Abstract ID:- 105

Abstract Topic:- Clinical Genetics

Abstract Title:- Genetic determinants of Provoked and Unprovoked Deep Vein Thrombosis in south Indian population

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Aims:-Dysregulated blood coagulation in the lower extremities is called Deep Vein Thrombosis (DVT), which leads to blockage of blood vessels. In worse conditions, it leads to pulmonary embolism (PE) due to dislodged blood clots from the vessels and causes life-threatening complications like cardiovascular collapse and death. In most cases, the reason behind the genetics of provoked & unprovoked DVT is unknown.We aimed to screen the genetic variants of F5, PLCG2, and FGG (which belong to the pathways of coagulation & platelets) and their role on provoked and unprovoked DVT occurrence in south Indian population.

Methods:- We recruited about 141 DVT patients and 145 healthy volunteers. The DNA was isolated from blood and its purity and integrity was checked. SNP genotyping of F5 (rs6025), PLCG2 (rs12445050), and FGG (rs2066865) polymorphism was done using 5'-hydrolysis chemistry by TaqMan Genotyping Assays (Applied Biosystems, USA). Genotyping was verified by Sanger Sequencing using 2% above genomic DNA samples. Statistical analysis was performed by IBM SPSS software, v.22.0 (IBM, USA).

Results:- Both provoked and unprovoked DVT sample sizes were statistically significant based on gender and different age groups. The genetic model of inheritances of DVT and healthy controls showed Co-Dominant, Dominant, and Over Dominant models were statistically significant in both univariate and multivariate (after age and gender adjusted) analysis of F5 (rs6025) and PLCG2 (rs12445050). In addition, the Additive model of rs6025 was also shown statistically significant in both univariate and multivariate analysis. This led to more than 7.3 and 1.7 times elevated risk of DVT with respect to F5 and PLCG2 respectively. The FGG (rs2066865) showed that the Co-Dominant, Dominant, and Additive models were significantly favour the disease progression more than 1.4-fold. The haplotype association of CCG pattern on the incidence of DVT showed significant protection as it was commonly observed in healthy controls. Genotype associations of CC/CT/GG, and CC/CT/GA of F5 (rs6025), PLCG2 (rs12445050), and FGG (rs2066865) patterns were statistically significant in provoked & unprovoked DVT and consistent after the adjustment with gender.

Conclusions:- Our data observed that the unprovoked male and left-sided DVT are more predominant compared to the others in the age group of 31 – 60 years in our South Indian DVT patients. The CC/CT/GG and CC/CC/GA genotype patterns of F5 (rs6025), PLCG2 (rs12445050), and FGG (rs2066865) of females in the age group of 21 - 30 years are more likely to be affected by provoked DVT. Collectively, males were more likely towards the unprovoked left-sided DVT; whereas females were towards provoked DVT.

Keywords:- Deep Vein Thrombosis (DVT), F5 (rs6025), PLCG2 (rs12445050), FGG (rs2066865), provoked and unprovoked DVT