TITLE: Species frequency and clonality in Klebsiella isolates producing NDM or co-producing KPC and NDM

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ABSTRACT:
Introduction: The *Klebsiella* genus has often been detected in serious health care-associated infections. The acquisition of multiple antimicrobial resistance genes, in particular those encoding carbapenemases, represents a major challenge in controlling its spread and in treating infections caused by this genus. Carbapenems are still the main antimicrobials used in the treatment of serious infections by Gram-negative bacilli in hospitalized patients and the main mechanism of resistance to this group of antimicrobials is the production of carbapenemases, particularly of the KPC and NDM types. KPC-2producers are widespread in Brazilian hospitals, while NDM-1 producers and KPC-2 and NDM-1 co-producers have an increasing incidence, but still do not exceed the frequency of KPC producers. The genus most frequently detected as a producer of NDM in Brazil is *Klebsiella*, but in the studies that studied the frequency of NDM in *Klebsiella* in Brazil, there is no differentiation between the species *K. variicola, K. Quasipneumoniae* and *K. pneumoniae*. Objective: To evaluate the frequency of species of the *K. pneumoniae* complex among isolates producing NDM or co-producing NDM and KPC. Methods: A total of 63 NDM-producing isolates of the *K. pneumoniae* complex, previously identified by MALDI-ToF-MS, from the collection of bacteria from Grupo Fleury, detected in 2018 and 2019, were analyzed. The production of metallo-β-lactamase was confirmed phenotypically using meropenem discs with EDTA and by PCR for *bla*NDM and *bla*KPC. Species identification was performed by multiplex PCR as previously described by Fonseca et al. The NDM and KPC co-producer isolates were also evaluated for their clonal relationship, by PFGE, after digestion with XbaI. Results: Among the 63 isolates analyzed, 3.2% were identified as *K. variicola*; 22.2% *K. quasipneumoniae* and 74.6% *K. pneumoniae*. As for the carbapenemase genes, 22.2% had the *bla*NDM and *bla*KPC genes and 77.8% had only *bla*NDM. The PFGE of the KPC and NDM co-producers showed that isolates from the same clonal groups are present in three major states in the country. Conclusions: *K. pneumoniae* was the predominant species among NDM producers, but *K. variicola* corresponds to about ¼ of the isolates. The presence of the same clone co-producer of NDM and KPC was observed in three Brazilian states.

Keywords: *Klebsiella;* NDM*;* co-producing NDM and KPC.

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