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Abstract Title:- Influence of KIF6- rs20455 (Trp719Arg) gene polymorphism as a pharmacogenetic marker for atorvastatin response in coronary artery patients of South India

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Aims:-Atorvastatin commonly prescribed, well-tolerated, and effective approach in management of high low-density lipoprotein cholesterol (LDL-C) and reduce the risk of vascular events in patients with coronary artery disease (CAD). Studies have also observed the association of risk allele of KIF6- rs20455 (Trp719Arg) polymorphism in reduction in cardiovascular events due to the modulation of statin response by KIF6-rs20455 (Trp719Arg) polymorphism. The non-carriers of the KIF6 719Arg variant seemed not to benefit from statin therapy. However, the results were inconsistent in various global studies. Hence the aim of the present study aimed to investigate the association KIF6-rs20455 (Trp719Arg) polymorphism with atorvastatin response (20mg/day) in South Indian CAD patients.

Methods:- Biochemical tests were performed using an automated analyzer (Architech/Aeroset, Abbott diagnostic kit, IL, USA) to measure glucose, total cholesterol (TCL), triglycerides (TG), LDL-C, high-density lipoprotein cholesterol (HDL-C), and very low-density lipoprotein (VLDL) and recorded the same at post-6-months atorvastatin treatment. Polymerase Chain-Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) Were Performed using Hpy-CH4III for KIF6-rs20455 (Trp719Arg) polymorphism. All statistical analyses were performed using IBM SPSS statistical software v.22 (SPSS Inc., IL, USA).

Results:- The genotype distributions of KIF6-rs20455 (Trp719Arg) polymorphism were in Hardy–Weinberg equilibrium. Paired t-test analysis demonstrated that post-atorvastatin treatment (20 mg/day) showed that Total Cholesterol (TCL), Triglycerides (TG), Low Density Lipoprotein (LDL-C), High Density Lipoprotein (HDL-C) and Very Low Density Lipoprotein (VLDL) were significantly reduced in CAD patients. The lipid-lowering impact revealed a substantial difference in KIF6-rs20455 (Trp719Arg) polymorphism between the pre- and post-treatment of atorvastatin. Combined homozygous mutant (719Arg/Arg) and heterozygous (719Trp/Arg) genotypes showed significantly increased reduction of LDL-C.

Conclusions:- The current study observed that the atorvastatin (20mg/dL) effectively reduce the lipid profile. We observed that the KIF6-rs20455 (Trp719Arg) polymorphism significantly modulates the LDL-C in post-atorvastatin treatment of CAD patients. Increasing the intensity of atorvastatin therapy may be advisable for patients who are positive for wild genotype (719Trp/Trp) variant for effective LDL-C reduction.

Keywords:- Coronary Artery Disease, Statin Response, Kinesin, Statin Efficacy, Single Nucleotide Polymorphism