Abstract

TLR4-dependent pro-inflammatory signaling has been involved in the initiation, progression, and plaque de-stabilization stages of atherosclerosis which is the underlying cause of myocardial infarction (MI). MI is caused by reduced blood flow in a coronary artery as a result of atherosclerosis & occlusion of an artery by an embolus or thrombus. Globally, there are 32.4 million MI cases each year. It has also been recommended that particularly early-onset MI shows familial clustering. The increased hazard if a first degree blood relative before the age of 55years for male family members while 65 years for female family members has had coronary heart disease The present research was designed to determine the association of *TLR4* gene with MI in Pakistani population. For this purpose, blood samples were collected from five families with positive family history of MI. The pro-band (patient) mean age was ±50.83 years while mean BMI of the pro-band (patient) was 30.20 kg/m^2. DNA was isolated and targeted sequence was amplified by primer specific PCR reaction. Genotyping was achieved by sanger sequencing. In this study, it was observed that smoking, air pollution, Body mass index, positive family history, diabetes and hypertension were strongly responsible for development of MI. In family clustering study, TT genotype of rs4986791 was found to be significantly associated with MI while heterozygous CT of same SNP representing carrier genotype in few family members of pro band. Other SNP (Asp299Gly; rs4986790) did not show any association with MI, all subjects were homozygous for normal AA genotype. We did not found any heterozygous condition with this SNP. In case control association study, we found T allele as a risk allele having significant association ($p < 0.05$) of variant rs4986791 with MI. Moreover, allele A of rs4986790 was found as protective allele for participants. In conclusion, increasing age, high BMI, smoking, air pollution, hypertension, diabetes and (Thr399Ile; rs4986791) polymorphism are linked with MI in Pakistani population. In contrast, there was no relationship found between rs4986790 and MI risk. By family clustering study for genetic analysis, those siblings have risk genotype can save themselves in future from onset of disease or can delay the disease onset by changing their life style. However other studies with greater sample size are needed to verify our results.

Keywords: Myocardial infarction, Family clustering, *TLR4 gene*