Genetic Analysis of Beta Globin Gene (HBB) in Transfusion-Dependent HBE/β-Thalassemia Patients

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Abstract

HbE/β-thalassemia is the most common form of β-thalassemia in Asia. It has various clinical manifestations ranging from very mild to severe. The most reliable and predictive factor of the disease phenotype is the nature of the β-globin gene mutation. Therefore, this study aimed to identify the spectrum of β-globin gene mutations among HbE/β-thalassemia patients, subsequently correlating the identified mutations with hematological parameters. A total of 204 transfusion-dependent HbE/β-thalassemia patients were randomly selected at Hospital USM and Ministry of Health hospitals in Malaysia. MARMS-PCR and CSGE were performed to screen for β-globin gene mutations. All genotyping results were confirmed and validated by DNA sequencing. The results were analyzed using SPSS version 22 and STATA SE. A total of 152 subjects were diagnosed as HbE/β-thalassemia. Thirteen compound heterozygous mutations were identified. The most prevalent compound heterozygous mutations were CD 26 (G→A) and IVS 1-5 (G→C) (36.2%), CD 26 (G→A) and IVS 1-1 (G→T) (26.9%), and compound heterozygous CD 26 (G→A) and IVS 1-1 (G→T) (11.8%). Two previously unreported rare mutations prevalent in Algerian populations, compound heterozygous CD 26 (G→A) and IVS 1-2 (T→C) and compound heterozygous CD 26 (G→A) and IVS 1-2 (T→A) were also discovered. The prevalent compound heterozygous mutations were statistically significant with MCH (p=0.033) and HbF level (p=0.008). This study showed the impact of genetic modifiers on genotype heterogeneity and clinical severity of the disease. A better understanding of the mechanism underlying the variety of phenotypes of this disease may lead to better future management plans.

Keywords: HbE/β-thalassemia; spectrum of β-globin gene mutations; MARMS-PCR.

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