J Metabolic Synd 2018, Volume 7
DOI: 10.4172/2167-0943-C1-009

Association of *VEGFA* variants with altered VEGF secretion and type 2 diabetes: A case control study

Sameh Sarray, Mohammed Jailani and Abrar K Al-Ansari
Arabian Gulf University, Bahrain

Background: Vascular endothelial growth factor (VEGF) contributes to type 2 diabetes (T2DM) pathogenesis and genetic variations in VEGFA gene were suggested to influence VEGF secretion and T2DM pathogenesis.

Aim: The aim of this study was to examine the potential association of specific VEGFA variants with altered VEGF levels and with T2DM.

Subjects & Methods: A retrospective case-control study, performed on 815 T2DM patients, and 805 healthy controls. VEGF levels were measured by ELISA. Genotyping of VEGFA variants was done by allelic exclusion method (real-time PCR).

Results: MAF of rs1570360, rs2010963, rs25648, rs833068, rs3025036 and rs3025039 were significantly different between T2DM cases and controls. Increased T2DM risk was associated with rs699947, rs1570360 and rs3025020, while reduced T2DM risk was seen with rs1547651, rs2010963, rs25648, rs3025036 and rs3025039 genotypes, thus assigning T2DM susceptibility and protection, respectively. Reduced VEGF levels were associated with rs833061, rs2010963 and rs3025039 heterozygosity and rs3025036 major allele homozygosity in T2DM cases, while increased VEGF levels were seen in rs833070 homozygous major allele genotype. Both rs699947 and rs1570360 were positively, while rs2010963 and rs3025036 were negatively correlated with fasting glucose. In addition, rs699947 was positively correlated with LDL-cholesterol and rs3025039 was positively correlated with diabetes duration, but negatively with HbA1c and triglycerides. Haploview analysis identified Block one containing eight loci and Block two with the remaining three loci. Haplotypes ACTGCCGG and AACGGCGA (Block 1) were negatively associated with T2DM, while haplotype CCC was positively and haplotype CGC (Block two) were negatively associated with T2DM.

Conclusion: This study confirms the contribution of altered VEGF secretion, resulting from genetic variation in VEGFA gene into T2DM pathogenesis, hence supporting role for VEGFA as T2DM candidate locus.

samehmss@agu.edu.bh

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