

ABSTRACT

Hyperglycemia is a hallmark of T2D, a multidimensional metabolic disease impacted by genetics as well as environmental factors. Purpose of this study was to inspect connection among T2D and *HNF1A* gene polymorphism in population of Pakistan, with focus on the potential for family inheritance patterns. Genetic analysis was performed on two SNPs, rs55783344 (*RsaI*) and rs1169288 (*MboI*). In accordance with WHO inclusion and exclusion criteria, blood samples were drawn from twenty families, including both diabetic and non-diabetic members. Genomic DNA was extracted and analyzed using PCR, Sanger sequencing, and RFLP. Positive history of family, lack of physical activity, high BP, and higher BMI were critical risk factors of T2D. Females (33.96%) were more likely to be affected by the diabetes compared to males (23.81%). The SNP at position rs1169288 was strongly associated with T2D ($P < 0.05$) especially among people with AC or CC genotype when compared with individuals with AA genotype. The SNP rs55783344 was not found significantly associated. The pedigree analysis indicated that the SNP rs1169288 SNP was significant risk factor for transmission of diabetes from one generation to next generation. These findings suggest that diabetes is a growing concern in Pakistan, with the rs1169288 polymorphism of *HNF1A* gene playing a significant role in its development ($P < 0.05$). The analysis of Mega 12 software showed a nucleotide modification at the *MboI* site resulted to change in amino acid sequence from Proline to Glutamine. Early diagnosis and prevention require wide-scale genetic screening.