

Epidemiology of Antimicrobial Use Among SARS-CoV-2 Positive and SARS-Cov-2 Negative Discharges in the US: A Multicenter Evaluation

Background

- Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged in December of 2019 and soon became pandemic.
- Previous viral epidemics have been associated with an increase in rates of super- or co-infections with other viruses, bacteria, anaerobes and fungi/yeast.
- There are limited and varied descriptions of antimicrobial usage among COVID-19 patients. Studies suggest that broad-spectrum antibiotic use is widespread among patients with COVID. Overuse of antimicrobials have deleterious effects, including the development of antibiotic resistance, increased risk for other infections, such as *Clostridium difficile*, and potential adverse events and toxicity.
- We evaluated antimicrobial use and culture source for US hospitalized patients among patients with and without laboratory confirmed SARS-CoV-2 infection.

Methods

- We conducted a multi-center, retrospective cohort study of hospitalized patients from 246 US acute care facilities admitted March 1 – May 31, 2020 (BD Insights Research Database [Becton, Dickinson and Company, Franklin Lakes, NJ]).
- Eligible admissions included all discharges with >1-day inpatient admission and a record of discharge or death between March 1, 2020 and May 31, 2020. Patients could have more than one admission within the time period.
- Admissions were classified into 2 groups based on a SARS-CoV-2 PCR test during or ≤7 days prior to hospitalization: (1) SARS-CoV-2 tested with a positive test result; and (2) SARS-CoV-2 tested with a negative test result for comparison.
- The frequency of antimicrobials received for ≥24 hours were categorized by class and by source of positive culture. Positive pathogens were identified by culture and molecular testing methods from blood, respiratory tract, urine, intra-abdominal, skin/wound and other sources. P value >0.05 were considered significantly different.

Results

- There were 141,621 admissions with SARS-CoV-2 testing with 12% resulting in a positive test.
- The highest rate of SARS-CoV-2 testing was among hospitals with >300 beds (62% of SARS-CoV-2 positive and 56% of SARS-CoV-2 negative admissions). Most of these facilities were urban (93%).

Figure 1. SARS-CoV-2 positivity by region and center, US

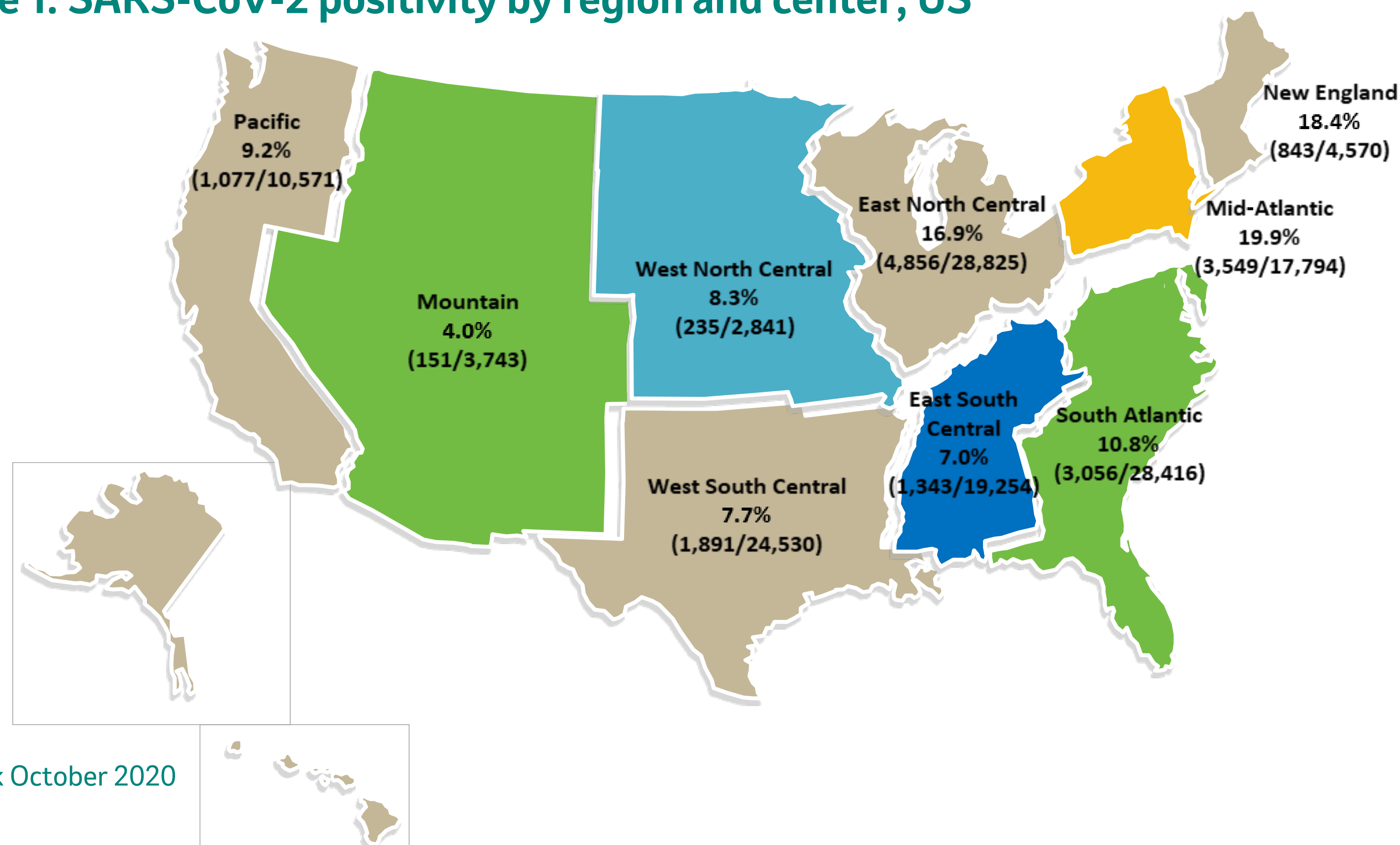


Table 1. Patient characteristics by those tested for SARS-CoV-2

Characteristic	Tested for SARS-CoV-2		P-value
	SARS-CoV-2 Positive Admissions (n=17,003)	SARS-CoV-2 Negative Admissions (n=124,618)	
Demographics			
Male sex, n (%)	9,026 (53.1%)	57,924 (46.5%)	<0.05
Age, mean ± SD, years	61.7 ± 18.0	58.5 ± 20.9	<0.05
ICU Admissions: n (%)	4,076 (24.0%)	21,060 (16.9%)	<0.05
Specimens collected for other pathogens, n (%)	16,637 (97.8%)	114,550 (91.9%)	<0.05
Specimens positive for other pathogens, n (% of admissions with specimens collected)	3,473 (20.4%)	24,442 (19.6%)	0.08

*Other pathogens were defined as any bacteria, fungus, or virus other than SARS-CoV-2.

Table 2: Antimicrobial classes prescribed by those tested for SARS-CoV-2

	SARS-CoV-2 Positive Admissions (n=17,003)	SARS-CoV-2 Negative Admissions (n=124,618)	P-value
Admissions Prescribed Antimicrobials* (duration ≥ 24 hours; n (%))	11,554 (68.0%)	56,286 (45.2%)	<0.05
Admission to Abx Start: mean ± SD, days	0.9 ± 2.6	0.9 ± 2.3	0.06
Duration of Abx: mean ± SD, days	6.1 ± 5.2	4.8 ± 4.5	<0.05
Most Common Antimicrobial Classes Prescribed as a % of Discharges Prescribed an Abx			
3rd/4th Gen Cephalosporins	8,679 (75.1%)	31,031 (55.1%)	<0.05
Glycopeptides	4,254 (36.8%)	23,586 (41.9%)	
Macrolides	7,482 (64.8%)	12,883 (22.9%)	
β-lactam/β-lactamase inhibitors	3,065 (26.5%)	17,997 (32.0%)	
Fluoroquinolones	800 (6.9%)	7,119 (12.6%)	
1st/2nd Gen Cephalosporins	432 (3.7%)	6,278 (11.2%)	
Tetracyclines	2,049 (17.7%)	5,625 (10.0%)	
Carbapenems	1,145 (9.9%)	5,068 (9.0%)	
Antifungals	579 (5.0%)	4,006 (7.1%)	
Anti-influenza agents	1,002 (8.7%)	998 (2%)	

*Admissions can be prescribed > 1 antimicrobial class

Table 3: Top 10 antimicrobials prescribed in respiratory, urine and blood positive admissions by SARS-CoV2 Status*

Respiratory Culture Positive Admissions			
	SARS-CoV-2 Positive (1,228)	SARS-CoV-2 Negative (n=5,435)	
Azithromycin	462 (37.6%)	Vancomycin	1,395 (25.7%)
Vancomycin	390 (31.8%)	Ceftriaxone	1,218 (22.4%)
Ceftriaxone	387 (31.5%)	Piperacillin-tazobactam	1,184 (21.8%)
Cefepime	328 (26.7%)	Azithromycin	1,089 (20.0%)
Piperacillin-tazobactam	265 (21.6%)	Cefepime	1,070 (19.7%)
Meropenem	195 (15.9%)	Meropenem	581 (10.7%)
Doxycycline	114 (9.3%)	Levofloxacin	432 (7.9%)
Linezolid	95 (7.7%)	Doxycycline	402 (7.4%)
Micafungin	71 (5.8%)	Metronidazole	394 (7.2%)
Levofloxacin	67 (5.5%)	Oseltamivir	286 (5.3%)
Urine Culture Positive Admissions			
	SARS-CoV-2 Positive (1,697)	SARS-CoV-2 Negative (10,077)	
Ceftriaxone	661 (39.0%)	Ceftriaxone	3,712 (36.8%)
Azithromycin	544 (32.1%)	Piperacillin-tazobactam	1,643 (16.3%)
Cefepime	339 (20.0%)	Vancomycin	1,630 (16.2%)
Vancomycin	324 (19.1%)	Cefepime	1,305 (13.0%)
Piperacillin-tazobactam	266 (15.7%)	Meropenem	985 (9.8%)
Meropenem	188 (11.1%)	Azithromycin	866 (8.6%)
Doxycycline	133 (7.8%)	Levofloxacin	605 (6.0%)
Linezolid	89 (5.2%)	Metronidazole	552 (5.5%)
Fluconazole	75 (4.4%)	Fluconazole	451 (4.5%)
Levofloxacin	74 (4.4%)	Ciprofloxacin	414 (4.1%)
Blood Culture Positive Admissions			
	SARS-CoV-2 Positive (n=1,020)	SARS-CoV-2 Negative (n=9,530)	
Vancomycin	229 (22.5%)	Ceftriaxone	1,712 (18.0%)
Azithromycin	219 (21.5%)	Vancomycin	1,558 (16.3%)
Ceftriaxone	213 (20.9%)	Piperacillin-tazobactam	1,347 (14.1%)
Cefepime	192 (18.8%)	Cefepime	1,064 (11.2%)
Piperacillin-tazobactam	145 (14.2%)	Meropenem	650 (6.8%)
Meropenem	110 (10.8%)	Azithromycin	592 (6.2%)
Micafungin	60 (5.9%)	Metronidazole	523 (5.5%)
Linezolid	55 (5.4%)	Cefazolin	399 (4.2%)
Doxycycline	48 (4.7%)	Levofloxacin	325 (3.4%)
Cefazolin	41 (4.0%)	Fluconazole	246 (2.6%)

*Patients can be prescribed > 1 antimicrobial

Results

- There were more males (53%) SARS-CoV-2 positive than negative (47%), and SARS-CoV-2 positive patients were older 62±18 years compared to those negative 59±21 years. (Table 1)
- About 1 in 4 admissions with COVID-19 had an ICU admission, which was significantly more than those tested negative. (Table 1)
- Both SARS-CoV-2 negative and positive patients had a high rate of other cultures collected (93%).
- The majority of SARS-CoV-2 positive patients were prescribed an antimicrobial (68%) and on average they received it within the first day of admission. Fewer SARS-CoV-2 negative admissions were prescribed an antimicrobial (45%); but both groups were prescribed antimicrobials within the first day of admission. (Table 1)
- SARS-CoV-2 positive admissions received a significantly longer duration of antimicrobials (6.1 ± 5.2 days) than those confirmed negative (4.8 ± 4.5 days). (Table 1)
- The classes of antimicrobials that were prescribed among those SARS-CoV-2 positive and negative admissions were significantly different. The most prevalent class prescribed among SARS-CoV-2 positive admissions was 3rd/4th generation cephalosporins (75%), followed by macrolides (65%) and glycopeptides (37%). (Table 2)
- Antimicrobials given were also different based on the source of the positive culture. (Table 3)

Study Limitations

- SARS-CoV-2 and other pathogen identification was based on local lab methodology and data entry, which is used for patient management, but may not be consistent across all the hospitals. Further, we did not assess COVID-19 disease severity, so it may be possible that there were patients with a history of COVID-19 still shedding virus or were not tested.
- These results are from the early phase of the pandemic and may not be representative of changing or current trends.
- Although source of infection was included in this study, it will be important for future studies to evaluate the pathogen for which the antimicrobial is targeted, and the appropriateness of the antimicrobial received.

Conclusions

- Antimicrobial use was higher among SARS-CoV-2 positive patients, despite similar rates of positive cultures among SARS-CoV-2 negative patients.
- Antimicrobials were prescribed within 24 hours from the time of admission among all patients.
- The high rates of antimicrobial use may highlight the high level of concern with potential bacterial superinfection among COVID-19 suspected patients. However, it may also be indicative of potential overuse of antimicrobials. Collateral damage from antimicrobial overuse among these patients could include increased selection of antimicrobial resistance, drug toxicity, adverse events and unnecessary treatment costs. Further studies are needed to determine the appropriateness of the antimicrobials and if they were discontinued when the causative pathogen was known.
- It will be important to continue to evaluate the utilization and appropriateness of antimicrobial use among COVID-19 patients to optimize treatment management and outcomes.

References

- Clancy CC, et al. Clinical Infectious Diseases 2020, c1aa524, <https://doi.org/10.1093/cid/c1aa524>
- Esper FP, et al. J Infect 2011;63:260-6.
- MacIntyre CR, et al. BMC Infect Dis 2018;18:637.
- Rawson TM, et al. Clinical Infectious Diseases, c1aa530, <https://doi.org/10.1093/cid/c1aa530>

