ABSATRACT

Thesis title: ADIPOQ, HHEX and KCNJ11 Gene Polymorphisms in Type II Diabetes.
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Aims and objectives: The present investigation aims to study the polymorphisms in adiponectin (ADIPOQ), HHEX and KCNJ11 genes to understand the predisposition and risk of Type 2 Diabetes. with the following objectives. The objectives of the study are (a) to investigate the known and novel Single Nucleotide Polymorphisms (SNPs) in conserved regions of ADIPOQ, HHEX and KCNJ11 genes, (b) to study the frequency distribution of identified SNPs in ADIPOQ, HHEX and KCNJ11 genes among Type 2 diabetic and control groups, (c) to study the role of SNPs in ADIPOQ, HHEX and KCNJ11 genes in conferring Type 2 diabetes predisposition and risk and (d) to study the underlying risk factors associated with these variations in development of Type 2 diabetic phenotype.

Materials and Methods: For this work, 5-10 ml of the peripheral blood samples was collected from 214 diabetic patients and 206 controls inhabiting Mysore district of Karnataka state in South India. The WHO (2006) criterion was followed to ascertain diabetes status. DNA was extracted by the phenol chloroform method. Primers were designed using Primer3 web based software and standardized using Gradient PCR. Cycle sequencing PCR was performed with the use of ABI prism BigDye Terminator Kits. Sequencing cleanup was performed following ethanol precipitation method. Purified products were sequenced on ABI 3730 Genetic Analyzer. Sequence data were checked for quality using ABI Sequence Analysis v5 software. Sequences were aligned with the use of SeqScape v2.5. References were obtained from RefSeq database. Quality trimming was performed. Electropherograms were checked for all the deviations. Genotypes were called after validation by two individuals.
**Results:** The present study has identified 16 novel variants in *ADIPOQ* gene and one of the variants (186570944) was a nonsense mutation which terminates translation at codon 33. No variants were observed in the *HHEX* gene indicating high conservation of the gene. None of the SNPs in the studied genes showed significant allelic association with type 2 diabetes. Although no variants were observed in *HHEX* gene, SNPs rs1111875 and rs5015480 near regions of the gene showed nominal associations with type 2 diabetes and fasting plasma glucose levels, indicating possible role of other genes in the *HHEX*/*IDF* region in developing diabetes in the present Mysore population. None of the SNPs in *KCNJ11* showed significant association with type 2 diabetes and other related phenotypes.

**Conclusion:** To conclude, the present study did not replicate the association of type 2 diabetes with previously reported SNPs in *ADIPOQ* and *KCNJ11* genes and nominally replicated association of type 2 diabetes with rs1111875 and rs5015480 SNPs near *HHEX* gene.