TITLE: EMERGENCE OF *BLA*$_{GES}$ AND *BLA*$_{CTX-M}$ IN A NOSOCOMIAL *KLEBSIELLA PNEUMONIAE* STRAIN ISOLATED IN A TEACHING HOSPITAL IN NORTHEAST OF BRAZIL

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ABSTRACT:
β-Lactamases are the most important mechanism of β-lactam drug resistance in Gram-negative bacteria. The GES enzymes have mainly been found in *Pseudomonas aeruginosa*, but the enzymes have also been observed in members of *Enterobacteriaceae*. The enzymes of the GES family differ from each other by one to four amino acid substitutions. Currently, the phylogenetically closest related β-lactamase to the GES family enzymes is BEL-1 from *P. aeruginosa* with identities ranging from 50% to 51%. Isolates producing GES enzymes with carbapenemase activity have been collected predominantly in Europe, South Africa and the Far East. The aim of the current study was to report the presence of the *bla*$_{GES}$ and *bla*$_{CTX-M}$ genes in clinical *Klebsiella pneumoniae* ESBL producer isolated from a newborn with nosocomial infection admitted in a teaching hospital in Sobral, Ceará, Northeast of Brazil. A clinical *K. pneumoniae* isolate carrying the extended-spectrum β-lactamase gene variant *bla*$_{GES}$ and *bla*$_{CTX-M}$ was recovered from a blood culture of a newborn preterm, with nine days of life, gestational age fixed 33 weeks and five days, weighing 1,742 grams, in the neonatal ICU in a teaching hospital in Brazil's Northeast from June 2015. The minimum inhibitory concentrations (MICs), resistance patterns, and phenotypic detection of ESBL production were determined using the Vitek® 2 compact automated system. Polymerase chain reaction (PCR) amplification was used to detect the presence of gene encoding GES and CTX-M enzymes. For amplification of *bla*$_{GES}$, as previously described, the following primers were used: 3'-AGCAGCTCAGATCGGTGTTG-5' and 3'-CCGTGCTCAGGATGAGTTG-5', and the pair of primers 3'-ATG TGCAGYACCAGTAA-5' (CTX-M 1/2-F) and 5'-CGCTGCCGGTTTTATCSCCC-3' (CTX-M 1/2-R) was used for amplification of a sequence of 512 base pairs for CTX-M family. The MIC for amikacin, ceftriaxone and cefuroxime was ≥ 64μg/mL, and additional resistance to ampicillin/sulbactam (MIC ≥32μg/mL) was observed. However, this strain analyzed demonstrated sensibility for carbapenems, ciprofloxacin, and tigecycline. These results show the emergence of *bla*$_{GES}$ and *bla*$_{CTX-M}$ in clinical *K. pneumoniae* strain in Brazil, suggesting a great potential for dissemination of *bla* genes into nosocomial pathogens. To our knowledge, the clinical *K. pneumoniae* isolate reported in this study, harboring *bla*$_{GES}$ and *bla*$_{CTX-M}$ genes, is the first report of this ESBL genes in nosocomial *K. pneumoniae* isolated from Brazil.

Keywords: Antimicrobial resistance; *bla*$_{GES}$ gene; CTX-M; *Klebsiella pneumoniae*; nosocomial infection.

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