ABSTRACT

Background

Carbapenem-resistant *Escherichia coli* (CREC) is a global public health threat, yet its emergence in neglected tropical disease (NTD) settings remains underexplored. Lymphatic filariasis (LF), characterized by chronic lymphedema and wounds, may create the conditions that pressure-select for antimicrobial resistance.

Methods

We performed whole-genome sequencing of six (6) CREC isolates from LF patients in endemic communities in Western Ghana. Genomic analysis was done to elucidate resistance mechanisms, virulence factors, mobile genetic elements, and clonal structure.

Findings

All 6 selected isolates exhibited phenotypic carbapenem resistance but lacked canonical carbapenemase genes. Resistance was linked with the presence of multiple efflux systems (e.g. *acrAB*, *medtEF*, *emrKY*), outer membrane modification genes (*eptA*, *pmrF*, *ugd*) linked to polymyxin tolerance, and variable β-lactamase profiles. Notably, virulence factors *ompA*, *astA*, and *ybt* co-occurred with resistance genes on plasmids and genomic islands. One isolate (ST131) showed a unique combination of resistance and virulence, with a virulome consistent with extraintestinal pathogenic *E. coli*. Core-genome phylogeny showed multiple lineage origins and isolate-specific accessory genomes.

Interpretation

Our results reveal a novel landscape of community-associated carbapenem resistance in *E. coli* from LF patients, driven by non-carbapenemase mechanisms, a silent development and spread of polymyxin resistance, and mobilome-driven pathoadaptation. These findings challenge healthcare-centric AMR surveillance paradigms and highlight the need to include NTD populations in the global antimicrobial resistance surveillance efforts.