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Wahyuhadi J *et al.*

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Dear Joni Wahyuhadi

Therapy for Asymptomatic and Mild Cases of COVID-19 patients in Indonesia
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60825
Indonesia

The APC for this article, once any discounts have been taken into account, is $1350.00

If you have any questions, please contact us as soon as possible.

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Dear Joni

Therapy for Asymptomatic and Mild Cases of COVID-19 patients in Indonesia Therapy for Asymptomatic and Mild Cases of COVID-19 patients in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

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Attached below is the revised manuscript for publication. Thank you very much for your assistance.

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Thank you for sending us your amended manuscript, and for your hard work on this so far.

There are a few queries which haven't been addressed in the attached, or which have arisen from your edits, so can you please take a look at the attached and address any outstanding queries?

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Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia

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Abstract

Background: Though coronavirus disease 2019 (COVID-19) has been designated as a global pandemic, its nature as a viral infection means that it is essentially a self-limiting disease. We studied the application of symptomatic, isolation, relaxation, nutrition and observation (SIRNO) therapy in patients with asymptomatic and mild symptoms of COVID-19 at a rescue hospital in Indonesia.

Methods: This is a retrospective cohort study involving 2122 patients who were admitted to Indrapura Field Hospital in Surabaya from 28 May 2020 to 20 September 2020. We analyzed demographic data, clinical signs and symptoms, laboratory data, therapy and clinical outcomes.

Result: The total sample of 2122 patients consisted of 1403 male patients (66.12%), and 719 female patients (33,88 %). The most common age range was 26-45 years, at 52.54% (1115 patients). The clinical symptoms of 1121 patients (52.8%) were asymptomatic, 977 patients (46%) had mild symptoms, and 24 patients (0.1%) had moderate symptoms. All patients received the SIRNO therapy method. From a total of 2122 patients, 1930 patients (90.9%) were cured, 181 patients (8.5%) are still being treated, seven patients (0.03%) were referred for indications of desaturation (SpO2 <94%), and four patients (0.01%) were moved to a referral hospital. Until 20 September 2020 as the final date studied, there were no patient deaths.

Conclusion: The SIRNO method provides excellent results in the management of COVID-19 at a rescue hospital for patients with asymptomatic and mild symptoms. Economic pharmacological research can initiate a follow-up study in order to objectively measure the effectiveness and efficiency of SIRNO treatment methods in patients with asymptomatic, mild symptoms of COVID-19, and the small number of 24 patients (0,1%) with moderate symptoms.

Keywords: Symptomatic, Isolation, Relaxation, Nutrition, Observation, COVID-19

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Introduction

Coronavirus disease 2019 (COVID-19) is a global public health issue that was confirmed as a pandemic in March 2020. Defined by the World Health Organization (WHO), COVID-19 is caused by a new coronavirus called the 2019-novel coronavirus (2019-nCoV)(1). However, the International Committee on Taxonomy of Viruses named the novel coronavirus as "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2)(2).

On September 21, 2020, a total of 30,675,675 confirmed COVID-19 cases were reported in more than 216 countries, including 954,417 deaths, resulting in a mortality rate of 3.1%. In Indonesia, the total number of cases was 248,852 with a death rate of 9,677, while in East Java the total number of cases was 40,708 (16.35%) with a mortality rate of 7.28 %, or 2,695 patients(3). As the number of COVID-19 sufferers in some countries continues to increase, as well as the deaths resulting from it, epidemiological studies are very important in order to determine the source of transmission and devise effective and efficient therapeutic methods(4). Although the understanding of COVID-19 epidemiology continues to develop, it is assumed that SARS-CoV-2 is primarily transmitted through droplets and close contact with a person that is carrying the virus(4) and the likelihood of death strongly depends on the methods of therapy and comorbidities found in patients.

COVID-19 has a very wide clinical output, from asymptomatic to severe and

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critical symptoms; more than 75% cases are asymptomatic cases(5). Among those symptomatic patients, clinical presentations of this include fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocytes count, and radiography evidence of pneumonia(6). Severe complications can include organ dysfunction, including shock, acute respiratory distress syndrome (ARDS), acute heart injury and acute kidney injury. These manifestations may continue and lead to death(7). The WHO recommended therapies for asymptomatic and mild symptomatic COVID-19 cases are symptomatic, isolation, and observation related to complaints as well as monitoring of vital signs and the progress of the disease. In addition, highly nutritional therapy(8) and relaxation are also needed in the form of light exercise, communication with fellow patients, a psychological approach and calming of the patient's soul with spiritual lectures and studies into religion, as well as a relaxed atmosphere in the hospital(9). This approach was based on the nature of viral infection which is a self-limiting disease. Viruses that enter the body will be countered by our body's defense system, either non-specific, natural or specific by antibodies.

If the body's non-specific defenses are unable to prevent the virus, then the virus will enter the cell, damage the cell and replicate itself. Antiviral drugs specifically for SARS-COV-2 are still in clinical trials, the administration of antiviral side effects damages the body's cells, so the type, time and dosage of its administration must be precise, in

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addition the effectiveness of virusidal against the virus that causes COVID-19 has not yet been empirically proven. A review of the economic pharmacology also needs to be considered, the efficiency and effectiveness of therapy is key to the success of the therapy method(10).

Kogabwilhan II Indrapuara Field Hospital is a specialized hospital that treats COVID-19 patients, which is confirmed by swab results with positive PCR (Polymerase Chain Reaction) examination infected with SARS-COV-2. The hospital was established for the treatment and isolation of COVID-19 patients without symptoms and with mild symptoms, in an effort to support COVID-19 services in existing referral hospitals. The initiator of the establishment of Indrapuara Field Hospital was the COVID-19 Control Task Force of East Java Province, with financing from the National Disaster centre and fully supported by the Provincial Government of East Java, military regional command V Brawijaya, East Java regional police, the Ministry of Health and the Commander of Joint Command Region II.

The purpose of this study is to describe application of symptomatic, isolation, relaxation, nutrition, and observation (SIRNO) therapy for asymptomatic and mild symptomatic patients at rescue field hospital.

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Methods

Study design

This study is a retrospective cohort study of COVID-19 patients who were admitted at Kogabwilhan II Indrapura Field Hospital from 28 May 2020 to 20 September 2020 in Surabaya, East Java Indonesia. The obtained data was downloaded from the electronic medical records with Inova Medika Solusindo application, including demographic data, clinical signs and symptoms, laboratory data, therapy and clinical outcomes (24).

Patient criteria

All patients with COVID-19 enrolled in this study diagnosed according to the guidelines for diagnostic criteria from *Clinical management of COVID-19: interim guidance* (World Health Organization, 27 May 2020). All patients suffered from the infection of SARS-CoV-2, ascertained in the laboratory (the results of RT-PCR/ Real-Time Polymerase Chain Reaction specific for SARS-CoV-2 was positive). Diagnosis of mild case patients is made based on the criteria of symptomatic patients and meets the definition of COVID-19 cases without evidence of viral pneumonia or hypoxia, and moderate cases of patients with clinical symptoms of pneumonia (fever, cough, dyspnea, rapid breathing) but no sign of severe pneumonia, including SpO2 ≥ 90% in the air of the room. All patients treated in Indrapura field hospital according to the criteria constitute the sample of the study.

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Data characteristics

Data demographic characteristics of patients were obtained with form collection from the electronic medical record. The collected information included age, gender, occupation, and domicile.

The patients' clinical data were data related to current and past patient medical history. Current signs and symptoms were fever, cough, shortness of breath, fatigue, anorexia, muscle pain, headache, chills, nausea and vomiting, diarrhea, and confusion. Patients' past history included hypertension, heart disease, diabetes, obesity, chronic obstructive pulmonary disease, liver disease. Serial vital signs included blood pressure, pulse, respiratory rate, body temperature, oxygen saturation, and body mass index. The date of onset of the disease is defined as the day when symptoms are first known. Determination of COVID-19 positivity was based on RT-PCR SARS-CoV-2 from naso/oropharyngeal swabs which were collected on the day of admission and evaluated when patients were discharged. Clinical outcome data, including recovery rates, length of treatment, referred cases and death cases, were also analyzed in this study.

SIRNO therapy

Symptomatic by providing therapy according to the complaints felt by the patient, such as

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the administration of antipyretics, anti diarrhea, decongestan, antitussive and so on.

Isolation by dividing into red zones for patients, which are not mixed between patients and service providers. The room includes a bed space, space for rest and a field for outdoor activities, as well as a garden.

Relaxation by doing gymnastics activities on the field, as well as deep breathing exercises. In addition, there are karaoke activities while still using masks and keeping distance, and regular spiritual and religious lectures and stress management.

Nutrition provided is adjusted to the patient's caloric needs and comorbidity. The type of food provided should also meet the balance of macro nutritional needs such as carbohydrates, proteins, fats, vitamins, and minerals.

Observations are divided into three shifts, each shift will enter the isolation zone for 3 hours to observe the patient's vital signs, complaints and progress. During observation, patients can also consult both physical and mental complaints such as sleep difficulty and restlessness. Patients can also contact the care team at any time online.

All patients are not given antiviral therapy or antibiotics.

Statistical analysis

Statistical analysis was performed using SPSS Version 24. All continuous data is presented as a mean ± standard deviation (SD) or median ± interquartile range (IQR). Categorical data

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is presented as numbers and percentages.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Dr. Soetomo Teaching Hospital (Surabaya, Indonesia), and Universitas Airlangga Faculty of Medicine (Surabaya, Indonesia). All participants have provided written consent for the usage of their data for research purposes.

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Results

Clinical characteristics

From the research period of 28 May to 20 September 2020, a total of 2122 patients were found to fit the research criteria. Of these, 1403 patients (66.12%) were men, with the most common age range of study subjects being 26-45 years of age at 52.54% (1115 patients), while 27.33% were 46-65 years, 17.58% were 12-25 years, 1.51% were 6-11 years and 1.03% were over 65 years. In total, 1656 patients were treated without comorbidities (78%) and 466 patients had comorbidities (21.9%). The most common comorbidities were hypertension, at 286 patients (13.47%), diabetes mellitus at 84 patients (3.95%), while 59 patients (2.78%) were obese. A small number of patients also had various comorbidities such as bronchial asthma, hypertensive heart disease, and coronary heart disease. In terms of patient occupation demographics, 946 patients (44.58%) worked as a private employee, followed by 219 patients (10.3%) as military and police, 130 patients (6.1%) as civil servants, and 73 patients (3.4%) as medical personnel, with details of 68 nurses (3.20%), four doctors (0.18%), and one midwife (0.04%) (Table 1).

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Signs and symptoms

Of the COVID-19 patients that were treated at Indrapura field hospital, there were 1121

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patients (52.8%) without complaint, 977 patients (46%) with mild symptoms, and 24 patients (0.1%) with moderate symptoms. The most common symptoms of COVID-19 were coughing in 325 patients (15.3%), followed by a cold in 132 patients (6.2%), anosmia in 110 patients (5.1%), fever in 93 patients (4.3%), nausea in 47 patients (2.2%), headaches in 46 patients (2.1%), and shortness of breath in 39 patients (1.8%). There were also other symptoms that patients complained about such as abdominal pain and diarrhea in 38 patients (1.7%) (Table 2).

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Swab RT-PCR SARS-CoV-2 results

All RT-PCR SARS-CoV-2 swab results were positive for patients treated at Indrapura field hospital. Recovered patients are patients with missing or mildly tolerated clinical symptoms after treatment without symptomatic drugs, and for whom swabs have been negative as much as two times. After leaving the hospital, 181 patients (8.5%) gave feedback related to post-treatment re-swab examination. Of these 181 patients, there were 52 patients (28.7%) who re-examined after exiting the Indrapura field hospital, while 129 patients (71.3%) did not do the re-swab. A total of 19 patients (37.3%) did the re-examination after more than 15 days of returning home, followed by eight patients (15.3%) on the 14th day, and the rest did the examination on the 6th day. Of the 52 patients who did the re-swab, we found 43 patients (82.8%) with negative results, and 9 patients (17.2%) with positive results (Table 2).

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Therapy

All patients treated in Indrapura field hospital received SIRNO therapy which was symptomatic (such as antitussive, expectorant, antipyretic, decongestan, bronchodilator), and involved isolation, relaxation, nutrition, and observation. In addition, patients also received therapy for comorbidities. Until 20 September 2020, 1907 patients (89.87%)

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received multivitamin therapy (Becefort), 337 patients (15.8%) received N-acetyl cystein therapy 200mg (NAC), 227 patients (10.6%) received decongestant therapy (such as Tremenza and Flutrop), 171 patients (8%) received paracetamol, and 97 patients (4.5%) received lorazepam for anxiety disorders. For hypertensive comorbid therapy, 197 patients (9.28%) received Amlodipine therapy 10mg and 190 patients (8.95%) received Amlodipine 5mg, while 26 patients (1.2%) received candesartan therapy 16mg and 21 patients (0.98%) received Candesartan 8mg. Patients with comorbid diabetes (as many as 37 patients, or 1.74%) received metformin therapy 500mg, Glimepiride therapy 2mg was received by 43 patients (2%), and 16 patients (0.75%) received insulin (Apidra, Novorapid, and Levemir). All patients in Indrapura field hospital had no antiviral therapy, nor corticosteroids (Table 3).

Clinical outcomes

From a total of 2122 patients, 1930 patients (90.9%) were cured, and 181 patients (8.5%) are still being treated. There were seven patients (0.03%) referred for indications of desaturation (SpO2 <94%), and four patients (0.01%) moved to a referral hospital. No patient died or returned home on their own request (0%). The highest number of patients treated in the Indrapura field hospital based on average length of stay (LOS) was in the group with a LOS of less than 7 days, which was 1399 patients in total (72.48%), followed by the group with a LOS of 8-14 days with 417 patients (21.6%), the group with a LOS of

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15-21 days with 91 patients (4.71%), and the group with a LOS of 22-28 with 20 patients (1.04%). Additionally, three patients (0.15%) were treated with a LOS of more than 28 days (Table 3).

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Discussion

COVID-19 has been reported to have caused the deaths of more than one million people, and the nature of viral infection remains a concern of many medical doctors worldwide. As for the asymptomatic and mild symptom cases, isolation and supportive therapy is the recommended approach(11). The clinical outcome was mainly affected by patient comorbidities, including old age, chronic metabolic diseases, obesity and long term viral exposure(12). Our data showed various medical comorbidities, with the most common being hypertension and diabetes mellitus. In addition, occupation-based analysis showed most patients were private employees, followed by military and police and civil servants. These occupations were occupations with high risk for contact with other people and high risk for COVID-19 infection(3).

In this study, there were 1238 patients without complaint (58.3%), 325 patients complained of coughing (15.3%), followed by 132 flu patients (6.2%), 110 anosmia patients (5.1%), and 93 fever patients (4.3%). Complaints of nausea, headache, tightness, abdominal pain, and diarrhea were less common. Gastrointestinal complaints were not found in COVID-19 patients in this study. Based on previous research by Ge *et al*, in 2019, we conducted retrospective research on confirmed patients for 10 months and obtained clinical manifestations of patients infected with SARS-CoV-2, ranging from mild non-specific symptoms to severe pneumonia with damage to organ function(13) Common symptoms are

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fever (77.4–98.6%), cough (59.4–81.8%), fatigue (38.1–69.6%), dyspepsia (3.2–55.0%), myalgia (11.1–34.8%), sputum production (28.2–56.5%), and headaches (6.5-33.9%)(13). Sore throat, rinorhea, chest pain, hemoptysis, conjunctiva congestion, diarrhea, nausea, and vomiting were less frequent(14). One study showed that 39.6% of the 140 confirmed COVID-19 patients had gastrointestinal symptoms, and 10.1% of patients experienced gastrointestinal discomfort at the onset(13). SARS-CoV-2, SARS-CoV, and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) infections have many similar clinical symptoms, including fever, cough, myalgia, and dyspnea(15). However, patients with SARS and MERS had more gastrointestinal symptoms (about a third) than COVID-19 patients(16).

The latest guidelines for the treatment of COVID-19 patients indicate that suspected and confirmed cases should be treated in isolated hospitals with effective isolation and protection conditions(17). As for asymptomatic and mild COVID-19 cases, the WHO recommends that COVID-19 patients are given symptomatic treatments such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration(7). In this study, it was found that all patients treated at Indrapura field hospital did not get antiviral therapy. The procedures were provided in the form of isolation, observation, and supportive therapy, symptomatic therapy, multivitamins, nutrition, and therapies for comorbidities such as amplodipine for hypertension, then therapy to reduce symptoms such as N-acetyl cystein

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(NAC), decongestants, and paracetamol. Indeed, there were several anti-viral drugs available for treating COVID-19 patients. Of the three clinical cohort studies, oseltamivir was used for antiviral therapy in 35.8% of patients, 89.9% of patients, and 92.7% of patients(18). Another study involved 99 COVID-19 patients, of which 76% received antiviral treatment, including oseltamivir, ganciclovir, and lopinavir and ritonavir tablets, with the duration of antiviral treatment is 3-14 days. Although oseltamivir was widely used in early cohort studies, its effectiveness in treating COVID-19 has not been so clear(13). To date, there is no evidence to recommend any specific anti-COVID-19 treatment.

Large-scale RCT (Randomized Controlled trial) COVID-19 drugs are still ongoing. The current use of chloroquine, hydroxychloroquine, oseltamivir, lopinavir/ritonavir, favipiravir, and remdesivir in COVID-19 management is currently based on small-scale clinical studies, which are not enough to draw strong conclusions about its efficacy and safety. Based on clinical pharmacological reviews, the decision to use this drug during the COVID-19 pandemic should consider its potential benefits and risks for patients, as the drug is likely to be effective, available and affordable, with the lowest risk to patients and the public(19). Therefore, the administration of antivirals is not recommended for infections with no symptoms. To date, isolation and close observation are still considered as better options for asymptomatic patients(20).

With this procedure, in this study, the obtained clinical outcome is 1399 patients

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(72.48%) with a LOS of less than 7 days, followed by 417 patients (21.6%) with a LOS of 8-14 days, 91 patients (4.71%) with a LOS of 15-21 days, 20 patients (1.04%) with a LOS of 22-28 days, and three patients (0.15%) were treated with a LOS of more than 28 days. In addition, eight patients were referred for clinical worsening indications, two patients moved hospitals, and one patient was in self-isolation. After leaving the hospital, there were 181 patients (8.5%) which gave feedback related to post-treatment re-swab examination. Of these 181 patients, there were 52 patients (28.7%) who were re-examined after exiting the Indrapura field hospital, while 129 patients (71.3%) did not do the re-swab. A total of 19 patients (37.3%) did re-examination after more than 15 days of returning home, followed by eight patients (15.3%) on the 14th day, and the rest did the examination on the sixth day. Of the 52 patients who did the re-swab, we found 43 patients (82.8%) with negative results, and nine patients (17.2%) with positive results.

There were several limitations to this study. Firstly, the included subjects in this study were asymptomatic and mild symptom patients without any comparison between the treated and untreated groups, hence we could not generate a good conclusion. Secondly, this study only covers one location with mostly Javanese patients. Since Indonesia does not only consist of Javanese people, a multi-center study involving more patients will give a more comprehensive understanding of the management of COVID-19 patients in Indonesia.

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Conclusion

The conclusion of this study is that SIRNO method provides excellent output in the management of COVID-19 at Indrapura field hospital. Economic pharmacological research can perform a follow-up study in order to objectively measure the effectiveness and efficiency of SIRNO treatment methods in asymptomatic and mild symptomatic infections of COVID-19.

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Data availability

Figshare: Demographic Information Indrapura Field Hospital Surabaya, Indonesia 2122.xlsx. https://doi.org/10.6084/m9.figshare.14412464.v2 (24)

The project contains the following underlying data:

- Demographic Information Indrapura Field Hospital Surabaya, Indonesia 2122.xlsx (Description of data file)

The data are not publicly available due to restrictions for ethical reasons, their containing information that could compromise the privacy of research participants. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Grant information

Declaration of interest

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Ethics Approval and consent to participate¶

The study protocol was approved by the Ethics Committee of Dr. Soetomo Teaching Hospital (Surabaya, Indonesia), and Universitas Airlangga Faculty of Medicine (Surabaya, Indonesia).¶

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Consent for Publication¶

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If your work was not funded by any grants, please state: 'The author(s) declared that no grants were involved in supporting this work'.

All authors declare there is no potential conflict of interest

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Acknowledgements¶

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Table Legends

Table 1. Demographic characteristics of patients at Indrapura Region II Joint Command Field Hospital

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Patient Demographics (n = 2122)	Value (%)
Gender	
Male	1403 (66.12%)
Female	719 (33.8%)
Age	
6-11 years	32 (1.51%)
12-25 years	373 (17.58%)
26-45 years	1115 (52.54%)
46-65 years	580 (27.33%)
> 65 years	22 (1.03%)
Occupation	
Private Employee	946 (44.58%)
Military and Police	219 (10.3%)
Civil Servant	130 (6.1%)
Student	123 (5.8%)
Company Employee	94 (4.43%)
Housewife	85 (4%)
Nurse	68 (3.2%)
Teacher	64 (3%)
Doctor	4 (0.18%)
Midwife	1 (0.04%)
Others (Retired, Unemployment)	388 (18.3%)
Comorbidity	
No comorbid	1656 (78%)
Hypertension	286 (13.47%)
Diabetes mellitus	84 (3.95%)
Obesity	59 (2.78%)
Asthma	12 (0.56%)
Hypertension Heart Disease	7 (0.33%)
Others (CHD, stroke, HIV)	18 (0.85%)

CHD: Coronary Heart Disease; HIV: Human Immunodeficiency Virus

Table 2. Clinical characteristics of patients at Indrapura Region II Joint Command Field

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Characteristics (n = 2122)	Value (%)
Severity	
No Symptoms	1121 (52.82%)
Mild	977 (46.04%)
Moderate	24 (1.13%)
Severe	0 (0%)
General Symptoms	
Cough	325 (15.3%)
Cold	132 (6.2%)
Anosmia	110 (5.1%)
Fever	93 (4.3%)
Nausea	47 (2.2%)
Headache	46 (2.1%)
Dyspnea	39 (1.8%)
Others (Abdominal pain, diarrhea)	38 (1.7%)
Swab RT-PCR SARS-CoV-2	
Positive	2122 (100%)
Feedback post-treatment	181 (8.5%)
Didn't do the re-swab	129 (71.3%)
Did the re-swab	52 (28.7%)
Re-swab >15 days	19 (37.3%)
Re-swab on day 14	8 (15.3%)
Re-swab on day 6	25 (48%)
Negative	43 (82.8%)
Positive	9 (17.2%)

RT-PCR SARS-CoV-2: *Reverse-Transcriptase Polymerase Chain Reaction Severe Acute Respiratory Syndrome Coronavirus 2*

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Table 3. Characteristics of therapy and clinical outcomes of patients at Indrapura

Region II Joint Command Field Hospital

Characteristics (n = 2122)	Value (%)
Symptomatic Therapy	
Multivitamins	1907 (89.87%)
N-acetylcystein 200mg	337 (15.8%)
Decongestants	227 (10.6%)
Paracetamol	171 (8%)
Lorazepam	97 (4.5%)
Comorbid Therapy	
Amlodipine 10mg	197 (9.28%)
Amlodipine 5mg	190 (8.95%)
Candesartan 16mg	26 (1.2%)
Candesartan 8mg	21 (0.98%)
Metformin 500mg	37 (1.74%)
Glimepiride 2mg	43 (2%)
Insulin	16 (0.75%)
Antiviral Therapy	0 (0%)
Corticosteroids Therapy	0 (0%)
Clinical Outcomes	
Cured	1930 (90.9%)
Being Treated	181 (8.5%)
Referred	7 (0.03%)
Died	0 (0%)
Length of Treatment	
< 7 days	1399 (72.48%)
8-14 days	417 (21.6%)
15-21 days	91 (4.71%)
22-28 days	20 (1.04%)
> 28 days	3 (0.15%)

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Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia

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Abstract

Background: Though coronavirus disease (COVID-19) has been designated as a global pandemic, its nature as a viral infection means that it is essentially a self-limiting disease. We studied the application of symptomatic, isolation, relaxation, nutrition and observation (SIRNO) therapy in patients with asymptomatic and mild symptoms of COVID-19 at a rescue hospital in Indonesia.

Methods: This is a retrospective cohort study involving 2122 patients who were admitted to Indrapura Field Hospital in Surabaya from 28 May 2020 to 20 September 2020. We analyzed demographic data, clinical signs and symptoms, laboratory data, therapy and clinical outcomes.

Result: The total sample of 2122 patients consisted of 1403 male patients (66.12%), and 719 female patients (33.88 %). The most common age range was 26-45 years, at 52.54% (1115 patients). The clinical symptoms of 1121 patients (52.8%)were asymptomatic, 977 patients (46%) had mild symptoms, and 24 patients (0.1%) had moderate symptoms. All patients received the SIRNO therapy method. From a total of 2122 patients, 1930 patients (90.9%) were cured, 181 patients (8.5%) are still being treated, seven patients (0.03%) were referred for indications of desaturation (SpO2 <94%), and four patients (0.01%) were moved to a referral hospital. Until 20 September 2020, the final date studied, there were no patient deaths.

Conclusion: The SIRNO method provides excellent results in the management of COVID-19 at a rescue hospital for patients with asymptomatic and mild symptoms. Economic pharmacological research can initiate a follow-up study in order to objectively measure the effectiveness and efficiency of SIRNO treatment methods in patients with asymptomatic, mild symptoms of COVID-19, and the small number of 24 patients (0,.1%) with moderate symptoms.

Keywords: Symptomatic, Isolation, Relaxation, Nutrition, Observation, COVID-19

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Introduction

Coronavirus disease (COVID-19) is a global public health issue that was confirmed as a pandemic in March 2020. Defined by the World Health Organization (WHO), COVID-19 is caused by a new coronavirus called the 2019-novel coronavirus (2019-nCoV)(1). However, the International Committee on Taxonomy of Viruses named the novel coronavirus as "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2)(2).

On September 21, 2020, a total of 30,675,675 confirmed COVID-19 cases were reported in more than 216 countries, including 954,417 deaths, resulting in a mortality rate of 3.1%. In Indonesia, the total number of cases was 248,852 with a death rate of 9,677, while in East Java the total number of cases was 40,708 (16.35%) with a mortality rate of 7.28 %, or 2,695 patients (3). As the number of COVID-19 sufferers in some countries continues to increase, as well as the deaths resulting from it, epidemiological studies are very important in order to determine the source of transmission and devise effective and efficient therapeutic methods (4). Although the understanding of COVID-19 epidemiology continues to develop, it is assumed that SARS-CoV-2 is primarily transmitted through droplets and close contact with a person that is carrying the virus (4) and the likelihood of death strongly depends on the methods of therapy and comorbidities found in patients.

COVID-19 has a very wide clinical output, from asymptomatic to severe and

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COVID-19 has a very wide clinical output, from asymptomatic to severe and critical symptoms; more than 75% cases are asymptomatic cases(4). Among those symptomatic patients, clinical presentations of this include fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocytes count, and radiography evidence of pneumonia(5). Severe complications can include organ dysfunction, including shock, acute respiratory distress syndrome (ARDS), acute heart injury and acute kidney injury. These manifestations may continue and lead to death(6). The WHO recommended therapies for asymptomatic and mild symptomatic COVID-19 cases are symptomatic, isolation, and observation related to complaints as well as monitoring of vital signs and the progress of the disease. In addition, highly nutritional therapy(7) and relaxation are also needed in the form of light exercise, communication with fellow patients, a psychological approach and calming of the patient's soul

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critical symptoms; more than 75% cases are asymptomatic cases (5). Among those symptomatic patients, clinical presentations of this include fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocytes count, and radiography evidence of pneumonia(6). Severe complications can include organ dysfunction, including shock, acute respiratory distress syndrome (ARDS), acute heart injury and acute kidney injury. These manifestations may continue and lead to death (7). The WHO recommended therapies for asymptomatic and mild symptomatic COVID-19 cases are symptomatic, isolation, and observation, related to complaints as well as the monitoring of vital signs and the progress of the disease. In addition, highly nutritional therapy (8) and relaxation are also needed in the form of light exercise, communication with fellow patients, a psychological approach and calming of the patient with spiritual lectures and studies into religion, as well as a relaxed atmosphere in the hospital (9). This approach was based on the nature of viral infection which is a self-limiting disease. Viruses that enter the body will be countered by our body's defense system, either naturally via non-specific defences, or specific antibodies.

If the body's non-specific defenses are unable to prevent the virus, then the virus will enter the cell, damage the cell and replicate itself. Antiviral drugs specifically for SARS-COV-2 are still in clinical trials, the administration of antiviral side effects damages the body's cells, so the type, time and dosage of its administration must be precise. In

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addition the effectiveness of virusidal against the virus that causes COVID-19 has not yet been empirically proven. A review of the economic pharmacology also needs to be considered, the efficiency and effectiveness of therapy is key to the success of the therapy method (10).

Kogabwilhan II Indrapuara Field Hospital is a specialized hospital that treats COVID-19 patients, which is confirmed by swab results with positive PCR (polymerase chain reaction) examination infected with SARS-COV-2. The hospital was established for the treatment and isolation of COVID-19 patients without symptoms and with mild symptoms, in an effort to support COVID-19 services in existing referral hospitals. The initiator of the establishment of Indrapuara Field Hospital was the COVID-19 Control Task Force of East Java Province, with financing from the National Disaster centre and fully supported by the Provincial Government of East Java, military regional command V Brawijaya, East Java regional police, the Ministry of Health and the Commander of Joint Command Region II.

The purpose of this study is to describe application of symptomatic, isolation, relaxation, nutrition, and observation (SIRNO) therapy for asymptomatic and mild symptomatic patients at rescue field hospital.

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Methods

Study design

This study is a retrospective cohort study of COVID-19 patients who were admitted at Kogabwilhan II Indrapura Field Hospital from 28 May 2020 to 20 September 2020 in Surabaya, East Java Indonesia. The obtained data was downloaded from the electronic medical records with the Inova Medika Solusindo application, including demographic data, clinical signs and symptoms, laboratory data, therapy and clinical outcomes (24).

Patient criteria

All patients with COVID-19 enrolled in this study diagnosed according to the guidelines for diagnostic criteria from *Clinical management of COVID-19: interim guidance* (World Health Organization, 27 May 2020). All patients suffered from the infection of SARS-CoV-2, ascertained in the laboratory (the results of RT-PCR [real-time polymerase chain reaction] specific for SARS-CoV-2 was positive). Diagnosis of mild case patients is made based on the criteria of symptomatic patients and meets the definition of COVID-19 cases without evidence of viral pneumonia or hypoxia, and moderate cases of patients with clinical symptoms of pneumonia (fever, cough, dyspnea, rapid breathing) but no sign of severe pneumonia, including SpO2 ≥ 90% in the air of the room. All patients treated in Indrapura field hospital according to the criteria constitute the sample of the study.

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Data characteristics

Data demographic characteristics of patients were obtained with form collection from the electronic medical record. The collected information included age, gender, occupation, and domicile.

The patients' clinical data were data related to current and past patient medical history. Current signs and symptoms were fever, cough, shortness of breath, fatigue, anorexia, muscle pain, headache, chills, nausea and vomiting, diarrhea, and confusion. Patients' past history included hypertension, heart disease, diabetes, obesity, chronic obstructive pulmonary disease, liver disease. Serial vital signs included blood pressure, pulse, respiratory rate, body temperature, oxygen saturation, and body mass index. The date of onset of the disease is defined as the day when symptoms are first known. Determination of COVID-19 positivity was based on RT-PCR SARS-CoV-2 from naso/oropharyngeal swabs which were collected on the day of admission and evaluated when patients were discharged. Clinical outcome data, including recovery rates, length of treatment, referred cases and death cases, were also analyzed in this study.

SIRNO therapy

Symptomatic by providing therapy according to the complaints felt by the patient, such as

the administration of antipyretics, anti diarrhea, decongestan, antitussive and so on.

Isolation by dividing into red zones for patients, which are not mixed between patients and service providers. The room includes a bed space, space for rest and a field for outdoor activities, as well as a garden.

Relaxation by doing gymnastics activities on the field, as well as deep breathing exercises. In addition, there are karaoke activities while still using masks and keeping distance, and regular spiritual and religious lectures and stress management.

Nutrition provided is adjusted to the patient's caloric needs and comorbidity. The type of food provided should also meet the balance of macro nutritional needs such as carbohydrates, proteins, fats, vitamins, and minerals.

Observations are divided into three shifts, each shift will enter the isolation zone for 3 hours to observe the patient's vital signs, complaints and progress. During observation, patients can also consult both physical and mental complaints such as sleep difficulty and restlessness. Patients can also contact the care team at any time online.

All patients are not given antiviral therapy or antibiotics.

Statistical analysis

Statistical analysis was performed using SPSS Version 24. All continuous data is presented as a mean ± standard deviation (SD) or median ± interquartile range (IQR). Categorical data

is presented as numbers and percentages.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Dr. Soetomo Teaching Hospital (Surabaya, Indonesia), and Universitas Airlangga Faculty of Medicine (Surabaya, Indonesia). All participants have provided written consent for the usage of their data for research purposes.

Results

Clinical characteristics

From the research period of 28 May to 20 September 2020, a total of 2122 patients were found to fit the research criteria. Of these, 1403 patients (66.12%) were men, with the most common age range of study subjects being 26-45 years of age at 52.54% (1115 patients), while 27.33% were 46-65 years, 17.58% were 12-25 years , 1.51% were 6-11 years and 1.03% were over 65 years. In total, 1656 patients were treated without comorbidities (78%) and 466 patients had comorbidities (21.9%). The most common comorbidities were hypertension, at 286 patients (13.47%), diabetes mellitus at 84 patients (3.95%), while 59 patients (2.78%) were obese. A small number of patients also had various comorbidities such as bronchial asthma, hypertensive heart disease, and coronary heart disease. In terms of patient occupation demographics, 946 patients (44.58%) worked as a private employee, followed by 219 patients (10.3%) as military and police, 130 patients (6.1%) as civil servants, and 73 patients (3.4%) as medical personnel, with details of 68 nurses (3.20%), four doctors (0.18%), and one midwife (0.04%) (Table 1).

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Signs and symptoms

Of the COVID-19 patients that were treated at Indrapura field hospital, there were 1121

patients (52.8%) without complaint, 977 patients (46%) with mild symptoms, and 24 patients (0.1%) with moderate symptoms. The most common symptoms of COVID-19 were coughing in 325 patients (15.3%), followed by a cold in 132 patients (6.2%), anosmia in 110 patients (5.1%), fever in 93 patients (4.3%), nausea in 47 patients (2.2%), headaches in 46 patients (2.1%), and shortness of breath in 39 patients (1.8%). There were also other symptoms that patients complained about such as abdominal pain and diarrhea in 38 patients (1.7%) (Table 2).

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Swab RT-PCR SARS-CoV-2 results

All RT-PCR SARS-CoV-2 swab results were positive for patients treated at Indrapura field hospital. Recovered patients are patients with missing or mildly tolerated clinical symptoms after treatment without symptomatic drugs, and for whom swabs have been negative as much as two times. After leaving the hospital, 181 patients (8.5%) gave feedback related to post-treatment re-swab examination. Of these 181 patients, there were 52 patients (28.7%) who re-examined after exiting the Indrapura field hospital, while 129 patients (71.3%) did not do the re-swab. A total of 19 patients (37.3%) did the re-examination after more than 15 days of returning home, followed by eight patients (15.3%) on the 14th day, and the rest did the examination on the 6th day. Of the 52 patients who did the re-swab, we found 43 patients (82.8%) with negative results, and 9 patients (17.2%) with positive results (Table 2).

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Therapy

All patients treated in Indrapura field hospital received SIRNO therapy which was symptomatic (such as antitussive, expectorant, antipyretic, decongestan, bronchodilator), and involved isolation, relaxation, nutrition, and observation. In addition, patients also received therapy for comorbidities. Until 20 September 2020, 1907 patients (89.87%) received multivitamin therapy (Becefort), 337 patients (15.8%) received N-acetyl cystein therapy

200mg (NAC), 227 patients (10.6%) received decongestant therapy (such as Tremenza and Flutrop), 171 patients (8%) received paracetamol, and 97 patients (4.5%) received lorazepam for anxiety disorders. For hypertensive comorbid therapy, 197 patients (9.28%) received Amlodipine therapy 10mg and 190 patients (8.95%) received Amlodipine 5mg, while 26 patients (1.2%) received candesartan therapy 16mg and 21 patients (0.98%) received Candesartan 8mg. Patients with comorbid diabetes (as many as 37 patients, or 1.74%) received metformin therapy 500mg, Glimepiride therapy 2mg was received by 43 patients (2%), and 16 patients (0.75%) received insulin (Apidra, Novorapid, and Levemir). All patients in Indrapura field hospital had no antiviral therapy, nor corticosteroids (Table 3).

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Clinical outcomes

From a total of 2122 patients, 1930 patients (90.9%) were cured, and 181 patients (8.5%) are still being treated. There were seven patients (0.03%) referred for indications of desaturation (SpO2 <94%), and four patients (0.01%) moved to a referral hospital. No patient died or returned home on their own request (0%). The highest number of patients treated in the Indrapura field hospital based on average length of stay (LOS) was in the group with a LOS of less than 7 days, which was 1399 patients in total (72.48%), followed by the group with a LOS of 8-14 days with 417 patients (21.6%), the group with a LOS of 15-21 days with 91 patients (4.71%), and the group with a LOS of 22-28 with 20 patients (1.04%). Additionally,

three patients (0.15%) were treated with a LOS of more than 28 days (Table 3).

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Discussion

COVID-19 has been reported to have caused the deaths of more than one million people, and the nature of viral infection remains a concern of many medical doctors worldwide. As for the asymptomatic and mild symptom cases, isolation and supportive therapy is the recommended approach(11). The clinical outcome was mainly affected by patient comorbidities, including old age, chronic metabolic diseases, obesity and long term viral exposure(12). Our data showed various medical comorbidities, with the most common being hypertension and diabetes mellitus. In addition, occupation-based analysis showed most patients were private employees, followed by military and police and civil servants. These occupations were occupations with high risk for contact with other people and high risk for COVID-19 infection(3).

In this study, there were 1238 patients without complaint (58.3%), 325 patients complained of coughing (15.3%), followed by 132 flu patients (6.2%), 110 anosmia patients (5.1%), and 93 fever patients (4.3%). Complaints of nausea, headache, tightness, abdominal pain, and diarrhea were less common. Gastrointestinal complaints were not found in COVID-19 patients in this study. Based on previous research by Ge *et al*. in 2019, we conducted retrospective research on confirmed patients for 10 months and obtained clinical manifestations of patients infected with SARS-CoV-2, ranging from mild non-specific symptoms to severe pneumonia with damage to organ function(13) Common symptoms are

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fever (77.4–98.6%), cough (59.4–81.8%), fatigue (38.1–69.6%), dyspepsia (3.2–55.0%), myalgia (11.1–34.8%), sputum production (28.2–56.5%), and headaches (6.5-33.9%)(13). Sore throat, rinorhea, chest pain, hemoptysis, conjunctiva congestion, diarrhea, nausea, and vomiting were less frequent(14). One study showed that 39.6% of the 140 confirmed COVID-19 patients had gastrointestinal symptoms, and 10.1% of patients experienced gastrointestinal discomfort at the onset(13). SARS-CoV-2, SARS-CoV, and MERS-CoV (Middle East respiratory syndrome coronavirus) infections have many similar clinical symptoms, including fever, cough, myalgia, and dyspnea(15). However, patients with SARS and MERS had more gastrointestinal symptoms (about a third) than COVID-19 patients(16).

The latest guidelines for the treatment of COVID-19 patients indicate that suspected and confirmed cases should be treated in isolated hospitals with effective isolation and protection conditions (17). As for asymptomatic and mild COVID-19 cases, the WHO recommends that COVID-19 patients are given symptomatic treatments such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration (7). In this study, it was found that all patients treated at Indrapura field hospital did not receive antiviral therapy. The procedures were provided in the form of isolation, observation, and supportive therapy, symptomatic therapy, multivitamins, nutrition, and therapies for comorbidities such as amplodipine for hypertension, then therapy to reduce symptoms such as N-acetyl cystein (NAC), decongestants, and paracetamol. Indeed, there were several anti-viral drugs

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Deleted: such as amplodipine for hypertension, then therapy to reduce symptoms such as N-acetyl cystein (NAC), decongestants, and paracetamol. Indeed, there were several anti-viral drugs available for treating COVID-19 patients. Of the three clinical cohort studies, oseltamivir was used for antiviral therapy in 35.8% of patients, 89.9% of patients, and 92.7% of patients(21). Another study involved 99 COVID-19 patients, of which 76% received antiviral treatment, including oseltamivir, ganciclovir, and lopinavir and ritonavir tablets, with the duration of antiviral treatment is 3-14 days. Although oseltamivir was widely used in early cohort studies, its effectiveness in treating COVID-19 has not been so ... [2]

available for treating COVID-19 patients. Of the three clinical cohort studies, oseltamivir was used for antiviral therapy in 35.8% of patients, 89.9% of patients, and 92.7% of patients(18). Another study involved 99 COVID-19 patients, of which 76% received antiviral treatment, including oseltamivir, ganciclovir, and lopinavir and ritonavir tablets, with the duration of antiviral treatment being 3-14 days. Although oseltamivir was widely used in early cohort studies, its effectiveness in treating COVID-19 has not been so clear (13). To date, there is no evidence to recommend any specific anti-COVID-19 treatment. Large-scale RCT (randomized controlled trial) COVID-19 drugs are still ongoing. The current use of chloroquine, hydroxychloroquine, oseltamivir, lopinavir/ritonavir, favipiravir, and remdesivir in COVID-19 management is currently based on small-scale clinical studies, which are not enough to draw strong conclusions about its efficacy and safety. Based on clinical pharmacological reviews, the decision to use this drug during the COVID-19 pandemic should consider its potential benefits and risks for patients, as the drug is likely to be effective, available and affordable, with the lowest risk to patients and the public (19). Therefore, the administration of antivirals is not recommended for infections with no symptoms. To date, isolation and close observation are still considered as better options for asymptomatic patients (20).

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With this procedure, in this study, the obtained clinical outcome is 1399 patients (72.48%) with a LOS of less than 7 days, followed by 417 patients (21.6%) with a LOS of 8-

14 days, 91 patients (4.71%) with a LOS of 15-21 days, 20 patients (1.04%) with a LOS of 22-28 days, and three patients (0.15%) were treated with a LOS of more than 28 days. In addition, eight patients were referred for clinical worsening indications, two patients moved hospitals, and one patient was in self-isolation. After leaving the hospital, there were 181 patients (8.5%) which gave feedback related to post-treatment re-swab examination. Of these 181 patients, there were 52 patients (28.7%) who were re-examined after exiting the Indrapura field hospital, while 129 patients (71.3%) did not do the re-swab. A total of 19 patients (37.3%) did re-examination after more than 15 days of returning home, followed by eight patients (15.3%) on the 14th day, and the rest did the examination on the sixth day. Of the 52 patients who did the re-swab, we found 43 patients (82.8%) with negative results, and nine patients (17.2%) with positive results.

There were several limitations to this study. Firstly, the included subjects in this study were asymptomatic and mild symptom patients without any comparison between the treated and untreated groups, hence we could not generate a good conclusion. Secondly, this study only covers one location with mostly Javanese patients. Since Indonesia does not only consist of Javanese people, a multi-center study involving more patients will give a more comprehensive understanding of the management of COVID-19 patients in Indonesia.

Conclusion

The conclusion of this study is that SIRNO method provides excellent output in the management of COVID-19 at Indrapura field hospital. Economic pharmacological research can perform a follow-up study in order to objectively measure the effectiveness and efficiency of SIRNO treatment methods in asymptomatic and mild symptomatic infections of COVID-19.

Data availability

Figshare: Demographic Information Indrapura Field Hospital Surabaya, Indonesia 2122.xlsx. https://doi.org/10.6084/m9.figshare.14412464.v2 (24)

The project contains the following underlying data:

- Demographic Information Indrapura Field Hospital Surabaya, Indonesia 2122.xlsx

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The data are not publicly available due to restrictions for ethical reasons, their containing information that could compromise the privacy of research participants. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Grant information

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If your work was not funded by any grants, please state: 'The author(s) declared that no grants were involved in supporting this work'.

Declaration of interest

All authors declare there is no potential conflict of interest

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Table Legends

Table 1. Demographic characteristics of patients at Indrapura Region II Joint Command Field Hospital

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Patient Demographics (n = 2122)	Value (%)
Gender	
Male	1403 (66.12%)
Female	719 (33.8%)
Age	
6-11 years	32 (1.51%)
12-25 years	373 (17.58%)
26-45 years	1115 (52.54%)
46-65 years	580 (27.33%)
> 65 years	22 (1.03%)
Occupation	
Private Employee	946 (44.58%)
Military and Police	219 (10.3%)
Civil Servant	130 (6.1%)
Student	123 (5.8%)
Company Employee	94 (4.43%)
Housewife	85 (4%)
Nurse	68 (3.2%)
Teacher	64 (3%)
Doctor	4 (0.18%)
Midwife	1 (0.04%)
Others (Retired, Unemployment)	388 (18.3%)
Comorbidity	
No comorbid	1656 (78%)
Hypertension	286 (13.47%)
Diabetes mellitus	84 (3.95%)
Obesity	59 (2.78%)
Asthma	12 (0.56%)
Hypertension Heart Disease	7 (0.33%)
Others (CHD, stroke, HIV)	18 (0.85%)

CHD: Coronary Heart Disease; HIV: Human Immunodeficiency Virus

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Table 2. Clinical characteristics of patients at Indrapura Region II Joint Command Field Hospital

Characteristics (n = 2122)	Value (%)
Severity	
No Symptoms	1121 (52.82%)
Mild	977 (46.04%)
Moderate	24 (1.13%)
Severe	0 (0%)
General Symptoms	
Cough	325 (15.3%)
Cold	132 (6.2%)
Anosmia	110 (5.1%)
Fever	93 (4.3%)
Nausea	47 (2.2%)
Headache	46 (2.1%)
Dyspnea	39 (1.8%)
Others (Abdominal pain, diarrhea)	38 (1.7%)
Swab RT-PCR SARS-CoV-2	
Positive	2122 (100%)
Feedback post-treatment	181 (8.5%)
Didn't do the re-swab	129 (71.3%)
Did the re-swab	52 (28.7%)
Re-swab >15 days	19 (37.3%)
Re-swab on day 14	8 (15.3%)
Re-swab on day 6	25 (48%)
Negative	43 (82.8%)
Positive	9 (17.2%)

RT-PCR SARS-CoV-2: *Reverse-Transcriptase Polymerase Chain Reaction Severe Acute Respiratory Syndrome Coronavirus 2*

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Table 3. Characteristics of therapy and clinical outcomes of patients at Indrapura Region II Joint Command Field Hospital

Characteristics (n = 2122)	Value (%)
Symptomatic Therapy	
Multivitamins	1907 (89.87%)
N-acetylcystein 200mg	337 (15.8%)
Decongestants	227 (10.6%)
Paracetamol	171 (8%)
Lorazepam	97 (4.5%)
Comorbid Therapy	
Amlodipine 10mg	197 (9.28%)
Amlodipine 5mg	190 (8.95%)
Candesartan 16mg	26 (1.2%)
Candesartan 8mg	21 (0.98%)
Metformin 500mg	37 (1.74%)
Glimepiride 2mg	43 (2%)
Insulin	16 (0.75%)
Antiviral Therapy	0 (0%)
Corticosteroids Therapy	0 (0%)
Clinical Outcomes	
Cured	1930 (90.9%)
Being Treated	181 (8.5%)
Referred	7 (0.03%)
Died	0 (0%)
Length of Treatment	
< 7 days	1399 (72.48%)
8-14 days	417 (21.6%)
15-21 days	91 (4.71%)

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22-28 days	20 (1.04%)
> 28 days	3 (0.15%)

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Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia

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Abstract

Background: Though coronavirus disease (COVID-19) has been designated as a global pandemic, its nature as a viral infection means that it is essentially a self-limiting disease. We studied the application of symptomatic, isolation, relaxation, nutrition and observation (SIRNO) therapy in patients with asymptomatic and mild symptoms of COVID-19 at a rescue hospital in Indonesia.

Methods: This is a retrospective cohort study involving 2122 patients who were admitted to Indrapura Field Hospital in Surabaya from 28 May 2020 to 20 September 2020. We analyzed demographic data, clinical signs and symptoms, laboratory data, therapy and clinical outcomes.

Result: The total sample of 2122 patients consisted of 1403 male patients (66.12%), and 719 female patients (33.88 %). The most common age range was 26-45 years, at 52.54% (1115 patients). The clinical symptoms of 1121 patients (52.8%)were asymptomatic, 977 patients (46%) had mild symptoms, and 24 patients (0.1%) had moderate symptoms. All patients received the SIRNO therapy method. From a total of 2122 patients, 1930 patients (90.9%) were cured, 181 patients (8.5%) are still being treated, seven patients (0.03%) were referred for indications of desaturation (SpO2 <94%), and four patients (0.01%) were moved to a referral hospital. Until 20 September 2020, the final date studied, there were no patient deaths.

Conclusion: The SIRNO method provides excellent results in the management of COVID-19 at a rescue hospital for patients with asymptomatic and mild symptoms. Economic pharmacological research can initiate a follow-up study in order to objectively measure the effectiveness and efficiency of SIRNO treatment methods in patients with asymptomatic, mild symptoms of COVID-19, and the small number of 24 patients (0,.1%) with moderate symptoms.

Keywords: Symptomatic, Isolation, Relaxation, Nutrition, Observation, COVID-19

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Introduction

Coronavirus disease (COVID-19) is a global public health issue that was confirmed as a pandemic in March 2020. Defined by the World Health Organization (WHO), COVID-19 is caused by a new coronavirus called the 2019-novel coronavirus (2019-nCoV)(1). However, the International Committee on Taxonomy of Viruses named the novel coronavirus as "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2)(2).

(21) (22)On September 21, 2020, a total of 30,675,675 confirmed COVID-19 cases were reported in more than 216 countries, including 954,417 deaths, resulting in a mortality rate of 3.1%. In Indonesia, the total number of cases was 248,852 with a death rate of 9,677, while in East Java the total number of cases was 40,708 (16.35%) with a mortality rate of 7.28 %, or 2,695 patients (3). As the number of COVID-19 sufferers in some countries continues to increase, as well as the deaths resulting from it, epidemiological studies are very important in order to determine the source of transmission and devise effective and efficient therapeutic methods (4). Although the understanding of COVID-19 epidemiology continues to develop, it is assumed that SARS-CoV-2 is primarily transmitted through droplets and close contact with a person that is carrying the virus (4) and the likelihood of death strongly depends on the methods of therapy and comorbidities found in patients.

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COVID-19 has a very wide clinical output, from asymptomatic to severe and critical symptoms; more than 75% cases are asymptomatic cases(4). Among those symptomatic patients, clinical presentations of this include fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocytes count, and radiography evidence of pneumonia(5). Severe complications can include organ dysfunction, including shock, acute respiratory distress syndrome (ARDS), acute heart injury and acute kidney injury. These manifestations may continue and lead to ... [1]

COVID-19 has a very wide clinical output, from asymptomatic to severe and critical symptoms; more than 75% cases are asymptomatic cases (5). Among those symptomatic patients, clinical presentations of this include fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocytes count, and radiography evidence of pneumonia(6). Severe complications can include organ dysfunction, including shock, acute respiratory distress syndrome (ARDS), acute heart injury and acute kidney injury. These manifestations may continue and lead to death (7). The WHO recommended therapies for asymptomatic and mild symptomatic COVID-19 cases are symptomatic, isolation, and observation, related to complaints as well as the monitoring of vital signs and the progress of the disease. In addition, highly nutritional therapy (8) and relaxation are also needed in the form of light exercise, communication with fellow patients, a psychological approach and calming of the patient with spiritual lectures and studies into religion, as well as a relaxed atmosphere in the hospital (9). This approach was based on the nature of viral infection which is a self-limiting disease. Viruses that enter the body will be countered by our body's defense system, either naturally via non-specific defences, or specific antibodies.

If the body's non-specific defenses are unable to prevent the virus, then the virus will enter the cell, damage the cell and replicate itself. Antiviral drugs specifically for SARS-COV-2 are still in clinical trials, the administration of antiviral side effects damages

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the body's cells, so the type, time and dosage of its administration must be precise. In addition the effectiveness of virusidal against the virus that causes COVID-19 has not yet been empirically proven. A review of the economic pharmacology also needs to be considered, the efficiency and effectiveness of therapy is key to the success of the therapy method (10).

Kogabwilhan II Indrapuara Field Hospital is a specialized hospital that treats COVID-19 patients, which is confirmed by swab results with positive PCR (polymerase chain reaction) examination infected with SARS-COV-2. The hospital was established for the treatment and isolation of COVID-19 patients without symptoms and with mild symptoms, in an effort to support COVID-19 services in existing referral hospitals. The initiator of the establishment of Indrapuara Field Hospital was the COVID-19 Control Task Force of East Java Province, with financing from the National Disaster centre and fully supported by the Provincial Government of East Java, military regional command V Brawijaya, East Java regional police, the Ministry of Health and the Commander of Joint Command Region II.

The purpose of this study is to describe application of symptomatic, isolation, relaxation, nutrition, and observation (SIRNO) therapy for asymptomatic and mild symptomatic patients at rescue field hospital.

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Methods

Study design

This study is a retrospective cohort study of COVID-19 patients who were admitted at Kogabwilhan II Indrapura Field Hospital from 28 May 2020 to 20 September 2020 in Surabaya, East Java Indonesia. This data range was chosen as the opening date of service of the Indrapura Field Hospital for COVID-19 patients. The obtained data was downloaded from the hospital electronic medical records, including demographic data, clinical signs and symptoms, laboratory data, therapy and clinical outcomes (24).

Patient criteria

All patients with COVID-19 enrolled in this study diagnosed according to the guidelines for diagnostic criteria from *Clinical management of COVID-19: interim guidance* (World Health Organization, 27 May 2020). All patients suffered from the infection of SARS-CoV-2, ascertained in the laboratory (the results of RT-PCR [reverse transcription polymerase chain reaction] specific for SARS-CoV-2 was positive). Diagnosis of mild case patients is made based on the criteria of symptomatic patients and meets the definition of COVID-19 cases without evidence of viral pneumonia or hypoxia, and moderate cases of patients with clinical symptoms of pneumonia (fever, cough, dyspnea, rapid breathing) but no sign of severe pneumonia, including SpO2 ≥ 90% in the air of the room. All patients treated in

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Indrapura field hospital according to the criteria constitute the sample of the study.

Data characteristics

Data demographic characteristics of patients were obtained with form collection from the electronic medical record. The collected information included age, gender, occupation, and domicile.

The patients' clinical data were data related to current and past patient medical history. Current signs and symptoms were fever, cough, shortness of breath, fatigue, anorexia, muscle pain, headache, chills, nausea and vomiting, diarrhea, and confusion. Patients' past history included hypertension, heart disease, diabetes, obesity, chronic obstructive pulmonary disease, liver disease. Serial vital signs included blood pressure, pulse, respiratory rate, body temperature, oxygen saturation, and body mass index. The date of onset of the disease is defined as the day when symptoms are first known. Determination of COVID-19 positivity was based on RT-PCR SARS-CoV-2 from naso/oropharyngeal swabs which were collected on the day of admission and evaluated when patients were discharged. Clinical outcome data, including recovery rates, length of treatment, referred cases and death cases, were also analyzed in this study.

SIRNO therapy

Symptomatic by providing therapy according to the complaints felt by the patient, such as the administration of antipyretics, anti diarrhea, decongestan, antitussive and so on.

Isolation by dividing into red zones for patients, which are not mixed between patients and service providers. The room includes a bed space, space for rest and a field for outdoor activities, as well as a garden.

Relaxation by doing gymnastics activities on the field, as well as deep breathing exercises. In addition, there are karaoke activities while still using masks and keeping distance, and regular spiritual and religious lectures and stress management.

Nutrition provided is adjusted to the patient's caloric needs and comorbidity. The type of food provided should also meet the balance of macro nutritional needs such as carbohydrates, proteins, fats, vitamins, and minerals.

Observations are divided into three shifts, each shift will enter the isolation zone for 3 hours to observe the patient's vital signs, complaints and progress. During observation, patients can also consult both physical and mental complaints such as sleep difficulty and restlessness. Patients can also contact the care team at any time online.

All patients are not given antiviral therapy or antibiotics.

Statistical analysis

Statistical analysis was performed using SPSS Version 24. All continuous data is presented

as a mean ± standard deviation (SD) or median ± interquartile range (IQR). Categorical data is presented as numbers and percentages.

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Dr. Soetomo Teaching Hospital (Surabaya, Indonesia), and Universitas Airlangga Faculty of Medicine (Surabaya, Indonesia). All participants have provided written consent for the usage of their data for research purposes.

Results

Clinical characteristics

From the research period of 28 May to 20 September 2020, a total of 2122 patients were found to fit the research criteria. Of these, 1403 patients (66.12%) were men, with the most common age range of study subjects being 26-45 years of age at 52.54% (1115 patients), while 27.33% were 46-65 years, 17.58% were 12-25 years , 1.51% were 6-11 years and 1.03% were over 65 years. In total, 1656 patients were treated without comorbidities (78%) and 466 patients had comorbidities (21.9%). The most common comorbidities were hypertension, at 286 patients (13.47%), diabetes mellitus at 84 patients (3.95%), while 59 patients (2.78%) were obese. A small number of patients also had various comorbidities such as bronchial asthma, hypertensive heart disease, and coronary heart disease. In terms of patient occupation demographics, 946 patients (44.58%) worked as a private employee, followed by 219 patients (10.3%) as military and police, 130 patients (6.1%) as civil servants, and 73 patients (3.4%) as medical personnel, with details of 68 nurses (3.20%), four doctors (0.18%), and one midwife (0.04%) (Table 1).

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Signs and symptoms

Of the COVID-19 patients that were treated at Indrapura field hospital, there were 1121

patients (52.8%) without complaint, 977 patients (46%) with mild symptoms, and 24 patients (0.1%) with moderate symptoms. The most common symptoms of COVID-19 were coughing in 325 patients (15.3%), followed by a cold in 132 patients (6.2%), anosmia in 110 patients (5.1%), fever in 93 patients (4.3%), nausea in 47 patients (2.2%), headaches in 46 patients (2.1%), and shortness of breath in 39 patients (1.8%). There were also other symptoms that patients complained about such as abdominal pain and diarrhea in 38 patients (1.7%) (Table 2).

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Swab RT-PCR SARS-CoV-2 results

All RT-PCR SARS-CoV-2 swab results were positive for patients treated at Indrapura field hospital. Recovered patients are patients with missing or mildly tolerated clinical symptoms after treatment without symptomatic drugs, and for whom swabs have been negative as much as two times. After leaving the hospital, 181 patients (8.5%) gave feedback related to post-treatment re-swab examination. Of these 181 patients, there were 52 patients (28.7%) who re-examined after exiting the Indrapura field hospital, while 129 patients (71.3%) did not do the re-swab. A total of 19 patients (37.3%) did the re-examination after more than 15 days of returning home, followed by eight patients (15.3%) on the 14th day, and the rest did the examination on the 6th day. Of the 52 patients who did the re-swab, we found 43 patients (82.8%) with negative results, and 9 patients (17.2%) with positive results (Table 2).

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Therapy

All patients treated in Indrapura field hospital received SIRNO therapy which was symptomatic (such as antitussive, expectorant, antipyretic, decongestan, bronchodilator), and involved isolation, relaxation, nutrition, and observation. In addition, patients also received therapy for comorbidities. Until 20 September 2020, 1907 patients (89.87%) received multivitamin therapy (Becefort), 337 patients (15.8%) received N-acetyl cystein therapy

200mg (NAC), 227 patients (10.6%) received decongestant therapy (such as Tremenza and Flutrop), 171 patients (8%) received paracetamol, and 97 patients (4.5%) received lorazepam for anxiety disorders. For hypertensive comorbid therapy, 197 patients (9.28%) received Amlodipine therapy 10mg and 190 patients (8.95%) received Amlodipine 5mg, while 26 patients (1.2%) received candesartan therapy 16mg and 21 patients (0.98%) received Candesartan 8mg. Patients with comorbid diabetes (as many as 37 patients, or 1.74%) received metformin therapy 500mg, Glimepiride therapy 2mg was received by 43 patients (2%), and 16 patients (0.75%) received insulin (Apidra, Novorapid, and Levemir). All patients in Indrapura field hospital had no antiviral therapy, nor corticosteroids (Table 3).

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Clinical outcomes

From a total of 2122 patients, 1930 patients (90.9%) were cured, and 181 patients (8.5%) are still being treated. There were seven patients (0.03%) referred for indications of desaturation (SpO2 <94%), and four patients (0.01%) moved to a referral hospital. No patient died or returned home on their own request (0%). The highest number of patients treated in the Indrapura field hospital based on average length of stay (LOS) was in the group with a LOS of less than 7 days, which was 1399 patients in total (72.48%), followed by the group with a LOS of 8-14 days with 417 patients (21.6%), the group with a LOS of 15-21 days with 91 patients (4.71%), and the group with a LOS of 22-28 with 20 patients (1.04%). Additionally,

three patients (0.15%) were treated with a LOS of more than 28 days (Table 3).

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Discussion

COVID-19 has been reported to have caused the deaths of more than one million people, and the nature of viral infection remains a concern of many medical doctors worldwide. As for the asymptomatic and mild symptom cases, isolation and supportive therapy is the recommended approach(11). The clinical outcome was mainly affected by patient comorbidities, including old age, chronic metabolic diseases, obesity and long term viral exposure(12). Our data showed various medical comorbidities, with the most common being hypertension and diabetes mellitus. In addition, occupation-based analysis showed most patients were private employees, followed by military and police and civil servants. These occupations were occupations with high risk for contact with other people and high risk for COVID-19 infection(3).

In this study, there were 1238 patients without complaint (58.3%), 325 patients complained of coughing (15.3%), followed by 132 flu patients (6.2%), 110 anosmia patients (5.1%), and 93 fever patients (4.3%). Complaints of nausea, headache, tightness, abdominal pain, and diarrhea were less common. Gastrointestinal complaints were not found in COVID-19 patients in this study. Based on previous research by Ge *et al*. in 2019, we conducted retrospective research on confirmed patients for 10 months and obtained clinical manifestations of patients infected with SARS-CoV-2, ranging from mild non-specific symptoms to severe pneumonia with damage to organ function(13) Common symptoms are

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fever (77.4–98.6%), cough (59.4–81.8%), fatigue (38.1–69.6%), dyspepsia (3.2–55.0%), myalgia (11.1–34.8%), sputum production (28.2–56.5%), and headaches (6.5-33.9%)(13). Sore throat, rinorhea, chest pain, hemoptysis, conjunctiva congestion, diarrhea, nausea, and vomiting were less frequent(14). One study showed that 39.6% of the 140 confirmed COVID-19 patients had gastrointestinal symptoms, and 10.1% of patients experienced gastrointestinal discomfort at the onset(13). SARS-CoV-2, SARS-CoV, and MERS-CoV (Middle East respiratory syndrome coronavirus) infections have many similar clinical symptoms, including fever, cough, myalgia, and dyspnea(15). However, patients with SARS and MERS had more gastrointestinal symptoms (about a third) than COVID-19 patients(16).

The latest guidelines for the treatment of COVID-19 patients indicate that suspected and confirmed cases should be treated in isolated hospitals with effective isolation and protection conditions (17). As for asymptomatic and mild COVID-19 cases, the WHO recommends that COVID-19 patients are given symptomatic treatments such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration (7). In this study, it was found that all patients treated at Indrapura field hospital did not receive antiviral therapy. The procedures were provided in the form of isolation, observation, and supportive therapy, symptomatic therapy, multivitamins, nutrition, and therapies for comorbidities randomized control trial ()such as amplodipine for hypertension, then therapy to reduce symptoms such as N-acetyl cystein (NAC), decongestants, and paracetamol. Indeed, there were several anti-

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Deleted: such as amplodipine for hypertension, then therapy to reduce symptoms such as N-acetyl cystein (NAC), decongestants, and paracetamol. Indeed, there were several anti-viral drugs available for treating COVID-19 patients. Of the three clinical cohort studies, oseltamivir was used for antiviral therapy in 35.8% of patients, 89.9% of patients, and 92.7% of patients(21). Another study involved 99 COVID-19 patients, of which 76% received antiviral treatment, including oseltamivir, ganciclovir, and lopinavir and ritonavir tablets ... [2]

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viral drugs available for treating COVID-19 patients. Of the three clinical cohort studies, oseltamivir was used for antiviral therapy in 35.8% of patients, 89.9% of patients, and 92.7% of patients(18). Another study involved 99 COVID-19 patients, of which 76% received antiviral treatment, including oseltamivir, ganciclovir, and lopinavir and ritonavir tablets, with the duration of antiviral treatment being 3-14 days. Although oseltamivir was widely used in early cohort studies, its effectiveness in treating COVID-19 has not been so clear (13). To date, there is no evidence to recommend any specific anti-COVID-19 treatment. Large-scale RCT (randomized controlled trial) COVID-19 drugs are still ongoing. The current use of chloroquine, hydroxychloroquine, oseltamivir, lopinavir/ritonavir, favipiravir, and remdesivir in COVID-19 management is currently based on small-scale clinical studies, which are not enough to draw strong conclusions about its efficacy and safety. Based on clinical pharmacological reviews, the decision to use this drug during the COVID-19 pandemic should consider its potential benefits and risks for patients, as the drug is likely to be effective, available and affordable, with the lowest risk to patients and the public (19). Therefore, the administration of antivirals is not recommended for infections with no symptoms. To date, isolation and close observation are still considered as better options for asymptomatic patients (20).

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With this procedure, in this study, the obtained clinical outcome is 1399 patients (72.48%) with a LOS of less than 7 days, followed by 417 patients (21.6%) with a LOS of 8-

14 days, 91 patients (4.71%) with a LOS of 15-21 days, 20 patients (1.04%) with a LOS of 22-28 days, and three patients (0.15%) were treated with a LOS of more than 28 days. In addition, eight patients were referred for clinical worsening indications, two patients moved hospitals, and one patient was in self-isolation. After leaving the hospital, there were 181 patients (8.5%) which gave feedback related to post-treatment re-swab examination. Of these 181 patients, there were 52 patients (28.7%) who were re-examined after exiting the Indrapura field hospital, while 129 patients (71.3%) did not do the re-swab. A total of 19 patients (37.3%) did re-examination after more than 15 days of returning home, followed by eight patients (15.3%) on the 14th day, and the rest did the examination on the sixth day. Of the 52 patients who did the re-swab, we found 43 patients (82.8%) with negative results, and nine patients (17.2%) with positive results.

There were several limitations to this study. Firstly, the included subjects in this study were asymptomatic and mild symptom patients without any comparison between the treated and untreated groups, hence we could not generate a good conclusion. Secondly, this study only covers one location with mostly Javanese patients. Since Indonesia does not only consist of Javanese people, a multi-center study involving more patients will give a more comprehensive understanding of the management of COVID-19 patients in Indonesia.

Conclusion

The conclusion of this study is that SIRNO method provides excellent output in the management of COVID-19 at Indrapura field hospital. Economic pharmacological research can perform a follow-up study in order to objectively measure the effectiveness and efficiency of SIRNO treatment methods in asymptomatic and mild symptomatic infections of COVID-19.

Data availability

Figshare: Demographic Information Indrapura Field Hospital Surabaya, Indonesia 2122.xlsx. https://doi.org/10.6084/m9.figshare.14412464.v2 (24)

The project contains the following underlying data:

- Demographic Information Indrapura Field Hospital Surabaya, Indonesia 2122.xlsx (This is part of the article Therapy for Asymptomatic and Mild Cases of COVID-19 Patients in Indonesia)

The data are not publicly available due to restrictions for ethical reasons, their containing information that could compromise the privacy of research participants. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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If your work was not funded by any grants, please state: 'The author(s) declared that no grants were involved in supporting this work'.

Declaration of interest

All authors declare there is no potential conflict of interest

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Table Legends

Table 1. Demographic characteristics of patients at Indrapura Region II Joint Command Field Hospital

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Patient Demographics (n = 2122)	Value (%)
Gender	
Male	1403 (66.12%)
Female	719 (33.8%)
Age	
6-11 years	32 (1.51%)
12-25 years	373 (17.58%)
26-45 years	1115 (52.54%)
46-65 years	580 (27.33%)
> 65 years	22 (1.03%)
Occupation	
Private Employee	946 (44.58%)
Military and Police	219 (10.3%)
Civil Servant	130 (6.1%)
Student	123 (5.8%)
Company Employee	94 (4.43%)
Housewife	85 (4%)
Nurse	68 (3.2%)
Teacher	64 (3%)
Doctor	4 (0.18%)
Midwife	1 (0.04%)
Others (Retired, Unemployment)	388 (18.3%)
Comorbidity	
No comorbid	1656 (78%)
Hypertension	286 (13.47%)
Diabetes mellitus	84 (3.95%)
Obesity	59 (2.78%)
Asthma	12 (0.56%)
Hypertension Heart Disease	7 (0.33%)
Others (CHD, stroke, HIV)	18 (0.85%)

CHD: Coronary Heart Disease; HIV: Human Immunodeficiency Virus

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Table 2. Clinical characteristics of patients at Indrapura Region II Joint Command Field Hospital

Characteristics (n = 2122)	Value (%)
Severity	
No Symptoms	1121 (52.82%)
Mild	977 (46.04%)
Moderate	24 (1.13%)
Severe	0 (0%)
General Symptoms	
Cough	325 (15.3%)
Cold	132 (6.2%)
Anosmia	110 (5.1%)
Fever	93 (4.3%)
Nausea	47 (2.2%)
Headache	46 (2.1%)
Dyspnea	39 (1.8%)
Others (Abdominal pain, diarrhea)	38 (1.7%)
Swab RT-PCR SARS-CoV-2	
Positive	2122 (100%)
Feedback post-treatment	181 (8.5%)
Didn't do the re-swab	129 (71.3%)
Did the re-swab	52 (28.7%)
Re-swab >15 days	19 (37.3%)
Re-swab on day 14	8 (15.3%)
Re-swab on day 6	25 (48%)
Negative	43 (82.8%)
Positive	9 (17.2%)

RT-PCR SARS-CoV-2: *Reverse-Transcriptase Polymerase Chain Reaction Severe Acute Respiratory Syndrome Coronavirus 2*

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Table 3. Characteristics of therapy and clinical outcomes of patients at Indrapura Region II Joint Command Field Hospital

Characteristics (n = 2122)	Value (%)
Symptomatic Therapy	
Multivitamins	1907 (89.87%)
N-acetylcystein 200mg	337 (15.8%)
Decongestants	227 (10.6%)
Paracetamol	171 (8%)
Lorazepam	97 (4.5%)
Comorbid Therapy	
Amlodipine 10mg	197 (9.28%)
Amlodipine 5mg	190 (8.95%)
Candesartan 16mg	26 (1.2%)
Candesartan 8mg	21 (0.98%)
Metformin 500mg	37 (1.74%)
Glimepiride 2mg	43 (2%)
Insulin	16 (0.75%)
Antiviral Therapy	0 (0%)
Corticosteroids Therapy	0 (0%)
Clinical Outcomes	
Cured	1930 (90.9%)
Being Treated	181 (8.5%)
Referred	7 (0.03%)
Died	0 (0%)
Length of Treatment	
< 7 days	1399 (72.48%)
8-14 days	417 (21.6%)
15-21 days	91 (4.71%)

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22-28 days	20 (1.04%)
> 28 days	3 (0.15%)

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Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

We have now accepted your article for publication in F1000Research. It will be sent to the typesetters and a member of the Production team will send you a proof in due course.

One of our editorial team will be assisting you with the peer review process of your article, and will be your main contact once the article is published.

Best wishes,

Matthew
The Editorial Team, F1000Research

Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com> 22 Juli 2021 19.28
Kepada: editorial@f1000research.com

Dear F1000 Research

Thank you very much for your email

Please let me know where and how much the payment that we need to made

Best regards
Joni
[Kutipan teks disembunyikan]

F1000.Research <research@f1000.com> 23 Juli 2021 14.43
Kepada: Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>, "F1000.Research.Editorial" <editorial@f1000research.com>

Dear Joni,

The APC for this article is $1,350, for which you will receive an invoice soon from our accounts team. The invoice will include instructions on how to pay your APC.

Best wishes,

Matthew

[Kutipan teks disembunyikan]
[Kutipan teks disembunyikan]

> [Kutipan teks disembunyikan]
> Information Classification: General

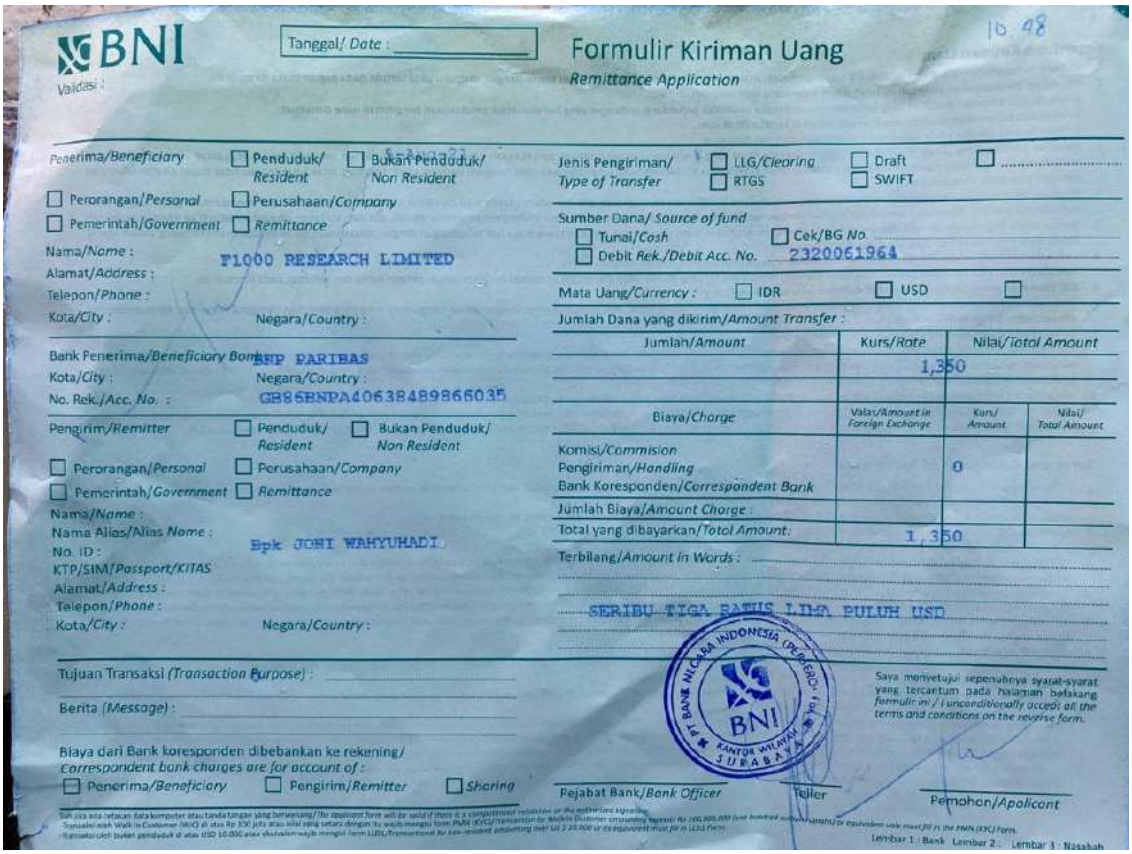
Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com> 13 Agustus 2021 20.14
Kepada: "F1000.Research" <research@f1000.com>

Dear F1000 Research Team

Attached below is the proof of payment for the article

Hopefully, the article can be published soon

Best Regards
Joni W



BNI

Tanggal/ Date :

Formulir Kiriman Uang
Remittance Application

Penerima/*Beneficiary* ☐ Penduduk/ *Resident* ☐ Bukan Penduduk/ *Non Resident*
☐ Perorangan/*Personal* ☐ Perusahaan/*Company*
☐ Pemerintah/*Government* ☐ *Remittance*
Nama/*Nome* : F1000 RESEARCH LIMITED
Alamat/*Address* :
Telepon/*Phone* :
Kota/*City* : Negara/*Country* :

Bank Penerima/*Beneficiary Bank* BNP PARIBAS
Kota/*City* : Negara/*Country* :
No. Rek./*Acc. No.* : GB86BNPA40638489866035

Pengirim/*Remitter* ☐ Penduduk/ *Resident* ☐ Bukan Penduduk/ *Non Resident*
☐ Perorangan/*Personal* ☐ Perusahaan/*Company*
☐ Pemerintah/*Government* ☐ *Remitter*
Nama/*Name* :
Nama Alias/*Alias Name* :
No. ID :
KTP/SIM/*Passport*/KITAS
Alamat/*Address* :
Telepon/*Phone* :
Kota/*City* : Negara/*Country* : Bpk JONI WAHYUHADI

Tujuan Transaksi (*Transaction Purpose*) :
Berita (*Message*) :

Biaya dari Bank koresponden dibebankan ke rekening/
Correspondent bank charges are for account of :
☐ Penerima/*Beneficiary* ☐ Pengirim/*Remitter* ☐ *Sharing*

Jenis Pengiriman/ *Type of Transfer* ☐ LLG/*Clearing* ☐ RTGS ☐ Draft ☐ SWIFT ☐
Sumber Dana/ *Source of fund*
☐ Tunai/*Cash* ☐ Cek/BG No.
☐ Debit Rek./*Debit Acc. No.* 2320061964
Mata Uang/*Currency* : ☐ IDR ☐ USD ☐
Jumlah Dana yang dikirim/*Amount Transfer* :

Jumlah/*Amount*	Kurs/*Rate*	Nilai/*Total Amount*
	1,350	

Biaya/*Charge*	Valas/*Amount in Foreign Exchange*	Kurs/ *Amount*	Nilai/ *Total Amount*
Komisi/*Commision*			
Pengiriman/*Handling*		0	
Bank Koresponden/*Correspondent Bank*			
Jumlah Biaya/*Amount Charge* :			
Total yang dibayarkan/*Total Amount*:		1,350	

Terbilang/*Amount in Words* : SERIBU TIGA RATUS LIMA PULUH USD

PT BANK NEGARA INDONESIA (PERSERO) TBK KANTOR WILAYAH JURABAYA

Saya menyetujui sepenuhnya syarat-syarat yang tercantum pada halaman belakang formulir ini / *I unconditionally accept all the terms and conditions on the reverse form.*

Pejabat Bank/*Bank Officer* Teller Pemohon/*Apolicont*

Lembar 1 : Bank Lember 2 : Lembar 3 : Nasabah

[Kutipan teks disembunyikan]

Invoice_5.PDF
32K

Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com> 17 Agustus 2021 15.35
Kepada: editorial@f1000research.com

Dear Matthew

Just to reconfirm that we already pay the publication fees, Please let us know if the payment has been accepted

Thank you
Best Regards
Joni

Pada tanggal Sel, 20 Jul 2021 pukul 17.22 <editorial@f1000research.com> menulis:

[Kutipan teks disembunyikan]

F1000.Research <research@f1000.com> 17 Agustus 2021 20.00
Kepada: Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>, "F1000.Research.Editorial" <editorial@f1000research.com>

Dear Joni,

I have sent a message to our accounts team, who deal with APC payments, to check that they've received your payment. I will let you know how they respond.

Best wishes,

Matthew

From: Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>
Sent: 17 August 2021 09:35
To: F1000.Research.Editorial <editorial@F1000Research.com>
Subject: Re: Your article 52833 is now accepted

Dear Matthew

[Kutipan teks disembunyikan]

[Kutipan teks disembunyikan]

> [Kutipan teks disembunyikan]
> Information Classification: General

F1000.Research <research@f1000.com> 19 Agustus 2021 14.23
Kepada: Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>, "F1000.Research.Editorial" <editorial@f1000research.com>

Dear Joni,

I've now heard back from our accounts team and they've confirmed receipt of your payment on the 6th of August.

Best wishes,

Matthew

From: Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>
Sent: 17 August 2021 09:35
To: F1000.Research.Editorial <editorial@F1000Research.com>
Subject: Re: Your article 52833 is now accepted

Dear Matthew

[Kutipan teks disembunyikan]

[Kutipan teks disembunyikan]

> [Kutipan teks disembunyikan]
> Information Classification: General

Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com> 31 Agustus 2021 19.18
Kepada: "F1000.Research" <research@f1000.com>

Dear F1000 Team

Thank you for the confirmation of the payment acceptance

If i may know, when will the article be published?

If there is anything that i need to provide, please let me know

Best regards
Joni
[Kutipan teks disembunyikan]

F1000.Research <research@f1000.com> 1 September 2021 14.13
Kepada: Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>, "F1000.Research" <research@f1000.com>

Dear Joni,

I can see from our notes that the production team has sent you the PDF proofs of your article, you will need to approve and return these (or specify any edits which need to be made) before the production team can continue with publication of the article. Once the PDF has been returned, your article should be published within a week.

[Kutipan teks disembunyikan]
[Kutipan teks disembunyikan]

> [Kutipan teks disembunyikan]
> [Kutipan teks disembunyikan]
>
> > [Kutipan teks disembunyikan]
> > Information Classification: General

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

The PDF of your article 52833 is ready for checking

2 pesan

production@f1000research.com <production@f1000research.com> 1 September 2021 17.49
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

Please click here to download the PDF proof of your F1000Research article.

Please find our query for this article:

1. In body text, incorrect reference citation "24" is given, whereas the specified reference is missing in reference field. Retained only the citation without reference link in body text. Kindly review and confirm whether the missing reference will be provided.

Please look through the article and let me know if it requires any corrections or if you are happy for it to be published as it is. Please also confirm the following details are correct:

- All author names are spelled correctly
- Authors are listed in the correct order
- Affiliations for all authors are accurate
- The information in the Copyright section is correct
- All figures and figure legends are correct
- All external files, including data files are correct
- All links within the article are working, and correct

Please note that connecting an ORCID account to F1000Research requires the account holder to sign in to both F1000Research and ORCID, **therefore it isn't possible for us to add ORCID badges for your co-authors on their behalf.** When the article is published, they will receive an email encouraging them to connect their ORCID account to F1000Research. If they do this, their ORCID badge will be displayed next to their name.

Corrections at this stage may require further typesetting and therefore cause some delays. If any corrections are necessary, please mark them directly on the PDF file using the commenting and markup tools in software such as Adobe Reader.

Please return your proof corrections to us via email - please note that after the article has been published, any requests for minor corrections will only be considered on a case-by-case basis. Therefore, we encourage you to check your proofs carefully at this stage.

If there are any outstanding queries on your reviewer suggestions, then we will be in touch with you shortly.

Best regards,

Jessica
The Editorial Team, F1000Research

Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com> 3 September 2021 09.53
Kepada: production@f1000research.com

Dear F1000 team

I am sorry that citation 24 actually refers to the figshare dataset. I think it can be erased

Hereby I confirmed that

- All author names are spelled correctly
- Authors are listed in the correct order
- Affiliations for all authors are accurate
- The information in the Copyright section is correct
- All figures and figure legends are correct
- All external files, including data files are correct
- All links within the article are working, and correct

Thank you very much

Best Regards
]oni Wahyuhadi

[Kutipan teks disembunyikan]

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

The PDF of your article 52833 is ready for checking

2 pesan

production@f1000research.com <production@f1000research.com> 1 September 2021 17.49
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

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Please find our query for this article:

1. In body text, incorrect reference citation "24" is given, whereas the specified reference is missing in reference field. Retained only the citation without reference link in body text. Kindly review and confirm whether the missing reference will be provided.

Please look through the article and let me know if it requires any corrections or if you are happy for it to be published as it is. Please also confirm the following details are correct:

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- Affiliations for all authors are accurate
- The information in the Copyright section is correct
- All figures and figure legends are correct
- All external files, including data files are correct
- All links within the article are working, and correct

Please note that connecting an ORCID account to F1000Research requires the account holder to sign in to both F1000Research and ORCID, **therefore it isn't possible for us to add ORCID badges for your co-authors on their behalf.** When the article is published, they will receive an email encouraging them to connect their ORCID account to F1000Research. If they do this, their ORCID badge will be displayed next to their name.

Corrections at this stage may require further typesetting and therefore cause some delays. If any corrections are necessary, please mark them directly on the PDF file using the commenting and markup tools in software such as Adobe Reader.

Please return your proof corrections to us via email - please note that after the article has been published, any requests for minor corrections will only be considered on a case-by-case basis. Therefore, we encourage you to check your proofs carefully at this stage.

If there are any outstanding queries on your reviewer suggestions, then we will be in touch with you shortly.

Best regards,

Jessica
The Editorial Team, F1000Research

Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com> 3 September 2021 09.53
Kepada: production@f1000research.com

Dear F1000 team

I am sorry that citation 24 actually refers to the figshare dataset. I think it can be erased

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- All author names are spelled correctly
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- Affiliations for all authors are accurate
- The information in the Copyright section is correct
- All figures and figure legends are correct
- All external files, including data files are correct
- All links within the article are working, and correct

Thank you very much

Best Regards
]oni Wahyuhadi

[Kutipan teks disembunyikan]

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

Your article is now published

1 pesan

production@f1000research.com <production@f1000research.com> 7 September 2021 22.44
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni,

I'm pleased to let you know that your article: "Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia" has just been published on F1000Research.

The Peer Review Process

We are now inviting the reviewers you have suggested. As part of their reports, reviewers are asked to provide a recommendation of 'Approved', 'Approved with Reservations' or 'Not Approved', and their report will be published alongside the article with their full name and affiliation. You will be able to respond to any published reports with a comment and/or by publishing revisions as a new version of your article – we will send you instructions on how to proceed when you begin to receive reports.

It is important that authors do not contact the reviewers directly, as this could result in invalidating their report.

Please note that we will ask you for additional reviewer suggestions if the invited reviewers decline. In order to avoid any delays with the peer review of your article, please continue to check your Suggest Reviewers page for updates and respond to any email requests as soon as you can.

Linking Your Data

Now that your article has been published and assigned a DOI (10.12688/f1000research.52833.1) we would strongly recommend that you include this DOI in the metadata of any published dataset associated with this article. If you would like assistance with this, please contact our editorial team.

Increasing Discoverability

Now that your article has been published, why not take advantage of the tools we provide to help maximize your article's reach and share your article using the Email and Share options on the article page.

Your article will be listed in ePMC shortly as a preprint, and then updated once it has passed peer review.

Regards

Zena Nyakoojo
Senior Managing Editor, F1000Research

Press releasing articles: Please avoid promoting articles in the media until the article has passed the open peer review process. Promotion on social media is encouraged once the article has been published; please ensure the full citation is included, as this contains the peer review status. F1000Research should be cited as the source of these articles with a link to the article.

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

First peer review report published

1 pesan

editorial@f1000research.com <editorial@f1000research.com> 4 Oktober 2021 19.16
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

We have just published a peer review report for your article on F1000Research, which you can read here.

If you wish to respond to the reviewer, please go to the link above and click 'Respond to this report' below the report. When responding to a peer review report, please try and make sure you are logged into the account that you originally used for the submission of this article, otherwise we cannot identify your response as being from an author. Please allow up to one working day for your comments to appear. If you 'Track' the article, you will automatically be alerted to any other reports or comments made.

NB: Your article will pass peer review and be indexed in PubMed, PMC, Scopus, Embase and other indexing sites, if you receive either two 'Approved' statuses, or two 'Approved with Reservations' statuses and one 'Approved' status from the reviewers.

In order to ensure that peer review proceeds quickly and you get at least one more report, we recommend that you suggest additional reviewers. Please visit Suggest Reviewers, where you will find a useful tool to help you find reviewers; you can also access this page via the article's record under My Research >> Submissions. See also our reviewer criteria and tips for finding reviewers.

We would recommend waiting for additional peer review reports before starting on any article revisions.

Best regards,

Trina
The Editorial Team, F1000Research

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

Peer review update for your article 52833

1 pesan

editorial@f1000research.com <editorial@f1000research.com> 9 Desember 2021 19.34
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

Your article has received 264 views and the PDF has been downloaded 22 times.

We have received a peer review report (with a status of: Approved with reservations) and other reviewers have agreed to review, but unfortunately their reports are very delayed, and potentially they may not be submitted. We would strongly recommend that you supply us with at least another 5 reviewer suggestions to minimize delay to the peer review process.

It sometimes happens that a reviewer who has agreed to review doesn't submit their report in a timely fashion, or doesn't provide one at all. Therefore we would recommend having some backup suggestions for reviewers to avoid any possible delay to peer review. Please send us your suggestions via Suggest Reviewers, where you will find a useful tool to help you find reviewers; you can also access this page via the article's record under My Research >> Submissions. See also our reviewer criteria and tips for finding reviewers.

Best regards,

Trina
The Editorial Team, F1000Research

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

Peer review update for your article 52833: urgent request for reviewers

1 pesan

editorial@f1000research.com <editorial@f1000research.com> 16 Desember 2021 01.06
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

I hope that you received my last email dated 09 December regarding issues with the peer review process for this article. F1000Research has an author-led peer review process, and I'm afraid without further suggestions for reviewers it is highly unlikely that your article will receive further reviews. We would strongly suggest that you supply us with at least another 5 reviewer suggestions to minimize any further delay to peer review.

Please send us your suggestions via your Suggest Reviewers page, where you will also find a useful tool to help you identify referee candidates (see also our reviewer criteria and tips for finding reviewers).

If you have any questions please don't hesitate to get in touch.

Best regards,

Trina
The Editorial Team, F1000Research

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

Peer review report published - article has not yet passed peer review

1 pesan

editorial@f1000research.com <editorial@f1000research.com> 22 Desember 2021 22.06
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

We have published another peer review report for your article in F1000Research at https://f1000research.com/articles/10-898/v1#referee-response-94781.

You have now received 2 peer review reports. Some of your reviewers had reservations and therefore your article has not yet passed peer review, which prevents it being indexed in bibliographic databases (*Once an article receives two 'Approved' statuses, or two 'Approved with Reservations' statuses and one 'Approved' status, it will be considered to have passed peer review).* Therefore, at this stage, we would encourage you to revise your article and publish a new version, together with a response to the reviewers. We will then contact the reviewers again for comments on your revision and an updated approval status.

For information on how to submit a new version, please visit Article Guidelines (new versions). Please bear in mind that new submissions need to be created and submitted using the submitting author's account.

If you wish to respond directly to the reviewer by adding a comment to their report (now, or at a later stage), please click the 'Respond to this report' button below the report. When responding to a peer review report, please try and make sure you are logged into the account that you originally used for the submission of this article, otherwise we cannot identify your response as being from an author. Please allow up to one working day for your comment to appear (comments explaining changes in the revised version of your article are usually published at the same time as the revised version).

Please kindly note our offices will be closed from 25 December to 3 January, which may cause delays in our response, but please don't hesitate to get in touch if you need any assistance, we're happy to help.

Best regards,

Trina
The Editorial Team, F1000Research

Gmail **Joni Wahyuhadi <joniwahyuhadi.rsudsoetomo@gmail.com>**

Regarding your article published in F1000Research

1 pesan

editorial@f1000research.com <editorial@f1000research.com> 22 Maret 2022 09.15
Kepada: joniwahyuhadi.rsudsoetomo@gmail.com

Dear Joni

Therapy for patients with asymptomatic and mild cases of COVID-19 in Indonesia
Wahyuhadi J, Triyono EA, Waloejo CS, Harianto A, Jaya HP, Aulia FA, Iswara ND, Harianto MA *et al.*

It's been a while since we've heard from you, so we wanted to check whether you were aware that your article has not yet passed peer review.

Your article has received peer review reports with the following status(es):

1 Approved
1 Approved with Reservations

To pass peer review, and be indexed in PubMed and Scopus, the article must receive at least two peer review reports with the status 'Approved' or at least two reports with the status 'Approved with Reservations' and one with the status 'Approved'.

Until now, we have assumed that you are in the process of revising your article in response to the peer review reports. However, as we have yet to receive your revisions, please can you update us on whether you are in the process of revising or intending to do so in the future. For information on how to submit a new version, please visit Article Guidelines (new versions).

If you need any assistance, please let us know and we will be happy to help - we look forward to hearing from you.

Best regards

Trina
The Editorial Team, F1000Research