

TITLE: Comparison of virulence genes detected in KPC-producing *Klebsiella pneumoniae* isolated from infection and colonization

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ABSTRACT:

KPC-producing *Klebsiella pneumoniae* (KPC-Kp) has become an important public health issue. In addition, *K. pneumoniae* possesses different virulence factors that contribute to its pathogenicity including lipopolysaccharide, capsular polysaccharide, adhesions, and siderophores. Besides that, the prior intestinal colonization by KPC-Kp has been identified as a risk factor associated with progression to infections. The purpose of this study was to compare the detection of virulence genes in KPC-Kp collected from human infection and colonization sources in Brazil. This study included 76 KPC-Kp isolates collected from different sources of hospitalized patients from 2009 to 2013 from 14 Brazilian states. The isolates were identified by conventional biochemical techniques. The gene *bla*_{KPC} was identified by PCR followed by Sanger sequencing. Multi-locus Sequence Typing (MLST) was performed to identify genetic similarities. The virulence factor-encoding genes *cf29a*, *ycfM*, *mrkD*, *fimH*, (adhesion), *entB*, *iroN*, *kfu*, *ybtS* (siderophores), *magA* (hypermucoviscous phenotype), *allS* (allantoin metabolism) were searched by PCR. The isolates were recovered from hospitals located in the states of Alagoas (1), Amazonas (1), Ceará (3), Federal District (15), Espírito Santo (9), Goiás (4), Maranhão (5), Minas Gerais (6), Mato Grosso (1), Paraíba (2), Pernambuco (9), Rio de Janeiro (12), Rio Grande do Sul (3), and Santa Catarina (5); comprising all geographical regions of the country. The isolates were collected in 2009 (1), 2010 (36), 2011 (20), 2012 (3), and 2013 (16), from colonization samples of rectal swabs (44), and infection sources (32) as blood (14), urine (9), catheter (5), and others (4). The MLST revealed 38 STs, with a prevalence of STs 11 (21%), 437 (14%), 340 (7%), and 37 (5%), being 47% from clonal complex 258 (CC258). The research for virulence determinants identified *entB* (100%), *fimH* (100%), *ycfM* (100%), *mrkD* (96%), *ybtS* (74%), *kfu* (13%), and *allS* (3%). The *iroN*, *magA* and *cf29a* genes were not detected. Most of isolates presented five (68%) virulence determinants, and there were no differences in the detection of virulence determinants between CC258 and non-CC258 isolates, both groups had \bar{X} =4.8 genes/isolate. Comparing the gene detection with the source isolation, we found a significant association between *ybtS* and rectal swab ($p=0.0005$).

These findings suggest a probable role of *ybtS* gene in the dynamic progression of intestinal colonization to infection by KPC-*Kp*.

KEYWORDS: *Klebsiella pneumoniae*; Virulence; KPC; Colonization; Infection.

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