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Abstract (poster session)

Detection of mutations associated with isoniazid resistance in multidrug-resistant *Mycobacterium tuberculosis* clinical isolates from Poland

T. Jagielski*, K. Roeske, M. Kaminski, M. Grzeszczuk, A. Napiórkowska, Z. Bakula, R. Stachowiak, E. Augustynowicz-Kopec, Z. Zwolska, J. Bielecki (Warsaw, PL)

Objective: The aim of this study was to investigate the prevalence of mutations in 7 genetic loci most frequently associated with isoniazid (INH) resistance in multidrug-resistant (MDR) *Mycobacterium tuberculosis* clinical isolates. **Material and Methods:** A total of 40 *M. tuberculosis* strains isolated from as many MDR-TB patients in Poland were included in the study. Mutations in 5 structural genes (*katG*, *inhA*, *ahpC*, *nat*, *ndh*), and 2 regulatory regions (*mabA-inhA*, *oxyR-ahpC*) were detected through PCR amplification of each locus, followed by their direct sequencing on both forward and reverse strands. The obtained nucleotide sequences were aligned against the reference sequences of the respective genes of *M. tuberculosis* reference strain H37Rv. The results were interpreted in the context of MIC values of INH and catalase activity of the strains tested. **Results:** Thirty-seven (92%) strains had mutations in the *katG* gene, with the *katG* S315T mutation being the most common (67%). Mutations at other 9 codons were distributed among 13 strains. Two strains with the wild-type 315 codon, and with the highest MIC values for INH (80 and 100 µg/mL) had unique nonsense mutations, that resulted in a severely truncated and nonfunctional catalase peptide. For the remaining 35 strains with *katG* mutations, the MICs of INH were within the range of 0.2–10 µg/mL. Thirty (75%) of those strains conserved their catalase activity. Six (15%) strains had single mutations in the *inhA* promoter region, and 2 of such strains had also single *inhA* structural gene mutations. Four strains harboured 4 different mutations in the *oxyR-ahpC* intergenic region. No mutations in the *ahpC* gene were found. Single polymorphisms in the *nat* and *ndh* genes were detected in 3 and 2 strains, respectively. Only one strain had no mutations in any of the analysed loci. **Conclusions:** The study revealed a high frequency of mutations within the *katG* gene, predominantly at codon 315, and the paucity of mutations in other inspected loci of the MDR strains. Detection of the *katG* S315T mutations may be useful for the prediction of MDR phenotype. Analysis of the *inhA*, *ahpC*, *nat*, *ndh*, *mabA-inhA*, and *oxyR-ahpC* genetic loci does not contribute considerably to the identification of multidrug resistance.