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Efficacy of Antiviral Medications in Decreasing Inflammation Levels Among Covid-19 Patients Experiencing Chronic Kidney Disease (CKD)

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A B S T R A C T

Individuals with Chronic Kidney Disease (CKD) face an elevated risk of severe COVID-19 infection. A comprehensive investigation into the effectiveness of antiviral medications in treating COVID-19 patients is imperative. The primary goal is to assess the severity of the illness and the efficacy of antiviral drugs in individuals with COVID-19 and CKD following antiviral treatment at Dr. Soedomo Trenggalek Hospital. This study adopts a cross-sectional approach, employing purposive sampling for sample selection. Retrospective data from 2022 medical records of COVID-19 patients diagnosed with CKD are analyzed. The research findings highlight the efficacy of antiviral drugs in diminishing inflammation levels in COVID-19 patients, as indicated by a significant p-value of 0.000. However, the leukocyte data proved inadequate in determining the reduction in inflammatory levels. Therefore, obtaining data on C-reactive protein (CVR) and lymphocytes is crucial for a more accurate measurement. The p-value for ClCr is 0.842

INTRODUCTION

The year 2020 was marked by the emergence of SARS-CoV-2, the virus causing COVID-19, which spread globally after originating in Wuhan, China, in December 2019. It led to a pandemic, as declared by the WHO, prompting Indonesia to declare a public health emergency related to COVID-19 (V.A.R.Barao et al., 2022).

COVID-19 resulted in significant illness and death. By December 2021, more than 273 million people were infected, with over 5.3 million deaths. Variations in symptoms and impacts raised concerns about risk factors like obesity, making individuals more vulnerable to COVID-19, prompting further research. In Indonesia, the first COVID-19 cases were announced in March 2020, and the numbers continued to rise. The surge in cases in 2021 demanded extra attention, with various virus variants spreading and reducing vaccine effectiveness (Yıldırım et al., 2022).

COVID-19 exhibits varying levels of severity, ranging from asymptomatic to critical. Chronic kidney disease (CKD) stands as a crucial risk factor, making patients vulnerable to serious complications, necessitating intensive care or ventilator support. Individuals with CKD are at higher risk of severe COVID-19. Tight prevention and monitoring are crucial, especially for those undergoing hemodialysis. While specific therapies are yet to exist, ongoing research aims to find effective antiviral medications (Rudiansyah et al., 2020).

Data from the Indonesian Renal Registry (2018) also indicates a CKD prevalence of 56% in males and 43% in females. This data aligns with information from several other countries regarding CKD prevalence by gender. There's been an increase in new chronic kidney failure patients from 2017 to 2018, almost doubling from around 30,831 to 66,433 patients (PERNEFRI, 2018).

According to data from the World Health Organization (WHO) in 2019, there were approximately 1.3 million CKD patients worldwide. CKD patients face a higher risk of death due to COVID-19 infection. This is attributed to changes in the immune system, including persistent systemic inflammation and immune suppression. Apart from attacking respiratory cells, the SARS-CoV-2 virus can also affect other organs such as the kidneys, ileum, and heart, especially during viremic conditions. This happens due to the expression of ACE2 receptors on proximal tubule epithelial cells, glomerular mesangial cells, and podocytes, which become targets for the COVID-19 virus (Sherina et al., 2023). Patients with chronic kidney failure tend to have a higher risk of severe COVID-19 infections. The RSUD dr. Soedomo Hospital in Trenggalek Regency, known for its handling of COVID-19 cases, serves as the research site to evaluate the use of antiviral drugs in COVID-19 patients with CKD (Prasetyawan, F., & Saristana, Y. 2023).

LITERATURE REVIEW

In this cross-sectional (non-experimental) study, researchers will collect retrospective data using 2022 medical records concerning COVID-19 diagnosed patients with CKD and will analyze the effectiveness of antiviral drugs in reducing inflammation levels. The cross-sectional (non-experimental) research method provides a clear understanding of the purposive sampling method employed, which involves specific considerations in selecting samples starting from the retrieval of medical records (Dr. Soedomo Trenggalek Regional General Hospital's medical records).

The study also investigates COVID-19 patients with CKD, examining leukocytes to observe reductions in inflammation levels. Additionally, it analyzes the effectiveness of antiviral drugs in reducing inflammation in patients with chronic kidney disease. This research aims to offer insights and determine the effectiveness and safety of antiviral drug usage in chronic kidney disease patients.

METHODOLOGY

This study is a cross-sectional analysis without experimental intervention. Using a deliberate selection method from medical records of COVID-19 patients who also suffer from Chronic Kidney Disease (CKD). Trying to understand the reduction in disease severity, treatment period, mortality rate, and side effects of antiviral drugs in patients with the same condition after undergoing treatment.

The research site is Dr. Soedomo Trenggalek with address Jl. DR. Sutomo No.2, Cengkong, Tamanan, Kec. Trenggalek, Trenggalek Regency, East Java 66311 and the research was conducted during August 2023.

The instruments used to collect data from medical records include patient demographic data, records of antiviral drug use, leukocyte test results, ClCr examinations, and Covid-19 tests.

Data analysis consists of two parts: Descriptive and Inferential. Descriptive Analysis uses percentages to explain the variables of antiviral drugs (independent) and Covid-19 patients with chronic kidney disease (dependent). The percentage value is calculated using the formula P=n/(Total Sample) x 100%.

Inferential analysis involves the Wilcoxon test to assess the effectiveness and safety of antiviral drugs in Covid-19 patients with chronic kidney disease. The decision making criteria are based on the following hypothesis test. If the Probability value is $< \alpha$ (0.05), there is a difference in the average and if the Probability value is $> \alpha$ (0.05), there is no difference in the average.

RESULTS AND DISCUSSION

During 2022, RSUD dr. Soedomo treated 50 patients diagnosed with Coronavirus Disease 2019 and comorbid conditions, namely chronic kidney disease. Patient demographic information is provided in Table 1 below:

Table 1. Data Demografi Pantients

Characteristics of patients	Numbers	
	Frequency	Percentage %
Age		
<15 year	4	8
16-35 year	7	14
36- 50 year	9	18
> 50 year	30	60
Gender		
Man	37	74
Woman	13	26
Total	50	100

Source: Primary data, 2023

The majority of patients (60%) were diagnosed with COVID-19 and chronic kidney disease at RSUD Dr. Soedomo Trenggalek is over 50 years old, with 74% being men. Age is a factor that increases the risk of a number of diseases due to decreased physiological function, including the influence on the immune system which is regulated by B cells and T cells (Fitriani, NI. 2020). Variations in the expression of ACE2 and TMPRSS2 receptors based on gender can explain variations in the severity and mortality rates due to COVID-19 (Di Gennaro, F., 2020).

Table 2. Length of Hospital Stay

	Numbers	
Length of Hospital Stay	Frequency	Percentage %
<3 day	12	24
4-7 day	36	72
>7 day	2	4
Total	50	100

Source: Primary data, 2023

Based on Table 2, the highest frequency occurred among patients with a hospital stay of 4-7 days, reaching a percentage of 72%.

Table 3. Outcome

Outcome	Numbers	
	Frequency	Percentage %
Recovered	36	72
Died	14	28
Total	50	100

Source: Primary data, 2023

From Table 3, it can be inferred that the largest average outcome is 'recovered,' with a frequency of 36, accounting for 72%. Meanwhile, the frequency of death is 14, representing 28%

Table 4. Frequency Antiviral Drugs

Drugs Name	Numbers	
	Frequency	Percentage %
Favipirafir	32	64
Remdesivir	18	36
Total	50	100

Source: Primary data, 2023

From tabel 3, At RSUD Dr. Soetomo, two types of antiviral medications, namely favipiravir and remdesivir, are predominantly employed. The utilization rate shows that favipiravir is used 64% of the time, followed by remdesivir at 36%. Favipiravir, possessing a broad antiviral spectrum, has been clinically validated for assessing its effectiveness in COVID-19 patients. Clinical trials have established its efficacy at maintenance doses ranging from 200 to 600 mg administered twice daily for a duration of 10 to 14 days, with various initial doses of 1600, 1800, and 2400 mg. However, the administration of favipiravir to patients with chronic kidney disease may result in accumulation, potentially leading to toxicity (Chen, N., 2020).

Meanwhile, remdesivir serves as a broad-spectrum antiviral agent effectively inhibiting RNA polymerase on RNA (RdRp), recommended for the treatment of hospitalized COVID-19 patients. Patients diagnosed with COVID-19 and chronic kidney disease exhibit a higher viral load compared to those without kidney ailments. Consequently, the standard dosage range of 250 mg/kg per day may not deliver an optimal treatment effect (ERA-EDTA & ERACODA, 2021).

Table 5. Safety and Effectiveness of Antiviral Drugs

Laboratory Data	Numbers				p-value
	Improvements	(%)	without improvements	(%)	
Leukocyte	34	68	16	32	0,000
ClCr	6	12	44	88	0,842

Source: Primary data, 2023

Based on Table 5, there is a significant 68% improvement observed in leukocyte counts, supported by a p-value of 0.000, indicating the efficacy of antiviral medication in reducing and ameliorating COVID-19 cases in patients concurrently suffering from chronic kidney disease. The normal range for leukocyte count is 4,800 to 10,800/µL, which serves as an inflammation marker in individuals affected by COVID-19. SARS-CoV-2 specifically targets ACE-2 receptors, prompting both viral replication and an inflammatory response within the human body (Humairo, A., 2021).

Additionally, the examination of ClCr indicated that there was no substantial improvement observed in 88% of cases, supported by a p-value of 0.842. This suggests that the administration of the antiviral drugs employed in this study may not be deemed safe for individuals with COVID-19 and chronic kidney disease. Notably, some patients showed signs of improvement due to hemodialysis treatment and vaccination. It's noteworthy that remdesivir is not advisable for patients with a GFR below 30 ml/min and creatinine levels >1 mg/dl unless the potential benefits significantly outweigh the risks. Meanwhile, the administration of favipiravir led to an initial decline in kidney function post-48 hours but showcased gradual improvement following therapy cessation (Gonzalez, M. E., 2021).

CONCLUSIONS AND RECOMMENDATIONS

The conclusion of this research indicates that leukocyte data is insufficient in determining the reduction in inflammation levels. Therefore, data on CVR and lymphocytes are necessary to measure a more precise decrease in inflammation levels. Additionally, concerning safety aspects, the use of antiviral drugs is not recommended for patients with chronic kidney disease, supported by the ClCr value of 0.842. In the case of administering favipiravir to COVID-19 patients with chronic kidney disease, strict monitoring of the patients' ClCr is essential, while the use of remdesivir can be administered as per the recommended dosage for a GFR above 30ml per minute.

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