

TITLE: CARBAPENEMASE-PRODUCING *Klebsiella pneumoniae* SEQUENCE TYPES 11 AND 16 CAUSING CO-INFECTION IN PATIENTS WITH COVID-19 IN A TERTIARY HOSPITAL, BRAZIL

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ABSTRACT:

Carbapenemase-producing *Klebsiella pneumoniae* (CPKP) is often associated with nosocomial infections leading to death. Reports of co-infection caused by CPKP in patients with coronavirus disease 2019 (COVID-19) have been recurrent and reported as a serious complication. Therefore, this study aimed to investigate and characterize the occurrence of CPKP causing infection in patients with COVID-19 admitted from May, 2020, to January, 2021, to intensive care units (ICU) in a tertiary hospital located in the state of São Paulo. Identification and antimicrobial susceptibility (AS) test were performed by automated system. Molecular typing was performed by *Xba*I-PFGE. Based on those results, representative isolates were selected for screening of *bla*_{KPC} and *bla*_{CTX-M}, as well as for MLST. A total of 142 isolates were recovered from tracheal aspirate (n=68), urine (n=59) or blood (n=15) from 109 patients. The AS profiles demonstrated that 73% of the isolates were carbapenem-resistant, and almost 27% of them were resistant to polymyxin B. The *Xba*I-PFGE typing distinguished 24 clusters, two of them with 14 and 13 isolates, respectively. Such isolates were obtained from different patients with up to six months among samplings. Furthermore, we also observed different strains causing co-infections in the same patient. Sixty-three isolates were selected based on *Xba*I-PFGE typing, only 2 susceptible to cephalosporins and carbapenems. The *bla*_{CTX-M} and *bla*_{KPC} genes were screened in 61 and 51 isolates, and were detected in 77% and 94%, respectively. CTX-M-1-like was the most prevalent variant (81%), followed by CTX-M-2-like (15%) and CTX-M-9-like (4%). Twelve different STs (11, 15, 16, 20, 29, 134, 258, 307, 405, 839, 1109 and 3506) were identified, being ST 11 (46%) and ST 16 (35%) the most detected, both harboring *bla*_{KPC} and *bla*_{CTX-M}. Our findings indicated that strains of the same clone, especially ST11 and ST16, are cause of serious infections in COVID-19 patients admitted in different periods in the same hospital, evidencing their transmission and circulation. Most of these strains were resistant to carbapenems, which are preventively used in COVID-19 patients at ICU admission. *bla*_{KPC} was the genetic determinant responsible for this phenotype. In addition,

a quarter of CPKP were resistant to polymyxin B, the last therapeutic option. All of this alert for the necessity for the correct adherence to infection control and prevention measures.

Keywords: *Klebsiella pneumoniae*, co-infection, COVID-19, antibiotic resistance, molecular typing

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