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Molecular genetics of *Mycobacterium tuberculosis* resistant to aminoglycosides and cyclic peptide testing by MTBDR*sl* in Armenia

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ABSTRACT

Objective/background: The GenoType MTBDR*sl* test rapidly detects resistance to ethambutol, fluoroquinolones, second-line aminoglycosides (amikacin [AMK] and kanamycin [KAN]), and cyclic peptides (capreomycin [CAP]) in *Mycobacterium tuberculosis*. According to data from Global Drug Resistance Surveillance Report (2007), Armenia is counted as a high-burden country for multidrug-resistant tuberculosis (MDR-TB). The estimated burden of MDR-TB in 2012 was 9.4 (7–12) and 43 (38–49) among retreatment TB cases. A total of 92 laboratory confirmed cases were reported to the World Health Organization (57 new and 35 previously treated) out of 511 cases tested for MDR-TB.

Methods: A set of 77 drug-resistant TB isolates during 2011 and 2012 period, being either acid-fast bacterium positive or negative but culture-positive resistant to isoniazid, rifampin, or both according to the GenoType MTBDR plus assay, were consecutively tested using GenoType MTBDR*sl*. *rrs* gene analysis and the results from GenoType MTBDR*sl* were compared with phenotypic drug resistance testing. The DNA preparation method was performed as recommended by the manufacturer (Genotype MTBDR plus version 1.0 and Genotype MTBDR*sl* version 2.0 Hain Lifescience Nehren, Germany).

Results: Aminoglycosides are key drugs for the treatment of MDR-TB. A total of 77 drug-resistant TB and four extensively drug-resistant *M. tuberculosis* isolates from Armenian TB patients were analyzed to characterize mutations within *rrs* and to compare with phenotypic drug resistance testing. Simultaneously, the following were identified: 65 (84.41%) *rrs* wild type (WT), 1 (1.3%) *rrs* WT MUT1 and MUT2 (WT; A1401G and G1484T), 1 (1.3%) *rrs* WT1, MUT1 (A1401G), 9 (11.7%) *rrs* WT1, MUT1 (A1401G), and 1 (1.3%) *rrs* WT1, MUT1. Mutation at position 1401 in *rrs* leads to resistance to KAN (7/77 = 9%), AMK (9/77 = 11.68%), and CAP (5/77 = 6.49%). Eleven (14.28%) streptomycin-resistant strains had a *rrs* mutation.

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Conclusion: Isolates with *rrs* structural gene mutations were cross-resistant to streptomycin, KAN, CAP, and AMK. Detection of the A1401G mutation appeared to be 100% specific for the detection of resistance to KAN and AMK. Being the first assessment, these data establish the presence of phenotypic drug-resistant and extensively drug-resistant strains using molecular profiling and are helpful in understanding aminoglycoside resistance on a molecular level.

Conflict of interest

There is no conflict of interest to declare.

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