

## Abstract

Type 2 diabetes (T2D) is one of the leading preventable cause of disease and death. It is a complex human disorder which is multi-factorial in nature where both genetic and environmental risk factors play a causal role in disease onset and progression. Genome wide association studies have confirmed more than thirty genes associated with T2D however, TCF7L2 is one of the most susceptible. TCF7L2 have been shown to be associated with T2D in multiple ethnic groups in the last decade but contradictory results were reported for Chinese and Pima Indian population. Although a number of TCF7L2 single nucleotide polymorphism (SNPs) have been studied in the European and Asian populations but the most strongly associated SNPs were rs12255372 and rs7903146. In the present study, the prevalence of TCF7L2 SNPs (rs12255372 and rs7903146) as well as the effect of risk factors that are associated with T2D was observed in Pakistani population.

A population based case-control study was carried out on 162 individuals including males (n=90) and females (n=72) with mean age 39 years ( $\pm 6.56$ ). The group was further sub grouped into cases (n=84) and controls (n=78) on the bases of diabetic and non-diabetic (healthy) individuals respectively. Demographic characteristics of subjects including age, body mass index (BMI) and fasting blood sugar (FBS) were recorded. Genetic analysis of each member of the population was carried out by tetra-primer ARMS-PCR (T-ARMS PCR) and the obtained data analyzed both descriptively and statistically by SPSS version 20. Hardy Weinberg Equilibrium (HWE) was applied to find out stratification in case-control subjects and in the entire population. Genotype, allele frequencies and chi-square was calculated to show significance of association among variables of case-controls, age, gender and BMI. Logistic regression analysis was applied to find out an association of variables with T2D. Linear regression was also used to find the effect size of genetic and environmental factors.

In case-control study of T2D associated TCF7L2 variant rs12255372, control subjects fall in Hardy Weinberg Equilibrium (HWE) with genotypes percentage 21.8%, 60.3% and 17.9% for GG, GT and TT, respectively whereas case subjects did not fall in HWE with genotypes percentage 13.2%, 71.4% and 15.4% for GG, GT and TT, respectively and appeared stratified due to the presence of lethal allele (51.2%). In cases, binary logistic regression analysis showed that GT genotype is significantly associated with T2D with p-value less than 0.05 ( $p=0.044$ ) and female gender was also strongly associated with T2D (OR= 1.77) although p-value was slightly insignificant.