Scientific Research Publishing

Advances in Infectious Diseases, 2023, 13, 508-520
https://www.scirp.org/journal/aid
ISSN Online: 2164-2656
ISSN Print: 2164-2648

The Effect of Dexamethasone versus Methylprednisolone in the Treatment of COVID-19 Patients in Jordan

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How to cite this paper: Al Ramahi, J.W., Hasan, N., Matar, A., Al-Ali, M.M., Abdulhadi, L., Kaf, D.A., Saadeh, W., Hamdan, N., Khalaf, H.A., Gharaibeh, M., Hamadallah, H., Bader, A., Atout, M., Mar'I, S.M. and Alhamed, T. (2023) The Effect of Dexamethasone versus Methylprednisolone in the Treatment of COVID-19 Patients in Jordan. *Advances in Infectious Diseases*, **13**, 508-520.
https://doi.org/10.4236/aid.2023.133041

Received: August 21, 2023
Accepted: September 19, 2023
Published: September 22, 2023

Abstract

Background: Previous studies focused on the treatment effect of steroids versus no steroids in treating severe COVID-19 patients, a few studies evaluated outcomes for treating those patients with either dexamethasone or methylprednisolone. Currently, we evaluate the difference in mortality associated with treating COVID-19 patients with dexamethasone versus methylprednisolone. **Methods:** With a retrospective multicenter study, records were reviewed for the admitted patients with severe COVID-19 during the peak of the severe COVID-19 pandemic. All admitted patients on dexamethasone or methylprednisolone were included. Patients were analyzed as all populations and propensity scores matched patients. Propensity scores were calculated for several confounders by the generalized linear model, and a "greedy" nearneighbor matching algorithm was used. Continuous variables with nonnormal distribution were analyzed by Wilcoxon signed rank test. Chi-squared and Fischer exact test analyzed categorical variables. P-values were adjusted by the Bonferroni method for both data cohorts. Body mass index was in categories. Radiological findings were divided into five categories. The outcomes: mortality, the need for home oxygen therapy, recovery, and residual symptoms on discharge were analyzed by an independent two-sample test for equality of proportions (with Yates correction), and logistic regression analy-

sis. **Results:** Among the 1128 reviewed records, patients on dexamethasone or methylprednisolone were 1071, and the propensity score-matched patients were 784: dexamethasone 393 and methylprednisolone 391. There was no significant difference in the characteristics of patients between the two steroids (p-value and adjusted p-value > 0.05) for most variables. PSM adjusted a few discrepant variables before analysis. The outcome of the unmatched patients demonstrated dexamethasone benefit in the need for home oxygen therapy (<0.001) and mortality (<0.01), but not for recovery and residual symptoms on home discharge (p-value > 0.05). However, matched patients demonstrated significantly lower mortality associated with dexamethasone treatment (difference −2.68%, 95%CI, −1.0, −0.004, p = 0.03, and OR 1.7, p = 0.017), and no difference for the other outcomes, including the need for home oxygen therapy (p-value > 0.05). **Conclusion:** Dexamethasone treatment caused significantly less mortality than methylprednisolone in treating our COVID-19 patients, but no significant difference in recovery, the need for home oxygen therapy, and residual symptoms on discharge.

Keywords

Dexamethasone, Methylprednisolone, COVID-19 Mortality, Home Oxygen, COVID-19 Recovery

1. Introduction

Soon after the WHO announcement of SARS-CoV-2 as a worldwide pandemic, cures were urgently recommended to treat the increasing deleterious health effects of the pandemic on patients; specific antivirals, other repurposed agents, and agents that suppress the hyper-inflammatory storm associated with SARS-CoV-2 infection were being evaluated at a fast pace [1]. The hyperinflammatory state associated with SARS-CoV-2 infection causes widespread tissue damage, especially in the lungs; its control is of paramount priority as was intervened in SARS-CoV and MERS-CoV where cytokine release syndrome was observed [2] [3]. Anti-inflammatory agents arose for the COVID-19 associated hyper-inflammatory syndrome, led by steroids due to their efficacy and relative safety [4], and are being prescribed extensively for moderate and severe cases, alone or combined with other agents [5]. The reasoned experience of treating patients with steroids for severe COVID-19 patients implied that low-dose steroid use might have been beneficial. Steroids available for use in hospitalized patients are dexamethasone and methylprednisolone among others. A leading published study demonstrated that dexamethasone significantly lowered mortality in severe COVID-19 patients. Also, methylprednisolone was evaluated for the same reason and found to bring a similar clinical benefit. A randomized clinical trial was conducted to test a range of potential treatments for COVID-19, including low-dose dexamethasone; it demonstrated that dexamethasone has an evident

35% day-28 mortality reduction in patients receiving either invasive mechanical ventilation but not among those receiving no respiratory support [6]. Another study cited a 67% reduction in mortality with using dexamethasone [7], and in a single-blind, randomized trial with the intention-to-treat (ITT) analysis, methylprednisolone pulse dose at 250 mg/day for three days remarkably lowered mortality compared with the standard care (5.9% versus 42.9%; $p < 0.001$) [8]. A comparative retrospective study of patients requiring invasive mechanical ventilation methylprednisolone at 1 mg/kg/day for ≥3 days reduced mortality compared with 6 mg dexamethasone for seven days [9]. Also, a time frame for initiating steroids was cited, *i.e.*, to use steroids if symptoms were >7 days, or the patient was hospitalized >72 hours off invasive mechanical ventilation [10]. Nonetheless, a Cochrane review on steroid treatment in patients with severe COVID-19 disease concluded that "Systemic corticosteroids plus standard care compared to standard care probably reduce the 30 days all-cause mortality (low to moderate-certainty evidence) slightly" [11].

In this retrospective cross-sectional study, we conducted a propensity-score matched study (PSM) with stabilized inverse probability of treatment weighting (SIPTW) of our hospitalized patients to evaluate the mortality effect difference between dexamethasone versus methylprednisolone.

2. Materials and Methods

2.1. Study Settings

Data for COVID-19 patients was collected from three participating hospitals (The Specialty, Jordan, and Al Khalidi) as a database during the peak of the COVID-19 pandemic. The study was a retrospective cross-sectional between (October 2020 to May 2021). Three studies were published earlier on different topics from the same database by our group [12] [13] [14]. Special units for managing patients with COVID-19 were allocated with an approximate capacity of 155-floor beds and 47 ICU beds. Data was uploaded into a cloud Excel sheet (Microsoft Corporation). Records were included as patients presented for admission in the participating hospitals. The internal review boards of the three hospitals approved the study (Specialty 108298/T/1/5, Al Khalidi KHMC/22/R/601, and Jordan JH/IRB/2020/12). No consent was needed as no added intervention was started, and no procedure or tissue specimen was examined for the purpose of the study but as a standard of care, following the "Declaration of Helsinki".

2.2. Inclusion Criteria

All patients with COVID-19 admitted to one of the three hospitals between October 2020 - May 2021 were included, 1128 records were reviewed for patients who stayed in the hospitals and were started on dexamethasone or methylprednisolone. None of the patients was excluded from the analysis including a few patients with malignancy (**Table 1**). In addition to the characteristics in **Table 1**, almost all patients were started on several medications like vitamin D in varying

Table 1. The characteristics of COVID-19 patients according to dexamethasone or methylprednisolone treatment allocation.

	All Patients				Propensity scores matched patients			
	Dexa N = 453[1]	Methyl N = 618[1]	p-value[2]	q-value[3]	Dexa N = 393[1]	Methyl N = 391[1]	p-value[2]	q-value[3]
Length of hospital stay	6.5 (5.2)	7.5 (6.1)	0.013	0.3	6.8 (5.4)	6.8 (5.3)	0.9	>0.9
Age	60 (15)	62 (15)	0.054	>0.9	62 (15)	62 (15)	0.7	>0.9
Sex								
female	174 (38%)	207 (33%)	0.10	>0.9	148 (38%)	141 (36%)	0.6	>0.9
male	279 (62%)	411 (67%)			245 (62%)	250 (64%)		
All symptoms	5.27 (2.34)	4.94 (2.16)	0.020	0.5	5.05 (2.32)	5.01 (2.10)	>0.9	>0.9
Comorbidities								
cardiac disease	6 (1.3%)	13 (2.1%)			6 (1.5%)	7 (1.8%)		
chronic lung disease	8 (1.8%)	21 (3.4%)			8 (2.0%)	10 (2.6%)		
diabetes mellitus	45 (9.9%)	64 (10%)			43 (11%)	41 (10%)		
Free	39 (8.6%)	5 (0.8%)			7 (1.8%)	3 (0.8%)		
hypertension	50 (11%)	72 (12%)	<0.001	<0.001	46 (12%)	49 (13%)	0.9	>0.9
malignancy	5 (1.1%)	8 (1.3%)			5 (1.3%)	6 (1.5%)		
obesity	9 (2.0%)	12 (1.9%)			9 (2.3%)	9 (2.3%)		
other chronic disease	21 (4.6%)	12 (1.9%)			11 (2.8%)	11 (2.8%)		
two or more	270 (60%)	411 (67%)			258 (66%)	255 (65%)		
Body mass index (BMI)[4]								
Underweight	1 (0.2%)	1 (0.2%)			1 (0.3%)	0 (0%)		
Healthy	90 (20%)	142 (23%)			83 (21%)	88 (23%)		
Overweight	188 (42%)	263 (43%)	0.7	>0.9	157 (40%)	169 (43%)	0.5	>0.9
Obesity Class 1	122 (27%)	153 (25%)			102 (26%)	97 (25%)		
Obesity Class 2	35 (7.7%)	41 (6.6%)			33 (8.4%)	27 (6.9%)		
Obesity Class3	17 (3.8%)	18 (2.9%)			17 (4.3%)	10 (2.6%)		
Tobacco	63 (14%)	68 (11%)	0.2	>0.9	54 (14%)	47 (12%)	0.5	>0.9
White blood cells								
4000 - 5000	41 (9.1%)	64 (10%)			37 (9.4%)	37 (9.5%)		
5000 - 11999	273 (60%)	364 (59%)	0.6	>0.9	239 (61%)	243 (62%)	>0.9	>0.9
less than 4000	32 (7.1%)	34 (5.5%)			26 (6.6%)	24 (6.1%)		
more than 12000	107 (24%)	156 (25%)			91 (23%)	87 (22%)		

Continued

Elevated LDH	261 (58%)	400 (65%)	0.018	0.4	228 (58%)	237 (61%)	0.5	>0.9
Elevated ferritin	368 (81%)	496 (80%)	0.7	>0.9	322 (82%)	310 (79%)	0.3	>0.9
Elevated C-reactive protein	448 (99%)	593 (96%)	0.004	0.091	388 (99%)	385 (98%)	0.8	>0.9
D. Dimer	273 (60%)	422 (68%)	0.007	0.2	239 (61%)	267 (68%)	0.029	0.7
Imaging								
ground glass	175 (39%)	214 (35%)			153 (39%)	149 (38%)		
lobar	29 (6.4%)	44 (7.1%)			28 (7.1%)	19 (4.9%)		
minimal infiltrate	134 (30%)	160 (26%)	0.13	>0.9	110 (28%)	110 (28%)	0.6	>0.9
Multi-lobar	102 (23%)	175 (28%)			90 (23%)	102 (26%)		
normal imaging	13 (2.9%)	25 (4.0%)			12 (3.1%)	11 (2.8%)		
Antivirals	274 (60%)	447 (72%)	<0.001	0.001	248 (63%)	261 (67%)	0.3	>0.9
Antibacterials	343 (76%)	445 (72%)	0.2	>0.9	302 (77%)	301 (77%)	>0.9	>0.9
Antifungals	52 (11%)	46 (7.4%)	0.024	0.5	40 (10%)	31 (7.9%)	0.3	>0.9
Interleukin 6 inhibitors	38 (8.4%)	103 (17%)	<0.001	0.002	33 (8.4%)	43 (11%)	0.2	>0.9
Colchicine	128 (28%)	127 (21%)	0.003	0.079	101 (26%)	89 (23%)	0.3	>0.9
Anticoagulants	429 (95%)	600 (97%)	0.047	>0.9	377 (96%)	374 (96%)	0.8	>0.9
Fever	92 (20%)	135 (22%)	0.5	>0.9	83 (21%)	84 (21%)	>0.9	>0.9
Oxygen saturation								
intermediate	166 (37%)	202 (33%)			139 (35%)	137 (35%)		
Low	197 (43%)	299 (48%)	0.3	>0.9	179 (46%)	185 (47%)	0.8	>0.9
normal	90 (20%)	117 (19%)			75 (19%)	69 (18%)		
Oxygen delivery method								
combined	22 (4.9%)	24 (3.9%)			16 (4.1%)	16 (4.1%)		
high flow	23 (5.1%)	20 (3.2%)			19 (4.8%)	14 (3.6%)		
IMV	18 (4.0%)	20 (3.2%)			17 (4.3%)	18 (4.6%)		
nasal prongs	195 (43%)	192 (31%)	<0.001	0.001	160 (41%)	147 (38%)	0.8	>0.9
NIMV	14 (3.1%)	29 (4.7%)			13 (3.3%)	11 (2.8%)		
nonbreathing mask	92 (20%)	137 (22%)			83 (21%)	86 (22%)		
room air	38 (8.4%)	98 (16%)			35 (8.9%)	48 (12%)		
simple mask	51 (11%)	98 (16%)			50 (13%)	51 (13%)		

[1]Mean (SD); n (%); [2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test; [3]Bonferroni correction for multiple testing; [4]BMI classes: https://www.cdc.gov/obesity/basics/adult-defining.html; Dexa: dexamethasone, Methyl: methylprednisolone, IMV: invasive mechanical ventilation, NIMV: non-invasive mechanical ventilation.

doses and durations, protein-pump inhibitors, acetylsalicylic acid, zinc tablets, Vitamin C, paracetamol, and multivitamins. Due to their universal use were not included as confounders.

2.3. Treatment Protocols

A currently updated COVID-19 management protocol is published by the Jordan Ministry of Health (last update: *Case Management protocol for COVID*-19, *MOH. June* 2023); dexamethasone 6 mg/day for 7 to 10 days or methylprednisolone 32 mg/day intravenously administered as 1 - 2 doses for 7 - 10 days [15]. The treating physicians dominated by chest specialty, and minimal Infectious Diseases service partially relied on the Ministry of Health protocol and literature updates; treating physicians prescribed dexamethasone and methylprednisolone in various doses and durations, doses for dexamethasone are mostly 6 mg/day for 7 - 10 days, and methylprednisolone as in MOH recommendations, a few prescribed 40 - 80 mg every 8 hours. Other agents prescribed by the treating physicians to some patients according to their own interpretation of their need for an agent based on the evolving literature; anticoagulants (Enoxaparin sodium, Apixaban, Rivaroxaban, and Fondaparinux), antivirals (Favipiravir, Remdesivir), and colchicine were added to the other confounders.

2.4. Classification of Radiological Findings

Infiltrates on chest radiography were described according to the severity of lung involvement as shown in a plain chest radiography and/or chest CT; lung involvement was classified into five categories; normal chest imaging, minimal infiltrate on imaging, a lobar infiltrate, diffuse ground glass appearance, and severe multilobe infiltrate, this classification somehow resembles a previously published chest radiography scoring system [16].

2.5. Statistical Analysis

Characteristics for all patients and propensity-matched patients were described (**Table 1**). Missingness in the various available variables for analysis was 751 (2.8%), and were imputed by multivariate imputations by chain equation "MICE" [17]. Propensity-score match tolerance (caliper) was 0.2 S.D. The matching method was the nearest neighbor (greedy) without replacement. Predictors entered were: Age, gender, length of hospital stay, the sum of recorded symptoms, comorbidities, BMI, Tobacco, ferritin level, C-RP, D-Dimer, LDH, imaging, antivirals, anticoagulants, antibacterials, antifungals, IL6-inhibitors, colchicine, documented temperature, blood oxygen saturation, oxygen delivery method, and peripheral white blood cells. A generalized linear model (logistic regression analysis) analysis was used to calculate the propensity scores of the confounders. Characteristics and outcomes of the patients were tabulated as all patients and PSM patients were allocated to dexamethasone and methylprednisolone. Characteristics were analyzed by the Wilcoxon rank sum test for non-normally distri-

buted covariates, Pearson's Chi-squared test, and Fisher's exact test for contingency categorical data. Corrections were made by adjusted p-values with the Bonferroni method (q-value). The Kruskal-Wallis's rank sum test analyzes the outcomes versus steroids and is found to come from a similar distribution (p = 0.3). Analysis was done by R, R-Studio (*R Core Team* (2023). https://www.R-project.org/, *RStudio Team* (2020). http://www.rstudio.com/.). With attached packages tidyverse [18] and gtsummary [19]. Outcomes were analyzed by Chi-squared and 2-sided tests for equality of proportions (two samples t-test) with Yates continuity correction and a generalized linear model. A p-value of <0.05 was considered significant.

3. Results

Among the 1128 reviewed records. The characteristics of patients who were on steroids (N = 1071), dexamethasone, or methylprednisolone, and the characteristics of the PSM patients (N = 784; dexamethasone 393 and methylprednisolone 391) were described in **Table 1**. There was no significant difference in the distribution of patients between the two steroids for age, sex, and body mass index into six categories, tobacco, white blood cells, serum ferritin, imaging categories, antibacterials, fever, and oxygen saturation (p-value > 0.05). The unbalanced characteristics for patients on steroids were: the length of hospital stay (p = 0.013), all-symptoms (p = 0.02), comorbidities, interleukin-6 inhibitors, oxygen delivery method, and antivirals (p < 0.001), elevated C-RP, D. Dimer (q-value), and colchicine (p < 0.01), elevated LDH (P0.018) antifungals (p = 0.024), and anticoagulants (p = 0.047), and all patients were balanced by propensity score and PSM (p > 0.05). The Bonferroni method's adjusted p-value for multiple comparisons did some characteristics balancing (p > 0.05) like the length of hospital stay, all symptoms, LDH, C-RP, D. Dimer, antifungals, colchicine, and anticoagulants. Frequency of symptoms on hospital admission was: fever 684 (12.59%), chills 527 (9.7%), sore throat 328 (6.04%), shortness of breath 908 (16.71%), cough 891 (16.4%), aches & pains 691 (12.72%), headaches 464 (8.45), loss of smell 358 (6.59%), loss of taste 364 (6.7%), diarrhea 152 (2.8%), rhinorrhea 67 (1.23%). In an analysis of symptoms, each symptom scored one and its absence a zero. Symptoms were summed up, their summary was (min = 0.0, Q1 = 3.0, median = 5.0, mean = 5.0, Q3 = 7.0, max = 11.0) **Figure 1**. For patients with zero symptoms were eight, the vast majority were three or more symptoms.

Outcome Analysis

All patients on methylprednisolone treatment did significantly better than dexamethasone for the need for home oxygen therapy after discharge (difference = 10.3%, 95% C.I., 4.1 - 16.0, p < 0.001), but mortality was more with methylprednisolone (difference = −6.0%, 95% C.I., −10.3, −1.9, p = 0.005). At the same time, there was no difference between dexamethasone and methylprednisolone for recovery and residual symptoms (p > 0.05) (**Table 2(a)**).

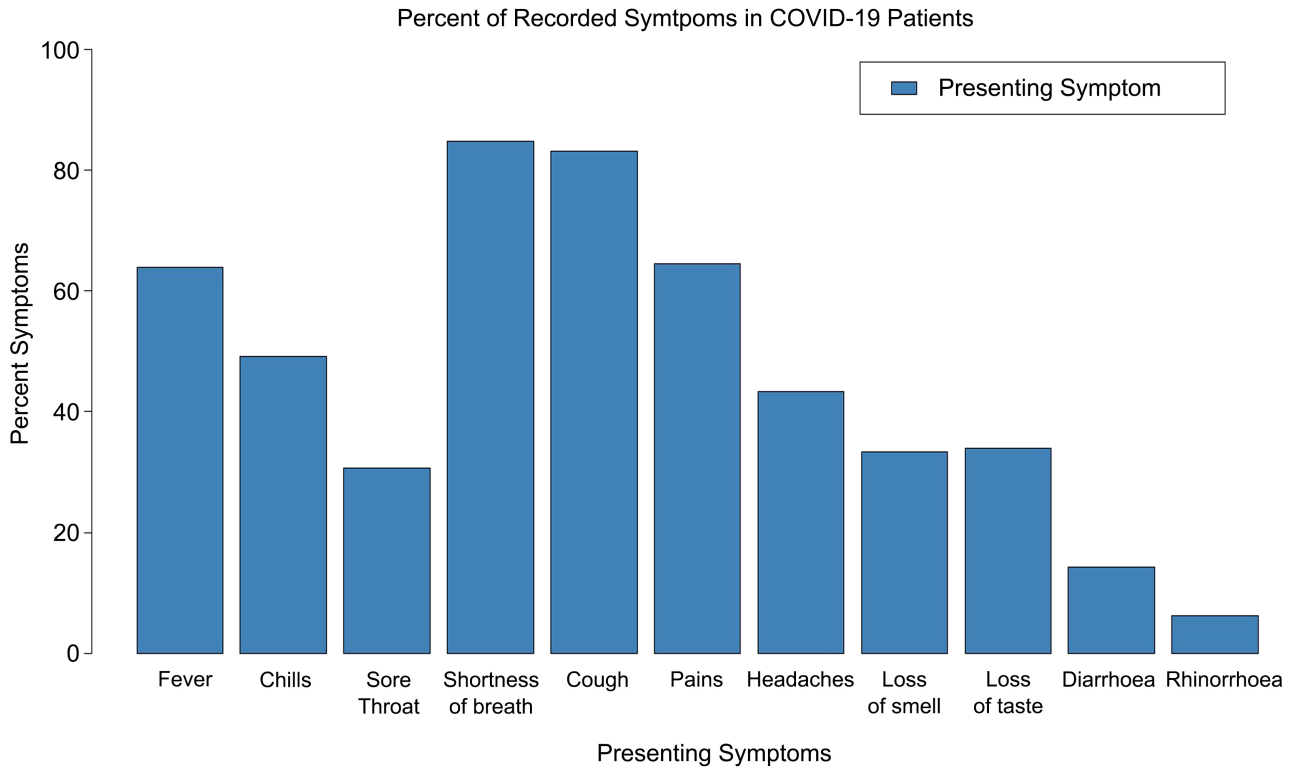

Figure 1. The distribution of symptoms for all COVID-19 patients treated with steroids at presentation.

PSM patients (**Table 2(b)**) demonstrated no significant difference for the outcomes examined: recovered (p = 0.93), residual symptoms (p = 1.0), and the need for home oxygen therapy (p = 0.22). Mortality associated with dexamethasone treatment was significantly lower than those treated with methylprednisolone (difference = 5.4%, 95% C.I., −10.4, 0.45, p = 0.03). The difference in mortality between the two steroids in PSM patients by a generalized linear model showed that treating with dexamethasone caused less mortality than treating with methylprednisolone (OR = 1.59, 95% C.I. 1.04, 2.45, p = 0.03), and with stabilized inverse probability of treatment weighting (SIPTW), it showed the same effect (OR = 1.70, 95% C.I. 1.10 - 2.66, p = 0.017).

4. Discussion

Though steroids appear similar, the question in the SARS-CoV-2 pandemic is; are they similar in treating COVID-19? An issue is a subject of debate. In this retrospective study, we conducted a propensity score and matching, with SIPTW enabling reasonable credibility in drawing conclusions on the causal effects (outcomes differences) [20].

We compared the outcomes of the difference in mortality, recovery, the need for home oxygen therapy on hospital discharge, and residual symptoms on discharge, between dexamethasone and methylprednisolone treatment in COVID-19 patients. Particularly, for the treating physicians in Jordan, the clinical experience is more with methylprednisolone and heavily relies on its use in

Table 2. (a) The outcome of treating COVID-19 patients with Dexamethasone or Methylprednisolone in the unmatched population; (b) The outcome of treating COVID-19 patients with dexamethasone or methylprednisolone in PSM and SIPTW populations.

(a)

Analysis of the causal effect (outcome) of selecting dexamethasone or methylprednisolone in the treatment of all COVID-19 patients (N = 1071)					
	Dexamethasone N (%)	**Methylprednisolone N (%)**	**Difference (%)**	**95% C.I.**	P[1]
Outcomes[2]	453 (42.3)	618 (57.7)	-----		
Recovered	159	238	3.4	−9.4, 2.6	0.281
Residual symptoms[3]	16 (3.53)	27 (4.36)	0.8	−3.4, 1.7	0.595
Needs home O_2	233 (51.9)	254 (41.1)	10.3	4.12, 16	<0.001
Death	45 (9.9)	99 (16.0)	6.0	−10.3, −1.9	0.005

[1]2-sided test for equality of proportions with continuity correction; [2]Chi-squared = 13.353, df = 3, p-value = 0.004 for the outcomes. Each outcome's percentage under dexamethasone or methylprednisolone is calculated for the proportion of both steroid treatments from the total for that specific outcome (4-sample test for equality of proportions without continuity correction); [3]One or more symptoms the patient presented with on admission. C.I.: Confidence interval.

(b)

Analysis of the outcomes for selecting dexamethasone or methylprednisolone in treating PSM and SIPTW COVID-19 patients (N = 784)						
	PSM patients				**SIPTW patients**	
Outcomes[1]	**Dexa N (%)**	**Methyl N (%)**	**95% C.I**	**p[2]**	**OR**	**P**
Recovered	146 (37.2)	143 (36.6)	−6.4, 7.6	0.93	1.04	0.8
Residual symptoms[3]	13 (3.3)	12 (3.0)	−2.4, 2.9	1.0	1.62	0.3
Needs home O_2	193 (49.1)	174 (44.5)	−2.6, 11.8	0.22	0.75	0.055
Death	41 (10.4)	62 (15.8)	−10.4, 0.45	0.03	1.70	0.017

Note that the number of PSM and SIPTW patients is the same. *See text for the mortality odds ratio in "outcome analysis". PSM: propensity score matched. Dexa: dexamethasone. Methyl: methylprednisolone. C.I.: Confidence interval; [1]Chi-squared = 5.3313, df = 3, p-value = 0.149 for all outcomes. Each outcome's percentage under dexamethasone or methylprednisolone is calculated for the proportion of both steroid treatments from the total for that specific outcome (2-sample test for equality of proportions with Yates continuity correction); [2]2-sided test for equality of proportions with Yates' continuity correction; [3]One or more symptoms the patient presented with on hospital discharge.

the different causes of ARDS. On the other hand, the use of dexamethasone is cost-effective, which is a genuine concern in resources constraint countries, (*https://rx-sales.biz/search?q=decadron+2+mg+cost*, *https://rx-storepills.biz/search?q=medrol+price&subid=ag2*) in addition, dexamethasone was the earliest evaluated steroid found to reduce mortality in the treatment of COVID-19 patients as was shown in the RECOVERY study [6],

despite patients having more critical radiological lesions [21]. However, another study showed that mortality was lower with methylprednisolone treatment at doses 1 mg/kg/day for three or more days in patients who required mechanical ventilation compared with dexamethasone dosed at least at 6 mg for ≥7 days (OR 0.48, 95% CI: 0.235 - 0.956, p = 0.04) [9]. Hitherto, dexamethasone was found to be equally effective in studies that compared both steroids focusing on mortality [22] [23]. Higher doses of dexamethasone (20 mg once daily for 5 days, followed by 10 mg once daily for an additional 5 days) compared with low-dose dexamethasone (6 mg once daily for 10 days) demonstrated the reduction in clinical worsening on day 11, with same mortality and recovery by day 28 [24] while high-dose methylprednisolone caused higher mortality 39% versus 18.6% [25] [26].

In this study, comparing the use of dexamethasone versus methylprednisolone demonstrated significantly higher mortality in patients with methylprednisolone treatment (2-sided test for equality of proportions p = 0.03), and (generalized linear model OR = 1.59, 95% C.I. 1.04 - 2.45, p = 0.03) in the PSM adjusted patients, and SIPTW patients (OR = 1.70, 95% C.I. 1.10 - 2.66, p = 0.017). At the same time, no significant difference was found for the other outcomes: recovery, the need for home oxygen therapy on hospital discharge, and residual symptoms on hospital discharge.

Our study did not evaluate chronological oxygen improvement for the treated patients for either steroid yet, we looked at the discharge need for oxygen as a surrogate maker of efficacy for both steroids, and both were equivalent in the PSM analysis (p = 0.22) and SIPTW analysis (OR = 0.75, 95%CI, 0.56, 1.00, p = 0.06). Although a study showed that methylprednisolone at standard doses (1 - 2 mg/kg/day) was better than dexamethasone in correcting PaO2/FiO2 ratios in severely sick ICU patients on mechanical ventilators, mortality was similar; meanwhile, high-dose steroids were found to be deleterious in recovery and caused more mortality [26]. But again, in Rana MA *et al.* study dexamethasone brought better chronological improvement in correcting PaO2/FiO2 ratios [26].

Both recovery and residual symptoms on discharge demonstrated no significant outcome differences for dexamethasone versus methylprednisolone in treating COVID-10 patients, whether analyzed as unmatched or PSM patients (p > 0.28).

5. Conclusion

No question is whether steroids' benefit in treating viral pneumonia/ARDS in COVID-19 patients exists, with mortality benefits revealed. In our study, an attempt was made to maximally control for many confounders by PSM and SIPTW to avoid bias while analyzing the outcomes maximally. In all cohorts, PSM and SIPTW analyzed patients, the mortality of patients with COVID-19 was significantly (p < 0.05) less with dexamethasone than with methylprednisolone. Despite our methodology of PSM analysis, which is believed to be robust in mini-

mizing bias in retrospective studies to a reasonable extent, a powered randomized controlled trial for a similar study concept needs to be planned to assure confidence in the outcome.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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