rs9376092 is a biomarker of severe HbE/Beta thalassemia

Nurul Fatihah Azman¹, Heba Alsaleh², Sarifah Hanafi¹, Noor Diana Rashid¹, Rosnah Bahar², Wan Zaidah Abdullah², Muhammad Farid Johan², Zilfalil Alwi³, *Rosline Hassan²

¹Department of Paediatrics, School of Medical Sciences, Universiti Sains Malaysia
²Department of eHaematology, School of Medical Sciences, Universiti Sains Malaysia
³Human Genome Centre, School of Medical Sciences, Universiti Sains Malaysia

roslin@usm.my

Abstract

The clinical presentation of HbE/Beta thalassemia (HbE/β-thalassemia) ranges from non-transfusion dependent thalassemia to transfusion dependent. There are genetic modifiers which influence the disease severity; primary, secondary and tertiary modifiers. The secondary modifier is associated with HBB locus, HBSIL-MYB and BCL11A gene. These genes ameliorate the disease severity of thalassemia. The aim of this study is to investigate the association of rs9376092 (A/C) among transfusion dependent HbE/β-thalassemia with disease severity. A total of 55 severe and 43 moderate HbE/β-thalassemia were compared with normal Malay control. The severity was classified based on clinical parameters: age at disease presentation and blood transfusion, pre transfusion hemoglobin (Hb) level, growth percentile and spleen size. The genotyping was conducted with Affymetrix SNP 6.0 array using DNAs. From the results and Manhattan plots, rs9376092 was associated with severity of disease (p-value 1.59 X 10⁻⁸ and 8.86 X 10⁻⁵ respectively). The mean of Hb F level amongst the patients was 26.49±20.18 (g/dL). The A allele of rs9376092 is frequent in severe cases with allele frequency ranging from 0.33-0.46. In conclusion, the rs9376092 is a common biomarker of severe HbE/Beta thalassemia. However, the underlying mechanism needs further investigation. In addition, this rs polymorphism is found in transfusion dependent HbE/β-thalassemia Malay, β₀ Thai-Chinese and Indonesian origin.

Keywords: transfusion dependent, HbE/Beta thalassemia, genetic modifiers, HBSIL-MYB

*Author for Correspondence