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A retrospective antibiotic prescribing assessment and examination of potential antibiotic stewardship targets in patients with COVID-19

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Objectives: Despite low rates of bacterial coinfection in patients admitted with COVID-19, antimicrobials are frequently prescribed. Our primary objective was to evaluate antimicrobial prescribing over time in patients admitted with COVID-19. The secondary objectives were to evaluate the role of ID providers in antimicrobial utilization, describe the rate of confirmed bacterial infection and determine factors associated with empirical antimicrobial prescribing in COVID-19.

Materials and methods: Retrospective review was performed for adult patients admitted to a tertiary care centre with COVID-19 between 1 March 2020 and 30 November 2020. Patient demographics, disease severity, risk factors for severe disease, clinical outcomes, antimicrobial prescribing and respiratory microbiological testing were collected and analysed. Prescribing trends were evaluated by month, and factors contributing to prescribing were established using univariate and multivariable analysis.

Results: Antibiotics were prescribed during admission in 37.9% of the study cohort, with 85.1% of patients who received antibiotics having therapy initiated within 48 h of admission. Antibiotic prescribing incidence increased with disease. Over the study period, antimicrobial prescribing rates decreased by 8.7% per month. Multivariable analysis found ICU admission, obtainment of procalcitonin values, intubation, heart failure, haemodialysis and nursing home residence were associated with empirical antimicrobial prescribing.

Conclusions: Unnecessary antimicrobial prescribing in patients with viral syndromes like COVID-19 continues to represent an area of concern. Antimicrobial stewardship efforts during COVID-19 should consider patient-specific factors associated with antibiotic prescribing. Recognition of such factors, in combination with application of well-established antimicrobial stewardship tactics, may serve to impact antimicrobial prescribing trends, even as patient volumes rise.

Introduction

During the COVID-19 pandemic, potential overuse of antimicrobials and resultant unintended consequences have been a concern of antimicrobial stewards.[1] This problem is driven by difficulty in differentiating between isolated viral illness and potential superimposed bacterial pneumonias or other infections. Bacterial or fungal coinfection have been estimated to occur in ∼10% of COVID-19 patients, with some reports demonstrating lower rates.[2–6] Despite low rates of bacterial coinfection, antimicrobial prescribing in inpatients with COVID-19 occurs in 50%–80% of admissions.[2,3,5–9] Empirical antimicrobial prescribing in patients with COVID-19 has failed to demonstrate improvement in patient outcomes.[7,10,11] The established overuse of antimicrobials in this patient population emphasizes the need for antimicrobial stewardship intervention, and application of fundamental stewardship strategies to patients with COVID-19 have been previously described.[12–17]

Early in the pandemic, we evaluated antimicrobial prescribing across the continuum of care in patients with COVID-19.[6] However, at that time, only a small number of inpatients were able to be included. As the pandemic progressed and our institution entered its surge, we sought to perform a more thorough evaluation of inpatient antimicrobial prescribing practices. Our primary

objective was to assess overall antimicrobial prescribing and prescribing changes over time for respiratory indications in patients with COVID-19. Secondary objectives included to examine the role of infectious diseases (ID) providers in antimicrobial utilization, describe rates of confirmed respiratory bacterial coinfection and associated organisms, and describe factors associated with empirical antimicrobial prescribing that could serve as noteworthy targets for future antimicrobial stewardship interventions.

Materials and methods

This retrospective cohort study was performed with approval of the institutional COVID-19 research committee and local institutional review board (IRB). Patients were included if they were adults (age ≥18 years), had positive SARS-CoV-2 PCR, an inpatient stay lasting >24 h between 1 March 2020 and 30 November 2020, and had authorized their medical information to be used in Minnesota as part of retrospective research. Patients were excluded if they were asymptomatic with positive PCR or if their last positive PCR was >30 days prior to index hospitalization with an admission diagnosis other than COVID-19. Patients were stratified by disease severity. Mild disease was defined as acute symptomatic disease without new or increased oxygen supplementation requirements, moderate disease as symptomatic disease with new or increased oxygen requirements, and severe disease as symptomatic disease resulting in ICU admission with or without mechanical ventilation.[6] A confirmed respiratory bacterial infection was defined by the isolation of a pathogen from a respiratory tract culture. When evaluating patient transfer status, local admission was defined as admission to our institution either through direct admission from the community or through the local emergency department (ED). ED transfer was defined as the transfer of a patient to our local ED as a result of evaluation in the ED of an outside hospital, and direct admission transfer was defined as transfer from an outside hospital admission to our facility for direct admission.

Antimicrobial data were collected for agents prescribed to treat a suspected or confirmed respiratory tract infection. Antimicrobials prescribed for other indications were not evaluated. The specialty responsible for antimicrobial discontinuation was determined by the provider specialty with the earliest documented mention of stopping antimicrobials. Antimicrobial utilization was collected in days of therapy. Spectrum of activity was reported utilizing a previously published spectrum score, with each antimicrobial assigned a value corresponding to its spectrum of activity, with larger scores indicative of broader spectrums.[18] Spectrum scores were reported as a whole and per day of antimicrobial therapy. Two antimicrobial agents, ceftolozane/tazobactam and cefiderocol, were encountered that were not scored as part of the originally published spectrum score. To appropriately account for their use, the scoring methodology applied by Gerber *et al.*[18] was applied by our study team (Table S1, available as Supplementary data at *JAC-AMR* Online). Cefiderocol was assigned a score of 6 and ceftolozane/tazobactam a score of 8.

Our institutional antimicrobial stewardship programme (ASP) performs prospective audit with intervention and feedback using real-time alerts (i.e. flags) to identify patients for review by ASP personnel (i.e. ID physicians/pharmacists). If indicated, recommendations on ASP flagged patients are passed along to the primary team. On 24 March 2020, our institution's ASP team instituted two new flags within our electronic health record (EHR) to facilitate the identification of COVID-19 patients and the stewardship of COVID-19 therapeutics as part of our prospective audit and feedback program.[14,15] The logic behind these flags remained fluid over time. When the enterprise encountered the first surge, the ongoing real-time review of each COVID-19 patient by ASP personnel became unrealistic, and on 11 August 2020 the initial flag intended to identify all patients with COVID-19 was refined to only include patients with active COVID-19 receiving empirical antimicrobial therapy for respiratory tract indications. In addition to the flags, passive education regarding avoidance of unnecessary antimicrobial prescribing in COVID-19 was widely distributed via an internal newsletter in September 2020. Given the multimodal approach with staggered implementation, assessment of the total impact of antimicrobial stewardship interventions was logistically difficult. In order to evaluate the changing patterns of prescribing over time, we chose to evaluate antimicrobial prescribing rates (total and empirical) by month and pre/post-implementation of the ASP flag (implemented 11 August 2020) specific to respiratory antimicrobial use in patients with COVID-19. Lastly, in the course of routine clinical care, ID could be formally consulted for the provision of therapeutic recommendations. During the study time frame, all COVID-19 inpatients were additionally evaluated remotely by a multidisciplinary expert COVID-19 panel including radiology, critical care, haematology and ID. All patients admitted with COVID-19 were discussed with this expert panel each morning. After evaluating the patient's clinical status, imaging and laboratory values, the panel would discuss and recommend available therapeutics to the primary and consulting teams.

Results are summarized using frequencies and percentages for categorical data, and either means and SDs or medians and IQRs for continuous data. Patient characteristics and antimicrobial utilization metrics were compared between disease severity groups using either χ^2 or Fisher's exact tests for categorical data, and either ANOVA or the Kruskal–Wallis test for continuous data as appropriate. Duration of antimicrobial therapy was compared between those initiated on antibiotics within 48 h and those initiated on antibiotics after 48 h using a Wilcoxon rank-sum test. For the overall antimicrobial prescribing rate, a 95% exact binomial CI was determined. Poisson regression was used to assess for changes in rates of antimicrobial prescribing over time. Logistic regression was used to assess whether factors were associated with the empirical use of antimicrobial agents. Stepwise selection was used to determine which variables went into the multivariable model, where $P = 0.20$ was the cut-off to enter the model and $P = 0.10$ was the cut-off to stay in the model. All tests were two-sided, and P values ≤0.05 were considered statistically significant. SAS version 9.4 software was used for all analyses (SAS Institute Inc., Cary, NC, USA).

Results

Total cohort demographics

A total of 654 patient encounters were included. Baseline demographics for the total cohort and by disease severity are displayed in Table 1. Of patients with severe disease, the median length of ICU stay was 6 days (IQR 3, 12) with 72 of 223 (32.3%) patient encounters resulting in endotracheal intubation with median duration of mechanical ventilation of 7.5 days (IQR 4, 13). Across all disease severities, 55 encounters (8.4%) represented readmissions for COVID-19 with 11, 20 and 24 being classified as mild, moderate or severe, respectively ($P = 0.2$). Procalcitonin (PCT) values were obtained within 24 h of admission in 170 (26%) patients. PCT values were more likely to be obtained in those with severe disease ($P < 0.001$) and median PCT values increased with increasing disease severity ($P < 0.001$). Formal consultation by ID occurred in 93.6% (612/654) of all cases. ID was more likely to be consulted in moderate (94.2%, 228/242) or severe cases (96.4%, 215/223) as compared with mild cases (89.4%, 169/189) ($P = 0.014$).

Antibiotic utilization

In the full cohort, 248 (37.9%) of patients received antimicrobials targeting suspected or confirmed bacterial respiratory infections. The incidence of antimicrobial prescribing increased with disease severity, with 16.9% (32/189), 29.8% (72/242) and 64.6% (144/223) of patients receiving respiratory antimicrobials during their

Table 1. Population demographics

Characteristics	All patients ($n = 654$)	Mild disease ($n = 189$)	Moderate disease ($n = 242$)	Severe disease ($n = 223$)	*P* value
Age, years, mean ± SD	63.6 ± 17.1	62.1 ± 18.2	65.3 ± 15.6	63.1 ± 17.6	0.12
Male, %	55.8	52.4	51.7	63.2	0.03
Race, %					0.42
White	76.1	74.1	81.4	72.2	
American Indian/Alaska Native	0.2	0	0	0.4	
Asian	5.4	6.3	3.3	6.7	
Black or African American	7.6	9	6.6	7.6	
Native Hawaiian	0.2	0	0	0.4	
Other	8	8.5	7	8.5	
Unknown	2.6	2.1	1.7	4	
Ethnicity, %					0.45
Hispanic or Latino	10.2	9	9.5	12.1	
Not Hispanic or Latino	84.6	85.7	86.8	81.2	
Unknown	5.2	5.3	3.7	6.7	
BMI, mean ± SD	32 ± 8	31.7 ± 8.6	32.3 ± 7.8	31.8 ± 7.7	0.69
Charlson Comorbidity Index, mean ± SD	5.8 ± 4.5	5.7 ± 4.5	5.9 ± 4.5	5.6 ± 4.6	0.65
Time between positive test and admission, days, median (IQR)	1 (0, 6)	1 (0, 5)	3 (0, 7)	1 (0, 5)	0.06
Length of stay, days, median (IQR)	7 (5, 11)	4 (3, 7)	6 (5, 9)	10 (7, 17)	<0.01
PCT obtained within 24 h of admittance, %	26	14.3	28.5	33.2	<0.01
PCT value, median (IQR)	0.2 (0.1, 0.6)	0.1 (0.1, 0.2)	0.2 (0.1, 0.4)	0.3 (0.1, 0.8)	<0.01
Death, %	10.6	1.1	3.7	26	<0.01
Transfer type, %					<0.01
Local admission (i.e. no transfer)	48	63	50.8	32.7	
ED transfer	20	21.2	24	14.4	
Direct admission	32	15.9	25.5	52.9	
Risk factors, %					
Age >60 years	62.8%	58.2%	66.5%	62.8%	0.21
BMI >30	54.1%	50.8%	55.4%	55.6%	0.55
Hypertension	55.4%	51.3%	59.5%	54.3%	0.22
Heart failure	14.7%	12.7%	16.5%	14.3%	0.53
Congenital heart disease	2.1%	0.5%	2.1%	3.6%	0.1
Coronary artery disease	17.7%	22.2%	17.4%	14.3%	0.11
Chronic lung disease/asthma	25.4%	24.3%	25.2%	26.5%	0.88
Diabetes	35.6%	30.7%	36.4%	39%	0.2
Immunocompromised	12.2%	13.2%	16.1%	7.2%	0.01
Nursing home resident	7.5%	5.3%	9.1%	7.6%	0.33
Chronic haemodialysis	3.8%	3.2%	5%	3.1%	0.51
Chronic liver disease	6.6%	5.8%	7.9%	5.8%	0.6
Pregnancy	1.2%	1.6%	0.8%	1.3%	0.76
Total risk factors, mean ± SD	1.7 ± 1.4	1.6 ± 1.2	1.7 ± 1.4	1.8 ± 1.5	0.9

admission in the mild, moderate and severe disease classifications, respectively ($P < 0.01$). Of the patients who received antibiotics, 85.5% (212/248) received empirical therapy within 48 h of hospital admission, with no significant difference identified between disease severities (90.9% mild versus 88.9% moderate versus 81.9% severe, $P = 0.24$). This considered, antimicrobial therapy was administered as empirical therapy within 48 h of hospitalization in 15.9% (30/189), 26.4% (64/242) and 52.9% (118/223) of the total populations of mild, moderate and severe disease, respectively ($P < 0.001$). However, it should be noted that 52.9% (118/223) of patients admitted with severe disease were admitted as the result of direct admission transfer, and, of these, 59.3% (70/118) received antibiotics within 48 h of admission. The ID consultation team was responsible for antimicrobial initiation in only 1.6% (4/248) of all encounters where an antibiotic was prescribed; however, they recommended antimicrobial discontinuation in 42.7% (106/248) of all encounters with an antimicrobial prescribed.

Antimicrobial utilization data are described in Table 2. The median length of antimicrobial therapy was 5 days in the total population, with significantly longer median durations of therapy being observed in those with severe disease (mild: 1 day versus moderate: 2 days versus severe: 6 days, $P < 0.01$). As such, total

Table 2. Antimicrobial utilization metrics

Characteristics	All patients ($n = 654$)	Mild disease ($n = 189$)	Moderate disease ($n = 242$)	Severe disease ($n = 223$)	*P* value
Receipt of respiratory antibiotics, %	37.9	16.9	29.8	64.6	<0.01
Patients with respiratory antibiotics who received first dose within 48 h of admission, %	85.4	90.9	88.9	81.9	0.24
Team responsible for antimicrobial initiation, %					<0.01
Emergency department	29.8	56.3	41.7	18.1	
Infectious diseases	1.6	3.1	0	2.1	
Primary inpatient team	68.5	40.6	58.3	79.9	
Team responsible for antimicrobial discontinuation, %					0.39
Emergency department	0.4	0	1.4	0%	
Infectious diseases	42.7	40.6	48.6	40.3	
Primary inpatient team	56.9	59.4	50	59.7	
Length of therapy, days, median (IQR)	5 (2, 7)	1 (1, 5)	2 (1, 5)	6 (4, 10)	<0.01
Total spectrum score, median (IQR)	38 (13, 62)	9.5 (9, 26)	18 (9, 45)	50 (31, 82)	<0.01
Spectrum score per day of antimicrobial therapy, median (IQR)	9 (7.3, 10)	9 (5, 9)	9, (7.3, 9.9)	9 (7.4, 10)	0.25
Antimicrobial days of therapy					N/A
Total antimicrobial days of therapy	2287	141	414	1732	
Amoxicillin	4	0	4	0	
Amoxicillin/clavulanate	56	0	26	30	
Ampicillin/sulbactam	2	0	0	2	
Azithromycin	316	28	102	186	
Aztreonam	15	0	2	13	
Cefadroxil	7	7	0	0	
Cefazolin	27	2	0	25	
Cefdinir	12	8	4	0	
Cefepime	365	27	37	301	
Cefiderocol	9	0	0	9	
Ceftolozane/tazobactam	27	0	0	27	
Ceftriaxone	471	36	114	321	
Cefuroxime	2	0	0	2	
Doxycycline	146	13	45	88	
Levofloxacin	56	6	22	28	
Meropenem	73	0	0	73	
Metronidazole	30	0	7	23	
Piperacillin/tazobactam	284	3	22	259	
Trimethoprim/sulfamethoxazole	41	0	0	41	
Vancomycin	344	11	29	304	

N/A, not applicable.

cumulative antimicrobial spectrum scores were higher in the patients with severe disease; however, when the spectrum score per day of antimicrobial therapy was evaluated, no significant difference was identified between any of the severity groups ($P = 0.25$). Antimicrobial durations of therapy were found to be shorter in patients who received empirical therapy within 48 h of hospitalization versus those initiated on antibiotics >48 h after admission (5 days [IQR 1, 7] versus 6 days [IQR 3.5, 9], $P = 0.034$).

A multiplicative decrease in antimicrobial prescribing rate over time of 8.7% per month was observed for all respiratory antimicrobial prescribing (incident rate ratio [IRR] per month: 0.92, 95% CI 0.87–0.69) and 9.9% per month for respiratory antimicrobial prescribing within 48 h of hospital admission (IRR per month: 0.9, 95% CI 0.86–0.95). This decrease in prescribing occurred despite an increase in COVID-19 related admissions during the study period (Figure 1). A statistically significant decrease in both total (51.8% [102/197] versus 31.9% [146/457], $P < 0.001$) and empirical (45.7% [90/197] versus 26.7% [122/457], $P < 0.01$) antibiotic prescribing was observed when comparing patients admitted before and after the implementation of the refined ASP flag.

Microbiological testing

Respiratory cultures were collected in 15.9% (104/654) of patients in the full cohort with 7.7% collected from bronchoalveolar lavage, 55.3% from expectorated sputum and 36.9% from tracheal

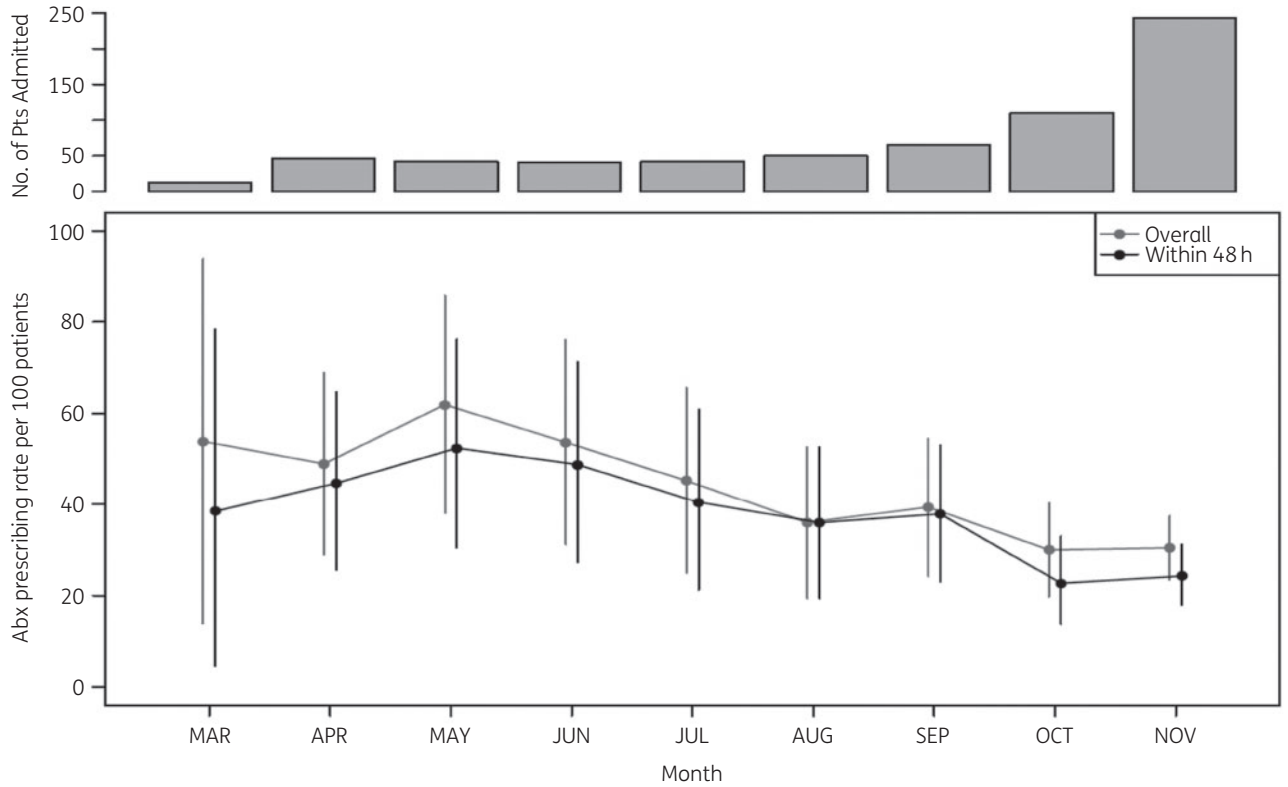

Figure 1. Full cohort antimicrobial prescribing rates and admissions by month. Abx, antibiotics; Pts, patients.

aspirate. Patients with severe disease were more likely to have bacterial respiratory cultures obtained than those with mild (34.1% [76/223] versus 3.7% [7/189], $P < 0.01$) or moderate disease (34.1% [76/223] versus 8.7% [21/242], $P < 0.001$). Additionally, time between admission and culture collection was longer in those with severe disease (3 days [IQR 1, 7]) as compared with mild (1 day [IQR 0, 1]) or moderate disease (1 day [IQR 0, 2]) ($P = 0.003$). A total of 64 isolates were identified from positive respiratory cultures (Figure 2). A specific pathogen was identified in the respiratory cultures of 47.1% (49/104) of patients who had cultures collected, without variation between disease severities, with 42.9% (3/7), 42.9% (9/21) and 48.7% (37/76) of cultures demonstrating growth of a pathogen in mild, moderate and severe disease, respectively ($P = 0.91$). *Staphylococcus aureus* was the most isolated pathogen and was isolated from 27 of the 49 patients with positive cultures, with 21 of 27 isolates being methicillin susceptible.

Factors associated with antimicrobial utilization

On univariate analysis (Table 3), factors found to be associated with empirical antimicrobial use included baseline coronary artery disease; residence in a nursing home; haemodialysis dependence; obtainment of a PCT value within 24 h of admission; admission to the ICU; intubation; calendar month of admission; transfer type (i.e. local admission versus direct admission transfer); evidence of infiltrate on chest imaging; severity of illness; and collection of respiratory cultures. Though collection of a PCT level within 24 h of admission was a factor associated with antimicrobial utilization, the median value was 0.2 ng/mL in both those who received empirical antimicrobials and those who did not ($P = 0.03$). Admission by direct admission transfer was associated with a statistically significant increase in empirical antimicrobial utilization as compared with local admission ($P < 0.001$) and admission by ED transfer ($P = 0.01$).

On multivariable analysis (Table 3), pre-existing heart failure; residence in a nursing home; haemodialysis dependence; obtainment of a PCT value within 24 h of admission; ICU admission, intubation; evidence of infiltrate on chest imaging; and collection of respiratory tract cultures were associated with empirical antimicrobial prescribing.

Discussion

The unnecessary utilization of antimicrobials in viral respiratory syndromes has long drawn the attention of antimicrobial stewards.[16] This has been acutely highlighted by the SARS-CoV-2 pandemic with early antimicrobial prescribing rates as high as 80%.[2,3,5–9]

During the first 9 months of the pandemic, we observed an overall rate of antimicrobial prescribing of 37.9%. Furthermore, 85.4% of patients that received antimicrobial therapy received their first dose within 48 h of admission. This high rate of empirical prescribing is starkly contrasted with a low rate of bacterial culture obtainment and isolation of a bacterial pathogen from respiratory cultures obtained during the hospital stay. During the study period, both active and passive methodologies were implemented to attempt to reduce unnecessary antibacterial prescribing in COVID-

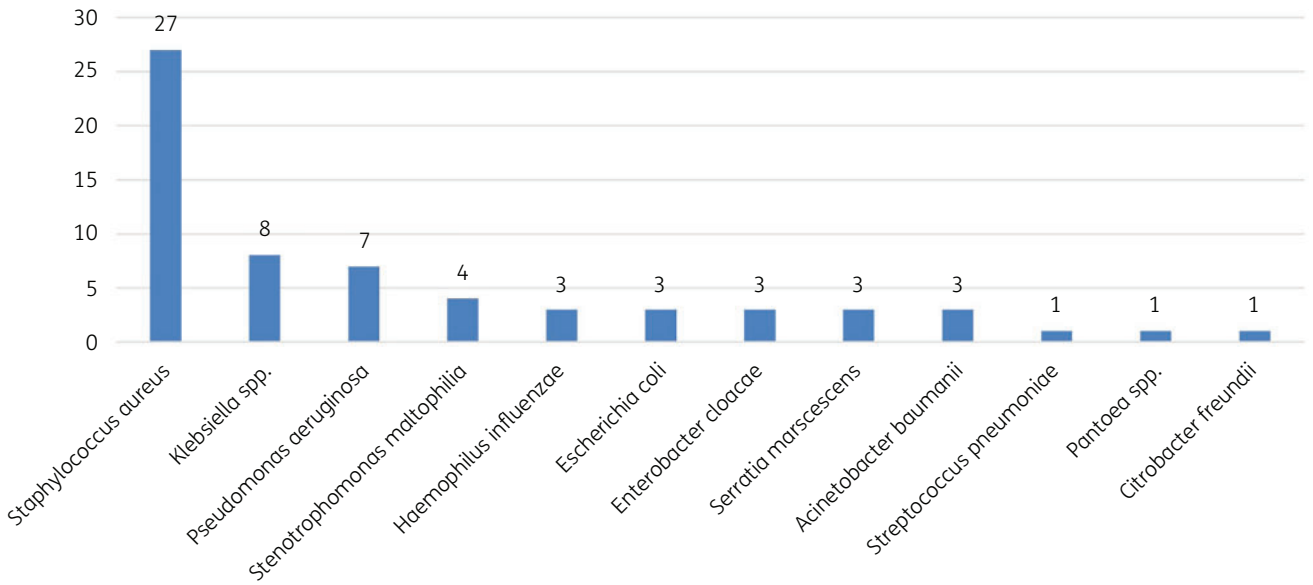

Figure 2. Count of organisms isolated from respiratory cultures.

19. This was accompanied by a high rate of formal ID consultation, with ID providers rarely being responsible for antibiotic initiation, but often recommended discontinuation. These interventions, likely along with the accumulation of time and experience with managing COVID-19, appear to have contributed to the observed trend in decreasing antimicrobial prescribing over time. Our study concluded with an empirical prescribing rate of 24.3% in November of 2020 despite the largest number of admissions in a single month during the study period ($n = 243$). While our rate of antimicrobial prescribing is notably lower than observed rates in other early publications, opportunities for improvement in antimicrobial prescribing in COVID-19 remain. Furthermore, the decrease in respiratory antibacterial prescribing over time demonstrates the utility of both passive and active antimicrobial stewardship techniques and the significance of ID involvement.

Use of a multivariable analysis, regarding empirical antimicrobial prescribing, identified that patients in the ICU potentially benefit from closest ASP review. Patients admitted to the ICU had the highest rate of culture collection amongst the disease severities and were also the most likely to receive antimicrobial therapy. Additionally, patients admitted to the ICU received therapy for significantly longer than those outside of the ICU, and intubation appeared to further increase the probability of empirical antimicrobial prescribing.

Though potentially a result of empirical prescribing practices rather than the cause, obtainment of PCT values and respiratory cultures occurred more commonly in ICU patients. Specifically, regarding respiratory cultures, the median time to culture obtainment was 3 days and antimicrobial initiation occurred within the first 24–48 h in 52.9% of that population. This may indicate that cultures were being obtained to guide therapy rather than determine its necessity. PCT is often touted as a tool to decrease antimicrobial use in adult ICU patients.[16] One study found the sensitivity and specificity of a PCT cut-off of 0.25 ng/mL in identifying bacterial respiratory coinfections to be poor at 0.71 and 0.53, respectively.[19] This yielded a positive predictive value of 0.015 and negative predictive value of 0.995. As such, some have concluded that PCT may lack utility for identifying patients with concurrent bacterial infection, but may be a tool to rule out bacterial coinfection and reduce unnecessary antimicrobial prescribing; however, this strategy is not supported by current community-acquired pneumonia guideline recommendations.[19,20] We noted that despite the median PCT value of 0.18, obtainment of PCT was significantly associated with receipt of respiratory antibiotics, which suggests either misapplication of the test or outright disbelief in the pneumonia threshold drawn from ICU literature. Our findings appear to illuminate an uncertainty regarding the utility of PCT given higher rates of PCT obtainment alongside longer durations of therapy in ICU patients. Clinical suspicion seems to supersede PCT values in antimicrobial decision-making. These factors should be further investigated.

Our study is not without limitations. First, inclusion of data from a single institution limits external validity of our findings. Our institution is based in a rural, primarily Caucasian setting and may not reflect the outcomes of more populous and diverse urban institutions, where the burden of COVID-19 may differ due to differences in demographic characteristics.[21] Second, we specifically set out to evaluate the rate of respiratory bacterial coinfection and did not evaluate the incidence of other bacterial coinfections and/or antimicrobial use related to other syndromes. This may have contributed to our rate of antimicrobial prescribing being lower than that observed in other publications that have accounted for other bacterial coinfections. Additionally, diagnosis with a bacterial respiratory tract infection required culture obtainment and not all patients included had respiratory tract cultures obtained, which may have led to underestimation of the true incidence of bacterial coinfection. Finally, our institution had the continuous presence of ID providers within an expert COVID-19 panel comprised of several disciplines including radiology, critical care and haematology. Such bandwidth may not be possible in other institutions, especially in areas of high disease prevalence. Hence, our results may not reflect the experience of institutions who struggled to provide a

Table 3. Univariate and multivariable analysis of factors potentially associated with empirical antimicrobial prescribing

	Univariate		Multivariable[a]	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age >60 years (Y versus N)	1.09 (0.77–1.53)	0.63		
Male sex (Y versus N)	1.11 (0.80–1.55)	0.54		
BMI >30 (Y versus N)	1.19 (0.86–1.66)	0.30		
Hypertension (Y versus N)	0.89 (0.64–1.23)	0.47		
Heart failure (Y versus N)	0.70 (0.43–1.14)	0.15	0.50 (0.28–0.90)	0.02
Congenital heart disease (Y versus N)	1.58 (0.54–4.61)	0.40		
Coronary artery disease (Y versus N)	0.61 (0.39–0.97)	0.037		
Chronic lung disease/asthma (Y versus N)	1.17 (0.80–1.69)	0.42		
Diabetes (Y versus N)	1.25 (0.89–1.76)	0.19		
Immunocompromising condition (Y versus N)	0.94 (0.57–1.56)	0.81		
Nursing home (Y versus N)	2.13 (1.19–3.83)	0.012	3.37 (1.68–6.79)	<0.01
Dialysis (Y versus N)	2.34 (1.05–5.22)	0.038	2.76 (1.15–6.63)	0.02
Chronic liver disease (Y versus N)	1.13 (0.59–2.16)	0.72		
Pregnancy (Y versus N)	0.69 (0.14–3.46)	0.65		
Charlson Comorbidity Index, median (IQR)	0.98 (0.95–1.02)	0.36		
PCT within 24 h of admittance (Y versus N)	3.46 (2.40–4.98)	<0.001	2.77 (1.84–4.16)	<0.01
ICU stay				
No ICU stay	Reference		Reference	
ICU stay—no intubation	3.53 (2.36–5.27)	<0.001	2.95 (1.92–4.55)	<0.01
ICU stay—intubated	8.48 (4.89–14.72)	<0.001	4.63 (2.37–9.02)	<0.01
Time between positive test and admission	1.01 (0.99–1.02)	0.57		
Transfer type				
Local admission (i.e. no transfer)	Reference			
ED transfer	1.19 (0.75–1.88)	0.46		
Direct admission	2.54 (1.75–3.68)	<0.001		
Radiographic changes (Y versus N)	7.49 (3.41–16.47)	<0.001	4.51 (1.96–10.40)	<0.01
Severity				
Mild	Reference			
Moderate	1.91 (1.18–3.09)	0.009		
Severe	5.97 (3.72–9.53)	<0.001		
Respiratory cultures collected (Y versus N)	5.06 (3.24–7.89)	<0.001	2.42 (1.39–4.20	<0.01
ID consulted (Y versus N)	1.38 (0.68–2.80)	0.37		

Y, yes; N, no.
[a]Variables included in the multivariable model were heart failure; nursing home residence; haemodialysis dependence; whether PCT values were collected within 24 h of admission; ICU stay/intubation; radiographic changes on chest imaging; and whether respiratory cultures were collected.

typical provider-to-patient ratio during periods of surge. These limitations considered; our study adds to the body of evidence suggesting low rates of bacterial respiratory coinfection in patients with COVID-19 and confirms the key role of multidisciplinary care with ID involvement in antimicrobial stewardship. It also confirms key targets for ASP initiatives to steward antimicrobials in this population (i.e. increasing disease severity and receipt of mechanical ventilation).[3,7,9]

Despite low rates of respiratory bacterial coinfection in patients with COVID-19, antimicrobials are commonly prescribed. The potentially unnecessary use of antibacterial therapy in these patients may be more common in patients on haemodialysis, admitted from nursing homes and/or with greater disease severity. Ongoing vigilance regarding the stewardship of antimicrobials remains of upmost importance in this patient population. The application of longstanding antimicrobial stewardship tactics, such as prospective audit with intervention and feedback, educational strategies and multidisciplinary team involvement, are likely to have an ongoing role in addressing antimicrobial overuse in COVID-19. Institutional ASPs should take an active role in intervening on unnecessary antimicrobial use in these patients by specifically understanding their local prescribing patterns, trending these patterns over time and identifying patient populations most likely to derive benefit from programmatic interventions.

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Transparency declarations

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Author contributions

R.W.S. contributed to study design, data collection, data analysis and manuscript writing. K.J. contributed to study design, data collection, data analysis and manuscript revisions. K.K. contributed to study design, data collection, data analysis and manuscript revisions. K.M contributed to study design, data collection and data analysis. J.C.O. contributed to study design, data obtainment and manuscript revisions. A.S. contributed to study design, data collection, data analysis and manuscript revision.

Supplementary data

Table S1 is available as Supplementary data at *JAC-AMR* Online

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