

ABSTRACT

Type 2 diabetes mellitus is a metabolic disorder which is characterized by hyperglycemia either due to improper functioning of insulin hormone or reduced secretion of insulin hormone. Both environmental and genetic factors are major risk factors, which are involved in onset of T2DM. Present research was designed to evaluate the association of genetics of *IRS1* gene with the development of T2DM in Pakistani population and also check its inheritance pattern among families. For achieving this purpose blood samples were taken from 13 families which included both diabetic (cases) and non-diabetic (control) individuals. Two SNP's from *IRS1* gene *rs1801278* (*AiuI*) and *rs1801276* (*DraIII*) were selected for the purpose of genetic analysis. For each individual genotypic analysis was performed by Sanger sequencing techniques and PCR-RFLP technique. As compared to males, females were at higher risk for T2DM. Important risk factors as positive family history (genetics) and obesity were appeared to be major factors in onset of T2DM. Genotypic analysis of *IRS1* SNP's *rs1801278* and *rs1801276* showed that only this SNP *rs1801278* was significantly associated with T2DM but *rs1801276* did not have any contribution in T2DM. The genotype G/A for *rs1801278*, both heterozygous GA and homozygous AA mutations were identified in diabetic patients were shown to be significantly associated with T2DM. While genotype C/C for *rs1801276*, both diabetic and non-diabetic individuals in family were shown the normal wild type genotype CC that meant, there was no association of SNP with T2DM. The genotypic and phenotypic pedigree analysis were shown that association of *rs1801278* SNP of *IRS1* in diabetic patients and their families may have surprisingly effect in next generation by cause this disease at any stage of their life period. While *rs1801276* polymorphism had no effect on T2DM. It was concluded that T2DM is a serious health hazardous and continuously effecting large number of Pakistani population. Secondly, *IRS1* gene polymorphism (*rs1801278*) have a significant role in the development of T2DM, but *IRS1* gene/variants (*rs1801276*) had no impact on genetic architecture T2DM. Positive family history, physical inactivity, high blood pressure, obesity and depression are increasing the chances of onset of T2DM.

Keywords

Insulin receptor substrate 1, T2DM, polymorphism, hyperglycemia