



**Karolinska
Institutet**

Institutionen för Mikrobiologi, Tumör och Cellbiologi, Karolinska Institutet,
Avdelningen för Beredskap, Smittskyddsinstitutet och
Faculty of Veterinary, Eduardo Mondlane University, Maputo, Mozambique

Molecular characterization of *Mycobacterium tuberculosis* isolates in Mozambique

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av

Sofia Omar Viegas

Huvudhandledare:

Medicine doktor Tuija Koivula
Karolinska Institutet
Institutionen för Mikrobiologi, Tumör
och Cellbiologi
Smittskyddsinstitutet
Avdelningen för Beredskap

Bihandledare:

Professor Gunilla Källenius
Karolinska Institutet
Institutionen för Klinisk Forskning
och Utbildning
Södersjukhuset

Betygsnämnd:

Docent Håkan Miörner
Universitetssjukhuset i Lund
Avdelningen för Klinisk Mikrobiologi
och Immunologi

Professor Vinod Diwan
Karolinska Institutet
Avdelningen för Internationell Hälsa

Docent Magnus Thore
Uppsala Universitet
Medicinsk Mikrobiologi
Centrallasarettet,
Västerås

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ABSTRACT

Tuberculosis (TB) is one of the major health problems in Mozambique. It is estimated that 27,000 deaths caused by TB occur each year with an estimated incidence and prevalence rate of 431 and 504 per 100,000 population respectively. Mozambique ranks 19th on the list of 22 high-burden TB countries in the world. A steady increase in the prevalence rate of HIV/AIDS and the emergence of drug-resistant bacilli makes the situation even more precarious. Moreover, Mozambique shares geographical borders with six other countries where TB is also endemic, i.e., South Africa, Swaziland, Zimbabwe, Zambia, Malawi and Tanzania. Different genotypes of *Mycobacterium tuberculosis* complex (MTC) predominate in different geographical regions of the world and have differences in virulence, clinical presentation as well as transmission potential.

This study described the molecular epidemiology of MTC in Mozambique, identified the predominant genotypes responsible for TB transmission and prevalence, and investigated the association between predominant spoligotypes and HIV sero-status. Furthermore, the study investigated the prevalence and transmission of the Beijing genotype in Mozambique.

For the epidemiological characterization, 445 *M. tuberculosis* isolates from seven different provinces of Mozambique were characterized by spoligotyping and resulting profiles were compared with the international spoligotyping database SITVIT2. It was found that the TB epidemic in Mozambique was caused by a wide diversity of spoligotypes with predominance of the Latin-American Mediterranean (LAM, n=165 or 37%); East African-Indian (EAI, n=132 or 29.7%); an evolutionary recent but yet ill-defined T clade, (n=52 or 11.6%) and the globally-emerging Beijing clone, (n=31 or 7%); nearly equally attributed both to ancestral and evolutionary modern *M. tuberculosis* lineages with an exceptionally high biodiversity documented for the EAI, LAM and T lineages. Furthermore, the presence of predominant lineages in neighboring countries indicates TB transmission by migration from one country to another, particularly to South Africa.

To investigate the prevalence and transmission of the Beijing genotype in Mozambique, a total of 543 *M. tuberculosis* isolates, from different regions of Mozambique were spoligotyped. Of these, 33 were of the Beijing lineage.

By combined use of spoligotyping and Region of Difference (RD) deletions, we found a predominant group of 25 isolates having deletions of RD105 and RD181. Another group of three isolates lacked RD150, a signature of the reference strain “sublineage 7” recently emerging in South Africa.

A comparison with South African Beijing strains, by Restriction Fragment Length Polymorphism (RFLP) and MIRU-VNTR, suggests multiple introductions of different sublineages leading to an emerging epidemic associated with HIV.

Moreover, the majority of the Beijing strains were found in the South Region of Mozambique, particularly in the capital, Maputo city (17%). Additionally, it was found that the Beijing strains were associated with HIV positive serostatus ($p=0.049$) but not with drug resistance.