# STUDY OF THE SEVERITY AND EARLY ANTIVIRAL TREATMENT FOR THE DURATION OF THE RECOVERY COVID-19 PATIENTS

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**ABSTRACT**

Late antiviral treatment can potentially cause the Covid-19 virus to replicate very quickly, so it is necessary to understand antiviral drugs and optimize treatment for Covid-19 patients. The study aimed to determine the correlation between the severity, speed of administration of antivirals, and the recovery time of Covid-19 patients. This type of research is an observational study with retrospective data collection on 94 Covid-19 medical records at "X" Hospital Cirebon from 316 populations in June-July 2021 according to inclusion criteria. The data analysis used was univariate and bivariate using Spearman's Rho. The 55–59-year age group (28.7%) was the most infected with Covid-19. There are more males than females (52.1% vs 47.9%). Favipiravir therapy (43.6%) was given the most. Moderate severity (74.5%) had the highest proportion. The speed of administration of antivirals was most initiated at 5-8 days (42.6%) after the onset of symptoms. The maximum recovery time for Covid-19 patients is 13-18 days (58.5%). A strong positive correlation between the speed of giving antivirals to the recovery time of Covid-19 patients (sig. 0.000) and the correlation coefficient of 0.659. Does not show a correlation between the severity of recovery time (sig. 0.113) and speed of antiviral administration to the severity of Covid-19 patients (sig. 0.297). There is a correlation between the early antiviral treatment and the recovery time of Covid-19 patients; the earlier antiviral therapy is given, the faster it will heal.

**Keywords:** Covid-19; Early antiviral treatment; Severity; Duration of recovery

## 1. INTRODUCTION

Many suspected Covid-19 patients are unwilling to be examined with a nasopharyngeal swab because they feel afraid, even though with the knowledge of Covid-19 disease from an early age, antiviral therapy will be immediately given and has the potential to accelerate healing or successful therapy. Although there are no transparent clinical trials, early timing of antiviral therapy can reduce the severity of the disease and prevent the development of Covid-19 disease (Xu et al., 2020).

Based on an analysis of Indonesian Covid-19 data on June 13, 2021, the increase in positive cases was 38.3% (39.999 vs 55.320), the number of deaths was 52.879 (2.77%) above the world average (90.92%), and the number of active cases was below the world average (6.92%). As of June 13, 2021, there was an increase in the number of cases in regencies/cities in high-risk zones of 29 (5.64%), medium-risk zones of 339 (65.95%), low-risk zones of 121 (23.54%, and green 25 (4.86%) (Satgas Covid-19, 2021).

The Covid-19 infection has a wide range of clinical symptoms, ranging from asymptomatic, mild symptoms, severe pneumonia, ARDS, and sepsis to septic shock. Based on the severity, around 80% of Covid-19 cases are in the mild or moderate group, as many as 13.8% are in severe or severe illness, and 6.1% are in critical condition. At the same time, asymptomatic infections

are still unknown  (WHO, 2020). The median time from symptom onset to clinical recovery is approximately two weeks for mild symptoms and 3-6 weeks for patients with severe or critical symptoms (WHO, 2020).

In Sofia, Bulgaria, from a 3-month study period from March 2020 to June 2020, 138 cases of Covid-19 were hospitalized, several cases showing clinical results of patient discharge with an increase of 87.7%, still under treatment at home sick about 8.0% and patients who were said to have died 4.3%. Of the nine patients who went through the intensive care unit, eight were intubated, and one was extubated and sent home after 49 days of hospitalization. Patients who died were based on comorbid diseases such as hypertension, cardiovascular disease, malignant disease, diabetes mellitus, and chronic obstructive pulmonary disease. Discharge from the hospital after two negative RTPCR (Reverse-Transcriptase Polymerase Chain Reaction) tests with a 24-hour interval between the two and clinical symptoms and IgG antibody presentation improved (Popov, G. T., *et. al.*, 2020).

To date, no antiviral treatment has been proven effective against the Covid-19 virus. Replication of the Covid-19 virus may be very active and fast at the beginning of the Covid-19 journey. Antiviral therapy has a significant impact before the disease condition develops into a hyperinflammatory state that can be a symptom of disease severity. Therefore, an understanding of antiviral drugs is needed in dealing with mild, moderate, severe, and critical symptoms, which aims to optimize treatment for sufferers of Covid-19. The recommended antiviral therapy is Lopinavir/Ritonavir, Remdesivir, Chloroquine or Hydroxychloroquine (NIH, 2021), Favipiravir, dan Oseltamivir (PDPI et al., 2020).

The condition of the Covid-19 pandemic in Indonesia, which continued to increase in the June-July 2021 period, the authors analyzed the severity, speed of administration of antiviral therapy, and the length of recovery for Covid-19 patients, which varied quite a lot from 316 positive cases undergoing isolation treatment at the hospital. X" Cirebon 2021 with only 94 medical records analyzed that met the inclusion criteria. The community and all relevant stakeholders must know that treating Covid-19 patients earlier will increase treatment success. This study aimed to determine the correlation between the severity of the disease, the speed at which antivirals were administered, and the length of recovery for Covid-19 patients.

## 2.  METHODS

This research is non-experimental with a correlational descriptive research approach. The population used was 316 Covid-19 medical records hospitalized in the isolation room of Cirebon "X" Hospital in June-July 2021. Sampling was carried out by purposive sampling based on predetermined inclusion-exclusion criteria, namely, only 94 patient medical records. The inclusion criteria are the medical records of Covid-19 patients undergoing treatment in the isolation room of the Gunung Jati Cirebon Hospital for the period June-July 2021, aged 25-60 years, positive Covid-19 PCR swab results, and having been given antivirals according to the Covid-19 edition of the Guidelines for Management (PDPI et al., 2020). Exclusion criteria included medical records of Covid-19 patients with asymptomatic severity, death, changes to antiviral therapy, forced discharge, and pregnant women. The independent variable in this study is the severity and speed of administering antivirals to Covid-19 patients, and the dependent variable is the recovery time for Covid-19 patients. The recovery time starts from the onset of symptoms until leaving the isolation room at Gunung Jati Hospital with negative RT-PCR results

### 2.1.  Research Path

The research begins with preparing a proposal; this is done to provide a summary of the research problem and methods for solving the problem. Then at the licensing stage, Ethical Clearance was obtained from the research ethics committee of RSD Gunung Jati Cirebon with Number 035/LAYAKETIK/KEPPKRSGJ/VII/2022. A research permit application letter was obtained from the Director of Cirebon "X" Hospital. The data collection stage was carried out by

observing the Covid-19 medical records for the June-July 2021 period by viewing and sorting patient data contained in the medical records by inclusion and exclusion. The researcher recorded the observed data in the data collection sheet. The data that has been collected is processed using SPSS software version 25. The data from the research results are presented in the form of a tabular diagram.

## 2.2. Data Analysis

### 2.2.1. Univariate Analysis

Univariate analysis in this study was used to describe the distribution of patient characteristics based on age, sex, the severity of Covid-19 patients, and the class of antiviral drugs given to Covid-19 patients in the isolation room of Cirebon "X" Hospital for the period June-July 2021. Analysis univariate presented tests were carried out in the form of frequency and percentage results.

### 2.2.2. Bivariate Analysis

The bivariate analysis is in the form of correlation analysis between variables, beginning with the data normality test using the Kolmogorov-Smirnov test to see if the data is normally distributed or not with the condition that if sig. > 0.05, then the data is normally distributed. Bivariate correlation analysis using Spearman's rho by looking at the value of Asymp sig. <0.05 indicates that the relationship between the two variables is correlated, while the P-value > 0.05 indicates that the two variables are not correlated. The bivariate value of the correlation with the direction of a perfect negative relationship is close to the coefficient -1, perfectly positive is close to the coefficient 1, and the coefficient of 0 indicates the direction of the relationship is not linear and is considered not correlated. The degree of relationship correlation value 0.00-0.199 indicates a very low correlation, 0.20-0.399 low correlation, 0.40-0.599 moderate correlation, 0.60-0.799 strong correlation, and 0.80-1.00 powerful correlation (Riadi, 2016). The bivariate analysis results are presented Kolmogorov-Smirnov test and Spearman's rho.

## 3. RESULTS AND DISCUSSION

### 3.1. The Characteristics of Covid-19 Patients

**Table 1** presents data on the characteristics of Covid-19 patients as follows.

**Table 1.** Characteristics of Covid-19 Patients

| Variable | Frequency | Percentage (%) |
|---|---|---|
| Age (years) | | |
| 25-29 | 2 | 2.1 |
| 30-34 | 8 | 8.5 |
| 35-39 | 5 | 5.3 |
| 40-44 | 8 | 8.5 |
| 45-49 | 15 | 16.0 |
| 50-54 | 26 | 27.7 |
| 55-59 | 27 | 28.7 |
| 60-64 | 3 | 3.2 |
| Sex | | |
| Man | 49 | 52.1 |
| Woman | 45 | 47.9 |

From the research results **Table 1** we can see that the 55-59-year-old category is the most infected with Covid-19; the older the age, the more organ function decreases, and so is elderly with comorbidities most vulnerable to needing Covid-19 treatment (Bulut & Kato, 2020). The prevalence of male sex is at a much higher risk of exposure to Covid-19 than women. This can be because most breadwinners and the backbone of the family are men who require them to leave the house (Fadilah, 2018). In addition, the lifestyle of men who are most active smokers can

increase the expression of the SARS-Cov-2 receptor, namely ACE-2, in the lungs (Mukherjee & Pahan, 2021).

### 3.2. The Characteristics of Therapy Covid-19 Patients

In **Table 2** the following data presents the characteristics of the disease's severity and therapy's characteristics.

**Table 2.** The Characteristics of Therapy Covid-19 Patients

| Variable | Frequency | Percentage (%) |
|---|---|---|
| Severity | | |
| Mild | 8 | 8.5 |
| Moderate | 70 | 74.5 |
| Severe | 15 | 16.0 |
| Critical | 1 | 1 |
| Antiviral Group | | |
| Oseltamivir | 13 | 13.8 |
| Favipiravir | 41 | 43.6 |
| Remdesivir | 40 | 42.6 |
| Early Treatment Antivirals (day) | | |
| 1-4 | 35 | 37.2 |
| 5-8 | 40 | 42.6 |
| 9-12 | 13 | 13.8 |
| 13-16 | 5 | 5.3 |
| 29-32 | 1 | 1.1 |
| Length of Recovery (day) | | |
| 1-6 | 3 | 3.2 |
| 7-12 | 21 | 22.3 |
| 13-18 | 55 | 58.5 |
| 19-24 | 8 | 8.5 |
| 25-30 | 5 | 5.3 |
| 31-36 | 1 | 1.1 |
| 43-48 | 1 | 1.1 |

In **Table 2** the results of the study showed that moderate severity was most commonly found in the number of samples studied. Meanwhile, the severity of the patient varies from patient to patient because the immune system of each patient is different in fighting the Covid-19 virus and is dynamic which can fluctuate due to various factors such as age, nutrition, hormones, comorbidities, and others (Amalia et al., 2020). The most common antiviral therapy given to Covid-19 patients is Favipiravir. Giving this antiviral is recommended following the Covid-19 Management Guidelines edition 3 for the mild, moderate, and severe/critical severity categories with a note of consideration by the DPJP (Doctor in Charge of the Patient) according to the patient's clinical condition to avoid DRP (Drug Related Problem) cases. The second number is Remdesivir; Remdesivir is an antiviral therapy that works by inhibiting RNA polymerase bound to viral RNA in vitro against SARS-Cov-1, SARS-Cov-2, and MERS-Cov. A double-blind, randomized, placebo-controlled trial of intravenous remdesivir in adults who tested positive for COVID-19 received an initial dose of 200 mg of remdesivir on day 1, followed by 100 mg daily until day 9 (Beigel, J. H., *et al*., 2020).

The speed of administration of antivirals is at most 5-8 days. These various antiviral initiations can also be caused by several factors such as patient immunity, the "X" hospital care service system related to 3T (Testing, Tracing, and Treatment), and individual concern for efforts to prevent Covid-19 is lacking, especially in 3T. The recovery time for Covid-19 patients, from the onset of symptoms to negative PCR results, was more experienced for 13-18 days. Based on the guidelines for managing Covid-19 edition 3, the length of isolation for moderate severity is calculated from 10 days after the onset of symptoms plus a minimum of 3 days without symptoms of fever and respiratory problems (PDPI et al., 2020). This means that the patient's recovery time

can differ for each individual due to several factors such as severity, immunity, and patient comorbidities.

### 3.3. The Correlation of Early Antivirals Treatment and Length of Recovery Covid-19 Patients

In **Table 3** the results of the correlation analysis are presented between the speed of administration of antivirals and the length of time to recover.

**Table 3.** The Correlation of Early Antivirals Treatment and Length of Recovery Covid-19 Patients

| Kolmogorov-Smirnov Test | Spearman's rho | | |
|---|---|---|---|
| Sig. | N | Sig. | Coeff. |
| 0.001 | 94 | 0.000 | 0.659 |

Explanation:
   Sig:    Significance
   N  :    Number of data
   Coeff: Coefficient of Correlation

The results of the study found that there was a relationship between the speed of giving antivirals and the length of recovery for Covid-19 patients with a positive and strong relationship. This is in line with the case studies that have been conducted by Wu et al., (2020) found that patients who received earlier and timely initiation of antiviral treatment were significantly correlated with the average Covid-19 recovery time with a correlation coefficient of 0.785 and a P value <0.001. The results of this research, which show that there is a correlation, can be used as a guideline in the management of Covid-19 to place more importance on giving antivirals as early as possible and on time after the appearance of symptoms and establishing a diagnosis so that the development of the virus in the body can be prevented from spreading from the start where the viral load is still small and has not spread area so that the patient's recovery time is faster. Giving antivirals quickly and precisely can potentially speed up patients' recovery and increase therapy success, bearing in mind that giving antivirals earlier will prevent more Covid-19 virus replication. The results of this study also prove that the antiviral therapy used at Cirebon "X" Hospital in the Covid-19 treatment pattern has good effectiveness against the Covid-19 virus so that the recovery process during hospitalization in the isolation room is following the guidebook. Management of Covid-19 edition 3.

### 3.4. The Correlation of Severity and Length of Recovery Covid-19 Patients

In **Table 4** the following presents the results of an analysis of the relationship between the severity of the recovery time for Covid-19 patients.

**Table 4.** Correlation of Severity and Length of Recovery Covid-19 Patients

| Kolmogorov-Smirnov Test | Spearman's rho | | |
|---|---|---|---|
| Sig. | N | Sig. | Coeff. |
| 0.000 | 94 | 0.113 | 0.165 |

Explanation:
   Sig.   : Significance
   N      : Number of data
   Coeff : Coefficient of Correlation

The study results showed no relationship between the severity level and the length of recovery for Covid-19 patients at Cirebon "X" Hospital. This is not in line with the research that has been done Wu et al., (2020), where patients who have a severe level of severity (2.50-18.70 days) can experience a much longer recovery period compared to the mild group (1.93-10.63 days) with a P-Value <0.001.

Many factors can cause differences between the results of these studies, namely comorbid illnesses, early administration of antivirals, levels of anxiety, and enthusiasm to recover for each Covid-19 patient, which can underlie the severity and prognosis of Covid-19 patients (Wu et al.,

2020). The most influencing factors cannot be determined precisely; of course, it depends on the patient's condition in the presence or absence of comorbidities, the administration of appropriate antivirals, and the enthusiasm of the patient to recover.

**3.5. The Correlation of The Early Antivirals Treatment and Severity of Covid-19 Patients**

The most important strategy for overcoming a pandemic is to prevent it from spreading broader, meaning that the spread of the Covid-19 virus needs to be fought as early as possible through early recognition of the virus and early antiviral treatment (Peng et al., 2020). Although there are no transparent clinical trials, early timing of antiviral therapy can reduce the severity of the disease and prevent the development of Covid-19 disease (Xu et al., 2020). The results of the analysis of the relationship between the speed of administration of antivirals and the severity of Covid-19 are presented in **Table 5**.

**Table 5.** Correlation of The Early Antivirals Treatment and Severity of Covid-19 Patients

| *Kolmogorov-Smirnov Test* | *Spearman's rho* | | |
|---|---|---|---|
| **Sig.** | **N** | **Sig.** | **Coeff.** |
| 0.000 | 94 | 0.297 | 0.109 |

Explanation:
   Sig  : Significance
   N    : Number of data
   Coeff  : Coefficient of Correlation

This study is not in line with the previous theory because there was no relationship between the speed of administration of antivirals and the severity of Covid-19 patients at Gunung Jati Hospital, Cirebon. This is also irrelevant to the results of research that has been conducted by Wu et al., (2020), which shows that early antiviral treatment can significantly slow the development of Covid-19 and improve patient prognosis with the obtained Odds Ratio (OR) value of 11.63 and P value of 0.001. This can happen because of the number of samples and different research methods.

This research is in line with Chron et al., (2020); even though patients had been given antiviral therapy, the mortality rate was still high (23%), and those who arrived earlier for hospitalization within 3 days of onset of symptoms and longer duration of hospitalization could therefore have a higher rate of organ failure compared with patients who came to the hospital after 1 week after the onset of symptoms had a mortality rate of 5% and a shorter length of stay.

In this study, there were several research limitations that made the research results less than optimal. There were discrepancies with what researchers expected, such as incomplete medical record data, a limited number of samples, laboratory results were not analyzed (such as blood tests, other co-infections, blood sugar, coagulation, and others), treatment of comorbidities or other diseases suffered by patients, radiological results, the guidelines for the management of Covid-19 used by researchers are different from studies that have been conducted in China, no observations were made of other supporting drugs for Covid-19 (such as antibiotics, supplements, convalescent plasma, and others), this study was conducted retrospectively. Hence, there is a possibility of causing recall bias which cannot be ruled out.

## 4. CONCLUSION

There is no correlation between severity and length of recovery, and there is no correlation between the early antiviral treatment and severity. However, the authors found a correlation that the earlier Covid-19 patients were given antiviral treatment, the patient prognosis would improve rapidly. It is therefore recommended that antiviral treatment be started on time and as early as possible while the viral load is low.

## 5. ACKNOWLEDGMENT

## 6. CONFLICT OF INTEREST

The author states that there is no conflict of interest in this research.

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