Characterization of Co-Infections in COVID-19 Patients (3-C's)

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Background

- Widely varying incidences of early (3-45%)[1,2] and late (16-41%)[2] co-infections have been reported in literature with a lack of consensus on the primary causal pathogen(s)
- Co-infections in previous respiratory viral outbreaks have shown to result in poorer patient outcomes
- Anti-infectives are often inappropriately initiated in COVID-19 patients with reports of empiric use in up to 75% of the patients[1]
- Identifying the incidence of co-infections, common pathogens and anti-infective prescribing practices will help guide future anti-infective use in COVID-19 patients

Objectives

- **Primary:**
  - To determine the rates of early (within 48hr of diagnosis) and late (≥48hr after diagnosis) co-infection, and to characterize the pathogens, source and onset of infections seen in COVID-19 patients
  - To determine the rates of inappropriate empiric anti-infective use upon COVID-19 diagnosis. Inappropriate early anti-infective use was defined as anti-infective use in patients without focal consolidation on CXR and/or WBC and neutrophil elevations
  - To determine the clinical outcomes including mortality, total hospital length of stay, and duration of mechanical ventilation (MV) in COVID-19 patients with and without co-infections
- **Secondary:**
  - To determine the anti-infective treatments utilized as well as the duration of treatment
  - To determine the rates of side effects associated with different antibiotics used in COVID-19 patients treated for bacterial co-infections (eg. *C.diff,* QT prolongation, rash, neutropenia, liver failure, acute renal failure)

Methods

- **Design:** Single-center retrospective cohort study
- **Study Dates:** January 1, 2020 to June 30, 2020
- **Inclusion:**
  - Diagnosed with COVID-19
  - Hospitalized at LGH between January 1, 2020 to June 30, 2020
- **Exclusion:** None
- **Analysis:** Descriptive Statistics

References

1. Langford BJ, So M, Raybardhan S, et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *Clin Microbiol Infect* 2020; 26: 1622–1629.

2. Musuuza JS, Watson L, Parmasad V, et al. Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: A systematic review and meta-analysis. *PLOS ONE* 2021; 16: e0251170.

Results

Table 1: Patient Characteristics

	Overall (n=48)
Age [Mean (SD) – Years]	69 (± 15.6)
Sex	
Male	35 (72.9%)
Highest Level of Care	
ICU	14 (29.2%)
Comorbidities	
Hypertension	21 (43.8%)
Atrial Fibrillation	9 (18.8%)
Dyslipidemia	9 (18.8%)
Diabetes (Non-Insulin Dependent)	8 (16.7%)
Diagnosis of COVID-19	
On Admission	30 (62.5%)
During Hospital Stay	11 (22.9%)
Signs/Symptoms	
Cough	34 (70.8%)
Dyspnea	29 (60.4%)
Fever	27 (56.3%)

Table 2: Early and Late Infections

	Overall (n=48)
Early Infection	3 (6.3%)
Confirmed	1 (2.1%)
Haemophilus influenzae (Sputum)	1
Suspected	2 (4.2%)
Sputum Cultures Completed	6 (12.5%)
Late Infection	7 (14.6%)
Confirmed	4 (8.3%)
Suspected	3 (6.3%)
Overall Number of Distinct Infections Treated	13
Ventilator Associated Pneumonia (VAP)	8
Aspiration Pneumonia	1
Bacteremia	3
Septic Shock	1
Onset [Mean (SD) – Days]	13 (±5.9)

Table 3: Late Infection Pathogens

	Overall Treated Infections (n=13)
VAP	
E. coli (ESBL)	1 (7.7%)
MSSA	1 (7.7%)
MRSA	1 (7.7%)
Pseudomonas aeruginosa	1 (7.7%)
Pseudomonas aeruginosa (β-Lactam Resistant)	1 (7.7%)
Bacteremia	
Staphylococcus epidermidis	2 (15.4%)
Candida albicans	1 (7.7%)

Table 5: Early and Late Anti-Infective Use

	Patients Treated with Empiric Anti-Infective (n=32)
Empiric Early Anti-Infective Used	32/48 (66.7%)
Inappropriate Early Anti-Infective Use	29 (90.6%)
Neither Focal Consolidation or WBC/Neutrophil Elevations	19 (65.5%)*
Only Focal Consolidations Present	5 (17.2%)*
Only WBC/Neutrophil Elevations Present	5 (17.2%)*
Early Anti-Infective Agents	
Ceftriaxone	26 (81.3%)
Azithromycin	22 (68.8%)
Piperacillin-Tazobactam	6 (21.9%)
Duration of Early Empiric Therapy [Mean (SD) - Days]	4.4 (±2.4)
Completed Course of Early Therapy	21 (65.5%)
Late Anti-Infective Agents (n=21)	
Piperacillin-Tazobactam	7 (33.3%)
Vancomycin	4 (19.0%)
Ceftazidime	2 (9.5%)
Duration of Late Anti-Infective Therapy [Median (IQR) – Days]	6.5 (6.3)

Table 6: Patient Outcomes and Rates of Antibiotic Associated Adverse Events

	Co-Infected Patients (n=10)	Non Co-Infected Patients (n=38)
Total Death by 28 Days	4 (40.0%)	8 (21.1%)
Discharged by 28 Days	2 (20.0%)	26 (68.4%)
Length of Hospital Stay [Median (IQR) – Days]	34.5 (36.3)	8.5 (13.5)
Requiring ICU Admission	6 (60.0%)	8 (21.1%)
Need for Mechanical Ventilation (MV)	6 (60.0%)	1 (2.6%)
MV Duration [Median (IQR) – Days]	20.5 (17.8)	3 (0)
Complications		
ARDS	6 (60.0%)	11 (28.9%)
AKI (Non-Antibiotic Related)	6 (60.0%)	8 (21.1%)
Renal Failure Requiring Dialysis (CRRT)	6 (60.0%)	0 (0.0%)
Any Antibiotic Associated Adverse Events	2 (20.0%)	0 (0.0%)
AKI	1 (10.0%)	
C. diff (Mild)	1 (10.0%)	

Limitations

- Single center study – small population
- Captured first wave of COVID-19 only
- Included patients that acquired COVID-19 during hospital stay
- Subjective symptom reporting and CXR interpretation
- Lack of sputum cultures may have limited detection of early co-infections pathogens

Conclusion

- Rates of early (6.3%) and late (14.6%) co-infections in our study were lower than those reported in literature. The majority of late infections occurred in ICU patients requiring MV
- Empiric antibiotics were started in 66.7% of the patients upon diagnosis of COVID-19 with 65.5% of those patients completing a course of antibiotics
- Sputum cultures should be ordered to help guide empiric anti-infective therapy
- Inappropriate use of early empiric anti-infectives was common (90.6%). Use of empiric antibiotics in COVID-19 patients with low suspicion of co-infection should be discouraged given the low rates of early infection identified
- Co-infected patients had higher rates of mortality and complications, longer hospital stays, and were more likely to require MV and ICU admission