Original Article

Increased Secondary Infection in COVID-19 Patients Treated with Steroids in New York City

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SUMMARY: Steroids are expected to be effective in the treatment of cytokine release syndrome, which is considered to be associated with severe cases of coronavirus disease 2019 (COVID-19). We aimed to investigate the use of steroids and its effects. We conducted a retrospective chart review and an analysis of 226 consecutive hospitalized patients with confirmed COVID-19. Patients were divided into those who received steroids (steroid group) and those who did not (no steroid group). Inverse probability weighted analysis was performed to assess the effect of steroids on in-hospital mortality. The steroid group had higher rates of preexisting hypertension and peripheral vascular disease as well as higher lactate dehydrogenase levels, d-dimer levels, and inflammatory markers than the no steroid group (all $P < 0.05$). The steroid group had significantly higher rates of multifocal pneumonia than the no steroid group at admission (75.4% vs. 50.3%, $P = 0.001$). Notably, the steroid group had higher rates of developing bacterial infection (25% vs. 13.1%, $P = 0.041$) and fungal infection (12.7% versus 0.7%, $P < 0.001$) during the hospital course than the no steroid group. After adjustment, it was observed that steroids did not decrease or increase in-hospital mortality (odds ratio [95% confidence interval]: 1.02 [0.60–1.73, $P = 0.94$]). There was an increase in bacterial and fungal infections with steroid use.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread globally since December 2019 (1). The World Health Organization declared a pandemic due to COVID-19 on March 11, 2020, and the number of deaths due to the COVID-19 pandemic has been rapidly increasing, with total cases exceeding 1.3 million globally (2). The United States (US) has eclipsed other countries and has the largest number of COVID-19 cases in the world, with more than 1 million cases confirmed as of May 2, 2020, with New York City as its epicenter. As of this date, the state of New York has nearly 590,000 cases (2). Since New York City reported its first confirmed COVID-19 patient on February 29, 2020, and their first confirmed death on March 14, 2020, the cases have grown at an astounding rate. The total number of deaths has risen exponentially to 18,491, with 172,354 patients suffering

from COVID-19 as of May 2, 2020 in New York City. While hospitals and healthcare systems needed to adapt rapidly to the unprecedented spread of this viral illness, physicians and healthcare workers struggled to understand the unpredictable consequences of the disease in afflicted patients, and the volume and pace by which these consequences presented.

The clinical manifestations of COVID-19 have from no symptoms whatsoever, to mild cough, fever, pneumonia, acute respiratory distress syndrome, multi-organ failure, and even death (3–5). Steroids are expected to be effective for the treatment of cytokine release syndrome, which is considered to be associated with severe cases of COVID-19. Previous observational studies supported this hypothesis; however, these did not assess side effects, such as bacterial and fungal infections (6,7). Since the release of the RECOVERY trial in June 2020, steroid use has become favorable in treatment recommendations (8–10). We aimed to evaluate the effect of early steroid use in this COVID-19 pandemic and review its impact on in-hospital mortality and outcomes, including the secondary infection rate.

MATERIALS AND METHODS

Data collection: We obtained the medical records of hospitalized patients with laboratory-confirmed COVID-19 from Mount Sinai Beth Israel Hospital, which is located in downtown Manhattan (11). The study protocol was approved by the Institutional Review Board (#20-00436) and conducted in

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accordance with the principles of the Declaration of Helsinki. Identification of COVID-19 patients required nasopharyngeal swabs, which were tested using polymerase chain reaction. Pathogenic detection was initially conducted in the Department of Health in New York City and LabCorp, subsequently transitioning to Mount Sinai Hospital's internal lab. Patients who presented at the hospital with respiratory symptoms or a viral prodrome and were suspected to have COVID-19 were tested and evaluated for admission. The decision to admit was largely provider-dependent and not based on any specific predetermined criteria since initially little was known about the disease.

After 502 consecutive COVID-19 tests, the first hospitalized patient with confirmed SARS-CoV-2 detection was identified on March 13, 2020. Subsequently, the next 226 hospitalized patients who were confirmed to have SARS-CoV-2 infection by March 31, 2020 were followed up until May 15, 2020. A retrospective review of patient electronic medical records was conducted, including data on demographics, clinical course, comorbidities, medications, and clinical outcomes by 2 authors (R.O. and T.M.). Cases were reviewed to determine if they met the criteria for systemic inflammatory response syndrome, as well as type 1 or type 2 myocardial infarction. Quick sepsis-related organ failure assessment was also calculated for all the patients admitted (12,13).

Study design: Patients were divided into 2 groups: those who were administered steroids (steroid group, 25.2% [$N = 57$]) versus those who were not administered steroids (no steroid group, 75.8% [$N = 169$]). Laboratory and imaging data during the hospital stay were collected, and the characteristics of hospital stay were also noted. The radiographic findings were reviewed by attending radiologists. Our institution initially used hydroxychloroquine for moderate cases, which were defined as those with a radiologic evidence of pneumonia or oxygen saturation $<94\%$. Completion of the treatment course was defined as a 5-day course of hydroxychloroquine, but discontinuation at discharge was also considered as completion of treatment (14).

The time course for clinical deterioration in all patients was reviewed, including the incidence of rapid response team (RRT) and code team triggers, whether cardiopulmonary resuscitation (CPR) was initiated during the hospital stay, and whether mechanical ventilation was ultimately used. Data on the incidences of bacterial and fungal infections were also collected and compared between the steroid and non-steroid groups. In addition, whether these incidences occurred in patients who were or were not administered tocilizumab was assessed in the steroid group.

Statistical analysis: Continuous variables were presented as mean $\pm$ standard deviation or median (interquartile range) as appropriate for the data distribution; categorical variables were expressed as percentages. The changes from baseline in the continuous variables were evaluated using Student's t -test or Mann-Whitney U test, and the χ^2 or Fisher's exact t -test was used to analyze the categorical variables. We also analyzed the effect of steroids on in-hospital mortality using inverse probability weighted analysis. A multivariate logistic regression model was

constructed to estimate the propensity score for steroid use.

Considering the total number of people in the steroid group ($N = 57$), 6 variables were chosen based on prior data. The following covariates were entered for multivariate logistic regression analyses: age, d-dimer level, multifocal pneumonia on chest X-ray (either posteroanterior film or anteroposterior film), use of tocilizumab, use of invasive mechanical ventilator, and stay in the intensive care unit (ICU). Age and d-dimer levels were recently reported as independent mortality predictors in COVID-19 patients (15). Although there are no specific radiographic features associated with COVID-19, bilateral multifocal opacities or consolidation are common chest X-ray findings (16). Since cytokine release syndrome with elevated interleukin-6 (IL-6) is associated with severe cases of COVID-19, IL-6 inhibitors such as tocilizumab are expected to be effective for its treatment (17,18). Despite a controversy regarding its clinical use, tocilizumab was used for selected patients with COVID-19 early in the hospital course with the rationale that it may prevent disease progression. Mechanical ventilation is associated with death in critical COVID-19 patients (19). In order to eliminate the imbalance between the steroid and no steroid groups, we conducted a sensitivity analysis on the effect of steroids on in-hospital mortality using inverse probability weighted analysis, limiting the number of patients who needed oxygen ($N = 152$, 67.3%). All statistical calculations and analyses were performed using SPSS (version 24, SPSS, Chicago, IL, USA), with $P < 0.05$ considered statistically significant.

RESULTS

Among the 226 patients, the mean age was 63.3 ± 16.8 years, and 57.1% were males. Among them, 35.4% were Caucasians, 19.0% were African Americans, and 44.3% were Hispanics. Regarding other demographics of interest, 4.4% were undomiciled, and 6.3% did not have a health insurance. Detailed baseline characteristics are shown in Tables 1 and 2. The steroid group had significantly lower oxygen saturation levels (94% [88, 96] versus 96% [94, 98], $P < 0.01$), a higher respiratory rate (22 [18, 26] vs. 20 [18, 23], $P = 0.002$), and were more likely to have preexisting hypertension, peripheral vascular disease, and a history of transplant compared to the no steroid group (Table 1).

Table 3 presents the baseline laboratory findings. The steroid group had a significantly higher baseline neutrophil count, glucose level, lactate dehydrogenase (LDH) level, and d-dimer level than the no steroid group (all $P < 0.05$). The steroid group also had significantly higher values of baseline inflammatory markers such as C-reactive protein, procalcitonin, ferritin, and IL-6 (all $P < 0.05$). Table 3 also describes the electrocardiogram and chest X-ray results. Electrocardiograms showed no significant differences (such as T-wave inversion) between the steroid and no steroid groups (Table 3). However, the steroid group had significantly higher proportions of multifocal pneumonia at admission, as shown in Table 3 (75.4% vs. 50.3%, $P = 0.001$).

Table 4 shows in-hospital treatment and outcomes. Within the steroid group, 63.2% of patients were

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Table 1. Baseline characteristics at admission; No steroid versus steroid

	Category		<i>P</i> value
	No steroid <i>N</i> = 169	Steroid <i>N</i> = 57	
Age	64 [51, 76]	70 [59.5, 79]	0.073
Male	59.2% (100/169)	50.9% (29/57)	0.27
BMI	28.3 [23.9, 32.1]	27.4 [24.3, 33.0]	0.92
Race	White 37.0% (61/165)	White 33.3% (19/57)	0.16
	Black 20.6% (34/165)	Black 15.8% (9/57)	
	Asian 9.7% (16/165)	Asian 21.1% (12/57)	
	Other 32.7% (54/165)	Other 29.8% (17/57)	
Hispanic	46.1% (76/165)	39.3% (22/56)	0.38
No Insurance	7.1% (12/169)	3.6% (2/56)	0.34
Medicare	45.0% (76/169)	64.3% (36/56)	0.012
Medicaid	34.3% (58/169)	39.3% (22/56)	0.50
Private insurance	59.8% (101/169)	58.9% (33/56)	0.91
Undomiciled	6.0% (10/168)	0.0% (0/57)	0.060
Shelter	4.8% (8/167)	0.0% (0/57)	0.092
Symptoms			
Fever	64.5% (107/166)	66.7% (38/57)	0.76
Myalgia	14.3% (24/168)	17.5% (10/57)	0.71
Chest pain	19.6% (33/168)	12.3% (7/57)	0.21
Malaise	28.0% (47/168)	26.3% (15/57)	0.81
Sore throat	6.0% (10/168)	10.5% (6/57)	0.25
Runny nose	8.3% (14/168)	12.5% (7/56)	0.47
Shortness of breath	58.3% (98/168)	68.4% (39/57)	0.18
Cough	67.3% (113/168)	78.9% (45/57)	0.095
Sputum	19.9% (27/136)	37.3% (19/51)	0.014
Abdominal pain	11.3% (19/168)	5.3% (3/57)	0.18
Nausea/Vomit	26.2% (44/168)	26.3% (15/57)	0.99
Diarrhea	26.8% (45/168)	17.5% (10/57)	0.16
Black diarrhea	3.3% (3/90)	0.0% (0/32)	0.30
Anosmia	0.6% (1/168)	0.0% (0/57)	0.56
Dysgeusia	0.0% (0/168)	0.0% (0/57)	-
Initial Vital			
Temperature (°C)	36.7 [36.2, 37.3]	37.2 [36.5, 37.8]	0.012
Heart rate (beat/min.)	96 [81, 111]	99 [84.5, 108]	0.68
SBP (mmHg)	133 [116, 150]	134 [117, 154]	0.42
DBP (mmHg)	80 [68, 88]	75 [65, 85]	0.15
MAP (mmHg)	95.7 [86.5, 108.8]	93.7 [84.2, 105.5]	0.66
RR (/min.)	20 [18, 23]	22 [18, 26]	0.002
SpO ₂ (%) at room air	96 [94, 98]	94 [88, 96]	<0.001
SIRS	1 [0.75, 2]	2 [1, 2]	0.20
qSOFA	0 [0, 1]	1 [0, 1]	0.68
Altered Mental Status	10.7% (18/168)	10.7% (6/56)	1.00
Aspirin	25.6% (43/168)	28.1% (16/57)	0.71
Anticoagulation	11.9% (20/168)	8.8% (5/57)	0.52
ACEI	17.9% (30/168)	14.0% (8/57)	0.51
ARB	15.0% (25/167)	26.3% (15/57)	0.053
Steroid use at home	1.2% (2/168)	3.5% (2/57)	0.25
Comorbidities			
Hypertension	54.4% (92/169)	75.4% (43/57)	0.005
Hyperlipidemia	40.2% (68/169)	43.9% (25/57)	0.63
DM	32.0% (54/169)	33.3% (19/57)	0.85
DM with insulin	8.9% (15/169)	8.8% (5/57)	0.27
CKD	11.3% (19/168)	17.5% (10/57)	0.23
COPD	6.5% (11/169)	10.5% (6/57)	0.32
Asthma	8.9% (15/169)	14.0% (8/57)	0.27

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CVA	6.5% (11/169)	7.0% (4/57)	0.89
PVD	4.7% (8/169)	12.3% (7/57)	0.048
Dialysis	3.6% (6/169)	1.8% (1/57)	0.50
Cirrhosis	1.8% (3/169)	3.5% (2/57)	0.44
CAD	19.5% (33/169)	21.1% (12/57)	0.80
Previous PCI	11.2% (19/169)	15.8% (9/57)	0.37
Previous CABG	4.7% (8/169)	5.3% (3/57)	0.87
Previous PE/DVT	5.9% (10/169)	5.3% (3/57)	0.85
History of AF	9.5% (16/169)	7.0% (4/57)	0.57
Previous CHF	13.6% (23/169)	8.9% (5/56)	0.36
History of cancer	6.5% (11/169)	10.5% (6/57)	0.32
Active cancer	1.2% (2/167)	0.0% (0/57)	0.41
History of transplant	0.0% (0/169)	3.5% (2/57)	0.014
HIV	5.9% (10/169)	5.3% (3/57)	0.85
Dementia	8.9% (15/169)	7.1% (4/56)	0.69
Schizophrenia	2.4% (4/169)	0.0% (0/57)	0.24
Other psychiatry diseases	15.6% (26/167)	19.3% (11/57)	0.51
Smoker			0.53
Current smoker	3.7% (6/163)	1.8% (1/57)	
Former smoker	25.2% (41/163)	31.6% (18/57)	

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; RR, respiratory rate; SIRS, systematic inflammatory response syndrome; qSOFA, quick sepsis related organ failure assessment; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; DM, diabetes mellitus; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; PVD, peripheral vascular disease; CAD, coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; PE/DVT, pulmonary embolism/deep vein thrombosis; AF, atrial fibrillation; CHF, congestive heart failure; HIV, human immunodeficiency virus.

Table 2. Steroid indication, regimen, and preliminary termination

Indication	%
COVID infection	89.5 (51/57)
Other	10.5 (6/57)
Asthma	3.5 (2/57)
COPD	1.8 (1/57)
Transplant organ	3.5 (2/57)
Gout	1.8 (1/57)
Steroid regimens	<i>N</i> = 57
Dexamethasone based	84.2 (48/57)
Dexamethasone 20 mg × 5 d, 10 mg × 5 d	47.4 (27/57)
Dexamethasone 10-day course, partial	15.8 (9/57)
Dexamethasone plus methylprednisolone	21.1 (12/57)
Prednisone, only	10.5 (6/57)
Methylprednisolone, only	1.8 (1/57)
Methylprednisolone plus prednisone	1.8 (1/57)
Hydrocortisone, only	1.8 (1/57)
Reasons for preliminary termination	
Patient died	15.8 (9/57)
Patient declined	1.8 (1/57)
Adverse events	0.0 (0/57)

COVID, corona virus disease; COPD, chronic obstructive pulmonary disease; d, day.

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Table 3. Baseline laboratory findings; no steroid versus steroid

	Category		<i>P</i> value
	No steroid <i>N</i> = 169	Steroid <i>N</i> = 57	
Complete blood count			
White blood cell, K/μL	6.8 [5.2, 9.0]	7.5 [5.1, 9.6]	0.35
Neutrophil, K/μL	4.9 [3.2, 6.6]	5.8 [4.1, 8.1]	0.018
Lymphocyte, K/μL	1.0 [0.7, 1.4]	0.9 [0.7, 1.3]	0.11
Hemoglobin, g/dL	13.6 [12.6, 15.0]	13.9 [12.8, 15.2]	0.45
Platelet, K/μL	170 [134, 218]	150 [120, 208]	0.18
Biochemistry panel			
Glucose, mg/dL	112 [96, 136]	125 [103, 166]	0.032
BUN, mg/dL	16 [11.5, 24]	20 [12, 27]	0.066
Creatinine, mg/dL	0.95 [0.69, 1.31]	0.98 [0.79, 1.33]	0.33
AST, U/L	37 [27, 52.3]	53 [40, 73]	<0.001
ALT, U/L	28 [19, 46]	39 [23.5, 53.5]	0.032
Total bilirubin, mg/dL	0.5 [0.4, 0.8]	0.5 [0.4, 0.6]	0.33
Albumin, g/dL			0.060
LDH, U/L	345 [256, 451]	448 [326, 593]	<0.001
CPK, U/L	140 [69, 311]	160 [70, 510]	0.71
Coagulation			
PT-INR	1.1 [1.0, 1.2]	1.0 [1.0, 1.2]	0.10
APTT (s)	31.8 [28.7, 36.8]	32.7 [29.2, 36.2]	0.98
D-Dimer, μg/mL	0.91 [0.58, 1.72]	1.12 [0.74, 2.22]	0.022
Fibrinogen, mg/dL	535 [353, 686]	588 [446, 733]	0.27
Inflammation marker			
CRP or hsCRP, mg/L	60.0 [30.4, 119]	121 [55.0, 190]	<0.001
Procalcitonin, ng/mL	0.11 [0.05, 0.28]	0.24 [0.09, 0.64]	<0.001
Ferritin, ng/mL	500 [273, 1072]	951 [429, 2184]	0.001
IL-6, pg/L	37.9 [19.3, 77.3]	99.9 [53.6, 170]	<0.001
Others			
pH (venous blood gas)	7.41 [7.37, 7.44]	7.39 [7.35, 7.43]	0.048
Lactate, mmol/L	1.3 [1.0, 1.8]	1.55 [1.23, 2.08]	0.019
BNP, pg/mL	33.6 [10.0, 179]	28.2 [10.0, 118]	0.55
Troponin T, ng/mL	0.01 [0.01, 0.04]	0.02 [0.01, 0.06]	0.084
ECG			
AF	4.7% (7/150)	3.6% (2/55)	0.29
PAC	3.3% (5/150)	3.6% (2/55)	0.92
PVC	3.3% (5/150)	3.6% (2/55)	0.92
CRBBB	6.7% (10/150)	5.5% (3/55)	0.75
CLBBB	2.0% (3/150)	0.0% (0/55)	0.29
T wave inversion	9.3% (14/150)	7.3% (4/55)	0.64
ST depression	1.3% (2/150)	0.0% (0/55)	0.39
ST elevation	0.6% (1/169)	3.5% (2/57)	0.096
Chest X ray			
Multifocal pneumonia	50.3% (85/169)	75.4% (43/57)	0.001
Lobular consolidation	0.6% (1/163)	1.8% (1/56)	0.43
Pleural effusion	6.1% (10/164)	10.7% (6/56)	0.25

BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine. aminotransferase; LDH, lactate dehydrogenase; CPK, creatine kinase; PT-INR, prothrombin time-international normalized ratio; APTT, activated partial thromboplastin time; CRP, c-reactive protein; hsCRP, high sensitivity c-reactive protein; IL-6, interleukin-6; AF, atrial fibrillation; CRBBB, complete right bundle branch block; CLBBB, complete left bundle branch block; PAC, premature atrial contraction; PVC, premature ventricular contraction.

Table 4. In-hospital treatments and outcomes; no steroid versus steroid

	Category		<i>P</i> value
	No steroid <i>N</i> = 169	Steroid <i>N</i> = 57	
Initial admission to ICU	9.5% (16/169)	29.8% (17/57)	<0.001
ICU stay	11.8% (20/169)	63.2% (36/57)	<0.001
Activation of RRT	3.6% (6/169)	14.0% (8/57)	0.005
Nosocomial infection	4.1% (7/169)	1.8% (1/57)	0.40
Treatment			
Hydroxychloroquine	79.3% (134/169)	96.5% (55/57)	0.002
Completion hydroxychloroquine	94.8% (127/134)	92.7% (51/55)	0.58
Azithromycin	56.8% (96/169)	75.4% (43/57)	0.012
Steroid pulse	0.0% (0/169)	0.0% (1/57)	1
Tocilizumab	1.8% (3/169)	35.1% (20/57)	<0.001
Bacterial infection	13.1% (19/145)	25% (14/56)	0.041
Fungal infection	0.7% (1/144)	12.7% (7/55)	<0.001
Vasopressor	2.4% (4/169)	36.8% (21/57)	<0.001
Phenylephrine	0.0% (0/169)	14.0% (8/57)	<0.001
Norepinephrine	2.4% (4/169)	36.8% (21/57)	<0.001
Vasopressin	0.0% (0/169)	14.0% (8/57)	<0.001
Epinephrine	0.0% (0/169)	3.5% (2/57)	0.014
Dobutamine	0.6% (1/169)	1.8% (1/57)	0.021
Oxygen	56.2% (95/169)	100% (57/57)	<0.001
Nasal Cannula	38.5% (65/169)	12.3% (7/57)	<0.001
Mask	10.7% (18/169)	15.8% (9/57)	0.30
High flow oxygen	2.4% (4/169)	15.8% (9/57)	<0.001
NPPV	1.2% (2/169)	5.3% (3/57)	0.070
IMV	3.6% (6/169)	50.9% (29/57)	<0.001
Tracheostomy	0.0% (0/169)	8.9% (5/56)	<0.001
Dialysis	1.2% (2/168)	10.9% (6/55)	0.001
Liver failure	0.6% (1/168)	1.8% (1/55)	0.42
VT	0.0% (0/169)	0.0% (0/55)	-
NSTEMI type 1	2.4% (4/169)	1.8% (1/57)	0.79
NSTEMI type 2	9.5% (16/169)	21.1% (12/57)	0.062
STEMI	0.6% (1/169)	3.5% (2/57)	0.096
Catheterization	0.6% (1/169)	0.0% (0/57)	0.56
VF/Pulseless VT	0.0% (0/169)	1.8% (1/57)	0.084
CPR	4.1% (7/169)	8.9% (5/56)	0.17
Length of stay	6 [4, 8]	15 [10.5, 19]	<0.001
Death	10.8% (18/167)	41.8% (23/55)	<0.001
Remains in hospital	1.2% (2/169)	3.5% (2/57)	0.25
Remains in ICU	0.0% (0/169)	1.8% (1/57)	0.084

ICU, intensive care unit; RRT, rapid response team; NPPV, noninvasive positive pressure ventilator; IMV, invasive mechanical ventilator; VT, ventricular tachycardia; NSTEMI, non-ST elevation myocardial infarction; STEMI, ST elevation myocardial infarction; VF, ventricular fibrillation; CPR, cardiopulmonary resuscitation.

admitted to the ICU during hospital course. RRT was activated for 6.2% of the total study cohort. Regarding treatments, the steroid group had higher proportions of hydroxychloroquine and azithromycin use than the no steroid group (Table 4). Additionally, tocilizumab was administered to 35.1% of the steroid group, significantly more than was administered to the no steroid group (1.8%) during the hospital course (Table 4). Notably, the

steroid group had higher rates of bacterial (25% versus 13.1%, $P = 0.041$) and fungal infections (12.7% versus 0.7%, $P < 0.001$) than the no steroid group during the hospital course (Table 5).

A subgroup analysis was performed in the steroid group to assess the use of tocilizumab, which showed that there was no significant difference in either bacterial or fungal infection rates between patients who

Table 5. Infectious profile of no steroid vs. steroid

Type of infection, type of diagnostic test, and detected organisms	No steroid (N = 169)	Steroid (N = 57)
Bacterial infection	11.2% (19/169)	24.6% (14/57)
Blood culture	3.0% (5/169)	1.8% (1/57)
Methicillin-sensitive <i>Staphylococcus aureus</i> (MSSA)	1.2% (2/169)	0% (0/57)
Viridans Streptococci	0.6% (1/169)	0% (0/57)
<i>Klebsiella aerogenes</i>	0% (0/169)	1.8% (1/57)
<i>Escherichia coli</i>	1.2% (2/169)	0% (0/57)
Urine culture	2.4% (4/169)	7.0% (4/57)
<i>Escherichia coli</i>	1.8% (3/169)	1.8% (1/57)
<i>Klebsiella pneumoniae</i>	0% (0/169)	3.5% (2/57)
<i>Enterococcus faecium</i>	0% (0/169)	1.8% (1/57)
<i>Streptococcus agalactiae</i>	0.6% (1/169)	0% (0/57)
<i>Enterococcus faecalis</i>	0.6% (1/169)	0% (0/57)
Respiratory culture	0% (0/169)	15.8% (9/57)
<i>Streptomonas multophila</i>	0% (0/169)	3.5% (2/57)
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	0% (0/169)	1.8% (1/57)
MSSA	0% (0/169)	3.5% (2/57)
<i>Escherichia coli</i>	0% (0/169)	1.8% (1/57)
<i>Pseudomonas aeruginosa</i>	0% (0/169)	1.8% (1/57)
<i>Klebsiella aerogenes</i>	0% (0/169)	1.8% (1/57)
<i>Klebsiella pneumoniae</i>	0% (0/169)	1.8% (1/57)
MRSA nasal swab	3.6% (6/169)	3.5% (2/57)
MRSA	0% (0/169)	1.8% (1/57)
MSSA	3.6% (6/169)	1.8% (1/57)
Other bacterial infection	2.4% (4/169)	0% (0/57)
	1.2% (2/169) liver abscesses, 0.6% (1/169) toe infection, 0.6% (1/169) bacterial vaginosis	
Fungal infection	0.6% (1/169)	12.3% (7/57)
<i>Candida</i> spp.	0% (0/169)	7.0% (4/57)
<i>Aspergillus fumigatus</i>	0.6% (1/169)	5.3% (3/57)
Blood test		
Aspergillus Galactomannan, performed	0.6% (1/169)	10.5% (6/57)
Fungiteli, performed	0.6% (1/169)	12.3% (7/57)
Fungiteli positive	Not Available	14.3% (1/7)
No other infectious work up	14.2% (24/169)	1.8% (1/57)

were or were not administered tocilizumab (Table 6). CPR was performed in 5.3% of the total patients with one shockable rhythm (1 out of 12 CPR, 8.3%), and the death rate for that group was 100%. Of all the patients in the steroid group, 41.8% died, which was 18.4% of the total patients (Table 4). To estimate the effect of steroids, an inverse probability weighted analysis was performed for adjustment. Interestingly, steroids did not decrease or increase in-hospital mortality (odds ratio (OR) [95% confidence interval (CI)]: 1.02 [0.60–1.73, $P = 0.94$]). Sensitivity analysis limiting patients who needed oxygen showed that steroids did not affect in-hospital mortality in this population (OR [95% CI]: 0.95 [0.54–1.68, $P = 0.87$]).

DISCUSSION

The salient findings of this cohort study are as follows: i) we provided a detailed description of clinical characteristics of a sample of patients representing the diverse urban population of New York City, especially those that differed between the steroid group and no steroid group; ii) the steroid group had higher rates of bacterial and fungal infection during the hospital course; iii) the steroid group had a mortality rate of 41.8%; and iv) steroid use did not show a decreased risk of in-hospital mortality after inverse weighted probability weighted analysis.

New York City is the epicenter of the COVID-19 crisis in the USA (20). Mount Sinai Beth Israel Hospital

Table 6. Infectious profile of steroid group: tocilizumab vs. no tocilizumab

Type of infection, type of diagnostic test, and detected organisms	Tocilizumab (N = 20)	No tocilizumab (N = 37)	P value
Bacterial infection	30% (6/20)	21.6% (8/37)	0.536
Blood culture	5% (1/20)	0% (0/37)	
<i>Klebsiella aerogenes</i>	5% (1/20)	0% (0/37)	
Urine culture	10% (2/20)	2.7% (1/37)	
<i>E.coli</i>	5% (1/20)	0% (0/37)	
<i>K. pneumoniae</i>	5% (1/20)	0% (0/37)	
<i>E. faecium</i>	0% (0/20)	2.7% (1/37)	
Respiratory culture	15% (3/20)	16.2% (6/37)	
<i>Streptomonas multophilus</i>	5% (1/20)	2.7% (1/37)	
MRSA	5% (1/20)	0% (0/37)	
MSSA	0% (0/20)	5.4% (2/37)	
<i>E. coli</i>	0% (0/20)	2.7% (1/37)	
<i>P. aeruginosa</i>	0% (0/20)	2.7% (1/37)	
<i>K. aerogenes</i>	5% (1/20)	0% (0/37)	0.219
<i>K. pneumoniae</i>	0% (0/20)	2.7% (1/37)	
MRSA nasal swab	5% (1/20)	2.7% (1/37)	
MRSA	5% (1/20)	0% (0/37)	
MSSA	0% (0/20)	2.7% (1/37)	
Fungal infection	20% (4/20)	8.1% (3/37)	
<i>Candida</i> spp.	15% (3/20)	2.7% (1/37)	
<i>Aspergillus fumigatus</i>	5% (1/20)	5.4% (2/37)	
Blood test	0% (0/20)	2.7% (1/37)	
Aspergillus Galactomannan	0% (0/20)	0% (0/37)	
Fungiteli	0% (0/20)	2.7% (1/37)	

has served the community of lower Manhattan through numerous crises such as 9/11 and the blackout, as well as hurricanes Irene and Sandy (11,21), and now serves the community during this rapidly evolving COVID-19 pandemic. The hospital has rapidly achieved a nearly 90% SARS-CoV-2 positive patient census in just a few short weeks and has expanded its volume and ICU capacity to more than triple its functioning census during this time to meet the needs of the community as of May 2, 2020. Our study describes the diversity of COVID-19 patient characteristics and the population impacted by the disease in New York City. Notably, we included variables such as homelessness, insurance status (which may be a surrogate for access to healthcare), and race/ethnicity. Our data showed that the steroid group had higher baseline LDH levels, d-dimer levels, and inflammatory markers such as C-reactive protein, procalcitonin, ferritin, and IL-6.

A previous observational study revealed favorable outcomes for steroid use in patients with COVID-19 (7). However, a review article concluded that this was due to survivor treatment bias (22). Previous data regarding steroid use in patients with influenza, severe acute respiratory syndrome, and Middle East respiratory syndrome did not reveal any benefit and demonstrated possible harm, such as increased mortality and delayed clearance of the virus (23,24). Recently, the RECOVERY trial from the United Kingdom showed

that dexamethasone use decreased the 28-day mortality in COVID-19 patients with oxygen support (8). Subsequent studies of steroid use in COVID-19 have also reported favorable outcomes in the steroid group (25–27). In addition, these recent trials suggested no association between an increase in the rate of secondary infection and steroid use, and only one fungal infection was reported to be related to steroid use. While our data showed no significant difference in mortality between the steroid group and no steroid group, it did, however, show higher rates of bacterial and fungal infections, which are concerning in patients with COVID-19.

In addition, our study raises doubts about the RECOVERY trial because our sensitivity analysis of the steroid group patients who needed oxygen showed that steroids did not affect in-hospital mortality in this population. These results could be related to other factors, such as patients in the steroid group being of older age. Furthermore, the CoDEX Randomized Clinical Trial, which applied the same steroid regimen as ours, did not reveal a significant difference in the secondary infection rate (27). Additionally, tocilizumab use in the steroid group did not have a significant effect on both bacterial and fungal infection rates.

Our study has several limitations. This study was conducted in a single-center hospital with a relatively small sample size. Despite adjustment, we could not eliminate all the confounding factors; however, our data

are valuable because previous data on steroid use is controversial and the study showed a higher incidence of bacterial and fungal infections and conducted a sensitivity analysis limiting patients who needed oxygen, which improved the study's robustness.

In conclusion, we provided a detailed description of the clinical characteristics of a sample representative of the diverse, multicultural, urban city of New York, especially for those that differed between the steroid and no steroid groups. Steroids increased the risk of bacterial and fungal infection; however, steroids did not decrease the risk of in-hospital mortality after adjustment, in the present study. Our study is meaningful because we investigated patient characteristics in detail in order to provide more information for physicians who treat COVID-19 patients in other parts of the country and the world.

Conflict of interest None to declare.

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