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Association of *gyrA* mutation in *Mycobacterium tuberculosis* isolates with phenotypic ofloxacin resistance detected by resazurin micro-titer assay

Asho Ali, Zahra Hasan, Sana Jafri, Raunaq Mehboob and Rumina Hasan
King Abdulaziz University, Saudi Arabia.

Background: Ofloxacin (OFX) is an important second-line anti-tuberculosis drug for the treatment of MDR-TB. This study aimed to compare mutations in quinolone-resistance determining regions (QRDR) of the *gyrA* and *gyrB* genes of *Mycobacterium tuberculosis* (MTB) isolates with MICs of OFX determined by resazurin micro-titer assay (REMA) on OFX resistance in isolates.

Methods: Thirty-nine MTB isolates collected during 2009 at the MTB bank were selected. This included 25 XDR, 3 MDR+OFX resistant and 11 OFX susceptible isolates (non-MDR). MICs for OFX were determined in duplicates by REMA method for the 39 MTB isolates as well as for control H37Rv strain. The presence of mutations in QRDR of the *gyrA* and *gyrB* genes was determined by sequencing. Then type of mutation identified on each codon was compared with MIC determined for OFX. The findings were also compared with the drug susceptibility results obtained by the proportion method.

Result: Mutations were observed in the *gyrA* gene of 18 out of 28 OFX resistant MTB isolates. Frequency of mutations were 14% (n=4), 4% (n=1) and 39% (n=11) on codons 90, 91 and 94 respectively. In addition, two isolates showed concurrent mutation i.e. on 90 plus 91 and 90 plus 96 codons. Codon 94 showed more high level (4-8 µg/mL) OFX resistance as compared to codons 90 and 91. None of the OFX resistant isolates exhibited mutation in *gyrB* gene. Mutations were not observed in *gyrA* and *gyrB* gene in all the OFX susceptible as well as in control MTB strain. Agreement between phenotypic and genotypic OFX susceptibility testing was 64%.

Conclusion: Results of this study supports the use of rapid, simple and inexpensive REMA method for OFX susceptibility testing particularly for MDR-TB isolates in resource limited settings. No significant association could be linked between type of mutated codon in *gyrA* gene and level of OFX resistance.

Biography

Asho Ali has completed her PhD at the age of 44 years from the Aga Khan University. She is Assistant Professor, Microbiology at the King Abdulaziz University, Jeddah, Saudi Arabia. She has extensive academic and research experience. Her research interests are infectious diseases; particularly tuberculosis, drug resistance in bacteria and molecular mechanisms of drug resistance. In her post-doctoral research work she has worked on molecular detection of drug resistance in Extensively Drug Resistant (XDR)-TB isolates. She has published more than 20 papers in reputed journals and has been serving as reviewer in many reputed journals.

asho.ali14@gmail.com

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