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ORIGINAL RESEARCH

Utilization of Antibiotics for Hospitalized Patients with Severe Coronavirus Disease 2019 in Al-Madinah Al-Munawara, Saudi Arabia: A Retrospective Study

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Background: Most patients admitted to intensive care units (ICUs) with severe Corona Virus Disease 2019 (COVID-19) pneumonia receive antibacterial antibiotics with little evidence of bacterial infections.

Objective: This study was designed to review the profiles of patients with severe COVID-19 pneumonia requiring intensive care, the rate of bacterial coinfection, the antibiotics used, and their relation to patient outcomes (death or recovery).

Methods: This was a retrospective study that reviewed the medical records of all patients with confirmed COVID-19 (n = 120) severe pneumonia admitted directly from the emergency room to the intensive care unit, at a public hospital during the period from May 2020 to April 2021. The data collected included patients' demographic and laboratory data, comorbidities, antibiotic treatment, and their outcome. Descriptive statistics, bivariate inferential analysis tests (chi-square and unpaired T-Tests) and multivariable binary logistic regression were performed.

Results: The mean age of the patients was 56.8 ± 16.5 years old, and among them, 74 (62.7%) were males. Of the included patients, 92 (77.0%) had comorbidities, 76 (63.3%) required mechanical ventilation and 30 (25%) died. All patients received empirical antibiotics for suspected bacterial coinfection. The most common antibiotics used were azithromycin (n = 97, 8%) and imipenem (n = 83, 9%). Ninety patients (75%) were on two empirical antibiotics. Early positive cultures for pathogens were found only in four patients (3.3%), whereas 36 (30%) patients had positive cultures 5–10 days after admission. The most frequently isolated pathogens were *Acinetobacter baumannii* (n = 16) and coagulase-negative Staphylococci (n = 14). In bivariate analysis empirical treatment with azithromycin resulted in a significantly lower mortality rate (p = 0.023), meanwhile mechanical ventilation, days of stay in intensive care unit, morbidities (e.g., lung disease), linezolid and, vancomycin use associated with mortality ($p< 0.05$). The adjusted logistic regression, controlling for age and gender, revealed that azithromycin antibiotic was more likely protective from mortality (OR= 0.22, 95%CI 0.06-0.85, p=0.028. However, patients with lung diseases and under mechanical ventilation were 35.21 and 19.57 more likely to die (95%CI =2.84-436.70, p=0.006; 95%CI=2.66-143.85, p=0.003, respectively).

Conclusion: Bacterial coinfection with severe COVID-19 pneumonia requiring intensive care was unlikely. The benefit of Azithromycin over other antibiotics could be attributed to its anti-inflammatory properties rather than its antibacterial effect.

Keywords: coronavirus disease 2019, antibiotics, intensive care unit, bacterial coinfection

Introduction

Since its start in December 2019, the Corona Virus Disease 2019 (COVID-19) pandemic had significantly affected the world in terms of health-care priorities and economic burden.[1] In general, the symptoms are mild to moderate in 80% of

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cases, severe in 20% of patients, and approximately 6% of affected patients require care in an intensive care unit (ICU).[2] About 90% of patients admitted to hospitals with COVID-19 pneumonia receive empirical antibiotics, without supporting evidence of a bacterial infection.[3] The type, dose, and justification for the empirical antibiotics for patients with COVID-19 have not yet been well established. These antibiotics are usually wide spectrum. As they are also expensive, developing countries usually suffer more because of limited resources.[4,5] Considering the risk of antibiotic-related adverse events, their impact on antimicrobial resistance, and burden on the economy, it appears that more efforts should be made to set a guideline for the use of anti-bacterial antibiotics for patients with severe COVID-19.

It was observed that during the other influenza pandemics, most deaths were due to superinfection rather than progressive, fatal pneumonitis, as is the case with COVID-19. Most deaths occurring during COVID-19 infection are because of the virulent virus and cytokine storm.[6–8] In their review of literature, Charles Feldman and Ronald Anderson reported that only 8% of patients with COVID-19 had coinfections, and those patients were either severely ill or eventually died.[9,10] In most cases, coinfections were misreported, and they appeared to be superinfections in the later stage of the illness.[10–12]

These superinfections are defined by the US Centers for Disease Control and Prevention (CDC) as an infection following a previous infection, whereas a coinfection is the infection that occurs concurrently with the initial infection at the beginning of the first presentation and not later.[13] Strangely enough, a distinction between the two is often unclear in the literature or in daily clinical practice.[10,14] Moreover, data on bacterial infections in patients with COVID-19 are deficient and not always consistent.[15] Recent studies reported the over-prescription of antibiotics in patients with COVID-19, which could increase the risk of antimicrobial resistance.[16,17]

The aim of this study was to review the profiles of patients with severe COVID-19 pneumonia requiring intensive care, the rate of bacterial coinfection, the antibiotics used, and their relation to patient outcomes (death or recovery).

Methods and Materials

Study Design and Setting

This was a retrospective study based on reviewing the medical records of 120 patients, corresponding to all patients admitted directly from the emergency room of Ohud Hospital (200 beds) public hospital and main isolation hospital for covid-19 patients in AL Madinah area to the ICU because of severe COVID-19 hypoxia in the period from May 2020 to April 2021.

Ethical Considerations

This study complies with the declaration of Helsinki. Its protocol was approved by the Research Committee reporting to the Ohud Hospital Health Gathering in Al-Madinah Al-Munawara branch of the Saudi Ministry of Health, as a part of the study of statins and COVID-19 (22–067). Informed consent was not required because of the retrospective nature of this study. However, the confidentiality of the data was assured; that is, the patients were assigned numerical identifiers. Access to data was restricted to the investigators, and the database was password protected.

Sampling Methods and Patients' Selection

Only patients who were confirmed to be COVID-19-positive by nasopharyngeal swab Reverse Transcription Real-Time Polymerase Chain Reaction (RT-PCR) were included. The review used an Excel sheet to extract the data of patients.

Study Variables, Measures, and Outcomes

Patients' demographics (eg, age and gender), comorbidities, the prescription of broad-spectrum antibiotics, positive cultures, the type of infection, the organisms isolated, and the impact of the broad-spectrum antibiotics used regarding the outcome (death or recovery) were extracted. As there is a national protocol provided by the Ministry of Health in Saudi Arabia stating detailed management of COVID-19 infections according to patient category (ie, antiviral therapy, dexamethasone, low-molecular-weight heparin, plasma, immunoglobulins, and interleukin-6 (IL6) blockers),[18] and this protocol is followed strictly by all critical care units in all Saudi hospitals, all patients included in this study were started

immediately on such a protocol upon admission to the ICU. Anti-bacterial antibiotics were started as physicians anticipate community acquired pneumonia as a superinfection or co-infection. The Saudi guidelines for the treatment of severe community acquired pneumonia are summarized in Table 1.[19]

Statistical Analysis

The data were imported from an Excel sheet into Statistical Package for Social Sciences (version 21; IBM Corp., Armonk, NY, USA) for analysis. Descriptive statistics were used to summarize the characteristics of the sample and the use of antibiotics. Continuous and categorical variables were reported as means ± standard deviations and frequencies with percentages, respectively. A multiple response questionnaire (MRQ) was developed to collect the data on comorbidities. This MRQ was processed and analyzed to rank the comorbidities in order. The chi-square test or Fisher's exact test and unpaired *t*-test were used to identify any statistically significant associations between categorical and continuous explanatory variables, with the dependent variable being hospital outcome (recovery or death). Binary logistic regression, controlling for age and gender, was performed to model the association of significant variables yielded from bivariate analysis with the dependent variables. A p value of <0.05 was considered statistically significant for all analysis.

Results

Demographics and Comorbidities Among Patients with COVID-19

Demographic characteristics and comorbidities among the patients included in this study are presented and summarized in Table 2. Of the 120 patients, 74 (61.7%) were males and 46 (38.3%) were females. The mean age of all patients was 56.8 ± 16.5 years old. Ninety-two (76.6%) patients had comorbidities of whom 28 had one comorbidity (23.3%) and the remaining patients had 2–5 comorbidities.

Figure 1 shows the patients with comorbidities (n = 92); the most common comorbidity was diabetes mellitus, which was found in 65 patients (70.7%), followed by hypertension in 62 patients (67.4%).

Table 1 Empirical Treatment of CAP: a Therapeutic Guideline

	First Line	**Alternative**
Out patient		
Young and otherwise healthy	Macrolid[b]	Doxycycline
Comorbid illness [c]or risk factors[d]	Second ceph[e] ± macrolide	macrolide β-Lactam /β-Lactamase inhibitor [f] or respiratory quinolones[g]
Hospitalized patients		
Ordinary cases	Second or third ceph[h] +macrolide β-Lactam /β-Lactamase inhibitor ± macrolide	Respiratory quinolones
With suspected aspiration		Clindamycin± macrolide
With bronchiectasis	Anti-pseudomonas third ceph + aminoglycoside ± macrolide.	Respiratory quinolones ± macrolide
Severe pneumonia		
No pseudomonas risk [j]	Third ceph + macrolide	Carbapenem[k] + macrolide
Pseudomonas risk	Anti-pseudomonas third ceph[i] + aminoglycoside[l] ± macrolide.	Carbapenem + aminoglycoside ± macrolide Anti-pseudomonas penicillin[m]+ aminoglycoside ± macrolide.

Notes: [a] Community acquired pneumonia. Regimen should be tailored upon results of microbiological testing. [b]For example, clarithromycin, azithromycin, roxithromycin. [c]For example, chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF). Cancer, diabetes mellitus (DM), hepatic or renal disease. [d]Risk factors; recent antibiotics within 3 months, age > 50 years, hospitalization, or immunosuppressive therapy within 3 months, drsp= drug resistant S.pneumoniae. [e]Second ceph= second generation cephalosporins (eg, cefuroxime, cephaclor, cefprozil) [f]Amoxycillin/clavulanate, ampicillin/sulbactam. [g]For example, moxifloxacin, levofloxacin, gatafloxacin, gemifloxacin. [h]Third cepf= third generation cephalosporins (cefotaxime, ceftriaxone). [i]For example, anti-pseudomonal third cephalosporin; ceftazidime, fourth cephalosporins; cefepime. [j]Structural lung disease, prior hospitalization, immunosuppressive therapy. [k]For example, imipenem, meropenem. [l]For example, gentamycin, tobramycin, amikacin.[m]For example, piperacillin-tazobactam, ticarcillin-clavulanic acid. Reprinted from *Int J Antimicrob Agents*. 20 Suppl 1. Memish ZA, Shibl AM, Ahmed QAA, Saudi Arabian Community-Acquired Pneumonia Working Group (SACAPWG). Guidelines for the management of community-acquired pneumonia in Saudi Arabia: a model for the Middle East region. S1–S12, ©copyright (2002), with permission from Elsevier.[19]

Table 2 Demographic Characteristics, Comorbidity and in Hospital Outcome of COVID-19 Patients (n = 120) Admitted in the Intensive Care Unit

Variable	Mean ± SD or F (%)
Age (mean/SD[a])	56.8 ± 16.5
Gender	
Female **Male**	46 (38.3) 74 (61.7)
High BMI[b](>29)	52 (43)
Comorbidities	
No morbidity One comorbidity Two comorbidities Three comorbidities Four comorbidities Five comorbidities	28 (23.3) 28 (23.3) 31 (25.8) 21 (17.5) 4 (3.3) 8 (6.7)
Outcomes	**Mean ± SD or F (%)**
Mechanical ventilation	
No Yes	44 (36.7) 76 (63.3)
ICU[c] stay days	12.6 ± 7.6
ICU outcome	
Recovered **Died**	90 (75) 30 (25)

Abbreviations: [a]SD, standard deviation; [b]BMI, body mass index; [c]ICU, intensive care unit.

Clinical Presentation at the Emergency Room and Laboratory Results

All 120 patients had severe pneumonia and hypoxia since their presentation to the emergency room and were admitted directly to the ICU. Twenty-six patients had hypotension, with a blood pressure of less than 90/60 mm Hg. The initial chest X-ray showed varying degrees of lung infiltration; bilateral peripheral infiltrate typical of COVID-19 pneumonia

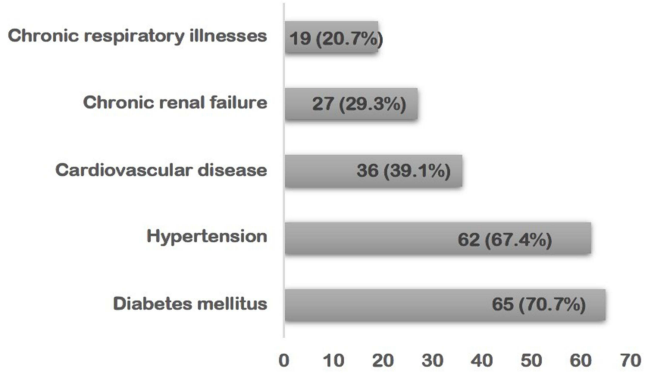

Figure 1 Percentages of Comorbidities Among Patients with Severe Covid-19.

was found in 83 patients (69.1%); right lung bronchopneumonia was found in 27 patients (22.5%); and left lung consolidation was found in 10 patients (8.3%).

Regarding laboratory results, 96 patients (80%) had normal leukocyte counts; leukocytosis was found in 22 patients (18.34%); and leukopenia with absolute lymphopenia was observed in two patients (1.6%). All patients had elevated levels of C-reactive protein (mean, 68.2 mg/dl; range, 7–156 mg/dl), D-dimer (mean 2231µg/l; range, 597–5580 µg/l), and serum ferritin (mean, 876 ng/mL; range, 255–3090 ng/mL). Data on procalcitonin levels were unavailable, so they were not evaluated in this study. Positive COVID-19 infection was confirmed in all included patients using RT-PCR of nasopharyngeal swab samples. HbA1c was uncontrolled (>6.5%) in 48 patients (40%), and elevated serum creatinine levels were found in 34 patients (28.3%). In addition to the applied management protocol for confirmed COVID-19 cases with severe pneumonia, all patients received empirical treatment with antibiotics while awaiting septic screening and culture reports. Samples from blood, respiratory secretions, and urine were submitted for gram stain and culture on day 1 of admission to the ICU. Repeated samples were resubmitted on days 5–10 if deterioration or superinfections were suspected.

Antibacterial Antibiotics Used and Outcomes

The most used antibiotic was azithromycin, which was used in 97 patients (80.8%), followed by imipenem, which was used in 83 patients (69.2%). Piperacillin/tazobactam was used in 31 patients (25.8%); vancomycin was used in 15 patients (12.5%); linezolid was administered in 35 patients (29.2%); fluoroquinolones (including; levofloxacin or moxifloxacin) were used in 67 patients (55.8%); ceftriaxone was administered in 10 patients (8.3%); amikacin was used in six patients (5%); and amphotericin B was used in 14 patients (12.1%) who continued to run fever after 7 days of admission, with positive culture of candida and when fungal hyphae appeared from any site. Most patients admitted to the ICU were treated with a combination of antibiotics: four antibiotics were used in three patients (2.5%); three antibiotics were administered in 23 patients (19%); two antibiotics were used in 90 patients (75%); and a single antibiotic was used in four patients (3.3%) (Table 3). There were 140 blood cultures, 130 sputum gram stains and cultures, 56 tracheal aspirate cultures, and 160 urine cultures performed. We found positive cultures for pathogens in only four (3.3%) patients from the samples taken as part of septic screen early on admission (within 24 h). All were coagulase-negative *Staphylococcus aureus*, whereas 36 (30%) patients had positive cultures later after 5–10 days of admission to the ICU, all

Table 3 Number and Percentage of Types of Antibiotic Used for COVID-19 Patients (n = 120) Admitted to the Intensive Care Unit

Use of Antibiotics	(%)
Azithromycin	
No	23 (19.2)
Yes	97 (80.8)
Imipenem	
No	37 (30.8)
Yes	83 (69.2)
Piperacillin/tazobactam	
No	89 (74.2)
Yes	31 (25.8)
Vancomycin	
No	105 (87.5)
Yes	15 (12.5)

(*Continued*)

Table 3 (Continued).

Use of Antibiotics	(%)
Linezolid	
No	85 (70.8)
Yes	35 (29.2)
Fluoroquinolone	
No	53 (44.2)
Yes	67 (55.8)
Ceftriaxone	
No	110 (91.7)
Yes	10 (8.3)
Amikacin	
No	114 (95.0)
Yes	6 (5)
Amphotericin B	
No	102 (87.9)
Yes	14 (12.1)

of which occurred after endotracheal intubation. The most frequently isolated pathogens at all sites were *Acinetobacter baumannii* (n = 16) and coagulase-negative Staphylococci (n = 14). Candida was isolated from six patients. No methicillin-resistant *Staphylococcus aureus* or other gram-negative organisms were isolated from the 120 patients included in this study.

The average duration of ICU stay was 12.6 ± 7.6 days. Seventy-six patients required mechanical ventilation (63.3%). Ninety patients (75%) recovered and were discharged from the ICU to the general ward and later returned home after improvement or complete recovery, whereas the remaining 30 patients (25%) died.

The mean age of the patients who died and their duration of stay in ICU were statistically significantly higher than those of the survivors (age: 64.7 ± 15.4 years old vs 54.1 ± 15.9 years; duration of ICU stay: 16.1 ± 8.3 days vs 11.4 ± 7.1 days). The mortality rate among patients with renal failure was statistically significantly higher than that among patients without renal failure (55.6% vs 16.1%, $p < 0.001$) and that among patients with hypertension, diabetes mellitus, and lung disease (33.9% vs 16.1%, $p = 0.027$; 36.9% vs 11.1%, $p = 0.001$; 57.9% vs 18.8%; $p \leq 0.001$, respectively). Finally, the mortality rate among patients who required mechanical ventilation was statistically significantly higher than that of those not requiring mechanical ventilation (38.2% vs 2.3%, $p < 0.001$).

Our results showed (Table 4) that the mortality rate among patients who were treated empirically with azithromycin was significantly lower than that among patients who did not receive the drug (20.6% for the azithromycin group vs 43.5% for the group without azithromycin, $p = 0.023$). Ceftriaxone had comparable results to azithromycin, though the results were insignificant, as the number of patients who received ceftriaxone was small. However, more deaths occurred among the linezolid and vancomycin groups.

Table 5 shows that the use of combinations of antibiotics did not yield statistically significant differences in death rates among patients with COVID-19 ($p > 0.05$). However, the combination of azithromycin and ceftriaxone seemed protective, although the results were marginally significant ($p = 0.065$). This could be because of the small sample size.

Binary logistic regression (Table 6) revealed that azithromycin antibiotic was more likely protective from death (OR= 0.22, 95% CI 0.06–0.85, p = 0.028). However, patients with lung diseases and under mechanical ventilation were 35.21 and 19.57 more likely to die (95% CI = 2.84–436.70, p = 0.006; 95% CI = 2.66–143.85, p = 0.003, respectively). Due to

Table 4 Death Rate Among Different Antibiotics Received

Antibiotic	Death F (%)	*P*-value
Azithromycin		
No	20 (43.5)	0.023
Yes	10 (20.6)	
Imipenem		
No	8 (21.6)	0.568
Yes	22 (26.5)	
Piperacillin/tazobactam		
No	10 (22.5)	0.279
Yes	20 (32.3)	
Vancomycin		
No	8 (21.0)	0.011
Yes	22 (53.3)	
Linezolid		
No	14 (16.5)	0.001
Yes	16 (45.7)	
Fluoroquinolone		
No	12 (22.6)	0.596
Yes	18 (26.9)	
Ceftriaxone		
No	30 (27.3)	0.065
Yes	0 (0.00)	
Amikacin		
No	0 (0.00)	0.335
Yes	30 (26.3)	
Amphotericin B		
No	4 (23.5)	0.741
Yes	24 (28.6)	

Table 5 Death Rate Among Combinations of Antibiotics Received

Antibiotics	Death F (%)	*P*-value
Azithromycin and Imipenem		
No	14 (26.9)	0.671
Yes	16 (23.5)	
Azithromycin and ceftriaxone		
No	30 (27.3)	0.065
Yes	0 (0.00)	

(*Continued*)

Table 5 (Continued).

Antibiotics	Death F (%)	*P*-value
Fluoroquinolone and ceftriaxone		
No Yes	30 (25.4) 0 (0.00)	0.100
Fluoroquinolone and imipenem		
No Yes	17 (25.4) 13 (24. 5)	0.100

Table 6 Logistic Regression Predicting Likelihood of Dying from COVID-19 Among Patients Admitted to ICU

Variables	B	Wald	AOR (95% CI)	*p*-value
Age	0.002	0.005	1.0 (0.96–1.05)	0.942
Sex	1.112	2.211	3.04 (0.70–13.16)	0.137
Azithromycin	−1.514	4.811	0.22 (0.06–0.85)	**0.028**
Mechanical ventilation	3.561	7.683	35.21 (2.84–436.70)	**0.006**
Days of stay in ICU	0.023	0.279	1.02 (0.94–1.12)	0.598
Lung disease	2.974	8.539	19.57 (2.66–143.85)	**0.003**
Linezolid	1.051	2.338	2.86 (0.74–10.99)	0.126
Vancomycin	1.219	1.563	3.39 (0.50–22.91)	0.211

Notes: Differences were considered statistically significant at *p* value < 0.05 and significant values are presented in bold type.
Abbreviations: AOR, adjusted odd ratio; 95% CI, 95% Confidence interval; B, beta coefficient; ICU, intensive care unit.

small sample size morbidities (hypertension, diabetes, renal failure) were statistically significantly associated with age at $p < 0.05$, as such did not enter the model and age was used as proxy for these variables.

Discussion

As the Covid-19 pandemic is running into its third year, there is a growing concern regarding the accompanying use of the broad spectrum antibiotics for the suspected bacterial CO-infections, a practice that carries a risk for increasing bacterial resistance. The current study aims to highlight the utilization of anti-bacterial antibiotics for confirmed covid-19 severe viral pneumonia and to answer the question needed based on positive cultures and patient outcomes.

Consistent with the findings of several previous studies, the COVID-19 infected patients requiring ICU admission included in this study were mostly males, with a male-to-female ratio of 2:1.[20] The mean age of the patients was 56.78 ± 16.54 years Approximately 76.7% of the patients in this study had various underlying chronic illnesses, among which the most common was type 2 diabetes mellitus, followed by hypertension and coronary artery disease, and renal impairment; the least number of patients had underlying chronic lung disease, such as bronchial asthma. Studies have reported similar data on comorbidities for patients with COVID-19 who required ICU admission because of severe hypoxia.[21,22] Among the patients in this study, 52% were obese. Similar results were found in other studies and previous reports of increased mortality with age, obesity, diabetes, length of hospital stay, and need for ICU admission and mechanical ventilation.[23–27] Clinical presentation was the most important reason for the initiation of empirical antibiotics, followed by the high laboratory markers of inflammation and typical radiology findings of pneumonia. This practice is similar to what was observed in other

studies.[2] The choice of the empirical antibiotics depended on physician experience and the national guidelines of community acquired pneumonia (CAP) treatment; (Table 1), therefore, most patients received antibiotic coverage for presumptive pneumococcal pneumonia, Staphylococcus, and atypical organisms (eg, azithromycin, fluoroquinolones, ceftriaxone, imipenem, and piperacillin/tazobactam). Later, after there were positive cultures, the antibiotic agents were either changed or combined with other agents (ie, vancomycin, linezolid, and amphotericin B). This practice was not supported by several studies that did not agree with the unrestricted empirical use of broad spectrum antibiotics.[28–30] However, the practice of empirical antibiotic coverage for CAP selected for the patients in this study agreed with the results of a survey conducted by 166 physicians from 23 countries and 82 hospitals.[2] Similar to other previous reports, unlike coinfection with other influenza viruses, we found low rates (3.2%) of early bacterial coinfection in patients with severe COVID-19. Additionally, later cultures revealed low rates of bacterial coinfection or superinfection (30%). Similar results were published from a UK secondary care setting (3.2%), showing early confirmed bacterial isolates identified 0–5 days after admission to the ICU.[31,32] In this study, only 0.03% of the patients received single antibiotics, whereas most patients (99.7%) were treated with a combination of antibiotics; 75% received three antibiotics. This could be explained by the critical condition of the patients upon admission and the presence of comorbid diseases in most of them, which could lead the treating physicians to use combinations to cover various suspected microorganisms. Combinations, including vancomycin or linezolid and amphotericin B, were used later, either when there was a poor response or when there was a positive culture indicating opportunistic infections; still, it did not improve these patients' chance of survival. Similar high percentages of antibiotic administration in patients with COVID-19 were also reported by Miranda et al and Langford et al.[26,32] Our results favored azithromycin, as there were fewer deaths when azithromycin was started early. It has been reported that azithromycin has activity at different points of the viral cycle and could protect against severe acute respiratory syndrome. It has a proven immunomodulatory activities and it can inhibit the cytokine production, enhance epithelial cell integrity, and prevent post recovery lung complications.[33,34] It has been also reported that azithromycin is associated with a reduced mortality and ventilation duration,[35,36] and, the early initiation of azithromycin in severe lung injury and acute respiratory distress syndrome has been reported to reduce the time to successful extubating from ventilation.[37,38] On the other hand, few other trials found no clinical benefits from the use of azithromycin in patients with COVID-19.[39] However, upon reviewing the use of azithromycin in the COALITION II study and other similar reports, we found that azithromycin was administered with hydroxychloroquine, which may have affected the benefit of azithromycin if it was used alone or in other combinations.[40]

Strengths and Limitations of the Study

This was a retrospective study which is inexpensive and time efficient. However, retrospective study inherits number of limitations in term of less control over variables.[40] In addition, the study included small sample size as only those patients directly admitted from emergency room to intensive care unit were included. Another limitation is that being done in one center, though Ohud Hospital was the referral center for Covid-19 patient in Madinah Area at the time this study was performed.

Conclusion

Unlike other influenza viruses, bacterial coinfection with severe COVID-19 pneumonia requiring intensive care management is unlikely, considering the low rate of positive cultures. Prolonged ICU stay and mechanical ventilation are associated with superinfection rather than coinfection. Empirical antibiotics with unproven benefits have been overused. Azithromycin was the only empirical antibiotic of benefit for severe CAP associated with COVID-19, a result that could be explained by its anti-inflammatory property rather than its antibacterial effect. Further studies are needed to highlight the problem of the overuse of empirical antibiotics, the burden of future resistance, and the cost-effectiveness of such a practice.

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Disclosure

The authors report no conflicts of interest in this work.

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