

RESEARCH ARTICLE

Whole genome sequences of multi-drug resistant *Escherichia coli* isolated in a Pastoralist Community of Western Uganda: Phylogenomic changes, virulence and resistant genes

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Abstract

Background

The crisis of antimicrobial resistance is already here with us, affecting both humans and animals alike and very soon, small cuts and surgeries will become life threatening. This study aimed at determine the whole genome sequences of multi-drug resistant *Escherichia coli* isolated in a Pastoralist Community of Western Uganda: phylogenomic changes, virulence and resistant genes.

Methods

This was a laboratory based cross sectional study. Bacterial isolates analyzed in this study were 42 multidrug resistant *E. coli* isolated from stool samples from both humans (n = 30) and cattle (n = 12) in pastoralist communities collected between January 2018-March 2019. Most of the isolates (41/42) were resistant to three or more antibiotics (multi-drug resistant) and 21/42 isolates were ESBL producers; 13/30 from human and 8/12 from cattle. Whole Genome Sequencing (WGS) was carried out at the facilities of Kenya Medical Research Institute-Wellcome trust, Kilifi, to determine the phylogenomic changes, virulence and resistant genes.

Results

At household level, the genomes from both human and animals clustered away from one another except for one instance where two human isolates from the same household clustered together. However, 67% of the *E. coli* isolated from cattle were closely related to those

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Abbreviations: ESBLs, Extended spectrum β -lactamases; CTAB, Cetyltrimethylammonium bromide; DNA, Deoxyribonucleic acid; CLSI, Clinical and Laboratory Standards Institute guidelines; WGS, Whole Genome Sequencing; AMR, antimicrobial resistance; QEPA, Queen Elizabeth National Park; UNCST, Uganda National Council for Science and Technology.

found in humans. The *E. coli* isolates were assigned to eight different phylogroups: A, B1, B2, Cladel, D, E, F and G, with a majority being assigned to phylogroup A; while most of the animal isolates were assigned to phylogroup B1. The carriage of multiple AMR genes was higher from the *E. coli* population from humans than those from cattle. Among these were Beta-lactamase; blaOXA-1: Class D beta-lactamases; blaTEM-1, blaTEM-235: Beta-lactamase; catA1: chloramphenicol acetyl transferase; cmlA1: chloramphenicol efflux transporter; dfrA1, dfrA12, dfrA14, dfrA15, dfrA17, dfrA5, dfrA7, dfrA8: [macrolide phosphotransferase](#); oqxB11: RND efflux pump conferring resistance to fluoroquinolone; qacL, qacEdelta1: quinolone efflux pump; qnrS1: quinolone resistance gene; sul1, sul2, sul3: sulfonamide resistant; tet(A), tet(B): tetracycline efflux pump. A high variation of virulence genes was registered among the *E. coli* genomes from humans than those of cattle origin.

Conclusion

From the analysis of the core genome and phenotypic resistance, this study has demonstrated that the *E. coli* of human origin and those of cattle origin may have a common ancestry. Limited sharing of virulence genes presents a challenge to the notion that AMR in humans is as a result of antibiotic use in the farm and distorts the picture of the directionality of transmission of AMR at a human-animal interface and presents a task of exploring alternative routes of transmission of AMR.

Background

The crisis of antimicrobial resistance is already here with us, affecting both humans and animals alike and very soon, small cuts and surgeries will become life threatening. Evidence of non-prescribed use of antimicrobials in livestock to mask ill farming practices and misuse of antibiotics in community pharmacies has been documented globally [1, 2]. Farmers use large amounts of antibiotics in livestock and this is now known as a key driver and recipe to accelerating emergency of antimicrobial resistance [3]. Resistant bacterial clones may spread from animals to humans rendering antibiotics less effective and increases mortality and morbidity in developing nations due to such bacteria [3]. Previous studies in Uganda report abuse of antimicrobials in animal husbandry as a major contributor to antimicrobial resistance emergence among microbes. Additionally, 40% of the persons who visit a health-care facility in Uganda are treated with antibiotics [4]. These antibiotics are mostly obtained without prescription in drug shops and community pharmacies in sub-therapeutic doses. Globalization of trade coupled with the revolutionization of travel has simplified distribution of resistant bacteria due to easy movement of humans and their goods including livestock across countries making the problem of antimicrobial resistance (AMR) global in nature.

The global spread of multi-drug resistant Enterobacteriaceae especially CTX-M type ESBLs and strains producing carbapenemases such as KPC and NDM warrant a multi-stake holder attention [5]. Resistance against certain antibiotic categories is already high in hospital settings in Uganda but resistance among bacteria from animals is not well documented. Introduction of bacteria with resistant genes into food animals as a result of antibiotic selection in veterinary medicine is now of great concern. Due to the routine consumption of certain antibiotics like tetracyclines in animal husbandry, undesirable shift of resistance towards potent second line