TITLE: CHARACTERIZATION OF PLASMIDS CARRYING *bla*$_{KPC}$ AND *bla*$_{NDM}$ GENES IN EXTENSIVELY DRUG-RESISTANT *KLEBSIELLA PNEUMONIAE* ISOLATES FROM BRAZIL.

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ABSTRACT:
Carbapenemase-producing *Klebsiella pneumoniae* has gained prominence due to its wide distribution, constituting a serious threat to public health and must be constantly monitored through epidemiological surveillance. The carbapenemases genes, like *bla*$_{KPC}$ and *bla*$_{NDM}$ usually are carried by plasmids that are fundamental genetic elements in the process of horizontal transmission genes. In this scenario, to understand the diversity of plasmids carrying carbapenemases genes, our group performed a genomic analysis of the plasmid profile of *K. pneumoniae* strains from different Brazilian regions. Genomes were sequenced using the Illumina platform, followed by assembly using Unicycler program. The Mob-recon tool was used to reconstruct individual plasmid sequences using the FASTA file from each genome and access plasmid's typing information, including replicon types. All quantitative analysis were performed using *perl* and *ssh* scripts from the generated data. Antibiotic susceptibility tests were performed using the disk diffusion technique, following the BrCast standards. Among 58 carbapenemase-producing *K. pneumoniae* investigated (KPC n=41, NDM n=14, and KPC plus NDM n=3), an extensive drug resistance profile was found for all. Were detected 61 plasmids encoding carbapenemases, which were grouped into 25 clusters, and classified in 24 different replicon types. Despite the plasmid diversity evidenced, we can highlight IncFIB and IncFII as important types carrying both *bla*$_{KPC}$ and *bla*$_{NDM}$ genes. Analyzing plasmids from KPC-producing *K. pneumoniae* (n=44), 32% contain IncFII, followed by IncFIB (29%), IncU (16%), IncX3 (14%), and IncN (14%). Among strains harboring KPC-plasmids, 59% belong to CC258. All isolates carrying plasmids containing only IncN replicon belong to CC258. A total of 44% strains from ST258 contain plasmids classified both as IncU and IncX3 (4/9). Among plasmids from NDM-producing *K. pneumoniae* (n=17), the most frequent replicon types were IncFII and IncFIB (47% for both). Therefore, we evidence a multiple pattern of plasmids/lineages dissemination among carbapenemase-producing *K. pneumoniae*. This reinforces the need for an ongoing understanding the content and dissemination of plasmids.

Keywords: plasmids, *Klebsiella pneumoniae*, antimicrobial resistance, IncFIB, IncFII.

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