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Mutations in rpoB, katG and inhA Genes: The Association with Resistance to Rifampicin and Isoniazid in Egyptian Mycobacterium tuberculosis Clinical Isolates

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Abstract : The rapid detection of TB and drug resistance, both optimizes treatment and improves outcomes. In the current study, respiratory specimens were collected from 155 patients. Conventional susceptibility testing and MIC determination were performed for rifampicin (RIF) and isoniazid (INH). Genotype MTBDRplus assay, which is a molecular genetic assay based on the DNA-STRIP technology and specific gene sequencing with primers for rpoB, KatG, and mab-inhA genes were used to detect mutations associated with resistance to rifampicin and isoniazid. In comparison to other categories, most of rifampicin resistant (61.5%) and isoniazid resistant isolates (47.1%) were from patients relapsed in treatment. The genotypic profile (using Genotype MTBDRplus assay) of multi-drug resistant (MDR) isolates showed missing of katG wild type 1 (WT1) band and appearance of mutation band katG MUT2. For isoniazid mono-resistant isolates, 80% showed katG MUT1, 20% showed katG MUT1, and inhA MUT1, 20% showed only inhA MUT1. Accordingly, 100% of isoniazid resistant strains were detected by this assay. Out of 17 resistant strains, 16 had mutation bands for katG distinguished high resistance to isoniazid. The assay could clearly detect rifampicin resistance among 66.7% of MDR isolates that showed mutation band rpoB MUT3 while 33.3% of them were considered as unknown. One mono-resistant rifampicin isolate did not show rifampicin mutation bands by Genotype MTBDRplus assay, but it showed an unexpected mutation in Codon 531 of rpoB by DNA sequence analysis. Rifampicin resistance in this strain could be associated with a mutation in codon 531 of rpoB (based on molecular sequencing), and Genotype MTBDRplus assay could not detect the associated mutation. If the results of Genotype MTBDRplus assay and sequencing were combined, this strain shows hetero-resistance pattern. Gene sequencing of eight selected isolates, previously tested by Genotype MTBDRplus assay, could detect resistance mutations mainly in codon 315 (katG gene), position -15 in inhA promotes gene for isoniazid resistance and codon 531 (rpoB gene) for rifampicin resistance. Genotyping techniques allow distinguishing between recurrent cases of reinfection or reactivation and supports epidemiological studies.

Keywords : M. tuberculosis, rpoB, KatG, inhA, genotype MTBDRplus
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