

Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. Concerns about antibiotic resistance are exacerbated in COVID-19 patients due to frequent antibiotic use, increase in mechanical ventilation and reusable equipment, conservation of PPE, and strain on hospital staff. We described cases with co-infection of carbapenem-resistant organisms (CRO) and SARS-CoV-2 and compared rates in the Massachusetts population.

Methods. All providers and hospitals are required to report CROs and SARS-CoV-2 to the Massachusetts Virtual Epidemiologic Network (MAVEN). We selected cases with both a positive SARS-CoV-2 test and a laboratory confirmed CRO from January through July 2020. We classified by which result occurred first and described demographic and clinical characteristics. We standardized the CRO case definition by excluding *CR-Pseudomonas aeruginosa* and calculated rates per 100,000 to assess the impact of SARS-CoV-2 on the population-based frequency of CROs. Analyses were conducted in SAS 9.4.

Results. 28 confirmed cases of SARS-CoV-2 infection were also diagnosed with a CRO. They were an average age of 71.8, 60.7% male, 67.9% white, and 64.3% were in congregate care prior to their diagnoses. Mortality was 5/28 (17.9%). The 23 (82.1%) with a positive SARS-CoV-2 result first were all hospitalized at least once compared to 40% in the CRO first group (p=0.003). 11 (47.8%) of the SARS-CoV-2 first were already admitted when they tested CRO positive; 7 (30.4%) were admitted for the CRO separately from COVID-19 treatment. None of the CRO first group were admitted for CRO infection. Average length of stay for the SARS-CoV-2 first group was higher than the CRO first group (62.3 days vs 11.0 days; p=0.049). Cases positive for CRO first were all infected with *CR-Escherichia coli* whereas those positive for SARS-CoV-2 first were infected with CRAB, CRPA, or a CRE (*Klebsiella oxytoca* or *Klebsiella pneumoniae*) (p< 0.0001). The rate of CRO/COVID coinfection was 0.203 per 100,000 population; the rates for January through July of CRO alone were 2.5 per 100,000 in 2020 and 2.4 per 100,000 in 2019.

Conclusion. Characteristics of individuals co-infected with CRO and SARS-CoV-2 differed by which diagnosis was made first; however, the SARS-CoV-2 pandemic did not impact the CRO population rate during the time frame studied.

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284. Antibiotic Prescribing Trends in Hospitalized Influenza Versus COVID-19 Patients at a Community-Based Health System

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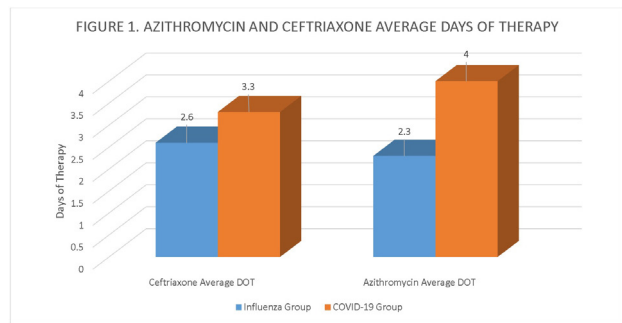
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Background. The 2019 coronavirus SARS-CoV-2 continues to affect global population health. Patients with severe disease that require hospitalization due to COVID-19 pneumonia remain at further risk of bacterial co-infections. There is limited evidence suggesting up to 3.5% bacterial co-infection upon admission and up to 13.5% of secondary infections after hospitalization for pneumonia yet antibacterial therapy usage remain as high, or even higher, than data seen for viral pneumonia, such as influenza. Unnecessary use of antimicrobial therapy may lead to further resistance and requires stewardship attention.

Methods. A single-center retrospective chart review was conducted in a community health system on all inpatient influenza admissions between October 1st 2019 to March 31st 2020 and all COVID-19 admissions during the same 6-month period one year later. Patients were excluded if age < 18, observation or emergency visit. The study aims to determine the percentage of patients that were prescribed antibacterial therapy during influenza season compared to during the COVID-19 pandemic.

Results. A total of 175 patients were included in the influenza group while 1411 patients were included in the COVID-19 group (Table 1). The percent of inpatients with positive bacterial respiratory cultures were 12% in both influenza and COVID-19 groups. Positive bacterial respiratory cultures collected within 48 hours of admission were 3.4% in the influenza group compared to 1.2% in the COVID-19 group. Seventy-three percent of patients in the influenza group received antibiotics during admission compared to 78% in the COVID-19 group. Azithromycin and/or ceftriaxone was most commonly prescribed (58% vs. 60%) (Figure 1). The median length of stay was 3 days in the influenza group compared to 5 days in the COVID-19 group. In hospital mortality was higher in the COVID-19 group (1.7% vs. 9%).

	Influenza Patients (10/1/2019 to 3/31/2020)	COVID-19 Patients (10/1/2020-3/31/2021)
Baseline Demographics		
Number of hospitalized patients	175	1411
Age (Median)	71	71
Male (%)	48.6	46.4
Primary Endpoint		
Received antibiotics (%)	73 (128/175)	78 (1105/1411)
Secondary Endpoints		
Hospital length of stay (median)	3	5
Hospital mortality (%)	1.7 (3/175)	9 (134/1411)
Patients in ICU (%)	18 (32/175)	15 (212/1411)
Percent of inpatients on azithromycin and/or ceftriaxone	58 (102/175)	60 (848/1411)
Ceftriaxone Average DOT	2.6	3.3
Azithromycin Average DOT	2.3	4
Patients with positive bacterial cultures (%)	12 (21/175)	12 (174/1411)
Percent of inpatients with positive bacterial respiratory cultures within first 48 hrs of admission (%)	3.4 (6/175)	1.2 (18/1411)
Percent of abnormal Procalcitonin Levels (%)	73 (99/136)	71 (1680/2357)
Average Procalcitonin value (ng/mL)	1.94	0.95
Top respiratory pathogens identified (count):	Methicillin-resistant <i>Staphylococcus aureus</i> , 3 <i>Staphylococcus aureus</i> , 2 <i>Enterobacter aerogenes</i> , 1 <i>Mycobacterium fortuitum</i> , 1 Acid-fast bacilli, 1 Serratia, 1	<i>Pseudomonas aeruginosa</i> , 16 <i>Staphylococcus aureus</i> , 8 <i>Streptococcus maltophilia</i> , 5 ESBL-producing <i>Klebsiella pneumoniae</i> , 5 <i>Klebsiella pneumoniae</i> , 4 Methicillin-resistant <i>Staphylococcus aureus</i> , 4



Conclusion. Despite the viral origin of influenza and COVID-19 and low incidence of bacterial infection, antibacterials were frequently prescribed in both indications but it appears to trend more so in the COVID-19 group. There is an opportunity to enhance antimicrobial stewardship for the treatment of COVID-19 in acute care settings.

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285. Outcomes and Antibiotic Use in Patients with COVID-19 Admitted to an Intensive Care Unit

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Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. Studies have shown the proportion of critically ill patients with COVID-19 receiving empiric antibiotics (ABX) greatly exceeds those with culture-proven bacterial co-infections. However, the benefits of continuing ABX in culture-negative (CxN) cases is unknown; this practice may increase the risks associated with ABX overuse. The purpose of this study was to evaluate outcomes and antibiotic use (AU) in intensive care unit (ICU) patients with COVID-19 based on culture results.

Methods. This was a multicenter, retrospective cohort study evaluating adults in an ICU for the first episode of ABX initiated following a confirmed COVID-19 diagnosis between September to December 2020. Blood and/or respiratory cultures must have been obtained within 24 hours (h) of ABX initiation. Patients were categorized into three groups: 1) CxN, ABX discontinued ≤ 72 h, 2) CxN, ABX continued > 72 h, or 3) Culture-positive (CxP). Data on AU was obtained from electronic medication administration records. The primary outcome was clinical success, defined as being discharged alive or > 2-point decrease in the World Health Organization Clinical Progression Scale score from day of ABX initiation to day 30.

Results. A total of 65 patients were included with 35.4% being CxP. ABX were discontinued ≤ 72 h in 23.8% of CxN patients. Methicillin-susceptible *Staphylococcus aureus* was the most common organism in 52.2% of CxP patients (66.7% respiratory; 16.7% blood; 16.7% both). Anti-methicillin-resistant *Staphylococcus aureus* and anti-pseudomonal antibiotics were the most prescribed for the initial regimen (Table 1). ABX de-escalation occurred in 58.5% of patients. Initial ABX duration was significantly longer in the CxP group (P < 0.01). No significant difference in clinical success was observed (Table 2). Although not significantly different, the highest rate of adverse events occurred in the CxN and ABX continued > 72 h group (40.6%).

Table 1. Antibiotic Use in ICU Patients with COVID-19

	Culture-negative, Antibiotics ≤ 72 h (n = 10)	Culture-negative, Antibiotics > 72 h (n = 32)	Culture-positive (n = 23)	P-value
Initial Antibiotic Regimen[*], n (%)				
Anti-MRSA	8 (80)	21 (65.6)	11 (47.8)	0.17
Anti-pseudomonal	8 (80)	27 (84.4)	14 (60.9)	0.13
Ceftriaxone	1 (10)	5 (15.6)	3 (13)	1
Cefazolin	0	0	4 (17.4)	0.02
Initial Regimen De-escalated, n (%)	2 (20)	19 (59.4)	17 (73.9)	0.02
Initial Regimen Continued (Not De-escalated/Escalated), n (%)	8 (80)	10 (31.3)	3 (13)	< 0.01
Duration of Therapy, Initial Regimen (days), median (IQR)	2 (1-3)	5 (4-6)	9 (6-13)	< 0.01
Antibiotics Re-started ≥ 24 h After Discontinuation, n (%)	4 (40)	15 (46.9)	5 (21.7)	0.16
Duration of Therapy, Total Antibiotics (days), median (IQR)	3 (2-6)	6 (5-14)	10 (7-17)	< 0.01

^{*}Categories of initial antibiotics administered in study:
 - Anti-MRSA: vancomycin, linezolid, ceftaroline; no patient received daptomycin for initial therapy
 - Anti-pseudomonal: ceftazidime, piperacillin-tazobactam, aztreonam
^{**}No broad-spectrum antibiotics targeting Gram-negative MDRO were given for initial therapy (carbapenems, ceftolozane-tazobactam, ceftazidime-avibactam, meropenem-vaborbactam, imipenem-relebactam, cefiderocol)

Abbreviations: ICU, intensive care unit; h, hours; MRSA, methicillin-resistant *Staphylococcus aureus*; IQR, interquartile range; MDRO, multidrug-resistant organisms

Comparisons were made using the chi-square test or Fisher's exact test for nominal variables and the Kruskal-Wallis test for continuous variables; P-values < 0.05 were considered statistically significant; All analyses were conducted using SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC)

Table 2. Clinical Outcomes and Adverse Events in ICU Patients with COVID-19

	Culture-negative, Antibiotics ≤ 72 h (n = 10)	Culture-negative, Antibiotics > 72 h (n = 32)	Culture-positive (n = 23)	P-value
Clinical Outcomes*, n (%) or median (IQR)				
Clinical Success	4 (40)	10 (31.3)	9 (39.1)	0.79
In-hospital Mortality	6 (60)	22 (68.8)	14 (60.9)	0.79
Time from Antibiotic Discontinuation to Re-start (days)	4.5 (2-7)	4 (2-8)	6 (4-6)	0.68
Time to ICU Discharge from Antibiotic Start (days)	8.5 (4-15)	11.5 (5.5-21)	11 (6-15)	0.57
Time to Hospital Discharge or Death from Antibiotic Start (days)	12.5 (4-16)	18.5 (6.5-25.5)	13 (8-34)	0.29
Adverse Events*, n (%)				
Total # Patients	2 (20)	13 (40.6)	7 (30.4)	0.44
AKI	1 (10)	8 (25)	4 (17.4)	0.71
MDRO	0	8 (25)	2 (8.7)	0.14
Antibiotic-related Rash	1 (10)	0	1 (4.3)	0.13
Drug Fever	0	1 (3.1)	0	1
<i>Clostridioides difficile</i> Infection	0	0	0	1

Definitions:

- **Clinical success:** discharged alive or > 2-point decrease in WHO 10-point Clinical Progression Scale score from day of antibiotic initiation to day 30
- **AKI:** increase in SCr ≥ 0.3 mg/dL or increase in SCr to ≥ 150-200% of baseline or urine output < 0.5 mL/kg/h for > 6 h (AKIN definition); assessed ≥ 24 h following initiation and up to 48 h following discontinuation of initial antibiotic regimen
- **MDRO:** MRSA, VRE, or Gram-negative bacteria resistant to one or more classes of antimicrobial agents per CDC definition

Abbreviations: ICU, intensive care unit; h, hours; IQR, interquartile range; AKI, acute kidney injury; MDRO, multidrug-resistant organism; WHO, World Health Organization; SCr, serum creatinine; AKIN, Acute Kidney Injury Network; MRSA, methicillin-resistant *Staphylococcus aureus*; VRE, vancomycin-resistant *Enterococcus*; CDC, Centers for Disease Control and Prevention

Comparisons were made using the chi-square test or Fisher's exact test for nominal variables and the Kruskal-Wallis test for continuous variables; P-values < 0.05 were considered statistically significant; All analyses were conducted using SAS Enterprise Guide 7.1 (SAS Institute Inc., Cary, NC)

Conclusion. In ICU patients with COVID-19, empiric broad-spectrum ABX are often overutilized with an inertia to de-escalate despite negative culture results, potentially increasing the risk of adverse events. This remains an important area for focused antimicrobial stewardship efforts to mitigate the development of multidrug resistance.

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286. Infectious Complications and Antimicrobial Utilization in Hospitalized Patients with COVID-19

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Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. Hospitalized patients with COVID-19 have created increased demands on health care infrastructure and resources. Bacterial and fungal infections have been reported and have increased the need for antimicrobial utilization. We performed a retrospective chart review to characterize bacterial infections and antibiotic utilization during the COVID-19 surge at our tertiary care center.

Methods. All patients diagnosed with COVID-19 using SARS-CoV-2 PCR admitted to MedStar Georgetown University Hospital from 01Mar2020 through 31Aug2020 were included in the analysis. Data was collected on hospital-wide antimicrobial utilization [mean days of therapy per 1000-patient-days (DOT)] during the 6-month surge and was compared to antimicrobial utilization during a 6-month period that preceded the COVID-19 surge. Clinical and microbiological data and patient outcomes were also collected and analyzed.

Results. A total of 238 patients met eligibility criteria during the observation period, of which 25.6% (n = 61) developed a bacterial, fungal, or viral co-infection. Culture-positive bacterial complications were seen in 21.8% (n = 52) with 32.8% (n = 20) having a multidrug resistant organism (MDRO). There was a statistically significant difference between COVID-19 patients with co-infection and those without for intubation (p < 0.001), vasopressor use (p < 0.001), and renal replacement therapy (p = 0.001). COVID-19 patients with co-infections had a longer mean length of stay (21.9 days vs 13.5 days, p < 0.001) and greater mortality (32.8% vs 20.6%, p = 0.006) compared to those without a co-infection, respectively.

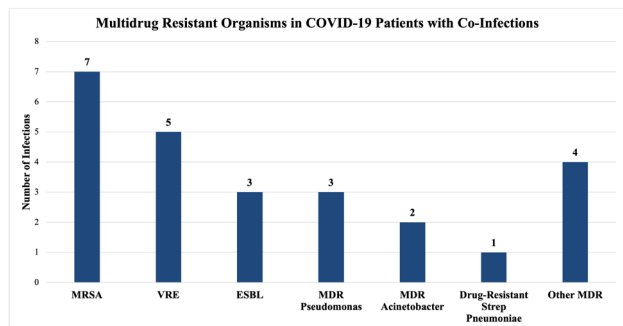
Mean antimicrobial utilization for the entire hospital population was 790.6 DOT during the COVID surge compared to 928.7 DOT during a 6-month period preceding the COVID surge (p < 0.001). For all COVID-19 patients, antimicrobial utilization was 846.9 DOT; however, this increased to 1236.4 DOT for COVID-19 patients with co-infections.

Table 1. Demographics

Complications, n (%)	Sample (n=238)	Co-infection (n=61)	P-value
Respiratory Support	193 (81.8)	53 (86.9)	0.180
Intubation	66 (27.7)	34 (55.7)	< 0.001*
Vasopressors	58 (24.4)	32 (52.5)	< 0.001*
Renal Replacement Therapy	48 (20.2)	21 (34.4)	0.001*
Length of hospital stay, mean (d ± SD)	13.53 ± 12.9	21.92 ± 18.2	<0.001*
Deceased	49 (20.6)	20 (32.8)	0.006*

Table 2. Antimicrobial Utilization in COVID-19 Patients

	Sample (N=238)	Co-Infection (n=61)	No Infection (n=177)
DOT per 1000-patient-days	846.9	1236.4	570.4
Mean Days of Antimicrobial Use	6.8	9.75	5.91
Median Days of Antimicrobial Use	5	6	4



Conclusion. Although hospital-wide antimicrobial utilization had decreased during the COVID surge, COVID-19 patients with co-infections demonstrated a disproportionate use of antimicrobial agents as well as ICU resources. As MDRO infections were relatively common, antimicrobial stewardship should be prioritized in the COVID-19 population.

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287. Characteristics and Outcomes of COVID-19 Patients with Candidemia at a Community Hospital in Chicago.

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Session: P-14. COVID-19 Complications, Co-infections, and Clinical Outcomes

Background. 1,416 patients with acute COVID-19 infection were admitted to our hospital in 2020. During that year we noticed an alarming increase in cases of nosocomial Candidemia: 26 versus an average of 2.8 cases per year over the previous 5 years. 19 of the 26 episodes (73%) of Candidemia occurred in patients who were admitted with acute COVID-19 infection. Recent reports suggest that hospitalized patients with COVID-19 are at increased risk for developing Candidemia, however their clinical characteristics, risk factors and outcomes have not been well described. We evaluated the risk factors and mortality of hospitalized COVID-19 patients with Candidemia.

Methods. We performed a retrospective chart review of 19 patients with Candidemia and confirmed COVID-19 infection at a 292-bed community teaching hospital in Chicago, Illinois from January through December 2020. We report a