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Epidemiological update of *mcr-1* producing Enterobacteriaceae clinical isolates from Argentina

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Background: Mobile polymyxins resistance mediated by *mcr* genes were recently described worldwide. *mcr-1* was generally found in *E. coli* isolates recovered from raw meat, animals, but also from human samples. This gene was mainly located in plasmids and no association with a specific clone was found. From 2012 to Oct-2017 we confirmed at the NRL, 130 colistin-resistant clinical isolates carrying *mcr* genes. The aim of the present study was to update the epidemiology of human *mcr*-producing isolates in Argentina.

Materials/methods: Colistin susceptibility was evaluated by dilution method and other antimicrobial agents by dilution or diffusion methods (CLSI). *mcr-1* and *mcr-2* genes were screened by standard PCR. Genetic relatedness was assessed by XbaI-PFGE. PCR multiplex to detect *E. coli* ST131, ST73, ST95 and ST69 clones was used. *Salmonella* spp.M1744 was used as recipient for biparental conjugation assays. S1-nuclease and DNA-hybridation was used for plasmid analysis.

Results: Until Oct-2017, 130/338 colistin-resistant ETB clinical isolates were confirmed at the NRL as positive for *mcr-1* and negative for *mcr-2*: 127 *E.coli*, 2 *Klebsiella pneumoniae* and 1 *Citrobacter amalonaticus*. These isolates were recovered from urine (74;57%), blood (17;13%) and other sites samples (39;30%). Isolates were submitted from 54 hospitals (10 provinces and Buenos Aires City). All strains were categorized as resistant to colistin (EUCAST: $\geq 4\mu\text{g/mL}$) with MIC₅₀/MIC₉₀/range: 8/8/4-16 $\mu\text{g/mL}$. Strains were resistance to: ampicillin (86%), nalidixic acid (82%), ciprofloxacin (65%), trimethoprim-sulfamethoxazole (50%), third generation cephalosporins (TGC) (48%), tetracycline (44%), minocycline (29%), gentamicin (21%), fosfomicin (21%), nitrofurantoin (4%), amikacin (3%) and imipenem (2%). All were susceptible to tigecycline. TGC-resistance was associated to (n): CTX-M (49); plasmidic-AmpC(7); SHV(2), PER(1). Two NDM (1 *E.coli* and 1 *C.amalonaticus*) and 1 KPC (*E.coli*) carbapenemases were detected. Among 110 *E. coli* analyzed by PFGE, 103 different pulsotypes were identified, 7 were repeatedly non-typeable. Of them, only two were ST131, two ST95 and three ST69. A ca. 60 kb IncI2-plasmid containing *mcr-1* was transferred by conjugation in nine *E.coli* isolates.

Conclusions: To date, *mcr-1* was mainly associated to highly diverse *E.coli* clones. The presence of an IncI2-plasmid in common could suggest the key role of horizontal dissemination among ETB clinical isolates from Argentina.