

Characteristics of COVID-19 Therapy Based on Disease Severity at Siloam Kebon Jeruk Hospital

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Abstract

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Introduction : COVID-19 is an infectious disease that can cause acute respiratory syndrome by droplet transmission. Along with the very fast spread of the virus which occurs in almost all countries, it is necessary to have therapies that can reduce the morbidity and mortality of patients infected with COVID-19. Various factors affect the administration of therapy so a management guideline is needed for medical personnel so that the administration of therapy can be consistent and efficient in accordance with scientific evidence. This study aims to determine the characteristics and therapeutic options of COVID-19 patients based on the severity of the disease so it can be an evaluation for policymakers and health workers in providing COVID-19 therapy.

Methods : This type of research is descriptive, and the research design is cross-sectional with a total population sampling. The study was conducted at Siloam Kebon Jeruk Hospital with a total of 135 respondents from secondary medical record data.

Results : The observed data include the characteristics of the respondents and the therapies for COVID-19 patients, which consist of antiviral, anti-inflammatory, and anticoagulant treatments. Based on the collected data, COVID-19 patients were predominantly male (55.6%) with an average age of 55 years. Many patients presented with moderate severity without requiring oxygen (34.1%) and were classified as having referred outcomes (47.4%). Antiviral therapy using favipiravir was predominantly administered to patients with mild to moderate severity, while remdesivir was mostly given to those with moderate to severe severity. Corticosteroids, such as dexamethasone and methylprednisolone, were the preferred choice for anti-inflammatory therapy (72.2%). Heparin was the most commonly used anticoagulant therapy across all severity levels, and antibiotics were administered to the majority of patients infected with COVID-19 (73.3%).

Conclusions : Evaluation of the low rate of use of corticosteroids and anticoagulants in COVID-19 patients is needed.

Introduction

The World Health Organization (WHO) officially classified the Coronavirus outbreak as a pandemic on March 11,

2020, due to its rapid global spread.¹ By July 6, 2021, Indonesia had reported 2,379,397 confirmed COVID-19 cases, with 62,908 deaths (2.6%). DKI Jakarta accounted for the highest number of cases,

totaling 482,264 (23.9%) and 7,922 deaths.² COVID-19 primarily affects the respiratory system and poses a significant health risk due to severe complications, including pneumonia.^{3,4} The clinical manifestations of COVID-19 include fever, cough, malaise, dyspnea, fatigue, anorexia, sneezing, and rhinitis.⁵ The disease is categorized into four levels of severity: asymptomatic, mild, moderate, and severe.⁶

The therapeutic approach to managing COVID-19 patients varies according to the severity of the disease and the treatment guidelines in use. Several factors influence the selection of therapy, including ethical considerations, medical professionalism, research evidence, a comprehensive understanding of the patient's condition, the identification of potential treatment options, patient consent to proposed interventions, implementation of the treatment plan, and evaluation of outcomes. Non-clinical factors, such as the patient's economic status, racial and cultural background, attitudes, beliefs, and the availability of healthcare resources, also play a critical role in clinical decision-making, adding layers of complexity.^{7,8}

Given the variability in therapeutic approaches, standardized clinical guidelines are essential to promote consistent and efficient treatment while reducing the gap between practice and evidence-based medicine.⁹ This study

seeks to analyze the characteristics of therapies provided to COVID-19 patients and their alignment with disease severity. The investigation focuses on evaluating therapy patterns for COVID-19 patients at Siloam Kebon Jeruk Hospital

Material And Methods

This study employs a descriptive observational design with a cross-sectional approach, utilizing secondary data from the medical records of COVID-19 patients treated at Siloam Kebon Jeruk Hospital. The sample consists of COVID-19 patients aged ≥ 18 years who received treatment at the hospital between December 2020 and August 2021. The collected data will be analyzed using statistical software.

Result

From a total of 135 respondents, the age distribution showed a mean of 55 years (SD ± 1.42). The majority of the sample comprised male patients, totaling 75 individuals (55.6%). The most prevalent severity level was moderate without oxygen support, with a proportion of 34.1%. Diabetes mellitus was the most common comorbidity, affecting 30.7% of patients, followed by hypertension at 27.4%. Additionally, 32 respondents (23.7%) presented with ≥ 2 comorbidities. The detailed characteristics of the respondents are presented in **Table 1**.

Table 1. Respondent Characteristics

Characteristic	Number (N = 135)
Gender	
Male	75 (55.6%)
Female	60 (44.4%)
Severity Level	
Mild	29 (21.5%)
Moderate without oxygen	46 (34.1%)
Moderate with oxygen	41 (30.4%)
Severe	19 (14.1%)
Comorbidities	
Diabetes mellitus	41 (30.4%)
Hypertension	37 (27.4%)
Heart disease	11 (8.1%)
Chronic kidney disease	11 (8.1%)
Asthma	7 (5.2%)
Chronic obstructive pulmonary disease (COPD)	2 (1.5%)
Cancer	2 (1.5%)
Autoimmune disease	0 (0%)
≥ 2 comorbidities	32 (23.7%)
Others	19 (14.1%)

Table 2 outlines the therapeutic interventions employed for COVID-19 patients included in the study. The data indicate that the most frequently utilized antiviral agent was favipiravir (48.9%), predominantly administered to individuals with mild to moderate disease severity who did not require oxygen supplementation (36%). Conversely, remdesivir emerged as the preferred antiviral for patients with moderate disease severity requiring oxygen support and severe cases, with a usage rate of 48.3%. Corticosteroids, serving as anti-inflammatory agents, were the second most common therapeutic

choice (23.7%). Their application was most pronounced in patients with moderate disease necessitating oxygen support. Within this category, dexamethasone was the predominant choice for patients with moderate disease requiring oxygen and for severe cases, whereas methylprednisolone was more frequently administered to patients with moderate disease not requiring oxygen supplementation. Additional anti-inflammatory interventions, including IL-6 receptor antagonists and intravenous immunoglobulin, were primarily reserved for patients with severe disease. Among anticoagulants, heparin was overwhelmingly the most utilized agent (87.5%), surpassing enoxaparin and rivaroxaban in frequency, with its use being highest among patients with moderate disease requiring oxygen support. Specific interventions such as spironolactone and convalescent plasma were exclusively administered to patients with moderate disease requiring oxygen support. Antibiotic therapy was implemented in 73.3% of cases, with the highest prevalence observed in moderate cases without oxygen supplementation (34.3%). N-acetylcysteine demonstrated the highest usage in moderate cases requiring oxygen, while the administration of hydroxychloroquine was evenly distributed among mild and moderate cases without oxygen support.

Table 2. Therapies Based on COVID-19 Disease Severity

Therapeutic Type	Mild (n=29)	Moderate w/o Oxygen (n=46)	Moderate w/ Oxygen (n=41)	Severe (n=19)	Total (n=135)
Antiviral Therapy					
Favipiravir	13 (27.1%)	14 (29.2%)	16 (33.3%)	5 (10.4%)	48 (35.6%)
Remdesivir	0 (0.0%)	13 (31.0%)	17 (40.5%)	12 (28.6%)	42 (31.1%)
Oseltamivir	4 (50.0%)	3 (37.5%)	1 (12.5%)	0 (0.0%)	8 (5.9%)
Anti-inflammatory Therapy					
Corticosteroids	2 (6.3%)	9 (28.1%)	11 (34.4%)	10 (31.3%)	32 (23.7%)
Dexamethasone	1 (3.8%)	5 (19.2%)	10 (38.5%)	10 (38.5%)	26 (19.3%)
Methylprednisolone	1 (16.7%)	4 (66.6%)	1 (16.7%)	0 (0.0%)	6 (4.4%)
IL-6 receptor antagonist	0 (0.0%)	0 (0.0%)	1 (14.3%)	6 (85.7%)	7 (5.2%)
Intravenous immunoglobulin	0 (0.0%)	0 (0.0%)	1 (25.0%)	3 (75.0%)	4 (3.0%)
Ivermectin	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (0.7%)
Anticoagulant Therapy					
Heparin	1 (4.8%)	2 (9.5%)	12 (57.1%)	6 (28.6%)	21 (15.6%)
Enoxaparin	0 (0.0%)	0 (0.0%)	1 (50.0%)	1 (50.0%)	2 (1.5%)
Rivaroxaban	0 (0.0%)	1 (100.0%)	0 (0.0%)	0 (0.0%)	1 (0.7%)
Angiotensin-Converting Enzyme II and RAAS Inhibitors					
Spirolactone	0 (0.0%)	0 (0.0%)	1 (100.0%)	0 (0.0%)	1 (0.7%)
Convalescent Plasma Therapy	0 (0.0%)	0 (0.0%)	2 (100.0%)	0 (0.0%)	2 (1.5%)
Antibiotic Therapy	14 (48.3%)	34 (34.3%)	33 (33.3%)	18 (18.2%)	99 (73.3%)
N-acetylcysteine Therapy	3 (8.6%)	12 (34.3%)	15 (42.9%)	5 (14.3%)	35 (25.9%)
Hydroxychloroquine Therapy	1 (50.0%)	1 (50.0%)	0 (0.0%)	0 (0.0%)	2 (1.5%)

Discussion

Data from the COVID-19 Task Force in Indonesia indicates that individuals aged 46–59 years and those over 60 years constitute the two largest age groups with the highest mortality rates among COVID-19 patients. This trend can be attributed to age-related degenerative processes that compromise immune function, rendering

older individuals more vulnerable to COVID-19 and increasing their risk of developing Acute Respiratory Distress Syndrome (ARDS).¹⁰ The higher prevalence of COVID-19 cases among males may be explained by various factors, including hormonal differences, behavioral patterns, lifestyle choices, and physiological disparities in immune system

responses between males and females, all of which influence susceptibility to SARS-CoV-2 infection.^{11–13} Regarding disease severity, findings are consistent with research by Kusumawardani, which identified moderate severity as the most common clinical presentation among COVID-19 patients.¹⁴ In terms of comorbidities, a similar pattern was observed in a study conducted at a hospital in Surakarta during the period from March to December 2020, where diabetes mellitus was the most frequently reported comorbidity, followed by hypertension.¹⁵

Favipiravir was predominantly used in mild to moderate cases. Based on reviews, favipiravir demonstrated a tolerable safety profile with manageable side effects, improved viral clearance within seven days, and clinical improvement during the first 14 days in mild to moderate cases. Its oral formulation facilitates easy administration.¹⁶ However, studies show no benefit in administering favipiravir to severe cases, highlighting the need for caution in its use for such patients. Furthermore, adding favipiravir to the standard care for severe cases does not improve clinical outcomes.^{17,18} In this study, five severe patients received favipiravir therapy, underscoring the need for further investigation into its efficacy in severe cases.

Oseltamivir, while more cost-effective than favipiravir for moderate COVID-19

cases, has demonstrated limited effectiveness.¹⁹ Recent in vitro studies and clinical usage showed that oseltamivir is ineffective against SARS-CoV-2, does not improve symptoms, and does not slow disease progression. Consequently, oseltamivir is unsuitable for COVID-19 treatment and is no longer recommended in the 2022 COVID-19 management guidelines.^{20,21}

Remdesivir was commonly used in moderate cases requiring oxygen and in severe cases. Current COVID-19 management guidelines recommend remdesivir for moderate and severe patients. Research indicates that remdesivir accelerates clinical recovery, reduces recovery time, and has an acceptable safety profile based on clinical trials.²²

Combination antiviral therapies were also noted. While some studies suggested that combining favipiravir and oseltamivir could expedite clinical recovery in severe influenza cases, there is no supporting evidence or recommendation for such combinations in COVID-19 management, especially given oseltamivir's ineffectiveness against SARS-CoV-2.²³

Corticosteroids, with their anti-inflammatory and immunosuppressive effects, were used to modulate immune response.¹⁵ Research shows that corticosteroids can reduce mortality among hospitalized COVID-19 patients, but their

benefits are limited to those requiring supplemental oxygen or mechanical ventilation. Their use in patients not requiring supplemental oxygen does not improve outcomes and may pose risks, leading to their exclusion from recommendations for such cases.²⁴ However, this study observed corticosteroid use in mild cases, contrary to COVID-19 management guidelines. This may reflect attempts to alleviate systemic symptoms and reduce the risk of COVID-19-induced ARDS. Further evaluation of this practice is necessary.²⁵

There is a hypothesis suggesting that methylprednisolone has higher pulmonary penetration compared to dexamethasone, alongside a trend towards lower mortality rates in patients receiving methylprednisolone, albeit without statistical significance.²⁶ Studies on the efficacy of dexamethasone versus methylprednisolone have demonstrated their significant effectiveness in controlling inflammatory markers and improving the PaO₂/FiO₂ ratio in moderate to severe COVID-19 cases.²⁷ However, this study found that only 31% and 34% of moderate and severe cases, respectively, received corticosteroid therapy, highlighting low usage and emphasizing the need to evaluate corticosteroid administration in these patients.

COVID-19-induced pulmonary symptoms are associated with a

hyperinflammatory response and cytokine storm involving interleukin and chemokine dysregulation. The cytokine storm leading to acute respiratory distress syndrome (ARDS) is a major cause of respiratory and lung damage in severe cases. IL-6 receptor blockers play a pivotal role in mitigating hyperinflammation, with IL-6 cytokine receptor blockade emerging as a promising therapy for severe SARS-CoV-2 cases.

The cytokine storm triggered by COVID-19 can lead to hyperinflammation and hypercoagulability due to dysregulated coagulation cascades. Pro-inflammatory activation, as part of cytokine release syndrome during SARS-CoV-2 progression, initiates a coagulation cascade that can result in thrombosis and widespread intravascular clot deposition. This disrupts organ blood supply, causing organ failure and death. Hence, anticoagulant therapy is crucial for preventing coagulopathies leading to thrombosis and thromboembolism, providing a favorable prognosis for COVID-19 patients. This study observed low anticoagulant use (33.3%) among moderate cases requiring oxygen and severe cases, warranting further investigation into its implementation.

Intravenous immunoglobulin is thought to be most beneficial when administered early, as patients begin to deteriorate but before respiratory failure occurs.^{28,29} Research indicates IVIG can

improve clinical outcomes, reduce disease duration, enhance oxygen saturation, and prevent the progression of lung lesions in severe COVID-19 cases refractory to standard treatment.^{30,31} However, in this study, only two patients received convalescent plasma therapy, likely due to the difficulty in obtaining plasma donors during the pandemic. While systematic reviews have shown convalescent plasma therapy offers no clear benefits, does not improve clinical recovery, and fails to reduce mortality risk in moderate or critical cases, further studies are required.³² The use of antibiotics in COVID-19 patients remains controversial, as bacterial co-infections in COVID-19 are relatively rare. Excessive antibiotic use poses risks, including increased resistance rates and higher mortality.^{33–35} This underscores the need for careful evaluation before administering antibiotics in COVID-19 management. N-Acetylcysteine, an antioxidant with antidotal properties, shows promise as both a therapeutic and preventive agent for COVID-19. Studies indicate that NAC significantly reduces the duration of extracorporeal membrane oxygenation (ECMO) use, shortens hospital stays, suppresses pro-inflammatory cytokine production, inhibits viral replication, and acts as an antioxidant.

These properties make NAC effective in reducing inflammation caused by COVID-19 infection.³⁶

Conclusion

The study results indicate that antiviral therapy was administered to 72.6% of COVID-19 patients, predominantly those with severe cases and moderate cases requiring oxygen. Anti-inflammatory therapy was given to 32.6% of patients, primarily those with severe disease, while anticoagulant therapy was administered to 17.8%, again mostly to those with severe conditions. This study emphasizes the importance of clinicians adhering to established guidelines when prescribing COVID-19 therapies. The findings can serve as a foundation for institutions to conduct further research on therapeutic approaches for COVID-19 patients, given the need for a thorough review of appropriate treatment strategies. Large-scale studies are needed to better understand the characteristics of therapy administration across different severity levels, which could guide the development of education and outreach programs aimed at ensuring healthcare professionals make informed and precise therapeutic decisions.

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