Identification and Clinical Impact of Antimicrobial Resistance in *Enterobacter* Spp. Among Filarial Lymphedema Patients in the Ahanta West District, Ghana.

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ABSTRACT

The human skin microbiome, comprising diverse microbes and their interactions with the host, is crucial to understanding disease development. Secondary skin and wound infections significantly contribute to the progression of lymphatic filariasis (LF)-related lymphedema. *Enterobacter spp*., although common gut commensals, are notable Gram-negative skin bacteria that pose a high risk of biofilm-associated opportunistic infections and antibiotic resistance, particularly in immunocompromised individuals. The Enterobacter cloacae complex (ECC), classified among the multidrug-resistant "ESKAPE" pathogens, highlights the urgent need for ongoing genomic surveillance and research to address these emerging threats. This study explores the genomic landscape of *E. cloacae* from chronic filarial lymphedema wounds to pinpoint the bacterial traits responsible for antibiotic resistance and potential differences in antibiotic susceptibility. In a cross-sectional cohort study across four LF-hyperendemic communities in Ghana's Ahanta West District, we collected wound samples from 28 symptomatic filarial lymphedema patients. Using the VITEK® 2 COMPACT system, we identify the Gram-negative bacteria and performed whole genome sequencing (WGS) on isolated *Enterobacter* spp. with the Illumina MiSeq platform for genomic analysis. Of the 22 Gram-negative isolates recovered, 5 (22.7%) were identified as belonging to the *Enterobacter cloacae* species complex. Genomic analysis of the five *E. cloacae* species reveals clonal relatedness among the strains, A001_s28, A004_s39, and A065_s34, evidenced by identical alleles at all seven MLST loci. In contrast, A002_s29 and A067_s22 showed distinct allele profiles, indicating ECC genetic diversity. While a core set of virulence genes (*csgB, csgD, csgE, csgF, csgG, entA, entB, entE, entS, fepA, fepB, fepC, fepD, fepG*) was present in all isolates, isolates A065 and A067 harboured an expanded repertoire. Alarming MDR was widespread, with isolates exhibiting resistance to beta-lactams, cephalosporins, carbapenems, and other antibiotic classes, driven by genes such as *blaTEM-1*, *blaCTX-M-15*, and *fosA*, along with efflux pumps and aminoglycoside-modifying enzymes. The combination of diverse virulence factors and widespread resistance mechanisms identified underscores the public health threat posed by these *E. cloacae* strains, particularly among this vulnerable population, emphasizing the need for stringent infection control and antibiotic stewardship to prevent their spread.