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Abstract Title: - Genetic polymorphisms in 9p21.3 associated with Coronary Artery Disease of South Indian population

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Aims: - Current genome-wide association studies (GWAS) have added a considerable number of loci to serve as genetic markers of coronary artery disease (CAD). Chr9p21.3 stands out for its relatively large effect size, high allele frequency of more than 50% and ethnic diversity. A 53 kb haplotype block in region on chromosome 9p21 that is associated with the risk of CAD which is the most supported association to arise from CAD GWAS to date. This locus overlaps with ANRIL, a non coding RNA gene of unknown function and genomic architecture. We aimed to study SNPs in the 9p21.3 region association in healthy controls and CAD cases of South Indian population.

Methods: - A total of 510 clinically diagnosed Coronary Artery Disease (CAD) patients and 532 age matched healthy controls included for the genetic study analyzing the GWAS annotated SNPs and its association with CAD of South Indian population. The present research study was approved by Institutional Ethics Committee of (IEC approval No. 03092010). Genomic DNA was isolated. Quality and Quantity were checked by NanoDrop Spectrophotometer and UV Gel documentation. In the present study CAD samples and health controls were screened for the SNPs: rs10757274, rs10757278 and rs10965244 were genotyped by Taqman SNP genotyping assay used for allelic discrimination and genetic effects were tested for each SNP and haplotype. DNA of all the study SNPs was sequenced by commercial DNA sequencing service (Macrogen Inc. Seoul, Korea) to confirm the genotyping results.

Results: - The 9p21.3 locus SNPs rs10757274, rs10757278 and rs10965244 were screened in the South Indian CAD and healthy controls to identify their association with CAD risk. All the three SNPs of 9p21.3 locus were in Hardy Weinberg Equilibrium (HWE) and Pearson's Chi-squared test was simulated p-value >0.05. The GG risk genotypes of SNPs rs10757274 and rs10757278 were significantly associated with CAD, with odds ratio (OR) 1.60 (95% CI; - (1.10 - 2.33), p=0.008 & 1.52 (95% CI; - 1.05 - 2.19), p=0.002

respectively. The SNP rs10965244 did not show any LD between either rs10757274 (D' = 0.45 & r =-0.14) or rs10757278 and (D'=0.43 & r =-0.13).

Conclusions: - The present study screened 3 SNPs (rs10757274, rs10757278 & rs10965244) of 9p21.3 locus amongst two linked 9p21.3 SNPs (rs10757274 and rs10757278) were strongly associated with the CAD risk independent of classical Cardio vascular risk factors. The haplotype analysis revealed that 'GGA' as CAD risk haplotype and 'AAA' as CAD protective haplotype in south Indians.

Keywords: - The 9p21.3 locus SNPs rs10757274, rs10757278 and rs10965244 were screened in the South Indian CAD and healthy controls to identify their association with CAD risk. All the three SNPs of 9p21.3 locus were in Hardy Weinberg Equilibrium (HWE) and Pearson's Chi-squared test was simulated p-value >0.05. The GG risk genotypes of SNPs rs10757274 and rs10757278 were significantly associated with CAD, with odds ratio (OR) 1.60 (95% CI; - (1.10 - 2.33), p=0.008 & 1.52 (95% CI; - 1.05 - 2.19), p=0.002 respectively. The SNP rs10965244 did not show any LD between either rs10757274 (D' = 0.45 & r =-0.14) or rs10757278 and (D'=0.43 & r =-0.13).