

Dynamics of TB mixed infections through space and time

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Abstract (200 words)

Mixed infections happen when at least two unrelated strains of the same pathogen can be detected in an individual. This has been linked to worse clinical outcomes in tuberculosis infections, as undetected strains presenting different antibiotic resistance profiles can lead to treatment failure. Here, we present a study of the extent of mixed infections in Georgia, a high-burden setting in which up to 11% of new TB cases are MDR/RR-TB. We obtained NGS data from cultures derived from surgery and sputum samples from 20 patients. Combined with a customized bioinformatics pipeline we enhanced the detection of multiple strains as opposed to just using a clinical sputum sample, identifying an unprecedented number of mixed infection cases of up to 40% of the patients analyzed. We also characterized transmission using 358 clinical samples and detected transmission clusters, several of which contained a sample from our surgery patients' dataset, allowing us to trace the history of several mixed infections. Our results suggest that the magnitude of mixed infections in high-burden settings is likely to be underestimated when only using sputum samples and they can be behind discrepancies between DST and WGS predictions if not properly assessed.