


## *Antiviral and Symptom Free Days for Confirmed Covid-19 Students*

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### **Abstract**

*Introduction: The limitations of health service facilities mean that Covid-19 case services are only for moderate and severe cases, while asymptomatic/mild cases are advised to self-isolate. The availability of antivirals for self-isolation patients is often limited, so the patient's recovery rate can be longer. The purpose of this study was to determine the difference in symptom-free days in Covid-19 patients who received and did not receive antivirals. Method: This type of analytic research is observational with a cross sectional approach. The research sample was 93 UMS students who were confirmed to have COVID-19 in March 2020 - August 2021. The research data was obtained by an online questionnaire. Data analysis was performed using the Mann Whitney test. Results: There were 32 self isolation Covid-19 patients who received antivirals (34.4%). In these patients, the symptom free days were 8.9 days; while the 61 patients (65.6%) who did not receive antivirals reported a symptom free day of 12.2 days. The Mann Whitney test obtained a p value = 0.023 indicating that there was a difference in symptom free days between Covid-19 patients who received and did not receive antivirals. Conclusion: Giving antivirals to self isolation Covid-19 patients shortens symptom free days.*

**Keywords:** Covid-19; self isolation; antiviral; symptom free day

## **Perbedaan Hari Bebas Keluhan Pasien Isolasi Mandiri yang Mendapat Antivirus**

### **Abstrak**

Latar Belakang: Keterbatasan fasilitas layanan kesehatan menyebabkan pelayanan kasus Covid-19 hanya diperuntukkan bagi kasus sedang dan berat, sedangkan kasus asimtomatik/ringan disarankan untuk melakukan isolasi mandiri (isoman). Ketersediaan antivirus untuk pasien isoman seringkali terbatas, sehingga tingkat kesembuhan pasien dapat lebih lama. Tujuan: Tujuan penelitian ini mengetahui perbedaan hari bebas keluhan pada pasien Covid-19 isoman yang mendapat dan tidak mendapat antivirus. Metode: Jenis penelitian analitik observasional dengan pendekatan cross sectional. Sampel penelitian 93 mahasiswa UMS terkonfirmasi covid-19 bulan Maret 2020 - Agustus 2021. Data-data penelitian diperoleh dari pembagian kuesioner secara daring. Analisis data dilakukan dengan uji *Mann Whitney*. Hasil: Pasien Covid-19 isoman yang mendapat antivirus berjumlah sebanyak 32 orang (34,4%). Pada pasien tersebut hari bebas keluhan adalah selama 8,9 hari; sedangkan dari 61 pasien (65,6%) yang tidak mendapat antivirus melaporkan hari bebas keluhan selama 12,2 hari. Uji *Mann Whitney* didapatkan nilai p = 0,023 menunjukkan bahwa terdapat perbedaan hari bebas keluhan antara pasien Covid-19 isoman yang mendapat dan tidak mendapat antivirus. Kesimpulan: Pemberian antivirus pada pasien Covid-19 isoman mempersingkat hari bebas keluhan.

**Kata kunci:** Antivirus; hari bebas keluhan; covid-19; isolasi mandiri

## 1. Introduction

Coronavirus disease 2019 (Covid-19) is a new disease that was first discovered in Wuhan China on December 31, 2019, and because of its very fast rate of spread, this disease was declared a pandemic by WHO on March 11, 2020. Covid-19 is caused by a virus. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2)[1]. The choice of antiviral use in the management of Covid-19 is very diverse, WHO recommends the use of chloroquine, a combination of ritonavir and lopinavir, a combination of ribavirin, ritonavir and lopinavir, darunavir, favipiravir, umifenovir, and nomaferon, and remdesivir that has passed phase 2 and 3 clinical trials. Several antivirals are being considered for Covid-19 therapy and some are in clinical trials. Provisional evidence shows the efficacy of remdesivir as a candidate for clinical improvement for Covid-19 in March 2020, namely that it can inhibit SARS-CoV-2 in vitro [2]. Phase 3 clinical trials of remdesivir are underway in the US, in China and in Italy [3]. The International Consensus of Pulmonologists recommends remdesivir, lopinavir/ritonavir, ribavirin, oseltamivir, and chloroquine/hydroxychloroquine, as well as other agents such as baricitinib darunavir/cobicistat, umifenovir, favilavir, and galidesivir [4].

According to *The Indonesian Food and Drug Authority* (2020) although there are no clinical comparison results of various types of antivirals in the treatment of Covid-19, according to the literature there are several potentially effective drugs that can be used for Covid-19 infection including chloroquine, hydroxychlorokine, azithromycin, favipiravir, lopinavir-ritonavir, and others. Treatment options can be tailored to the patient's condition, and affordability. However, the combination of several antiviral drugs should be avoided because their safety is still debatable [3]. Due to the very fast rate of disease transmission, and limited health care facilities, which are more focused on moderate and severe cases of Covid-19, asymptomatic cases or mild symptoms are advised to self-isolation [5]. However, the availability of antivirals for self isolation patients is often limited. Although in the end self isolation patients also recovered, but the recovery can be longer than patients who receive antivirals. The identification of symptom free days in confirmed COVID-19 patients who are self isolation between those receiving and not receiving antivirals appears to have not been well explored, so it is important to investigate.

## 2. Methods

This type of research is analytic observational with a cross sectional design. The sample of this study was a total of 93 confirmed Covid-19 UMS students from various faculties and departments who performed self isolation between March 2020-August 2021. Students who were recruited as samples were those who were proven to be confirmed positive for Covid-19, were willing to participate in the study, signed the informed consent, filled out the questionnaire completely, and was an active student attending lectures. Students with comorbidities such as heart disease, chronic lung disease, cancer, diabetes mellitus, obesity and hypertension were excluded from this study. The research data was obtained from distributing questionnaires online (on the network) using Google Form. The length of the symptomfree day is calculated on the day the student is confirmed positive for Covid-19 and no longer complains of symptoms. Antiviral status was differentiated between patients who received and did not receive antivirals. The type of antivirus you get can be favipiravir/avigan or oseltamivir. Hypothesis testing was carried out with the Mann Whitney test at p below 0.05. This study was in accordance with the research protocol and met the principles of research ethics as evidenced by the approval of given by the research sample

and approval by the Health Research and Ethics Commission of the Medical Faculty of UMS Number: 1.087 / XII / HREC / 2021.

### 3. Results and Discussion

#### Characteristics of Research Samples

The characteristics of students who are confirmed to be Covid-19 are shown in Table 1. Age characteristics showed that almost all patients were in the age range of 18-25 years (95.7%) or classified as late teens. Some of the patients (64.5%) were women, and most were from the general medical faculty (21.5%) while the least were from the economics and architectural engineering faculties with 1.1% each.

**Table 1.** Characteristics of confirmed Covid-19 patients

| Sample characteristics      | n  | %    |
|-----------------------------|----|------|
| Age group                   |    |      |
| 18-25 years old             | 89 | 95.7 |
| 26-35 years old             | 4  | 4.3  |
| Gender                      |    |      |
| Man                         | 33 | 35.5 |
| Woman                       | 60 | 64.5 |
| Faculty                     |    |      |
| General medicine            | 20 | 21.5 |
| Dentistry                   | 13 | 14   |
| Economy                     | 1  | 1.1  |
| Islam                       | 2  | 2.2  |
| Science of nutrition        | 4  | 4.3  |
| Public health               | 5  | 5.4  |
| Physiotherapy               | 6  | 6.5  |
| Communication & informatics | 3  | 3.2  |
| Nursing                     | 3  | 3.2  |
| Pharmacy                    | 15 | 16.1 |
| FKIP                        | 13 | 14   |
| Law                         | 3  | 3.2  |
| Industry                    | 4  | 4.3  |
| Architecture                | 1  | 1.1  |

## Perception of Danger Level and Description of Covid-19 Status

Descriptions of student perceptions regarding the level of danger of Covid-19 as well as a description of the disease are shown in Table 2. Half of the patients (50.5%) stated that Covid-19 was a very dangerous disease. The origin of Covid-19 transmission was obtained from family members (49.5%), followed by infection from the surrounding environment (29%) and the least infected from the workplace (1.1%). According to smoking history, almost all patients did not smoke (96.8%). Almost all patients (92.5%) said they were symptomatic and 7.5% said they were asymptomatic. In symptomatic patients, the most frequently reported duration of symptoms was 8-14 days (by 53.5% of patients).

**Table 2.** Description of Perception of Danger Level and Status of Covid-19

| Description                                | n  | %    |
|--|----|------|
| Perception of the danger level of covid-19 | n  | %    |
| Not harmful                                | 1  | 1.1  |
| Just the same                              | 4  | 4.3  |
| Quite dangerous                            | 41 | 44.1 |
| Very dangerous                             | 47 | 50.5 |
| Origin of transmission                     |    |      |
| Do not know                                | 6  | 6.5  |
| Public places                              | 9  | 9.7  |
| Celebration                                | 2  | 2.2  |
| Surrounding environment                    | 27 | 29   |
| Family                                     | 46 | 49.5 |
| Hospital                                   | 2  | 2.2  |
| Workplace                                  | 1  | 1.1  |
| Smoke                                      |    |      |
| Yes  | 3  | 3.2  |
| Not  | 90 | 96.8 |
| Symptom                                    |    |      |
| With                                       | 86 | 92.5 |
| Without                                    | 7  | 7.5  |
| Symptoms days                              |    |      |
| ≤7 days                                    | 26 | 28   |
| 8-14 days                                  | 51 | 54.8 |
| > 14 days                                  | 16 | 17.2 |

## Description of self isolation status and antiviral usage

Next is a description of self isolation status and antiviral usage which is presented in Table 3. Some patients (60.2%) did self isolation between 10 - 14 days, and the rest (39.8%) did self isolation <10 days. The place/location of self isolation is the patient's house (77.4%). Most of the patients (94.6%) stated that they were taking medication and the level of adherence to taking medication was 82.8%. The number of patients who received antivirals was less (34.4%) than those who did not receive antivirals (65.6%). The average symptom free days were between 8-14 days, which was indicated by 54.8% of patients, followed by symptom free days <7 days in 28% of patients and symptom free days >14 days in 17.2% of patients. Post-self isolation symptoms reported by 37,6 %.

**Table 3.** Description of Self isolation and Uses of Antivirus

| Description of Self isolation and Uses of Antivirus | n  | %    |
|---|----|------|
| Days of self isolation                              |    |      |
| < 10 days   | 37 | 39.8 |
| 10 – 14 days  | 56 | 60.2 |
| > 14 days   | 0  | 0.0  |
| Self isolation location                             |    |      |

| Description of Self isolation and Uses of Antivirus | n  | %    |
|---|----|------|
| UMS hostel/hostel                                   | 13 | 14   |
| Hotel   | 1  | 1.1  |
| Boarding house                                      | 2  | 2.3  |
| House   | 73 | 78.5 |
| Hospital area                                       | 3  | 3.2  |
| Centralized facilities                              | 1  | 1.1  |
| Take medicine                                       |    |      |
| Yes   | 88 | 94.6 |
| Not   | 5  | 5.4  |
| Compliance with taking medication                   |    |      |
| Yes   | 77 | 82.8 |
| Not   | 16 | 17.2 |
| Got antiviral                                       |    |      |
| Yes   | 32 | 34.4 |
| Not   | 61 | 65.6 |
| Symptom free days                                   |    |      |
| ≤7 days   | 26 | 28.0 |
| 8-14 days   | 51 | 54.8 |
| > 14 days   | 16 | 17.2 |
| Symptoms of post self isolation                     |    |      |
| Yes   | 35 | 37.6 |
| No  | 58 | 62.4 |

### Differences in symptom free days according to anti-viral treatment

Table 4 shows that the average symptom free days in the group of patients receiving antivirals was  $8.9 \pm 3.51$  days; while in the group of patients who did not receive antivirals it was  $12.2 \pm 8.80$  days ( $p = 0.023$ ). Students with confirmed Covid-19 who received antiviral had faster symptom free days compared to students who did not receive antiviral.

**Table 4.** The results of the analysis of the difference in Covid-19 symptom free days according to the provision of antiviral

| Giving antiviral  | n  | Mean $\pm$ SD   | <i>p-value</i> |
|-------------------|----|-----------------|----------------|
| Yes               | 32 | $8.9 \pm 3.51$  | 0.098*         |
| Not               | 61 | $12.2 \pm 8.80$ | 0.000**        |
| <i>p-value</i> ** |    | 0.023***        |                |

n = number of patients, \* = Shapiro Wilk test, \*\* = Kolmogorov Smirnov test, \*\*\* = Mann Whitney test

## Discussion

Self isolation patients who received antivirals showed shorter symptom free days, namely  $8.9 \pm 3.51$  days, while patients who did not receive antivirals experienced symptom free days at  $12.2 \pm 8.80$  days. These findings are relevant to the systematic review reported by Rejo et al. that the administration of an antiviral (remdesivir) resulted in faster symptom free days (9-10 days) than in patients who were not given antivirals [6]. Guidelines for the management of Covid-19, whether published for the first time or the latest, recommend the use of antivirals in mild to moderate self isolation patients [7]. In this study, the types of antiviral given to self isolation patients were oseltamivir or favipiravir (avigan).

Giving antiviral can shorten the symptom free days, this is because each antiviral has an anti-infection mechanism. Remdesivir is a type of nucleotide analog drug that works by inhibiting viral RNA dependent RNA polymerase (RdRp), so that viral RNA stops prematurely and inhibits Covid-19 virus replication at an early stage [8]. Favipiravir is an antiviral recommended for emergency use. This drug has a mechanism of action similar to remdesivir, namely inhibiting the RdRp virus (influenza) and is a prodrug with the active

form of favipiravir-RTP and is a CYP2C8 inhibitor, while oseltamivir is a prodrug of oseltamivir carboxylate and is a neuramidase inhibitor in the Cov-2 virus which also functions to inhibit replication. Virus [9].

Symptom free days in this study were also associated with the onset of symptoms exhibited by the patients. Patients with symptom onset <7 days experienced fewer symptom free days (11.1 days) than patients with symptom onset 8-14 days (11.49 days) and >14 days (13 days). This could be due to psychological effects, where patients with a longer onset of symptoms experience an anxiety syndrome so that it can slow down the recovery of their clinical condition. Anxiety due to Covid-19 can trigger psychological reactions that have an impact on biological reactions and trigger the hormone cortisol so that it disrupts emotional stability. This can affect the immune system. Deficiency Immunity can weaken the body's ability to fight the malignancy of the Covid-19 virus so that the recovery rate will take longer [10].

Patients who have a smoking habit were not excluded from this study because of the limited number of study samples. However, these two did not become a confounding factor in the relationship between antiviral use and Covid-19 symptom free days. In this study, the patient's anxiety condition was unknown, so that was one of the limitations of this study. Another limitation is not knowing the reason why after self isolation, there are patients who still feel symptoms of Covid-19. Another factor that is thought to affect the symptom free day is the support of family or closest people. The results of previous studies stated that family support provided important benefits for the patient's recovery. Providing support to patients can prevent patients from feeling anxious/depressed and increase the patient's enthusiasm to fight the disease so that the recovery rate can be obtained faster [11]. The family support given to patients was also unknown in this study, in terms of the location of self isolation, more patients underwent self isolation at home but the symptom free days were longer (11 days) than patients who underwent isolation at the hotel (7 days), boarding house (8 days), or a friend's house (7 days).

Covid-19 patients who live with their families may still receive adequate support. Patients with Covid-19 who live far from their families find it more difficult to obtain the necessary support. During this pandemic, social support becomes even more important. Many Covid-19 patients who live far from their families receive social support from their friends, neighbors, teachers, co-workers or others [12]. The social support received by this patients after they were infected with covid-19 taught them to be more empathetic towards their surroundings. Furthermore, this social support is thought to improve the physical and mental health of covid-19 patients [13].

Many students were not recruited in this study because not all who were exposed to Covid-19 had their conditions checked or went to health care facilities to be confirmed positive/negative for Covid-19. Symptom free days in this study may also be caused by the symptomatic drug obtained. This study also has a weakness, namely that it has only been carried out on a student population who has no comorbidities, and a swab evaluation is not carried out to determine whether or not the patient has recovered. The sample of this study was also not differentiated according to when the initial time of administration of antiviral was carried out, and the clinical degree of the disease was not identified by laboratory examination and doctors judgement whether it was mild or moderate.

## 4. Conclusion

Giving antivirals to self isolation patients can shorten the days of symptoms or it can also be said that giving antivirals accelerates the achievement of symptom free days. However, this research still needs to be followed up with similar studies that consider the



anxiety factor in patients and their family support, also consider the time factor for initial administration of antivirals, the degree of disease, the presence of comorbidities, and the results of the swab evaluation. The community should provide support in any form, even if it is small, because it is very important for Covid-19 patients healing processed.

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