Design and implementation of a novel assay for a selected *SERPINC1*gene variant in a cohort of Portal Vein Thrombosis patients in the Sri Lankan population.

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Background & Objectives: Portal vein thrombosis (PVT), is a thromboembolic disorder with a genetic etiology. In developing countries, 40% of portal hypertension are attributed to PVT. Anti-thrombin (AT) deficiency is a major risk factor for venous thromboembolic disorders. The AT precursor is encoded by the *SERPINC1* gene. A comprehensive literature review revealed that a variant of the *SERPINC1* gene (rs2227589, g.5301G>A), is associated with an increased risk of thrombosis in South Asian populations. The objective of this study was to design and implement an assay for determining the presence of the *SERPINC1* g.5301G>A gene variant in the Sri Lankan population.

Method (s) and Results: This retrospective study comprised of 80 individuals clinically diagnosed with PVT, who had been referred to the Human Genetics Unit, Faculty of Medicine, University of Colombo, for genetic screening after obtaining written informed consent for future studies. A novel tetra-primer amplification refractory mutation system-polymerase chain reaction (T-ARMS-PCR) assay was designed and optimized to genotype the variant rs2227589, in the *SERPINC1* gene. The optimized protocol was validated by Sanger sequencing. The allele frequency for the benign variant (G/G) and the heterozygous for the pathogenic variant (G/A) was 62.4% and 31.2%, respectively. No homozygotes for the pathogenic variant were identified. The minor allele frequency for the g.5301G>A genotype was 0.01 (chi squared = 0.98) according to the Hardy Weinberg equilibrium.

Conclusions (Significance and Impact of the Study): The designed T-ARMS-PCR assay can be implemented to genotype the rs2227589 variant of the *SERPINC1* gene. This assay can be introduced as a sensitive, specific, and simple diagnostic technique for testing genetic variants associated with PVT.

Conflict of interest disclosure: The authors declare no potential conflicts of interest, whether scientific, financial and personal.

Keywords: PVT, Thrombosis, *SERPINC1*, Anti-thrombin, T-ARMS PCR