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Cost-Effectiveness Analysis of Favipiravir and Remdesivir as COVID-19 Treatment in South Tangerang, Banten Province - Indonesia

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Abstract

COVID-19 is a contagious ailment primarily attributed to the severe acute respiratory syndrome coronavirus. Indonesia persists in confronting the COVID-19 pandemic, and South Tangerang City has emerged as one of the municipalities in Indonesia that has been significantly affected. There are two categories of medications employed for COVID-19 treatment according to government policies, namely favipiravir and remdesivir. This study aims to assess the cost-effectiveness of favipiravir and remdesivir medications at the South Tangerang General Hospital, Indonesia. The present study employs a retrospective research design characterized by a quantitative approach, utilizing cross-sectional methodologies. The analysis mostly consists of descriptive techniques. The sample consisted of 479 individuals, with 246 individuals receiving outpatient treatment and 233 undergoing inpatient treatment. The inclusion criteria for this study consisted of individuals diagnosed with COVID-19 who had tested positive for the antiviral medications favipiravir and remdesivir. The findings indicated that the Average Cost-Effectivenss Ratio (ACER) for inpatients treated with favipiravir was IDR 2,354,319,859, but for those treated with remdesivir, it amounted to IDR 3,501,513,488. Regarding the outpatient population utilizing favipiravir, the total expenditure amounts to IDR 420,083,118. Similarly, patients utilizing remdesivir incur a total expenditure of IDR 797,282,432. It is worth noting that the Cost-Effectivenss Ratio (CER) for patients using favipiravir is IDR 1,545,621, whereas patients using remdesivir have a CER of IDR 2,309,705. This study makes a valuable contribution to the existing body of research by demonstrating the cost-effectiveness of favipiravir. Consequently, future studies investigating the overall effectiveness of favipiravir in COVID-19 patients must employ more comprehensive criteria.

Keywords*:* COVID-19, CEA, favipiravir, remdesivir

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Introduction

The COVID-19 virus has disseminated across many global regions, including Southeast Asia, which ranks fourth in terms of recorded cases. Specifically, Southeast Asia has reported a total of 61,191,036 confirmed COVID-19 cases, with 806,499 fatalities.[1] Indonesia continues to grapple with the ongoing COVID-19 pandemic. According to national data, the cumulative number of verified COVID-19 cases in the country stands at 6,811,780, with a corresponding total of 161,865 deaths. The Banten Province is ranked fifth in terms of the number of cases, with a total of 363,348 reported cases and 2,982 fatalities. South Tangerang City, located in Banten Province, has recorded the highest number of COVID-19 instances within the region, amounting to 120,513 cases and resulting in 786 fatalities.[2]

The South Tangerang General Hospital serves as a designated healthcare facility for treating and managing people diagnosed with COVID-19. The hospital has observed a notable rise in the number of COVID-19 patients. This is evident from the data indicating that in 2020, there were 236 patients, followed by 1,056 patients in 2021, and further escalating to 1,240 patients in 2022. The COVID-19 pandemic presents a significant problem for hospitals due to the relatively high financial burden associated with managing patients affected by the virus. Hospitals are mandated to establish isolation facilities for patients, as well as provide additional medical interventions such as antiviral medications, oxygen therapy, and intensive care.[3]

The escalation of COVID-19 cases in Indonesia has led to a heightened need for medications that exhibit promising potential and have been identified as crucial components in COVID-19 treatment protocols. As per an official document titled "Decree of the Minister of Health number HK. 01.07/MENKES/4826/2021" about the maximum retail price of medications during the COVID-19 pandemic, the government has identified a total of eleven distinct categories of pharmaceuticals. To date, there remains a lack of targeted therapeutic interventions or treatments for the management of COVID-19.[4]

According to a study conducted by Rahmandani et al., in 2021, the research findings indicate that the ACER of oseltamivir IDR 4,419,677 was lower than the CER of favipiravir IDR 4,615,014. Consequently, the utilization of the more economically advantageous drug is oseltamivir in comparison to favipiravir.[5]

Methods

The present study employs a retrospective research design, adopting a quantitative approach and utilizing a cross-sectional method. The analysis primarily focuses on descriptive statistics, and the data collection process involves retrieving retrospective information from secondary sources. The present study utilizes secondary data comprising medical record data and billing data obtained from the South Tangerang General Hospital, specifically about patients diagnosed with COVID-19.

The present investigation was carried out during the period spanning from July 2022 to August 2023. The participants in this study consisted of individuals who tested positive for COVID-19, underwent COVID-19 medication therapy, and fulfilled the specified inclusion and exclusion criteria at the South Tangerang General Hospital in 2022.

The aforementioned inclusion criteria pertain to patients who have received a positive confirmation for COVID-19 and were currently receiving treatment at South Tangerang City Hospital. Additionally, these

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criteria encompass COVID-19 patients who were utilizing favipiravir and remdesivir medications, as well as those who have been deemed cured by medical professionals based on negative results from the Real-Time Polymerase Chain Reaction (RT-PCR) test.

The sampling technique employed in this study utilized a non-probability sampling approach, namely the purposive sampling method. The researchers employed the Lemeshow formula to ascertain the sample size utilized in this investigation. The findings indicate that the sample size for outpatients was 245.9, rounded to 246 samples. Similarly, the sample size for inpatients was 232.5, rounded up to 233 samples.

The present work has obtained ethical approval from the Ethics Committee for Medical and Health Research at Universitas Gadjah Mada. The document in question is an acceptance letter with the reference code KE/FK/1319/EC/2023.

Results and Discussions

Characteristics of Respondents

This study examined the demographic features of the respondents, including their age, gender, and medication usage. The data presented in Table 1 reveals that the age group exceeding 51 years has the highest prevalence of COVID-19 cases among both outpatients and inpatients in South Tangerang city, accounting for 35% and 37.8% respectively. Moreover, the prevalence of COVID-19 predominantly affects individuals of the female gender in both outpatient and inpatient settings, with respective proportions of 66.3% and 61.4%. Furthermore, in the context of pharmaceutical interventions for managing COVID-19 cases in South Tangerang city, a significant proportion of patients, specifically 78.5% of outpatients and 70.8% of inpatients, were administered favipiravir as the primary medication.

Ages

Based on the data collected in this study, it was observed that individuals who received inpatient and outpatient therapy with the medications favipiravir and remdesivir exhibited a higher proportion of respondents aged 51 years and above. Specifically, 35% of outpatients and 37.8% of inpatients fell into this age category.

Age is considered to be a significant risk factor in the transmission of the COVID-19 virus. This assertion is substantiated by a study undertaken by Dyana Sarvati in 2023, the study elucidates that the senior population represents a susceptible age group that is prone to a range of illnesses, including COVID-19.[6] The findings of this study are consistent with prior research conducted by Halimbar et al, 2023, at the Hajj Hospital in the East Java Province, which demonstrated that individuals between the ages of 51 and 60 exhibited the highest prevalence of COVID-19 infection.[7]

Sex

The demographic attributes of the respondents were collected in order to identify the individuals who participated in this study as COVID-19 patients. These attributes encompassed gender and age. According to the findings of this study, the gender distribution of COVID-19 patients receiving both inpatient and outpatient care was predominantly female. (66.3% of inpatients and 62.2% of outpatients). The findings of this study align with the statistics published on the official website of the government, which indicates a higher prevalence of COVID-19 cases among females compared to males in Indonesia. The findings of this study are further corroborated by Fathurrahman et al in 2023, which posits a higher prevalence of female patients relative to male patients.[8]

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In addition, the COVID-19 pandemic has had a significant impact on the physical and psychological well-being of working moms, leading to increased workload and stress levels. These factors can have detrimental effects on the body's immune system, as highlighted by Safarina et al in 2021.This finding aligns with the research conducted by Khaerunnisa et al., in 2022, which suggests that women have a higher susceptibility to stress when confronted with novel situations.[8-10]

Pharmaceuticals

Remdesivir and Favipiravir are antiviral agents that have demonstrated efficacy in individuals with moderate to severe symptoms. These medications belong to the class of prodrug nucleotide analogues and are capable of inhibiting the RNA polymerase of the COVID-19 virus. In vitro studies have indicated their potential action against the SARS-CoV-2 virus.[11] The findings of this study indicate that the medications utilized by individuals diagnosed with COVID-19 throughout the 2022 timeframe, whether they were admitted to the hospital or received treatment as outpatients, predominantly consisted of Favipiravir. Specifically, 78.5% of outpatients and 70.8% of inpatients were discovered to have been prescribed this particular drug, as illustrated in Table 1.

The findings of the aforementioned study align with previous research conducted at the East Java Province Hajj Hospital, which indicates that the utilization of favipiravir is more prevalent among COVID-19 patients at the hospital as compared to remdesivir.[7] A previous study conducted by revealed that the utilization of the antiviral medication Favipiravir was more prevalent among COVID-19 patients in comparison to oseltamivir.[5]

The figure represents the total count of patients who have been prescribed and are currently utilising the pharmaceutical compounds known as favipiravir and remdisivir. Out of a total of 165 patients, 130 individuals, constituting 78.8% of the sample, utilised favipiravir. In contrast, a significant proportion of patients (79.4% or 54 out of 68) in the remdesivir group exhibited positive outcomes.

The efficacy of a medicine can be determined by the reduction in recovery time observed among patients. A recent study conducted at the East Java Province Hajj Hospital revealed that the average length of stay (LOS) for patients treated with favipiravir was 11.22 days, which was the shortest LOS seen. Conversely, patients treated with remdesivir had the greatest LOS, with an average of 13.13 days.[7] This phenomenon arises due to the utilisation of favipiravir, a purine nucleic acid analogue that has been authorised for the therapeutic management of influenza. The efficacy of this compound lies in its ability to effectively impede the RNA Polymerase (RdRp) of several viruses, including influenza, norovirus, and Ebola virus.[12]

Based on the preceding discourse, it is advisable that all healthcare personnel engaged in the provision of inpatient care consistently adhere to the Standard Operating Procedures governing the management of patients afflicted with COVID-19. It is imperative for all officers to possess knowledge regarding the specific classification of COVID-19 medication that aligns with the level of severity exhibited by the infection. The selection of appropriate complementary medication can potentially enhance the rate of recovery among COVID-19 patients receiving inpatient care.

Upon contrasting outpatients and inpatients in Table 3, it can be observed that favipiravir exhibits the best level of efficacy in treating patients with COVID-19. The efficacy rate of favipiravir for individuals receiving outpatient

Table 1. Characteristics Respondents

Characteristics of Respondents	Outpatients		Inpatients	
	n	%	n	%
Ages				
<25	40	16.3%	24	10.3%
26-30	31	12.6%	25	10.7%
31-35	24	9.8%	24	10.3%
36-40	25	10.2%	28	12.0%
41-45	18	7.3%	19	8.2%
46-50	22	8.9%	25	10.7%
>51	86	35.0%	88	37.8%
Sex				
Male	83	33.7%	90	38.6%
Female	163	66.3%	143	61.4%
Pharmaceuticals				
Favipiravir	193	78.5%	165	70.8%
Remdesivir	53	21.5%	68	29.2%

Table 2. COVID-19 Patients Length of Stay

Length Of Stay (LOS)	The specific pharmaceutical interventions for COVID-19 Patients			
	Favipiravir (n=165)		Remdesivir (n=68)	
	N	%	N	%
1-5 Days	29	17,6%	10	14,7%
6-10 Days	130	78,8%	54	79,4%
11-20 Days	6	3,6%	3	4,4%
>21 Days	0	0	1	1,5%
Total	165	100%	68	100%

The LOS for individuals diagnosed with COVID-19 is notably reduced to a range of 6 to 10 days when considering the administration of favipiravir and remdesivir medications

care is 78%, but for those receiving inpatient care, it is 71%. Based on the findings of the study, it can be inferred that the efficacy of favipiravir is attributed to its demonstrated effectiveness against positive-stranded RNA viruses, including noroviruses and flaviviruses. Hence, it exhibits antiviral properties against the SARS-CoV-2 virus. The findings indicate that the administration of favipiravir yields positive outcomes in enhancing the clinical condition of individuals afflicted with COVID-19.

Nowadays, favipiravir has been granted approval and is being employed as a therapeutic intervention for COVID-19 in several nations. According to the available published statistics and literature, the nations that have been reported to utilise favipiravir include China, Hungary, India, Korea, Poland, Portugal, Russia, Serbia, Thailand, and Turkey.[13,14]

Comparable findings were observed among individuals receiving inpatient care. The total cost of remdesivir for inpatients is IDR 9,005,714 or USD 586.04, which is considered to be relatively high. In the interim, it is noteworthy to mention that the price of Favipiravir is at IDR 7,232,512 or USD 470.65. The presumed rationale behind the substantial cost disparity between administering remdesivir to outpatients versus

Table 3. Comparative Analysis of the Efficacy of Drug Therapy between Outpatient and Inpatient COVID-19 Patients

Pharmaceutical interventions for COVID-19	Number of Outpatients	Effectiveness Parameters	Pharmaceutical Effectiveness (%)
Favipiravir	193	$= \frac{\text{Total patients who started recovery}}{\text{Total patients}} x\ 100\%$	78%
Remdesivir	53	$= \frac{\text{Total patients who started recovery}}{\text{Total patients}} x\ 100\%$	22%
Total		246	100%
Pharmaceutical interventions for COVID-19	Number of Inpatients	Effectiveness Parameters	Pharmaceutical Effectiveness (%)
Favipiravir	165	$= \frac{\text{Total patients who started recovery}}{\text{Total patients}} x\ 100\%$	71%
Remdesivir	68	$= \frac{\text{Total patients who started recovery}}{\text{Total patients}} x\ 100\%$	29%
Total		233	100%

inpatients is that hospitalisation allows for greater oversight and control of the patient, whereas home-based treatment affords patients more autonomy and independence from direct medical supervision. The expenses associated with remdesivir treatment for outpatients are higher.

The mean expenditure for COVID-19 treatment per individual amounts to IDR 43,595,339.94. The component with the greatest average cost is the accommodation room, which amounts to IDR 10,690,794.62, or 24.52% of the overall average cost. Conversely, the lowest average cost is attributed to professional services such as physiotherapy, dietitians, and other related expenses, amounting to IDR 3,042.64.14 The study findings indicate that the direct expenses incurred by patients for medical services, specifically laboratory and radiology, were found to be the most substantial for both inpatients and outpatients who were prescribed remdesivir.

In the case of inpatients, the costs amounted to IDR 1,391,037, whereas for outpatients, the expenses reached IDR 2,342,446. Similarly, patients utilising favipiravir incurred direct costs of IDR 1,580,758 for inpatients and IDR 2,151,522 for outpatients. Based on the findings of the study, it can be observed that laboratory support examinations impose the greatest financial burden in comparison to the overall costs of pharmaceuticals and medical gas for both inpatients and outpatients.[16]

The findings presented in Table 6 demonstrate the ACER calculations for both inpatient and outpatient COVID-19 cases. The ACER for inpatients treated with favipiravir is observed to be IDR 2,354,319,859, while for those treated with remdesivir, it amounts to IDR 3,501,513,488. Regarding the individuals receiving outpatient care, the expenditure on the medication Favipiravir totals IDR 420,083,118, while those utilising the drug remdesivir incur a cost of IDR 797,282,432.

The utilisation of alternative therapies that demonstrate greater cost-effectiveness is contingent upon the identification of alternative therapies that exhibit lower ACER is in comparison to conventional therapies.

Table 4. Average Direct Medical Costs of Outpatient COVID-19 Patients in South Tangerang City

Pharmaceutical interventions for COVID-19	Everage of Pharmaceutical Costs (IDR)	Average Outpatient Rate (IDR)	Average Outpatient Treatment Rate (IDR)	Average Laboratory Costs (IDR)	Average Radiology Costs (IDR)	Average Total Costs (IDR)
Favipiravir	20.445	75.000	4.263.225	1.908.522	243.000	6.510.191
Remdesivir	558.877	75.000	8.663.934	2.234.446	108.000	11.640.256

The highest cost for remdesivir is observed in outpatient COVID-19 patients, amounting to IDR 11,640,256 or USD 757.48. In contrast, the expenses borne by patients for favipiravir are significantly reduced, amounting to approximately 50% less at a total of IDR 6,510,191 or USD 423.65

Table 5. Average Direct Medical Costs of Inpatients COVID-19 Patients in South Tangerang City

Pharmaceutical interventions for COVID-19	Everage of Pharmaceutical Costs (IDR)	Average cost of medical support (IDR)	Average cost of inpatient room (IDR)	Average cost of Physician Treatment (IDR)	Average cost of paramedical measures (IDR)	Average inpatient cost (IDR)	Average Total Costs (IDR)
Favipiravir	20.410	1.219.085	1.580.758	1.178.636	2.601.739	631.883	7.232.512
Remdesivir	559.622	1.391.037	1.696.176	1.301.462	3.274.750	782.668	9.005.714

Table 6. Results of Calculation of ACER for Outpatients and Inpatients of COVID-19 patients

Pharmaceutical interventions for COVID-19	Total Healthcare Costs (IDR)	Effectiveness	ACER
Outpatients			
Favipiravir	327.664.832	78%	420.083.118
Remdesivir	175.402.135	22%	797.282.432
Inpatients			
Favipiravir	1.671.567.100	71%	2.354.319.859
Remdesivir	1.015.438.900	29%	3.501.513.448

Table 7. The results of the calculation of the Cost Effectiveness Ratio (CER) for COVID-19 patients in South Tangerang City

Pharmaceutical interventions for COVID-19	Rata-Rata Nilai		CER (IDR)
	Average of Total Direct Costs (IDR)	*Length Of Stay* (LOS)	
Favipiravir	10.355.664	6,70	1.545.621
Remdesivir	15.798.385	6,84	2.309.705

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When considering the ACER of inpatients and outpatients, it can be observed that the efficacy of the COVID-19 medication favipiravir surpasses that of remdesivir. Favipiravir demonstrates a favourable cost-effectiveness profile, characterised by a low overall direct expenditure and a high level of efficacy. In contrast, the utilisation of remdesivir is associated with a substantial overall direct expenditure coupled with limited efficacy. A research investigation carried out in Saudi Arabia examined the cost-effectiveness of treating COVID-19 patients with favipiravir in comparison to those treated with remdesivir, revealing a cost-effectiveness rate of 65.6%.[17] The study was replicated at the DR. Soetomo General Hospital to assess the efficacy of favipiravir drug therapy in comparison to remdesivir. The findings indicated that favipiravir exhibited an effectiveness rate of 85.17%, suggesting that its utilization is more economically advantageous than remdesivir.[18]

Table 7 presents data on the efficiency of interventions for COVID-19 patients, together with their corresponding average total direct medical expenses. By utilising this information, one may determine the CER. Consequently, there is no requirement to perform the calculation of the Incremental Cost Effectiveness Ratio (ICER). Based on the findings from the computation of CER, it is evident that patients administered with favipiravir exhibit a CER of IDR 1,541,021, whereas patients receiving remdesivir have a CER of IDR 2,309,705.

The CER result signifies that there is a difference in the cost of inpatient treatment between patients utilising the drugs favipiravir and remdesivir. Specifically, for each additional day of inpatient treatment, the cost for patients using favipiravir is IDR 1,545,621, but for patients using remdesivir, the cost is IDR 2,309,705.

The findings of this study are consistent with the research conducted by Halimbar, et al in 2023, which suggests that favipiravir exhibits greater cost-effectiveness compared to tremdesivir. The research conducted by Setiadi and Nur aligns with the findings of Halimbar, indicating that favipiravir exhibits superior efficacy compared to oseltamivir and remdesivir. This is evident from the observed duration of treatment, as patients receiving therapy with favipiravir experience a more rapid rate of recovery.[19]

Alternative perspectives from several studies suggest that a higher mortality rate is observed among people utilising remdesivir compared to those who experience recovery. In the interim, a greater proportion of patients who received favipiravir exhibited recovery compared to those who had mortality.[20]

A study conducted in Bali also provides evidence supporting the efficacy of favipiravir in comparison to remdesivir and oseltamivir. The research was carried out over a duration of 14 days, including a total of 192 individuals. Among them, 96 patients received favipiravir, while the remaining 96 patients were administered remdesivir and oseltamivir.

The study observed a cohort of 96 individuals who received favipiravir medication therapy and found that they exhibited improved health outcomes, namely a reduction in fever and respiratory issues, compared to those who did not receive the treatment.[21]

Conclusions

The data collected from the respondents indicates that a majority of the individuals receiving inpatient and outpatient care for COVID-19 at the South Tangerang General Hospital were female patients. Furthermore, the average age of these patients exceeded 51 years. The analysis conducted by researchers

has also examined the utilisation of COVID-19 medications, revealing that the drug Favipiravir is the predominant choice among patients, as opposed to the drug Remdesivir. The investigation yielded findings indicating that the medicine Favipiravir exhibits characteristics that render it a cost-effective option for the treatment of COVID-19. This conclusion is based on its superior efficacy and comparatively lower expenses in comparison to the drug Remdesivir. In order to expedite the rate of recovery for the patient, while simultaneously reducing the financial burden. The findings of this study may serve as a valuable resource for guiding medicine selection in the treatment of people afflicted with COVID-19 or other related illnesses.

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None Declared

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