Assessing gene expression of coagulation factors and Factor XIII polymorphisms in type 2 diabetes mellitus patients

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Background: Type 2 diabetes mellitus (T2D) is characterized by chronic hyperglycaemia, inflammation and coagulopathies due cytokine activation of platelets. The aim of the study is to assess FXIII mRNA levels and identification of factor XIII SNPs (Val34Leu and Tyr204Phe) in T2D and control subjects in a South African cohort.

Methods: Following ethical approval (269/2017), control (n=30/100) and T2D patients’ (n=63/100) blood samples were collected by venepuncture in citrated tubes. Total RNA followed by cDNA synthesis was prepared from whole blood. Quantitative PCR was used to assess mRNA levels of XIII, calculated using $2^{-\Delta\Delta CT}$. Genomic DNA was isolated from whole blood and used for PCR amplification of FXIII subunit A Val34Leu and Tyr204Phe. Amplicons were restricted enzymatically to assess genotypes. Thromboelastography (TEG) was used to assess clot kinetics (reaction time (R-time), clotting time, alpha angle and maximum amplitude).

Results: Significant variation in FXIII mRNA was found between T2D and controls with a mean relative fold increase of 21.37±11.20 (p=0.042). R-time was 2-fold higher in T2D (11.0 vs. controls: 4.89; p=0.097) and other kinetics remained unchanged. Genotype frequencies for controls ($\chi^2=0.0089$, p=0.92) and T2D ($\chi^2=2.286$, p=0.13) passed Hardy-Weinberg equilibrium. Haplotype analysis showed a higher frequency of the variant in controls compared to T2D (Val: 67% vs. 85%, respectively, p=0.0105). FXIII Tyr204Phe SNPS were absent in both groups.

Conclusion. The FXIII Val34Leu variant was more frequent in controls. The plausible mechanism for greater reaction time and overexpression of FXIII may be attributed to the hyperactivity of FXIII in T2D patients.

Keyword: Type 2 diabetes. Coagulation. Factor XIII.