Medical Sains : Jurnal Ilmiah Kefarmasian
Vol. 9 No. 3, July - September 2024
https:/ojs.stfmuhammadiyahcirebon.ac.id/index.php/iojs

REAL WORLD DATA : ANTIVIRUS SELECTION IN COVID-19 PATIENTS AT PKU MUHAMMADIYAH GAMPING HOSPITAL

Hazena Misgi Damayanti[1*], Dyah Aryani Perwitasari[1], Irma Risdiana[2], Muhammad Husnul Kuluq[1]
[1]*Pharmacy, Faculty of Pharmacy, Ahmad Dahlan University, Indonesia*
[2] *Pharmacy Installation of PKU Muhammadiyah Gamping Hospital, Indonesia*
**Email Corresponding: hazenamisgi@gmail.com*

Submitted: December 21, 2023 ***Revised: May 28, 2024*** ***Accepted: July 14, 2024***

ABSTRACT

COVID-19 is a disease that requires antivirals, such as favipiravir and remdesivir, which have been recommended in Indonesia. Choosing the right antiviral agent can affect the length and total cost of hospitalization. The impact of COVID-19 can cause a decline in health and the economy, if not treated effectively. This study aimed to determine the average length of hospitalization and total cost of hospitalization for COVID-19 patients based on the selection of favipiravir and remdesivir antivirals at the PKU Muhammadiyah Gamping Hospital from August 2022-August to 2023 based on *real world data*. The research method was Observational research with a descriptive research design and retrospective data collection was used. During this period, 306 patients were diagnosed with COVID-19. A total of 171 patients met the inclusion criteria, including 130 patients using favipiravir antivirus and 41 patients using remdesivir antivirus. The results of this study are the average length of hospitalization of the patient group with antiviral favipiravir was 4.1 days and the patient group with antiviral remdesivir was 5 days and the average total cost of hospitalization of the patient group with antiviral favipiravir was IDR 12,377,415 and the average total cost of the patient group with antiviral remdesivir was IDR 14,428,132. The conclusion of this study is that the use of favipiravir antiviral therapy is more effective when viewed from the perspective of length of hospitalization and total cost of hospitalization; therefore, these results can be applied under the same conditions in the treatment of COVID-19.

Keywords: Antivirus, COVID-19, *Real World Data*, Length of Hospitalization, Costs

INTRODUCTION

On March 11, 2020, COVID-19 was declared a global pandemic by the *World Health Organization* (WHO). *Severe Acute Respiratory Syndrome Coronavirus-2* (SARS-CoV-2) causes this disease. The virus first appeared in Wuhan City, Hubei Province, China in December 2019 (Hu *et al*., 2021). COVID-19 is a respiratory disease that can cause shortness of breath, coughing, muscle aches, fatigue, and fever and can sometimes lead to pneumonia (Rothan & Byrareddy, 2020). On March 15, 2020, a COVID-19 case was confirmed in Yogyakarta, and on March 20, 2020, the governor of Yogyakarta declared a public health emergency. COVID-19 cases continue to increase in unstable situations, as is the case throughout Indonesia. Yogyakarta reported since the first pandemic occurred in Yogyakarta until February 28, 2023 there were 230,389 confirmed cases, 6,082 deaths and 224,248 recoveries Sleman became the first region in Yogyakarta to be confirmed positive for COVID-19 after the first two national cases, while the lowest case was in Kulonprogo Regency, where Kulonprogo was the last affected area in DIY. The first case of Kulonprogo was confirmed on March 26, 2020 (Arif *et al*. 2021). COVID-19 can spread through tiny droplets that come out of the mouth or nose when sneezing or coughing, which then fall onto surrounding objects. If we hold objects contaminated with droplets and then touch areas of

the body, such as the mouth, eyes, or nose, we can be infected with COVID-19 (Kemenkes RI, 2020). The first case of COVID-19 was reported on March 2, 2020, and the number continued to increase until August 31, 2023, when the Ministry of Health reported 6,812,127 confirmed cases of COVID-19, with 161,879 deaths, 6,642,003 recoveries, and 8,245 patients still being treated.

Viral infections cause COVID-19. Therefore, an appropriate antiviral treatment strategy is essential to reduce losses (Simsek Yavuz & Unal, 2020). The 4th edition of the COVID-19 management guidelines approved by the BPOM and Emergency Use Authorization (EUA) in January 2022 states that remdesivir and favipiravir antivirals can be used based on severity, and oseltamivir should only be administered to COVID-19 patients suspected to be infected with influenza viruses (BPOM, 2022). Mortality and length of hospitalization can indicate the effectiveness of the antiviral treatment. Gender, severity, comorbidities, age, and viral load are factors that can affect the outcome of therapy (Rico-Caballero *et al*., 2022).

According to the Indonesian Society of Internal Medicine Specialists, antivirals used in Indonesia for COVID-19 patients are based on symptom severity (Burhan *et al*., 2020). Antivirals that have been used for COVID-19 patients in several countries are lopinavir/ritonavir, remdesivir, oseltamivir, chloroquine, hydroxychloroquine and favipiravir (Zhong *et al*., 2020). COVID-19 emergency treatment in Indonesia consists of two antiviral drugs, favipiravir and remdesivir. Favipiravir has been used as an experimental treatment in China and other countries, and has shown good results in reducing the number of COVID-19 infections. The Food and Drug Administration (FDA) has granted approval for remdesivir antivirals to be used as an antiviral treatment for COVID-19 in pediatric and adult patients undergoing hospitalization (Y Furuta T komeno, 2017). The choice of antivirals may affect the length of hospital stay and total hospital costs. In hospitals, the length of hospital stay is a standard that indicates how long a patient has been admitted. Patients who have been admitted receive treatment according to their respective diagnoses (Nasarah *et al*., 2022). Hospitalization days that are extremely long can cause losses, such as reducing the coverage of hospital health services, increasing patient care costs, increasing Bed Occupancy Rate (BOR), and extravagance for hospitals due to higher operational costs (Soejono & Fitriana, 2018).

Real world data include raw data collected from electronic health records, claims databases, and patient-generated data. These data may include patient demographic information, diagnosis, treatment, laboratory results, and a final patient summary at discharge (Zou *et al*., 2020). Analysis of real-world data generates real-world evidence, which is clinical evidence that provides information about the use and potential benefits or risks of a drug. COVID-19 treatment decisions must consider the safety, efficacy, quality, and economic value. The selection of effective drugs, which means that the cost of treatment is affordable for the community and has good clinical results, is an important economic factor (Rosyidah *et al*., 2022). A cost-effectiveness analysis is needed to correlate the costs required with the results produced must be done before choosing which treatment strategy has the best treatment results. Based on research at Haji Surabaya Hospital from April 2021-October to 2021, the use of favipiravir antiviral therapy can reduce the total cost of care and length of hospitalization compared to remdesivir antiviral therapy. This result also applies to Dr. Doris Sylvanus Hospital, which shows that the use of favipiravir antivirals can shorten the length of hospitalization compared to the use of remdesivir antivirals. The purpose of this study was to determine the average length of hospitalization and average total cost of hospitalization for COVID-19 patients based on favipiravir and remdesivir antivirals at PKU Muhammadiyah Gamping Hospital between August 2022-August 2023.

RESEARCH METHODS

This was an observational study with a descriptive research design and retrospective data collection using electronic medical record data of COVID-19 patients at PKU Muhammadiyah Gamping Hospital. The electronic medical records included medication

administration records, Integrated Patient Progress Notes (CPPT), diagnostic support results, and discharge summaries. Electronic medical record data for COVID-19 patients were taken from August 2022-August to 2023. Secondary data in the form of electronic medical records that met the inclusion criteria were used.

Inclusion Criteria
1. Patients ≥ 18 years old with a positive diagnosis of COVID-19
2. Patients receive single antiviral therapy

Exclusion Criteria
1. Patient passed away while undergoing treatment
2. Patients who have incomplete medical records
3. Patient is referred to another health facility
4. Patient discharged at own request

Equipment and Materials
Electronic medical record data were used in this study. The materials for this research were medication administration records, Integrated Patient Progress Notes (CPPT), diagnostic support results, and discharge summaries.

Research Procedure
1. Preparation Stage
In this preparatory stage, a proposal was prepared, and ethical committee approval (ethical clearance) was obtained from the ethics committee of Ahmad Dahlan University the number 012309226 and a research permit at PKU Muhammadiyah Gamping Hospital.
2. Implementation Stage
Data collection was carried out at the PKU Muhammadiyah Gamping Hospital on all patients diagnosed with COVID-19 between August 2022-August 2023 and included in the inclusion criteria. Electronic Medical Record data were obtained in the form of patient medical record (RM) numbers, patient names, drug administration records, Integrated Patient Progress Notes (CPPT), diagnostic support results, and discharge summaries.
3. Final Stage of Research
Data processing was carried out in Microsoft Excel in the form of percentages, followed by the preparation of a research publication document.

Data Analysis

No	Parameter	Analysis	Variables	Measurement Types
1	Patient Demographic Data	The researcher counted the total of patients with their respective percentages categories of antiviral use. Percentage = number of each category / total number of patients whose data were used in the study X 100%	1. Gender 2. Age 3. Domicile Origin 4. Education Level 5. Marriage Status	Descriptive Analysis
2	Number of Comorbidities	The researcher calculated the total number of patients who had comorbid	1. Total comorbidities	Descriptive analysis

		diseases with the percentage for each category of antiviral use. Percentage = number of patients with each number of comorbidities / total number of patients used each antiviral in the study X 100%			
3	Degree of severity	The researcher calculated the total number of patients who had different degrees of severity with the percentage of each category of antiviral use. Percentage = number of patients with severity level / total number of patients used each antiviral in the study X 100%	1.	Degree of severity	Descriptive Analysis
4	Length of hospitalization	The researcher calculated the average length of stay for patients with each category of antiviral use. Average length of stay = total length of stay/total number of patients used each antiviral in the study	1.	Length of Hospitalization	Descriptive Analysis
5	Total hospitalization cost	The researcher calculated the average total hospitalization cost for patients with each category of antiviral use. Average total hospitalization cost = total hospitalization cost/total number of patients used each antiviral in the study	1.	Total hospitalization cost	Descriptive Analysis

The analysis was carried out descriptively, including data on patient characteristics obtained from medical records (gender, age, education level, domicile, marital status, and comorbidities). Other data included the type of antiviral used, length of hospitalization, and total cost. The collected data were then analyzed descriptively and presented as percentages (%).

RESULTS AND DISCUSSION

There were 306 patients were diagnosed with COVID-19 in the period August 2022-August 2023 at PKU Muhammadiyah Gamping Hospital, and 171 patients met the inclusion criteria. The characteristics of the study subjects can be categorized based on gender, age, domicile origin, marital status, education level, and comorbidities. The description of the characteristics of the research subjects can be seen in **Table I**.

Table I. Characteristics of Research Subjects

Patient Characteristics	Favipiravir (n=130)		Remdesivir (n=41)	
	Total	Percentage (%)	Total	Percentage (%)
Gender				
Male	61	46,9	25	61,0
Female	69	53,1	16	39,0
Age				
18-27 Years	26	20,0	3	7,3
28-37 Years	14	10,8	2	4,9
38-47 Years	10	7,7	2	4,9
48-57 Years	15	11,5	3	7,3
58-67 Years	25	19,2	12	29,3
68-77 Years	27	20,8	12	29,3
78-87 Years	12	9,2	6	14,6
88-97 Years	1	0,8	1	2,4
Domicile Origin				
Sleman District	55	42,3	23	56,1
Not Sleman District	75	57,7	18	43,9
Education Level				
≤ SMA	107	82,3	37	90,2
>SMA	23	17,7	4	9,8
Marriage Status				
Marry	93	71,5	35	85,4
Unmarried	26	20,2	2	4,9
Widow	10	7,7	3	77,3
Widower	1	0,8	1	2,4

Demographic data of confirmed and treated COVID-19 patients ernawaat PKU Muhammadiyah Gamping Hospital included 86 male patients, with a percentage of 50.3%, and 85 female patients, with a percentage of 49.7%. According to data collected from 137 countries on January 18, 2021, 49.1% of COVID-19 patients were female and 50.9% were male (Athena Nguyen *et al.*, 2020). However, habits practiced by men, such as smoking, can worsen lung conditions and overall health (Vardavas & Nikitara, 2020). Angiotensin I converting enzyme 2 (ACE2) and interleukin 6 (IL-6) levels are higher in men, resulting in stronger inflammatory responses (Jun Mi *et al.*, 2020). The immune systems of women are stronger than those of men. Immunoglobulin B cell production, CD8+T cell cytotoxic activity, and CD4+T cell counts are all higher in females than in males (Peckham *et al.*, 2020). While the hormone estrogen enhances immune responses in women, there is evidence that testosterone decreases them (Pradhan & Olsson, 2020).

This is in line with research by Ernawati (2021) in Pati Regency in 2020, which found that 53% of men were confirmed positive for COVID-19 and 47% of women; the same results were also in accordance with the research of Agus Styawan (2020), which showed that men in Indonesia were more likely to be exposed to COVID-19 than women, with 51.5% of men and 47% of women confirmed positive. This is due to the fact that women are more compliant with health protocols than men (Riyadi & Larasaty, 2020). The

risk of contracting COVID-19 in men is higher than that in women owing to the mobility of men (Warsida *et al*., 2013). The difference in the X chromosome in women, which is more dominant than in men, can affect the immune system (Seftiya & Kosala, 2021). According to epidemiological data from various countries, the risk of exposure to COVID-19 is higher in men than that in women. However, other studies have shown otherwise.

Another demographic data point is age. In this study, the most confirmed age of COVID-19 was 68-77 years old, with 39 patients, or 22.8% of the total patients. Adults have a stronger adaptive immune system; therefore, the virus attacks longer because of higher levels of neutralizing antibodies. At the start of the pandemic, the WHO stated that the elderly are more vulnerable to COVID-19 because the immune system can weaken with age. However, all people are susceptible to COVID-19 infection (Pierce *et al*., 2020). Elderly people and those with other diseases may have a higher risk of contracting COVID-19. A decreased immune system in the elderly and people with other diseases is a triggering factor. This can worsen the patient's condition and lead to death. Conflicting theories on COVID-19 have emerged from ongoing research. Currently, the global standard for COVID-19 epidemiological data is gender and age, which are used as prognostic factors for patients (Kemenkes RI, 2020).

78 patients treated at the PKU Muhammadiyah Gamping Hospital were residents of Sleman Regency, while the remaining 93 patients came from outside Sleman Regency. This shows that the spread rate of COVID-19 outside the Sleman Regency is higher than that inside it. Population density is an environmental factor affecting the spread of infectious diseases. This was related to the spread of the disease. Diseases transmitted through small droplets in air spread quickly in areas with high population densities (Mardiana, 2018). In addition, the frequency of interactions between people in an area increases because of the high population density (Edriani *et al*., 2021). The number of cases that have been confirmed positive for COVID-19 continues to increase, encouraging the community to raise awareness about how to prevent the transmission of the virus. Public awareness will reduce the transmission of COVID-19; therefore, there are no new cases. People can prevent COVID-19 independently in their homes and with their own awareness. Increased education and social media in the community can increase efforts to prevent the virus (Gannika & Sembiring, 2020). The majority of patients in this study had an education level ≤ high school as much as 84.2%. The level of education shows how high a person's health knowledge and understanding of the disease are. A higher level of education can increase knowledge and disease prevention behaviors (Gannika & Sembiring, 2020).

Regarding the marital status of COVID-19 patients in this study, 74.9% of patients were married and 16.4% were unmarried, which requires compliance in carrying out care and treatment. One way to obtain a sense of physical and psychological comfort during times of stress is to obtain support from the family and environment. Fithri *et al*. (2022) showed that the chances of married respondents being compliant in undergoing treatment were 1.1 times. This could be caused by concerns that the disease can spread to their partners and families, which encourages them to protect themselves and their partners so that they can recover faster.

The number of COVID-19 comorbidities in August 2022-August 2023 period in **Table II**.

Table II. Number of Comorbidities in COVID-19 Patients

Number of comorbidities	Favipiravir		Remdesivir	
	Total	Percentage	Total	Percentage
0 Comorbid	60	46,2%	9	22%
1 Comorbid	38	29,2%	11	26,8%
2 Comorbidities	25	19,2%	15	36,6%
3 Comorbidities	5	3,8%	5	12,2%
4 Comorbidities	2	1,5%	1	2,4%

According to patient clinical characteristics data, individuals with more comorbidities have a higher risk of exposure to COVID-19 than those with fewer or no comorbidities (Rahmandani *et al*., 2021). Patients who were confirmed positive for COVID-19 at PKU Muhammadiyah Gamping Hospital had 0 comorbid in 69 patients, 1 comorbid in 49 patients, 2 comorbid in 40 patients, 3 comorbid in 10 patients and 4 comorbid in 3 patients.

The types of COVID-19 comorbidities in the August 2022-August 2023 period are shown in **Table III**.

Table III. Types of Comorbidities in COVID-19 Patients

Comorbidity Type	Total	Percentage
Hypertension	63	36,8%
Diabetes Mellitus	25	14,6%
Cardiovascular Disease	25	14,6%
Respiratory Disease	9	5,2%
Kidney Disease	8	4,6%
Nerve Disorders	4	2,3%

Patients treated at PKU Muhammadiyah Gamping Hospital had as many as 63 patients with hypertension. The treatment of patients with comorbidities with proper medical care is very important to improve survival because SARS CoV-2 infection becomes more detrimental when infected with other people (Ejaz *et al*., 2020). COVID-19 positive patients have more severe hypertension than patients without comorbidities because of the binding of the SARS-CoV-2 virus with the ACE2 receptor, which can reduce anti-inflammatory function and increase the amount of Angiotensin II, thereby increasing blood pressure. As a result, COVID-19 positive patients have a higher risk of death than patients without comorbidities (Ejaz *et al*., 2020). A common treatment for patients with hypertension is the use of ACE-2 inhibitors and angiotensin receptor blockers (ARBs). Higher use of these inhibitors may upregulate the expression of ACE-2 receptors, which may increase the susceptibility to SARS-CoV-2 infection (Fang *et al*., 2020). A total of 25 patients had diabetes mellitus as a comorbidity, which could be due to the increased number of ACE2 receptors and impaired ability of phagocytic cells; patients with diabetes are more susceptible to infection. Impaired T-cell function and elevated levels of ACE-2 and interleukin-6 (IL-6) are targets of attack (Ejaz *et al*., 2020). Therefore, higher lung inflammation and lower insulin levels may be due to a dysregulated immune response to increased ACE-2 receptor and furin expression. The virus threatens individuals with diabetes mellitus. In addition, the main factors responsible for COVID-19 in diabetic patients include impaired T cell function and increased levels of interleukin-6 (IL-6) cells (Kulcsar *et al*., 2019).

The presence of ACE-2 receptors in heart muscle cells increases the risk of COVID-19 in patients who already have cardiovascular disease. Patients with cardiovascular disease are at a higher risk of developing acute coronary syndrome due to acute infections. This can lead to a decreased immune response. This syndrome increases with myocardial demand, which ultimately leads to myocardial injury or infarction, as well as an increase in COVID-19 cases mediating atherosclerosis, procoagulant activation, and hemodynamic instability leading to ischemia and thrombosis. COVID-19 patients often have cardiovascular comorbidities, which require immediate treatment to reduce mortality and morbidity (Yang *et al*., 2020). ACE 2 and ARB-containing therapies for cardiovascular diseases may protect the lungs. In contrast, the ACE 2 protein allows SARS-CoV-2 to enter the body (Ernawati, 2021).

SARS-CoV-2 can infect the lungs and other respiratory systems. Therefore, individuals with congenital diseases such as chronic respiratory disorders are more susceptible to COVID-19 and are more likely to experience more severe symptoms. Asthma,

pulmonary fibrosis and chronic obstructive pulmonary disease (COPD) are some of the congenital respiratory disorders to watch out for. COPD treatment using ACEs and ARBs facilitates the entry of SARS-CoV-2 into the body, making it a risk factor for COVID-19. Individuals with asthma have a delayed innate antiviral immune response and problems with IFN- secretion, which increases the risk of more severe disease. Asthma can be associated with SARS (1.4%) and MERS (13%), causing the symptoms to worsen, similar to other chronic lung diseases. History suggests that asthma may be a risk factor for COVID-19 infection. However, there is no evidence of SARS-CoV-2 infection in asthmatic patients (Ejaz *et al*., 2020). Chronic kidney disease (CKD) is a congenital disease that can worsen COVID-19 symptoms. The immune system can also be compromised by dialysis. As a result, if a patient is infected with COVID-19, the patient's body will face the infection more difficult. The aim is to increase the secretion of enzymes, including angiotensin-converting enzyme (ACE-2) and dipeptidyl peptidase-4 (Ejaz *et al*., 2020).

Cardiovascular disease, chronic obstructive pulmonary disease, hypertension, diabetes mellitus, chronic liver disease, and cancer are comorbidities that increase the risk of exposure to COVID-19. Individuals with diabetes mellitus as a comorbid disease are more susceptible to COVID-19. Other comorbidities include chronic liver disease and cancer. Patients with chronic liver disease and cancer are more susceptible to COVID-19 transmission. This is related to chemotherapy and surgery, which cause immunosuppressive reactions and increase cytokine levels. As a result, the immunity of patients with chronic liver disease decreases, making them more vulnerable to COVID-19 (Ernawati, 2021). n addition, WHO states that asthma, diabetes mellitus, and heart disease make a person more vulnerable to the effects of COVID-19. Patients with cardiovascular disease, heart failure, valvular heart disease, hypertension, peripheral vascular disease, and congenital heart disease experience more severe heart conditions as a result of COVID-19 transmission (Fuadi & Irdalisa, 2020).

The severity of COVID-19 in the August 2022-August 2023 period is shown in Table IV.

Table IV. Degree of Severity of COVID-19 Patients

Degree of Severity	Antivirus Favipiravir		Antivirus Remdesivir		Total	
	Total	Percentage	Total	Percentage	Total	Percentage
Mild	0	0%	1	0,6%	1	0,6%
Moderate	128	74,8%	34	19,9%	162	94,7%
Severe	2	1,2%	6	3,5%	8	4,7%

COVID-19 is classified into asymptomatic, mild, moderate, severe, and critical depending on the severity of the symptoms. A total of 128 patients using favipiravir antiviral therapy and 34 patients using remdesivir at the PKU Muhammadiyah Gamping Hospital had moderate severity. The 4th edition of the COVID-19 management guidelines approved by the BPOM and the Emergency Use Authorazation (EUA) in January 2022 states that remdesivir and favipiravir antivirals can be used based on moderate to severe severity, and oseltamivir should only be administered to COVID-19 patients suspected to be infected with influenza viruses (BPOM, 2022).

The average length of hospitalization in the favipiravir antiviral therapy group was 4.123 ± 2.217 days, whereas that the in remdesivir antiviral therapy group was 5 ± 2.179 days. There were 130 (76%) patients who received favipiravir antiviral therapy and 41 (24%) patients who received remdesivir antiviral therapy. These results contradict research conducted by Hamdi M.Nur *et al*., (2022) showed that the length of hospitalization of patients receiving remdesivir antivirals was 1 day shorter than that of patients receiving favipiravir antivirals, but this was not statistically significant. The study Hamdi M.Nur *et al.* (2022) was conducted using analytical observational methods and a retrospective research design. These results are comparable to those of Riptasari *et al.* (2022), with clinical

evidence parameters Number Needed to Treat (NNT) in 140 research subjects according to inclusion at RSUD dr. Doris Sylvanus and 70 subjects each using favipiravir and remdesivir with results showing that the length of hospitalization for favipiravir antivirals is shorter than remdesivir antivirals, with the results of hospitalization for favipiravir antivirals averaging 8.8 days, while the results of hospitalization for remdesivir antivirals averaged 9.3 days. This result is also comparable to that of Halimbar (2023), which showed that the length of hospitalization using antiviral favipiravir was shorter, with an average result of 11.22 days when compared to the use of antiviral remdesivir with an average result of 13.13 days. Many studies have been conducted using a wide range of drugs from several categories, but none have provided consistent and effective results. Antivirals, such as favipiravir, are still being studied to find effective antiviral therapies. In addition, other antiviral drugs such as remdesivir, ribavirin, oseltamivir, and lopinavir have also been used in many countries (Liu *et al*., 2020).

Favipiravir and remdesivir are antimetabolite broad-spectrum RNA polymerase inhibitors that are structurally related to the naturally occurring RNA structural elements. Both drugs are prodrugs that must be activated intracellularly to exert effects through a variety of different mechanisms of action. Clinical trials have shown an association between remdesivir and an increased frequency of adverse events compared to favipiravir. Nevertheless, the data obtained with remdesivir resulted in FDA approval on October 22, 2020 for the treatment of COVID-19. Currently, remdesivir is recommended by several treatment guidelines for COVID-19 patients. Antiviral favipiravir is beneficial when administered to COVID-19 cases with mild and moderate symptoms, whereas remdesivir is more beneficial in cases with severe symptoms (Al-Ardhi *et al*., 2022). According to research conducted by Ara Perveen *et al*. (2021), antiviral and favipiravir antiviral therapy has proven effective for treating COVID-19 patients. Antivirals showed clinical improvement in severe and critical patients when compared to the control group or standard care (Al-Abdouh *et al*., 2020).

The results of the favipiravir antiviral therapy group had an average total hospitalization cost of Rp 12,377,415 ± 12,391,264 while the use of remdesivir antiviral had an average total hospitalization cost of Rp 14,428,132 ± 7,310,691. This total cost includes direct costs in the form of medical costs, which include healthcare costs, use of hospital facilities, laboratory costs, doctor consultation fees, drug costs, nurse service costs, and non-medical costs, which include ambulance fees. The results above show that the group using favipiravir antiviral had a lower average total cost of hospitalization than the group using remdesivir antiviral. This result contradicts the study of Danty (2023), which concluded that remdesivir antiviral therapy is the most cost-effective drug for the treatment of COVID-19 patients when compared to using favipiravir antivirals; however, the average length of hospitalization was the same as the research method in the form of descriptive analytics using retrospective data, with data for the period 2020-2022 at Madiun City Hospital. These results are comparable to those of Halimbar (2023), which showed that the average total cost of treatment using favipiravir antivirals was lower than that of the remdesivir antiviral group, and there was a significant difference in the total direct medical costs between the favipiravir antiviral group and the remdesivir antiviral group. The limitations of this study are that inferential statistical analysis was not performed because the study subjects were determined by the time period, namely August 2022-August 2023, and there was no analysis of the relationship between patient characteristics, length of hospitalization, and total treatment costs.

CONCLUSIONS

The conclusion of this study was that the average length of hospitalization for the group of patients given favipiravir antiviral was 4.1 days with an average total cost of hospitalization of Rp 12,377,415 and the average length of hospitalization for the group of patients given remdesivir antiviral was 5 days with an average total cost of hospitalization of Rp 14,428,132. In this study, the use of favipiravir antiviral therapy was more effective when viewed from the perspective of length of hospitalization and total cost of hospitalization.

REFERENCES

Agus Styawan, D. (2020). Pandemi COVID-19 dalam Perspektif Demografi. *Seminar Nasional Official Statistics*, *2020*(September), 182–189.

Al-Abdouh, A., Bizanti, A., Barbarawi, M., Jabri, A., & Kumar, A. (2020). *Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information . January*.

Al-Ardhi, F. M., Novotny, L., Alhunayan, A., & Al-Tannak, N. F. (2022). Comparison of remdesivir and favipiravir - the anti-Covid-19 agents mimicking purine RNA constituents. *Biomedical Papers*, *166*(1), 12–20. https://doi.org/10.5507/bp.2021.063

Ara Perveen, R., Nasir, M., Murshed M, M., Naznin, R., & Ahmed, S. N. (2021). Remdesivir and Favipiravir Changes Hepato-Renal Profile in COVID-19 patients: A Cross Sectional Observation in Bangladesh. *International Journal of Medical Science and Clinical Invention*, *8*(01), 5196–5201. https://doi.org/10.18535/ijmsci/v8i01.03

Arif, N., Respati, D., Sumunar, S., Khotimah, N., Cahyani, E., Susena, Y., Ariyanto, R. A., & Yogyakarta, U. N. (2021). Comparative Study of COVID-19 Spatial Distribution in Yogyakarta and Gorontalo. *Geomedia*, *19*(1), 46–53. https://journal.uny.ac.id/index.php/geomedia/article/view/40166/15722

Athena Nguyen, Jordan Hoffmann, Laura Baines, Ratha Ra, R. E. (2020). *Rapid Gender Analysis during COVID-19 Pandemic*. *September*, 1–49.

BPBD DIY. (2019). *Bpbd Diy*. http://bpbd.jogjaprov.go.id/pusdalops-pb

BPOM-Badan Pengawas Obat dan Makanan. (2022). *Informatorium Obat Covid-19 Di Indonesia Edisi 4 Badan Pengawas Obat Dan Makanan Republik Indonesia*.

Burhan, E., Susanto, A. D., Nasution, S. A., Ginanjar, E., Pitoyo, W., Susilo, A., & Dkk. (2020). Pedoman Tatalaksana COVID-19 edisi 3. In *Pdpi, Perki,Papfi,Perdatin,Idai*. https://www.papdi.or.id/download/983-pedoman-tatalaksana-covid-19-edisi-3-desember-2020

Danty, M. S., & Madiun, U. P. (2023). *Analisis efektivitas biaya penggunaan obat Favipiravir pada pasien COVID-19 di RSUD Kota Madiun*. 101–106.

Edriani, T. S., Rahmadani, A., & Noor, D. M. M. (2021). Analisis Hubungan Kepadatan Penduduk dengan Pola Penyebaran COVID-19 Provinsi DKI Jakarta menggunakan Regresi Robust. *Indonesian Journal of Applied Mathematics*, *1*(2), 51. https://doi.org/10.35472/indojam.v1i2.353

Ejaz, H., Alsrhani, A., Zafar, A., Javed, H., Junaid, K., Abdalla, A. E., Abosalif, K. O. A., Ahmed, Z., & Younas, S. (2020). COVID-19 and comorbidities: Deleterious impact on infected patients. *Journal of Infection and Public Health*, *13*(12), 1833–1839. https://doi.org/10.1016/j.jiph.2020.07.014

Ernawati, A. (2021). Tinjauan Kasus COVID-19 Berdasarkan Jenis Kelamin, Golongan Usia, dan Kepadatan Penduduk di Kabupaten Pati. *Jurnal Litbang: Media Informasi Penelitian, Pengembangan Dan IPTEK*, *17*(2), 131–146. https://doi.org/10.33658/jl.v17i2.280

Fang, L., Karakiulakis, G., & Roth, M. (2020). Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *The Lancet Respiratory Medicine*, *8*(4), e21. https://doi.org/10.1016/S2213-2600(20)30116-8

Fithri, N. K., Amalia, R., & Anggraeni, D. T. (2022). Determinan Kepatuhan Masyarakat Urban pada Protokol Kesehatan dalam Mencegah Penyebaran Covid-19 di Era Kebiasaan Baru. *JKMI: Jurnal Kesehatan Masyarakat Indonesia*, *17*(2), 24–32.

Fuadi, T. M., & Irdalisa. (2020). Covid 19: Antara Angka Kematian dan Angka Kelahiran. *Jurnal Sosiologi Agama Indonesia (JSAI)*, *1*(3), 199–211. https://doi.org/10.22373/jsai.v1i3.767

Gannika, L., & Sembiring, E. E. (2020). Tingkat Pengetahuan dan Perilaku Pencegahan Coronavirus Disease 2019 (COVID-19) pada Masyarakat Sulawesi Utara. *NERS: Jurnal Keperawatan*, *16*(2), 83–89.

http://ners.fkep.unand.ac.id/index.php/ners/article/view/377

Halimbar, A. N. . L. A. . & R. D. (2023). Cost-Effectiveness Analysis of Remdesivir and Favipiravir Therapy for the Treatment of Covid-19 in Adult Patients At the Hajj Regional General Hospital, East Java Province. *Jurnal Scientia*, *12*(01), 348–354.

Hamdi M.Nur, A., Muflihah, H., & Ary Lantika, U. (2022). Hubungan antara Pemberian Remdesivir dan Durasi Rawat Inap Dibandingkan Favipiravir pada Pasien Covid-19. *Bandung Conference Series: Medical Science*, *2*(1), 319–325. https://doi.org/10.29313/bcsms.v2i1.755

Hu, B., Guo, H., Zhou, P., & Shi, Z. L. (2021). Characteristics of SARS-CoV-2 and COVID-19. *Nature Reviews Microbiology*, *19*(3), 141–154. https://doi.org/10.1038/s41579-020-00459-7

Jun Mi, Weimin Zhong, Chaoqun Huang, Li Tan, & Lili ding. (2020). Gender, Age and Comorbidities as the main factors in patient with COVID-19 pneumonia. *Am J Transl Res*, *12*(10), 6537–6548.

Kemenkes RI. (2020). Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MenKes/413/2020 Tentang Pedoman Pencegahan dan Pengendalian Corona Virus Disease 2019 (Covid-19). *MenKes/413/2020*, *2019*, 1–207. https://covid19.go.id/p/regulasi/keputusan-menteri-kesehatan-republik-indonesia-nomor-hk0107menkes4132020

Kemenkes RI. (2020). Keputusan Menteri Kesehatan Republik Indonesia Nomor HK.01.07/MenKes/413/2020 Tentang Pedoman Pencegahan dan Pengendalian Corona Virus Disease 2019 (Covid-19). *MenKes/413/2020*, *2019*, 207.

Kulcsar, K. A., Coleman, C. M., Beck, S. E., & Frieman, M. B. (2019). Comorbid diabetes results in immune dysregulation and enhanced disease severity following MERS-CoV infection. *JCI Insight*, *4*(20), 1–18. https://doi.org/10.1172/jci.insight.131774

Liu, K., Chen, Y., Lin, R., & Han, K. (2020). Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information. *Journal of Infection*, *80*(6), 14–18. https://www.journalofinfection.com/article/S0163-4453(20)30116-X/fulltext

Mardiana, D. E. (2018). The Influence of Immunization and Population Density to Diphtheria's Prevalence in East Java. *Jurnal Berkala Epidemiologi*, *6*(2), 122. https://doi.org/10.20473/jbe.v6i22018.122-129

Nasarah, M., Utami R, H., Sumiyati, Y., & Subhan, A. (2022). Pengaruh Favipiravir dan Remdesivir Pada Pasien Covid-19 dengan Komorbid Penyakit Kardiovaskular & Hipertensi Terhadap Luaran Klinis Di RSUP Fatmawati Jakarta. *Poltekita : Jurnal Ilmu Kesehatan*, *16*(3), 296–308. https://doi.org/10.33860/jik.v16i3.1613

Peckham, H., de Gruijter, N. M., Raine, C., Radziszewska, A., Ciurtin, C., Wedderburn, L. R., Rosser, E. C., Webb, K., & Deakin, C. T. (2020). Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. *Nature Communications*, *11*(1), 1–10. https://doi.org/10.1038/s41467-020-19741-6

Pierce, C. A., Preston-Hurlburt, P., Dai, Y., Aschner, C. B., Cheshenko, N., Galen, B., Garforth, S. J., Herrera, N. G., Jangra, R. K., Morano, N. C., Orner, E., Sy, S., Chandran, K., Dziura, J., Almo, S. C., Ring, A., Keller, M. J., Herold, K. C., & Herold, B. C. (2020). Immune responses to SARS-CoV-2 infection in hospitalized pediatric and adult patients. *Science Translational Medicine*, *12*(564), 1–17. https://doi.org/10.1126/scitranslmed.abe8120

Pradhan, A., & Olsson, P. E. (2020). Sex differences in severity and mortality from COVID-19: are males more vulnerable? *Biology of Sex Differences*, *11*(1), 1–11. https://doi.org/10.1186/s13293-020-00330-7

Rahmandani, A., Sarnianto, P., Anggriani, Y., & Dermawan Purba, F. (2021). Analisis Efektivitas Biaya Penggunaan Obat Antivirus Oseltamivir dan Favipiravir pada Pasien Covid-19 Derajat Sedang di Rumah Sakit Sentra Medika Cisalak Depok. *Majalah Farmasetika*, *6*(Suppl 1), 133. https://doi.org/10.24198/mfarmasetika.v6i0.36667

Rico-Caballero, V., Fernández, M., Hurtado, J. C., Marcos, M. A., Cardozo, C., Albiach, L., Agüero, D., Ambrosioni, J., Bodro, M., Chumbita, M., De la Mora, L., Garcia-Pouton, N., Gonzalez-Cordón, A., Dueñas, G., Hernandez-Meneses, M., Inciarte, A., Laguno, M., Leal, L., Macaya, I., … Tuset, M. (2022). Impact of SARS-CoV-2 viral load and duration of symptoms before hospital admission on the mortality of hospitalized COVID-19 patients. *Infection*, *50*(5), 1321–1328. https://doi.org/10.1007/s15010-022-01833-8

Riptasari, R. D., Rahem, A., & Purnamayanti, A. (2022). Perbandingan Keberhasilan Terapi Antivirus Favipiravir dan Remdesivir pada Pasien Covid-19 di RSUD dr. Doris Sylvanus. *Jurnal Surya Medika*, *8*(1), 125–128. https://doi.org/10.33084/jsm.v8i1.3453

Riyadi, & Larasaty, P. (2020). Factors Affecting Community Compliance With Health Protocols In Preventing The Spread Of Covid-19). *Seminar Nasional Official Statistics 2020: Pemodelan Statistika Tentang Covid-19*, *19*, 45–54.

Rosyidah, K. A., Primananda, A. Z., Sabaan, W., & Sukoharjanti, B. T. (2022). R Eformasi P Elayanan K Esehatan P Rimer P Ada P Uskemas R Awat. *Indonesia Jurnal Farmasi*, *7*(1), 52–62.

Rothan, H. A., & Byrareddy, S. N. (2020). The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity*, *109*(February), 102433. https://doi.org/10.1016/j.jaut.2020.102433

Seftiya, A., & Kosala, K. (2021). Epidemiologi Karakteristik Pasien Covid-19 di Kalimantan Utara. *Jurnal Sains Dan Kesehatan*, *3*(5), 645–653. https://doi.org/10.25026/jsk.v3i5.542

Şimşek Yavuz, S., & Ünal, S. (2020). Antiviral treatment of covid-19. *Turkish Journal of Medical Sciences*, *50*(SI-1), 611–619. https://doi.org/10.3906/sag-2004-145

Soejono, C. H., & Fitriana, I. (2018). The Difference in Length of Stay, Quality of Life, and Cost Effectiveness of Care for Geriatric Patients in Acute Care for Elderly Dr. Cipto Mangunkusumo National Hospital Before and After National Health Insurance Program Implementation. *EJournal Kedokteran Indonesia*, *6*(1). https://doi.org/10.23886/ejki.6.9398.

Vardavas, C. I., & Nikitara, K. (2020). COVID-19 and smoking: A systematic review of the evidence. *Tobacco Induced Diseases*, *18*(March), 1–4. https://doi.org/10.18332/tid/119324

Warsida, R. Y., Adioetomo, S. M., & Pardede, E. (2013). Pengaruh Variabel Sosio-Demografis terhadap Mobilitas Ulang-Alik di Jabodetabek. *Jurnal Ekonomi Dan Pembangunan Indonesia*, *13*(2), 159–176. https://doi.org/10.21002/jepi.v13i2.489

Y Furuta, T komeno, T. N. (2017). Polymerase Activity (%) 100 μ mol / L Favipiravir Favipiravir-RMP Control. *Proc Jpn Acad Ser B Phys Biol Sci.*, *93*(7), 449–463. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5713175/pdf/pjab-93-449

Yang, J., Zheng, Y., Gou, X., Pu, K., Chen, Z., Guo, Q., Ji, R., Wang, H., Wang, Y., & Zhou, Y. (2020). Prevalence of comorbidities and its effects in coronavirus disease 2019 patients: A systematic review and meta-analysis. *International Journal of Infectious Diseases*, *94*, 91–95. https://doi.org/10.1016/j.ijid.2020.03.017

Zhong, H., Wang, Y., Zhang, Z., Liu, Y., Le, K., Cui, M., & Yu, Y. (2020). *Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information . January*.

Zou, K. H., Li, J. Z., Imperato, J., Potkar, C. N., Sethi, N., Edwards, J., & Ray, A. (2020). Harnessing real-world data for regulatory use and applying innovative applications. *Journal of Multidisciplinary Healthcare*, *13*, 671–679. https://doi.org/10.2147/JMDH.S262776