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Literature Review

The Cure Rate of COVID-19 Patients with Comorbid Hypertension

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ABSTRACT

Introduction: *Coronavirus Disease 2019 (COVID-19) is an outbreak that has resulted in a global pandemic. In 2020, 185 countries were affected, and more than 3,000,000 cases have been reported worldwide, with more than 210,000 deaths. COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV 2), an RNA virus that can cause respiratory system disorders. Hypertension, commonly called high blood pressure, is a health problem that often occurs in the community because its prevalence is relatively high throughout the world. Approximately 7.5 million deaths, or 12.8% of all annual deaths in the world, are caused by hypertension. Generally, the presence of comorbid hypertension in COVID-19 can worsen the patient's condition.* ***Methods:*** *This literature review study aims to determine the recovery rate of COVID-19 patients with comorbid hypertension. Journals in this literature review used three databases, including Google Scholar, PubMed, and Science Direct, using the keywords COVID-19 with Hypertension and COVID-19 with Hypertension. The literature search was adjusted based on the inclusion and exclusion criteria.* ***Results:*** *The search results obtained 25 journals consisting of 4 national journals and 21 international journals. The results showed that the average recovery rate for COVID-19 patients with comorbid hypertension*

was 75.40%. Factors influencing the recovery rate of COVID-19 patients with comorbid hypertension include ACE-2, ACEI/ARBs, age, male, and cytokines. ***Conclusions:*** *It can be concluded that the presence of comorbid hypertension affects the recovery rate of COVID-19 patients.*

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1. INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is an outbreak that has resulted in a global pandemic.[1,2] In 2020, 185 countries have been affected, and more than 3,000,000 cases have been reported worldwide, with more than 210,000 deaths.[3–5] The severe acute respiratory syndrome coronavirus causes COVID-19- 2 (SARS-CoV 2), an RNA virus.[6–8]

SARS-CoV-2 is unlike coronaviruses previously known to cause the common cold (229E, OC43, NL63, and HKU1) but is similar to the Severe Acute Respiratory Syndrome (SARS) severe acute respiratory syndrome coronavirus.[9] SARS-CoV 2 infection is caused by binding of the viral surface spike protein (S) to the human Angiotensin Converting Enzyme 2 (ACE-2) receptor after activation of the spike protein by Transmembrane Protease Serine-2 (TMPRSS2).[10] ACE2 is expressed in the lung, mainly in alveolar type II cells, and appears to be a central portal of entry.[11] High ACE2 is also expressed in the heart, counteracting the effects of angiotensin II in circumstances of excessive renin-angiotensin system activation, such as hypertension.[12]

Hypertension, commonly called high blood pressure, is a health problem often occurring in society because its prevalence is relatively high worldwide.[12] Approximately 7.5 million deaths, or 12.8% of all annual deaths in the world, are caused by hypertension.[12] It is estimated that up to 1.56 billion adults will suffer from hypertension by 2025.[13] Hypertension is high arterial BP.[12] According to the Joint National Committee 7 (JNC 7), systolic BP <120 mmHg and diastolic BP <80 mmHg are normal blood pressure. A person is called hypertensive if systolic BP ≥140 mmHg and/or diastolic BP ≥ 90 mmHg.[14]

Hypertension is the most common comorbid condition in the community related to COVID-19.[15] Studies in China[15] and Italy[16] have shown a potential association between comorbid hypertension and SARS-CoV-2 infection. Comorbid hypertension hurts COVID-19 disease outcomes, which will result in worse conditions. Based on these data, the author feels the need to further examine the recovery rate of COVID-19 patients with comorbid hypertension.

2. METHODS

The research design used is the Literature Study method with the Literature Review type. The reference or literature search strategy was carried out through the Google Scholar, PubMed, and Science Direct databases using COVID-19 with Hypertension and COVID-19 with Hypertension. The literature search was adjusted based on the inclusion and exclusion criteria. Inclusion criteria include 1) the period of journal publication from 2019-2021, 2) the theme or content of the research journal is

related to the recovery rate of COVID-19 patients with comorbid hypertension, 3) the type of journal used is a research journal, not a literature study, 4) national or international journals, 5) the journal is a full-text journal. The exclusion data includes 1) journals published below 2019 and above 2021, 2) journals that only show abstract text, and 3) journals that do not discuss the recovery rate of COVID-19 patients with comorbid hypertension.

Journal searches using Google Scholar found 31,645 journals, PubMed 3,180 journals and Science Direct 7,158. So, that is a total of 41,983 journals. Then, screening was carried out to obtain journals based on inclusion and exclusion criteria. The screening results amounted to 48 journals. The journals analyzed and used as data in this study were 25 journals, four national journals, and 21 international journals.

3. RESULTS

3.1 Recovery Rate of COVID-19 Patients with Comorbid Hypertension

The analysis results of 25 journals regarding the recovery rate of COVID-19 patients with comorbid hypertension are listed in Table 1 and Figure 1.

Table 1. Percentage of each journal regarding the recovery rate of COVID-19 patients with comorbid hypertension

No	Researcher Name	Cure Rate (%)	Mortality Rate (%)
1.	Emami et al.[17]	83,33	16,67
2.	Rodilla et al.[18]	70,16	29,84
3.	Huang et al.[19]	75,22	24,78
4.	Hasanah dan Wahyudi[20]	83,33	16,67
5.	Abayomi et al.[21]	91,9	8,1
6.	Moftakhar et al.[22]	86,87	13,13
7.	Zhang et al.[23]	90,67	9,33
8.	Wang et al.[24]	76,81	23,19
9.	Zhong et al.[25]	89,46	10,54
10.	Fang et al.[26]	99,52	0,48
11.	Deng et al.[27]	31,04	68,96
12.	Zhou et al.[28]	55,17	44,83
13.	Osibogun et al.[29]	86,33	13,67
14.	Iaccarino et al.[30]	84,31	15,69
15.	Amiruddin et al.[31]	42,42	57,58
16.	Chen et al.[32]	41,94	58,06
17.	Karyono dan Wicaksana[33]	80,94	19,06
18.	Widjaja et al.[34]	63,64	36,36

19.	Drew and Adisasmita[35]	84,15	15,85
20.	Khan et al.[36]	95,2	14,58
21.	Cheng et al.[37]	62,86	37,14
22.	Basu et al.[38]	54,44	45,56
23.	Yao et al.[39]	83,22	16,78
24.	Gao et al.[40]	96	4
25.	Pan et al.[41]	76,17	23,83
	Total	1885,10	624,68
	Average	**75,40%**	**24,99%**

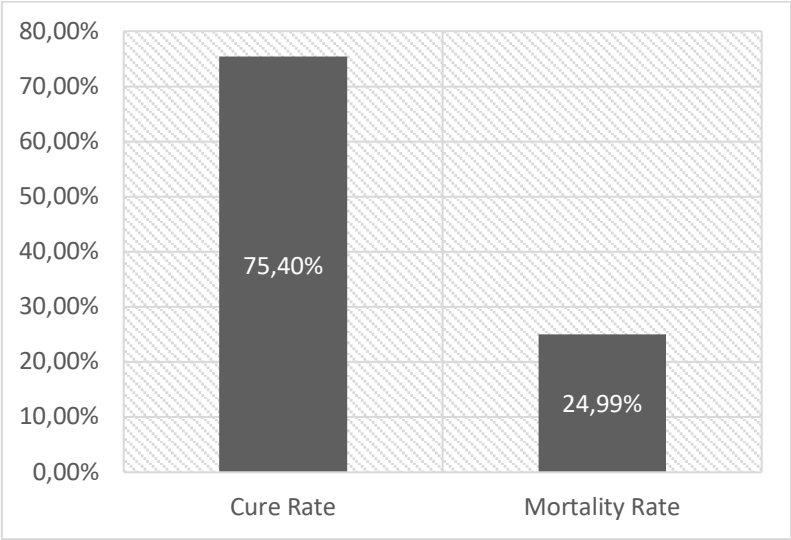

Figure 1. The average percentage of 25 journals regarding the recovery rate of COVID-19 patients with comorbid hypertension

The percentage of data on cure rate and mortality rate listed in each journal above was obtained from data processing results that took into account the number of samples and characteristics of the samples used in each study.

3.2 Factors Affecting the Recovery Rate of COVID-19 Patients with Comorbid Hypertension

Based on the analysis of 25 journals, several factors can affect the recovery rate of COVID-19 patients with comorbid hypertension, including ACE-2, ACE-I/ARBs, Age, Male and Cytokines. The percentage of how much these factors can affect the recovery rate of COVID-19 patients with comorbid hypertension is presented in Table 2 and Figure 2.

Table 2. Percentage of each journal regarding factors that affect the recovery rate of COVID-19 patients with comorbid hypertension

No	Researcher Name	ACE-2	ACE-I /ARBs	Age	Male	Cytokines
1.	Emami et al.[17]		✓	✓		
2.	Rodilla et al.[18]			✓		
3.	Huang et al.[19]		✓			✓
4.	Hasanah dan Wahyudi[20]	✓	✓			
5.	Abayomi et al.[21]			✓		
6.	Moftakhar et al.[22]	✓	✓	✓	✓	✓
7.	Zhang et al.[23]		✓	✓		
8.	Wang et al.[24]			✓		
9.	Zhong et al.[25]			✓		✓
10.	Fang et al.[26]			✓	✓	
11.	Deng et al.[27]		✓			
12.	Zhou et al.[28]	✓		✓		✓
13.	Osibogun et al.[29]			✓		
14.	Iaccarino et al.[30]			✓		
15.	Amiruddin et al.[31]			✓	✓	✓
16.	Chen et al.[32]			✓	✓	
17.	Karyono dan Wicaksana[33]	✓		✓	✓	
18.	Widjaja et al.[34]	✓				
19.	Drew and Adisasmita[35]	✓		✓	✓	
20.	Khan et al.[36]			✓	✓	
21.	Cheng et al.[37]			✓		
22.	Basu et al.[38]			✓	✓	
23.	Yao et al.[39]			✓		
24.	Gao et al.[40]		✓			
25.	Pan et al.[41]					✓
	Total	6	7	19	8	6
	Percentage	**13,04%**	**15,22%**	**41,30%**	**17,39%**	**13,04%**

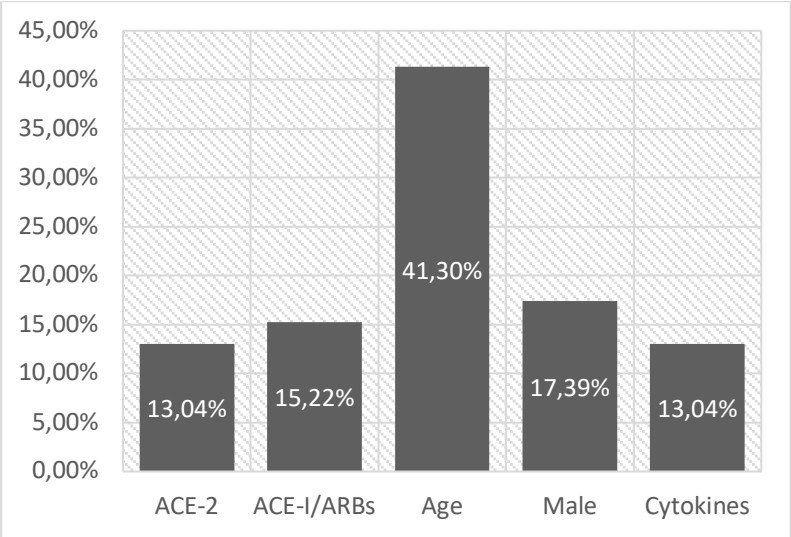

Figure 2. Average percentage of 25 journals on factors affecting the recovery rate of COVID-19 patients with comorbid hypertension

4. DISCUSSIONS

Data regarding the recovery rate of COVID-19 patients with comorbid hypertension in 25 journals used in this thesis averaged 75.40%. The factors that influence the recovery rate of COVID-19 patients with comorbid hypertension include:

1. ACE-2

Angiotensin Converting Enzyme 2 (ACE-2) is the primary receptor for SARS-COV-2.[42,43] This enzyme is widely expressed in various organs, which makes them susceptible to this virus. Other studies have shown that populations with hypertensive disease tend to have more ACE2 receptors, which may make it easier for SARS-CoV-2 to disseminate in the body or facilitate its entry into target cells and prolong viral clearance time.[44,45]

2. ACEI/ARBs

Some studies suggest that the use of ACE-I and ARBs may increase the expression of ACE-2, thereby increasing the virus binding field and making the most vulnerable. Mechanistically, however, ACE-2 also plays a role in catalyzing Angiotensin II into Angiotensin 1-7, resulting in enhanced anti-inflammatory effects. Experimental observations on this function were seen in 1128 COVID-19 hypertensive patients and revealed a significant reduction in the mortality rate of patients receiving ACEIs/ARBs.[46]

3. Age

Age is the main factor with the highest percentage that affects that influence the recovery rate of COVID-19 patients with comorbid hypertension.[47] The younger person is the higher the recovery rate compared to older age.[48] This happens because older age is associated with acute respiratory distress syndrome (ARDS) and mortality. Thus, older age associated with mortality may be due to a weakened immune response. Older age is associated with more comorbidities. Therefore, it may worsen the condition if infected with COVID-19.

4. Male

The immune system differs between men and women. Women may be less susceptible to viral infections, as they are related to the hormones estrogen and

progesterone. These hormones can help boost innate and adaptive immune responses, and many immune genes are linked to the X chromosome. High immune reactivity after a viral infection in women may speed up the viral clearance process but, on the other hand, may lead to immune pathogenicity and autoimmunity.

5. Cytokines

Cytokine imbalance may be an explanation for the correlation between hypertension and severe COVID-19. Increasing clinical data have shown a link between worsening COVID-19 and cytokine storms, such as elevated levels of IL-6, IL-7, granulocyte-macrophage colony-stimulating factor, and tumour necrosis factor. Previous clinical studies have found that increases in these cytokines are also associated with the development of hypertension. An important example is that IL-6 has been observed to be closely associated with the poor prognosis of COVID-19 patients, which is also one of the critical cytokines regulating the immune inflammatory response in hypertension.

In journal by Deng et al.[27], Amiruddin et al.[31], and Chen et al.[32] listed in Table 1, there is data on a higher percentage of mortality rates than cure rates. This result contrasts the other journals in the same table, which reported more cure rates than mortality rates. This difference is because:

1. Deng et al.[27]

In this study, patients who came to the hospital were already seriously ill. In addition, most of the patients in this study were middle-aged and elderly. The average age of patients who died was 69, which is a risk factor for death.

2. Amiruddin et al.[31]

This study used more male subjects, totaling 31 people (67.4%) and women, totaling 15 people (32.6%), where most of them 33 of them had comorbid hypertension. Based on previous research showing the role of gender on morbidity and mortality in COVID-19 patients, male patients with COVID-19 are more at risk of experiencing poor conditions and death. In addition, this study found that patients aged 60 years and over were more significant in the non-survivor group compared to the survivor group.

3. Chen et al.[32]

This study used research subjects aged ≥60 years, namely 156 people, compared to ages 40-60 years, namely 68 people and ages <40 years, namely 53 people, where from the data obtained, hypertension comorbidities are dominant among other comorbidities. In addition, there were more research subjects with male gender, namely 171 people, compared to 103 women. Based on previous research, it shows that older age and male gender are more at risk of producing more severe conditions or death.

5. CONCLUSION

It can be concluded that the recovery rate of COVID-19 patients with comorbid hypertension is 75.40%, higher than the death rate of 24.99%. Factors affecting the recovery rate of COVID-19 patients with comorbid hypertension are increased ACE-2, consumption of ACEI/ARBs antihypertensive drugs, older age, male gender and cytokine imbalance.

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Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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