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Abstract Topic:- Statistical genetics and genetic epidemiology

Abstract Title:- Development and validation of SNP markers in relation to type 2 diabetes: A molecular epidemiology study in Central Indian population

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Aims:-Type 2 diabetes mellitus (T2DM), a metabolic disorder characterized by insulin resistance and relative insulin deficiency, is a multi-factorial complex disease of major public health importance. Several risk factors are associated with T2DM, including genetics, obesity, lifestyle, dietary habits, and age. According to WHO, India has approximately 77 million T2DM cases and around 25 million pre-diabetic people and considered as the diabetes capital of the world. The genome-wide association study (GWAS) has revealed significant association of various genes with T2DM. However, many of such variants were not studied in Indian population. In this study, we have developed SNP based molecular assays for BCL11A (rs243021), PPARG (rs11715073) and SNX7 (rs9727115) and validated in Central Indian population. Along with these 3 newly developed markers, HSD11B1 (rs12086634) polymorphism was also assessed for association with type 2 diabetes cases.

Methods:- A case-control study design was followed. Type 2 diabetes cases and controls were enrolled as per the guidelines of American Diabetes Association based on point of care HbA1C levels. Demographic and anthropometric parameters of all enrolled subjects were recorded and different biochemical and laboratory parameters were generated. Genome wide association studies were reviewed to identify potential genes for development of SNP based markers. Amplification Refractory Mutation System (ARMS) PCR assay was developed for PPARG (C/G) and PCR-RFLP was developed for BCL11A (G/A) and SNX7 (G/A) polymorphism and genotyping was performed. A subset of samples was sequenced to verify the designed assays. using restriction fragment length polymorphism – polymerase chain reaction for, as well as allele specific amplification refractory mutation system (ARMS) polymerase chain reaction for PPARG (C/G) and HSD11B1 (T/G). An odds ratio and 95% confidence interval were calculated to determine the association of gene polymorphisms with T2DM and related parameters.

Results:- A total of 296 participants of age group 30 – 70 years including 143 T2DM (84 male and 59 female) and 155 (87 male and 68 female) healthy individuals, from Bhopal city in Central India were enrolled. A significant difference was observed in various biochemical and anthropometric parameters between T2DM patients and healthy controls. The association analysis indicated that gene BCL11A SNP rs243021 (G/A) and HSD11B1 SNP rs12086634 (T/G) were significantly associated with T2DM [OR 1.62, CI (1.02 – 2.58), p = 0.041; OR 0.38, CI 0.19 – 0.73, p = 0.012), while PPARG SNP rs11715073 and SNX7 SNP rs9727115 were not associated with T2DM.

Conclusions:- The results of our study indicated that the BCL11A rs243021 and HSD11B1 rs12086634 associated with T2DM while PPARG rs11715073 and SNX7 rs9727115 were not, in population Bhopal, Central

India. Further studies are required to cross-validate our findings using a geographically diverse Indian population.

Keywords:- Type 2 diabetes mellitus, insulin resistance, single nucleotide polymorphism, genome-wide association study, molecular epidemiolog