World Academy of Science, Engineering and Technology
International Journal of Health and Medical Engineering
Vol:10, No:10, 2016

Insulin Receptor Substrate-1 (IRS1) and Transcription Factor 7-Like 2 (TCF7L2) Gene Polymorphisms Associated with Type 2 Diabetes Mellitus in Eritreans

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Abstract : Background: Type 2 diabetes mellitus (T2DM) is a complex, degenerative, and multi-factorial disease, which is culpable for huge mortality and morbidity worldwide. Even though relatively significant numbers of studies are conducted on the genetics domain of this disease in the developed world, there is huge information gap in the sub-Saharan Africa region in general and in Eritrea in particular. Objective: The principal aim of this study was to investigate the association of common variants of the Insulin Receptor Substrate 1 (IRS1) and Transcription Factor 7-Like 2 (TCF7L2) genes with T2DM in the Eritrean population. Method: In this cross-sectional case control study 200 T2DM patients and 112 non-diabetes subjects were participated and genotyping of the IRS1 (rs13431179, rs16822615, 16822644rs, rs1801123) and TCF7L2 (rs7092484) tag SNPs were carries out using PCR-RFLP method of analysis. Haplotype analyses were carried out using Plink version 1.07, and Haploview 4.2 software. Linkage disequilibrium (LD), and Hardy-Weinberg equilibrium (HWE) analyses were performed using the Plink software. All descriptive statistical data analyses were carried out using SPSS (Version-20) software. Throughout the analysis p-value ≤0.05 was considered statistically significant. Result: Significant association was found between rs13431179 SNP of the IRS1 gene and T2DM under the recessive model of inheritance (OR=9.00, 95%CI=1.17-69.07, p=0.035), and marginally significant association found in the genotypic model (OR=7.50, 95%CI=0.94-60.06, p=0.058). The rs7092484 SNP of the TCF7L2 gene also showed markedly significant association with T2DM in the recessive (OR=3.61, 95%CI=1.70-7.67, p=0.001); and allelic (OR=1.80, 95%CI=1.23-2.62, p=0.002) models. Moreover, eight haplotypes of the IRS1 gene found to have significant association withT2DM (p=0.013 to 0.049). Assessments made on the interactions of genotypes of the rs13431179 and rs7092484 SNPs with various parameters demonstrated that high density lipoprotein (HDL), low density lipoprotein (LDL), waist circumference (WC), and systolic blood pressure (SBP) are the best T2DM onset predicting models. Furthermore, genotypes of the rs7092484 SNP showed significant association with various atherogenic indexes (Atherogenic index of plasma, LDL/HDL, and CHLO/HDL); and Eritreans carrying the GG or GA genotypes were predicted to be more susceptible to cardiovascular diseases onset. Conclusions: Results of this study suggest that IRS1 (rs13431179) and TCF7L2 (rs7092484) gene polymorphisms are associated with increased risk of T2DM in Eritreans.

Keywords : IRS1, SNP, TCF7L2, type 2 diabetes
Conference Title : ICDTT 2016 : International Conference on Diabetes Treatment and Therapy
Conference Location : New York, United States
Conference Dates : October 10-11, 2016