



## RESEARCH ARTICLE

# Bacterial infections and patterns of antibiotic use in patients with COVID-19

Alvaro Goncalves Mendes Neto MD<sup>1</sup>  | Kevin Bryan Lo MD<sup>1</sup> | Ammaar Wattoo MD<sup>1</sup> | Grace Salacup MD<sup>1</sup>  | Jerald Pelayo MD<sup>1</sup> | Robert DeJoy III DO<sup>1</sup> | Ruchika Bhargav DO<sup>1</sup> | Fahad Gul MD<sup>1</sup> | Eric Peterson DO<sup>1</sup> | Jeri Albano MD<sup>1</sup> | Gabriel Patarroyo-Aponte MD<sup>1,2,3</sup> | Janani Rangaswami MD<sup>1,2</sup> | Zurab Azmaiparashvili MD, MSc<sup>1</sup>

<sup>1</sup>Department of Medicine, Albert Einstein Medical Center Philadelphia, Philadelphia, Pennsylvania

<sup>2</sup>Sidney Kimmel College of Thomas Jefferson University, Philadelphia, Pennsylvania

<sup>3</sup>Division of Pulmonary and Critical Care and Sleep Medicine, Albert Einstein Medical Center Philadelphia, Philadelphia, Pennsylvania

## Correspondence

Alvaro Goncalves Mendes Neto, MD, Albert Einstein Medical Center, 5501 Old York Road Philadelphia, PA 19141.

Email: [GoncalvA@einstein.edu](mailto:GoncalvA@einstein.edu)

## Abstract

Bacterial coinfection is associated with poor outcomes in patients with viral pneumonia, but data on its role in the mortality of patients with coronavirus disease 2019 (COVID-19) is limited. This is a single-center retrospective analysis of 242 patients with confirmed COVID-19 admitted to both intensive care and non-intensive care settings. Bacterial coinfection was determined by the presence of characteristic clinical features and positive culture results. Multivariable logistic regression was used to analyze the association of concomitant bacterial infection with inpatient death after adjusting for demographic factors and comorbidities. Antibiotic use pattern was also determined. Bacterial coinfection was detected in 46 (19%) patients. Genitourinary source was the most frequent, representing 57% of all coinfections. The overall mortality rate was 21%. Concomitant bacterial infections were independently associated with increased inpatient mortality (OR, 5.838; 95% CI, 2.647-12.876). Patients with bacterial coinfection were relatively older ( $71.35 \pm 11.20$  vs  $64.78 \pm 15.23$ ;  $P = .006$ ). A total of 67% of patients received antibiotic therapy, yet 72% did not have an obvious source of bacterial infection. There was a significantly higher rate of inpatient mortality in patients who received antibiotics compared to those who did not (30% vs 5%;  $P < .0001$ ). Bacterial coinfection in COVID-19 is associated with increased mortality.

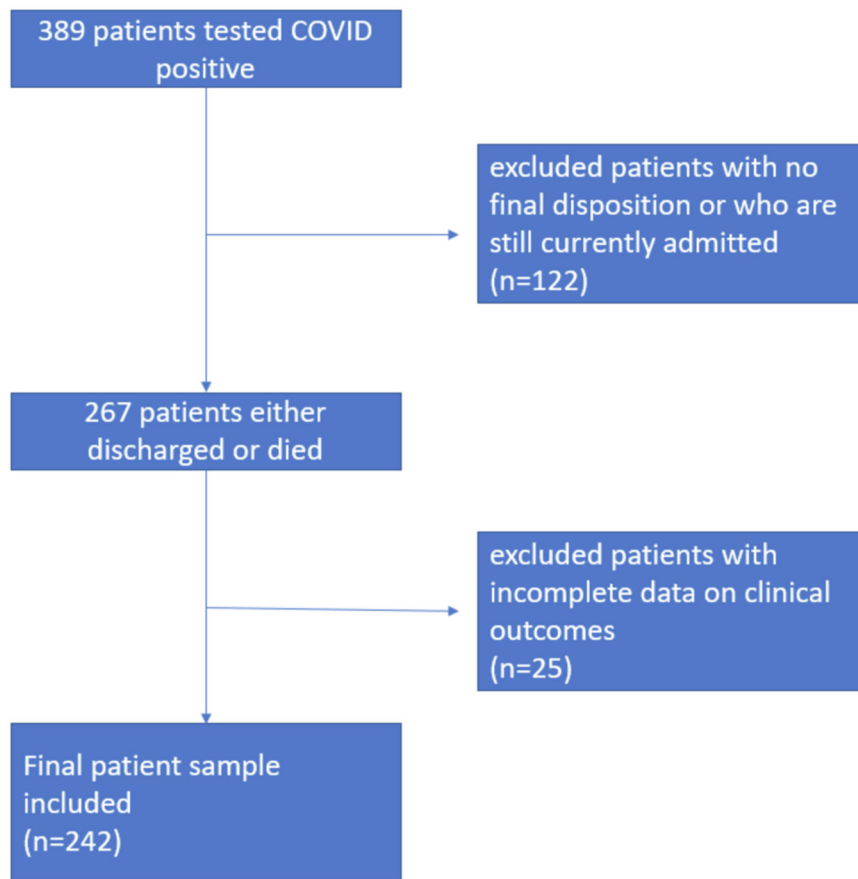
## KEYWORDS

antibiotic use, coinfections, inflammation, pandemics, SARS-CoV-2

## 1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a newly emerged viral pathogen causing pneumonia that can progress to hypoxic respiratory failure, adult respiratory distress syndrome (ARDS), and multiorgan failure.<sup>1</sup> These may include acute kidney injury, myocarditis, and thromboembolic disease among others.<sup>2-4</sup> At present, the effect of Coronavirus disease 2019 (COVID-19) on susceptibility to

bacterial infections, however, is still unclear. Other viral pathogens, such as influenza virus and rhinovirus, have been shown to predispose patients to bacterial infections and resultant increased mortality.<sup>5</sup> Mechanisms for coinfection, while not completely understood, center on impaired function and integrity of the respiratory epithelium.<sup>6</sup> Bacteremia, when reported, is presumed to be secondary to respiratory infection.<sup>7</sup> An association with increased non-respiratory infections has not been shown with previously known viral pathogens.

**FIGURE 1** Patient selection

This study aims to determine the incidence of bacterial coinfection in hospitalized patients with COVID-19. Furthermore, we aim to evaluate the association of bacterial coinfection and empiric antibiotic therapy with the clinical outcomes of patients admitted with COVID-19.

## 2 | PATIENTS AND METHODS

### 2.1 | Study design, participants, and data collection

This study is a single-center retrospective analysis of all patients >18 years old admitted between 3/1/2020 and 4/24/2020 with a confirmed diagnosis of COVID-19 via reverse transcriptase-polymerase chain reaction assay (RT-PCR) performed on nasopharyngeal swab specimens. We included patients in both the intensive care unit (ICU) and non-ICU settings. The patients were identified using a registry of all COVID-19 patients admitted to our hospital. We excluded patients who were still admitted at the time of analysis. Demographic and clinical factors, including age, gender, race, and comorbidities, were extracted from electronic medical records with a standardized data collection form. Bacterial coinfection was determined by the presence of characteristic clinical features and positive blood, sputum, urine, or tissue culture results. Patterns of antibiotic use were also tabulated. Informed consent was waived since this was a retrospective study. IRB approval was obtained. IRB number: 2020-436.

### 2.2 | Statistical analysis

Demographic variables were summarized using percentages for categorical variables and means for continuous variables. Categorical variables were compared using  $\chi^2$  testing. Continuous variables were compared using *t* tests. For skewed data, the Mann-Whitney *U* test was used to identify any significant difference. A *P* < .05 was considered statistically significant. Multivariable logistic regression was used to analyze the association of concomitant bacterial infection with inpatient mortality after adjusting for demographic factors and comorbidities. The 95% confidence intervals and odds ratios were provided as appropriate. All analyses were performed using the IBM SPSS Statistics for Windows, version 23.0.

## 3 | RESULTS

### 3.1 | Demographic and comorbidities

A total of 389 patients were evaluated and tested positive via RT-PCR for COVID-19. A total of 122 patients were excluded as they were still admitted at the time of analysis. The 25 patients with incomplete clinical data were excluded, leaving a final sample of 242 patients (see Figure 1). In the final sample of 242 patients, the mean age  $\pm$  SD was  $66 \pm 14.75$ . Almost half of the patients were female (119), and 70% (170) were African American. Prevalent chronic medical conditions included

hypertension (74%;  $n = 179$ ), diabetes mellitus (49%;  $n = 119$ ), and chronic obstructive pulmonary disease (COPD) or asthma (19%;  $n = 46$ ) (see Table 1).

### 3.2 | Patient mortality and bacterial coinfection

The overall mortality in our sample was 21.5% ( $n = 52$ ), while the rate of concomitant bacterial infection was 19% ( $n = 46$ ). Patients with coinfection were relatively older compared to those without. Genitourinary infections were the most common (57%), followed by skin infections (10%), and respiratory infections (8%) (see Figure 2). The most common organism was *E. coli* (26%). More than a quarter of patients with concomitant bacterial infection had documented bacteremia. The rates of steroid use were also significantly higher among patients with bacterial co-infections vs those without (37% vs 19%;  $P = .018$ ) (see Table 1). There was a significantly higher rate of inpatient mortality (50% vs 15%;  $P < .0001$ ) and a need for mechanical

ventilation (44% vs 17%;  $P < .0001$ ) among patients with concomitant bacterial infection compared to those without (see Figure 3). Even after adjusting for demographic factors and comorbidities, concomitant bacterial infections were still independently significantly associated with increased inpatient mortality (OR, 5.838; 95% CI, 2.647-12.876;  $P < .0001$ ) (see Table 2). Looking at the subgroup of urinary tract infections only, there was still a significantly higher rate of inpatient mortality (50% vs 18%;  $P < .0001$ ). Even after adjustment for demographic factors and comorbidities by multivariable regression, urinary tract infections were still independently associated with inpatient death (OR, 4.224; 95% CI, 1.692-10.540;  $P < .002$ ).

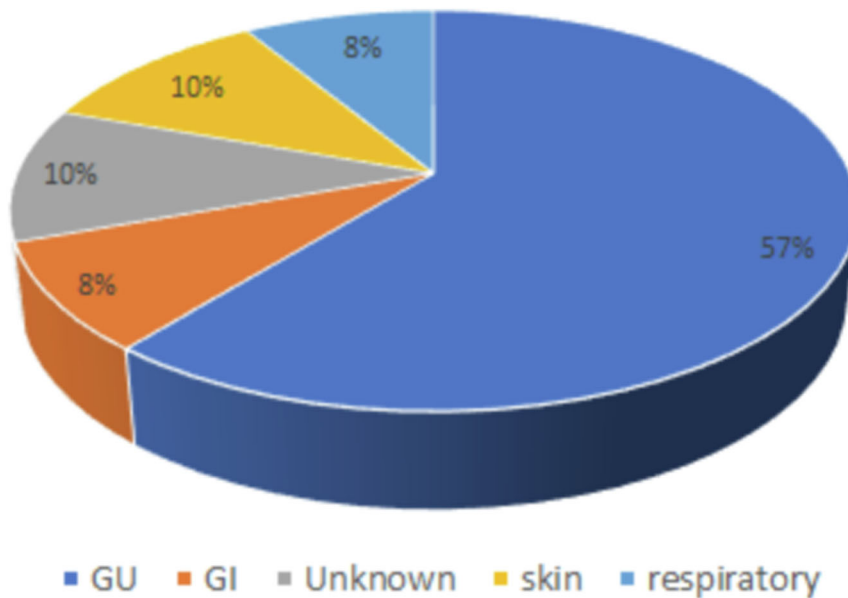
### 3.3 | Patterns of antibiotic use

In terms of antibiotic prescribing patterns, 67% ( $n = 162$ ) of all patients received antibiotics. The 72% of these patients did not have an obvious source of bacterial infection. The most common antibiotics

**TABLE 1** Clinical characteristics of the patients at baseline

Characteristics	Bacterial co-infection ( $n = 46$ (%))	None $n = 196$ (%)	P value
Age median (mean $\pm$ SD)	71.35 $\pm$ 11.20	64.78 $\pm$ 15.23	.006
Female gender $n$ (%)	23 (50)	96 (49)	1.000
Ethnicity $n$ (%)			
African American	27 (58)	144 (74)	
Caucasian	3 (8)	14 (7)	.184
Hispanic	6 (13)	20 (10)	
Other	10 (23)	18 (9)	
Comorbidities			
BMI (mean $\pm$ SD)	27.36 $\pm$ 9.11	29.86 $\pm$ 9.20	.105
COPD	6 (13)	24 (12)	.809
Asthma	0 (0)	18 (9)	.028
Heart Failure	7 (15)	28 (14)	.819
Atrial fibrillation	8 (17)	16 (8)	.095
Liver cirrhosis	3 (6)	5 (3)	.179
Diabetes	24 (52)	94 (48)	.627
Chronic kidney disease	10 (22)	32 (16)	.391
End stage renal disease on dialysis	2 (4)	17 (9)	.542
Coronary artery disease	10 (22)	35 (18)	.532
Hypertension	36 (78)	144 (74)	.577
Obesity	17 (37)	80 (41)	.739
COVID-19 treatment			
Hydroxychloroquine	27 (59)	118 (60)	.868
Steroids	17 (37)	38 (19)	.018
Tocilizumab	5 (11)	16 (8)	.563
Clinical outcomes			
Inpatient death	23 (46)	29 (15)	<.0001
Need for CRRT/HD	7 (15)	17 (9)	.180
Need for vasopressors	20 (43)	29 (15)	<.0001
Need for intubation	20 (43)	34 (17)	<.0001

FIGURE 2 Bacterial infections



used were cefepime (45%), ceftriaxone (54%), vancomycin (48%), and azithromycin (47%). There was a significantly higher rate of inpatient mortality in patients who received antibiotics compared to those who did not (30% vs 5%;  $P < .0001$ ). A subgroup analysis looking at patients who received antibiotic therapy showed that all inflammatory markers were statistically significantly elevated except for ferritin compared to patients who did not receive antibiotics (see Table 3).

#### 4 | DISCUSSION

This retrospective single-center study determined that bacterial coinfection in patients with COVID-19 is common and is associated with an increased risk of inpatient mortality. At present, there is limited data regarding bacterial coinfection in COVID-19 in the United States. Only one case series in Washington reported a 4.8% bacterial coinfection

rate.<sup>8</sup> This is comparatively lower to the coinfection rate in our population (19%). Most of the reported case series and cohort studies from China and Spain showed similarly lower coinfection rates.<sup>9-17</sup> In a meta-analysis of hospitalized ICU and non-ICU COVID-19 patients, only 7% had bacterial coinfection.<sup>18</sup> Higher rates of coinfection in our study population is explained by a relatively sicker patient population with higher rates of hypertension and diabetes mellitus, as well as higher body mass index (BMI) compared to the aforementioned COVID-19 studies. There are proposed theories that patients with cardiometabolic comorbidities tend to have higher rates of bacterial coinfection in viral infection due to an underlying dysregulated immune response. Diabetes mellitus itself is known to downregulate effective T-cell and neutrophil response.<sup>19</sup> It causes decreased innate immune response via ineffective chemotaxis, phagocytosis, and bactericidal activity of neutrophils and macrophages leading to susceptibility to secondary bacterial infection.<sup>20</sup> In addition, these cardiometabolic comorbidities, especially if uncontrolled, have

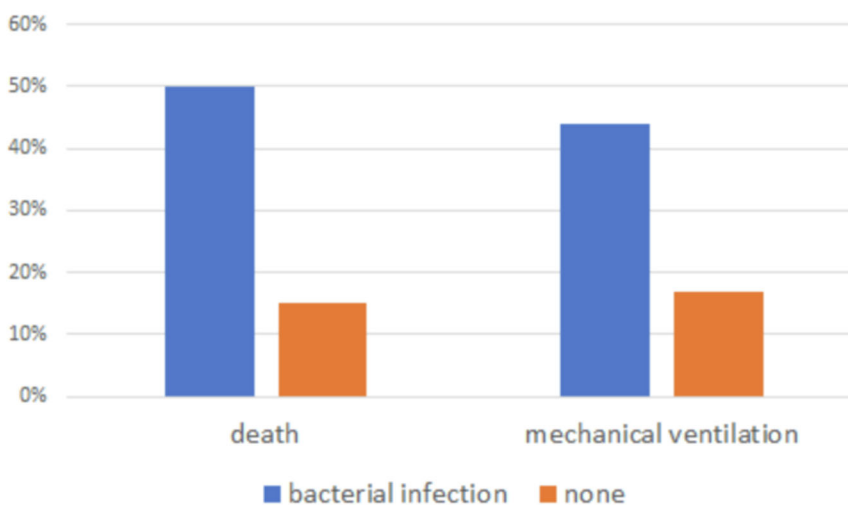


FIGURE 3 Mortality and mechanical ventilation

**TABLE 2** Multivariable logistic regression on factors associated with inpatient mortality

Characteristics	Odds ratio (95% CI)	P value
Age	1.048 (1.015-1.082)	.005
Male	(referent)	
Female	0.795 (0.373-1.697)	.553
BMI	1.015 (0.969-1.062)	.537
African American	(referent)	
Caucasian	2.130 (0.391-11.608)	.382
Hispanic	0.515 (0.120-2.211)	.372
Others	1.654 (0.570-4.802)	.355
Diabetes	1.560 (0.699-3.481)	.277
CKD	0.713 (0.267-1.902)	.499
Hypertension	0.932 (0.348-2.494)	.888
COPD	0.823 (0.275-2.466)	.728
CAD	1.281 (0.470-3.494)	.629
HF	2.233 (0.796-6.266)	.127
HIV	0.723 (0.056-9.403)	.804
Bacterial infection	5.838 (2.647-12.876)	<.0001

chronically increased pro-inflammatory cytokines such as interleukin-1 (IL-1), IL-6, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and c-reactive protein (CRP).<sup>21-25</sup> With the link of higher angiotensin-converting enzyme-2 (ACE-2) receptors compared to the general population, these patients may have higher viral intracellular inoculation resulting in more cellular pyroptosis.<sup>28-28</sup> Combination of chronic pro-inflammatory state and higher cellular pyroptosis by COVID-19 predispose these patients with cardiometabolic comorbidities to an amplified cytokine storm.<sup>29</sup> Such unregulated pro-inflammatory response promotes immune dysregulation, tissue damage, and pre-disposition to bacterial coinfection.<sup>30,31</sup>

To our knowledge, no other studies have specifically reported concurrent urinary tract infection (UTI) among COVID-19 patients. This is the first report showing UTI affecting more than half (57%) of our COVID-19 population. Previously reported organisms were generally respiratory pathogens such as *Mycoplasma pneumoniae*, *Pseudomonas aeruginosa*, and *Haemophilus influenzae*.<sup>18</sup> However, our

**TABLE 3** Differences in inflammatory markers in patients treated with antibiotics vs without

	With antibiotics median (IQR)	Without antibiotics median (IQR)	P value
Ferritin	925 (380-2181)	687 (215-1542)	.108
D-dimer	2110 (1095-3405)	1195 (705-2802)	.006
Procalcitonin	0.25 (0.1-1.12)	0.11 (0.06-0.33)	.003
CRP	144 (65-236)	47 (24-131)	.002
LDH	466 (317-609)	333 (241-435)	.001

study identified *Escherichia coli* and *Enterobacter cloacae* as the most commonly isolated pathogens, consistent with the UTI. These can be attributed to a spectrum of diseases, ranging from asymptomatic bacteriuria and lower UTI to acute pyelonephritis. Because of the possibility of asymptomatic bacteriuria among our patients with documented urinary infections we did a subgroup analysis looking at just urinary infections to make sure that the effects were not driven by co-infections from other sources. Even after subgroup analysis and inclusion in the multivariable model, the associations with mortality have remained the same. This connotes that even microbial colonization may be a sign of a dysregulated immune response in patients with COVID-19. Studies have shown that susceptibility to such infections can be an indicator of defective innate mucosal immune system with resultant failure to distinguish and mount a response to commensal pathogens.<sup>32</sup> Another possible explanation is the high prevalence of diabetes mellitus in our study, which make the studied population susceptible to UTI.<sup>33</sup>

Mortality was observed in 50% of our COVID-19 patients with concomitant bacterial infection (OR, 5.838;  $P < .0001$ ). In a previously reported meta-analysis, COVID-19 patients with bacterial coinfection were more likely to die with pooled OR of 5.82.<sup>18</sup> Wang et al<sup>12</sup> also reported bacterial infection to be a predictor of increased mortality in older patients. The presence of coinfection may not be causative of worse clinical outcomes but rather signify clinical deterioration. As cytokine storm promotes dysregulated innate immune responses, vulnerable patients are predisposed to bacterial coinfection. More so, our study showed that patients who had bacterial coinfection were significantly older. The elderly population is known to have increased pro-inflammatory cytokines and decreased anti-inflammatory cytokines. Age-related pathophysiologic processes include alteration of ACE-2 receptor expression, excess reactive oxygen species (ROS) production, and alteration of autophagy.<sup>34</sup>

Our study also showed that patients with bacterial co-infection had significantly higher rates of steroid use. Theoretically, glucocorticoids are anti-inflammatory agents that help prevent the progression of cytokine storm and subsequent dysregulation of the immune system. Though there are mixed data regarding the benefits of corticosteroids in COVID-19,<sup>35</sup> the RECOVERY trial showed promising benefits in severe COVID-19, and among those recruited after the first week of their illness.<sup>36</sup> Our results differ likely due to selection bias in that patients who developed bacterial coinfection as a result of immune dysregulation were likely sicker and received higher corticosteroid doses due to a more severe COVID-19 disease process. This is manifested by the higher rates of need for vasopressors, mechanical ventilation, and renal replacement therapy (RRT) in this patient group.

More than half of the patients received antibiotics in this study. The 72% of these did not have laboratory evidence of bacterial infection, findings similar to the study of Rawson et al.<sup>37</sup> This can be attributed to the presentation of severe COVID-19 as a systemic inflammatory response syndrome (SIRS) and therefore, empiric broad-spectrum coverage might have been warranted. Additionally, this study observed that patients placed on antibiotics had poorer outcomes and higher inflammatory markers. This can be due to

selection bias, given that sicker patients are more likely to be started on empiric antibiotic coverage. Given the high rates of use of empiric antibiotics with no evidence of bacterial infections, proper antibiotic stewardship in the setting of COVID-19 remains a challenge.

## 5 | LIMITATIONS

This is a single-center retrospective study with a predominantly African American population, which may limit generalizability. Clinical characteristics defining bacterial coinfection were varied and dependent on the patient's presentation (ie, fever, hypothermia, increased sputum production), which could also be attributed to COVID-19 infection. Patients in ICU were sedated and intubated; thus, historical data on signs and symptoms may have been limited in helping to determine bacterial co-infection in this population subgroup. The rates of a urinary source of bacterial infection may be overestimated as asymptomatic bacteriuria may be hard to distinguish from UTI, especially in patients who are unable to provide history and/or manifest systemic responses that may be masked by the concomitant COVID-19 infection. Also, UTIs were not further stratified as community-acquired or nosocomial.

Findings on antibiotic use should be interpreted with caution as there may be a form of selection bias. Association between antibiotic usage and increased mortality may be reflective of a sicker patient population and may not be indicative of causative effect.

## 6 | CONCLUSION

Concomitant bacterial infections in patients with COVID-19 are relatively common and are significantly associated with higher inpatient mortality.

### CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

### ORCID

Alvaro Goncalves Mendes Neto  <https://orcid.org/0000-0003-1280-624X>

Grace Salacup  <http://orcid.org/0000-0002-0003-2040>

### REFERENCES

- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323(13):1239-1242.
- Hirsch JS, Ng JH, Ross DW, et al. Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int*. 2020;98:209-218.
- Siripanthong B, Nazarian S, Muser D, et al. Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management [published online ahead of print, 2020 May 5]. *Heart Rhythm*. 2020. <https://doi.org/10.1016/j.hrthm.2020.05.001>
- Abou-Ismaïl MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. *Thromb Res*. 2020;194:101-115.
- Morris DE, Cleary DW, Clarke SC. Secondary bacterial infections associated with influenza pandemics. *Front Microbiol*. 2017;8:1041.
- Prasso JE, Deng JC. Postviral complications: bacterial pneumonia. *Clin Chest Med*. 2017;38(1):127-138.
- Cawcutt K, Kalil AC. Pneumonia with bacterial and viral coinfection. *Curr Opin Crit Care*. 2017;23(5):385-390.
- Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA*. 2020;323(16):1612-1614.
- Zhao D, Yao F, Wang L, et al. A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias. *Clin Infect Dis*. 2020;71:756-761.
- Zhang JJ, Dong X, Cao YY, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. *Allergy*. 2020;75(7):1730-1741. <https://doi.org/10.1111/all.14238>
- Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study [published online ahead of print, 2020 April 8]. *Lancet Respirat Med*. 2020;8(5):475-481.
- Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical Features of 69 Cases With Coronavirus Disease 2019 in Wuhan, China. *Clin Infect Dis*. 2020;71(15):769-777. <http://doi.org/10.1093/cid/ciaa272>
- Mo P, Xing Y, Xiao Y, et al. Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China [published online ahead of print, 2020 Mar 16]. *Clin Infect Dis*. 2020. <http://doi.org/10.1093/cid/ciaa270>
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020;395(10223):497-506.
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395(10223):507-513.
- Feng Y, Ling Y, Bai T, et al. COVID-19 with different severities: a multicenter study of clinical features. *Am J Respir Crit Care Med*. 2020;201(11):1380-1388.
- Barrasa H, Rello J, Tejada S, et al. SARS-CoV-2 in Spanish intensive care: early experience with 15-day survival in Vitoria [published online ahead of print, 2020 Apr 9]. *Anaesthesia Crit Care Pain Med*. 2020. <http://doi.org/10.1016/j.accpm.2020.04.001>
- Lansbury L, Lim B, Baskaran V, Lim WS. Co-infections in people with COVID-19: a systematic review and meta-analysis. *J Infect*. 2020;81:266-275.
- Casqueiro J, Casqueiro J, Alves C. Infections in patients with diabetes mellitus: a review of pathogenesis. *Indian J Endocrinol Metab*. 2012;16(suppl 1):S27-S36.
- Dooley KE, Chaisson RE. Tuberculosis and diabetes mellitus: convergence of two epidemics. *Lancet Infect Dis*. 2009;9(12):737-746.
- Chamarthi B, Williams GH, Ricchiuti V, et al. Inflammation and hypertension: the interplay of interleukin-6, dietary sodium, and the renin-angiotensin system in humans. *Am J Hypertens*. 2011;24(10):1143-1148.
- Phosat C, Panprathip P, Chumpathat N, et al. Elevated C-reactive protein, interleukin 6, tumor necrosis factor alpha and glycemic load associated with type 2 diabetes mellitus in rural Thais: a cross-sectional study. *BMC Endocr Disord*. 2017;17(1):44.



23. Colwell JA. Inflammation and diabetic vascular complications. *Diabetes Care*. 1999;22(12):1927-1928.
24. Fatkhullina AR, Peshkova IO, Koltsova EK. The role of cytokines in the development of atherosclerosis. *Biochemistry*. 2016;81(11):1358-1370.
25. Dharmashankar K, Widlansky ME. Vascular endothelial function and hypertension: insights and directions. *Curr Hypertens Rep*. 2010;12(6):448-455.
26. Verdecchia P, Cavallini C, Spanevello A, Angeli F. The pivotal link between ACE2 deficiency and SARS-CoV-2 infection. *Eur J Intern Med*. 2020;76:14-20.
27. Iannelli A, Favre G, Frey S, et al. Obesity and COVID-19: ACE 2, the missing tile. *Obes Surg*. 2020:1-3.
28. deLucena TM, da Silva Santos AF, de Lima Fabrício BR, de Albuquerque Borborema ME, de Azevêdo Silva J. Mechanism of inflammatory response in associated comorbidities in COVID-19. *Diabetes Metab Syndrome: Clin Res Rev*. 2020;14:597-600.
29. Tay MZ, Poh CM, Rénia L, MacAry PA, Ng LF. The trinity of COVID-19: immunity, inflammation and intervention. *Nat Rev Immunol*. 2020;20:1-2.
30. De Jong MD, Simmons CP, Thanh TT, et al. Fatal outcome of human influenza A (H5N1) is associated with high viral load and hypercytokinemia. *Nature Med*. 2006;12(10):1203-1207.
31. Picchianti Diamanti A, Rosado MM, Pioli C, Sesti G, Laganà B. Cytokine release syndrome in COVID-19 patients, a new scenario for an old concern: the fragile balance between infections and autoimmunity. *Int J Mol Sci*. 2020;21(9):3330.
32. Ambite I, Nagy K, Godaly G, Puthia M, Wullt B, Svanborg C. Susceptibility to urinary tract infection: benefits and hazards of the antibacterial host response. *Urinary Tract Infect Mol Pathogen Clin Manag*. 2017:523-554.
33. Hamdan HZ, Kubbara E, Adam AM, Hassan OS, Suliman SO, Adam I. Urinary tract infections and antimicrobial sensitivity among diabetic patients at Khartoum, Sudan. *Ann Clin Microbiol Antimicrob*. 2015;14(1):26.
34. Meftahi GH, Jangravi Z, Sahraei H, Bahari Z. The possible pathophysiology mechanism of cytokine storm in elderly adults with COVID-19 infection: the contribution of "inflamm-aging". *Inflamm Res*. 2020;69:1-5.
35. Veronese N, Demurtas J, Yang L, et al. Use of corticosteroids in coronavirus disease 2019 pneumonia: a systematic review of the literature. *Front Med*. 2020;7:170.
36. Horby P, Lim WS, Emberson J, et al. Effect of dexamethasone in hospitalized patients with COVID-19: preliminary report [published online ahead of print, 2020 Jul 17]. *MedRxiv*. 2020. <https://doi.org/10.1056/NEJMoa2021436>
37. Rawson TM, Moore LS, Zhu N, et al. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing [published online ahead of print, 2020 May 2]. *Clin Infect Dis*. 2020. <https://doi.org/10.1093/cid/ciaa530>

**How to cite this article:** Goncalves Mendes Neto A, Lo KB, Wattoo A, et al. Bacterial infections and patterns of antibiotic use in patients with COVID-19. *J Med Virol*. 2021; 93:1489-1495. <https://doi.org/10.1002/jmv.26441>