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Identification of anti-TB therapy induced ADRs genetic markers using In-Silico approaches

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Introduction: Adverse drug reactions (ADRs) are associated with clinical morbidity and, in severe cases, even mortality. Globally billions of dollars are spent on managing these ADRs for common and uncommon diseases. Due to these reasons drug resistant strains have emerged and are now a serious challenge to TB eradication. To effectively deliver the available treatment regimen and ensure patient compliance it is important to manage ADRs more efficiently. Recent studies have demonstrated that drug outcomes are patient-specific and can, therefore be predicted. A few of these drugs, including a few administered for TB, have shown excellent correlation with response rates and development of ADRs.

Method: ADRs selected based on frequency of occurrence (≥1%). Anti-TB drugs were reviewed to identify the candidate genes (DMETs, HLA). Genes analysed with different web tools and databases to extract their SNPs. MAF >0.01 shortlisted using NCBI Gene and dbSNP databases (built 141). SNPs which lay in a functional domain of the gene were prioritized using SNPinfo web server (www.snpinfo.niehs.nih.gov/). Additionally, same analysis was done for Indian population.

Result: We identified 10 genes which maybe directly linked to ADRs to various anti-TB drugs, 4 of these have been documented earlier. Nearly 47 genes were identified for indirect association with ADRs by virtue of them being off-targets of the drugs. Lastly, 5 genes were reported for their allelic association with anti-TB DIH. To our knowledge, this is the first review reporting a list of possible genetic markers in context to TB ADRs to such a vast extent.

Conclusions: New gens are identified that may be associated potentially with anti-TB drug ADRs. This would translate into not just patient welfare but would also save billions of dollars spent annually on managing drug induced ADRs.

Reference:

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