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ANALYSIS OF THE RELATIONSHIP OF COVID-19 SYMPTOMS WHICH RECEIVE FAVIPIRAVIR AND LENGTH OF TREATMENT IN THE INPATITION OF DR. ISKAK TULUNGAGUNG

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ABSTRACT

Coronavirus disease 2019 or commonly called COVID-19 is an infectious disease caused by SARS-CoV-2. Favipiravir is a broad-spectrum antiviral drug so it has potential antiviral action against SARS-CoV-2 which is an RNA virus. This research aims to find out the relationship between Covid-19 symptoms when receiving favipiravir and the length of treatment of patients hospitalized at RSUD Dr. Iskak Tulungagung. Observational research with descriptive retrospective methods in COVID-19 patients' moderate symptoms with Favipiravir therapy at RSUD dr. Iskak Tungagung period July - September 2021. Data collection using the calculation of the Slovin formula to determine the number of patient samples. Analysis analysis using SPSS by carrying out the Chi-square test. The results of the study were obtained from 146 patients, the pattern of using Favipiravir was given at a dose (2x1600mg) on the first day followed by (2x600mg) on the second day and so on with the most giving range of 1-7 days.

KEYWORDS *Favipiravir, COVID-19, Moderate Symptoms*

INTRODUCTION

Coronavirus disease 2019 or what is commonly called COVID-19 is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is a new type of coronavirus that has never been identified in humans before. COVID-19 was declared a pandemic by WHO on March 11 2020 (Ministry of Health of the Republic of Indonesia, 2020). Globally, the number of positive cases of COVID-19 on June 14 2021 was reported to have exceeded 177 million people. Cases continue to increase and spread rapidly to

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various countries outside China(WHO, 2021). Positive cases of COVID-19 are also increasing and spreading rapidly in Indonesia. According to data from the Ministry of Health, as of July 17 2021, it was reported that 2,832,755 people were confirmed positive for COVID-19 with 72,489 deaths (Annisa, 2021).

The pathophysiology of SARS-CoV-2 basically attacks cells in the human respiratory tract. The S protein in the virus binds to the cellular receptor in the form of ACE2. The virus will bind to the receptor and penetrate the cell. Inside the cell, SARS-CoV-2 duplicates genetic material and synthesizes proteins and then forms new virus particles that will appear on the surface of the cell (Susilo et al., 2020). The clinical manifestations of COVID-19 are generally mild and develop gradually. Patients with moderate symptoms have clinical signs of pneumonia such as cough, fever, shortness of breath and no signs of severe pneumonia (PDPI et al., 2020).

In principle, management of COVID-19 patients is carried out using pharmacological and non-pharmacological therapy. Treatment for COVID-19 patients also depends on the degree of symptoms. Pharmacological therapy for COVID-19 patients with moderate symptoms is given multivitamins, antiviral drugs (Favipiravir / Remdesivir), LMWH/UFH anticoagulants. Symptomatic treatment can also be given to COVID-19 patients with moderate symptoms, such as paracetamol (Decree of the Minister of Health of the Republic of Indonesia, 2021).Favipiravir is a broad-spectrum antiviral drug approved in Japan for the treatment of influenza. In addition to inhibiting influenza viruses, Favipiravir also shows inhibitory effects on various other RNA viruses such as arenaviruses, bunyaviruses, flaviviruses and filoviruses that cause dengue fever (Du & Chen, 2020). Therefore, Favipiravir has potential antiviral action on SARS-CoV-2 which is an RNA virus (Dong et al., 2020).

Based on the background above, it is necessary to conduct research to determine the relationship between COVID-19 symptoms when receiving favipiravir and the length of treatment in patients who are inpatients at RSUD dr. Iskak Tulungagung.

RESEARCH METHODS

The research carried out was a cross sectional study, namely observing patient data using medical record data. Data collection was carried out retrospectively by processing patient medical record data with inclusion criteria, namely COVID-19 patients with moderate and severe symptoms who received Favipiravir at RSUD dr. Iskak Tulungagung for the period July – September 2021 with complete Medical Health Record data. Data collection uses the Slovin Formula calculation to determine the number of patient samples. Data were carried out with descriptive univariate analysis looking at socio-demographics (age, gender, comorbidities), favipiravir treatment patterns, length of treatment and bivariate analysis looking at the relationship between Covid-19 symptoms who received favipiravir and the patient's length of stay in the hospital using Chi-square statistical analysis.

RESULTS AND DISCUSSION

Based on the results of research conducted at RSUD dr. Iskak Tulungagung using a retrospective method using patient Health Medical Record (RMK) data for the period July – September 2021. The sample of COVID-19 patients with moderate and severe symptoms with Favipiravir was 146 samples. A total of 72 samples with moderate symptoms and 74 samples with severe symptoms.

Patient Demographic Data

Table 1. Types Gender of COVID-19 Patients with Moderate Symptoms

Gender	Amount	Percentage (%)
Man	75	51.4
Woman	71	48.6
Total	**146**	**100**

In Table 1, it was found that the percentage of male patients was greater, namely 39 patients (54%) compared to 33 female patients (46%). Male patients tend to have higher rates of severity and mortality. Lifestyle differences between men and women may also contribute to the greater degree of susceptibility to COVID-19 observed in men. Smoking is associated with an increased risk of poor COVID-19 outcomes (Mukherjee & Pahan, 2021). In addition, it is known that in general the immune response is stronger in women than in men (Mi et al., 2020).

Table 1. Age of COVID-19 Patients

Age (years)	Amount	Percentage (%)
15-24	13	8.9
25-34	19	13.0
35-44	37	25.3
45-54	42	28.8
55-64	22	15.1
>65	13	8.9
Total	**146**	**100**

*Ministry of Health of the Republic of Indonesia, 2022

Based on Table 2, the highest number of results was obtained, namely at the age of 45-54 years, as many as 20 patients (28%). Data from research byScript et al., (2021)It was found that the largest age range for COVID-19 patients was 31-54 years. The majority of patients are infected with SARS-CoV-2 as mild or moderate symptoms (Guo et al., 2020). Survival in elderly patients is lower compared to younger patients. The cause may be due to relatively poor nutritional status and immune function which can cause damage to the immune defense function and develop into severe pneumonia thereby increasing the risk of deathn(Mi et al., 2020).

Table2. Disease History of COVID-19 Patients

Disease History	Amount	Percentage (%)
Diabetes	33	39.8
Hypertension	16	19.3
VTE	6	7.2
Heart	5	6.0
Asthma	9	10.8
Dyspepsia	4	4.8
Cancer	1	1,2
Autoimmune	2	2,4
CKD	2	2,4
TB	2	2,4
Vertigo	1	1,2
CVAs	1	1,2
COPD	1	1,2
Total	**83**	**100**

*1 patient can have more than 1 history of disease and/or no history of disease

Based on Table 3, DM is the most common comorbidity in COVID-19 patients, followed by hypertension. According to research, the use of ACE inhibitors and ARBs can increase ACE2 receptors, thus facilitating the entry of viruses (Wang et al., 2021). Diabetes is one of the most common comorbidities that can cause multisystem complications. The long-term effects of elevated blood sugar (hyperglycemia) can lead to a weakened immune system and increased susceptibility to infectious processes such as COVID-19 (Bajgain et al., 2021). The pathophysiology related to comorbid diabetes in COVID-19 patients was explained by Wu et al., (2020) that the immune system in diabetes patients decreases due to abnormal blood glucose levels, which results in dysregulation and decreased immune response. As a result, patients with comorbid diabetes are vulnerable to SARS-CoV-2.

Favipiravir Usage Patterns

Table 4. Usage Patterns

Therapy and Dosage Regimen	Amount	Percentage (%)
Favipiravir (2x1600mg – 2x600mg) po	146	100
Total	**146**	**100**

In Table 4 there is only a single therapy pattern of Favipiravir given to all COVID-19 patients with moderate and severe symptoms at RSUD dr. Iskak was 146 patients (100%). Based on research results, the Favipiravir dose is in accordance with the guidelines in Indonesia, namely given (2x1600mg) po on the first day then (2x600mg) po on days 2-5 and can be extended up to 7 days (Decree of the Minister of Health of the Republic of Indonesia, 2021).The research results showed that the duration of use of favipiravir was 1-7 days. The research results

obtained on the duration of use of Favipiravir are in accordance with guidelines in Indonesia. According to a study by Chen et al., (2020) Favipiravir showed better ability in clinical recovery rates reducing symptoms of fever and cough with doses given (2x1600mg) po on the first day then (2x600mg) on days 2-7.

Length of Hospital Admission for COVID-19 Patients with Moderate and Severe Symptoms

Table 5. Length of Hospital Admission

Old MRS	Amount	Percentage (%)
≤ 14 days	127	87
> 14 days	19	13
Total	**146**	**100**

Table 5 shows that the length of treatment for COVID-19 patients with moderate and severe symptoms at the Dr. Regional General Hospital. Iskak Tulungagung is different. Treatment for ≤ 14 days was 127 patients (87%) and treatment for > 14 days was 19 patients (13%). A study by Solaymani-Dodaran et al., (2021) The average length of hospital stay for COVID-19 patients on Favipiravir therapy who were discharged was 7 days. Likewise with research according to Hassanipour et al., (2021)Favipiravir showed clinical improvement after 7 and 14 days of hospitalization compared to those receiving other drugs. According to the Indonesian Ministry of Health in 2021, the effective length of treatment ranges from 1-14 days. If it is more than 14 days, the medication is declared ineffective.

Relationship between symptoms and length of treatment

The data obtained was first tested for normality with Kolmogorov-Smirnof. The results of the significance normality test were 0.344 and 0.520 which showed a value > 0.05 so it was normally distributed.

Table 6. One-Sample Kolmogorov-Smirnov Test

		Covid Symptoms	Length of Treatment
N		146	146
Normal Parameters, b	Mean	1.51	1.13
	Std. Deviation	,502	,338
Most Extreme Differences	Absolute	,344	,520
	Positive	,337	,520
	negative	-.344	-.350
Statistical Tests		,344	,520
Asymp. Sig. (2-tailed)		,000c	,000c

a. Test distribution is Normal.
b. Calculated from data.
c. Lilliefors Significance Correction.

The Chi-square test was carried out on the data, then a significant value was obtained showing a P value = 0.002, which states that the Asymptotic Significance value is less than 0.05, thus indicating a relationship between the symptoms of Covid-19 who received favipiravir and the length of stay for COVID-19 patients in inpatient hospital Dr. Isaac. By using the right antiviral with the way the drug works according to the patient's condition, it will be more helpful for the patient's improvement. From these results, the antiviral drug Favipiravir provides significant therapeutic outcomes in terms of patient length of stay, by working against RNA by inhibiting the viral polymerase enzyme.

Table 7. Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	9.822a	1	,002		
Continuity Correction b	8,341	1	,004		
Likelihood Ratio	10,692	1	,001		
Fisher's Exact Test				,002	,001
Linear-by-Linear Association	9,755	1	,002		
N of Valid Cases	146				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 9.37.
b. Computed only for a 2x2 table

CONCLUSION

From the research results, a significant value was obtained showing a P value = 0.002, which states that the Asymptotic Significance value is less than 0.05, thus indicating a relationship between the symptoms of Covid-19 when receiving favipiravir and the length of stay for COVID-19 patients in the inpatient hospital at Dr. Isaac.

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