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| RESEARCH ARTICLE

Management of Hypertension in Patients with Pneumonia Covid 19: A Literature Review

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| ABSTRACT

COVID-19 is an infectious respiratory disease caused by SARS-CoV-2. Originating from Wuhan, China, it spread quickly to the entire world. In just 6 months, it's reported no less than 7.700.000 confirmed cases by June 2020. The cause is severe acute respiratory syndrome coronavirus-2. Many organs are affected by Covid-19, especially the heart and lungs. Cardiovascular damage is frequently detected in patients with this condition. We can find troponin and/or creatine kinase increasing. Cytocine storm in Covid-19 can result towards multiple organ failure (MOF), which is life threatening. Cytocine storm manifested in excessive inflammation, hiperferritinemia, a marked increase in proinflammatory cytokines, hemodinamic instability, and lastly, multi organ failure, which can be fatal. From clinical symptoms, many of the patients developed pneumonia and severe acute respiratory distress syndrome, which is the main death cause of Covid-19. Hypertension and heart problems appear to be the highest comorbidity in patients diagnosed with COVID-19 pneumonia and health risk in the environment. Multisystem involvement of severe COVID-19 patients necessitates a holistic approach to managing COVID-19-associated hypertension.

| KEYWORDS

COVID-19, Hypertension, Pneumonia, Health-risk

| ARTICLE INFORMATION

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1. Introduction

In March 2020, the World Health Organization (WHO) declared the Severe Acute Respiratory Syndrome (SARS-CoV-2) outbreak, also known as Corona Virus and Disease 2019 (COVID-19), a pandemic. This disease has caused more than 180,000 deaths worldwide as of April 2020, with approximately 635 occurring in Indonesia. Currently, 29 countries have reported confirmed or suspected cases of COVID-19. According to information from February 12, 2020, the global mortality rate is 2.1% (PDPI, 2020). On July 18, 2020, according to the most recent data from WHO, 83,130 people in Indonesia were diagnosed with COVID-19, with 3,957 deaths (WHO, 2020). Numerous studies have helped clarify the clinical profile of SARS-CoV-2 infection, revealing that chronic morbidities such as hypertension, diabetes, obesity, and cardiovascular disease are major risk factors for disease severity and prognosis (Pititto et al., 2020).

Hypertension is the most prevalent comorbidity in COVID-19 pneumonia patients. According to preliminary data from China and the United States, hypertension appears to be the most prevalent comorbidity among COVID-19 pneumonia patients, accounting for approximately 30% of the population (Yang et al., 2020). In addition, according to data collected by the COVID-19 task force in October 2020, 50.5% of the total number of HIV-positive patients were found to have comorbidities, with hypertension constituting the largest percentage. More COVID-19 pneumonia patients with comorbid hypertension are hospitalized than those

without comorbid hypertension. Patients with comorbid hypertension appear to be associated with a worse prognosis and more severe symptoms of COVID-19 pneumonia (Kulkarni et al., 2020).
Initial treatment of hypertensive patients The European Society of Hypertension (ESH) recommends initiating hypertension treatment with renin-angiotensin system blocker (RAS blocker) medications. However, the community is still divided over whether administering this class of drugs can facilitate coronavirus entry into the body. This study aimed to explore the literature regarding COVID-19 pneumonia patients with comorbid hypertension, as hypertension is the leading cause of high mortality rates worldwide and the most prevalent comorbid in COVID-19 pneumonia patients.

2. Methodology

Various databases were used throughout the literature search. The studies considered for inclusion in this review were limited to those that met the primary objective of this review, which was to identify evidence of attitudes regarding the Management of Hypertension in Patients with Pneumonia Covid 19.

3. Result and Discussion

Pneumonia Covid-19 through SARS-CoV-2 are RNA viruses with a protein spike on their surface. Covid-19 virus protein spike binding to Angiotensin converting enzyme (ACE-2) facilitates virus infection of lung cells. It is fatal and rapidly spreading. SARS-CoV-2 is more resistant to stainless steel and plastic than to cardboard and copper. According to reports, the virus can survive on these surfaces for up to 72 hours. Transmission is primarily through droplets, and common symptoms include difficulty breathing, joint and muscle pain, headaches, diarrhea, nausea, and bloody coughing. However, A reverse transcriptase polymerase chain reaction (RT-PCR) test can detect the virus 1-2 days before symptoms appear. Within 5-6 days after the onset of symptoms, the viral load reaches its peak approximately 10 days later. After an average of 8–9 days, severe cases of COVID-19 progress to acute respiratory distress syndrome (ARDS). The average incubation period is approximately four to five days (Tay, 2020).

According to the Indonesian Lung Doctors Association, COVID-19 can cause a variety of clinical symptoms in infected patients. The most common symptoms of mild pneumonia include fever, cough, and shortness of breath. There were no indications of severe pneumonia. Tachypnea (breathing rate greater than thirty times per minute), severe respiratory distress, or oxygen saturation of less than ninety percent of the air around the patient are indicators of severe pneumonia in adult patients (Burhan, 2020).

The protease inhibitor lopinavir is widely used for the treatment of HIV and is a potential candidate for the treatment of COVID-19. Lopinavir is combined with another protease inhibitor, ritonavir (lopinavir/ritonavir, marketed under the brand names Kaletra and Aluvia) (Doward, 2020).

Inosine pranobex (IP), also known as isoprinosine or methisoprinol, is a synthetic compound consisting of a 3:1 molar ratio of p-acetamido benzoate salt of NN dimethylamino-2-propanol and inosine. Non-clinical and clinical studies have demonstrated that inosine pranobex can influence humoral as well as cell-mediated immunity, which is essential for preventing viral infection (Maini, 2020).

Fluoroquinolones are synthetic antimicrobial agents with a broad spectrum derived from quinolones with a fluorine atom attached to the central ring. A recent study demonstrated that fluoroquinolones can inhibit SARS CoV-2 replication. Specifically, levofloxacin is thought to scavenge neutrophil-derived hydroxyl radicals and inhibit NO production, resulting in a decrease in oxidative stress markers and NO metabolites in the lungs of H1N1 influenza virus-infected animals (Karampela, 2020).

Hypertension (21.1%), diabetes (9.7%), cardiovascular disease (8.4%), and other respiratory diseases (1.5%) were the most prevalent comorbidities of COVID-19 (Yang, 2020). According to the official CDC website, the death toll in the United States reached 161,392 by August 2020, with 35,272 patients diagnosed with comorbid hypertension.

It is still unclear whether COVID-19 pneumonia and hypertension have a direct relationship. The elderly patient population exhibited a high mortality rate associated with COVID-19 pneumonia. Patients with hypertension become susceptible to SARS-CoV-2 as a result of the association between hypertension and old age, where target organ damage frequently occurs in elderly patients, resulting in changes to the cardiovascular system (Kurkani et al., 2020).

Patients aged 76 years have a history of hypertension, but no damage to the organ of interest has been observed. This may explain why the patient's disease progression and prognosis are relatively favorable compared to those of other hypertensive patients.

The guidelines for hypertension management recommended by the Indonesian Doctors Association refer to 2 international

guidelines, namely the American College of Cardiology (ACC)/American Heart Association (AHA) 2017 and the European Society of Cardiology (ESC)/European Society of Hypertension (ESH) 2018.

According to the ESC/ESH Guidelines for the management of arterial hypertension in 2018, hypertension is defined as a systolic blood pressure of > 140 mmHg and/or a diastolic blood pressure of > 90 mmHg. The classifications for blood pressure and degrees are summarized in the following table (Williams, 2018).

Table 1 Hypertension categories

Category	Systolic (mmHg)		Diastolic (mmHg)
Optimal	<120	and	<80
Normal	120- 129	and/or	80-84
High Normal	130-139	and/or	85-89
Hypertension grade 1	140-159	and/or	90-99
Hypertension grade 2	160-179	and/or	100-109
Hypertension grade 3	180	and/or	110
Isolated systolic hypertension[b]	140	and	<90

[a]BP category is defined according to seated clinic BP and by the highest level of BP, whether systolic or diastolic.

[b]Isolated systolic hypertension is graded 1, 2, or 3 according to SBP values in the ranges indicated.

The same classification is used for all ages from 16 years.

BP = blood pressure; SBP = systolic blood pressure

Diuretics, beta blockers, calcium channel blockers (CCBs), angiotensin converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARBs) are the recommended antihypertensive drug classes. According to the patient's condition, antihypertensive drugs are selected based on the presence or absence of contraindications. In patients who have been prescribed antihypertensive medications, it is necessary to monitor the development of side effects.

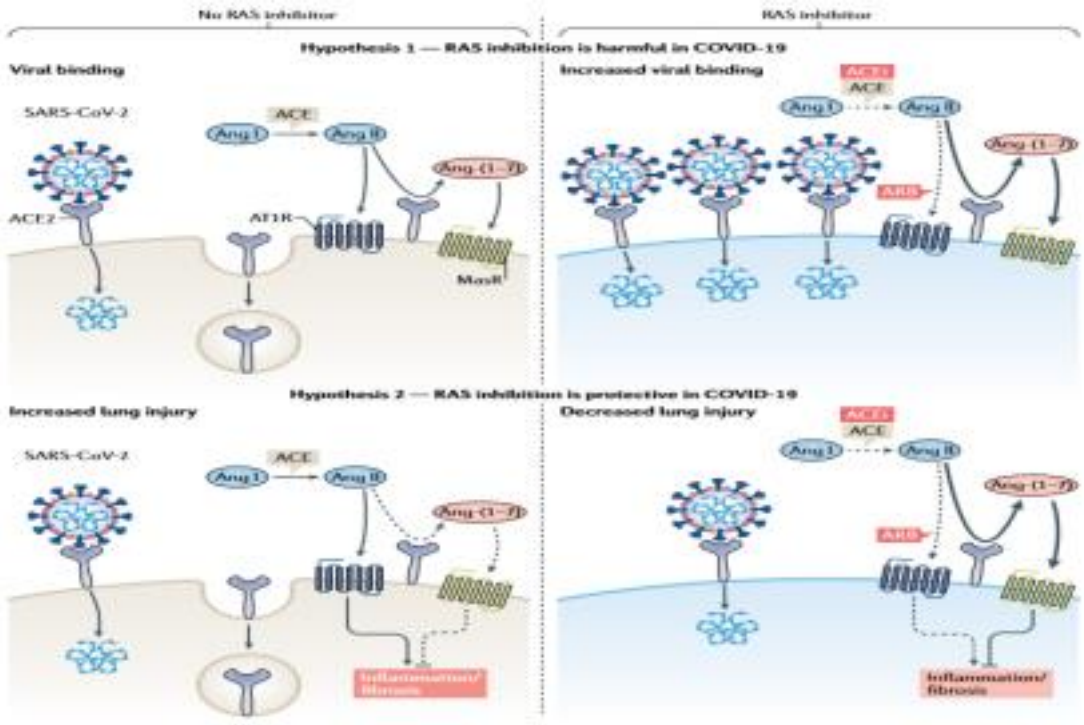

Figure 1 *RAAS mechanism of antihypertensive drugs. Sources:* South et al., 2020

ACEIs and ARBs are RAAS inhibitors and are regarded as first-line medications for the majority of hypertensive patients. However, the continued use of ACEIs/ARBs in COVID-19 patients has been controversial. In animal studies, the use of ACEIs and ARBS can increase the expression of the ACE2 receptor, which is a known cellular receptor and a necessary entry point for SARS-CoV2 infection (Zhang, 2020). In addition, the mechanism of inhibition of the renin-angiotensin system (RAS) by angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) may be detrimental or protective against COVID-19. There are two possible explanations for this. SARS-CoV-2 enters cells by binding to enzymes, as hypothesized.

Angiotensin 2 conversion enzyme (ACE2) The addition of ACEi or ARB can increase ACE2, thereby increasing the likelihood of viral entry. Angiotensin II (Ang II) is responsible for lung injury by activating the angiotensin type 1 receptor (AT1R), resulting in inflammation and fibrosis. Reducing Ang II production with ACEi or blocking the action of Ang II-AT1R with ARBs increases Ang-(1-7) formation by ACE2 and activation of Mas receptors (MasR), which attenuates inflammation and fibrosis and, consequently, attenuates inflamed lungs and injury circumstances (South, 2020). In contrast, ACE 2 expression decreases following SARS infection, resulting in RAS hyperactivation and a worsening of the progression of pneumonia. Therefore, the administration of ACEI/ARB may be advantageous by inhibiting RAS hyperactivation induced by ACE2 downregulation, thereby preventing acute lung injury and the risk of respiratory distress (Zhang, 2020).

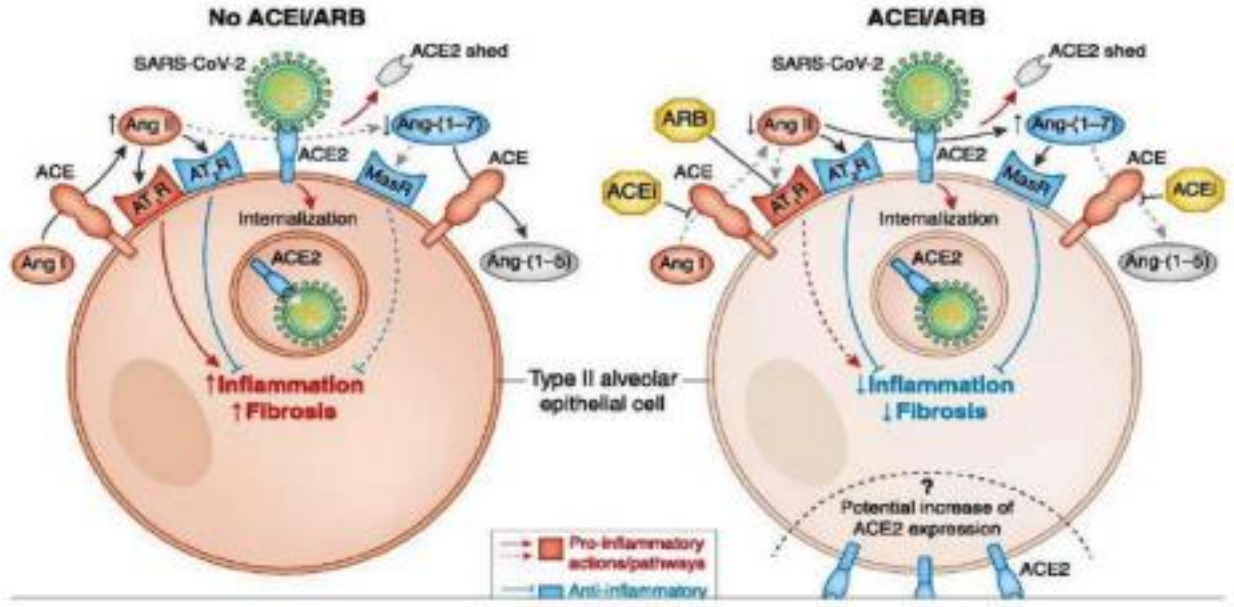

Figure 2 SARS-CoV-2 binds to ACE-2. Sources: Sparks et al., 2020

The left image explains when SARS-CoV-2 binds to ACE2 as its receptor via the spike protein (S). ACE2 will be released into the bloodstream, increasing angiotensin II levels and decreasing angiotensin (1-7). This circumstance will activate the inflammatory and fibrotic mechanisms. In contrast, the image on the right demonstrates that ACEI/ARB therapy will inhibit angiotensin II and increase angiotensin (1-7) in order to reduce the inflammatory response and angiotensin II fibrosis.

Although studies demonstrate that RAAS inhibitors can increase ACE2 expression in animals, there are insufficient data to determine whether these findings are applicable to humans, and no studies have evaluated the effects of RAAS inhibitors on COVID-19. Patients at high risk, such as those with heart failure or myocardial infarction, should discontinue RAAS inhibitors immediately. It is recommended that RAAS-inhibiting hypertension medications be continued in stable patients who are at risk, is being evaluated, or have COVID-19 until additional data becomes available (Tignanelli, 2020). According to the COVID-19 management protocol compiled by the association of pulmonary doctors, cardiovascular specialists, internal medicine specialists, anesthesiologists and intensive therapy doctors, as well as the association of Indonesian pediatricians, hypertensive patients should continue to receive ACEi and ARB class hypertension medications, a person with COVID-19 pneumonia.

Although there is still a growing controversy in the community, ACEi and ARB antihypertensive drugs can continue to be prescribed to patients in accordance with the established protocol for hypertension management.

4. Conclusion

The purpose of this study was to review the literature concerning COVID-19 pneumonia patients with comorbid hypertension. In conclusion, hypertension is the leading cause of high global mortality rates and the most prevalent comorbidity in COVID-19 pneumonia patients. Although there is still a growing controversy in the community, ACEi and ARB antihypertensive drugs can continue to be prescribed to patients in accordance with the established protocol for hypertension management. Multisystem involvement in patients with severe COVID-19 necessitates an interdisciplinary strategy for managing COVID-19-associated hypertension. This literature review is limited by its reliance on previously published research and the absence of a systematic method, such as a systematic review because there is still a lack of relevant research. Therefore, we recommend that future research employ a more effective method of systematic review to examine the relevant literature.

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