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Abstract Title:- Association of NOS2A and TLR4 gene polymorphisms with susceptibility to tuberculosis in Manipuri population of northeast India.

Presenting author name :- Reena Haobam

Presenting author institute:- Manipur University

Co-authors name:- Anupama Pandey, Heikrujam Nilkanta Meitei

Co-authors institute:- Manipur University, Imphal

Aims:- This study aims to investigate the polymorphism in NOS2A (Nitric oxide synthase 2A) and TLR4 (Toll-like receptor 4) genes, and their association with susceptibility to TB in the Manipuri population of northeast India.

Methods:- In a case-control study including 495 subjects- 220 TB patients and 275 control individuals, the TaqMan allelic discrimination assay was used to study the genetic polymorphism, and Gries's Test was used to determine the serum NO levels.

Results:- Three SNPs, two for NOS2A (rs8078340 and rs2274894) and one for TLR4(rs4986791), were analyzed in the study. For one of the SNP (rs8078340) of NOS2A, a significant difference in the genotypic and allelic frequencies was observed between the case and control groups ($p < 0.05$; AA genotype OR=30.288, 95% CI: 1.703-538.44 and A allele OR=2.937, 95%CI: 1.762-4.896). However, for the second SNP (rs2274894), only the T allele (with OR= 1.464; 95%CI: 1.080-1.983, $p < 0.05$) was observed to be associated with susceptibility to TB. For the TLR4 gene, the genotypic and allelic frequencies of the SNP marker (rs4986791) were found to be significantly associated with TB susceptibility ($p < 0.05$). Homozygous CC genotype (OR=2.114; 95%CI: 1.081-4.135, $p < 0.05$) and C allele (OR=2.30; 95%CI: 1.205-4.39; $p < 0.05$) were observed to be associated with TB susceptibility. Analysis of serum NO levels shows significant differences between the study groups. Patients with susceptibility-associated AA genotype for NOS2A (rs8078340) show significantly higher serum NO levels compared to the GG and GA genotypes. However, no significant difference in serum NO levels was observed between different genotype groups for the SNP marker (rs2274894).

Conclusions:- Significant associations of homozygous AA genotype and allele A of the NOS2A (rs8078340), minor allele T of NOS2A (rs2274894), and allele C and homozygous CC genotype of TLR4 (rs4986791) with TB susceptibility were observed in the study. Patients with the AA genotype of NOS2A (rs8078340) show a higher serum NO level, suggesting its role in greater expression of the NOS2A gene.

Keywords:- Nitric oxide synthase, Toll-like receptor 4, gene polymorphism, susceptibility to tuberculosis, TaqMan allelic discrimination assay