



# Impact of Corticosteroid on Covid-19 Pneumonia Patients

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## ABSTRACT

**Background:** Globally over 704,753,890 had COVID-19. Out of which 7,010,681 died compared to 12,031 deaths in Nepal out of 1,003,450 cases nationwide.<sup>1</sup> Corticosteroids because of their anti-inflammatory effect may have a beneficial effect/s on COVID-19 patients. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the pathogen responsible for the coronavirus disease 2019 (COVID-19) pandemic, which has resulted in global healthcare crises and strained health resources. Corticosteroids are a potential therapeutic agent for patients with COVID-19 pneumonia. The RECOVERY (Randomised Trials in COVID-19 Therapy) trial provided data on the mortality benefits of corticosteroids.

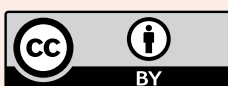
**Aim:** The study aims to see the effect of corticosteroids on COVID-19 patient outcomes concerning disease progression, length of hospital stay, 28-day mortality, and use of resources like ventilator.

**Method:** Single Hospital-based Prospective observational study among RT-PCR positive for COVID-19 patients admitted at Kathmandu Medical College Teaching Hospital from June 01, 2021–July 31<sup>st</sup>, 2021 requiring oxygen therapy. Patients were grouped into either usual care, including symptomatic treatment only, or a group receiving both usual care and corticosteroid.

**Results:** This study included 160 RT-PCR-positive cases. There were 53 patients with mild symptoms and 107 with moderate symptoms. Patients with mild symptoms who received standard care had an odds ratio of 1.875 for progression to moderate and severe COVID-19 compared to those who received both standard care and corticosteroid. Similarly, patients with moderate symptoms who received standard care had an odds ratio of 1.8 for progression to severe and critical COVID-19 compared to those who received both standard care as well as corticosteroids. Among patients with mild symptoms, the overall use of a ventilator was 35.85% and mortality was 13.21%. Similarly, in patients with moderate symptoms at presentation, a ventilator was needed in 33.64% and mortality was 24.30%.

**Conclusion:** Though corticosteroids seem to have a beneficial role in preventing disease progression, they failed to show a statistically significant reduction of ventilator use and mortality benefit amongst groups.

**Keywords:** Covid-19 pneumonia, Coronavirus, and Corticosteroid, Ventilator.



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## INTRODUCTION

Globally over 704,753,890 had COVID-19. Out of which 7,010,681 died compared to 12,031 deaths in Nepal out of 1,003,450 cases nationwide.<sup>1</sup> Majority of cases are asymptomatic to mildly symptomatic, ranging from almost 81%, severe to 14%, and critical to approximately 5% of total COVID-19 cases. In fact, targeting the group with early and effective management plans and preventing them from

further deterioration will rationalize the healthcare resource utilization patient outcomes.

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In the RECOVERY study, treatment with dexamethasone conferred a survival benefit among participants who required supplemental oxygen without invasive mechanical ventilation at enrollment: 23.3% of the participants in the dexamethasone group died within 28 days of enrollment compared with 26.2% in the standard-of care arm (rate ratio 0.82; 95% CI, 0.72–0.94). Center for Disease Control, USA (CDC) also recommended corticosteroids for patients requiring oxygen support and ventilator assistance upon National Institute of Health COVID management protocol.<sup>2</sup> Recommendations on the use of corticosteroids for COVID-19 are largely based on data from the RECOVERY trial<sup>3,4</sup>, a large, multicenter, randomized, open-label trial performed in the United Kingdom. This trial compared hospitalized patients who received up to 10 days of dexamethasone to those who received the standard of care. Mortality at 28 days was lower among patients who were randomized to receive dexamethasone than among those who received the standard of care.<sup>5</sup> This benefit was observed in patients who were mechanically ventilated or required supplemental oxygen at enrollment. No benefit of dexamethasone was seen in patients who did not require supplemental oxygen at enrollment. Conversely, Dexamethasone (6 mg per day) tends to increase clotting factor and fibrinogen concentrations. Thus, it is plausible for exogenous glucocorticoids to precipitate clinical thrombosis.<sup>6</sup>

Though Adaptive COVID-19 Treatment Trial ACT-1 trial claimed to have the beneficial effect of Remdesivir if used early in the course of disease in those requiring low flow oxygen in terms of improved time to recovery. On the contrary, studies like RECOVERY trial, SOLIDARITY trial failed to show any significant outcome. Although, several monoclonal antibodies like anti-IL-6, and others have been studied; none proved beneficial. Undoubtedly, the development of vaccines in a short period is commendable.

**METHODS:**

This was a single hospital-based Prospective observational Study. Ethical approval was taken from the Institutional Review Committee of Kathmandu Medical College Teaching Hospital- KMC-IRC (2005202105). All patients admitted at KMCTH from June 01, 2021 –July 31<sup>st</sup>, 2021 coming with fever, cough, dyspnea, myalgia, fatigue, loss of taste, loss of smell, etc. in various combinations were classified as mild or moderate based on WHO COVID-19 Classification as mild, moderate, severe and critical enrolled and their records were kept. Patients were grouped into Usual care/Standard care (SC) or SC plus Corticosteroid. Results were analyzed using statistical tools like MS Excel and percentage prevalence, the association was measured using p-value by chi-square test, odds ratios were calculated and the final report was prepared.

**RESULTS:**

During the study period, a total of 160 positive COVID-19 cases were admitted at KMCTH and were included in the

study. There were no statistically significant differences in age, gender, comorbid conditions, and critical care illness between those who did and did not receive corticosteroids. When comparing the usual care/standard arm (SC) vs. usual care/standard plus corticosteroid arm, among patients with mild symptoms, the odds ratio of progressing to a more severe form was 1.875 times higher than those patients receiving corticosteroid as shown in Table 1 below. Similarly, in patients with moderate symptoms, the odds ratio of progressing to a more severe form in patients receiving only standard care was 1.8 times higher than those patients receiving corticosteroids as shown in Table 1 below.

**Table 1:** Progression of disease among patients with different levels of symptoms and care modalities

Mild Symptoms (N=53)				
	Remains mild	Progresses to moderate	Progresses to severe	Progresses to critical
Standard care(SC) n=29	8 (27.59 %)	9 (31.03 %)	7 (24.14 %)	5 (17.24 %)
SC Plus Corticosteroid care (standard care and steroid) n=24	10 (41.67 %)	7 (29.17 %)	5 (20.83 %)	2 (8.33 %)

Moderate Symptoms (N=107)				
	-	Remains moderate	Progresses to severe	Progresses to critical
Standard care n=30	-	17 (56.67 %)	7 (23.33 %)	6 (20 %)
SC Plus Corticosteroid care (standard care and steroid) n= 77	-	54 (70.12 %)	17 (22.08 %)	6 (7.80 %)

The overall length of hospital stay among the patients who presented with mild symptoms, who were given standard care was 4-9 days for those who remained mild, 5-10 days for those who progressed to moderate, 7-15 days for those who progressed to severe and also 7-15 days for those who progressed to critical. The patients with plus care also had the same length of stay in the hospitals. Whereas in patients with moderate symptoms and receiving standard care, the overall length of hospital stay was 5-9 days for those who remained moderate, 12-20 days for those who progressed to severe, and 20-30 days for those who progressed to critical. Similarly, in moderate symptoms patients with plus care, the overall length of hospital stay was 5-7 days for those who remained moderate, 10-13 days for those who progressed to severe, and 20-27 days for those who progressed to critical.

Among patients with mild symptoms, the overall use of a ventilator was 35.85 % and mortality was 13.21 %. Similarly, in patients with moderate symptoms at presentation, a ventilator was needed in 33.64 % and mortality was 24.30

%. However, no statistical significance ( $p$ -value $>0.05$ ) was found either in terms of a patient requiring ventilators or mortality benefit was seen among patients receiving SC Plus corticosteroid when analyzed as a group as shown in Table 2 below. Moreover, there was no significant difference in outcome (ventilator use and mortality) among patients with SC Vs. SC plus corticosteroid care in patients with mild symptoms and moderate symptoms when analyzed separately.

**Table 2:** Ventilator use and mortality among patients with different levels of symptoms and care modalities

	Mild Symptoms (n=53)		Moderate symptoms (n=107)	
	Standard care (29)	SC Plus corticosteroid (24)	Standard care (30)	SC Plus Corticosteroid (77)
Ventilator	12 (41.38 %)	7 (29.17 %)	13 (43.33 %)	23 (29.87 %)
Mortality	4 (13.79 %)	3 (12.5 %)	9 (30 %)	17 (22.08 %)

## LIMITATION:

Single center, prospective observational study with small sample size.

## DISCUSSION:

The effects of corticosteroids in the treatment of viral pneumonia and acute respiratory distress syndrome (ARDS) have been the subject of controversy over decades, including several studies over the last 15 years. The majority of studies report a detrimental effect of corticosteroids for the treatment of influenza viral pneumonia, including studies during the H1N1 influenza outbreak of 2009–2010<sup>7,8</sup> and subsequent studies with H5N1 influenza pneumonia<sup>9</sup>. Corticosteroid in COVID-19 is a double-edged sword. Hence, to reap its benefit at the cost of minimal adverse effects is an art of using scientific data on an individual basis rather than a one-size-fits-all dictum.

Our observation of having no significant difference between groups who did receive corticosteroids and who did not is similar to a study conducted by Kam Sing Ho et al.<sup>10</sup> and contrary to RECOVERY TRIAL<sup>4</sup> in terms of mortality. Moreover, study by Liu J, et. al and Gerard Moreno<sup>1</sup> et. al, showed the increased odds of death in patients treated with corticosteroids persisted among propensity-matched subjects (OR = 1.64, 95% CI 1.05–2.57, P = 0.032)<sup>11,12</sup>. The findings differ from study to study because of the different patient populations, timing of initiation of corticosteroid therapy, and threshold for use of Invasive mechanical ventilator.

Similarly, our finding of having an increased odds ratio of progression to severe disease was in line with the systemic review finding by Mario Cruciani et. al.<sup>13</sup> and Yang Li et. al.<sup>14</sup>.

The outcome concerning disease progression, ventilator use, and mortality do not depend only on disease severity but also on the timing of use of corticosteroid; specifically before the beginning of cytokine storm, i.e. the earlier the better. In terms of overall length of hospital stay, we did not find any statistically significant difference between either usual care (SC) OR SC plus corticosteroid arm.

## CONCLUSION:

Though Corticosteroids seem to have a beneficial role in preventing disease progression, but they failed to show a statistically significant reduction of ventilator use and mortality benefit amongst groups.

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