Molecular characterization of NDM-1-Producing *Klebsiella pneumoniae* isolates from Rio de Janeiro, Brazil

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Resumo:

New Delhi Metallo-β-lactamase (NDM), first identified in a *K. pneumoniae* (2008) became the focus of worldwide attention due to the rapid dissemination and limitation of antimicrobial therapeutical options. Since the first description of this gene in Brazil (2013), in a *Providencia rettgeri* isolate, some reports of NDM-1-producing isolates from diverse species have been described in different Brazilian states, suggesting a rapid spread in this country. In this study, we characterized 16 NDM-1-producing *K. pneumoniae* isolates from Rio de Janeiro state, Brazil. Bacterial identification was performed by conventional techniques, antibiotic susceptibility was determined by disk diffusion method and Etest, phenotypic carbapenemase production was tested by double-disk diffusion test with EDTA, boronic acid and cloxacillin, the presence of virulence and resistance genes was investigated by PCR and sequencing. PCR was used to determine the flanking region of bla_{NDM-1} gene. PFGE and MLST were carried out to investigate the genetic relatedness. The strains were recovered between Sep/2013 and Sep/2014 from surveillance rectal swabs (7), urine (3), blood (4), catheter tip (1) and liquor (1) samples from non-consecutive patients in different hospitals of three cities of Rio de Janeiro state. The isolates were not susceptible to all β-lactams (100%), except for aztreonam (69%), gentamicin, ciprofloxacin and sulfamethoxazole/trimethoprim (75%). Nevertheless the isolates remained susceptible to amikacin (81%), fosfomycin/trometamol (94%), polymyxin B (81%), and tigecycline (69%). PFGE and MLST analysis identified different pulsotypes and sequence types, suggesting that the spread of the bla_{NDM-1} gene in Rio de Janeiro is not related to specific clones. All strains were positive phenotypically for metallo-β-lactamase production and possessed $bla_{NDM-1.}$ Other resistance genes were also found (bla_{KPC}, bla_{TEM}, bla_{SHV}, bla_{CTX-M}, *rmtD*, *qnrA*, *qnrB*, *qnrS*, *aadA*, *aadB*, *aac(3)-Iia*, *aac(6')-Ib*). Virulence genes observed were *entB* (100%), *fimH* (100%), *yfcM* (100%), *mrkD* (100%), *allS* (6%), *kfU* (75%), and *ybt*S (25%). The bla_{NDM-1} gene was found associated to IS*Aba125* upstream and ble_{MBL} gene downstream. These results indicate the diversity of NDM hosts even in the same species, and the rapid and easy spread. We also highlight the presence of an NDM-producing *K. pneumoniae* polymyxin B resistant which increases a concern since the therapeutic options become more limited.

Palavras-chaves: NDM-1, *Klebsiella pneumoniae*, virulence, Rio de Janeiro

Agência Fomento: CNPq, CAPES, FAPERJ