**REAL WORLD DATA: EFFECTIVENESS OF**

**COVID-19 TREATMENT IN SEVERE SYMPTOMS PATIENTS AT RS PKU MUHAMMADIYAH GAMPING IN AUGUST**

**2022-2023**

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***Submitted: December 21, 2023 Revised: December 6, 2024 Accepted:*** ***December 20, 2024***

**ABSTRACT**

Severe COVID-19 has created significant real-world clinical challenges, particularly in the management of critically ill patients in intensive care units. The disease is often accompanied by serious complications, such as acute respiratory distress syndrome (ARDS), multiple organ damage, and increased risk of mortality, particularly in individuals with risk factors such as advanced age and comorbidities. Real World data provide evidence related to effectiveness as patients are observed from admission to discharge. This study aimed to obtain an overview of the effectiveness of COVID-19 treatment with severe symptoms at RS PKU Muhammadiyah Gamping in August 2022-2023. This observational study used a descriptive research design. Data collection was retrospective and was obtained from medical records. Descriptive analyses were conducted including patient characteristics, drug usage, and therapy effectiveness. This study obtained data from 45 patients who met the inclusion criteria for severe COVID-19. The majority of the patients were male (66.7%), aged ≥60 years (77.8%), and had hypertension as a comorbidity (21.7%). The most commonly used antiviral drugs were favipiravir (48.8%), antibiotic levofloxacin (44.4%), corticosteroid dexamethasone (53.3%), vitamin Prove C+Prove D3 (33.3%), and anticoagulant warfarin (28.9%). Therapy provided to patients with severe COVID-19 at PKU Muhammadiyah Gamping Hospital from August 2022 to 2023 yielded effectiveness percentages for each therapeutic outcome. These outcomes included SpO2 values ≥93% in 88.9% of cases, temperature improvement to <38.0°C in 88.9%, respiratory rate improvement to <30x/minute in 88.4%, improvement in cough symptoms in 84.4%, and patient discharge with recovery in 71.1%. The therapy provided to patients with severe COVID-19 at PKU Muhammadiyah Gamping Hospital from August 2022 to 2023 yielded effectiveness percentages for each therapeutic outcome. These outcomes included SpO2 values ≥93% in 88.9% of cases, temperature improvement to <38.0°C in 88.9%, respiratory rate improvement to <30x/minute in 84.4%, improvement in cough symptoms in 84.4%, and patient discharge with recovery in 71.1%.

**Keywords:** covid-19, effectiveness, real world data

# INTRODUCTION

Respiratory tract infections caused by the coronavirus disease (COVID-19) can manifest symptoms ranging from common flu-like conditions to life-threatening situations, including severe acute respiratory syndrome (SARS). The first documented case of COVID-19 was recorded in Wuhan, Hubei Province, China in December 2019. Since then, this disease has spread globally. On March 11, 2020, the World Health Organization (WHO) declared the Novel Coronavirus infection (2019-nCoV) a Public Health Emergency of International Concern (PHEIC) [(Kemenkes RI, 2022)](#kemenkes). Severe symptoms of COVID-19 are characterized by conditions such as a respiratory rate exceeding 30 breaths per minute and peripheral capillary oxygen saturation (SpO2) of 93% or lower. Additionally, elevated body temperature (>38°C), a positive result on Real-Time Polymerase Chain Reaction (RT-PCR) diagnostic testing, and complaints of cough are indicative features [(MacKenzie & Smith, 2020).](#macken)

As of the information released by the World Health Organization (WHO) on June 7, 2023, until the present moment, there have been over 7 million confirmed cases of COVID-19 worldwide, with a death toll exceeding 6 million. Based on data collected up to August 6, 2022, there were more than 1.5 million confirmed cases and over 200,000 deaths in Indonesia [(BPOM-Badan Pengawas Obat dan Makanan, 2022).](#bpom)

Since the beginning of the pandemic, several potential drug candidates have emerged for the treatment of COVID-19, including lopinavir/ritonavir, interferon alfa 2b, umifenovir, chloroquine, remdesivir, favipiravir, and anti-inflammatory drugs (such as corticosteroids and other molecules). These drugs are considered to be repurposed or off-label medications, indicating their use for purposes other than those originally intended [(Gil-Del-Valle *et al*., 2023).](#gildel)

Real World Data (RWD) refers to health-related data collected routinely, often generated from electronic health records that can provide information about health status. RWD are increasingly playing a crucial role in informing global health decision-making, particularly in Asia. The COVID-19 pandemic has accelerated the use of digital technology and has presented opportunities to expand the utilization of Real World data [(Kc *et al*., 2023).](#kcs) Real World data can provide evidence regarding the effectiveness of COVID-19 patient treatments, as patients are observed from hospital admission to discharge, and drug therapy is initiated during inpatient care. This study aimed to obtain an overview of the effectiveness of COVID-19 treatment for severe symptoms at the PKU Muhammadiyah Gamping Hospital from August 2022 to 2023.

# RESEARCH METHODS

This was an observational study that employed a descriptive research design with retrospective data collection. Data were obtained from medical records covering the period from August 2022 to 2023. Ethical approval was obtained from the Universitas Ahmad Dahlan Yogyakarta the reference number: 012309226. The sampling technique utilized in this study was purposive sampling, where the subjects were selected deliberately based on certain characteristics that are considered representative of the population and the sample is taken because it is considered important and purposive sampling allows focus on relevant groups to explore the issue.

**Research Procedure**

The research commenced in the preparation phase, which included crafting a research proposal and obtaining research ethics approval. The study involved the collection of secondary data regarding patient information acquired from patients’ medical records during hospitalization at PKU Muhammadiyah Gamping Hospital. The retrieved data pertained to the emergency department assessment, drug administration records, integrated patient progress notes (CPPT), diagnostic support results, and patient discharge summaries.

This study was conducted at PKU Muhammadiyah Gamping Hospital, involving all COVID-19 patients meeting the inclusion criteria. Inclusion criteria included patients over 18 years old diagnosed with COVID-19, receiving antiviral, antibiotic, corticosteroid, vitamin, and anticoagulant therapies; COVID-19 patients with complete medical records; patients exhibiting severe symptoms according to the classification outlined in the COVID-19 Management Guidelines, 4th Edition, 2022; and patients with severe COVID-19 symptoms. The exclusion criterion was incomplete medical records of COVID-19 patients. Operational definitions for this study included defining patients as individuals diagnosed with COVID-19 and treated at the PKU Muhammadiyah Gamping Hospital in 2022-2023. ICD-10 (International Statistical Classification of Diseases and Related Health Problems, Tenth Revision) was employed for accurate coding of COVID-19 diagnoses. The operational definition of severe symptoms of COVID-19 includes patients exhibiting clinical symptoms such as a respiratory rate >30 breaths per minute and SpO2 ≤93% [(MacKenzie & Smith, 2020)](#macken). COVID-19 therapy refers to the management of patients with COVID-19. In this context, therapy involves the administration of antiviral, antibiotic, corticosteroid, vitamin, and anticoagulant treatments to patients [(Burhan *et al*., 2022)](#burhan), and the outcomes of the therapy involve monitoring various parameters to assess its effectiveness. The therapeutic outcomes utilized were SpO2 data, temperature, Respiratory Rate (RR), and subjective data such as cough and mortality. Effectiveness was defined as the percentage of patients with therapeutic outcomes of SpO2, temperature, Respiratory Rate, subjective data such as cough, and mortality from each parameter reaching normal values.

Data Analysis

The analysis was conducted descriptively, encompassing patient characteristics obtained from medical records (age, gender, education, marital status, comorbidities), and the use of antiviral, antibiotic, corticosteroid, vitamin, and anticoagulant medications, including the specific drug names. Therapeutic outcomes derived from medical record data include SpO2, temperature, Respiratory Rate (RR), subjective data such as cough and mortality, and whether they improve after receiving antiviral, antibiotic, corticosteroid, vitamin, and anticoagulant therapy. The collected data were then subjected to descriptive analysis and presented in percentage (%) format.

# RESULTS AND DISCUSSION

This research was conducted on COVID-19 patients at PKU Muhammadiyah Gamping Hospital between August 2022 and 2023. Research ethics approval was obtained from Universitas Ahmad Dahlan Yogyakarta under reference number 012309226. The total study population comprised 306 patients, of whom 45 met the inclusion criteria. Patient characteristics were categorized based on gender, age, and comorbidities.

Based on the research findings, the majority of patients were male, totaling 30 patients (66.7%), with the majority of patients aged over 60 years, totaling 35 patients (77.8%). The education level of the majority was below or equivalent to high school, with 38 patients (84.4%), and the most common comorbidity was hypertension, with 10 patients (21.7%).

In this study, the majority of patients were male, accounting for 66.7%. This result was higher than the findings of [Seftiya and Kosala (2021)](#seftiya), which showed that 57.5% of COVID-19 patients in North Kalimantan were male. [Maler' study (2022)](#maler) reported that 56.7% of COVID-19 patients were male. Another study by [Naya *et al.,* (2022)](#naya) found that 53.4% of COVID-19 patients were male. The description of patient characteristics can be observed in **Table I**.

**Table I. Demographic Characteristics of COVID-19 Patients with Severe Symptoms**

|  |  |  |
| --- | --- | --- |
| **Characteristics** | **Number of Patients**  **(n=45)** | **Percentage (%)** |
| **Gender** | | |
| Man | 30 | 66.7 |
| Woman | 15 | 33.3 |
| **Age** | | |
| >60 Years | 35 | 77.8 |
| ≤60 Years | 10 | 22.2 |
| **Comorbidity** | | |
| Hypertension | 10 | 21.7 |
| Hypertension+Diabetes mellitus | 6 | 13.0 |
| Hypertension+Stroke | 4 | 8.7 |
| Diabetes mellitus | 3 | 6.5 |
| Hypertension+Cardiovascular | 3 | 6.5 |
| Stroke | 2 | 4.3 |
| Hypertension+Stroke+Diabetes Mellitus | 2 | 4.3 |
| No Comorbidities | 2 | 4.3 |
| COPD | 1 | 2.2 |
| CKD | 1 | 2.2 |
| Myasthemia gravis | 1 | 2.2 |
| Hypertension+CKD | 1 | 2.2 |
| Hypertension+Asthma | 1 | 2.2 |
| Hypertension+ALS | 1 | 2.2 |
| Hypertension+ALO | 1 | 2.2 |
| Hypertension+COPD | 1 | 2.2 |
| DM+CKD | 1 | 2.2 |
| DM+Cardiovascular | 1 | 2.2 |
| Stroke+Diabetes Mellitus | 1 | 2.2 |
| Hypertension+Stroke+Asthma | 1 | 2.2 |
| Hypertension + Diabetes Mellitus + Cardiovascular | 1 | 2.2 |

This disease tends to affect males more than females [(Nanda, 2021).](#nanda) Women (XX) were more influenced by the X chromosome than were men (XY). The female immune system is more dominant than that of males because of the association of the X chromosome with numerous genes related to both the innate and adaptive immune systems, along with various effectors that regulate the activity of cytokine receptors and act as mediators and regulators of the immune system [(Sarvasti, 2020).](#sarvasti) Women have a higher percentage of CD4+ T cells in their immune system due to the presence of the X gene on the chromosome, strengthening their defense against viral infections and inflammation. After viral infection, women produce less inflammatory interleukin-6 than men, and this correlates with higher survival rates in women. Compared with men, women generate more antibodies, and their levels persist longer in the bloodstream [(Conti, 2020).](#conti)

In this study, the majority of the patients were aged ≥60 years (82 %). This result is lower than the findings of [Naya *et al.* (2022),](#naya) where the highest prevalence of COVID-19 occurred in the elderly group (84.5 %). Another study conducted by [Amartya Noor *et al.,* (2023)](#amartya), reported that 68% of COVID-19 patients fell within the age range of 60-65 years.

In addition to gender, advanced age can increase the risk of contracting COVID-19. This is because individuals aged ≥ 60 years often suffer from chronic diseases, making them more vulnerable to virus infections. Weakening immune defenses makes it challenging for the body to combat infections, and reduced elasticity of lung tissues increases susceptibility to diseases such as COVID-19, and inflammation can pose a threat, leading to organ [damage (Nanda, 2021)](#nanda). This study aligns with research by [Suhaera *et al.,* (2022)](#suhaera) as aging and COVID-19 are interrelated due to the aging process causing a decline in the anatomy and physiology of the body, rendering individuals more susceptible to diseases. Existing comorbidities also weaken the body and increase the risk of COVID-19.

Comorbidities refer to concurrent diseases accompanying COVID-19, obtained from patient medical records. The majority of the comorbidities in this study were hypertension (21.7 %). This result is lower than the findings of [Salsabilla *et al.* (2023),](#salsabilla) who indicated that the highest comorbidity among COVID-19 patients was hypertension (60.5 %).

The immune system functions less effectively in the presence of concurrent diseases. Individuals with hypertension may experience decreased immunity, limiting their ability to produce antibodies useful in fighting infectious diseases [(Hong *et al.,* 2020)](#hong). ACE-2 receptors, which are often found in the heart and respiratory system, are the entry mechanism of SARS-CoV-2 into the human body. Therefore, individuals with cardiovascular comorbidities, such as hypertension, are more likely to contract COVID-19 and experience more severe clinical symptoms [(Rahayu *et al.,* 2021).](#rahayu)

The therapy profile results for COVID-19 patients with severe symptoms at PKU Muhammadiyah Gamping Hospital revealed that favipiravir was used in 48.9% of cases, levofloxacin in 44.4%, dexamethasone in 53.3%, proven C+Prove D3 in 33.3%, and warfarin in 28.9%. The results are presented in **Table II**.

**Table II. Therapy Profile of COVID-19 Patients with Severe Symptoms**

|  |  |  |  |
| --- | --- | --- | --- |
| **Drug Class** | **Drug Name** | **(n=45)** | **(%)** |
| Antivirus | Favipiravir | 22 | 48.9 |
| Remdesivir | 18 | 40.0 |
| Favipiravir+Remdesivir | 3 | 6.7 |
| Not Using Antivirus | 2 | 4.4 |
| Antibiotics | Levofloxacin | 20 | 44.4 |
| Not Using Antibiotics | 6 | 13.3 |
| Azitromicyn | 4 | 8.9 |
| Ceftriaxone | 3 | 6.7 |
| Ceftazidime+Levofloxacin | 3 | 6.7 |
| Ceftazidime | 1 | 2.2 |
| Azitromicyn+Levofloxacin | 1 | 2.2 |
| Ceftazidime+Azitromicyn | 1 | 2.2 |
| Ceftriaxone+Cefixime | 1 | 2.2 |
| Levofloxacin+Meropenem | 1 | 2.2 |
| Ceftriaxone+Azitromicyn+Cefotaxime | 1 | 2.2 |
| Cefixime+Azitromicyn+Ceftriaxone | 1 | 2.2 |
| Ceftriaxone+Ceftazidime+Levofloxacin+Azitromicyn | 1 | 2.2 |
| Azitromicyn+Ceftriaxon | 1 | 2.2 |
| Corticosteroids | Dexamethasone | 24 | 53.3 |
| Do not use corticosteroids | 12 | 26.7 |
| Methylprednisolone | 6 | 13.3 |
| Hydrokortisone | 1 | 2.2 |
| Methylprednisolone+Dexamethasone | 1 | 2.2 |
| Dexamethasone+Hydrokortisone | 1 | 2.2 |
| Vitamin | Prove C+Prove D3 | 15 | 33.3 |
| Prove C+Prove D3+Neurosanbe | 14 | 31.1 |
| Not Using Vitamins | 3 | 6.7 |
| Prove D3 | 3 | 6.7 |
| Mecobalamin | 3 | 6.7 |
| Mecobalamin+Neurosanbe+Prove D3+Prove C | 2 | 4.4 |
| Prove C | 1 | 2.2 |
| Mecobalamin+Prove D3 | 1 | 2.2 |
| Neurosanbe+Peove C | 1 | 2.2 |
| Prove C+Vitamin B+Prove D3 | 1 | 2.2 |
| Prove D3+Mecobalamin+Prove C | 1 | 2.2 |
| Anticoagulants | Not Using Anticoagulants | 24 | 53.3 |
| Warfarin | 13 | 28.9 |
| Heparin | 1 | 2.2 |
| Enoxaparin | 4 | 8.9 |
| Warfarin+Enoxaparin | 1 | 2.2 |
| Warfarin+Fondaparinux | 1 | 2.2 |
| Enoxaparin+Rivaroxaban | 1 | 2.2 |

Based on the medical records of COVID-19 patients with severe symptoms at PKU Muhammadiyah Gamping Hospital, the use of antiviral favipiravir amounted to 48.9%. These findings were lower than those reported by [Haqim *et al*. (2023)](#haqim), where the use of antiviral favipiravir was reported to be 54.24%. In patients with mild to severe or critical symptoms, favipiravir is recommended as therapy according to the COVID-19 Management Guidelines in Indonesia. Another study conducted by [Satriyani *et al*. (2023)](#satriyani), involving patients with moderate, severe, and critical COVID-19, showed that 99 patients (50.8%) were treated with favipiravir.

Favipiravir works selectively and has the potential to inhibit the RNA-dependent RNA polymerase (RdRp) of RNA viruses, inducing changes in RNA transversion that render the virus nonviable. After metabolism, favipiravir transforms into its active form, favipiravir ribofuranosyl 5'-triphosphate. In addition to the absence of human DNA polymerase subunits α, β, and γ (up to 100 g/mL), favipiravir is metabolized in the liver and does not cause clinically significant drug interactions, thus avoiding toxic effects [(BPOM-Badan Pengawas Obat dan Makanan, 2022).](#bpom)

In this study, the most commonly used antibiotic was levofloxacin, accounting for 44.4% of cases. This result is lower than the findings [of Kelana *et al.* (2021),](#kelana) where the study indicated that levofloxacin was the most frequently used antibiotic in COVID-19 patients, with a percentage (62.5 %). Another study by [Nasarah *et al.* (2022)](#nasarah) reported that levofloxacin is the most frequently used antibiotic (41 %). [Hutahean (2020)](#hutahean) reported that 33% of COVID-19 patients used levofloxacin.

Levofloxacin belongs to the respiratory fluoroquinolone group and constitutes the majority of antibiotics used in this study. Fluoroquinolone antibiotics can inhibit the replication of SARS-CoV-2 and suppress the production of proinflammatory cytokines such as interleukin-1 and tumor necrosis factor-alpha (TNF-α) [(Karampela & Dalamaga, 2020).](#karampela)

In this study, the use of the corticosteroid dexamethasone amounted to 53.3%.This result is higher than the findings of [Nasarah *et al.* (2022)](#nasarah), where 49% of patients used dexamethasone. Another study by [Cartika *et al.,* (2022)](#cartika) indicated that 78.4% of COVID-19 patients used dexamethasone, and in the research by [Ramadhan *et al.,* (2021)](#ramadhan), dexamethasone was used in 376 prescriptions, accounting for 97.92%.

The anti-inflammatory effect of dexamethasone involves the inhibition of proinflammatory genes, such as interleukin-1, interleukin-2, interleukin-6, interleukin-8, TNF, INF-gamma, VEGF, and prostaglandin, which encode cytokines and acute inflammatory responses [(Ahmed & Hassan, 2020).](#ahmed)

In this study and other research, dexamethasone was more commonly used because of the administration of short-term steroids in most COVID-19 trials (10 days of dexamethasone, 3–7 days of methylprednisolone). Steroids are unlikely to cause hyperglycemia or worsen glycemic control in diabetic patients. The occurrence of a 30-50% reduction in insulin-stimulated glucose uptake in skeletal muscle cells contributes to postprandial hyperglycemia, along with a 50-70% decrease in hepatic glycogenolysis in diabetic patients using corticosteroids. Corticosteroids also have a direct inhibitory effect on β-cells. Lipotoxicity from lipolysis can have similar effects on β-cells. The effects of steroids are usually temporary and reversible after discontinuation. The corticosteroids used in COVID-19 patients are methylprednisolone, a short-acting glucocorticoid with a duration of 4-6 hours, and dexamethasone, a long-acting steroid with steroid-induced hyperglycemia lasting more than 24 hours after the last dose, with minimal decline after overnight fasting [(Kumar *et al.,* 2020).](#kumar)

The type of vitamin administered to COVID-19 patients in this study was Prove C+Prove D3 (33.3 %).This percentage is lower than that reported by [Muliyani *et al.* (2022),](#muliyani) which indicated that 61% of COVID-19 patients used vitamin D. Another study by [Ramadhan *et al.* (2021)](#ramadhan) stated that 44.59% of COVID-19 patients received vitamin D3 therapy. Another study conducted by [Maharianingsih *et al*. (2022)](#maharia) stated that 142 patients (71%) received a combination of intravenous vitamins C and D.

Vitamins can reduce cytokine storms caused by innate immunity. By activating macrophages, vitamin D decreases the synthesis of Th1 cytokines and increases the production of anti-inflammatory cytokines. Genes associated with antioxidants, such as glutathione reductase and glutamate-cysteine ligase modifier subunit, are expressed. Administration of vitamin D increases glutathione synthesis and inhibits the action of bacteria and viruses [(Juli *et al.,* 2020).](#juli)

Supplementation with vitamin D3 may be an effective, accessible, and well-tolerated supplement as a treatment for COVID-19. This is because vitamin D supplementation can regulate RAS, innate immunity, and adaptive immunity, as well as physical barriers. Vitamin D enhances immunomodulatory and anti-inflammatory activities, potentially limiting the increase in cytokine levels caused by COVID-19 infection. [(Annweiler *et al.,* 2020).](#annweiler)

Vitamin C can protect the body from the damaging effects of free radicals because it is an antioxidant that can neutralize free radicals by donating one of its electrons, thus ending the electron reaction that lacks a pair and resulting in a stable compound. This mechanism forms the basis for vitamin C prevention of cell and tissue damage that can result from various infectious diseases, including COVID-19. When entering the body through respiration, it is recognized by antibodies, and vitamin C increases the epithelial barrier integrity, natural killer cell activity, neutrophil chemotaxis, and phagocytosis. Additionally, routine vitamin C supplementation can enhance innate immune responses and improve immunological effects against SARS-CoV-2 infection, potentially aiding the treatment of COVID-19. [(Abobaker *et al.,* 2020).](#abobakar)

Anticoagulants are used in COVID-19 patients to prevent the risk of coagulopathy-related thrombosis. In this study, the use of the anticoagulant warfarin was 28.9%. This result is lower than the findings of [Wong *et al.* (2021)](#wong), where the study indicated that 60.6% of patients used warfarin with an average age of 79 years. Another study by [Schaefer *et al.* (2019)](#schaefer) reported that 62.5% of 4086 patients used warfarin monotherapy.

The results of the therapy outcome parameter profiles for COVID-19 patients at the PKU Muhammadiyah Gamping Hospital are shown in **Table III**.

**Table III. Profile of Therapy Outcome Parameters in COVID-19 Patients with Severe Symptoms**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Therapeutic Outcome Parameter** | **Hospital Admission (n=45)** | | **Out of Hospital**  **(n=45)** | |
| **Normal** | **Abnormal** | **Normal** | **Abnormal** |
| SpO2 | 2.2% | 97.8% | 88.9% | 11.1% |
| Temperature | 68.9% | 31.1% | 88.9% | 11.1% |
| Respiratory rate | 0 % | 100% | 84.4% | 15.6% |
| Cough | 20% | 80% | 84.4% | 15.6% |
| Mortality | 0% | 100% | 71.1% | 28.9% |

Therapeutic outcomes are the goals of therapy. Therapeutic outcomes can include improvements in the patient's clinical condition, worsening of the patient's clinical condition, or absence of clinical improvement. Improved therapeutic outcomes mean that patients experience improved values of SpO2, temperature, respiratory rate, cough, and lower mortality after receiving therapy, whereas worsened therapeutic outcomes occur if patients do not show improvement after therapy administration. Achieving favorable therapeutic outcomes involves addressing symptoms as quickly as possible and limiting the spread of infection and complications [(Widiyastuti *et al.,* 2023).](#widiyastuti)

Severe symptoms of COVID-19 are characterized by conditions such as a respiratory rate >30 breaths per minute, SpO2 ≤93% at room temperature, and fever (>38°C) [(Burhan *et al.,* 2022)](#burhan). These data served as parameters for assessing the effectiveness of treatment for severe COVID-19 symptoms in this study. This study showed that 88.9% of patients experienced an improvement in SpO2 values (≥93%), while 11.1% of patients had SpO2 values below the normal range. These results are lower than those of [Syaifulloh *et al*. (2020),](#syaifullah) who reported that 92% of the patients experienced SpO2 improvement. This difference may be because the majority of patients in the study by [Syaifulloh *et al*. (2020)](#syaifullah). Another study conducted by [Kurniawan *et al.,* (2022)](#kurniawan), showed that 60 individuals (75%) with moderate to severe COVID-19 symptoms experienced improvement in SpO2 values (>93%). In a study conducted by [Stone *et al.* (2022)](#tone), it was found that among 19 COVID-19 patients with severe symptoms, SpO2 values increased from 86.7% before treatment to 93.3% after treatment.

In this study, 53.3% of the patients used dexamethasone therapy, and 88.9% of the patients experienced an increase in SpO2 values (>93%). This is consistent with the findings of [Tomazini *et al.*, (2020)](#toma) in the RECOVERY study conducted in the UK, involving 6,425 hospitalized COVID-19 patients. The study showed that the COVID-19 patient group requiring additional oxygen or mechanical ventilation experienced significant clinical improvement after receiving additional dexamethasone medication at a dose of 6 mg per day for 10 days.

In the study conducted by [Widiyastuti *et al*. (2023)](#widiyastuti), 88 patients (61.11%) who used levofloxacin experienced clinical improvement after 5 days of antibiotic use, as assessed by normal body temperature (36.0-37.0°C), absence of cough, absence of dyspnea, absence of chest pain, no pleural effusion as indicated by X-ray results, respiratory rate ≤24x/minute, normalization or normal leukocyte count, and discharge approval by the doctor.

In this study, 88.9% of patients experienced temperature improvement (<38.0°C), and levofloxacin antibiotics were used by 44.4% of patients. These results are higher than those of [Kurniawan *et al.,* (2022)](#kurniawan) where 59 individuals (73.75%) with moderate to severe COVID-19 symptoms experienced temperature improvement.

In addition to temperature improvement, improvement in respiratory rate values is also used as a therapeutic outcome parameter. In this study, 88.4% of the patients experienced an improvement in respiratory rate values (<30x/minute). This result is lower than that of the study by [Syaifulloh *et al.* (2020)](#syaifullah), which showed that 88% of COVID-19 patients experienced improvement in respiratory rate; this could be because the majority of patients were age range–26-45 years. Another study by [Yulianto *et al.* (2023)](#yulianto) showed that 52% of patients experienced an improvement in respiratory rate values.

The next therapeutic outcome parameter was improvement in the cough symptoms. In this study, the majority of patients presented with cough symptoms and 84.4% experienced improvement. This result is consistent with the findings of [Khaerunnisa *et al.* (2022)](#khaerunnisa), which showed that 84.1% of COVID-19 patients experienced improvement in cough symptoms. This could be because the patients in the study by [Khaerunnisa *et al.* (2022)](#khaerunnisa) had mild to moderate symptoms, whereas this study focused on patients with severe symptoms who had less severe cough symptoms.

In this study, 71.1% of the discharged patients experienced improvement, whereas 28.9% were discharged. This result is lower than that of the study by [Maharianingsih *et al.* (2022)](#maharia), in which 162 patients (81%) recovered; this could be due to the smaller number of patients in this study. Another study by [Ramatillah and Isnaini (2021)](#ramatillah) reported that 22 individuals (81.5%) achieved clinical recovery.

In this study, 48.9% of the patients used antiviral favipiravir. This aligns with the findings of [Hadiatussalamah *et al.* (2023)](#hadiatuss), in which patients received a combination of antiviral, antibiotic, corticosteroid, anticoagulant, and convalescent plasma therapy, with favipiravir showing an effective rate with clinical recovery in 30 patients (34.1%), as determined by the WHO ordinal scale for COVID-19 disease progression and recovery. The study also indicated a significant association between the types of antivirals, specifically favipiravir and remdesivir, and the clinical outcomes. The percentage of patients improving in the favipiravir group, 44 patients (50%), was greater than in the remdesivir group, 31 patients (35.3%). Similar results were found in the study by [Damayanti *et al.* (2021),](#damayanti) who stated that favipiravir could enhance clinical improvement in COVID-19 patients at the end of the isolation period compared to other antivirals.

A systematic review involving 7 clinical trials with 6250 severe COVID-19 patients concluded that the use of corticosteroids in COVID-19 patients significantly reduced mortality rates and prevented disease progression. Corticosteroids play a role in suppressing immune dysfunction, leading to cytokine storms in COVID-19 patients [(Ma *et al.,* 2021).](#mas) Dexamethasone is the most extensively studied corticosteroid and has been shown to improve clinical outcomes in patients with severe COVID-19 [(Tomazini *et al.,* 2020)](#toma).

Patients with severe or critical symptoms are at risk of mortality owing to weakened immune responses, leading to virus replication and tissue damage. Conversely, an excessive immune response can result in tissue damage. The reaction triggered by an exaggerated immune response is called a cytokine storm, which is characterized by a rapid increase in cytokine production as an infection response. The rapid increase in proinflammatory cytokine production can lead to inflammatory infiltration in the lung tissues, causing damage to the epithelial and endothelial parts of the lungs. This damage can result in multiorgan failure, ARDS, or death [(Haq *et al.,* 2021).](#haq)

One of the conditions that affect the elderly is reduced competence of the immune system, caused by a decline in both the innate and adaptive immune systems. This results in a decrease in the number of immune response-related cells, such as TLR receptors and receptors on the surface of monocytes and macrophages, as well as in the number of neutrophils, dendritic cells, and T lymphocytes. The mortality rate of elderly patients is also influenced by the ability of B lymphocytes to differentiate [(De Wit *et al.,* 2016).](#dewit)

The limitation of this study is that data collection was only conducted from August 2022 to 2023, resulting in a small number of patients with severe COVID-19 available for analysis. Additionally, the researchers did not investigate the dosage of medication administered to the patients, thus preventing the identification of other factors influencing the effectiveness of treatment in patients with severe COVID-19.

# CONCLUSION

The therapy provided to patients with severe COVID-19 at PKU Muhammadiyah Gamping Hospital from August 2022 to 2023 yielded effectiveness percentages for each therapeutic outcome. These outcomes included SpO2 values ≥93% in 88.9% of cases, temperature improvement to <38.0°C in 88.9%, respiratory rate improvement to <30x/minute in 84.4%, improvement in cough symptoms in 84.4%, and patient discharge with recovery in 71.1%.

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