

TITLE: Resistome, mobilome and virulome of international high-risk clones of multidrug-resistant *Escherichia coli* in water sources

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ABSTRACT:

Extra-intestinal pathogenic *Escherichia coli* (ExPEC) and Diarrheagenic *E. coli* (DEC) are related to urinary tract infections and diarrheal diseases, respectively. Bacterial resistance to antimicrobials is a public health problem since multidrug-resistant (MDR) bacteria are being widely reported worldwide. Aquatic environments have been acting as reservoir and disseminator of MDR bacteria as well as the acquired antimicrobial resistance genes (ARGs). This study aimed to characterize by whole genome sequencing (WGS) MDR *E. coli* isolates obtained from water sources in Brazil. The bacterial isolation was performed using water samples from rivers and streams located in different cities of the São Paulo State. Thirty-four antimicrobials were tested and then, five MDR *E. coli* isolates were selected for WGS analysis. All isolates were resistant to ampicillin, non-extended spectrum cephalosporins, quinolones and fluoroquinolones, streptomycin and trimethoprim. Resistance to other antimicrobials was also detected, including extended-spectrum cephalosporins, aztreonam, tetracyclines, aminoglycosides, sulfonamides and chloramphenicol. Resistome analysis showed ARGs to β -lactams (*bla*_{CTX-M-14}, *bla*_{CTX-M-15}, *bla*_{TEM-1B}), fluoroquinolones (*qnrS1*), tetracyclines (*tetA*, *tetB*), aminoglycosides (*aadA2*, *aadA5*, *aac(3)-IId*, *aph(3'')-Ib*, *aph(6)-Id*, *aph(3')-Ia*), macrolides [*mph(A)*, *mdf(A)*, *Inu(F)*], trimethoprim (*dfrA8*, *dfrA14*, *dfrA17*), sulfonamides (*sul1*, *sul2*, *sul3*) and phenicols (*floR*). Mutations in quinolone resistance-determining regions of GyrA (Ser83Leu; Asp87Asn), ParC (Ser80Ile; Glu84Val; Glu84Gly) and ParE (Ile355Thr; Ser458Ala; Ile529Leu) were also detected. Mobilome analysis showed the plasmids families IncR, IncF (-2, -18, -48, -57), IncFIA1, IncFIB (-1, -49, -54), IncX1, IncN, Col440I, ColpVC and p0111. Virulome analysis showed the presence of several virulence genes, such as *iss*, *gad*, *iroN*, *iha*, *ipfA*, *sat*, *cma*, *air* and *eilA*. In addition, high-pathogenicity island (HPI) was detected in two isolates. According to virulome results, two isolates were classified as Enteroaggregative *E. coli* (EAEC). MLST, phylo-group and *fimH* typing revealed five different associations (i.e. B2-ST131/CC131-*fimH*30, B1-ST1665-*fimH*31, F-ST648/CC648-*fimH*27, B1-ST223/CC155-*fimH*32 and F-ST354/CC354-*fimH*58). This study reports the presence of international high-risk clones of MDR CTX-M-14-, CTX-M-15- and QnrS1-producing *E. coli* in Brazilian water sources, which is of great concern.

Keywords: CTX-M-like; *Escherichia coli*; MDR; QnrS1; Water.

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