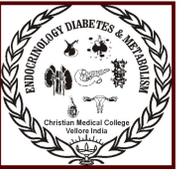




Do TCF7L2 Polymorphisms increase the risk of Gestational Diabetes Mellitus in India



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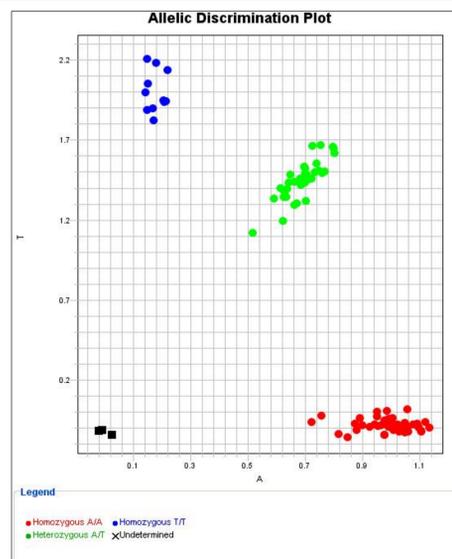
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INTRODUCTION

Genetic predisposition along with environmental factors plays a significant role in the development of polygenic type 2 diabetes mellitus (T2D). Among the diabetogenic genes, the transcription factor 7-like 2 (TCF7L2) gene remains the strongest genetic determinant of T2D risk in humans. TCF7L2 encodes a high mobility group (HMG) box-containing transcription factor that plays a key role in the Wnt (wingless-related integration) signaling pathway. Epidemiological studies suggest an association between gestational diabetes mellitus (GDM) and T2D. Our aim was to investigate whether TCF7L2 variants that have previously been associated with type 2 diabetes would also confer risk for gestational diabetes mellitus.

METHODS

During the period Jan-2012 to April 2013, DNA extraction was done in 166 unrelated women (117 women with gestational diabetes mellitus, 49 non-diabetic control subjects) using the Genra puregene blood method. The primers were validated by Sanger sequencing (3130 genetic analyzer). We genotyped 3 TCF7L2 polymorphisms (rs7903146, rs1225372 and rs4506565) using TaqMan allelic discrimination assay in the molecular laboratory, Endocrinology, Diabetes & Metabolism, Christian Medical College, Vellore. Data Analysis was done with SPSS 17,R.



SNP	Position(NCBI)	Genotype	Patients	Control	Hetero OR(95% CI)	P-Value	Homo OR(95% CI)	P-value
rs7903146	114748339	CC	55	27				
		CT	46	18	1.84(0.551-2.544)	0.666	1.776(0.503-6.263)	0.37
		TT	16	4				
rs1225372	114798892	GG	70	33				
		GT	38	14	1.354(0.618-2.966)	0.449	1.404(0.242-8.119)	0.705
		TT	8	2				
rs4506565	114746031	AA	53	27				
		AT	47	17	1.411(0.652-3.05)	0.382	3.75(0.750-18.53)	0.08
		TT	17	2				

Logistic regression analysis for GDM patients and controls

RESULTS & DISCUSSION

In a India population, we have found that the odds ratio (OR) of TCF7L2 polymorphisms rs4506565, rs7903146, rs1225372 were 3.75(C.I=0.75-18.53, P=0.08), 1.77 (C.I=0.503-6.263,P=0.37) and 1.40 (C.I=0.24-8.11, P=0.70) respectively, when compared with controls for the occurrence of gestational diabetes. The Common variants of TCF7L2 (rs7903146,rs1225372 and rs4506565) have been shown to be associated with diabetes mellitus in European (Cauchi et al. 2007) and Asian population (Chandak et al. 2006, Alami et al. 2012) [OR=1.3-1.9]. The association of GDM with these TCF7L2 variants is varied in different populations viz., Mexican Americans (OR=2.49 [95% CI 1.17-5.31]; $p = 0.018$), Arab women (OR=2.370, (95% of CI 1.010-5.563, $p = 0.047$) and Scandinavian women (OR=1.49 [95% CI 1.28-1.75], $p = 0.049$).

CONCLUSIONS

The TCF7L2 polymorphism rs4506565 showed a trend towards association with the occurrence of gestational diabetes, when compared to the other two common polymorphisms in TCF7L2 (rs7903146, rs1225372). This is the first data of TCF7L2 polymorphism associations with GDM from Indian population. However, to confirm our findings further studies need to be performed in a larger population.

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