Carbapenem-resistant *Klebsiella pneumoniae* in ICU-admitted COVID-19 patients: Keep an eye on the ball

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**Abstract**

Here we report on seven intensive care unit (ICU) patients with coronavirus disease 2019 (COVID-19)-related acute respiratory distress syndrome (ARDS) who developed positive rectal swabs and invasive infections due to carbapenemase-producing *Klebsiella pneumoniae* (CP-Kp). Notwithstanding the infection prevention measures introduced during the COVID-19 pandemic and changes in the hospitalised population, attention to CP-Kp infections must remain high, especially in the critically ill setting.

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1. Introduction

Bacterial and viral infections are common complications of viral pneumonia, especially in critically-ill patients, as evidenced during the 2003 severe acute respiratory syndrome coronavirus (SARS-CoV) epidemic, when Gram-negative bacteria (GNB) and *Candida* caused the largest number of secondary infections [1]. It follows that assessing the risk of difficult-to-treat bacterial superinfections such as those caused by GNB is crucial in all suspected cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; 2019 novel coronavirus) infection [2].

Patients with coronavirus disease 2019 (COVID-19) are, in fact, particularly at risk of developing superinfections, especially those caused by multidrug-resistant (MDR) pathogens, despite the improvements in infection control procedures worldwide adopted during the COVID-19 outbreak, the changes in overall hospital admissions for other conditions [3], the considerably younger age and the absence of multiple co-morbidities [4].

Due to the fact that, prior to the COVID-19 outbreak, Italy had an endemic situation regarding the spread of MDR infections, mainly due to carbapenemase-producing *Klebsiella pneumoniae* (CP-Kp) [5], we evaluated the incidence and time course of CP-Kp infections during their intensive care unit (ICU) stay in a cohort of ICU patients affected by COVID-19-related acute respiratory distress syndrome (ARDS).

2. Materials and methods

From 1 March to 20 May 2020, all COVID-19 patients with ARDS admitted to the ICU at ‘Città della Salute e della Scienza’ Hospital in Turin (Italy) were studied. Bloodstream infection (BSI) and ventilator-associated pneumonia (VAP) were defined according to the European Centre for Disease Prevention and Control (ECDC). Matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF), Microscan WalkAway plus System (Beckman Coulter, Brea, CA, USA) and MASTDISCS® *Combi Carba plus* disk system (Mast Group Ltd., Bootle, UK) were used for bacterial identification, antimicrobial susceptibility testing and to characterise carbapenemase-producing isolates, respectively. Detection of carbapenem resistance genes was carried out using an Xpert Carba-R assay (Cepheid, Sunnyvale, CA, USA). Antimicrobial susceptibility was
Among 35 patients, 7 had a positive rectal swab for CP-Kp and bilateral pulmonary infiltrates (Table 1). Six patients developed invasive infections and one patient was colonised by CP-Kp during their ICU stay (two patients were positive for CP-Kp at ICU admission). Six of the seven patients were transferred from other hospitals. The median [interquartile range (IQR)] Sequential Organ Failure Assessment (SOFA) score, Simplified Acute Physiology Score (SAPS) and Acute Physiology and Chronic Health Evaluation (APACHE) II score at ICU admission were, respectively, 12 (11-13), 54 (51–60) and 25 (24–26), whilst the median (IQR) MULBSTA score [6] was 9 (9–10). The median (IQR) duration of COVID-19 symptoms before hospital admission was 7 (4–7) days, whilst the median (IQR) duration of ICU stay and mechanical ventilation was 34 (24–40) days and 34 (23–40) days, respectively.

The median (IQR) time between CP-Kp infection and hospital and ICU admission was 13 (12–19) days and 12 (7–15) days, respectively. Six patients developed VAP and five had contextual BSI, in all of five of whom the infection resulted in septic shock with high vasopressor requirement.

All of the patients received hydroxychloroquine, five of them received antiviral treatment and four were treated with tocilizumab. Corticosteroids were given in all but one patient (dexamethasone 8 mg every 8 h, with variability according to different hospitals in transferred patients). At ICU admission, 71.4% of patients had lymphopenia. All patients had been previously treated with broad-spectrum antibiotics (all of them with β-lactams, five with azithromycin, two with doxycycline and three with vancomycin), in five cases with a documented prior bacterial co-infection before CP-Kp, including three VAP and two BSI caused by *Pseudomonas aeruginosa* (n = 2), extended-spectrum β-lactamase (ESBL)-producing *K. pneumoniae* (n = 1), coagulase-negative staphylococcus (n = 1) and *Enterococcus faecium* (n = 1), respectively. We observed two deaths within 28 days and five deaths in the ICU in seven patients. Mortality related to CP-Kp septic shock was 28.6%.

### 4. Discussion

Few articles are reporting about secondary infections in COVID-19, but some data confirm that superinfections were identified in 13.5–44% of ICU patients owing to various pathogens, including MDR-GNB [2].

Known risk factors for the development of CP-Kp infections do not appear fully applicable in this cohort of patients [4]. In fact, our population was relatively young and free of significant co-morbidities, except obesity (57.1%). The reduction in hospital access for all causes [3], apart from those due to COVID-19, should, at least theoretically, have contributed to a reduction in the dissemination of MDR pathogens. Furthermore, infection control procedures are highly implemented in the context of the COVID-19 pandemic to ensure safety for healthcare workers, maximising contact precautions.

Conversely, factors potentially implicated in the risk of MDR infections are increased patient transfer caused by the pandemic affecting the whole of Northern Italy, previous broad-spectrum antibiotic treatment before hospital admission, the presence of other previous invasive bacterial co-infection, and the severity of the patient cohort requiring venovenous extracorporeal membrane oxygenation (VV-ECMO) support in 71.4% of cases and continuous renal replacement therapy in 28.6%. In particular, in patients undergoing ECMO, colonisation by MDR-GNB is frequent.
Gastrointestinal colonization with multidrug-resistant Gram-negative bacteria during extracorporeal membrane oxygenation: effect on the risk of subsequent infections and impact on patient outcome. Ann Intensive Care 2019;9:141, doi: http://dx.doi.org/10.1186/s13613-019-0615-7.

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