

## Abstract

*TLR4* gene is an important gene in the immune system that induces inflammation in the body. Gene polymorphism in the *TLR4* gene can cause chronic inflammation, one of the main reasons for type 1 and type 2 diabetes. The two most studied SNPs of this gene rs4986790 and rs4986791 have been reported to be strongly associated with diabetes mellitus among different ethnicities. However, the results for these two SNPs are inconsistent among different populations. This study aims to understand the role of *TLR4* gene polymorphism (896A>G and 1196C>T) in the predisposition of diabetes Mellitus in the Pakistani population. For this purpose, a case-control study was conducted by collecting blood samples from 25 healthy people and 25 diabetic patients. PCR and DNA sequencing methods were used to analyze the polymorphism for the rs4986790 and rs4986791. Genotypic, allelic frequencies, and haplotype analysis were then examined by using SHEsis software. The results indicated that both SNPs (rs4986790 and rs4986791) were associated with an increased risk of diabetes mellitus among the Pakistani population. The GG genotype of rs4986790 and TT genotype of rs4986791 were found to be associated with DM as these genotypes have higher frequencies (0.520,0.560 respectively) in the case group. The risk alleles G and T (G (0.74, OR=0.066924, 95% CI=0.19-0.61, p=0.00005, df=1), (T (0.760, OR=0.04, 95% CI= 0.16-0.65, p=0.00001, df=1) shows its strong association with DM. Further, the haplotype analysis (chi-square= 50.930167, p=0.00005) and linkage disequilibrium values ( $r^2=0.660$ ) also prove that the rs4986790 and rs4986791 are positively associated with diabetes mellitus in Pakistan.

**Keywords:** Diabetes mellitus, *TLR4* gene, genetic polymorphism, Pakistani population