

Analysis of selected glutathione S-transferase gene polymorphisms in Malaysian type 2 diabetes mellitus patients with and without cardiovascular disease

ABSTRACT

Type 2 diabetes mellitus (T2DM) is believed to be associated with excessive production of reactive oxygen species. Glutathione S-transferase (GST) polymorphisms result in decreased or absent enzyme activity and altered oxidative stress, and have been associated with cardiovascular disease (CVD). The present study assessed the effect of GST polymorphisms on the risk of developing T2DM in individuals of Malaysian Malay ethnicity. A total of 287 subjects, consisting of 87 T2DM and 64 CVD/T2DM patients, as well as 136 healthy gender- and age-matched controls were genotyped for selected polymorphisms to evaluate associations with T2DM susceptibility. Genomic DNA was extracted using commercially available kits, and GSTM1, GSTT1, and α -globin sequences were amplified by multiplex polymerase chain reaction. Biochemical parameters were measured with a Hitachi autoanalyzer. The Fisher exact test, the chi-square statistic, and means \pm standard deviations were calculated using the SPSS software. Overall, we observed no significant differences regarding genotype and allele frequencies between each group ($P = 0.224$ and 0.199 , respectively). However, in the combined analysis of genotypes and blood measurements, fasting plasma glucose, HbA1c, and triglyceride levels, followed by age, body mass index, waist-hip ratio, systolic blood pressure, and history of T2DM significantly differed according to GST polymorphism ($P < 0.05$). Genetically induced absence of the GSTT1 enzyme is an independent and powerful predictor of premature vascular morbidity and death in individuals with T2DM, and might be triggered by cigarette smoking's oxidative effects. These polymorphisms could be screened in other ethnicities within Malaysia to determine further possible risk factors.

Keyword: Glutathione S-transferase; Cardiovascular disease; Malaysia; Type 2 diabetes mellitus