

**Paper ID: PT-05****Genetic Basis of Anti-Tuberculosis Drug-Induced Liver Injury (AT-DILI)****Plenary Talk**

Heikrujam Nilkanta Meitei<sup>1</sup>, Anupama Pandey, Bidyarani Devi Konjengbam<sup>1</sup>, and  
Reena Haobam<sup>1</sup>

<sup>1</sup>Department of Biotechnology, Manipur University, Canchipur, Imphal-795003, Manipur, India

Email: reena\_haobam@rediffmail.com / reena\_haobam@manipuruniv.ac.in

**Abstract**

Anti-tuberculosis drug-induced liver injury (AT-DILI) is a severe adverse drug reaction associated with using anti-tuberculosis medications. Isoniazid, rifampicin, and pyrazinamide are potentially hepatotoxic drugs used in TB treatment. The rate of AT-DILI ranges from 2 to 28%, and this is also attributed to genetic factors. Drug metabolism genes are the major targets for association studies with AT-DILI. Some of the major genes that have been reported to be associated with DILI are N-acetyltransferase 2 (*NAT2*), glutathione S-transferase gene (*GSTM1*, *GSTT1*), Pregnane X receptor (*PXR*) etc. The present study aims to determine the prevalent genotypes of *NAT2*, *PXR*, *ABCB1*, *GSTs*, and their association with AT-DILI in the Manipuri population of India. About 450 individuals, including both controls and cases, were recruited, and genotyping of *NAT2*, *PXR*, *ABCB1*, and *GST* genes was performed using the Taqman allelic discrimination assay. Liver function tests (LFT) were also conducted to assess the liver injuries. Ten genotypes of *NAT2* were observed in the population. About 51.2% of the population were of the intermediate acetylator genotype of *NAT2*, and the variant allele 'T' of the *PXR* and *ABCB1* genes were observed to be 21.0% and 58%, respectively. The null genotypes of *GSTT1* and *GSTM1* were found to be 37.8% and 68.0%, respectively. LFT analysis in 32 follow-up patients showed that about 75% of patients developed mild AT-DILI after two months of TB treatment. Case-control analysis showed that the null genotypes of *GSTT1* and *GSTM1*, and the slow acetylator genotype of *NAT2* were associated with AT-DILI. The study revealed that most Indian Manipuri populations were carriers of ancestral alleles for *NAT2*, *PXR*, and *ABCB1*. However, the null mutation of the *GSTT1* and *GSTM1* genes was highly prevalent in the population, and they could be significant contributors to AT-DILI in TB patients along with the slow acetylator genotype of *NAT2*.

**Keywords:** Genetic polymorphism, Drug-induced liver injury, Liver function test, Drug metabolism genes, N-acetyltransferase 2, Glutathione S-transferase