

The genomic epidemiology of shigellosis in South Africa

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Shigellosis, a leading cause of diarrhoeal mortality and morbidity globally, predominantly affects children under five years of age living in low- and middle-income countries. While whole genome sequence analysis (WGS) has been effectively used to further our understanding of shigellosis epidemiology, antimicrobial resistance, and transmission, it has been under-utilised in sub-Saharan Africa. In this study, we applied WGS to large sub-sample of surveillance isolates from South Africa, collected from 2011 to 2015, focussing on *Shigella flexneri* 2a and *Shigella sonnei*. We find each serotype is epidemiologically distinct. The four identified *S. flexneri* 2a clusters having distinct geographical distributions, and antimicrobial resistance (AMR) and virulence profiles, while the four sub-Clades of *S. sonnei* varied in virulence plasmid retention. Our results support serotype specific lifestyles as a driver for epidemiological differences, show AMR is not required for epidemiological success in *S. flexneri*, and that the HIV epidemic may have promoted *Shigella* population expansion.

Shigellosis is the second leading cause of diarrhoeal death, globally^{1,2}, with the greatest disease burden on those living in low- and middle-income countries^{1,2}. Of further concern is the high burden of disease among children under five years old (around 30% of cases and 38% of deaths), with repeat childhood infections bringing long-term health consequences, including stunted growth, impaired cognitive abilities, and chronic, functional bowel disorders^{3–10}.

The causative agents, a group of Gram-negative bacteria called *Shigella*, are convergently evolved specialised pathogens of *E. coli*¹¹. Made up of four serogroups (*S. flexneri*, *S. sonnei*, *S. boydii* and *S. dysenteriae*), they share an enteroinvasive pathogenesis mediated by acquisition of the large invasion, or virulence, plasmid (pINV)¹². Each serogroup is epidemiologically distinct, though *S. flexneri* and *S. sonnei* are of primary importance due to their global distribution and high prevalence (accounting for approximately 90% of the global shigellosis

burden)^{12–15}. The two serogroups are also genetically distinct; *S. sonnei* has only one serotype and is highly clonal, while *S. flexneri* is far more diverse genetically and serotypically (having >20 different serotypes)¹⁶. Whole genome sequence analysis (WGS) on large temporo-geographical collections of both serogroups has established new genomic nomenclatures, complementing traditional serological distinctions. These differentiate *S. flexneri* into eight phylogroups, and *S. sonnei* into five Lineages, and subsequently Clades and sub-Clades^{16,17}.

The serogroups are also thought to have distinct ecologies, with a switch from *S. flexneri* dominance to *S. sonnei* being linked with increasing industrialisation¹⁸. This may be due to reduced *Fleximonas shigelloides* exposure in industrialised settings leading to reduced cross-protection against *S. sonnei* from their shared O-antigen^{19,20}. Though differences in pathogen lifestyle may also be involved, genetic

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Epidemiology Of Theilerosis In Africa

JG Myers



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