

# Kelainan trombosit dan aktivasi koagulasi pada penderita thalassemia mayor yang sudah dan belum mengalami splenektomi di Indonesia = Platelet changes and activation of coagulation in splenectomized and non-splenectomized patients with thalassemia major in Indonesia

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## Abstrak

Di Indonesia, thalassemia mayor merupakan salah satu masalah kesehatan karena morbiditas dan mortalitasnya yang tinggi. Thalassemia mayor ditandai dengan anemia berat sejak usia anak-anak dan memerlukan transfusi teratur untuk mempertahankan kadar hemoglobin. Untuk mengurangi kebutuhan akan transfusi darah, dilakukan splenektomi. Trombosis merupakan salah satu komplikasi thalassemia yang banyak dilaporkan di berbagai negara, tetapi di Indonesia sampai saat ini belum ada laporan. Trombosit dan sistem koagulasi memegang peranan dalam patogenesis trombosis. Tujuan penelitian ini adalah untuk mendapatkan gambaran mengenai kelainan trombosit serta aktivasi koagulasi pada penderita thalassemia mayor yang sudah maupun yang belum di-splenektomi di Indonesia.

Desain penelitian ini potong lintang. Subyek penelitian terdiri dari 31 orang penderita thalassemia mayor yang sudah displenektomi (kelompok splenektomi) dan 35 orang penderita thalassemia mayor yang belum mengalami splenektomi (kelompok nonsplenektomi). Untuk menilai fungsi trombosit, dilakukan pemeriksaan agregasi trombosit terhadap adenosin difosfat (ADP), aktivasi trombosit dinilai dengan mengukur kadar  $\epsilon$ -tromboglobulin ( $\epsilon$ -TG), sedangkan aktivasi koagulasi dinilai dengan pemeriksaan D-dimer.

Hasil penelitian ini menunjukkan bahwa jumlah trombosit pada kelompok splenektomi lebih tinggi secara bermakna dibandingkan kelompok non-splenektomi ( $549.260 \pm 251.662/\epsilon$  vs  $156.000/\epsilon$ ; (kisaran  $34.000-046.000/\epsilon$ );  $p < 0,001$ ). Demikian pula agregasi trombosit terhadap ADP 1 pM maupun 10 pM lebih tinggi secara bermakna pada kelompok splenektomi dibandingkan dengan kelompok non-splenektomi (1 pM: 17,3% (kisaran 1,9-104,0%) vs 5,2% (kisaran 0,5-18,2%);  $p < 0,001$  dan 10 pM: 91,2% (kisaran 27,3-136,8%) vs  $55,93 \pm 17,27\%$ ;  $p < 0,001$ ). Kadar  $\epsilon$ -TG lebih tinggi secara bermakna pada kelompok splenektomi dibandingkan kelompok non-splenektomi ( $178,81 \pm 86,3$  IU/ml vs  $100,11 \pm 40,0$  IU/ml;  $p < 0,001$ ). Kadar D-dimer juga lebih tinggi secara bermakna pada kelompok splenektomi dibandingkan non-splenektomi walaupun keduanya masih dalam rentang normal ( $0,2 \epsilon$ /g/ml (kisaran  $0,1-0,7$  g/ml) vs  $0,1 \epsilon$ /g/ml (kisaran  $0,1-0,8 \epsilon$ /g/ml)).

Dari hasil penelitian ini, disimpulkan bahwa pada penderita thalassemia mayor di Indonesia terdapat jumlah trombosit dan fungsi agregasi yang bervariasi, sedangkan aktivasi trombosit meningkat, tetapi belum dapat dibuktikan adanya aktivasi koagulasi. Pada penderita thalassemia mayor yang sudah displenektomi didapatkan trombositosis, serta agregasi trombosit terhadap ADP dan aktivasi trombosit yang lebih tinggi dibandingkan dengan penderita yang belum di-splenektomi.

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Thalassemia major is one of the health problem in Indonesia due to its high morbidity and mortality. Thalassemia major is characterized by severe anemia presenting in the first years of life and requires regular transfusions to maintain hemoglobin level. Splenectomy is performed to decrease the need for transfusion. Thrombosis is one of the complications widely reported in patients with thalassemia in many parts of the world, but until now, there had been no report on this complication in Indonesia. Platelet and the coagulation system play a role in the pathogenesis of thrombosis. The aim of this study was to obtain the pattern of changes in platelet count, function and activation level, and activation of coagulation in patients with thalassemia major patients in Indonesia.

The design of this study was cross-sectional. The subjects were 31 splenectomized and 35 non-splenectomized patients with thalassemia major. Platelet aggregation to adenosine diphosphate (ADP) was performed to assess platelet function;  $\alpha$ -thromboglobulin level was used as marker of platelet activation, and D-dimer for activation of coagulation.

The result of this study revealed a significantly higher platelet count in splenectomized compared to non-splenectomized patients ( $549.260 \pm 251.86210$  vs  $156.000 \pm 34.000$  (34.000- 46.000);  $p < 0.001$ ). Platelet aggregation to ADP were significantly higher in splenectomized patients than non-splenectomized group, both to 1 pM (17.3% (range 1.9-104M%) vs 5.2% (range 0.5-118.2%);  $p < 0.001$ ) and 10  $\mu$ M ADP (91.2% (range 27.3-136.8%) vs 55.93  $\pm$  17.27%;  $p < 0.001$ ).  $\alpha$ -thromboglobulin level was significantly higher in splenectomized patients compared to non-splenectomized patients ( $178.81 \pm 86.3$  IU/rnl vs  $100.11 \pm 40.0$  IU/ml;  $p < 0.001$ ). D-dimer level was also significantly higher in the splenectomized group compared to non-splenectomized group although both had values within normal range ( $0.2 \text{ pg/ml}$  (range 0.1-0.7  $\mu$ g/ml) vs  $0.1 \text{ pg/ml}$  (range 0.1-0.8  $\mu$ g/ml)).

We concluded that the platelet count and function were varied, while platelet activation level was increased in patients with thalassemia major in Indonesia, but activation of coagulation was not established. We also concluded that in splenectomized patients there were thrombocytosis and increased platelet aggregation to ADP and platelet activation level compared to non-splenectomized patients.