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Original Article

Internal Medicine Section

Efficacy of Dexamethasone and Methylprednisolone in COVID-19 Pneumonia Patients in Kolkata, India: A Retrospective Cohort Study

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ABSTRACT

Introduction: Since the outbreak of Coronavirus Disease 2019 (COVID-19) in China, the epidemic has rapidly spread all over the world in just a few months. Different steroids have been proven effective in treating COVID-19 pneumonia. However, comparative efficacy data between different steroids have been evaluated in a few studies from various parts of the world. To date, no study with a large number of patients has been conducted in the eastern part of India.

Aim: To compare the efficacy of dexamethasone and methylprednisolone in terms of outcomes and disease progression in COVID-19 pneumonia patients.

Materials and Methods: This retrospective cohort study included 377 patients with moderate and severe COVID-19 pneumonia admitted to Medical College and Hospital from May 2020 to December 2020, Kolkata, West Bengal, India. Patient records were divided into two groups based on the type of steroids administered (dexamethasone and methylprednisolone). Clinical, laboratory, treatment, and outcome data were tabulated for analysis. Demographic patterns in the two groups were compared, and efficacy was analysed in terms of hospital course (hospital stay length, type of respiratory support received) and final outcome (cured or death) in both groups. The data collected were analysed using Statistical Package for Social Sciences (SPSS) software version 29.0. Qualitative variables were expressed as counts and percentages, while quantitative variables were presented as mean±Standard Deviation (SD).

Results: There were no significant differences between the two treatment groups based on demographic features (age, sex), co-morbidities (diabetes, hypertension, etc.), disease severity (hypoxia, hypotension) on admission day, and smoking status. The study showed that methylprednisolone significantly reduced the requirement for high-flow oxygen (p-value=0.002), Non Invasive Ventilation (NIV) (p-value=0.001), and invasive ventilation (p-value=0.001) compared to dexamethasone. However, there was no significant difference (p-value=0.800) in the duration of hospital stay between the methylprednisolone and dexamethasone treatment groups. Kaplan-Meier survival analysis also showed a significant survival benefit among patients who received methylprednisolone compared to dexamethasone (log-rank p-value=0.039).

Conclusion: The present study concludes that in COVID-19 pneumonia, the administration of methylprednisolone leads to a significant reduction in mortality and the need for high-flow oxygen, NIV, and invasive ventilation compared to dexamethasone.

Keywords: Co-morbidity, Coronavirus disease-2019, Efficacy, Steroids

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) was first reported in late December 2019 in Wuhan, China [1]. Since the sudden outbreak of COVID-19 in parts of China, the epidemic rapidly spread all over the world in just two months. On March 11, 2020, the World Health Organisation (WHO) declared the COVID-19 outbreak as an pandemic. Several waves of coronavirus infections have hit different countries around the globe since then. Different variants were also identified during these periods, causing several waves in many countries [2].

The pathological process of severe COVID-19 pneumonia involves inflammation in lung tissue characterised by the destruction of the deep airway and alveolar region [3]. Lung injury is caused by immune responses triggered by COVID-19, leading to the activation of immune cells and the outpouring of pro- and anti-inflammatory cytokines. Histology from COVID-19 affected lung tissues revealed diffuse alveolar damage and mucinous exudate, which is somewhat similar to Acute Respiratory Distress Syndrome (ARDS) [3]. This altered immune response, in terms of cytokine-mediated injury, leads to COVID-19 pneumonia, which can be fatal, if left untreated. Various agents, such as steroids and tocilizumab, have been tried to halt these immune-mediated injuries [4].

Steroids (methylprednisolone or dexamethasone) are classical immunosuppressive drugs that are important in stopping or delaying the progression of pneumonia and cytokine storms. Wu C et al., found that the administration of methylprednisolone appeared to reduce the risk of death in COVID-19 pneumonia patients with ARDS [5]. In another study, Zhou W et al., showed the clinical benefits of low-dose steroids in treating critically-ill patients with COVID-19 pneumonia [6]. The Randomised Evaluation of Covid-19 Therapy (RECOVERY) trial concluded that dexamethasone reduced deaths by one-third in ventilated patients and by one-fifth in other patients receiving oxygen only. These findings suggest that treating around eight ventilated patients or about 25 patients who needed oxygen alone with dexamethasone would save one death [7]. Meta-analysis of steroids in COVID-19 pneumonia shows that data on methylprednisolone are limited [8].

Several studies have compared the efficacy of dexamethasone and methylprednisolone in treating COVID-19 pneumonia patients. Fatima SA et al., found in 100 recruited patients that both dexamethasone and methylprednisolone are equally effective in treating moderate to severe COVID-19 pneumonia [9]. Another group studied 86 patients and concluded that in hypoxic

COVID-19 patients, methylprednisolone is better compared to dexamethasone [10]. Another study found that hospital mortality was lower, and hospital length of stay was higher among COVID-19 pneumonia patients receiving methylprednisolone compared to dexamethasone [11].

Prompted by different studies showing differences in opinion regarding the benefits of methylprednisolone and dexamethasone in treating moderate and severe COVID-19 pneumonia, authors undertook a study that aimed to compare the efficacy of dexamethasone and methylprednisolone in terms of outcomes and disease progression in COVID-19-infected moderate and severe patients admitted to Medical College and Hospital, Kolkata, West Bengal, India, in the year 2020. In eastern India, no such study has been done to date. The present study analysed a significantly large number of patients, which is lacking in other studies from different parts of the world.

MATERIALS AND METHODS

The present retrospective cohort study was conducted at Medical College, Kolkata, which was designated as a dedicated tertiary level COVID-19 hospital in West Bengal during the COVID-19 pandemic. The records of patients admitted in the year 2020 (May to December) were analysed. This is a retrospective cohort study, so all admitted cases that fulfilled the inclusion and exclusion criteria were included. No sample size calculation is needed. The study was approved by the Institutional Ethics Committee (IEC) at Medical College, Kolkata (Ref No: MC/KOL/IEC/NON-SPON/729/06/2020 dated: 06/07/2020).

Inclusion criteria:

- Moderate and severe pneumonia cases were selected for analysis.
- Patients who received steroids (methylprednisolone or dexamethasone) were included.
- Patients whose data were complete in terms of clinical parameters, laboratory results, and treatment details.

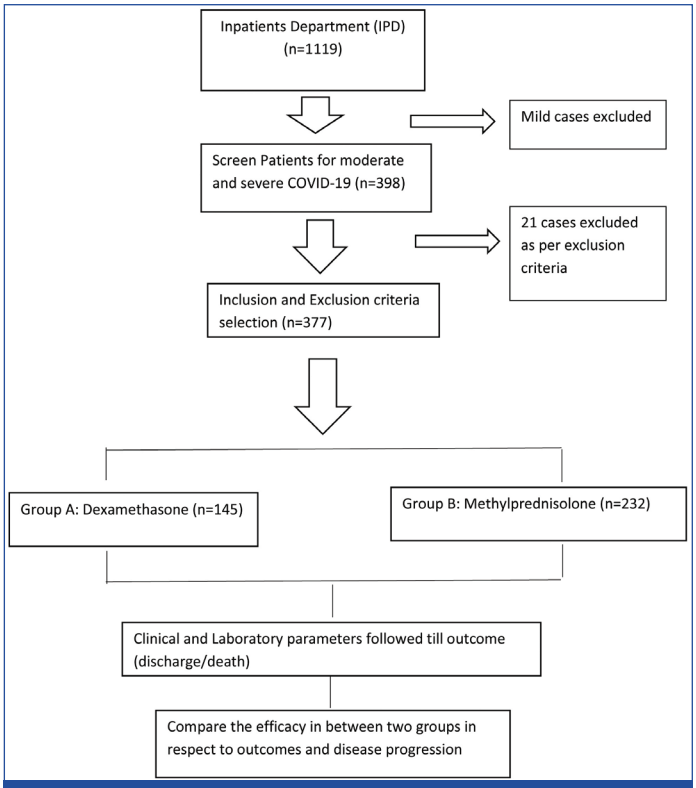
Exclusion criteria:

- Paediatric patients (<12 years old).
- Pregnant patients/lactating mothers.
- Those who were on steroids previously for indications other than COVID-19 pneumonia.
- Patients who received other immunosuppressive drugs for COVID-19 (such as tocilizumab/baricitinib).
- Patients who received convalescent plasma.

Study Procedure

Flow diagram for selecting the methylprednisolone and dexamethasone treatment groups in patients with COVID-19 pneunomia has been depicted in [Table/Fig-1]. A total of 1119 patients' records were considered. After excluding mild cases, 398 cases had moderate or severe pneumonia. Total of 21 patients were excluded according to the specified criteria. Among the 377 recruited patients, 232 received methylprednisolone alongside standard treatment, and 145 received dexamethasone alongside standard treatment for COVID-19 pneumonia.

A total of 377 patients with moderate and severe COVID-19 infection were enrolled after selection based on the inclusion and exclusion criteria. Their hospital records were analysed to determine the types of steroids received. They were divided into two groups: one group received methylprednisolone, and the other group received dexamethasone along with the standard of care as per the Indian National Treatment Protocol. Steroids were administered to patients according to their severity for the required period as outlined in the national treatment protocol for COVID-19 management in India [12]. Records from both treatment groups (methylprednisolone and dexamethasone) were analysed for daily clinical and laboratory parameters.



[Table/Fig-1]: Flow diagram of selection of methylprednisolone and dexamethasone treatment groups in patients with COVID-19.

Study Definition:

- **COVID-19 infection:** A patient hospitalised with a positive Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) or Rapid Antigen Test (RAT) from a nasopharyngeal swab or other respiratory sample.
- **Mild COVID-19 cases:** Patients without evidence of breathlessness or hypoxia (normal saturation), only fever, cough, and other constitutional symptoms [13].
- **Moderate COVID-19 cases:** Defined as the presence of clinical features of dyspnoea and/or hypoxia, fever, cough, including SpO_2=90-94% on room air, respiratory rate ≥24/minute [13].
- **Severe COVID-19 cases:** Defined as patients with clinical signs of pneumonia plus any one of the following: a) respiratory rate >30/minute; b) severe respiratory distress with SpO_2 <90% on room air [13].
- **Dose of steroids used:** Clinical management protocol in India recommends moderate cases are to be treated with methylprednisolone 0.5 to 1 mg/kg/day for 3-5 days and for severe cases 1.0-2.0 mg/kg/day for 7-10 days (dexamethasone 0.1-0.2 mg/kg/day for moderate cases; 0.2-0.4 mg/kg/day for severe cases) [13].

  Binary outcomes evaluated included the need for high flow oxygen {Non-rebreathing Mask (NRBM) or High Frequency Nasal Oxygen (HFNO)}, NIV, Invasive Mechanical Ventilation (IMV), and death. Time-to-event outcomes evaluated included time to hospital discharge and time to death. All-cause mortality in both groups.
- **Laboratory results:** Laboratory data used in present study includes all recorded results obtained during the hospital stay of each patient. Laboratory results included haematology data {White Blood Cell (WBC) count, neutrophil, lymphocyte, and platelet count and Erythrocyte Sedimentation Rate (ESR)}; immunological and biochemical inflammatory markers {Interleukin-6 (IL-6), C-reactive Protein (CRP), D-dimer, Ferritin, Lactate Dehydrogenase (LDH), Procalcitonin, blood urea,

creatinine, Serum Glutamic Pyruvic Transaminase (SGPT), Serum Glutamic Oxaloacetic Transaminase (SGOT), Bilirubin, Prothrombin Time (PT)/International Normalised Ratio (INR), serum electrolytes}; radiology data (Chest X-ray findings, High Resolution Computed Tomography (HRCT) Thorax- CT severity index), respiratory data {Arterial Oxygen Partial Pressure (PaO_2)/ Fractional Inspired Oxygen (FiO_2)}.

These laboratory results helped to assess the severity of the patient and monitor the course of the patient during the hospital stay.

STATISTICAL ANALYSIS

The data collected were analysed using standard statistical methods with SPSS software version 29.0. Qualitative variables were expressed as counts and percentages, while quantitative variables were presented as mean±Standard Deviation (SD). A univariate analysis was then conducted to compare variables (demographic details, co-morbidity data, and presenting clinical status) between two groups of patients receiving corticosteroids. The comparison of values was performed using the two-tailed student's t-test or the Mann-Whitney U test for quantitative variables, and the Chi-square or Fisher's exact test for qualitative variables. Outcome comparisons between the two groups were analysed using the Chi-square test and t-test. Survival between the two groups was compared using Kaplan-Meier curves.

RESULTS

A total of 377 patients were enrolled in present clinical study, with 232 receiving methylprednisolone alongside the standard treatment and 145 receiving dexamethasone alongside the standard treatment. The baseline demographic data of the patients in present study has been depicted in [Table/Fig-2]. Authors found that there was no significant variation between the two treatment groups based on demographic features, co-morbid conditions, disease severity on admission day (SpO_2 at admission), and smoking status.

Characteristics		Methylprednisolone (n=232)	Dexamethasone (n=145)	p-value*
Sex	Male	145 (62.50%)	89 (61.38%)	0.489
	Female	87 (37.50%)	56 (38.62%)	
Age (year) Mean±Standard Deviation (SD)		47.13±18.43	47.37±19.04	0.900
Underlying diseases	Diabetes	58 (25.00%)	38 (26.21%)	0.117
	Hypertension	60 (25.86%)	36 (24.83%)	0.079
	IHD	49 (21.12%)	29 (20.00%)	0.786
	CKD	09 (03.88%)	08 (05.52%)	0.142
	Cancer	23 (09.91%)	14 (09.66%)	0.524
SpO_2 <90%		22 (09.48%)	14 (09.66%)	0.062
Hypotension (SBP <100 mmHg)		07 (03.02%)	05 (03.45%)	0.084
Smoker		33 (14.22%)	18 (12.41%)	0.054

[Table/Fig-2]: Demography and co-morbidity status of patients and admission status in two groups (N=377).
IHD: Ischaemic heart disease: SBP: Systolic blood pressure: CKD: Chronic kidney disease
*Chi-square, t-test

The duration of hospital stay was also compared. The mean length of hospital stay was 12.89±2.84 days in the methylprednisolone group and 12.97±2.94 days in the dexamethasone group (p-value=0.800) [Table/Fig-3]. Therefore, there was no significant difference in the duration of hospital stay between the methylprednisolone and dexamethasone treatment groups.

In the methylprednisolone group, 30.17% of patients required high-flow oxygen (NRBM/HFNO) during their stay, compared to 39.31% in the dexamethasone group (p-value=0.002) [Table/Fig-3]. Thus, there was a significant difference in the requirement for high-flow oxygen {Non Rebreathing Mask (NRBM)/High Flow Nasal Oxygen (HFNO)} between the two treatment groups, with methylprednisolone significantly reducing the need for high-flow oxygen compared to dexamethasone.

Outcome	Methylprednisolone (n=232)	Dexamethasone (n=145)	p-value*
Hospital stays (days) mean±Standard Deviation (SD)	12.89±2.84	12.97±2.94	0.800
High flow oxygen (NRBM/ HFNO)	70 (30.17%)	57 (39.31%)	0.002
Non Invasive Ventilation (NIV)	12 (05.17%)	07 (06.21%)	0.001
Invasive ventilation	04 (01.72%)	02 (02.07%)	0.001
Deceased	54 (23.28%)	51 (35.17%)	0.012

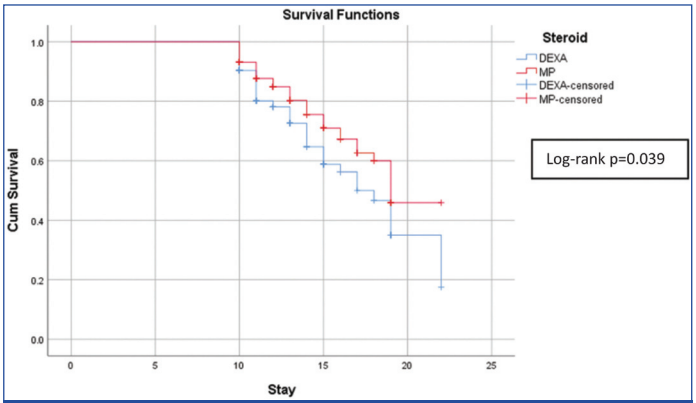
[Table/Fig-3]: Outcome of patients in two treatment groups (N=377).
*Chi-square, t-test

In the methylprednisolone group, 5.17% of patients required NIV, compared to 6.21% in the dexamethasone group (p-value=0.001) [Table/Fig-3]. Therefore, there was a significant difference in the requirement for NIV between the two treatment groups, with methylprednisolone significantly reducing the need for NIV compared to dexamethasone.

In the methylprednisolone group, 1.72% of patients required invasive ventilation, compared to 2.07% in the dexamethasone group (p-value=0.001) [Table/Fig-3]. Thus, there was a significant difference in the requirement for invasive ventilation between the two treatment groups, with methylprednisolone significantly reducing the need for invasive ventilation compared to dexamethasone.

In the methylprednisolone treatment group, 54 (23.28%) patients succumbed to death, whereas in the dexamethasone treatment group, 51 (35.17%) patients died in the hospital. The difference in mortality rates between the two treatment groups was statistically significant (p-value=0.012) [Table/Fig-3]. Therefore, methylprednisolone significantly reduces mortality compared to dexamethasone in moderate/severe COVID-19 patients.

Kaplan-Meier survival analysis showed a significant survival benefit among patients who received methylprednisolone compared to dexamethasone (log-rank p-value=0.039) [Table/Fig-4].



[Table/Fig-4]: Kaplan Meier's survival analysis in two treatment groups.

When comparing treatment effects in the methylprednisolone and dexamethasone groups in relation to the severity of the disease, authors found that in moderate pneumonia, methylprednisolone had lower mortality compared to dexamethasone (12.72% vs. 40.54%) (p<0.001). In severe pneumonia, dexamethasone-treated patients had lower mortality compared to methylprednisolone-treated patients (33.33% vs. 54.23%) (p-value=0.009) [Table/Fig-5]. Therefore, in severe cases of COVID-19, dexamethasone is significantly superior to methylprednisolone in reducing mortality. In moderate cases of COVID-19, methylprednisolone is significantly superior to dexamethasone in reducing mortality.

Severity	Survival	Methylprednisolone (n=173)	Dexamethasone (n=37)	p-value*
Moderate (n=210)	Cured	151 (87.28%)	22 (59.46%)	<0.001
	Deceased	22 (12.72%)	15 (40.54%)	
Severity	**Survival**	**Methylprednisolone (59)**	**Dexamethasone (108)**	**p-value***
Severe (n=167)	Cured	27 (45.76%)	72 (66.67%)	0.009
	Deceased	32 (54.23%)	36 (33.33%)	

[Table/Fig-5]: Severity and survival in treatment groups.
*Chi-square, t-test

DISCUSSION

In present study, authors found that there was no significant variation between the two treatment groups based on demographic features, co-morbid conditions, disease severity on admission day (SpO_2 at admission), and smoking status that might affect the outcome in the two treatment groups in terms of outcome. The present study showed a significant beneficial effect of methylprednisolone in the patients' treatment course compared to dexamethasone. Methylprednisolone significantly reduces the requirement for high-flow oxygen (NRBM/HFNO), NIV, and invasive ventilation compared to dexamethasone. The present study also showed that there was no significant difference in the duration of hospital stay between the methylprednisolone and dexamethasone treatment groups. Furthermore, methylprednisolone significantly reduces mortality compared to dexamethasone in moderate/severe COVID-19 patients (23% vs. 35%). In present study, Kaplan-Meier survival analysis also showed a significant survival benefit among patients who received methylprednisolone compared with dexamethasone (log-rank p-value=0.039). On sub-analysis regarding disease severity, it was found that in severe cases of COVID-19, dexamethasone is significantly superior, while in moderate cases of COVID-19, methylprednisolone is significantly superior in terms of reducing mortality. Since the emergence of COVID-19, steroids have been a cornerstone in the standard treatment protocol for treating moderate and severe COVID-19 cases worldwide. Different types of steroids and regimens have been approved in various parts of the world. Braude AC and Rebuck AS studied the lung penetration of steroids and found that methylprednisolone has higher lung penetration [14]. Fadel R et al., showed that an early short course of methylprednisolone reduced mortality and improved other composite outcome indicators [15]. Thus, methylprednisolone can be a better immunosuppressive agent in the treatment of COVID-19 and in improving its respiratory complications.

The present study included 377 patients (methylprednisolone=232; dexamethasone=145). The two groups had a mean age of around 47 years. The present study included relatively younger patients compared to other studies. All co-morbidities (such as diabetes, hypertension, CKD, etc.) were evenly distributed between the two groups, and at admission, patients in both groups had similar clinical statuses (such as hypoxia, hypotension, etc.).

Fatima SA et al., studied 100 patients from Lahore, Pakistan, of which 35 patients received dexamethasone and 65 were in the methylprednisolone group [9]. The mean age of patients was 57.91 years in the dexamethasone group and 54.86 years in the methylprednisolone group. They included patients who received tocilizumab or convalescent plasma. There were significant co-morbidities (diabetes, hypertension, etc.) that were evenly distributed between the two groups.

Ranjbar K et al., evaluated 86 patients from Iran in a prospective manner [10]. They assigned two groups: methylprednisolone (2 mg/kg/day; intervention group) or dexamethasone (6 mg/day; control group). Data were assessed based on a 9-point WHO ordinal scale extending from uninfected (point 0) to death (point 8). They excluded patients with uncontrolled diabetes mellitus, uncontrolled hypertension, and non hypoxic patients.

Canaan M et al., studied 121 mechanically ventilated COVID-19 patients retrospectively, with 53 receiving methylprednisolone and 68 receiving dexamethasone [11]. Pinzón MA et al., conducted an ambispective cohort study with survival analysis of 216 patients diagnosed with severe COVID-19 pneumonia in Taiwan [16]. One group received dexamethasone 6 mg QD for seven to 10 days, and the other group received a high dose of methylprednisolone of 250 to 500 mg/day for three days, with a subsequent change to oral prednisone 50 mg/day for 14 days.

Rana MA et al., analysed 60 participants retrospectively from Lahore [17]. The dexamethasone group received 8 mg twice daily, and the methylprednisolone group received 40 mg twice daily for eight days. El Mezzeoui S et al., retrospectively studied 513 COVID-19 patients admitted to the intensive care unit in Morocco [18]. The first group was treated with intravenous (1 mg/kg) or oral methylprednisolone, and the second group was treated with intravenous dexamethasone 6 mg/kg per day.

Buso R et al., retrospectively studied 246 patients from two steroid efficacy comparison groups in Italy [19]. The doses of the two steroids were dexamethasone 6 mg once daily or methylprednisolone 60 mg/day for atleast 10 days. Ko JJ et al., from California, USA, studied 262 patients prospectively [20]. The doses of steroids were methylprednisolone 1 mg/kg/day for three days and dexamethasone 6 mg for seven days.

Mogali SM and Qureshi MF from Karnataka, India, studied 130 patients retrospectively [21]. The two groups had differences in co-morbidities (44.6% vs. 32.4%), making the study weak.

The present study concluded that methylprednisolone did not reduce the duration of hospital stay compared to dexamethasone. However, methylprednisolone was significant in reducing the requirement for HFNO/NRBM in present study. Fatima SA et al., showed no significant difference in the duration of hospital stay, and there was no mention of NRBM/HFNO requirement [9]. Ranjbar K et al., and Canaan M et al., both showed methylprednisolone to be superior in reducing the duration of hospital stay [10,11]. In both of these studies, there was no measurement of NRBM/HFNO requirement.

Pinzón MA et al., found that the methylprednisolone group significantly reduced hospital stays and transfers to the intensive care unit, but there was no mention of NRBM/HFNO requirement [16]. Rana MA et al., did not study the duration of hospital stay or NRBM/HFNO requirement. El Mezzeoui S et al., concluded that the dexamethasone-treated group had a good evolution with a significant reduction in oxygen supplementation, but there was no mention of the duration of hospital stays [18].

Buso R et al., showed no differences in the requirement for critical care support or the duration of hospital stay between the two groups [19]. Ko JJ et al., did not study the duration of hospital stay or NRBM/HFNO requirement [20]. Mogali SM and Qureshi MF found no difference between dexamethasone and methylprednisolone in terms of hospital stay duration or the requirement for HFNO/NRBM [21].

Fatima SA et al., showed no significant difference in invasive ventilation or mortality [9]. Ranjbar K et al., found methylprednisolone to be superior in reducing invasive ventilation and mortality compared to dexamethasone. Canaan M et al.,'s study showed that methylprednisolone had numerically lower mortality, but not statistically significant, and dexamethasone was found to be better in severe COVID-19 pneumonia (mechanical ventilation) [11]. Pinzón MA et al., found that the methylprednisolone group significantly reduced transfers to the intensive care unit and mortality, although there was no specific mention of invasive ventilation [16]. Rana MA et al., did not mention mortality, ventilation/NRBM/HFNO requirements [17]. Mogali SM and Qureshi MF found no difference between dexamethasone and methylprednisolone in terms of NIV, mechanical ventilation, and also did not find any mortality benefit [21].

El Mezzeoui S et al., concluded that the dexamethasone-treated group had a good outcome with a significant reduction in oxygen supplementation, lower use of invasive ventilation, and a significant reduction in mortality compared with the methylprednisolone group. The present study had more severe patients in the dexamethasone arm [18]. Buso R et al., showed no differences in mortality between the two steroid groups, and there were no significant differences in the requirement for critical care support between the two groups [19]. Ko JJ et al., found that in patients with COVID-19 requiring mechanical ventilation, methylprednisolone was superior to dexamethasone [20]. However, in patients who did not require mechanical ventilation, both steroids decreased mortality to low rates, and no difference between the two steroids was detected.

In the current study, we found that in severe cases of COVID-19, dexamethasone is significantly superior to methylprednisolone in reducing mortality. Conversely, in moderate cases of COVID-19, methylprednisolone is significantly superior to dexamethasone in reducing mortality. Fatima SA et al., showed no significant improvement in temperature, CRP, or oxygen levels in the two steroid groups, and no superiority was found between the two groups [9]. Ranjbar K et al., found that the methylprednisolone group demonstrated significantly better clinical status compared to the control group on day 5 and day 10 of admission [10]. Canaan M et al.,'s study showed that the time interval between steroid administration and death was significantly lower in the methylprednisolone group compared to the dexamethasone group [11]. However, the time interval between hospital admission and steroid administration was significantly higher in the methylprednisolone group compared to the dexamethasone group. Additionally, the time interval between hospital admission and ICU admission was significantly lower in the methylprednisolone group compared to the dexamethasone group. Pinzón MA et al., found that after completing 4 days of treatment with parenteral corticosteroids, laboratory markers (CRP, D-Dimer, Lactate dehydrogenase) decreased significantly in the group that received methylprednisolone [16]. Rana MA et al., found that both steroid therapies are effective in controlling inflammation markers (CRP), with dexamethasone significantly improving the P/F ratio in COVID-19 patients [17]. Mogali SM and Qureshi MF showed methylprednisolone to be superior in improving oxygen levels and laboratory marker status [21]. El Mezzeoui S et al., concluded that patients treated with dexamethasone had more critical lung lesions compared to patients treated with methylprednisolone, and these patients showed good progress with a significant reduction in oxygen supplementation and significant improvement in biological parameters (CRP and white blood cells) [18]. Buso R et al., showed no differences in viral clearance time between the two groups [19]. Ko JJ et al., did not study laboratory parameters [20]. The present study did not analyse data on laboratory parameters. Results from various studies worldwide analysing the efficacy of methylprednisolone were compared with the results of present study as shown in [Table/Fig-6] [9-11,16-21].

Authors name	Treatment groups	Hospital stay	(NRBM or HFNO)	Non Invasive Ventilation (NIV)	Invasive ventilation	Mortality	Others
Fatima SA et al., [9]	MP (1 mg/kg/day)× 5 days vs. Dexa (8 mg/day)×5 days (included patients who got tocilizumab or convalescent plasma)	In Dexa group, there were 15 critically ill patients who were shifted to Intensive Care Unit (ICU) and seven of them needed ventilatory support, whereas in MP group 22 had to be admitted in ICU with 8 patient needing ventilator	Not studied	Not studied	Both same	Six patients died among those who received Dexa while 10 patients died among those receiving MP	In patients receiving Dexa, there was a significant reduction in mean temperature. There was significant reduction in CRP In MP group, the mean reduction in temperature was from 100.66 F on day 0-98.7 F on day 5. Mean oxygen requirement reduced from 11.8 L to 7.8 L. Mean CRP reduced from 129.8 to 59.07 in 5 days (p<0.0001)
Ranjbar K et al., [10]	MP* (2 mg/kg/day) vs. Dexa# (6 mg/day) [excluded patients with uncontrolled diabetes mellitus, uncontrolled hypertension and non hypoxic patients]	Mean length of hospital stay was 7.43±3.64 4days and 10.52±5.47 days in the MP and Dexa groups, respectively	Not studied	Not studied	Ventilator was significantly lower in the MP group than in the Dexa group (18.2% vs 38.1%)	MP was better	MP group demonstrated significantly better clinical status compared to the Dexa group at day 5 and day 10 of admission
Canaan M et al., [11]	Dose not mentioned (only mechanically ventilated patients were included)	In hospital length of stay (p=0.307) were lower among the MP group	NA	NA	NA	In-hospital mortality was lower among COVID-19 patients receiving MP, compared to the Dexa group, though not significantly (Hazard Ratio (HR), 0.64; 95% CI: 0.35-3.17)	The time interval between hospital admission and steroid administration was significantly higher among the MP group compared to the Dexa group (32.3 h vs. 8.4 h, p<0.001). The time interval between hospital admission and ICU admission was significantly lower among the MP group, compared to the Dexa group (90.7 h vs. 429.5 h, p=0.002)
Pinzón MA et al., [16]	MP (250-500 mg/ day×3 days vs. Dexa 6 mg/day×10 days (Only included severe COVID-19 pneumonia)	MP	-	-	-	At 30-day follow-up, 92.6% were alive in MP vs 63.1% of those who received Dexa	Patients in the Dexa group evolved to severe ARDS£ in a higher proportion (26.1% vs 17.1% than the MP group). After completion 4 days of treatment with parenteral corticosteroid, laboratory markers$ of severity decreased significantly in the group that received MP
Rana MA et al., [17]	Dexa 8 mg BD× 8 days vs. MP 40 mg BD×8 days	-	-	-	-	-	Steroid therapy is effective in controlling inflammation markers (CRP), and especially Dexa is significantly effective in improving the P/F ratio in COVID-19 patients

Mogali SM and Qureshi MF [21]	Dose not mentioned (Two groups had difference in co-morbidities (44.6% vs 32.4%)	No difference in Dexa and MP in terms of hospital stay	No difference	No difference	No difference	Both same	MP is superior in improving oxygen and laboratory marker status
El Mezzeoui S et al., [18]	Dexa 6 mg/kg/day vs MP 1 mg/kg Both 7 days (in intensive care unit)	-	-	-	Dexa treated group had good evolution with a significant reduction of oxygen supplementation	Dexa treated group had good evolution with a significant reduction of oxygen supplementation	Dexa causes significant reduction of oxygen supplementation and biological parameters (CRP and white blood cells)
Buso R et al., [19]	MP 60 mg/day vs. Dexa 6 mg/day Both at least 10 d (only non intensive care patients)	Both same	-	-	-	Both same (no differences in requirement of critical care support)	Need for intensive or semi-intensive care- same in both groups Time to viral clearance- same in both groups
Ko JJ et al., [20]	MP (1 mg/kg/d)× ≥3 day vs. Dexa (6 mg/kg/d)×≥7 d	-	-	-	MP is better	In patients with COVID-19 requiring mechanical ventilation, methylprednisolone was superior to dexamethasone. But, in patients who did not require mechanical ventilation, both steroids decreased mortality to low rates and no difference between the 2 steroids was detected	-
This study	MP and Dexa as per Indian protocol and severity	Both same	MP	MP	MP	MP	Severe COVID-19- Dexa is better Moderate COVID-19-MP is better

[Table/Fig-6]: Studies evaluating parameters in respect to favouring steroids [9-11,16-21].
*MP: Methylprednisolone: #Dexa: Dexamethasone: ^NA: Not applicable

Limitation(s)

The present study had several limitations, including a relatively small sample size in each group. There is limited data on complications and other outcome measures. There is a lack of follow-up data after discharge because the patients who survived in the hospital may have died shortly after discharge. Some patients also presented late at the tertiary care hospital. No data regarding radiological features were analysed. Considering the limitations of present study, further randomised controlled trials with larger patient populations and subsequent follow-up for a few months would suggest a more significant beneficial effect of methylprednisolone in patients with COVID-19 pneumonia.

CONCLUSION(S)

The present study concludes that for hospitalised patients with COVID-19 pneumonia, methylprednisolone significantly reduces the need for NRBM/HFNO, NIV, and invasive ventilation compared to dexamethasone. However, the duration of hospital stay in these two steroid-treated patient groups remains non significant. There is a definite mortality benefit of methylprednisolone over dexamethasone in moderate and severe COVID-19 pneumonia patients. For severe COVID-19 pneumonia, dexamethasone is beneficial, while for moderate pneumonia, methylprednisolone is beneficial. The present study clearly analysed the effects of the two most commonly used steroids, methylprednisolone and dexamethasone, in COVID-19 pneumonia. This difference in efficacy between the two steroids may be clinically significant, if used judiciously in future waves of COVID-19.

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