Genetic modifiers contributing to phenotypic heterogeneity of Hb E/β-Thalassemia

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Abstract

Hb E/Beta-thalassemia disease has the highest number of transfusion dependent thalassemia patients in Kedah. HbE/Beta-Thalassemia disease is clinically variable. Several genetic modifiers have been reported to play an important role in disease severity. To determine genetic factors that can predict phenotypic severity of patients with Hb E/β-thalassemia diseases and to assess the relationship between the genotype and phenotype of the disease based on a scoring system. Total of 68 samples was recruited from thalassemia clinic. Data used in this study is retrospectively evaluated. Clinical features were recorded based on scoring system for the classification of β-thalassemia/Hb E disease severity. Hematological analysis was performed. Molecular studies were performed for both alpha and beta globin chain using dot blot and reverse dot blot hybridization, multiplex ARMS PCR. Detection of Gγ-globin gene (158 (C>T) XmnI polymorphism) was performed using Restriction Fragment Length Polymorphism (RFLP). Based on the scoring system, 10% of cases were characterized as mild, 44.5% as moderate and 45.5% severe cases. β/βE genotype associated with mild disease severity include βIVS1,βE, β28/βE and βIVS1.5/βE. Mixed of β/βE genotype such as βIVS1/βE, βIVS1.5/βE, βCD41/42/βE, βNS 1-25 bp del/βE, βIVS1/βE, βCD36/C/βE, βIVS1/βE, βIVS1/βE associated with moderate phenotype. Majority of severe phenotypic cases showed βE/βE genotype which include βIVS1/βE, βIVS1.5/βE, βCD41/42/βE, βIVS1/βE, βIVS1/βE and βIVS1/βE. For XMN1 polymorphism, 97% of the samples showed heterozygous state Xmn1 -158 Gγ polymorphism (C-T). This study has showed a variety of primary modifiers as compared to the previous study. Coinheritance of alpha thalassemia or red cell ovalostomatocytes (SEAO) showed milder and moderate phenotype. Further study on genetic variants that regulates Hb F is recommended.

Keywords: genetic modifiers; Hb E/β-thalassemia

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