greater COVID-19 disease severity.
COVID-19 is reported to have taken countless people all over the world. However, the most common COVID-19-related mortality was found in patients with comorbidity. Several studies reveal that individuals with chronic health conditions such as diabetes mellitus and hypertension can increase the risk of mortality from COVID-19.12,14,17 Individuals with pulmonary tuberculosis also have a 2-fold higher risk of COVID-19-related mortality than non-TB patients.10

Concerning the background described, a study that discusses the severity and mortality risk of COVID-19 in a particular group is crucial since COVID-19 continues to pose a health threat worldwide. Identifying the risk of severe symptoms in COVID-19 patients with comorbidity cannot be ignored because this group is more vulnerable to COVID-19 infection. This study aims to provide a narrative review of available literature to find the relationship between hypertension, diabetes mellitus, and pulmonary tuberculosis (TB) comorbidities with the severity of COVID-19 symptoms. This review also reports the level of compliance in COVID-19 preventive behaviors among patients with comorbidity.

METHOD

This study used a narrative literature review method. A review was conducted on scientific articles that discussed the severity of COVID-19 symptoms among patients with comorbidity and their compliance in implementing COVID-19 preventive behaviors. A literature search was performed online using Google Scholar and PubMed databases. The authors explored the relevant kinds of literature using several keywords, including "COVID-19 and Comorbidity", "COVID-19 and Hypertension", "COVID-19 and Diabetes Mellitus", "COVID-19 and Pulmonary Tuberculosis", and "COVID-19 Preventive Behaviors among Patients with Comorbidity". This study determined several inclusion criteria, including scientific articles published in journals between January 2020 and March 2022. The sources of articles are limited to those using Bahasa Indonesia and English, and articles that have been published are open access.

The authors obtained 21,500 articles and selected eight articles compatible with the inclusion criteria in this study. Articles were involved based on the applicability to the topic and then reviewed descriptively. The results of all articles are summarized in a matrix containing the year of publication, author's name, article title, and research settings. The summary matrix of the eight articles is analyzed to conclude and answer the purposes of this literature review.

RESULTS AND DISCUSSION

This study summarized eight articles discussing the severity of COVID-19 symptoms among patients with comorbidity. The comorbidities were limited to hypertension, diabetes mellitus, and pulmonary tuberculosis. Among the selected articles, three analyzed the relationship between hypertension and the severity of COVID-19 symptoms. Furthermore, four articles specifically studied
the relationship of diabetes mellitus with the severity of COVID-19 symptoms, while three articles focused on pulmonary tuberculosis. The two articles included in this study analyzed more than one type of comorbidity at once.

Table 1. The Characteristics of Included Articles

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<td>April 2021</td>
<td>2. A history of hypertension comorbidity increases the risk 10.59 times for experiencing COVID-19 related mortality</td>
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<td>3. Multivariate analysis showed a history of hypertension comorbidity increased the risk of COVID-19 related mortality by 2.45 times</td>
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2. Diabetes mellitus comorbidity can increase susceptibility and worsen symptoms in COVID-19 patients |
2. Individuals with diabetes mellitus comorbidity are 16.5 times more likely to experience a worsening COVID-19 symptoms than individuals without diabetes mellitus comorbidity  
3. COVID-19 cases in individuals with tuberculosis comorbidity experienced symptoms development an average of 3.3 |
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<td>7</td>
<td>2021</td>
<td>Song, W., Zhao, J., Zhang, Q., Liu, S., Zhu, X., An, Q., Xu, T., Li, S., Liu, J., Tao, N., Liu, Y., Li, Y. &amp; Li, H.¹⁰</td>
<td>COVID-19 and Tuberculosis Coinfection: An Overview of Case Reports/Case Series and Meta-Analysis</td>
<td>August 2021</td>
<td>1. COVID-19 patients with tuberculosis comorbidity are 2.21 times more likely to experience severe symptoms than other COVID-19 patients 2. COVID-19 patients with tuberculosis comorbidity are also 2.27 times more likely to die than other COVID-19 patients</td>
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Generally, COVID-19 can infect humans and show a wide range of clinical manifestations. The appearance of symptoms in an infected person is a form of the body's response to infection.\(^\text{18}\) Patients with mild symptoms might experience uncomplicated acute respiratory tract infections such as fever, cough, loss of appetite, malaise, sore throat, and headache.\(^\text{19}\) Treatment for those patients can be carried out by self-isolation at home or health care facilities for a predetermined time. Meanwhile, in severe cases, patients could suffer fever, cough, dyspnea, unexplained loss of taste or smell, weakness and fatigue, headache, diarrhea, and myalgia. Other patients with severe symptoms might encounter shortness of breath, changes in respiratory rate, and decreased oxygen saturation. Those patients require hospital treatment, a ventilator, or an ICU.\(^\text{11}\)

Moreover, a COVID-19-infected person also risks complications.\(^\text{14}\) The complications can end up with a deleterious effect on the patient due to multiple organ failure, shock, acute respiratory distress syndrome, heart failure, arrhythmias, renal failure, and, eventually, mortality.\(^\text{14}\) Various studies have shown that several factors might influence the risk of infection and severity of COVID-19 symptoms in individuals. One of them is the occurrence of comorbidity reported to aggravate the symptoms experienced by the patient.

**Hypertension Comorbidity with the Severity of COVID-19 Symptoms**

Hypertension is one of the major health problems among adults worldwide because of its high prevalence.\(^\text{23}\) Moreover, hypertension is the most common comorbidity in COVID-19 patients.\(^\text{12}\) COVID-19 patients with hypertension comorbidity accounted for 52.1% globally.\(^\text{12}\) Based on the studies reviewed, COVID-19 patients with hypertension might be at increased risk for the severity of COVID-19 symptoms.\(^\text{19}\) Moreover, a study found that hypertension could predict the COVID-19 severity.\(^\text{17}\) The severity of symptoms experienced by COVID-19 patients with hypertension also might increase the risk of mortality. In those patients, there is a 2.5-fold increased risk of COVID-19-related mortality compared with COVID-19 patients without hypertension.\(^\text{17,18}\) Another study also reported that 15.8% of COVID-19 patients with hypertension have died.\(^\text{19}\)

All of the articles reviewed in this study show a significant relationship between hypertension comorbidity with the severity of COVID-19 symptoms. The significant relationship is due to the metabolic inflammation commonly encountered by patients with hypertension.\(^\text{17}\) Metabolic inflammation can interfere with the immune system through decreased macrophage and lymphocyte activity; however, it can weaken immune function and an individual’s ability to fight infection.\(^\text{17}\) Furthermore, the severity of COVID-19 symptoms in people with hypertension might be attributable to an increased incidence of thrombotic complications, as those groups have a higher risk of thrombotic events.\(^\text{17}\) In that incidence, patients will lose a protective enzyme that increases the expression of ACE-2 (Angiotensin Converting Enzyme-2).\(^\text{19}\) The high expression of ACE-2 causes the virus to bind with
the receptor cells in endothelial and is dysfunctional in vascular endothelial cells, causing the virus to be more easily disseminated in the body, worsening symptoms and increasing the risk of mortality.\textsuperscript{18,19}

**Diabetes Mellitus Comorbidity with the Severity of COVID-19 Symptoms**

Diabetes Mellitus is a chronic non-communicable disease that can weaken the immune system.\textsuperscript{24} However, diabetes mellitus is the second position as the most prevalent comorbidity among COVID-19 patients, accounting for 33.6\% of all cases.\textsuperscript{12} A study stated that diabetes mellitus comorbidity could increase the probability of COVID-19 severity by 5.29 times.\textsuperscript{22} Another study also reported an increased risk of COVID-19 severity in diabetes mellitus patients by 1.55 times.\textsuperscript{19} Diabetes mellitus is also associated with COVID-19 for worsening the patient’s condition.\textsuperscript{17,20} A study involving COVID-19 patients in Jakarta Athletes Village, Indonesia, reported that 84.6\% of patients with diabetes mellitus experienced worsening symptoms.\textsuperscript{4} The study revealed that the increased risk of worsening COVID-19 symptoms in patients with diabetes mellitus was 16.5 times higher than in those without diabetes mellitus.\textsuperscript{4} In addition, COVID-19 patients with diabetes mellitus were also related to the risk of Acute Respiratory Distress Syndrome (ARDS), hospitalization, extended ICU care and ventilator usage, with an odds ratio of 2.75.\textsuperscript{17} Furthermore, diabetes mellitus comorbidity could also increase the mortality risk in COVID-19 patients.\textsuperscript{17} A study showed an increased mortality risk of 2.95 times in COVID-19 patients with diabetes mellitus than in patients without diabetes mellitus.\textsuperscript{22}

This review found that people with diabetes mellitus were at risk for more severe COVID-19 symptoms than those without similar comorbidity. Patients with diabetes mellitus are more susceptible to infection due to metabolic inflammation, interfering with the immune system.\textsuperscript{17} People with diabetes mellitus will suffer a weakened immunological function which reduces the ability to fend off infection.\textsuperscript{17} Furthermore, people with Diabetes Mellitus are also prone to inflammation caused by increased Angiotensin Converting Enzyme-2 (ACE2). However, more viruses can attach and replicate.\textsuperscript{25} The presence of immune system dysfunction in people with diabetes mellitus can also lead to a cytokine storm that produces hyper inflammation and affects the severity and risk of mortality from COVID-19.\textsuperscript{25} Another study suggests that COVID-19 infection can accelerate organ damage in people with diabetes mellitus.\textsuperscript{4} The severity of COVID-19 symptoms in individuals with diabetes mellitus might also be contributed by the link between induced hypercoagulation activity, myocardial infarction development, and cerebrovascular thrombosis.\textsuperscript{22} COVID-19 infection in patients with diabetes mellitus can trigger conditions of high metabolic stress that cause an increase in blood glucose levels and abnormal glucose variability.\textsuperscript{20} Individuals with uncontrolled hyperglycemia also have a greater chance of mortality from COVID-19 because of impaired immune response and enhanced pathogen virulence.\textsuperscript{19,20} In addition, infection by microorganisms and viruses in the pancreas could also cause inflammation, thereby reducing its function. As a result, no hormones for metabolic activities, such as insulin, are secreted.\textsuperscript{4}
Pulmonary Tuberculosis with the Severity of COVID-19 Symptoms

Pulmonary tuberculosis is among the most frequent infectious diseases in developing countries. Based on the Global Tuberculosis Report, Indonesia ranks third with the highest pulmonary tuberculosis cases globally, after India and China. As both infectious diseases attack the respiratory tract, pulmonary tuberculosis is recognized to have a relationship with COVID-19, increasing the risk of infection, symptoms, and rapid development. A study revealed that people with active or latent pulmonary tuberculosis are more prone to acquire severe COVID-19 symptoms and develop clinical manifestations more quickly than those without this infection. A study also reported a 2.27-fold increased risk of severe COVID-19 symptoms in patients with pulmonary tuberculosis than in those without pulmonary tuberculosis. Another study found that the percentage of COVID-19 patients with pulmonary tuberculosis who experienced severe and critical conditions was significantly higher (78%) than cases with mild or moderate symptoms (22%). The study stated that COVID-19 patients with pulmonary tuberculosis experienced symptoms development 3.3 days faster than those without pulmonary tuberculosis. Furthermore, symptom development was reported to occur on average on the ninth day after the onset of symptoms. Moreover, pulmonary tuberculosis comorbidity in COVID-19 patients might increase mortality risk. The increased mortality risk among COVID-19 patients with pulmonary tuberculosis is 2.21 times higher than those without the disease.

Generally, patients diagnosed with pulmonary tuberculosis can show symptoms and signs such as a chronic cough lasting more than two weeks, night sweats, fever, and weight loss. One study found that the lungs of patients with pulmonary tuberculosis exhibit a high expression of ACE-2, which enhances the effect of COVID-19 not only through immunosuppressive but also through increased ACE-2 expression. In addition, the increasing prevalence of dyspnea in COVID-19 patients with pulmonary tuberculosis is also one aspect that triggers the severity of COVID-19 symptoms. In elderly patients with pulmonary tuberculosis, dysregulation in the immune response and systemic inflammation are commonly reported, affecting the symptoms of COVID-19 experienced. Another study found that COVID-TB patients with hypertension, dyspnea, and higher leukocyte counts had a higher mortality rate.

The Compliance of COVID-19 Preventive Behaviors among Patients with Comorbidity

This study reviews the adherence level of COVID-19 patients with comorbidity in implementing COVID-19 preventive behaviors. A study on COVID-19 patients with diabetes mellitus showed that more than half of the respondents (53.3%) had COVID-19 preventive behaviors at a good level. While, 46.7% of the remaining respondents had an inadequate level of COVID-19 preventive behaviors. A similar study reported that comorbidity in COVID-19 patients is related to adherence to COVID-19 preventive behaviors. Most COVID-19 patients with comorbidity were observed to have high adherence to implementing COVID-19 preventive behaviors (88.7%).

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preventive behaviors included several health protocols such as washing hands, wearing a mask, keeping distance, avoiding crowds, and strengthening immunity.²⁹

This study concluded that individuals with comorbidity tend to have good COVID-19 preventive behaviors. A study of COVID-19 patients with hypertension showed a significant relationship between the attitudes of hypertensive patients and COVID-19 preventive behaviors.³⁰ The belief of hypertension patients about the spread of COVID-19 makes them have an evaluation of the body’s susceptibility to COVID-19 transmission.²⁸ Therefore, people with hypertension are more vigilant in shaping their lifestyles.²⁸ Individuals with comorbidity were also found to have higher anxiety levels in the face of a pandemic.²⁹ The higher anxiety levels motivate them to comply with health protocols such as washing hands, wearing masks, keeping their distance, staying away from crowds, and strengthening immunity.²⁹ In addition, individuals with a history of comorbidity tend to have a high awareness of self-protection.²⁹

Based on existing facts, COVID-19 can be transmitted through direct contact with an infected person and droplets.³¹ Deterrence and mitigation activities could be critical to handling COVID-19 in the population.³¹ People in close contact with COVID-19 or care for them are a high-risk group for infection. Therefore, individuals with comorbidity also require attention in preventing COVID-19 because of their higher risk of severe symptoms and mortality. Based on this review, it can be concluded that COVID-19 patients with hypertension, diabetes mellitus, and pulmonary tuberculosis comorbidity tend to develop more severe symptoms and have a greater mortality risk than their counterparts. However, if properly diagnosed and treated, COVID-19 patients with comorbidity will respond well and improve clinical and laboratory indicators.²⁰

In addition, individuals with comorbidity were shown to have high compliance in practicing COVID-19 preventive behaviors, such as washing hands, wearing a mask, keeping distance, avoiding crowds, and strengthening immunity. Patients with comorbidity should take all necessary precautions to avoid getting infected with COVID-19 since they have the worst prognosis. These precautions include maintaining hand hygiene, avoiding touching eyes, nose, and mouth, and applying cough or sneezing etiquette by covering the nose and mouth with the upper arm or tissue, then throwing the tissue in the trash. Furthermore, wearing a medical mask and practicing hand hygiene after disposing of the mask, keeping a distance from people, and limiting going to public areas unless necessary are preventive measures that can be applied.³¹

In this study, there are numerous limitations. Firstly, the authors only utilize search engines such as Google Scholar and PubMed. In addition, the context of the comorbidities evaluated is also limited to several types. The authors only discuss research results on hypertension, diabetes mellitus, and pulmonary tuberculosis comorbidities. However, these results adequately describe the COVID-19 condition in patients with comorbidity.
CONCLUSIONS AND SUGGESTIONS

The authors concluded that COVID-19 patients with hypertension or diabetes mellitus or pulmonary tuberculosis were more vulnerable to severe COVID-19 symptoms. COVID-19 patients with these comorbidities also have a greater risk of mortality. Due to the higher risk in this group, they tend to apply good COVID-19 preventive behaviors to protect themselves from COVID-19 infection and the severity of its symptoms. The authors suggest that individuals with comorbidity must adhere to the COVID-19 protocols, which include washing hands, keeping distance, using masks, avoiding crowds, and strengthening immunity.

REFERENCES


