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# THE ASSOCIATION BETWEEN COMORBID HYPERTENSION AND THE SEVERITY OF COVID-19 AT NATIONAL EMERGENCY HOSPITAL WISMA ATLIT KEMAYORAN JAKARTA

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## ABSTRACT

*The severity of COVID-19 is influenced by many factors, one of which is comorbid hypertension. The National Emergency Hospital Wisma Atlit Kemayoran is a special hospital and the only hospital that treats patients from severe to asymptomatic. This study aims to look at the association between comorbid hypertension and the severity of COVID-19. The design of this study was a case control conducted from October to November 2022. The data used was the secondary data from the medical records of patients at National Emergency Hospital Wisma Atlit Kemayoran in 2021. The case group totaled 288 research subjects who experienced COVID-19 with moderate and severe symptoms, while the control group totaled 302 research subjects who experienced COVID-19 with mild and asymptomatic symptoms. The results showed a statistically significant association between hypertension and the severity of COVID-19 with OR 3.40, 95% CI 1.88 to 6.34 and p-value <0.001. There is also a statistically significant association between comorbid hypertension and the severity of COVID-19 with Adjusted OR 3.33, 95% CI 1.79 to 6.13 and p-value <0.001 after being controlled by age, vaccination status, and education level. It is hoped to be an illustration that the management of hypertension is very important in order to prevent the worsening of the condition in COVID-19 patients.*

***Keywords:*** *COVID-19, the severity, comorbid , hypertension.*

## ABSTRAK

Tingkat keparahan COVID-19 dipengaruhi oleh banyak faktor, salah satunya adalah komorbid hipertensi. Rumah Sakit Darurat Penanganan COVID-19 (RSDC) Wisma Atlit merupakan rumah sakit khusus dan satu-satunya rumah sakit yang merawat pasien dari gejala berat sampai tanpa gejala. Penelitian ini bertujuan untuk melihat hubungan komorbid hipertensi dengan tingkat keparahan COVID-19. Desain penelitian ini adalah kasus kontrol dan dilakukan sejak Oktober-November 2022. Data yang digunakan adalah data rekam medis pasien RSDC Wisma Atlit tahun 2021. Kelompok kasus berjumlah 288 responden penelitian yang mengalami COVID-19 dengan gejala sedang dan gejala berat sedangkan kelompok kontrol berjumlah 302 responden penelitian yang mengalami COVID-19 dengan gejala ringan dan tanpa gejala. Hasil penelitian menunjukkan hubungan yang signifikan secara statistik antara komorbid hipertensi dengan tingkat keparahan COVID-19 dengan nilai OR 3.40, 95% CI 1.88 – 6.34 dan nilai p <0,001. Terdapat pula hubungan yang signifikan secara statistik antara komorbid hipertensi dengan tingkat keparahan COVID-19 dengan OR *adjusted* 3.33, 95% CI 1.79 – 6.13 dan nilai p <0,001 setelah dikontrol variable umur, status vaksinasi dan tingkat pendidikan. Hal ini diharapkan bisa menjadi gambaran bahwa penanggulangan penyakit hipertensi sangatlah penting agar dapat mencegah perburukan keadaan pada pasien COVID-19.

**Kata Kunci:** COVID-19, tingkat keparahan, komorbid, hipertensi

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## Introduction

The severity of COVID-19 is determined based on clinical symptoms, laboratory results, and chest radiographic images, which are divided into asymptomatic infections, mild symptoms, moderate symptoms, and severe symptoms.[1] Data from the Ministry of Health states that 81% of COVID-19 sufferers recovered on their own without special treatment or in other words, experienced COVID-19 without symptoms or mild symptoms, then as many as 14% of patients experienced a severe condition, and the remaining 5% fell to a critical stage.[2] Factors that influence the severity of COVID-19 sufferers include age, gender, immune system, and comorbid diseases such as hypertension, diabetes mellitus, COPD, heart disease, and chronic kidney disease.[3,4] In addition, the severity of COVID-19 is also affected by the patient's vaccination status. Patients who have not or are not vaccinated have a higher risk of severity and death.[5]

One of the factors that greatly affect the severity of COVID-19 is the presence of comorbidities. Comorbidities are co-morbidities that the patient previously had. In Indonesia, data shows that the co-morbidities that most often accompany confirmed cases of COVID-19 are diabetes mellitus (9.4%), hypertension (9.2%) and heart disease (4.8%).[4,6] Hypertension is one of the comorbidities that many people in Indonesia experience. A person is diagnosed with hypertension if the systolic blood pressure is ≥140 mmHg and or the diastolic blood pressure is ≥90 mmHg on two different measurements.[7] Data shows that there are 1.28 billion people with hypertension aged 30-79 years worldwide.[8] Based on the 2018 Basic Health Research (Riskesdas) data, the prevalence of hypertension in people aged ≥18 years is 34.11%. This figure is higher when compared to the prevalence in 2013, which was only 25.8%.[9]

Hypertension is known to have a clear mechanism to affect the severity of COVID-19 patients, resulting in a worsening of the condition. The SARS-CoV-2 virus uses the Angiotensin Converting Enzyme (ACE) 2 receptor to arrive at target cells. This impairs the activity of ACE 2, which is involved in the conversion of angiotensin 2 to angiotensin (1-7). Disruption of angiotensin production (1-7) also disrupts vascular homeostasis and causes vasoconstriction resulting in an increase in blood pressure which will eventually worsen the condition of patients with a history of comorbid hypertension.[10] Recent research states that patients with comorbid cardiovascular disease are at greater risk of contracting COVID-19 at a severe level through the mechanism of endotheliitis. COVID-19 affects not only lung parenchyma epithelial cells through ACE 2 but also endothelial cells throughout the body, causing overall endothelial damage and inflammation, or what is called endotheliitis.[11] This is in line with several previous studies conducted by Parveen et al. (2020), which stated that hypertension is positively related to the severity of patients with an OR value of 2.69 with 95% CI 1.27 to 5.73.[12] In Indonesia, research related to and which contains how

big the association is is still very minimal, especially at the National Emergency Hospital *Wisma Atlit Kemayoran Jakarta*.

National Emergency Hospital *Wisma Atlit Kemayoran Jakarta* is an emergency hospital dedicated to treating patients with COVID-19 since March 2020. This hospital was previously an accommodation for athletes who will compete in the 2018 Asian Games. This hospital was one of the largest hospitals in the world for handling COVID-19 patients. This hospital has its own specialty because it can treat patients with various levels of severity ranging from patients with no symptoms, mild symptoms, and moderate symptoms to severe symptoms, in contrast to other hospitals, which usually can only treat patients with moderate and severe symptoms.[13,14] This is, of course, very useful if research is carried out at the National Emergency Hospital *Wisma Atlit* because we can see firsthand the difference between the severity of COVID-19. A study conducted at National Emergency Hospital *Wisma Atlit*, which reviewed the epidemiological picture and patient characteristics, found that there was indeed a significant difference between the severity of COVID-19 patients who were divided into asymptomatic patients, mild symptoms and severe symptoms with comorbidities suffered with a p-value <0.001.[15] There is no research that has looked at how big the association between comorbid hypertension is with the severity of COVID-19, especially at the National Emergency Hospital *Wisma Atlit Kemayoran Jakarta*. Based on this background, this study aims to look at the association between hypertension comorbidities and the severity of COVID-19 at the National Emergency Hospital *Wisma Atlit Kemayoran Jakarta* in 2021.

## Methods

A case-control study design was used in this research, and it was conducted from October to November 2022. The data used were medical record data of patients at the National Emergency Hospital *Wisma Atlit Kemayoran Jakarta* in 2021. In this study, identification of the case group and the control group were identified. The case group was COVID-19 patients with moderate-severe symptoms, while the control group was COVID-19 patients with mild-asymptomatic symptoms who visited or were treated at National Emergency Hospital *Wisma Atlit* in 2021. The minimum sample size was 302 respondents for each group. The comparison between the case group and the control group is 1:1. Respondents were selected using consecutive sampling techniques in the case group and simple random sampling in the control group. This difference was due to the selection of research respondents; the number of respondents in the case group (with moderate-severe symptoms of COVID-19) could not meet the minimum sample size due to incomplete medical record data, so the data analysis could not be carried out. The available data were as many as 288 research respondents in the case group. Then all data was entered and analyzed (consecutive sampling). The power of this research was 99%. The case and control groups were then examined

retrospectively to see if there were any risk factors, namely the presence of comorbid hypertension, taking into account covariates such as age, sex, education, vaccination status, comorbid diabetes mellitus, comorbid heart disease, and comorbid asthma.

The severity of COVID-19, comorbid hypertension, comorbid diabetes mellitus, comorbid heart disease, and comorbid asthma were determined based on the diagnosis stated in the patient's medical record (categorized as yes or no). Patient age was categorized into elderly patients (> 60 years) and non-elderly (<60 years). Gender was categorized into male and female. The education level of the research respondents was divided into basic education (elementary-junior high school), secondary education (high school and equivalent), and higher education (diploma, bachelor, master, specialist, and doctoral). The patient's vaccination status was categorized as either vaccinated or not vaccinated.

Data analysis was carried out univariate, bivariate, and multivariate using tests appropriate to the type of data for each variable. Univariate analysis was carried out on all respondents to see the distribution and frequency of the independent variable (comorbid hypertension) and other variables such as age, gender, occupation, education, comorbid diabetes mellitus, comorbid COPD, and comorbid heart disease on the severity of COVID-19. Bivariate analysis was carried out to see the association of the severity of COVID-19 with the independent variable (comorbid hypertension) and other variables such as age, gender, occupation, education, comorbid diabetes mellitus, comorbid COPD, and comorbid heart disease before controlling for variables that could potentially become confounders. Bivariate analysis used the association size of crude Odds Ratio (OR). Multivariate analysis was carried out to determine the association between comorbid hypertension and the severity of COVID-19 after controlling for the confounder variable. Multivariate analysis used the adjusted Odds Ratio (OR) to see the association. This research was approved by the Ethics Committee for the National Emergency Hospital *Wisma Atlit Kemayoran Jakarta*, Number: 054/KERSDCWA/2021.

## Results

Based on the table 1, it was seen that the number of research respondents who were analyzed was 288 respondents in the case group and 302 respondents in the control group. The number of respondents in the case group was less than in the control group/*references*. Bivariate analysis showed a statistically significant association between comorbid hypertension and the severity of COVID-19 with OR 3.39, 95% CI 1.88 to 6.34 and p-value <0.001. Respondents with comorbid hypertension have a risk of 3.39 times getting COVID-19 with moderate–severe symptoms compared to those with mild symptoms–asymptomatic COVID-19.

**Table 1. The Association between the Severity Level of COVID-19 and Comorbid Hypertensionand Other Variables**

| Variable | Case | Control | P-value | OR | (95% CI) |
|---|---|---|---|---|---|
| | n ( %) | n (%) | | | |
| **Hypertension** | | | | | |
| Yes | 51 (17.71) | 18 (5.96) | <0.000 | 3.40 | 1.88 – 6.34 |
| No | 237 (82.29) | 284 (94.04) | | | |
| **Age** | | | | | |
| ≥60years (elderly) | 25 (8.68) | 14 (4.64) | 0.04 | 1.95 | 0.95 – 4.15 |
| <60years (not elderly) | 263 (91.32) | 288 (95.36) | | | |
| **Gender** | | | | | |
| Male | 145 (50.35) | 142 (47.02) | 0.41 | 0.88 | 0.63 – 1.22 |
| Female | 143 (49.65) | 160 (52.98) | | | |
| **Education Level** | | | | | |
| College | 123 (42.71) | 60 (19.87) | <0.000 | 1.98 | 1.22 – 3.26 |
| High School | 133 (46.18) | 144 (47.68) | | | |
| Junior High School | 32 (11.11) | 98 (32.45) | | | |
| **Vaccination Level** | | | | | |
| Not vaccinated | 181 (62.85) | 77 (25.50) | <0.000 | 4.94 | 3.42 – 7.14 |
| Vaccinated | 107 (37.15) | 225 (74.50) | | | |
| **Diabetes Mellitus** | | | | | |
| Yes | 14 (60.87) | 9 (39.13) | 0.24 | 1.66 | 0.65 – 4.42 |
| No | 274 (48.32) | 293 (51.68) | | | |

Table 1 also showed that there was a statistically significant association between the age factor and the severity of COVID-19 with was OR 1.95, 95% CI 0.95 to 4.15 and p-value 0.04, which meant that respondents who were elderly (> 60 years old) have a 1.95 times risk of getting COVID-19 with moderate–severe symptoms compared to having mild symptoms–no symptoms of COVID-19.

The education level of the research respondents also showed that there was a statistically significant association with the severity of COVID-19 with OR was 1.98, 95% CI 1.22 to 3.26 and p-value <0.001, which meant that respondents with higher education have a 1.98 times risk of getting COVID-19 with moderate–severe symptoms compared to having mild symptoms–asymptomatic COVID-19.

A statistically significant association was also seen between vaccination status and the severity of COVID-19 with OR was 4.94, 95% CI 3.42 to 7.14 and p-value <0.001. Respondents who did not vaccinate against COVID-19 had 4.94 times the risk of getting COVID-19 with moderate-severe symptoms compared to getting COVID-19 with mild symptoms-asymptomatic.

**Table 2. Final Model of the Association between Comorbid Hypertension and COVID-19 Severity after Controlling Variables Age, Vaccination Status and Education Level**

| Variable | P-value | Adjusted OR | (95% CI) |
|---|---|---|---|
| Hypertension Comorbid | <0.001 | 3.33 | 1.79 – 6.13 |
| Age | 0.13 | 1.80 | 0.83 – 3.90 |
| Vaccination Status | <0.001 | 5.33 | 3.67 – 7.68 |
| Education Level | <0.001 | 1.70 | 1.30 – 2.21 |

Multivariate analysis on the table 2 was carried out to model a causal association between hypertension comorbidities and the severity of COVID-19 using the logistic regression method (causal model). The method used to obtain an appropriate model is using the backward elimination procedure model by removing the covariate variables one by one and comparing changes in the OR values of the main independent variables. The confounder variable was a covariate variable that had an OR change value of >10%. After the procedure was carried out, it was found that the confounders in this study were age, vaccination status, and education level, so these variables were included in the model to control for the OR (adjustment) value, and the adjusted OR value was 3.33, 95% CI 1.79 to 6.13 and p-value <0.001, which mean that respondents with comorbid hypertension have a 3.33 times risk of getting COVID-19 with moderate-severe symptoms compared to getting COVID-19 with mild-no symptoms after controlling for age, vaccination status and education level. There was a statistically significant association between hypertension co-morbidities and the severity of COVID-19 after controlling for age, vaccination status, and education level.

## Discussion

Multivariate analysis was carried out to model a causal association between hypertension comorbidities and the severity of COVID-19 using the logistic regression method (causal model). The method used to obtain an appropriate model is using the backward elimination procedure model by removing the covariate variables one by one and comparing changes in the OR values of the main independent variables. The confounder variable was a covariate variable that had an OR change value of > 10%. After the procedure was carried out, it was found that the confounders in this study were age, vaccination status, and education level, so these variables were included in the model to control for the OR (adjustment) value, and the adjusted OR was 3.33, 95% CI 1.79 to 6.13 and p-value <0.001, which meant that respondents with comorbid hypertension have a 3.33 times risk of getting COVID-19 with moderate-severe symptoms compared to getting COVID-19 with mild-no symptoms after controlling for age, vaccination status and education level. There was a statistically significant association between hypertension co-morbidities and the severity of COVID-19 after controlling for age, vaccination status, and education level.

The severity of COVID-19 based on the symptoms that appearedwas divided into asymptomatic, mild, moderate, and severe COVID-19.[3,16] This assessment was based on clinical manifestations, physical examination, and supporting examinations obtained. In asymptomatic COVID-19 sufferers, the patient did not feel any symptoms. Complaints felt in patients with mild symptoms of COVID-19 are fever, cough, fatigue, shortness of breath, decreased appetite, nausea, vomiting, anosmia (loss of taste) and ageusia (loss of taste). In COVID-19, mild symptoms were not found that pneumonia occurred. COVID-19 sufferers with moderate symptoms experienced clinical symptoms of pneumonia such as fever, cough, and shortness of breath, but no signs have been found or SpO2 >93% with room air. In patients with severe COVID-19 symptoms, the patientexperienced clinical symptoms of pneumonia in the form of fever, cough, shortness of breath, and fast breathing plus one of these symptoms, namely respiratory frequency >30 x/minute or severe respiratory distress or SpO2 <93% in room air.[16,17]

The SARS-CoV-2 virus used the Angiotensin Converting Enzyme (ACE) 2 receptor to arrive at target cells.[18] This interferes with the activity of ACE 2, which was involved in the conversion of angiotensin 2 to angiotensin (1-7). Disruption of angiotensin production (1-7) also disrupts vascular homeostasis and causes vasoconstriction resulting in an increase in blood pressure which eventually worsen the condition of patients with a history of comorbid hypertension. In addition, there were other mechanisms in the form of an increase in angiotensin 2, which caused an increase in the permeability of blood vessels, including the pulmonary vessels, which has the potential to cause pulmonary edema.[19,20]

In patients with comorbid hypertension, it was known that actually the number of ACE 2 increases due to impaired conversion of angiotensin 2 to angiotensin (1-7). This increased number of ACE 2 was found in many important organs such as the lungs, arteries, heart, and others which will make it easier for the SARS-CoV-2 virus to enter host cells and develop. This lead to an increase in cellular response that triggers pro-inflammatory cells to come out and lead to an increase in excess cytokines, which in turn has the potential to become a pro-inflammatory cytokine storm.[19,21]

A recent research stated that patients with comorbid cardiovascular disease were at greater risk of contracting COVID-19 at a severe level through the mechanism of endotheliitis. COVID-19 affects not only lung parenchyma epithelial cells through ACE2 but also endothelial cells throughout the body, causing overall endothelial damage and inflammation, or what is calledendotheliitis. The features of endotheliitis consist of the accumulation of lymphocytes, plasma cells and macrophages beneath the endothelial cells and in the perivascular space. Endothelial cells play an important role in the regulation of vascular tone and the maintenance of vascular homeostasis. The development of endotheliitis shifted the vascular balance resulting in vasoconstriction with ischemia of the organs, inflammation with associated tissue edema, and a

procoagulant state. According to research on male patients, smoking, hypertension, diabetes mellitus, obesity and other cardiovascular diseases are very susceptible to endothelial dysfunction, so if you were exposed to COVID-19, you would be at high risk of experiencing COVID-19 with severe severity. Many of these results have been found from autopsies on corpses since the pandemic occurred.[11] The results of this study were in line with the existing theory that there was a statistically significant association between hypertension comorbidities and the severity of COVID-19 with adjusted OR was 3.33, 95% CI 1.79 to 6.13 and p-value <0.001.

In this study, the confounders which could influence the results of the study included age, vaccination status and level of education. The researcher included this confounder together with the final model to control the OR (OR adjusted) value, so it was hoped that the presence of the confounder did not affect the research results. In the multivariate analysis, the adjusted OR was 3.33, 95% CI 1.79 to 6.13 and p-value <0.001, which meant that respondents with comorbid hypertension have a 3.33 times risk of getting COVID-19 with moderate-severe symptoms compared to getting COVID-19 with mild-no symptoms after controlling for age, vaccination status and education level. These results were in line with a study conducted by Lippi et al. (2020), which showed that there was a association between comorbid hypertension and the severity of COVID-19 patients which resulted in death of 2.5 times higher than patients who did not have comorbid hypertension.[22] These results were also the same as a study conducted by Pranata et al. (2020) which showed that hypertension was associated with worsening patient conditions with an RR value of 2.11 with a 95% CI: 1.85 to 2.40.[23] A similar study conducted by Parveen et al., (2020) stated that hypertension was positively related to the patient's severity with an OR value of 2.69 with 95% CI 1.27 to 5.7.[12] A total of 53 systematic reviews and meta-analyses looked at the association of comorbid hypertension as COVID-19 exposure with severity (assessment based on ICU admission, need for mechanical ventilation, clinical disease progression, a combination of these conditions, or death) using both retrospective and prospective designs. Revealed that hypertension is strongly related to the severity of COVID-19. Nine main studies stated that the estimated association or risk is adjusted with the variables included in the regression model including age, sex, clinical symptoms, and other co-morbidities, indicating that hypertension is associated with a higher risk of severity and death in COVID-19 patients.[24] This is also in line with a study conducted by Fang et al. (2020) which stated that comorbid hypertension and diabetes mellitus, male sex and active smokers had strong epidemiological evidence to influence the severity and prognosis of COVID-19 disease.[25] A systematic review and meta-analysis study conducted by Mudatsir et al., (2021) also revealed the same thing by observing 19 studies involving 1.934 COVID-19 patients with mild symptoms and 1,644 COVID-19 patients with severe symptoms. The study showed that several comorbidities, including chronic respiratory

disease, cardiovascular disease, diabetes mellitus, and hypertension were more common among COVID-19 patients with severe symptoms than COVID-19 patients with mild symptoms.[26]

## Conclusion

The results of the study showed a statistically association between comorbid hypertension and the severity of COVID-19 at National Emergency Hospital *Wisma Atlit Kemayoran Jakarta* in 2021. Respondents with comorbid hypertension had a risk of 3.33 times to get COVID-19 with moderate–severe symptoms compared to COVID-19 with mild symptoms–asymptomatic after controlling for age, vaccination status, and education level. It was hoped that the results of this studyserved as an illustration that managing comorbid hypertension was very important in order to prevent worsening of the condition in COVID-19 patients sopatients did not fall into severe severity.

Management of comorbid hypertension in Indonesia was pursued through the activities of the Integrated Development Post Program (*POSBINDU*) for Non-Communicable Diseases (*PTM*) at first-level health facilities for early detection and monitoring of risk factors for non-communicable diseases including comorbid hypertension. In addition, the presence of *PTM posbindu* was a means of community empowerment through increasing community participation and increasing awareness of PTM risks. It was hoped that people who participated in posbindu can implement CERDIK behavior, namely by C: regular health checks, E: get rid of cigarette smoke, R: stimulate physical activity, D: healthy and balanced diet, I: adequate rest, and K: manage stress. This was very useful in managing comorbid hypertension in the community.

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## Conflict of Interest

There is no conflict of interest whatsoever in writing this article.

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