

# Burden of Hyperglycemia in Patients Receiving Corticosteroids for Severe COVID-19

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## Abstract

Although corticosteroid therapy is the standard of care for all patients hospitalized with severe coronavirus disease 2019 (COVID-19), the studies demonstrating the mortality–benefit ratio of corticosteroids were limited to fully evaluate their adverse effects. To determine the severity of corticosteroid-induced hyperglycemia in patients with and without diabetes mellitus, we retrospectively collected data from the medical records of patients hospitalized with COVID-19 before and after corticosteroids were the standard of care. Corticosteroid-induced hyperglycemia was more severe in patients hospitalized with COVID-19 with diabetes than those without diabetes. Additionally, patients with diabetes required higher doses of correctional insulin per day when on corticosteroid therapy, suggesting that intensive point-of-care glucose monitoring could be limited in patients without diabetes mellitus and support cautionary use of corticosteroids in patients with COVID-19 discharged with supplemental oxygen.

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Corticosteroids have become standard of care for patients hospitalized with severe COVID-19.<sup>1,2</sup> Although studies have shown that corticosteroids reduce inpatient mortality and are generally safe, they are limited by their inability to assess complications, such as the impact of corticosteroid-induced hyperglycemia.

Corticosteroids adversely impact blood glucose homeostasis, particularly in patients with diabetes mellitus.<sup>3</sup> Several hospitalized cohorts with COVID-19 exhibited up to 40% patients with diabetes mellitus.<sup>4</sup> Additionally, admission hyperglycemia has been associated with worse hospital outcomes in patients with COVID-19.<sup>4,5</sup> The present study attempted to investigate a differential impact of corticosteroid-induced hyperglycemia from dexamethasone use in patients hospitalized for severe COVID-19 with and without diabetes mellitus.

## METHODS

The present retrospective study was conducted in adult patients with severe COVID-19 pneumonia admitted before and after

corticosteroids became the standard of care (May–July 2020) in our urban tertiary care academic medical center in Los Angeles County. Data were collected from the time of admission or start of corticosteroids and followed for 10 days or until patient discharge or death. Patients with an alternative indication for corticosteroids or those under continuous intravenous insulin therapy were excluded from the study. Correctional insulin dosing was used to compensate for COVID-19 exposures in additional nursing staff and the high nursing workload. Correctional insulin dosing frequency was used as a surrogate for COVID-19 exposures and workload to nursing staff. No funding was received for this study.

## RESULTS

The present study evaluated 122 patients, of which 63 received 6 mg of dexamethasone per day and 59 did not receive corticosteroids. The baseline characteristics between the two groups were similar (Table 1). The differences between the groups in blood glucose measurements, administration of correctional insulin,

TABLE 1. Baseline Characteristics<sup>a</sup>

	No dexamethasone (n=59)	Dexamethasone (n=63)	P value
Age (y) median (range)	52 (24-87)	56 (23-84)	.52 <sup>b</sup>
Female, n (%)	29 (49)	25 (39)	.29 <sup>c</sup>
Race/ethnicity, n (%)			
Black	4 (6.8)	5 (8)	
White, non-Hispanic	1 (1.7)	1 (1.6)	
Hispanic/Latinx	52 (88.1)	49 (77.8)	
Other	2 (3.4)	8 (12.7)	
Body mass index, mean (range), kg/m <sup>2</sup>	31 (18.3-57)	32.3 (16.0-65.6)	.49 <sup>b</sup>
Prior diagnosis of diabetes mellitus <sup>b</sup> , n (%)	23 (39)	35 (55.5)	
HbA1c, mean% (STD, n)	8.8% (2.6%, n=26)	8.9% (2.6%, n=36)	.88 <sup>b</sup>
Highest required O <sub>2</sub> supplementation			.14 <sup>d</sup>
Low flow, n (%)	26 (44.1)	22 (34.9)	
High flow nasal canula, n (%)	17 (28.8)	29 (46)	
Mechanical ventilation, n (%)	16 (27)	12 (19)	
Duration of hospitalization, median (IQR)	7 (5-13)	8 (5-13)	
Days on dexamethasone, median (IQR)	0	7.3 (5-10)	

<sup>a</sup>HbA1c, hemoglobin A1c; IQR, interquartile range; STD, standard deviation.

<sup>b</sup>Unpaired two-tailed Student's t-test

<sup>c</sup>Type I & type II diabetes mellitus combined because of inability to confirm on chart review specific diagnosis

<sup>d</sup>Pearson's  $\chi^2$  test

and infectious complications are summarized in Table 2. The overall 10-day median blood glucose level was higher in patients who received dexamethasone than in those who did not. The effect was more obvious in patients with diabetes than in those without (median 234 mg/dL vs 176 mg/dL;  $p < .005$ ). Dexamethasone use in patients with diabetes mellitus was also associated with higher doses of correctional insulin per day and more days with at least 1 correctional intervention. The difference in the number of doses of correctional insulin per day or the proportion of days with at least one dose of correctional insulin among patients without diabetes mellitus who received dexamethasone and those who did not was statistically nonsignificant. No evidence of increased early infectious complications was observed with dexamethasone.

## DISCUSSION

Hyperglycemia is a crucial adverse effect of dexamethasone therapy in patients hospitalized with severe COVID-19 with diabetes mellitus. These outcomes exhibited a downstream influence on an increasing number of nursing interventions, a surrogate for both workload and exposures to infectious patients. Patients

without diabetes mellitus receiving dexamethasone exhibited clinically similar median blood glucose levels and correctional requirements to those not receiving dexamethasone, suggesting that avoiding standardized intensive blood glucose monitoring in these patients may not put the patients at increased risk and would potentially reduce workload and exposures in nurses. On the other hand, patients with diabetes mellitus would be appropriate for continued POC blood glucose monitoring and the provision of correctional insulin. Current guidelines do not recommend for or against discharging patients still requiring supplemental oxygen with corticosteroids.<sup>1</sup> However, for patients discharged with corticosteroids with diabetes mellitus may benefit from close monitoring.

The present study has certain limitations. The retrospective single-center design and relatively small sample size prevents the generalization of the findings. Additionally, the follow-up was limited to 10 days, which may be too short to capture occult infections or other typical corticosteroid-associated adverse effects. POC glucose checks were not routinely ordered for patients without diabetes mellitus, which could have limited the sensitivity for

**TABLE 2. Average Blood Glucose, Administration of Correctional Insulin, and Infectious Complications in Patients Who Did and Did Not Receive Corticosteroids<sup>a</sup>**

	No dexamethasone (n=59)	Dexamethasone (n=63)	P value
10-day average blood glucose, median (IQR)	117 mg/dL (104-176)	175 mg/dL (122.2-249)	<.005 <sup>b</sup>
10-day average blood glucose, those <i>without</i> diabetes, median (IQR)	106.9 mg/dL (96-113.6)	118.4 mg/dL (111.1-143.6)	<.005 <sup>b</sup>
10-day average blood glucose, those <i>with</i> diabetes mellitus, median (IQR)	176 mg/dL (133.4-192.7)	234.4 mg/dL (208-273.8)	<.005 <sup>b</sup>
<b>Correctional Insulin</b>			
Proportion of days with $\geq 1$ correctional dose per days hospitalized or on dexamethasone <sup>c</sup>			
No diabetes mellitus, (95% confidence interval)	0.04 (-0.01-0.09)	0.08 (-0.01-0.18)	.39 <sup>d</sup>
Diabetes mellitus, (95% confidence interval)	0.61 (0.44-0.77)	0.88 (0.76-1.0)	.006 <sup>b</sup>
Number of correctional doses per day hospitalized or on dexamethasone			
No diabetes mellitus, (95% confidence interval)	0.09 (-0.04-0.22)	0.22 (-0.05-0.48)	.36 <sup>d</sup>
Diabetes mellitus, (95% confidence interval)	1.54 (1.04-2.03)	2.81 (2.31-3.24)	<.001 <sup>d</sup>
<b>Infectious Complications<sup>f</sup></b>			
No diabetes mellitus	3 of 34	1 of 28	.62 <sup>e</sup>
Diabetes mellitus	3 of 25	5 of 35	>.99 <sup>e</sup>

<sup>a</sup>IQR, interquartile range.<sup>b</sup>Mann-Whitney test, significance level 0.05<sup>c</sup>For example, patients with diabetes mellitus receiving dexamethasone received at least one dose of correctional insulin on 80% of days they were on dexamethasone, on average.<sup>d</sup>Unpaired two-tailed Student's t-test<sup>e</sup>Fisher exact test<sup>f</sup>Infectious complications with steroids: invasive candidiasis; hospital acquired pneumonia (2 patients, 2 instances); urinary tract infection (3 patients, 4 instances). Infectious complications with no steroids: invasive candidiasis; hospital acquired pneumonia; urinary tract infection (2 patients, 2 instances); *C. difficile* colitis; bacteremia due to *Klebsiella* sp.

post-prandial glucose in these patients. Furthermore, utilization of correctional insulin may have been influenced by the variability in the use of maintenance or prandial insulin as this was not standardized.

Corticosteroids reduced mortality in hospitalized patients with severe COVID-19.<sup>2</sup> The present study highlighted hyperglycemia as a vital complication of this therapy, specifically in patients with diabetes mellitus. These analyses could impact healthcare personnel utilization and a consistent scarcity during surges by reducing intensive blood glucose monitoring in patients without diabetes mellitus. Further research could evaluate the incidence and potential complications of hyperglycemia in patients discharged from clinics or emergency departments on corticosteroids.

## CONCLUSION

Corticosteroid-induced hyperglycemia is a crucial complication of corticosteroid therapy

for severe COVID-19, particularly in patients with diabetes mellitus compared with those without diabetes.

## POTENTIAL COMPETING INTERESTS

E.S.D. has been a consultant for and has received research support from GileadMerck, and GlaxoSmithKline/ViiV Healthcare. The other authors report no competing interests. No funding was received for this study.

## SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <http://www.mcpiqjournal.org>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

**Abbreviations and Acronyms:** POC, point-of-care

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