Thrombin Activatable Fibrinolysis Inhibitor (TAFI) Plasma Levels and Thr325Ile Genetic Polymorphism in a Cohort of Egyptian Sickle Cell Disease Patients and Impact on Disease Severity

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Abstract

Background: Thrombin is a critical protease modulating thrombosis as well as inflammation which are one of the main pathophysiological mechanisms in sickle vasculopathy, and its levels were reported to be high in sickle cell disease (SCD). The thrombin-thrombomodulin complex activates an inhibitor of fibrinolysis called TAFI acting by reducing plasmin affinity for its substrate hindering fibrinolysis. **Objective:** We aimed to determine the influence of the Thr325Ile single nucleotide polymorphism on TAFI antigen levels and potential effects on the severity of SCD in a cohort of Egyptian patients. **Methods:** Genotyping of Thr325lle polymorphism using Taq-Man SNP genotyping assay and TAFI level measurement using an Enzyme-Linked Immunosorbent Assay (ELISA) were performed for 80 SCD patients and 80 health control subjects. **Results:** Plasma TAFI levels were higher in SCD patients with Thr325Ile polymorphism, yet the difference was not statistically significant (p=0.204). SCD patients with polymorphic genotypes had a greater number of hospital admissions (p=0.03), Ten patients with acute chest syndrome had the homozygous polymorphic genotype (GG), and all patients with pulmonary hypertension had the polymorphic genotype (6 were homozygous [GG] and 5 were heterozygous [GA]). SCD patients complicated with pulmonary hypertension showed significantly higher plasma TAFI levels (p= 0.044). **Conclusion:** The analysis of Thr325Ile polymorphism combined with plasma TAFI level possibly suggests that the analyzed SNP could influence plasma levels and subsequently disease severity and hospitalization rate, which might be regarded as predictors for complex disease.

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