Title: FIRST DETECTION OF COLISTIN RESISTANCE MEDIATED BY MCR-1 IN *Salmonella* Choleraesuis ISOLATED IN HUMAN FROM BRAZIL.

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ABSTRACT:

Polymyxins are one group of antimicrobials polypeptides divided in A, B, C, D and E (colistin) active against the majority of gram-negative bacilli. Although, this drug present high toxicity, mainly neurotoxicity and nephrotoxicity, it being replaced at decade of 1980's for new antimicrobials of others class presenting less toxicity, but returned in decade of 1990's after the increase of infections for carbapenemase-producing Enterobacteriaceae as last option therapeutic. However, some enterobacteria strains could present resistance for this class of antimicrobials, mainly mediated by chromosomal determinants (through the modification of lipide A, reducing the affinity of polymyxin). In 2016, the first case of mobile colistin resistance (mcr-1) mediated by plasmids was reported in *Escherichia coli*. Since then, *mcr-1* gene was detected in several Gram-negative bacteria, including *Salmonella spp*. In this study, 150 *Salmonella* strains isolated from human and non-human sources between 2017 and 2019 were screened by the polymyxin drop test (at concentration of 16µg/ml of polymyxin B and colistin). Three strains (2%) of *Salmonella* presented resistance to the drop test and such phenotype was confirmed by polymyxin B and colistin broth microdilution tests, with both values of minimal inhibitory concentrations (MIC) >16µg/mL (resistant). *mcr-1* gene was detected by Polymerase Chain Reaction only in one strain of *Salmonella* Choleraesuis (466/18), and further sequenced. *mcr-2, mcr- 3, mcr-4*, and *mcr-5* genes were not detected. Additional resistances were detected (disk-diffusion) to nalidixic acid, ampicillin, chloramphenicol, streptomycin, tetracycline, and sulfonamides for 466/18 strain. Conjugative transfer of *mcr-1* was successfully achieved to *E.coli* J53 as the recipient. S1-nuclease-PFGE detected a transferable plasmid of 40kb, likely responsible for the occurrence of *mcr-1* gene (*mcr-1* gene was detected by PCR in the transconjugant). The colistin MIC of the transconjugant 466/18-trans strain increased 4-fold (4 mg/L) compared with the recipient *E.coli* J53 strain (1 mg/L) MIC test, and 16-fold to Polymyxin B. To the best of our knowledge, this is the very first report of mcr-*1* in *Salmonella* Choleraesuis strain from human source. This finding underscores the urgent need of continuous surveillance for early detection and containment of this resistance determinant to preserve the therapeutic options for the treatment of severe salmonellosis.

Key-words: *Salmonella* spp., polymyxins, MCR-1, drop test.