

ABSTRAK

PERFORMA DIAGNOSTIK *SINGLE NUCLEOTIDE POLYMORPHISM* (SNP) rs9399137 DAN rs72872548 DENGAN EKSPRESI *PHOSPHATIDYLSERINE* PADA SEL DARAH MERAH (*PS-EXPOSED RBCs*) SEBAGAI MODEL PREDIKTOR TINGKAT KEPARAHAN BETA-THALASSEMIA

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Mutasi gen beta globin merupakan penyebab utama beta-thalassemia, yaitu suatu penyakit hereditas yang ditandai oleh penurunan atau tidak adanya sintesis rantai polipeptida globin, sehingga produksi Hb menjadi tidak adekuat. Pada pasien beta-thalassemia, peroksidasi lipid membran eritrosit pasca transfusi, dapat meningkatkan ekspresi *phosphatidylserine* pada sel darah merah (*PS-Exposed RBCs*), yang berperan dalam aktivasi faktor koagulasi V dan X, sehingga memicu trombotik. Beberapa *Single Nucleotide Polymorphism* (SNP) diketahui berhubungan dengan dengan gen pengekspresi penyakit ini, diantaranya rs9399137 pada region HBS1L-MYB dan rs72872548 pada gen HbE. Penelitian ini bertujuan untuk mengidentifikasi spesifisitas dan sensitivitas kombinasi SNP rs9399137, rs72872548 dengan *PS-Exposed RBCs* dalam memprediksi tingkat keparahan pasien beta-thalassemia. Penelitian ini merupakan studi observasi laboratorik, yang melibatkan 32 orang pasien beta-thalassemia. Pemeriksaan SNP rs9399137 dan rs72872548 dilakukan menggunakan metode PCR dan sekuensing DNA, sedangkan ekspresi *PS-Exposed RBCs* menggunakan metode ELISA. Hasil penelitian menunjukkan bahwa genotipe TT merupakan genotipe yang paling banyak ditemukan pada SNP rs9399137 (66,7%), sedangkan genotipe CC paling dominan pada SNP rs72872548 (82,1%). Penggunaan masing-masing marker SNP rs9399137, SNP rs72872548, dan *PS-Exposed RBCs* sebagai prediktor tunggal tingkat keparahan memiliki sensitivitas dan spesifisitas yang tidak cukup baik. SNP rs9399137 memiliki sensitivitas 92,30% dan spesifisitas 57,14%, SNP rs72872548 sensitivitas 92,86% dan spesifisitas 28,57% dan PS memiliki sensitivitas sebesar 64,71% dan spesifisitas 86,67%. Model kombinasi gabungan SNP rs9399137, SNP rs72872548 dan *PS-Exposed RBCs* sebagai model prediktor tingkat keparahan, memiliki sensitivitas (84,6%) dan spesifisitas (71,4%) yang paling optimal dengan nilai diskriminasi yang baik (AUC=0,852; 95% CI: 0,701–0,974). **Simpulan:** Model pemeriksaan kombinasi SNP rs9399137, SNP rs72872548 dan ekspresi PS merupakan model prediktor tingkat keparahan beta-thalassemia terbaik dengan sensitivitas dan spesifisitas yang optimal, dibandingkan parameter tunggal.

Kata kunci: Beta-thalassemia, *PS-Exposed RBCs*, *Single Nucleotide Polymorphism* (SNP), SNP rs9399137, SNP rs72872548

ABSTRACT

DIAGNOSTIC PERFORMANCE OF SINGLE NUCLEOTIDE POLYMORPHISM (SNP) rs9399137 AND rs72872548 WITH PHOSPHATIDYLSERINE EXPRESSION IN RED BLOOD CELLS (PS- EXPOSED RBCS) AS A PREDICTOR MODEL FOR BETA- THALASSEMIA SEVERITY

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Mutations in the beta-globin gene are the primary cause of beta-thalassemia, a hereditary disorder characterized by reduced or absent synthesis of globin polypeptide chains, resulting in inadequate hemoglobin (Hb) production. In patients with beta-thalassemia, post-transfusion erythrocyte membrane lipid peroxidation can increase the exposure of phosphatidylserine on red blood cells (PS-exposed RBCs), which plays a role in the activation of coagulation factors V and X, thereby triggering thrombosis. Several single nucleotide polymorphisms (SNPs) have been reported to be associated with the expression of this disease, including rs9399137 located in the HBS1L-MYB region and rs72872548 in the HbE gene. This study aimed to identify the sensitivity and specificity of a combination of SNP rs9399137, SNP rs72872548, and PS-exposed RBCs in predicting the severity of beta-thalassemia. This study was a laboratory-based observational study involving 32 patients with beta-thalassemia. Genotyping of SNP rs9399137 and rs72872548 was performed using PCR and DNA sequencing, while PS-exposed RBC levels were measured using an ELISA-based method. The results showed that the TT genotype was the most frequently observed genotype for SNP rs9399137 (66.7%), whereas the CC genotype was the most dominant for SNP rs72872548 (82.1%). The use of SNP markers rs9399137, SNP rs72872548, and PS-Exposed RBCs as single predictors of severity had insufficient sensitivity and specificity. SNP rs9399137 had a sensitivity of 92.30% and a specificity of 57.14%, SNP rs72872548 a sensitivity of 92.86% and a specificity of 28.57%, and PS had a sensitivity of 64.71% and a specificity of 86.67%. The combined model of SNP rs9399137, SNP rs72872548 and PS-Exposed RBCs as a severity predictor model, has the most optimal sensitivity (84.6%) and specificity (71.4%) with good discrimination value (AUC=0.852; 95% CI: 0.701–0.974). **Conclusion:** The combined examination model of SNP rs9399137, SNP rs72872548 and PS expression is the best beta-thalassemia severity predictor model with optimal sensitivity and specificity, compared to single parameters.

Keyword: Beta-thalassemia, PS-Exposed RBCs, Single Nucleotide Polymorphism (SNP), SNP rs9399137, SNP rs72872548