

## Comparative Study of Mutations Associated with Second Line Drug Resistance and Genetic Background of Mycobacterium tuberculosis Strains

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**Abstract :** Background: Performance of Genotype MTBDRsl (Hain Life science GmbH Germany) for detection of mutations associated with second-line drug resistance is well known. However, less evidence regarding the association of mutations and genetic background of strains is known which, in the future, is essential for clinical management of anti-tuberculosis drugs in those settings where the probability of particular genotype is predominant. Material and Methods: During this retrospective study, a total of 259 MDR-TB isolates obtained from pulmonary TB patients were tested for second-line drug susceptibility testing (DST) using Genotype MTBDRsl VER 1.0 and compared with BACTEC MGIT-960 as a reference standard. All isolates were further characterized using spoligotyping. The spoligo patterns obtained were compared and analyzed using SITVIT\_WEB. Results: Of total 259 MDR-TB isolates which were screened for second-line DST by Genotype MTBDRsl, mutations were found to be associated with *gyrA*, *rrs* and *emb* genes in 82 (31.6%), 2 (0.8%) and 90 (34.7%) isolates respectively. 16 (6.1%) isolates detected mutations associated with both FQ as well as to AG/CP drugs (XDR-TB). No mutations were detected in 159 (61.4%) isolates for corresponding *gyrA* and *rrs* genes. Genotype MTBDRsl showed a concordance of 96.4% for detection of sensitive isolates in comparison with second-line DST by BACTEC MGIT-960 and 94.1%, 93.5%, 60.5% and 50% for detection of XDR-TB, FQ, EMB, and AMK/CAP respectively. D94G was the most prevalent mutation found among (38 (46.4%)) OFXR isolates (37 FQ mono-resistant and 1 XDR-TB) followed by A90V (23 (28.1%)) (17 FQ mono-resistant and 6 XDR-TB). Among AG/CP resistant isolates A1401G was the most frequent mutation observed among (11 (61.1%)) isolates (2 AG/CP mono-resistant isolates and 9 XDR-TB isolates) followed by WT+A1401G (6 (33.3%)) and G1484T (1 (5.5%)) respectively. On spoligotyping analysis, Beijing strain (46%) was found to be the most predominant strain among pre-XDR and XDR TB isolates followed by CAS (30%), X (6%), Unique (5%), EAI and T each of 4%, Manu (3%) and Ural (2%) respectively. Beijing strain was found to be strongly associated with D94G (47.3%) and A90V mutations by (47.3%) and 34.8% followed by CAS strain by (31.6%) and 30.4% respectively. However, among AG/CP resistant isolates, only Beijing strain was found to be strongly associated with A1401G and WT+A1401G mutations by 54.5% and 50% respectively. Conclusion: Beijing strain was found to be strongly associated with the most prevalent mutations among pre-XDR and XDR TB isolates. Acknowledgments: Study was supported with Grant by All India Institute of Medical Sciences, New Delhi reference No. P-2012/12452.

**Keywords :** tuberculosis, line probe assay, XDR TB, drug susceptibility

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