

ABSTRAK

Thalassaemia β memiliki heterogenitas genetik dan klinis yang berbeda dalam berbagai populasi. Tujuan penelitian adalah untuk menentukan jenis mutasi pada gen β , gen pengubah genetik lokus *XmnI*, BCL11A, HBS1L-MYB, dan aspek fenotipe pasien Thalassaemia di Banyumas, Jawa Tengah, Indonesia.

Penelitian menggunakan desain penelitian *cross sectional study*. Subyek adalah semua pasien dengan diagnosis Thalassaemia dalam *database* Yayasan Thalassaemia Indonesia (YTI) Banyumas. Jenis mutasi pada gen globin β ditentukan dengan teknik *Polymerase Chain Reaction-Restriction Fragment Length Polymorphism* (PCR-RFLP), *Amplification-Refractory Mutation System* (ARMS), dan *direct sequencing*. Alel-alel pada lokus *XmnI*, SNPs rs11886868, rs766432, rs9399137 dikarakterisasi menggunakan teknik PCR-RFLP dan ARMS sesuai dengan primer dan enzim restriksi yang sesuai. Status klinis pasien Thalassaemia diukur dengan skor derajat klinis Sriciphai. Data dianalisis secara deskriptif selanjutnya dilakukan uji multivariat sesuai dengan karakteristik data. Hasil pengujian dianggap bermakna bila $p < 0,05$ pada interval kepercayaan 95%.

Penelitian menemukan bahwa frekuensi alel mutasi gen β sebagai berikut : IVS-1-5 (G>C) (43,5 %), Cd26 (HbE) (28,2%), IVS-1-1 (G>A) (5%), Cd15 (TGG>TAG) (3,8%), IVS-1-1(G>T)(3,1%), Cd35 (-C) (2,4%), serta di bawah 1 % adalah Cd41/42 (-TTCT), Cd8/9 +G, Cd19 (AAC>AGC), Cd123/124/125(-ACCCCACC), IVS-1-2 (T>C), Cd17 (AAG>TAG), Cd40 (-G), CAP +1 (A>C). Data penelitian memperlihatkan bahwa alel *XmnI* memiliki frekuensi alel minor 14 %. Alel C pada rs11886868 pada populasi subyek di Banyumas adalah alel mayor dengan frekuensi 78 %. Distribusi alel rs766432 dan rs9399137 memiliki distribusi yang hampir serupa pada berbagai populasi dunia (18-19 %). *XmnI*, rs766432 dan rs11886868 pada kelompok HbE/Thalassaemia β berhubungan secara signifikan baik pada kadar HbF maupun derajat klinis pasien ($p < 0,05$). Sedangkan alel rs9399137 HBS1L-MYB tidak menunjukkan hubungan yang serupa ($p > 0,05$). Pada kelompok homozigot Thalassaemia β^0/β^0 maupun Thalassaemia β^0/β^+ (*severe*) polimorfisme lokus *XmnI*, rs766432, rs11886868, dan rs9399137 tidak berhubungan secara signifikan dengan derajat klinis pasien ($p > 0,05$).

Kesimpulan penelitian adalah sebagai berikut; mutasi gen β paling banyak adalah alel IVS-1-5 (G>C) dan Cd26 (HbE) dengan persentase 43,5 % dan 28,2 %. Polimorfisme lokus *XmnI*, rs766432, rs11886868 (BCL11A) pada pasien HbE/Thalassaemia β berhubungan secara signifikan dengan derajat klinis, sedangkan rs9399137 (HBS1L-MYB) tidak berhubungan. Polimorfisme lokus *XmnI*, rs766432, rs11886868, dan rs9399137 pada pasien homozigot Thalassaemia β^0/β^0 maupun Thalassaemia β^0/β^+ (*severe*) tidak berhubungan secara signifikan dengan derajat klinis.

Kata Kunci : Thalassaemia β , *XmnI*, BCL11A, HBS1L-MYB, clinical appearance

ABSTRACT

Beta Thalassemia has different genetics and clinical heterogeneity in various populations. The research objective was to determine the types of mutations in β gene, a genetic modifier gene of *XmnI* locus, BCL11A, HBS1L-MYB, and phenotype aspects of Thalassaemia patients in Banyumas, Central Java, Indonesia.

The study used cross sectional study design. The subjects were all patients with a diagnosis of thalassemia in the database of the Indonesia Thalassaemia Foundation (YTI) Banyumas. The type of mutation in the β globin genes was determined by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP), Amplification-Refractory Mutation System (ARMS), and direct sequencing. Alleles at the *XmnI* locus, SNPs rs11886868, rs766432, rs9399137 were characterized using PCR-RFLP and ARMS technique in accordance with appropriate primers and restriction enzymes. Clinical status of Thalassaemia patients were measured using Sriciphai clinical score. Data were analyzed descriptively then performed multivariate test in accordance with the characteristics of the data. The test results are considered significant if $p < 0.05$ on 95% confidence intervals.

The study found that the mutation allele frequency of β genes were as follows: IVS-1-5 (G>C) (43.5%), Cd26 (HbE) (28.2%), IVS-1-1 (G>A) (5 %), Cd15 (TGG>TAG) (3.8%), IVS-1-1 (G>T) (3.1%), Cd35 (-C) (2.4%), and below 1% were CD41/42 (-TTCT), CD8/9 + G, CD19 (AAC>AGC), Cd123/124/125 (-ACCCCACC), IVS-1-2 (T>C), Cd17 (AAG>TAG), CD40 (-G), CAP +1 (A>C). Data showed that the *XmnI* allele have a minor allele frequency of 14%. C allele at rs11886868 in the subject of Banyumas population is a major allele with a frequency of 78%. Rs766432 and rs9399137 allele distribution has a similar distribution to the various populations of the world (18-19%). *XmnI*, rs766432 and rs11886868 in the HbE/ β Thalassaemia group associated significantly with HbF levels or clinical score patients ($p < 0.05$), while rs9399137 HBS1L-MYB alleles did not show a similar relationship ($p > 0.05$). In homozygous β^0/β^0 Thalassaemia and β^0/β^+ (severe) Thalassaemia *XmnI* polymorphisms, rs766432, rs11886868, and rs9399137 did not significantly associate with the degree of clinical scores ($p > 0.05$).

The conclusion of the study was as follows; most mutations in β genes are alleles of IVS-1-5 (G>C) and Cd26 (HbE) with a percentage of 43.5% and 28.2%. *XmnI* polymorphism loci, rs766432, rs11886868 (BCL11A) in patients HbE/ β Thalassaemia significantly associated with clinical degrees, while rs9399137 (HBS1L-MYB) was not related. *XmnI* polymorphism loci, rs766432, rs11886868, and rs9399137 in patients with homozygous Thalassaemia β^0/β^0 and Thalassaemia β^0/β^+ (severe) was not significantly related to the clinical degree.

Keywords : Thalassaemia β , *XmnI*, BCL11A, HBS1L-MYB, clinical appearance