

## Involvement of HLA-DR/DQ, ApoE and ACE I/D Gene Polymorphisms in Development of Secondary Complication in South Indian T2DM Patients

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**ABSTRACT** The gene loci such as HLA (DRB1\* and DQB1\*), ACE I/D and ApoE were implicated in the spectrum of type 2 diabetes mellitus (T2DM) leading to secondary complications such as hypertension, retinopathy and cardiac complications. Two hundreds T2DM patients and 151 controls for ACE and ApoE and 156 T2DM patients and 102 controls for HLA-DRB1\* and DQB1\* were genotyped by PCR methods. The overall frequency of D allele (ID + DD) was higher in T2DM patients than controls ( $P = 0.056$ ). Consistently higher frequency of ID genotype was noticed in T2DM patients (pooled) (69.50%), T2DM- without complications (71.71%) and T2DM- with complications (68.31%) than controls (49%). The genotype II was significantly elevated in controls than T2DM ( $p=0.0002$ ), T2DM-WOC ( $p=0.0005$ ) and T2DM-WC ( $p=0.0002$ ). Further, we observed a complete absence of genotype II in patients with retinopathy, genotype DD in patients with hypertension and retinopathy and both II and DD genotype in patients with hypertension and neuropathy, conferring longevity and/or survival benefit to T2DM patients with these complications. The ApoE carrier  $\epsilon 2$  ( $P = 0.007$ ) and  $\epsilon 4$  ( $P = 0.003$ ) were strongly associated with T2DM. A preferential co-occurrence of ACE-ApoE was observed for ID-2/3 combination ( $P = 0.001$ ) and ID-3/4 ( $P = 0.269$ ) in T2DM patients than controls. For HLA, the allele frequency was the highest for DRB1\*03 in patients than the controls (15.70 vs. 5.88%) and for DRB1\*07 in controls than T2DM patients (23.52 vs. 12.17%) affording a susceptible and protective roles of these alleles respectively. Heterozygote combinations were preferentially seen in T2DM patients of higher age groups than controls.