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P0920 Epidemiology and evolutionary genetics of Klebsiella pneumoniae in antimicrobial-resistant clones using whole-genome sequencing

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Background: *Klebsiella pneumoniae* is increasingly recognised as a serious threat to human life due to multidrug-resistant (MDR) and hypervirulent strains causing life-threatening infections globally. Here we used *K. pneumoniae* genomic data to quantify basic parameters of MDR epidemiology and to understand the relationship between common clonal groups, the genetic diversity of antimicrobial resistance (AMR) and to address the co-occurrence and the order in which MDR occurs at the genetic level.

Materials/methods: A whole genome single nucleotide polymorphism phylogeny and metadata from 3,585 *K. pneumoniae* isolates were retrieved from the NCBI database. Sequence types (STs) and clonal groups (CGs) were identified by comprehensive searches of the Pasteur MLST database and metadata of the original publications. AMR genes were identified using two databases, namely the Comprehensive Antibiotic Research Database and NCBI Pathogen Detection. Co-occurrence analysis was based on a probabilistic model of species co-occurrence using the R 'cooccur' package. Ancestral reconstruction was performed using three alternative approaches (maximum parsimony, maximum likelihood and stochastic mapping) in R.

Results: Beta-lactamase genes were the most frequent AMR genes identified, followed by aminoglycoside resistance genes. CG258 consisting of approximately 70% of isolates was the most prevalent clone. Furthermore, 85% of CG258 strains contained AMR genes that confer resistance to at least three antibiotic drug classes. CG258 co-occurrence analysis showed positive associations between AMR genes that confer resistance to four antibiotic drug classes, namely carbapenem, aminoglycoside, fluoroquinolone and fosfomycin. *OmpK37* was identified in CG258I at 34%, CG43 at 15% and CG143 at 41%. For the co-occurrence analysis, there was a positive association between extended-spectrum beta-lactamase producing genes and aminoglycoside resistance genes ($p < 0.05$). Aminoglycoside resistance genes had a positive association with fluroquinolone and fosfomycin resistance genes in more than 80% of selected CGs ($p < 0.01$). Colistin resistant isolates were not identified. An analysis of four clades suggested that emergence of resistance against carbapenem was always preceded by the emergence of resistance against aminoglycoside.

Conclusions: This study provides an example of the use of publicly available whole genome databases for studying genetic mechanisms behind AMR evolution, thus making online genomics a powerful tool for AMR surveillance.