The Clinical Manifestation of SARS-CoV-2 in Critically Ill Patients with *Klebsiella pneumoniae* NDM Hospitalized in the ICU of a Modular Hospital during the Third Wave of the Pandemic in Poland—An Observational Cohort Study

Aneta Guzek 1, Zbigniew Rybicki 2, Agnieszka Woźniak-Kosek 1 and Dariusz Tomaszewski 3,*

1 Department of Laboratory Diagnostics, Military Institute of Medicine, 04-141 Warsaw, Poland; aguzek@wim.mil.pl (A.G.); awozniak-kosek@wim.mil.pl (A.W.-K.)
2 Department of Anaesthesiology and Intensive Therapy, Military Institute of Medicine, 04-141 Warsaw, Poland; zrybicki@wim.mil.pl
3 Department of Anaesthesiology and Intensive Therapy, Military Institute of Aviation Medicine, 01-755 Warsaw, Poland

* Correspondence: dariusz.tomaszewski@wiml.waw.pl

Abstract: There is limited information on the clinical characteristics of critically ill patients infected with SARS-CoV-2 and *Klebsiella pneumoniae* NDM. The objective of this study was to describe such a group of patients hospitalised in the intensive care unit of a large academic hospital during the third wave of the COVID-19 pandemic in Poland. Between 1 March and 30 June 2021, 103 patients were hospitalised, of whom 23 (22.3%) were positive for *K. pneumoniae* NDM; 14 (61%) of those patients died. Their hospitalisation time varied between 9 and 47 days. Five of the 23 patients (21.7%) were otherwise healthy. In contrast, the others suffered from cardiovascular problems (11, 47.8%), obesity (6, 26.1%), diabetes (5, 21.7%), neurological problems (4, 17.4%), or kidney disease (1, 4.3%); 4 (17.4%) were heavy smokers, and 1 (4.3%) had a history of alcohol abuse. *K. pneumoniae* NDM was isolated from urine samples of all patients. In 17 patients (73.9%), it was also isolated from other sources: from the respiratory tract in 10 (43.8%), from the blood in 2 (8.7%), and the central venous catheter was contaminated in 1 case (4.3%). Fourteen of the patients (60.9%) were colonised *K. pneumoniae* NDM. In four patients (17.4%), bacterial and fungal coinfection occurred. In one case (4.4%), two fungal species, *Candida albicans* and *Candida glabrata*, were isolated simultaneously. The most frequently administered antimicrobial agent was colistin (60.9%), followed by meropenem (47.8%), vancomycin (47.8%), ceftriaxone (34.8%), linezolid (30.4%), piperacillin/tazobactam (30.4%), and trimethoprim/sulfamethoxazole (30.4%). Other less-frequently administered agents included amikacin, amoxicillin/clavulanate, tigecycline, ciprofloxacin, fosfomycin, clindamycin, and cloxacillin. Fluconazole was administered in 14 patients (60.7%) and micafungin was administered in 2 (8.7%).

Keywords: COVID-19; critically ill; *Klebsiella pneumoniae* NDM

1. Introduction

Until now, more than 300 million patients [1] have been infected with SARS-CoV-2. Many of them have required hospitalisation and critical care. The admission rates to the intensive care unit (ICU) have varied from 5% to 12% in Italy [2,3], from 5% to 26% in China [4,5], and from 5% to 81% in the United States and Canada [6–8]. These rates indicate that no less than 15 million patients have been hospitalised in ICUs. Patients hospitalised in the ICU have numerous issues, and the problem of bacterial infections and antimicrobial resistance is also a challenge. Although the relationship between SARS-CoV-2 disease and antimicrobial resistance has not been resolved, some authors [9–12] suggest such a relation.
Regardless of the answer, there is no doubt that any other infection increases the duration and cost of hospitalisation and may worsen the patient’s outcome.

This study aims to describe the characteristics, clinical presentation, antimicrobial treatment, and outcomes of patients with COVID-19 and infected with *Klebsiella pneumoniae* New Delhi metallo-β-lactamase (NDM) hospitalised in the ICU of a large academic hospital during the third wave of the COVID-19 pandemic in Poland.

### 2. Material and Methods

#### 2.1. Study Design

This was an observational cohort study. The study design was approved by the institutional Bioethical Committee (37/WIM/2021 of 15 December 2021). Informed concern was waived because no intervention was involved, and no patient identifying information was included.

#### 2.2. Setting

This study was performed in an ICU designated for critically ill patients infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The ICU was a department of a modular hospital, a part of the Military Institute of Medicine, a 1000-bed academic hospital, and a regional trauma centre. This modular hospital was designed for the treatment of patients infected with SARS-CoV-2. There were 60 beds, including 12 beds in the ICU.

#### 2.3. Participants

We analysed the data of all critically ill patients infected with the SARS-CoV-2 hospitalised between 1 March and 30 June 2021, during the third wave of the COVID-19 pandemic in Poland, from whom *K. pneumoniae* NDM had been isolated. No other eligibility criteria were applied.

According to the European Centre for Disease Prevention and Control [13], to perform active surveillance and identify high-risk patients, we performed a swab test (from the respiratory tract or rectal) upon admission of patients to the ICU. Such tests were repeated every seven days of hospitalisation. In every case when the patient had a fever (core temperature ≥38 °C), blood samples were withdrawn and submitted for microbiological testing.

#### 2.4. Microbiological Analysis

Bacteria were identified with the VitekMS (bioMérieux, Marcy-l’Étoile, France), an automated microbial identification system that uses matrix-assisted laser desorption/ionization-time of flight (MALDI-ToF) mass spectrometry. Antimicrobial susceptibility was determined for all positive samples except rectal swabs. The broth microdilution method and the automated VITEK-2 system (bioMérieux) were used. The results were read according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria [14]. The presence and nature of carbapenemase determinants were assessed by molecular testing of bacterial isolates using either a polymerase chain reaction (PCR)-based platform (Xpert-Carba R assay, Cepheid, Sunnyvale, CA, USA) or a lateral flow immunochromatographic assay (RESIST-5 OOKNV, CORIS, BioConcept, Gembloux, Belgium).

#### 2.5. Study Size

Due to the retrospective nature of this study, its size was not determined before the start of the project.

#### 2.6. Statistical Methods

Collected data were archived and analysed with Microsoft Excel software. Descriptive statistics were used for analysis. The figure was prepared with DataGraph software.
3. Results

Between 1 March and 30 June 2021, in the ICU of the modular hospital, 103 patients were hospitalised, including 60 men (58.25%, aged 20–88 years) and 43 women (41.75%, aged 34–97). Twenty-three (22.33%) were positive for multidrug-resistant (MDR) *K. pneumoniae* NDM. All of them were analysed, and no data were missed. Fourteen of 23 patients died (60.87%), and 9 (39.13%) survived. The duration of hospitalisation was between 9 and 47 days (median 22, interquartile range 17–34). The characteristics of the analysed patients, their comorbidities, and empiric and targeted antimicrobial therapy are presented in Table 1. Five of 23 patients (21.74%) were otherwise healthy. Of the 23 patients who were positive for *K. pneumoniae* NDM, 11 (47.83%) suffered from cardiovascular problems, including arterial hypertension (8/23, 34.78%) and heart disease (3/23, 13.04%). Six (26.09%) suffered from obesity, five (21.74%) from diabetes, four (17.39%) had some neurological problems, four (17.39%) were heavy smokers, one (4.35%) suffered from chronic kidney disease, and one (4.35%) had a history of alcohol abuse.

Of the 23 patients positive for *K. pneumonia* NDM, 8 were women (34.78%), and 15 were men (65.22%). The pathogen was isolated from the urine of all patients. In 6 cases (26.09%), this was the only positive sample; in the other 17 patients (73.91%), *K. pneumoniae* NDM was isolated from other sources: from the respiratory tract in 10 (43.48%), from blood samples in 2 (8.70%). The central venous catheter tip was contaminated in 1 case (4.35%). Fourteen of the 23 patients (60.87%) were colonised with *K. pneumoniae* NDM.

Of the 23 patients infected with *K. pneumoniae* NDM, some had superimposed infections. Specifically, 10 cases (43.84%) were positive for MDR *Acinetobacter baumannii*, 2 (8.70%) were positive for *Pseudomonas aeruginosa*, and 1 (4.35%) was positive for methicillin-resistance *Staphylococcus aureus* (MRSA). Moreover, in 4 of 23 patients (17.39%), bacterial and fungal coinfection occurred: in 2 (8.70%) *Candida albicans*, in 1 (4.35%) *Candida glabrata*, and in 1 case (4.35%) both *C. albicans* and *C. glabrata* were isolated simultaneously.

Antimicrobial susceptibility and resistance of *K. pneumoniae* NDM strains isolated from urine samples of all 23 patients were presented in Table 2. The most frequently administered antimicrobial agent was colistin (18/23, 78.26%), followed by meropenem (11/23, 47.83%), vancomycin (11/23, 47.83%), ceftriaxone (8/23, 34.78%), linezolid (7/23, 30.43%), piperacillin/tazobactam (7/23, 30.43%), trimethoprim/sulfamethoxazole (7/23, 30.43%), amikacin (5/23, 21.74%), amoxicillin/clavulanate (3/23, 13.04%), tigecycline (3/23, 13.04%), ciprofloxacin (2/23, 8.70%), fosfomycin (2/23, 8.70%), clindamycin (1/23, 4.35%), and cloxacillin (1/23, 4.35%). Fluconazole was administered in 14 of 23 patients (60.87%), and micafungin was administered in 2 of 23 patients (8.70%). In one case (4.35%), antimicrobial therapy was not administered. The detailed information on the antimicrobials administered in empiric and targeted therapy is shown in Figure 1.
| Patient Number | Age, Gender | Comorbidities | Duration of Hospitalization (Days) | COVID Treatment | Empiric Antimicrobial Treatment | Targeted Antimicrobial Treatment | Origin of K. pneumoniae Isolates | Superimposed Infection | Days from ICU Admission to the Isolation of K. pneumoniae NDM in Urine | The Highest Concentration of IL-6 | The Highest Concentration of PCT | The Highest Concentration of CRP | Outcome | Occurrence of Clostridioides difficile |
|----------------|-------------|---------------|----------------------------------|-----------------|-------------------------------|-------------------------------|-------------------------------|------------------------|-----------------------------------------------------------------------------|-------------------------------|-------------------------------|-------------------------------|---------|-------------------------------|
| 1              | 71, M       | hypertension, Multiple sclerosis | 17                  | remdesivir, steroids, plasma of convalescents | vancomycin, meropenem, fluoroquinolone | colistin | urine, respiratory tract, rectum | 6                  | 7                                                                            | 14.7                          | 0.46                          | 30.1                          | died    | no                             |
| 2              | 73, M       | diabetes      | 35                  | remdesivir, steroids, clarithromycin | vancomycin, meropenem, fluoroquinolone | colistin | urine, respiratory tract, rectum | P. aeruginosa, C. glabrata | 21                                                                         | N/A                          | 0.21                          | 29.4                          | alive   | no                             |
| 3              | 46, M       | diabetes, obesity | 9                   | steroids | vancomycin, fluoroquinolone | colistin | urine | A. baumannii | 2                      | N/A                          | 0.53                          | 23.4                         | died    | no                             |
| 4              | 39, M       | hypertension, obesity, depression | 14                  | steroids | ceftriaxone, meropenem, linezolid, fluoroquinolone | urine, respiratory tract | 14                            | 140.7                         | 4.17                         | 13.3                          | died    | no                             |
| 5              | 66, F       | hypertension, diabetes, hemophilia, thrombocytopenia | 23                  | steroids | vancomycin, PIP, TAZO | TMT, SMX | urine, respiratory tract | A. baumannii | 9                      | N/A                          | 20.39                         | 67.7                         | died    | no                             |
| 6              | 79, F       | epilepsy, atherosclerosis | 30                  | steroids | amox/clav | colistin | urine, respiratory tract | 13                  | N/A                          | 0.14                          | 5.0                          | alive   | yes                            |
| 7              | 71, M       | hypertension, alcohol abuse | 18                  | steroids | amox/clav, vancomycin | colistin | TMT, SMX | urine | MRSA, P. aeruginosa | 8                             | 180.7                         | 0.12                          | 14.8                         | alive   | no                             |
| 8              | 66, F       | CHD           | 26                  | remdesivir, steroids | ceftriaxone, colistin | TMT, SMX, linezolid | urine | A. baumannii, C. albicans | 4                             | N/A                          | 5.04                          | 27.8                         | alive   | no                             |
| 9              | 45, F       | obesity, hypothyroidism | 17                  | remdesivir, steroids | vancomycin, meropenem, colistin | linezolid, fluoroquinolone | urine, respiratory tract | A. baumannii, C. albicans | 5                             | N/A                          | 0.26                          | 32.8                         | died    | no                             |
| 10             | 20, M       | CHD, heart failure, myelodysplastic syndrome, history of stroke | 36                  | remdesivir, steroids | ceftriaxone, clindamycin, vancomycin | colistin | urine, respiratory tract, rectum | A. baumannii, C. albicans | 4                             | N/A                          | 5.04                          | 27.8                         | alive   | no                             |
| 11             | 76, M       | CHD, heart failure, myelodysplastic syndrome, history of stroke | 34                  | steroids, plasma of convalescents | ceftriaxone, clindamycin, vancomycin | amox/clav | urine | 30                  | N/A                          | 29.99                         | 21.6                          | alive   | yes                            |
| 12             | 74, F       | meningioma    | 16                  | remdesivir, steroids, plasma of convalescents | vancomycin, meropenem, fluoroquinolone | colistin | urine, respiratory tract | 14                            | 394.8                         | 2.28                          | 41.1                         | died    | no                             |
| 13             | 78, M       | hypertension | 47                  | steroids | ceftriaxone, clindamycin, PIP, TAZO | colistin | TMT, SMX, amikacin, fluoroquinolone | urine | A. baumannii, C. albicans, C. glabrata | 5                             | N/A                          | 8.59                          | 48.0                         | died    | yes                            |
| 14             | 48, M       | hypertension, diabetes, morbid obesity | 29                  | steroids | ceftriaxone, colistin | fosfomycin, linezolid | TMT, SMX | Blood culture tip, urine, respiratory tract | A. baumannii | 10                        | N/A                          | 46.53                         | 26.0                         | died    | no                             |
| 15             | 67, M       | CHD, hypertension, diabetes, renal failure | 21                  | steroids | meropenem, linezolid | colistin | fluoroquinolone | urine | A. baumannii, C. albicans | 8                             | 189.1                         | 1.18                          | 30.1                         | died    | no                             |
### Table 1. Cont.

| Patient Number | Age, Gender | Comorbidities | Duration of Hospitalization (Days) | COVID Treatment | Empiric Antimicrobial Treatment | Targeted Antimicrobial Treatment | Origin of K. pneumoniae Isolates | Superimposed Infection | Days from ICU Admission to the Isolation of K. pneumoniae NDM in Urine | The Highest Concentration of IL-6 | The Highest Concentration of PCT | The Highest Concentration of CRP | Outcome | Occurrence of Clostridioides difficile |
|----------------|-------------|---------------|-----------------------------------|-----------------|-------------------------------|---------------------------------|---------------------------------|----------------------|---------------------------------------------------------------|--------------------------|-----------------------------|---------------------------|----------|----------------------------------|
| 16             | 44, M       |               | 22                                | steroids        | vancomycin meropenem fluconazole | colistin amikacin               | blood urine respiratory tract rectum | A. baouenevi            | 3                               | 670.2       | 30.6                        | 27.6         | died                      | no                      |
| 17             | 35, F       | obesity       | 22                                | steroids        | PIP/TAZO linezolid             | colistin amikacin TMT/SMX       | urine                           | A. baouenevi            | 13                              | NA          | 12.71                      | 14.9         | alive                     | no                      |
| 18             | 70, M       | hypertension  | 19                                | vancomycin meropenem fluconazole chloramphenicol | * | urine respiratory tract rectum | A. baouenevi            | 13                              | NA                              | 1.7                    | 33.4                     | died                      | no                    |
| 19             | 77, F       | hypertension  | 18                                | netidoxime      | chloramphenicol               | * | urine respiratory tract rectum | A. baouenevi            | 12                              | NA          | 0.31                       | 27.3         | died                      | no                      |
| 20             | 61, M       | steroids   | 33                                | tocilizumab     | chloramphenicol PIP/TAZO       | colistin amikacin               | urine respiratory tract rectum | A. baouenevi            | 6                               | 1331.5      | 2.83                        | 23.7         | alive                     | no                      |
| 21             | 61, M       | steroids   | 38                                | chloramphenicol | PIP/TAZO                     | colistin tigecycline fosfomycin fluconazole | urine respiratory tract rectum | A. baouenevi            | 22                              | 89.8        | 0.40                       | 21.8         | alive                     | no                      |
| 22             | 45, M       | obesity     | 12                                | steroids        | none                          | * | urine                           |                  | 6                               | NA          | 0.67                       | 15.4         | died                      | no                      |
| 23             | 58, M       | steroids   | 34                                | steroids        | PIP/TAZO meropenem vancomycin  | colistin TMT/SMX fluconazole    | urine                           |                  | 25                              | NA          | 0.44                       | 33.9         | alive                     | no                      |

CHD—coronary heart disease; CRP—C reactive protein (values in mg/dL); F—female; M—male; MRSA—methicillin resistant Staphylococcus aureus; amox/clav—amoxicillin/clavulanate; IL-6—interleukin 6 (normal range <5.9 pg/mL); PIP/TAZO—piperacillin/tazobactam; PCT—procalcitonin, serum concentration (ng/mL); TMT/SMX—trimethoprim/sulfamethoxazole; * patient died before targeted antimicrobial treatment was administered.
Table 2. Antimicrobial susceptibility and resistance of K. pneumoniae NDM strains isolated from urine samples of all 23 patients.

| Antimicrobial Agent       | Susceptibility | Resistance |
|---------------------------|----------------|------------|
|                           | n   | Percent   | n   | Percent   |
| amikacin (AM)             | 0   | 0.0%      | 23  | 100%      |
| amoxicillin/clavulanate (AMC) | 0   | 0.0%      | 23  | 100%      |
| cefepime (FEP)            | 0   | 0.0%      | 23  | 100%      |
| cefotaxime (CTX)          | 0   | 0.0%      | 23  | 100%      |
| ceftazidime (CAZ)         | 0   | 0.0%      | 23  | 100%      |
| cefuroxime (CF)           | 0   | 0.0%      | 23  | 100%      |
| cefuroxime axetil (CFA)   | 0   | 0.0%      | 23  | 100%      |
| ciprofloxacin (CIP)       | 0   | 0.0%      | 23  | 100%      |
| colistin (CS)             | 18  | 78.26%    | 5   | 21.74%    |
| fosfomycin (FOS)          | 12  | 52.17%    | 11  | 47.83%    |
| gentamycin (GN)           | 2   | 8.70%     | 21  | 91.30%    |
| imipenem (IMI)            | 0   | 0.0%      | 23  | 100%      |
| meropenem (MEM)           | 0   | 0.0%      | 23  | 100%      |
| norfloxacin (NOR)         | 0   | 0.0%      | 23  | 100%      |
| piperacillin/tazobactam (TZP) | 0   | 0.0%      | 23  | 100%      |
| tigecycline (TGC)         | 1   | 4.35%     | 22  | 95.65%    |
| tobramycin (TOB)          | 0   | 0.0%      | 23  | 100%      |
| trimethoprim/sulfamethoxazole (SXT) | 11  | 47.83%    | 12  | 52.17%    |

Figure 1. Antimicrobial agents administered in empiric and targeted therapy in critically ill COVID-19 patients hospitalized in ICU infected with Klebsiella pneumoniae NDM.

4. Discussion

In total, 23 of 103 patients (22.33%) hospitalised in the ICU between 1 March and 30 June 2021, mainly men, had a positive microbiological result for K. pneumoniae NDM.
The incidence of carbapenem-resistant *K. pneumoniae* isolation and the gender profile of the patients was similar to the data of Mędrzycka-Dąbrowska et al. [15]. Contrary to their data, in our study, the pathogen was most commonly isolated from urine, not samples from the respiratory tract or the blood.

The incidence of *K. pneumoniae* NDM in our cohort was quite similar to the results of Bentivegna et al. [16], who reported a higher incidence of MDR pathogens in COVID-19 departments compared with other hospital wards (29% vs. 19%), as well as the findings reported by Montrucchio et al. [17]. The high incidence of *K. pneumoniae* NDM may result from complex thoracic pathology related to the COVID-19 infection, mechanical ventilation, exposure to carbapenems and β-lactam/β-lactamase inhibitors, renal replacement therapy, transfusions, and extended inpatient stay [18].

The SARS-CoV-2 infection has a profound impact on the immune system of the infected patients. We still do not know whether coronavirus infection triggers a typical immune response, with cooperation between the natural killer (NK) cells and natural antibodies. However, there is no doubt that the individual immune response is essential in determining the clinical course of SARS-CoV-2 infection [19]. Some parameters were proposed as indicators of individual reactions to the virus and are related to the infection’s clinical course. Hu et al. [20] found a decreased number of lymphocytes, including CD4, CD8, and NK cells, in severe COVID-19 patients. Our study did not analyse the number and changes in such cell lines.

The meta-analysis of Feng et al. [21] found PCT > 0.5 ng/mL, CRP > 10 mg/L a risk factors for disease progression in patients with COVID-19. Moreover, Sayah et al. [22] found that the cut-off value for prediction of mortality is: for IL-6: 83 pg/L (sensitivity 96.3%, specificity 87.6%), for CRP: 15.1 mg/dL (sensitivity 70.4%, specificity 80.0%), for PCT: 0.16 ng/mL (sensitivity 96.3%, specificity 70.5%). In our analysis, of the patients who exceeded these values, 4/7 (57.14%) in the IL-6 group, 14/21 (66.67%) in the PCT group, and 13/19 (68.42%) in the CRP group died. However, a relatively small number of participants makes the comparison of such results pretty difficult.

We administered steroids to all patients to decrease the coronavirus-induced cytokine storm. However, Karruli et al. [23] suggest that MDR infections were more frequent when steroid therapy was administered. It may be one of the reasons for the high incidence of such infections in our cohort.

The information on the relations between the administration of remdesivir and MDR incidence is limited. Nevertheless, it could be pretty challenging to find such a link.

We administered tocilizumab in one case only. Data from Aljuhani et al. [24] revealed the lack of association between such treatment and the incidence of MDR.

The most frequently administered antimicrobial agent in our cohort was colistin, followed by meropenem, vancomycin, ceftriaxone, linezolid, piperacillin/tazobactam trimethoprim/sulfamethoxazole, amikacin, amoxicillin/clavulanate, tigecycline, ciprofloxacin, fosfomycin, clindamycin, and cloxacillin. Comparing such data with the results of other authors is quite tricky, mainly due to the limited data regarding antimicrobial treatment in critically ill patients with COVID-19. In their analysis of 19 studies from China, the United States, Brazil, and Denmark comprising 2834 patients infected with SARS-CoV-2, Chedid et al. [25] found that the primary rate of antibiotic usage was 74%, and the most frequently used antimicrobials were fluoroquinolones, followed by ceftriaxone and azithromycin. Carbapenems were used quite seldomly. One must bear in mind that comparing the whole population of patients infected with SARS-CoV-2 with those who require critical care may produce a critical bias. However, the wide use of antimicrobial agents facilitates the spread of MDR pathogens [26].

The higher incidence of MDR pathogens in patients with COVID-19 compared with the non-COVID-19 population resulting from comprehensive administration of broad-spread antimicrobial agents and selection of resistant pathogens, has been confirmed by Liew et al. [27]. Moreover, the presence of *K. pneumoniae* NDM in the patient room environment, the number of invasive procedures, the inappropriate use of personal protective equipment, and the
transmission of pathogens between caregivers and patients may play a role in the aetiology and incidence of such infections [28].

In four of 23 cases (17.4%), we observed both bacterial and fungal infection. These patients died. Such incidence is much higher than noted by Rawson et al. [29], Nori et al. [30], or Hughes et al. [31]. The higher coinfection rate may be the consequence of the patients’ immune state or the fact that all patients analysed in our study received steroids. However, the data reported by Baiou et al. [32] did not support such an observation.

Fourteen of 23 patients positive for *K. pneumoniae* NMD carried this bacterium (60.9%). In recent years, the spread of carbapenemase-producing *K. pneumoniae* has increased in hospitalised patients [33]. However, there are limited data on its incidence in the population of hospitalised patients infected with SARS-CoV-2.

The main limitations of our study are its retrospective design, the lack of clonality data of *K. pneumoniae* NDM isolates, and the fact that it is a single-centre report of only 23 cases; therefore, it is difficult to generalise our results. Moreover, we did not consider the consumption of antimicrobial agents in the study period. Our analysis did not determine how many patients had their position changed to prone. This information could provide some insight because Tiri et al. [10] found that 67% of patients who had changed their posture to a prone position were colonised by carbapenem-resistant Enterobacteriaceae compared with 37% of patients whose posture had not been changed.

5. Conclusions

In conclusion, the high incidence of *K. pneumoniae* NDM in our study may result from the clinical profile of hospitalized patients, frequent administration of steroids, and excessive workload of medical personnel, which, due to deficiencies, may lower the standard of sanitary care. Identifying these causes is necessary to reduce the incidence of MDR pathogens and, consequently, improve treatment outcomes.

**Author Contributions:** Conceptualization, A.G., Z.R. and D.T.; Data curation, A.W.-K.; Formal analysis, A.G. and D.T.; Investigation, A.G.; Methodology, A.G.; Project administration, A.G., Z.R., A.W.-K. and D.T.; Visualization, D.T.; Writing—original draft, A.G., Z.R. and D.T.; Writing—review & editing, A.G., Z.R., A.W.-K. and D.T. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of the Military Institute of Medicine (protocol code 37/WIM/2021 of 15 December 2021).

**Informed Consent Statement:** Informed consent was waived because no intervention was involved, and no patient identifying information was included.

**Data Availability Statement:** The data presented in this study are available on request from the corresponding author.

**Acknowledgments:** The authors would like to thank Marcin Moźański and Anna Rychlik for their valuable effort and help to collect the clinical data.

**Conflicts of Interest:** The authors declare no conflict of interest.

**References**

1. COVID-19 Coronavirus Pandemic. Available online: https://www.worldometers.info/coronavirus/ (accessed on 7 January 2022).
2. Grasselli, G.; Pesenti, A.; Cecconi, M. Critical Care Utilization for the COVID-19 Outbreak in Lombardy, Italy: Early Experience and Forecast During an Emergency Response. *JAMA* 2020, 323, 1545. Available online: https://jamanetwork.com/journals/jama/fullarticle/2763188 (accessed on 7 January 2022). [CrossRef] [PubMed]
3. Livingston, E.; Bucher, K. Coronavirus Disease 2019 (COVID-19) in Italy. *JAMA* 2020, 323, 1335. [CrossRef] [PubMed]
4. Wang, D.; Hu, B.; Hu, C.; Zhu, F.; Liu, X.; Zhang, J.; Wang, B.; Xiang, H.; Cheng, Z.; Xiong, Y.; et al. Clinical Characteristics of 138 Hospitalized Patients with 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. *JAMA* 2020, 323, 1061. [CrossRef] [PubMed]
5. Wu, Z.; McGoogan, J.M. 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, 1239. [CrossRef]

6. Murthy, S.; Archambault, P.M.; Atique, A.; Carrier, F.M.; Cheng, M.P.; Codan, C.; Daneman, N.; Dechert, W.; Douglas, S.; Fiest, K.M.; et al. Characteristics and outcomes of patients with COVID-19 admitted to hospital and intensive care in the first phase of the pandemic in Canada: A national cohort study. *Can. Med. Assoc. Open Access J.* 2021, 9, E181–E188. [CrossRef]

7. Arentz, M.; Yim, E.; Klaff, L.; Lokhandwala, S.; Riedo, F.X.; Chong, M.; Lee, M. Characteristics and Outcomes of 21 Critically Ill Patients with COVID-19 in Washington State. *JAMA* 2020, 323, 1612. [CrossRef]

8. Richardson, S.; Hirsch, J.S.; Narasimhan, M.; Crawford, J.M.; McGinn, T.; Davidson, K.W.; Barnaby, D.P.; Becker, L.B.; Chelico, J.D.; Cohen, S.L.; et al. Presenting Characteristics, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area. *JAMA* 2020, 323, 2052. [CrossRef]

9. Porretta, A.D.; Baggiani, A.; Arzilli, G.; Casigliani, V.; Mariotti, T.; Mariottini, F.; Scardina, G.; Sironi, D.; Totaro, M.; Barnini, S.; et al. Increased Risk of Acquisition of New Delhi Metallo-beta-Lactamase-Producing Carbapenem-Resistant Enterobacteriaceae (NDM-CRE) among a Cohort of COVID-19 Patients in a Teaching Hospital in Tuscany, Italy. *Pathogens* 2020, 9, 635. [CrossRef]

10. Tiri, B.; Sensi, E.; Marsiliani, V.; Cantarini, M.; Priante, G.; Vernelli, C.; Martella, L.A.; Costantini, M.; Mariotti, A.; Andreani, P.; et al. Antimicrobial Stewardship Program, COVID-19, and Infection Control: Spread of Carbapenem-Resistant Klebsiella Pneumoniae Colonization in ICU COVID-19 Patients. What Did Not Work? *J. Clin. Med.* 2020, 9, 2744. [CrossRef]

11. Kampmeier, S.; Tönnes, H.; Correa-Martinez, C.L.; Mellmann, A.; Schwierzeck, V. A nosocomial cluster of vancomycin resistant enterococci among COVID-19 patients in an intensive care unit. *Antimicrob. Resist. Infect. Control* 2020, 9, 154. [CrossRef]

12. Nori, P.; Szymczak, W.; Puius, Y.; Sharma, A.; Cowman, K.; Gialanella, P.; Fleischner, Z.; Corpuz, M.; Torres-Isasiga, J.; Bartash, R.; et al. Emerging Co-Pathogens: New Delhi Metallo-beta-lactamase producing Enterobacteriaceae Infections in New York City COVID-19 Patients. *Int. J. Antimicrob. Agents* 2020, 56, 106179. [CrossRef] [PubMed]

13. European Centre for Disease Prevention and Control. Risk Assessment on the Spread of Carbapenemase-Producing Enterobacteriaceae (CPE): Through Patient Transfer between Healthcare Facilities, with Special Emphasis on Cross-Border Transfer; Publications Office: Luxembourg, 2011. Available online: https://data.europa.eu/8or/doi/10.2900/59034 (accessed on 7 January 2022).

14. Clinical Breakpoints—Breakpoints and Guidance. Available online: https://www.eucast.org/clinical_breakpoints/ (accessed on 7 January 2022).

15. Mędrzycka-Dąbrowska, W.; Lange, S.; Zorena, K.; Dąbrowski, S.; Ozga, D.; Tomaszek, L. Carbapenem-Resistant Klebsiella pneumoniae Infections in ICU COVID-19 Patients—A Scoping Review. *J. Clin. Med.* 2021, 10, 2067. [CrossRef] [PubMed]

16. Bentivegna, E.; Luciani, M.; Arcari, L.; Santino, I.; Simmaco, M.; Martelletti, P. Reduction of Multidrug-Resistant (MDR) Bacterial Infections during the COVID-19 Pandemic: A Retrospective Study. *Int. J. Environ. Res. Public Health* 2021, 18, 1003. [CrossRef] [PubMed]

17. Montrucchio, G.; Corcione, S.; Sales, G.; Curtoni, A.; de Rosa, F.G.; Brazzi, L. Carbapenem-resistant Klebsiella pneumoniae in ICU-admitted COVID-19 patients: Keep an eye on the ball. *J. Glob. Antimicrob. Resist.* 2020, 23, 398–400. [CrossRef]

18. Mathers, A.J.; Vegesana, K.; German-Mesner, I.; Ainsworth, J.; Pannone, A.; Crook, D.W.; Sifri, C.D.; Sheppard, A.; Stoesser, N.; Peto, T.; et al. Risk factors for Klebsiella pneumoniae carbapenemase (KPC) gene acquisition and clinical outcomes across multiple bacterial species. *J. Hosp. Infect.* 2020, 104, 456–468. [CrossRef]

19. Salinas, A.F.; Mortari, E.P.; Terreri, S.; Quintarelli, C.; Pulvirenti, F.; Di Cecca, S.; Guercio, M.; Milito, C.; Bonanni, L.; Auria, S.; et al. SARS-CoV-2 Virus Induced Atypical Immune Responses in Antibody Defects: Everybody Does their Best. *J. Clin. Immunol.* 2021, 41, 1709–1722. [CrossRef]

20. Hu, C.; Li, J.; Xing, X.; Gao, J.; Zhao, S.; Xing, L. The effect of age on the clinical and immune characteristics of critically ill patients with COVID-19: A preliminary report. *PLoS ONE* 2021, 16, e0248675. [CrossRef]

21. Feng, X.; Li, S.; Sun, Q.; Zhu, J.; Chen, B.; Xiong, M.; Cao, G. Immune-Inflammatory Parameters in COVID-19 Cases: A Systematic Review and Meta-Analysis. *Front. Med.* 2020, 7, 301. [CrossRef]

22. Sayah, W.; Berkane, I.; Guermache, I.; Sabri, M.; Lakhal, F.Z.; Rahali, S.Y.; Djidjeli, A.; Merah, F.; Belaid, B.; Berkani, L.; et al. Interleukin-6, procalcitonin and neutrophil-to-lymphocyte ratio: Potential immune-inflammatory parameters to identify severe and fatal forms of COVID-19. *Cytokine* 2021, 141, 155428. [CrossRef]

23. Karruli, A.; Boccia, F.; Gagliardi, M.; Patauner, F.; Uris, M.P.; Sommese, P.; de Rosa, R.; Murino, P.; Ruocco, G.; Corcione, A.; et al. Multidrug-Resistant Infections and Outcome of Critically Ill Patients with COVID-19 Disease 2019: A Single Center Experience. *Microb. Drug Resist.* 2021, 27, 1167–1175. [CrossRef]

24. Aljuhani, O.; Al Sulaiman, K.; Alshabasy, A.; Eljaaly, K.; Al Shaya, A.I.; Nourdeelne, H.; Aboudeif, M.; Al Dosari, B.; Alkhalaif, A.; Korayem, G.B.; et al. Association between tocilizumab and emerging multidrug-resistant organisms in critically ill patients with COVID-19: A multicenter, retrospective cohort study. *BMC Infect. Dis.* 2021, 21, 1127. [CrossRef] [PubMed]

25. Chedid, M.; Waked, R.; Haddad, E.; Chetata, N.; Saliba, G.; Choucay, J. Antibiotics in treatment of COVID-19 complications: A review of frequency, indications, and efficacy. *J. Infect. Public Health* 2021, 14, 570–576. [CrossRef] [PubMed]

26. Artega-Livasia, K.; Pinzas-Acosta, K.; Perez-Abad, L.; Panduro-Correa, V.; Rabaan, A.A.; Pecho-Silva, S.; Dámaso-Mata, B. A multidrug-resistant *Klebsiella pneumoniae* outbreak in a Peruvian hospital: Another threat from the COVID-19 pandemic. * Infect. Control Hosp. Epidemiol.* 2021, 43, 267–268. [CrossRef] [PubMed]
27. Liew, Y.; Lee, W.H.; Tan, L.; Kwa, A.L.; Thien, S.Y.; Cherng, B.P.; Chung, S.J. Antimicrobial stewardship programme: A vital resource for hospitals during the global outbreak of coronavirus disease 2019 (COVID-19). *Int. J. Antimicrob. Agents* 2020, 56, 106145. [CrossRef] [PubMed]

28. Amarsy, R.; Jacquier, H.; Munier, A.L.; Merimèche, M.; Berçot, B.; Mégarbane, B. Outbreak of NDM-1-producing Klebsiella pneumoniae in the intensive care unit during the COVID-19 pandemic: Another nightmare. *Am. J. Infect. Control* 2021, 49, 1324–1326. [CrossRef] [PubMed]

29. Rawson, T.M.; Moore, L.S.; Zhu, N.; Ranganathan, N.; Skolimowska, K.; Gilchrist, M.; Satta, G.; Cooke, G.; Holmes, A. Bacterial and Fungal Coinfection in Individuals with Coronavirus: A Rapid Review to Support COVID-19 Antimicrobial Prescribing. *Clin. Infect. Dis.* 2020, 71, 2459–2468. [CrossRef] [PubMed]

30. Nori, P.; Cowman, K.; Chen, V.; Bartash, R.; Szymczak, W.; Madaline, T.; Katiyar, C.P.; Jain, R.; Aldrich, M.; Weston, G.; et al. Bacterial and fungal coinfections in COVID-19 patients hospitalized during the New York City pandemic surge. *Infect. Control Hosp. Epidemiol.* 2021, 42, 84–88. [CrossRef]

31. Hughes, S.; Troise, O.; Donaldson, H.; Mughal, N.; Moore, L.S.P. Bacterial and fungal coinfection among hospitalized patients with COVID-19: A retrospective cohort study in a UK secondary-care setting. *Clin. Microbiol. Infect.* 2020, 26, 1395–1399. [CrossRef]

32. Baiou, A.; Elbuzidi, A.A.; Bakdach, D.; Zaqout, A.; Alarbi, K.M.; Bintahe, A.A.; Ali, M.M.; Elarabi, A.M.; Ali, G.A.; Daghfal, J.; et al. Clinical characteristics and risk factors for the isolation of multi-drug-resistant Gram-negative bacteria from critically ill patients with COVID-19. *J. Hosp. Infect.* 2021, 110, 165–171. [CrossRef]

33. Parisi, S.G.; Bartolini, A.; Santacatterina, E.; Castellani, E.; Ghirardo, R.; Berto, A.; Franchin, E.; Menegotto, N.; de Canale, E.; Tommasini, T.; et al. Prevalence of Klebsiella pneumoniae strains producing carbapenemases and increase of resistance to colistin in an Italian teaching hospital from January 2012 to December 2014. *BMC Infect. Dis.* 2015, 15, 244. [CrossRef]