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ORIGINAL ARTICLE

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Empirical antibiotic therapy in COVID-19 ICU pulmonary coinfections

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ABSTRACT

Introduction: The rapid emergence and global spread of COVID-19 have underscored the critical need for understanding patient characteristics, clinical outcomes, and the microbiological landscape within intensive care settings. The study aims to identify the most common microbes causing pulmonary coinfections in COVID-19 ICU patients and to determine the optimal empirical antimicrobial treatment for this patient population.

Material and methods: In the following single-center retrospective cohort study, we collected medical data on 201 patients admitted to the ICU due to COVID-19. Further, we identified the primary causative pathogens of pulmonary coinfection. The study outcomes were death or ICU discharge.

Results: The study analyzed 201 COVID-19 patients in the ICU, revealing a balanced distribution between those with (52%) and without (48%) pulmonary infections. In our cohort, the mean BMI was 33.0. The subgroup with pulmonary coinfections did not show statistically significant differences in the prevalence of diabetes and hypertension compared to those without such coinfections. Patients with pulmonary infections exhibited more severe respiratory compromise, necessitating increased mechanical ventilation and extended ICU stays. Pathogen isolation highlighted *Staphylococcus aureus*, *Enterobacter cloacae*, and *Enterococcus faecalis* as predominant, with a notable shift towards resistant strains like *Klebsiella pneumoniae* ESBL and *Acinetobacter baumannii* MDR post-48 hours of admission. Antibiotic susceptibility testing underscored the effectiveness of specific agents against MSSA, while revealing variable resistance patterns among *Enterobacter cloacae* and *Enterococcus faecalis*, particularly against Daptomycin and Levofloxacin. The most commonly used antibiotics were ceftriaxone and levofloxacin.

Conclusions: The number of used antibiotics, including broad-spectrum, increased the occurrence of multi-drug resistant bacteria.

Keywords: COVID-19, ICU, antimicrobial use; COVID-19; hospital-acquired infections, superinfection

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Introduction

The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has posed unprecedented challenges to global healthcare systems, particularly in managing critically ill patients requiring intensive care unit (ICU) admission.

Bacterial coinfections in the respiratory tract, while not uncommon in viral pneumonias, pose a particular challenge in COVID-19 due to the overlapping clinical features and the heightened inflammatory response associated with the virus. The prevalence of these coinfections and their impact on patient outcomes necessitates a careful approach to diagnosis and treatment, especially in the high-stakes environment of the ICU.

Managing bacterial coinfections in COVID-19 patients, particularly those in critical care, often involves using empirical antibiotic therapy. While this approach is necessary in the face of diagnostic uncertainty, it risks contributing to antibiotic resistance, primarily when broad-spectrum agents are employed without specific bacterial identification and susceptibility data.

According to the study, 14% of patients hospitalized in the ICU for COVID-19 have bacterial coinfection [1]. Considering the severe condition of patients admitted to ICU in their previous hospitalizations, we are often forced to administer broad-spectrum antibiotics, which may increase antimicrobial resistance.

Despite the widespread adoption of empirical antibiotic protocols in ICUs worldwide, there remains a significant gap in the literature regarding optimizing antibiotic use for COVID-19-associated bacterial pulmonary coinfections. The study aims to delineate the prevalent microbial agents responsible for pulmonary coinfections in COVID-19 patients admitted to the ICU. Furthermore, we seek to evaluate the efficacy of current empirical antimicrobial treatments to optimize therapeutic strategies for this vulnerable patient cohort.

Materials and methods

Study design and population

This retrospective cohort study was carried out at a single center, adhering to the guidelines outlined in the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. The study encompassed 235 adults diagnosed with COVID-19 who were treated in the ICU of the University Clinical Hospital in Bialystok, Poland, from March 3, 2020, to July 1, 2021. The following criteria determined eligibility for participation: being over 18 years of age, having a confirmed acute COVID-19 infection through reverse transcription polymerase chain reaction (RT-PCR) testing of nasal and pharyngeal swabs or secretions from the lower respiratory tract, and requiring ICU admission due to SARS-CoV-2 infection. Exclusions were made for pregnant individuals and those admitted to the ICU for non-COVID-19 reasons, such as elective surgeries or other emergencies. Ultimately, 201 participants were deemed eligible, with 97 (48%) of these developing pulmonary coinfections. A flowchart detailing participant selection is depicted in Figure 1. Pulmonary coinfection positivity requires the collection of positive microbiological samples from the respiratory system. The diagnosis of pulmonary coinfections necessitated fever or other laboratory evidence of infection, with a positive microbiological sample identified more than 48 hours post-admission considered nosocomial.

The initiation of antibiotic therapy was guided by clinical evaluation, factoring in signs of infection such as fever and the results of microbiological tests.

A comprehensive description of VAP (ventilator-associated pneumonia) and BSI (bloodstream infection) in this population is included in these studies [2, 3].

Statistical analysis

SARS-CoV-2 patients' data were entered into a predefined institutional database. We summarized continuous data as either mean ± standard deviations (SDs). Frequencies and percentages were used to detail categorical variables. The Shapiro-Wilk test was employed to assess the normality of data distribution. For continuous variables, t-tests or Mann-Whitney tests

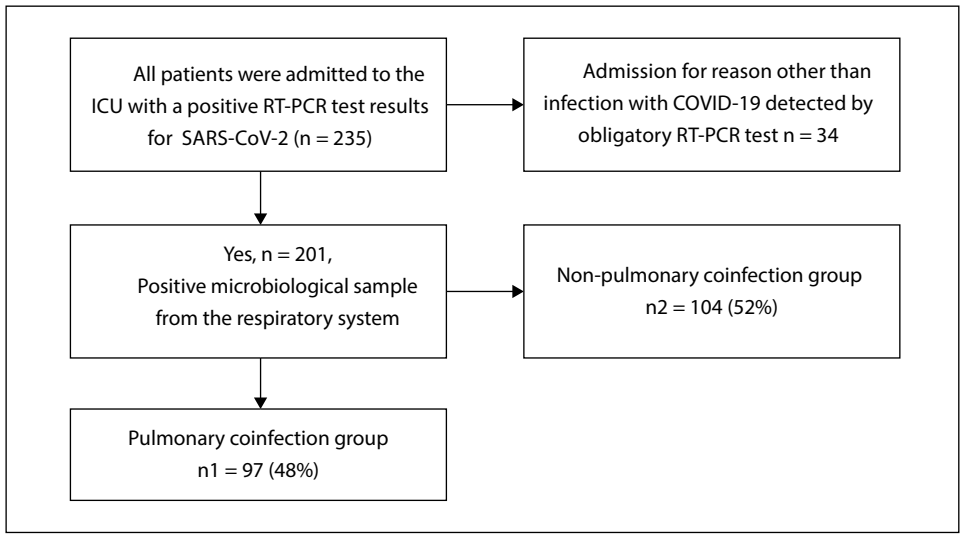

Figure 1. Flowchart of patient screening and inclusion. ICU — intensive care unit; SARS-CoV-2 — severe acute respiratory syndrome coronavirus 2; COVID-19 — coronavirus disease 2019; RT-PCR — reverse transcription-polymerase chain reaction

Table 1. Characteristics of patients with COVID-19 at ICU admission, risk factors for developing pulmonary infection, disease course, treatment, and outcomes

Headcount	Non-pulmonary infection n1 = 97 (48%)	Pulmonary infection n2 = 104 (52%)	All n = 201	*p*-value
Baseline and demographic				
BMI (± SD)	32.0 (7.5)	33.9 (22.6)	33.0 (17.0)	0.432
Female — no. (%)	50 (51.5)	37 (35.6)	87 (43.3)	0.024
Age (± SD) [years]	67.5 (11.9)	64.8 (12.1)	66.1 (12.1)	0.107
Diabetes mellitus	26 (26.8)	34 (32.7)	60 (29.9)	0.441
Atrial fibrillation	12 (12.4)	16 (15.4)	28 (13.9)	0.550
Hypertension	58 (59.8)	63 (61.2)	121 (60.5)	0.885
Obesity	18 (18.6)	25 (24.5)	43 (21.6)	0.389
Chronic heart failure	23 (23.7)	23 (22.3)	46 (23.0)	0.867
On arrival in the ICU				
APACHE II (± SD)	29.6 (9.0)	28.5 (7.0)	29.1 (8.0)	0.352
PaO2/FiO2 (± SD) [mmHg]	143.0 (92.5)	111.9 (54.6)	126.9 (76.7)	0.004
Acute kidney failure — no. (%)	35 (36.1)	34 (32.7)	69 (34.3)	0.657
CRP (± SD) [mg/L]	82.7 (91.1)	84.8 (89.8)	83.7 (90.2)	0.869
D-dimer (± SD)	4.7 (5.1)	3.2 (3.6)	3.9 (4.4)	0.082
INR (± SD)	1.4 (0.3)	1.3 (0.3)	1.4 (0.3)	0.063
Interleukin 6 (± SD) [pg/mL]	371.8 (795.6)	513.8 (936.2)	451.4 (876.9)	0.358
Absolute neutrophils ($\times 10^3/\mu$L)	10.4 (7.3)	10.6 (6.6)	10.5 (6.9)	0.897
Procalcitonin (± SD) [ng/mL]	3.5 (11.4)	1.2 (3.9)	2.3 (8.4)	0.054
White blood cells ($\times 10^3/\mu$L) (± SD)	13.2 (9.1)	12.5 (9.9)	12.9 (9.5)	0.586
FIO2 mean (SD)	0.8 (0.2)	0.8 (0.2)	0.8 (0.2)	0.116
During hospitalization				
Length of stay at ICU (± SD) [days]	8.6 (6.6)	16.8 (11.3)	12.8 (10.1)	< 0.001
Mechanical ventilation — no. (%)	81 (83.5)	102 (98.1)	183 (91.0)	< 0.001
Mechanical ventilation duration (± SD) [days]	7.2 (6.7)	14.8 (9.3)	11.2 (9.0)	< 0.001
Infusion of NMBAs at least 1 day (%)	49 (50.5)	86 (82.7)	135 (67.2)	< 0.001
Corticosteroids — no. (%)	82 (84.5)	95 (91.3)	177 (88.1)	0.191
Prone Position — no. (%)	33 (34.0)	46 (44.2)	79 (39.3)	0.151
Antibiotics — no. (%)	83 (85.6)	99 (95.2)	182 (90.5)	0.028
Not ARDS	9 (9.3)	0 (0.0)	9 (4.5)	0.007
ARDS Mild	11 (11.3)	9 (8.7)	20 (10.0)	0.007
ARDS moderate	35 (36.1)	41 (39.4)	76 (37.8)	0.007
ARDS severe	42 (43.3)	54 (51.9)	96 (47.8)	0.007
After 24 hours of ICU hospitalization				
CRP (± SD) [mg/L]	68.2 (75.4)	70.2 (72.3)	69.3 (73.4)	0.871
D-dimer (± SD)	5.2 (5.5)	5.2 (5.3)	5.2 (5.3)	0.995
INR (± SD)	1.4 (0.3)	1.3 (0.3)	1.4 (0.3)	0.934

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Table 1 cont. Characteristics of patients with COVID-19 at ICU admission, risk factors for developing pulmonary infection, disease course, treatment, and outcomes

Headcount	Non-pulmonary infection n1 = 97 (48%)	Pulmonary infection n2 = 104 (52%)	All n = 201	*p*-value
Interleukin 6 (± SD) [pg/mL]	284.4 (349.2)	306.3 (427.6)	297.0 (391.5)	0.864
Absolute neutrophils ($\times 10^3/\mu L$)	11.7 (5.4)	9.7 (5.4)	10.6 (5.4)	0.342
Neutrophils Percent (± SD)	79.7 (22.8)	70.2 (31.2)	74.6 (27.5)	0.371
Procalcitonin (± SD) [ng/mL]	2.9 (8.2)	1.0 (3.1)	1.9 (6.0)	0.081
White Blood Cells ($\times 10^3/\mu L$) (±SD)	14.1 (8.8)	12.5 (11.0)	13.2 (10.0)	0.365
After 48 hours of ICU hospitalization				
CRP (± SD) [mg/L]	53.6 (63.8)	51.8 (68.9)	52.6 (66.6)	0.879
D-dimer (± SD)	5.1 (5.4)	4.2 (4.6)	4.6 (4.9)	0.570
INR (± SD)	1.3 (0.3)	1.3 (0.2)	1.3 (0.2)	0.120
Interleukin 6 (± SD) [pg/mL]	427.6 (450.8)	148.3 (167.4)	218.1 (287.6)	0.006
Absolute neutrophils ($\times 10^3/\mu L$)	11.6 (6.7)	8.5 (5.1)	9.8 (5.9)	0.142
Neutrophils Percent (± SD)	68.1 (33.3)	79.2 (7.6)	74.5 (22.6)	0.168
Procalcitonin (± SD) [ng/mL]	2.0 (5.6)	0.9 (2.1)	1.3 (4.0)	0.115
White Blood Cells ($\times 10^3/\mu L$) (± SD)	15.6 (10.3)	12.5 (11.0)	13.9 (10.8)	0.106
After 72 hours of ICU hospitalization				
CRP (± SD) [mg/L]	86.8 (73.2)	75.7 (69.0)	81.0 (71.0)	0.275
D-dimer (± SD)	2.8 (4.4)	2.7 (3.9)	2.8 (4.1)	0.874
INR (± SD)	1.3 (0.3)	1.2 (0.2)	1.2 (0.3)	0.165
Interleukin 6 (± SD) [pg/mL]	424.8 (905.7)	420.2 (772.2)	422.4 (835.7)	0.969
Absolute neutrophils ($\times 10^3/\mu L$)	7.6 (8.2)	7.1 (6.7)	7.3 (7.4)	0.589
Neutrophils Percent (± SD)	50.8 (42.1)	54.0 (40.5)	52.5 (41.2)	0.581
Procalcitonin (± SD) [ng/mL]	3.2 (9.6)	0.8 (2.5)	1.9 (6.9)	0.016
White Blood Cells ($\times 10^3/\mu L$) (± SD)	14.8 (8.6)	13.5 (9.2)	14.1 (8.9)	0.319
Outcome				
Death — no. (%)	54 (55.7)	67 (64.4)	121 (60.2)	0.262

The results are reported as a number (percentage) for categorical variables and median [IQR] and SD for continuous variables. APACHE II — Acute Physiology and Chronic Health Evaluation II; ARDS — acute respiratory distress syndrome; NMBAs — neuromuscular blocking agents; ICU — intensive care unit

were utilized for bivariate analysis, while chi-square or Fisher's exact tests were chosen for categorical variables. All tests were two-tailed. A p-value of less than 0.05 was deemed statistically significant.

Results

Table 1 shows baseline demographics, the average body mass index (BMI) slightly differed between the two groups without statistical significance (p = 0.432). A notable difference was observed in the sex distribution, with a significantly higher percentage of females in the non-pulmonary infection group (p = 0.024).

The PaO2/FiO2 ratio was significantly lower in the pulmonary infection group, suggesting more severe respiratory compromise (p = 0.004).

During the hospitalization, significant differences emerged in the length of ICU stay, mechanical ventilation (MV) necessity and duration, and the use of neuromuscular blocking agents (NMBAs), all higher in the pulmonary infection group, indicating more severe

Table 2. Pathogens isolated from the respiratory system are divided by the time of collection

Pathogens	Up to 48 hours since admission	After 48 hours since admission
Staphylococcus aureus	27	18
Enterobacter cloacae	5	2
Enterococcus faecalis HLAR	4	13
Haemophilus influenzae	4	0
Enterococcus faecalis	4	6
Klebsiella pneumoniae ESBL	4	55
Klebsiella pneumoniae	3	6
Escherichia coli	3	3
Staphylococcus aureus MLSBK MRR MRSA	3	4
Enterococcus faecium HLAR	3	0
Corynebacterium species	3	4
Streptococcus	2	0
Staphylococcus epidermidis MLSBK MRR	2	1
Streptococcus viridans	2	2
Staphylococcus epidermidis MRR	2	2
Klebsiella pneumoniae ssp pneumoniae ESBL	1	2
Staphylococcus aureus MRR MRSA	1	0
Escherichia coli ESBL	1	6
Corynebacterium striatum	1	0
Staphylococcus cohnii ssp cohnii MLSBK MRR	1	0
Staphylococcus haemolyticus MRR	1	0
Acinetobacter baumannii MDR	1	59
Streptococcus mitis/oralis MLSBK	1	0
Staphylococcus warneri MRR	1	0
Pseudomonas aeruginosa	1	0
Delftia acidovorans	1	2
Burkholderia gladioli	1	1
Proteus mirabilis ESBL	1	5
Klebsiella pneumoniae MBL	1	45
Acinetobacter baumannii	0	9
Enterococcus faecium VRE	0	7
Proteus mirabilis	0	7
Stenotrophomonas maltophilia	0	5
Klebsiella pneumoniae OXA-48	0	5
Citrobacter freundii	0	4
Enterococcus faecium	0	3
Pseudomonas aeruginosa MBL	0	3
Staphylococcus haemolyticus	0	2
Staphylococcus haemolyticus MLSBK MRR	0	2
Streptococcus agalactiae	0	1
Enterobacter hormaechei	0	1
Klebsiella oxytoca ESBL	0	1
Citrobacter braakii	0	1
Enterobacter cloacae complex	0	1
Hafnia alvei	0	1
Klebsiella oxytoca	0	1

HLAR — high-level aminoglycoside resistance; ESBL — extended spectrum beta-lactamases; MLSBK MRR MRSA — methicillin, lincosamide-streptogramin B, ketolide resistance, methicillin-resistant staphylococcus aureus, MR — methicillin resistance; MLSBK MRR: methicillin, lincosamide-streptogramin B, ketolide resistance, MBL — metallo-beta-lactamase, MDR — multidrug-resistant; VRE — vancomycin-resistant enterococci; OXA-48 — OXA-48 carbapenemase; MLSBK MRR — methicillin; lincosamide-streptogramin B; ketolide resistance

disease courses. Corticosteroid use and prone positioning did not significantly differ, while antibiotic use was more prevalent in the pulmonary infection group ($p = 0.028$).

The outcomes section reveals that the mortality rate was higher in the pulmonary infection group (64.4%) compared to the non-pulmonary group (55.7%), although this was not statistically significant ($p = 0.262$).

Table 2 presents that during the initial 48 hours post-admission, the most frequently isolated pathogen was *Staphylococcus aureus,* which was identified in 27 cases. Other bacteria of significant prevalence within this timeframe included *Enterococcus faecalis* HLAR, *Haemophilus influenzae, Enterococcus faecalis*, and *Klebsiella pneumoniae* ESBL, each found in four instances.

In contrast, the bacterial profile dramatically shifted 48 hours after admission. *Acinetobacter baumannii* MDR emerged as the dominant organism, detected in 59 instances. *Klebsiella pneumoniae* ESBL was closely followed by 55 identifications, and *Klebsiella pneumoniae* MBL was noted 45 times.

Regarding the resistance patterns, extended spectrum beta-lactamases (ESBL), metallo-beta-lactamase

(MBL), and multidrug-resistant (MDR) patterns were most commonly observed in the isolated bacterial strains. Additionally, a significant number of strains demonstrated high-level aminoglycoside resistance (HLAR) and methicillin, lincosamide-streptogramin B, and ketolide resistance (MLSBK MRR), with the latter also presenting in methicillin-resistant *Staphylococcus Aureus* (MRSA) strains.

Methicillin-sensitive *Staphylococcus aureus*, *Enterococcus faecalis,* and *Enterobacter cloacae* dominated the cultures collected on the first two days. Notably, of our study group of 201 people, positive respiratory cultures were obtained in the first 48 hours in 87 people (43%).

Interestingly, alarm pathogen infections also occurred during the first two days of stay. If we look at the pathogens cultured after 48 hours, our attention is drawn to the contribution of multidrug-resistant strains in the pathogenesis of the infections. Of the 294 positive cultures, the most common bacteria were *Klebsiella pneumoniae* ESBL, multidrug-resistant *Acinetobacter* and *Klebsiella pneumoniae* MBL.

The most commonly used antibiotics were ceftriaxone (n = 122) and levofloxacin (n = 127). Broad-spectrum antibiotics such as meropenem (n = 102) and vancomycin (n = 67) were used frequently. Antibiotic susceptibility of the most commonly cultured bacteria is presented in Table 3. It is apparent from this chart that the levofloxacin spectrum covers *Enterobacter cloacae in* 100% and *Enterococcus faecalis* in 80%.

Discussion

Key findings include a significant burden of pulmonary infections among ICU admissions, with these patients experiencing more severe respiratory compromise, higher mechanical ventilation requirements, and extended ICU stays. The microbiological analysis revealed a diverse array of pathogens, with a notable shift towards antibiotic-resistant strains such as Klebsiella pneumoniae ESBL and Acinetobacter baumannii MDR post-48 hours of admission. Antibiotic susceptibility testing highlighted various agents' efficacy and resistance challenges against isolated pathogens.

Studies show that 7% of patients with SARS-CoV-2 infection have a bacterial coinfection, and 14–40% of patients in ICU [1, 4, 5]. Most of these patients were admitted after a few days of hospitalization, often had already started empirical antibiotic therapy, and did not always have cultures taken on admission to other departments. This would also explain why we obtained multidrug-resistant drug cultures in the out-of-hospital group. Because patients had already started antibiotic therapy, we did not obtain positive cultures in patients with obvious signs of bacterial infection. It is worth noting that patients admitted to the ICU are a particular group of patients, those with the most severe course of disease, often with a history of multiple hospitalizations, some of whom are colonized with multidrug-resistant nosocomial flora. Reports show 70.4% use of antibiotics in COVID-19 patients(6), and 80.3% in severe patients [7] compared to 90.5% in our study.

These results elucidate the susceptibility patterns of common pathogens to various antibiotics, providing valuable insights for effective antimicrobial therapy in the clinical setting. The data emphasize the need for continued surveillance of antibiotic susceptibility to ensure the appropriate selection of therapeutic agents in combating bacterial infections.

As studies show, most often cultured bacteria in severe community-acquired pneumonia are gram-positive cocci such as *Streptococcus pneumoniae* and *Staphylococcus aureus*, Enteric Gram-negative bacilli, *H. influenzae, Legionella species, P. aureginosa* [7, 8]. This differs from our results, and no patient had proven S. pneumoniae infection. It may be due to effective antimicrobial treatment before admission to ICU. We did not routinely run tests for *Legionella*, *Mycoplasma* and *Chlamydophila* infection; perhaps the proportion of these agents would be higher in such cases.

The most commonly used antibiotics were levofloxacin and ceftriaxone. These results match those observed in earlier studies and treatment guidelines for severe community-acquired pneumonia. The most common etiological factors justify the choice of ceftriaxone as a first-line antibiotic. Its spectrum includes *Streptococcus pneumoniae*, methicillin-susceptible *Staphylococcus aureus*, and *Enterobacteriaceae*. Due to its pharmacokinetic properties, it is a good option for treating lower respiratory tract infections.

In our research, where the primary causative agent was MSSA, ceftriaxone may seem controversial. Ceftriaxone in a single daily dose shows against MSSA, mainly a bacteriostatic effect. Because of the critical state of patients in the ICU, a bactericidal effect is crucial. According to studies, a bactericidal effect of 97% can be achieved with a dose of 2g twice daily [8], the standard dosage in our unit. Adequate dosing when using broad-spectrum antibiotics is crucial. We are most concerned about situations when the dose is too low or the interval between doses is too long, which may result in a lack of therapeutic effect but carries a risk of complications such as *Clostridioides infection*. We have not

Table 3. Antibiotic susceptibility of the most commonly cultured pathogens

Antibiotics	Staphylococcus aureus MSS	Enterobacter cloacae	Enterococcus faecalis
Amikacin	76%	75%	n/a
Ceftaroline	100%	n/a	n/a
Ciprofloxacin	12%	61%	64%
Daptomycin	100%	n/a	0%
Erythromycin	97%	n/a	n/a
Gentamicin	100%	61%	n/a
Clindamycin	99%	n/a	n/a
Cloxacillin	100%	n/a	n/a
Levofloxacin	0%	100%	81%
Linezolid	100%	n/a	100%
Oxacillin	100%	n/a	n/a
Rifampicin	100%	n/a	n/a
Teicoplanin	99%	n/a	n/a
Tetracycline	95%	n/a	38%
Tigecycline	100%	20%	100%
Trimethoprim/Sulfamethoxazole	100%	61%	55%
Vancomycin	100%	n/a	100%
Amoxicillin/Clavulanic Acid	n/a	0%	n/a
Aztreonam	n/a	86%	n/a
Cefepime	n/a	29%	n/a
Cefotaxime	n/a	18%	n/a
Ceftazidime	n/a	34%	n/a
Cefuroxime Axetil	n/a	0%	n/a
Ceftriaxone	100%	n/a	n/a
Imipenem	n/a	100%	0%
Colistin	n/a	100%	n/a
Meropenem	n/a	100%	n/a
Piperacillin	n/a	86%	n/a
Piperacillin/Tazobactam	n/a	34%	100%
Ticarcillin - Clavulanic Acid	n/a	86%	n/a
Tobramycin	n/a	61%	n/a
Ampicillin	n/a	n/a	100%
Nitrofurantoin	n/a	n/a	95%
Quinupristin/Dalfopristin	n/a	n/a	5%
Streptomycin Synergy	n/a	n/a	74%

n/a — not applicable

confirmed *Streptococcus pneumoniae* infection in any patient. Our microbiology laboratory did not determine the sensitivity of MSSA to ceftriaxone, but given the data in the literature, we assumed it is sensitive [9–11].

According to SSC guidelines, patients with suspected bacterial infections received empirical antimicrobial treatment [12]. As far as levofloxacin is concerned, its efficacy in treating atypical bacterial infections cannot be overestimated. Of all the fluoroquinolones, it causes the fewest adverse reactions. However, it should be noted that it may cause QTc prolongation and promote Clostridioides infection.

Finally, several significant limitations need to be considered. First is the retrospective nature of the study. Second, we have not routinely performed antigen tests for *Streptococcus pneumoniae* and *Legionella pneumoniae*. Also, these findings cannot be extrapolated to all patients due to the characteristics of ICU patients and differences in the prevalence of different bacteria depending on geographical location.

This investigation is limited by its confinement to a single institution. These factors inherently introduce biases and restrict the study due to its reliance on pre-existing medical documentation. Despite these drawbacks, the substantial number of participants and the rigorous data compilation approach enhance the credibility of our findings.

Empirical antibiotic therapy represents a major challenge in modern medicine. This has become particularly evident in the era of the COVID-19 pandemic.

We identified frequent bacterial pulmonary coinfection in patients with severe COVID-19 with a predominance of methicillin-sensitive *Staphylococcus aureus*. Using levofloxacin and ceftriaxone in high doses twice a day seems reasonable. However, it is advisable to use them as briefly as possible with early de-escalation or administration of targeted therapy. Bacterial infection is a risk factor for prolonged hospitalization, the need for broad-spectrum antibiotics and, therefore, the selection of resistant strains, prolonged mechanical ventilation and consequently, high mortality.

Article information

Author contributions: *Conceptualization, MB and EWC; methodology, EWC; software, EWC; validation, MB; formal analysis, MB; investigation, EWC; resources, MB; data curation, MB; writing — original draft preparation, EWC; writing — review and editing, SLC, EWC; visualization, MB, KB; supervision, EWC, JRŁ, PD; project administration, MB, SLC. All authors have read and agreed to the published version of the manuscript.*

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Institutional review board statement: *The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Medical University of Bialystok, Poland (protocol code: APK.002.242.2021, date of approval: 29.04.2021).*

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