

L-24 EPIDEMIOLOGY OF CARBAPENEMASE PRODUCING ENTEROBACTERIALES IN THE CZECH REPUBLIC

**IBRAHIM BITAR^{a*}, MONIKA DOLEJSKA^a, COSTAS
C PAPAGIANNITSIS^b, JAROSLAV HRABAK^a**

^a Department of Microbiology, Faculty of Medicine, Charles University, Alej svobody 76, Plzeň, 32300, Czech Republic,

^b Department of Microbiology, University Hospital of Larissa, Larissa, 41334, Greece
ibrahimbitar5@gmail.com

Carbapenemases are versatile β -lactamases capable of hydrolyzing carbapenem antibiotics. They are classified into Ambler classes A, B, and D. Class A carbapenemases, such as *Klebsiella pneumoniae* carbapenemase (KPC) and Guyana extended-spectrum β -lactamase (GES), hydrolyze penicillins, cephalosporins, carbapenems, and aztreonam. Class B carbapenemases, defined by their metallo- β -lactamase (MBL) structures, hydrolyze all β -lactams except aztreonam. While class D carbapenemases, including oxyacillin-hydrolyzing carbapenemase (OXA) enzymes, have decreased hydrolyzing activity against carbapenems and penicillins.

In this study, we deliberate the emergence, gene transition, and continuous spread of carbapenemase-producing *Enterobacterales* in the Czech Republic, to develop a snapshot of the epidemic distribution in correlation to carbapenem resistance gene (CRG) repertoire, we explored the genomes of 791 different *Enterobacterales* collected between 2018–2023. Understanding the factors that cause CRE to spread so successfully in the Czech Republic is crucial to curtail its dissemination and prevent it from becoming nationally untreatable.



Fig. 1. Carbapenemases distribution in the Czech Republic; circles in orange, red, green, dark blue, yellow corresponds to NDM-4, NDM-5, NDM-1, KPC and OXA-48-Like respectively

Out of the 791 isolates sequenced, 212 were NDM producers with 68 NDM-4, 44 NDM-5 and 100 NDM-1. Moreover, 99/791 were KPC producers, 79 were OXA-48 like producers and 12 VIM-producers.

Regarding NDM-4; a major clonal outbreak has been detected in Plzeň. 30/68 was identified as *E. hormaechei* ST 182. *C. freundii* ST100 also played a role in the outbreak but in smaller numbers. Nevertheless, even with the detection of this clonal outbreak, the gene was carried on an IncX3 plasmid that has been identified in the same hospital 7 years ago, and thus dissemination is mainly plasmid mediated.

NDM-5 was also identified as a clonal outbreak of *E. coli* ST 38 in Brno. The gene here is carried within the chromosome and the outbreak is deemed as clonal.

NDM-1 corresponds to most of the cases with different outbreaks of: *K. pneumoniae* ST321 in Ceska Lipa (#9), *K. pneumoniae* (36 different STs) and *P. mirabilis* (#13) in Cesky Brod, *K. pneumoniae* (#8) in Ostrava and 50 *K. pneumoniae* (mainly ST11) in Prague. The data shows that all genes are carried on different plasmid types and sizes and rarely on chromosome indicating the involvement of different plasmids in the dissemination of this variant.

Regarding KPC, 54 isolates of different species and STs in Hradec Kralove with *E. Hormaechei* ST421 being the most abundant (#9) and 22 isolates of different species and STs in Prague. Again, the data shows that all genes are carried on different plasmid types and sizes and rarely on chromosome indicating the involvement of different plasmids in the dissemination of this variant.

Finally, OXA-48 were the most abundant in both Plzeň and Prague where the data shows the dissemination is plasmid mediated by the well previously described IncL plasmid in the Czech Republic and the world.

In conclusion, the data shows that there are multiple factors that is mediating carbapenem resistance in the Czech Republic, ranging from clonal outbreaks such the *E. coli* NDM-5 in Brno to plasmid mediated like the NDM-4 IncX3 plasmid in Plzeň and Prague. To a smaller extent, integrons are also playing a role such as Int110 in the cases of VIMs. Continues monitoring is required to deal with rapid dissemination.

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