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## **THE EFFECT OF HYPERTENSION COMORBIDITIES ON THE SEVERITY OF COVID-19 PATIENTS**

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### **ABSTRACT**

**Background:** Coronavirus disease 2019 (COVID-19) is an infectious disease caused by SARS-CoV-2. In some individuals, this virus causes no symptoms, but in other individuals, it can cause severe symptoms, respiratory failure, and even death. Based on research on COVID-19 patients with comorbidities such as hypertension, diabetes, chronic heart or kidney disease, and also chronic lung disease. has a high rate of severity and mortality, Covid-19 patients with hypertension co-morbidities have a higher number of ACE-2 receptors, as a result, the coronavirus is easier for the body to enter, increasing the risk of mortality in covid-19 patients

**Objective:** Knowing the severity of COVID-19 patients with hypertension comorbidities.

**Method:** Literature study with systematic review using 26 articles in national and international journals as a reference to produce conclusions.

**Results:** Hypertension patients are at risk of suffering from COVID-19 2.109 times greater than those without hypertension co-morbidities. This is proven by 35.43% of COVID-19 sufferers having hypertension co-morbidities. COVID-19 patients with hypertension co-morbidities have a severe severity of 1.85 times greater which requires ICU care on average 23.9%, use mechanical ventilation at 16.8%, experience ARDS, and the risk of death is 2.36 times greater.

**Conclusion:** COVID-19 patients with hypertension comorbidities have a poor prognosis and even death compared to patients without hypertension comorbidities.

**Keywords:** Hypertension, co-morbidities, COVID-19

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## INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease that was first discovered in Wuhan, China in 2019. COVID-19 is caused by SARS-CoV-2 which can infect anyone and cause different symptoms and levels of seriousness for each individual. (1) COVID-19 can be spread through droplets, which are water particles > 5-10 micrometers in diameter. Spread can occur when communicating at close range, coughing, and sneezing, and can be through direct contact with exposed objects. The COVID-19 virus is an RNA (Ribo Nucleic Acid) virus belonging to the order nidovirales, which consists of the Coronaviridae, Roniviridae, Mesoniviridae, and Arteriviridae families. The Coronaviridae family is divided into two subfamilies namely Coronavirinae and Torovirinae. The Coronavirinae subfamily consists of 4 genera, namely alpha, beta, gamma, and delta. The genera that can infect humans are the beta and alpha genera. (2,3).

The global prevalence of COVID-19 cases with comorbidities is 57.7% and without comorbidities is 42.3%, where hypertension is one of the highest comorbidities suffered by COVID-19 patients, namely 27.4%. Patients with hypertension are at high risk of exposure to COVID-19, but this risk can be reduced by carrying out management to achieve normal blood pressure or a stable condition. (4,5) Severity in COVID-19 patients with hypertension comorbidities is due to increased expression of the Angiotensin-Converting-Enzyme 2 (ACE2) receptor, making them susceptible to COVID-19 infection. The SARS-CoV-2 virus causes increased capillary

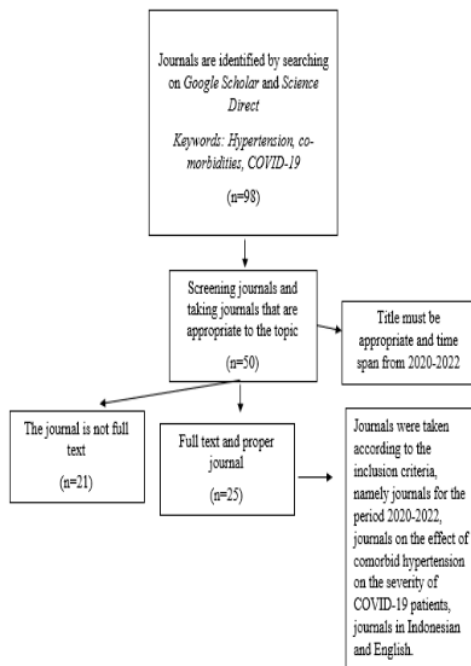
permeability, necrosis of the airway epithelium, and mucus production, resulting in difficulty breathing, Acute Respiratory Distress Syndrome (ARDS), and an increased risk of death. Hypertension can lead to chronic kidney failure which will exacerbate the symptoms of COVID-19 and increase the risk of death. (6,7)

According to data from the Ministry of Health in Indonesia on July 22, 2023, there were 6,812,141 cases, of which 162,026 died. Many comorbid diseases were found, one of which was hypertension with a percentage of 9.2%.

## METHOD

Literature study with systematic review by collecting reference data from trusted scientific research journals relating to the severity of COVID-19 patients associated with hypertension comorbidities, spanning 2020-2023, national and international journals.

Figure 1: Literature Review Stages



## RESULTS AND DISCUSSION

Concomitant diseases are diseases that have been suffered before, in the case of COVID-19 there are several co-morbidities, which are commonly found, namely hypertension, diabetes mellitus, chronic obstructive pulmonary disease, kidney failure, and obesity. Co-morbidities that exist in COVID-19 patients can worsen the condition and even risk death. (6,8)

Co-morbidities present in COVID-19 patients correlate with poor clinical outcomes. Several co-morbidities are risk factors for the severity of COVID-19 patients and can have an impact on death. In Aisyiyah's research (2022), Herlina (2022) states that hypertension is the most common type of comorbid disease, while research by Wei, Qiao, Chen (2021) and Fresan, C<sub>11</sub>vara (2021) found 16.3% and 16.8% of COVID-19 patients had hypertension. (9),(10),(11), And(12)Zhang and Tao's research stated

that 26.1%, 26.8%, and 12.9% of COVID-19 patients had hypertension cohorts in the wild-type, delta, and omicron variant cohorts, while Chen, Liu, Qin, Rua<sub>11</sub>Zeng, and Zhang's research found 29.9% of COVID-19 patients were hypertension patients. Huang's Research (2020) 36.5%, Dita's Research, 52.1%, Zhao's Research, (2021) 63.6%, Sato's Research, Fanning, 73% of COVID-19 patients have hypertension co-morbidities. After analyzing the average comorbidities of hypertension, 35.34% was obtained from this research. (1,11-17)

Hypertension co-morbidities according to research by Nanda, and Indaryati, (2021) states that there is an effect of hypertension co-morbidities (p-value = 0.007 <0.05) on the incidence of COVID-19 where hypertension has a risk of being infected with COVID-19 by 2.109 times higher than patients who do not have hypertension similar to the Senewe study (2021) which states that patients with hypertension comorbidities have 1.90 times the risk of suffering from COVID-19 compared to those without hypertension comorbidities. This is because in hypertensive patients there is an increase in ACE-2 expression so that the risk of infection with SARS-CoV-2 is higher.(1,2,16,17)

The pathogenesis of COVID-19 first infects through respiratory cells, then the <sub>13</sub>velope spike virus in the form of a glycoprotein binds to angiotensin-converting enzyme 2 (ACE-2) which is present in the alveolar epithelium, cornea, and conjunctiva resulting in duplication of genetic material and protein synthesis. Exposure to the SARS-CoV-2 virus makes the body respond immune with an antigen mechanism by APC which will stimulate T cells and B cells to form IgM

and IgG. If the virus can evade the host's immune response by replicating in double-membrane vesicles that do not have pattern recognition receptors (PRRs), the virus cannot be recognized and infection occurs. The severity of infection is determined by the cytopathic effect of the virus and its ability to overcome the immune response. A weak immune response in the individual causes viral replication and tissue damage. As a result, clinically appearing in Covid-19 infection can be asymptomatic, mild symptoms, severe, and even cause death.(2,9,13)

Hypertension is an inflammatory disease due to endothelial dysfunction, in hypertensive patients there is a higher expression of ACE 2 compared to patients who are not hypertensive, causing an increased risk of COVID-19 infection. ACE 2 is a receptor for the virus that causes COVID-19 which is found in many specific organs and can cause organ failure. Treatment of hypertension using ACEI (Angiotensin-converting enzyme inhibitors) and ARB (Angiotensin receptor blockers) is thought to increase the expression of ACE 2 in humans. This may increase susceptibility to viral entry and propagation into host cells in patients with hypertension.(2,9,11)

Hypertension co-morbidities are a risk factor for the severity of COVID-19 patients, this has been shown to increase the risk of severity and require ICU treatment, and increase mortality. In Isik's study (2022) it was found that comorbid hypertension has a higher risk of death than other comorbidities. Hypertension can increase the risk of death in Covid-19 patients by 1.15 times (Adhani, 2022)(21), 1,585 times

(Herlina, 2022)(22), 2.2 times (Wulandari, 2021)(7), 4.53 times (Choirunnisa and Helda, 2022)(20) compared with COVID-19 cases without comorbid hypertension.(7.20–22)

Chen's research (2022) stated that the hypertension group had a higher mortality rate than the non-hypertension group, where the rate of hospitalization in the intensive care unit (ICU) in the hypertension group (12.8%) was higher than in the non-hypertension group (5.3%). Shah's research (2021) states that the prevalence of hypertension in COVID-19 appears to be higher in patients with high severity, which includes the use of intensive care units, use of mechanical ventilation, ARDS, or death. Another study from China showed that almost 58% of COVID-19 patients who required intensive care had hypertension. Two other studies reported that 48% of COVID-19 patients who died had comorbid hypertension. Antos' research (2021) based on comparative analysis identified hypertension with an odds ratio of 34,(11,14,23,24)

Zhao's research (2021) shows an increased risk of severe COVID-19 complications in individuals with hypertension. Gunawan's research (2020) states that hypertension can worsen the condition of COVID-19 patients by up to 2.5 times. Huang's study (2021) stated that compared to non-hypertensive patients, hypertensive patients had a higher mortality rate (24.8%), a higher proportion of severe patients (63.7%), a higher proportion of patients who received non-invasive mechanical ventilation (16.8%), and a higher proportion of patients transferred to the intensive care unit (ICU) (23.9%). In

Dita's study (2021) in patients who had comorbid hypertension, there was a worsening and severity of SARS-CoV-2 infection due to an increase in the binding of the virus to target cells that utilized ACE-2.(1,2,6,11,25)

Co-morbidities causing COVID-19 patients are substantially associated with significant morbidity and mortality. Patients with hypertension co-morbidities have a high prevalence of infection with SARS-CoV-2. SARS-CoV-2 uses protein S (Spike) to attach to host cells using receptors in the form of ACE2 and enters cells after division. ACE2 is involved in the RAAS system. In hypertension co-morbidities, the RAAS is dysregulated and hypertensive patients often use (ACEis) as their therapy, and experimentally show an increase in ACE2 expression. Clinical data are showing a relationship between worsening COVID-19 and cytokine storms, namely increased cytokines associated with the development of hypertension. In hypertension co-morbidities with COVID-19,(16,20).

Co-morbidities contribute to a decrease in the body's functional reserves, thereby reducing the capacity and ability to fight infection. Hypertensive co-morbidities are associated with strong ACE-2 receptor expression and higher release of proprotein convertase which increases viral entry into host cells. The outcome of COVID-19 patients is thought to be related to the patient's severity at the time of admission, namely moderate-severe. In the hypertensive patient group, moderate and severe severity were directly proportional to the percentage of deaths in this group. Previous studies have found that more than 50% of COVID-19 patients experience sepsis.

Viral infection is the only reason for sepsis. Sepsis is a common complication directly caused by infection with SARS-CoV-2.(2,9,11)

## CONCLUSION

COVID-19 patients with hypertension co-morbidities have a poor prognosis and even death compared to patients without hypertension co-morbidities. Hypertension patients are at risk of suffering from COVID-19 2.109 times greater than those without hypertension co-morbidities. This is proven by 35.43% of COVID-19 sufferers having hypertension co-morbidities. COVID-19 patients with hypertension co-morbidities have a severe severity of 1.85 times greater which requires ICU care on average 23.9%, use mechanical ventilation at 16.8%, experience ARDS, and the risk of death is 2.36 times greater.



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