Detection of XMN1-Gγ Polymorphism Among Patients with HbE/Beta Thalassaemia in North East Malaysia

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The incidence of HbE/beta (HbE/β) thalassaemia is increasing in Asian countries, including Malaysia. HbE/β thalassaemia is widely acknowledged to have a diverse phenotypic spectrum despite having the same primary genetic background [1,2,3]. Thus, there are HbE/β thalassaemia patients who receive unnecessary treatments which leads to side effects [4], reduced quality of life and wasting health care resources. Ideally, the treatment and management of thalassaemia patients are individually tailored in order to minimise side effects and optimise health care costs. Genetic variants have been widely acknowledged to influence the variability of human phenotypes. Presence of unique genetic modifiers are believed to cause the diversity in HbE/β thalassaemia severity. Milder disease course has been found to be highly associated with Xmn1-Gγ polymorphism (rs7482144), a SNP at HBG2 promoter [1,5,6,7]**.** So far, there is no association study between Xmn1-Gγ polymorphism and HbE/beta thalassaemia disease severity in Malaysia. This study aims to optimise PCR-RFLP technique for detection of Xmn1-Gγ polymorphism, to determine the frequency of Xmn1-Gγ polymorphism in HbE/β thalassaemia patients and finding its association with the severity of HbE/β thalassaemia patients. This hospital-based cross-sectional study was performed using archived genomic DNAs from 58 subjects with their respective research pro formas. Selected datas were extracted from the pro formas in order to classify patients into 3 disease severity groups using the scoring system by Sripichai *et al*., (2008) based on 6 parameters. The archived genomic DNAs were genotyped employing Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) technique. The genotypes were categorised into homozygous variant, heterozygous and homozygous wild type. The genotypes detected were then validated using DNA sequencing analysis. Appropriate statistical analysis was used to determine the association of Xmn1-Gγ polymorphism with the clinical severity of HbE/β thalassaemia. This study had successfully optimised the PCR-RFLP technique for detection of Xmn1-Gγ polymorphism. Out of 58 subjects, the Xmn1-Gγ polymorphisms were detected in 40 subjects (69%) with the majority being heterozygous (CT) (n=38, 66%) and there were only 2 (3%) homozygous variant (TT)

subjects. Homozygous wild type (CC) were detected in 18 (31%) subjects. There were no significant association of Xmn1-Gγ polymorphism with the severity of HbE/β thalassaemia patients with p-value of 0.65 for genotype and 0.58 for allele, respectively. In conclusion, this study showed no significant association of Xmn1-Gγ polymorphism with milder disease severity of HbE/β thalassaemia patients. This can be a true finding for the patients in North East Malaysia or due to small sample size. Thus we recommend to have a larger study in order to validate the association of Xmn1-Gγ polymorphism with HbE/β thalassaemia severity. In addition, there may be other genetic factors that interact with Xmn1-Gγ polymorphism as it was not possible to consistently predict phenotype and severity from the presence of Xmn1-Gγ polymorphism alone.

Keywords: HbE, beta, HbE/β, thalassaemia, Xmn1-Gγ polymorphism

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