

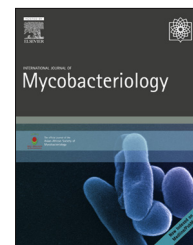


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Association of slow recovery of *Mycobacterium africanum*-infected patients posttreatment with high content of Persister-Like bacilli in pretreatment sputum

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ABSTRACT

Objectives/Background: *Mycobacterium africanum* that causes 40% of tuberculosis (TB) in West Africa grows more slowly in culture and has similar transmission capacity compared with *Mycobacterium tuberculosis*, but *M. africanum*-exposed contacts progress more slowly to active disease. The presence of lipid body (LB) containing *M. tuberculosis* complex (MTBC) cells in sputum samples has been associated with mycobacterial transcriptomes indicating slow or no growth and persister-like antibiotic tolerance. Slow-growing bacilli have been found to display a persister-like phenotype with the accumulation of LBs and drug tolerance. Our previous study showed that the body mass index and lung damage resolution on chest X-ray were significantly improved slower in *M. africanum*-infected patients post-treatment than in *M. tuberculosis*-infected patients; however, the reason for this remains unclear. Therefore, we hypothesized that these differences could be either due to significant differences in drug resistance between the MTBC lineages or a difference in their content of persisters, as indicated by the percentage of LP-positive bacilli in sputum.

Methods: Sputum isolates collected before treatment from patients with TB were subjected to drug susceptibility testing using the BD BACTEC MGIT 960 SIRE kit. The percentage of acid-fast bacilli (AFB) and LB-positive bacilli in pretreatment sputum was determined by a dual staining procedure using Auramine O and LipidTOX Red neutral lipid stain, respectively, and fluorescence microscopy imaging.

Results: Out of the 77 isolates tested, 9 showed resistance to at least one drug and only 2 showed multidrug (rifampicin and isoniazid) resistance among *M. tuberculosis*-infected patients. The percentage of AFB-positive smears was similar between the two groups ($p = 0.821$), whereas that of LP-positive bacilli was significantly higher ($p = 0.0059$) in *M. africanum*-infected patients' sputa ($n = 24$) than in *M. tuberculosis*-infected patients' sputa

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($n = 36$). In addition, the bacillary lengths were significantly higher in *M. africanum*-infected patients' sputa than in *M. tuberculosis*-infected patients' sputa ($p = 0.0007$). A high frequency of LP-positive bacilli in pretreatment sputum was associated with a poor body mass index and lung damage on chest X-ray improvement following anti-TB treatment in both the groups ($r^2 = 0.022$; $p = 0.017$).

Conclusion: The slow clinical recovery of *M. africanum*-infected patients compared with *M. tuberculosis*-infected patients posttreatment may be at least partially associated with the persistence of drug-tolerant “fat and lazy” bacilli.

Conflicts of interest

The authors have no conflicts of interest to declare.