TITLE: FIRST REPORT OF BKC-1-PRODUCING *KLEBSIELLA PNEUMONIAE* (KPN) OUTBREAK IN A TEACHING HOSPITAL - SÃO PAULO, BRAZIL

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ABSTRACT:
BKC-1 is a class A carbapenemase first described among Brazilian KPN isolates in 2015. Only five KPN isolates carrying *bla*$_{BKC-1}$ were reported so far. However, the frequency of BKC-1 might be underestimated because the producing isolates usually show low carbapenem MICs due to BKC-1 weak carbapenemase activity. The aim of this study was to characterize microbiologically BKC-1-producing KPN isolates involved in the first reported outbreak that occurred in São Paulo, Brazil. A total of 647 KPN clinical isolates with decreased carbapenem susceptibility were retrospectively selected from the bacterial collection of a teaching hospital in São Paulo, between 2008 and 2017. The isolates were screened for *bla*$_{BKC-1}$ by PCR. For those isolates positive for *bla*$_{BKC-1}$ the presence of other resistance genes was also investigated. All amplicons were submitted to DNA sequencing. Bacterial identification was confirmed by MALDI-TOF MS. The genetic similarity was performed by PFGE and MLST and the antimicrobial susceptibility profile was determined by EUCAST broth microdilution (BMD): Sixteen BKC-1-producing KPN isolates were detected (2.47%) during 2010 (n=1), 2011 (n=14), and 2012 (n=1). Such isolates were recovered from different hospital units and clinical specimens, as following as: 68.8% (11/16) from blood; 18.8% (3/16) from tracheal aspirate; and 6.3% (1/16) from post-operative wound cultures. The PFGE analysis showed two distinct patterns. Fourteen isolates belonged to cluster A (A1, n=13; A2, n=1) and two isolates belonged to cluster B. The 14 isolates belonging to cluster A were very similar to those five BKC-1-producing KPN previously published. One isolate included in cluster A1 belongs to ST442. The MIC_{50}/MIC_{90} values were, respectively: 8/512 µg/mL for meropenem (range, ≤1 to 512), 8/128 µg/mL for imipenem (range, 2 to 256), 32/512 µg/mL for ertapenem (range, ≤1 to 1,024), and 32/128 µg/mL for polymyxin B (range, ≤0.125 to 128). High MICs were also observed for ceftriaxone, cephalothin, cefoxitin, aztreonam, and ciprofloxacin for all BKC-1 producing isolates. Interestingly, the co-production of *bla*$_{BKC-1}$ and *bla*$_{KPC-2}$ genes was also identified in five isolates included in cluster A1. We reported for the first time an outbreak caused by BKC-1-producing KPN isolates in Brazil after a surveillance study. Our data shows that the BKC-1 dissemination is ongoing within Brazilian hospitals and, worst, not recognized by clinical labs and infection control teams.

Keywords: *Klebsiella pneumoniae*, BKC-1, carbapenem, outbreak.

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