27th ECCMID Vienna, Austria 22 – 25 April 2017
The congress of ESCMID

Session: OS175 Origin, dissemination and impact of mcr genes

Category: 3b. Resistance surveillance & epidemiology: Gram-negatives

25 April 2017, 09:00 - 09:10
OS0866

MCR-1 dispersion in clinically relevant clones of multidrug-resistant and copper-tolerant Salmonella from Portugal

Joana Campos*[1], Luís Cristino[2], Sofia Ribeiro[2], Joana Vanessa Cordeiro Melro Mourão[3], Patricia Antunes[4], Luisa Maria Vieira Peixe[3]

[1]*Requimte – Rede de Quimica e Tecnologia; Laboratório de Microbiologia, Faculdade de Farmácia, Universidade Do Porto*

[2]*Faculdade de Ciências Da Nutrição e Alimentação, Universidade Do Porto*

[3]*Requimte/Ucibio, Laboratório de Microbiologia, Faculdade de Farmácia, Universidade Do Porto*

[4]*Faculdade de Ciências Da Nutrição e Alimentação, Universidade Do Porto. Ucibio/Requimte. Laboratório de Microbiologia, Faculdade de Farmácia*

Background: Colistin is frequently the only therapeutic alternative in infections with multidrug-resistant Gram-negative bacteria. The first transferable gene conferring colistin resistance, *mcr-1* gene, was recently described in *Enterobacteriaceae* from several sources in China. Further worldwide reports of *mcr-1*, and of its variant *mcr-2* until now sporadic, have been associated mostly with animal sources, suggesting that its emergence is due to extensive colistin use in food-producing animals. However, the possibility of other antimicrobial agents (e.g. metals) contributing to their emergence has not been demonstrated. In this study, the presence of *mcr* genes in several *Salmonella* serotypes/clones obtained from different sources and regions of Portugal (2002-2016) was investigated, as well as, their possible relationship with presence of genes conferring tolerance to metals widely used in food-animal production.

Material/methods: We analysed a total of 1351 *Salmonella* isolates (2002-2016) of at least 66 serotypes, from several sources (human clinical cases/food products/food-animal production settings/aquatic environments) and regions, for the presence of *mcr-1* and *mcr-2* genes by PCR/sequencing. The isolates with *mcr* genes were further tested for susceptibility to colistin and

other antibiotics (ampicillin-A/chloramphenicol-C/ciprofloxacin-Cp/gentamicin-G/kanamycin/meropenem/nalidixic acid-Na/pefloxacin-P/streptomycin-S/sulfametoxazole-Su/tetracycline-T/trimethoprim-Tr/cefepime/ceftazidime/cefotaxime/cefoxitin-Fx/amoxicillin-clavulanic acid) by microdilution and/or disk diffusion methods, according to EUCAST/CLSI. Further, detection of other antibiotic resistance and MT genes (copper/silver-*pcoD*+*silA*/tellurium-*terF*/mercury-*merA*) (PCR/sequencing), conjugation assays, plasmid characterization (presence of *ISApl*1/PCR-PBRT/pMLST/sequencing), genomic location (I-CeuI/S1-PFGE-hybridization) and clonal relatedness (XbaI-PFGE/MLST) were performed.

Results: In this study, *mcr-2* was not detected, but *mcr-1* was present in 1.3% (n=17/1351) of the studied isolates, including of clinical origin (CL; n=5/674), pork-products (P; n=11/442) and food-animal production settings (FP; n=1/59), from several regions between 2011 and 2016. All presented resistance $MIC_{Colistin}$=4-8 mg/L and co-resistance to other antibiotics and mostly carried several MT genes, particularly to copper (all but one carrying *silA*+*pcoD* on the chromosome). They belonged to clinically relevant MDR clones of *S.*1,4,[5],12:i:- [n=13-ST34/STnew-European clone-CL+P+FP-ASSuT±CCpP(Na)GTr], *S.*Typhimurium [n=2-ST34-European clone-P-ASSuTTr±FxCpP(Na)C; n=1-ST19-DT104 clone-CL-ACSSuT] or *S.*Rissen (n=2-ST469-P-ACSSuTr±T), frequently associated with pig production and human infections. The *mcr-1* gene, some associated with *ISApl1* (n=6/17), was located in IncX4 (n=7/~35kb/4 transferable/three serotypes) or IncHI2 (n=7/200-300kb-ST4-*terF*±*merA*/all transferable/*S.*1,4,[5],12:i:-/ *S.*Typhimurium; n=3/~120kb-non-typeable-*terF*+*merA*/non-transferable/*S.*1,4,[5],12:i:-) plasmids. Transferability of *mcr-1* was associated with a 32-64 fold increase in $MIC_{Colistin}$ and, in some isolates, with acquisition of multidrug-resistance and/or metals tolerance genes (*terF, merA*).

Conclusions: Our study evidenced the acquisition of *mcr-1* by clinically relevant MDR *Salmonella* clones, with probable origin in pigs, in Portugal since at least 2011. The dissemination of those successful MDR clones and/or plasmids with *mcr-1* is of concern, being copper tolerance a relevant feature for maintenance/amplification of *mcr-1* in *Salmonella,* which raises questions about metal-based interventions in food-producing animals (e.g. copper) to reduce colistin use and contain *mcr-1* dissemination.