TITLE: DISSEMINATION OF MULTIDRUG RESISTANT *KLEBSIELLA PNEUMONIAE*: EVALUATION OF *BLA*$_{CTX-M}$ AND VIRULENCE FACTORS IN CLINICAL KPC-2-PRODUCING ISOLATES

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ABSTRACT

Klebsiella pneumoniae is often involved with healthcare-associated infections in Brazil, and has a great ability to develop or acquire antimicrobial resistance. This study investigated the clonal dissemination and prevalence of sequence types (STs) in clinical strains of *K. pneumoniae* carrying *bla*$_{CTX-M}$ and *bla*$_{KPC}$ genes, as well as the presence of genes encoding virulence factors. Non-duplicated 60 *K. pneumoniae* isolates were randomly selected from a collection recovered from inpatients at the Clinical Hospital of the Federal University of Uberlândia (HC-UFU) from June 2009 to July 2015. Were selected 30 carbapenem-sensitive (KpSC) strains isolated from infections; 30 carbapenem-resistant *K. pneumoniae* (KpRC) strains, 20 isolated from infections and 10 from colonizations. For investigation of the *bla*$_{CTX-M}$ and *bla*$_{KPC}$ resistance genes and its association with virulence genes (*fimH, fimA, wabG, iucC, rmpA, ecpA, mrkD* and *khe*), the strains were evaluated by PCR. DNA sequencing was performed to confirm the presence of *bla*$_{KPC-2}$ gene. The pulsotypes, STs and clonal complexes (CCs) were determined by PFGE and MLST, respectively. Significant differences were found when patients infected by KpSC and KpRC were compared, especially the high previous use of β-lactams (53%), carbapenems (73.3%) and polymyxin B (43.3%) in KpRC group. Inadequate therapy, although prevalent in 56.7% of the patients, was much higher (70%) among those with KpRC infections. Regarding the presence of resistance genes, 80% of strains carried *bla*$_{CTX-M}$ gene and 100% of carbapenem-resistant isolates the *bla*$_{KPC-2}$ gene. Virulence genes were detected with high frequencies in both groups, not associated with resistance to carbapenems. However, among the KpRC strains, the *fimH*, *fimA* and *wabG* genes were predominant (83%). It was observed polyclonal dissemination of strains with predominance of MLST STs 11 and 340, belonging to the clonal complex 258. The knowledge of the virulence factors and the pathogenic potential of ESBL and carbapenemases-producing *K. pneumoniae* contribute to a better understanding of colonization, pathogenicity and persistence of these microorganisms in the hospital environment and can provide tools to improve the treatment of serious infections as well as subsidies to improve infection control and prevention measures.

Keywords: polyclonality, multiresistance, carbapenems, virulence

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