

TITLE: DETECTION OF MOBILE COLISTIN RESISTANCE GENE (*mcr-1*) IN HUMAN CLINICAL STRAINS OF *Escherichia coli*.

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ABSTRACT:

Polymyxin resistance is being reported increasingly in clinical strains. This resistance was detected in a new plasmid-mediated transferable resistance determinant, the *mcr-1* (mobile colistin resistance) gene. MCR-1 was originally detected in commensal *Escherichia coli* from pigs, but not long after it was associated with infectious diseases in humans. In Brazil, the *mcr-1* gene was first reported in humans in a clinical strain of *E. coli* in august 2016. Therefore, our group standardized a real-time PCR assay to detect this gene on routine MDR (multi-drug resistance) clinical strains received at a public health laboratory in Paraná. We tested all MDR strains (n=2150), including carbapenem and colistin-resistant *Enterobacteriaceae* from August, 2016 to May, 2017. PCR protocol was applied according to Chabou et. al, 2016, using specific primers and probe designed to target two different regions of the *mcr-1* gene. The *mcr-1* gene was detected in twelve *E. coli* isolates (0,56 %) recovered from eleven patients. This samples were collected in eight hospitals from different cities in Paraná (Curitiba, Londrina, Cascavel and Irati). The first isolate was sampled in October, 2016. Out of this twelve isolates, seven were from rectal swabs and five from infected samples (one from urine, two from prosthesis, one from sterile liquid and one from secretion). Four strains (4/12) confirmed to be resistant to polymyxin, exhibiting a MIC of 4 µg/ml by broth microdilution. All others strains (8/12) had a susceptible MIC of 2 µg/ml. Automated tests (Vitek-2[®], Microscan[®]) and E-Test[®] gave unreliable results for MICs such as major errors and very major errors. These isolates exhibited a multidrug-resistant phenotype, where one was resistant to carbapenems, eight to fluorquinolones and one presented an intermediated result for tygeciclin. Besides that, nine strains produced extended-spectrum-β-lactamase activity and *bla*_{KPC} and *bla*_{NDM} genes were not detected. These results showed that *E. coli mcr-1* positive strains, although have low frequency, are disseminated in clinical samples in Paraná state. Moreover, it was possible to verify that just *E.coli* species are carrying this gene and, surprisingly, most of them (75%) do not exhibit polymyxin resistance. The presence of *mcr-1* in clinical strains is alarming and requires a broader surveillance, aiming its mitigation in Brazil.

Keywords: Brazil, *E. coli*, *mcr-1* gene, real time PCR.

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