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Prolonged Corticosteroid Usage and Associated Infectious Complications in Adult Patients with COVID-19

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INTRODUCTION

- The National Institutes of Health (NIH) strongly recommends corticosteroids, specifically dexamethasone, for hospitalized patients who require supplemental oxygen for the treatment of COVID-19 to improve survival. [1]
  - Based on the RECOVERY trial, a large single center trial, demonstrated reduced mortality at 28 days using dexamethasone 6mg daily for up to 10 days.[2]
  - Equivalent doses to dexamethasone may be used.
  - The greatest benefit has been seen with patients who require mechanical ventilation.
  - The recommended dose of dexamethasone is 6mg intravenously or orally once daily for 10 days or until hospital discharge.
- It is not specified within the NIH recommendations if patients should receive therapy for up to 10 days or until hospital discharge, whichever will come first.[1,2]
  - In clinical practice, prescribers may continue therapy, especially in those who remain symptomatic after a 10-day course
- Extended corticosteroid therapy increases risk for severe bacterial or fungal infections thus complicating treatment and prolonging hospital stay. [3,4,5]
  - Retrospective chart review of 226 patients identified significantly higher rates of bacterial infection (25% vs. 13.1%, P=0.041) and fungal infection (12.7% vs. 0.7%, P<0.001) during hospital course.[3]
  - Case reports of patients testing positive for *aspergillus fumigate* and *bacillus cereus* have been associated with prolonged corticosteroid use without previous patient risk factors.[4,5]

OBJECTIVES

To explore the incidence of secondary infections during extended durations of corticosteroid use for the treatment of COVID-19 infection.

METHODS

- A retrospective study of patients at Jamaica Hospital Medical Center and Flushing Hospital Medical Center between September 2020 and May 2021 with a diagnosis of respiratory failure secondary to COVID-19 infection.
- Patients who were diagnosed with a new, lab-confirmed secondary infection during admission for COVID-19 infection were included.
  - Secondary infection must present at least 48 hours after admission
  - Additional variables included past medical history, clinical presentation, days on corticosteroids at time of secondary infection, treatment and outcome of secondary infection, days on anti-infective prior to development of secondary infection, total length of stay, and disposition.
- No comparison group due to lack of appropriate comparison group in our database.
- Qualitative analysis completed with SPSS v 27.0 and R

RESULTS

- Of the 3,000 COVID-19 admission within the timeframe, 73 patients were included (**Table 1**).
  - No patient received immunomodulators for COVID-19 treatment, including those approved for Emergency Use.
  - Patients had a median of 18 days on corticosteroid (range 10-65 days) prior to first positive culture.
- There were 130 positive cultures identified in blood, urine, and sputum samples yielding 34 clinically relevant organisms including K.pneumoniae and P. aeruginosa (**Figure 1**).
- Hospital courses were complicated by septic shock (68.5%), change in lung function (76.7%), and acute organ damage (57.5%) and 55 patients expired with this hospital admission **(Table 3).**

Table 1: Baseline Characteristics*

		N = 73
Age, years (Range)		68 (36-93)
BMI, kg/m² (Range)		34 (15-66)
Male, %		51
Institution		
	Jamaica Hospital Medical Center, n (%)	39 (53)
	Flushing Hospital Medical Center, n(%)	34 (47)
Past Medical History		
	Endocrine, n (%)	36 (49.3)
	Cardiac, n (%)	45 (61.6)
	Neurological, n (%)	16 (21.9)
	Gastro-intestinal, n (%)	9 (12.3)
	Respiratory, n (%)	14 (19.1)
	Genitourinary, n (%)	6 (8.2)
	Prior Infection, n (%)	17 (23.3)
	Risk Factors for Infection, n (%)¥	13 (17.8)
Cumulative Corticosteroid Use, days (Range)		21 (10-73)
Prior to Secondary Infection		
	Antibiotic Use, days (Range)	10 (1-33)
	Antiviral Use, days (Range)	0 (0-49)
	Antifungal Use, days (Range)	0 (0-22)
	Corticosteroid Use, days (Range)	18 (10-65)

* All results are reported as median (range) unless otherwise reported.
¥ Includes history of lines, ports, ventilator use, and prior corticosteroid usage before hospitalization.

Table 3: Hospital Course and Disposition*

		N = 73
Number of Pathogens		1 (1-5)
Total LOS, days (Range)		30 (11-87)
MICU LOS, days (Range)		15 (1-34)
Complications Attributed to Secondary Infection		
	Septic Shock, n (%)	50 (68.4)
	Further Change in Lung Function, n (%)	56 (76.7)
	Acute Organ Damage, n (%)¥	42 (57.5)
Disposition		
	AMA, n (%)	1 (1.4)
	Expired, n (%)	55 (75.3)
	Discharged, n (%)€	16 (21.9)
	Discharged to hospice care, n (%)	1 (1.4)

LOS = length of stay; MICU = Medical Intensive Care Unit; AMA = against medical advice
* All results are reported as median (range) unless otherwise reported.
¥ Includes damage to the brain, kidney, liver and heart; excludes damage to the lungs.
€ Includes patients who were discharged from the institution to home or a nursing facility.

Figure 1: Pathogens by Source

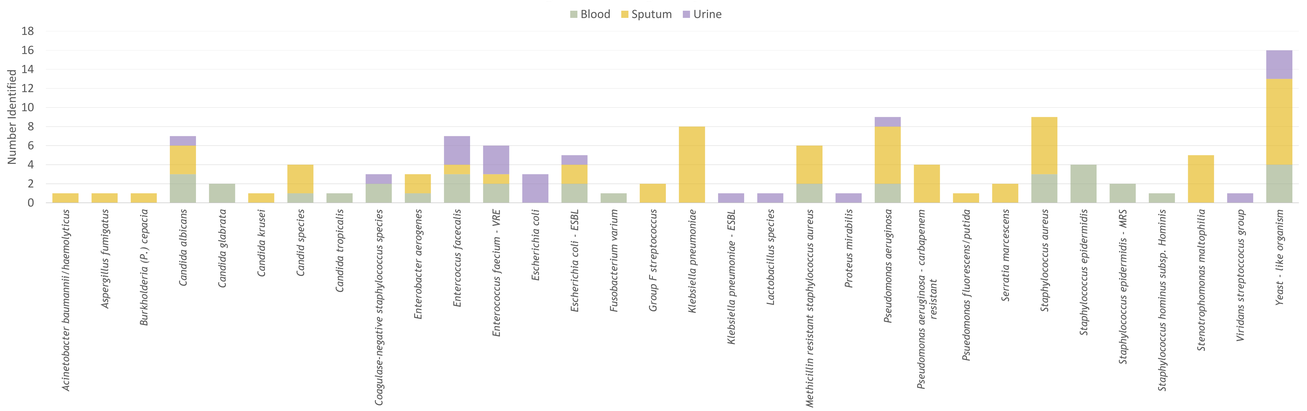

Table 2: Pathogen Grouped By Person

Pathogen	Number Isolated	Age, years (Average)	BMI, kg/m² (Average)	Discharged*	Expired
Acinetobacter baumannii/haemolyticus	1	63	27	Yes	
Aspergillus fumigatus	1	58	33		Yes
Burkholderia (P.) cepacia	1	78	29	Yes	
Candida albicans	5	73	28		Yes
Candida glabrata	2	71	28		Yes
Candida krusei	1	84	23		
Candid species	3	65	33		Yes
Candida tropicalis	1	58	33		Yes
Coagulase-negative *staphylococcus species*	3	68	35		Yes
Enterobacter aerogenes	3	75	28		Yes
Entercoccus facecalis	6	63	30		Yes
Enterococcus faecium - VRE	5	73	32		Yes
Escherichia coli	3	76	26		Yes
Escherichia coli - ESBL	4	78	28		Yes
Fusobacterium varium	1	87	32		Yes
Group F streptococcus	2	79	30	Yes	Yes
Klebsiella pneumoniae	8	67	28		Yes
Klebsiella pneumoniae - ESBL	1	68	26		Yes
Lactobacillus species	1	78	29	Yes	
Methicillin resistant *staphylococcus aureus*	5	50	31		Yes
Proteus mirabilis	1	42	32		Yes
Pseudomonas aeruginosa	8	71	27		Yes
Pseudomonas aeruginosa - carbapenem resistant	4	68	27		Yes
Psuedomonas fluorescens/putida	1	93	23		Yes
Serratia marcescens	2	47	39	Yes	Yes
Staphylococcus aureus	6	62	30		Yes
Staphylococcus epidermidis	4	75	29		Yes
Staphylococcus epidermidis - MRS	2	76	22	Yes	
Staphylococcus hominus subsp. Hominis	1	55	49	Yes	
Stenotrophomonas maltophilia	5	73	34		Yes
Viridans streptococcus group	1	50	25	Yes	
Yeast - like organism	13	69	31		Yes

VRE = vancomycin resistant enterococcus; ESBL = extended spectrum beta-lactamase; MRS = methicillin-resistant staphylococcus
* Includes patients who were discharged from the institution to home or a nursing facility

DISCUSSION/CONCLUSIONS

- Patients with COVID-19 infections being treated with extended durations of corticosteroid therapy of greater than 10 days have high rates of secondary infections.
  - Patients could have multiple secondary infections that were mostly found in sputum cultures.
- The use of extended durations of corticosteroids was not shown to improve patient outcomes and patients continued to deteriorate despite treatment.
  - Majority of patients had complications affecting multiple organ systems.
  - Complications could also be attributed to COVID-19 disease progression.
- Given there is limited information suggesting improved outcomes with these prolonged courses, risk to benefit analysis must be carefully considered.

REFERENCES

1. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed 2 June 2021.
2. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with COVID-19—preliminary report. N Engl J Med. 2020;Published online ahead of print. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32678530.
3. Obata R, Maeda T, Rizk D, Kuno T. Increased secondary infection in COVID-19 patients treated with steroids in New York City. Jpn J Infect Dis . 2020 Dec 25. doi: 10.7883/yoken.JJID.2020.884. Online ahead of print.
4. Sasoni N, Rodriguez Müller M, Posse G, González J, Leonardelli F, Garcia-Effron G. SARS-CoV-2 and Aspergillus section Fumigati coinfection in an immunocompetent patient treated with corticosteroids. Rev Iberoam Micol. 2021;38(1):16-18. doi:10.1016/j.riam.2020.11.001
5. Osakwe N. A case of Bacillus cereus bacteremia in a COVID-19 patient treated with steroids. IDCases. 2020;21:e00855. Published 2020 May 30. doi:10.1016/j.idcr.2020.e00855

DISCLOSURES

The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation