

## Endokan Sebagai Penanda Kebocoran Plasma Pada Pasien Demam Berdarah Dengue = Endocan as a Marker of Plasma Leakage in Dengue Patients

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### Abstrak

Latar belakang: Demam berdarah dengue (DBD) merupakan salah satu penyakit infeksi terpenting di berbagai negara tropis dan subtropis. Kebocoran plasma merupakan salah satu penanda infeksi dengue berat. Namun, beberapa metode diagnostik kebocoran plasma yang direkomendasikan oleh WHO memiliki berbagai kekurangan untuk digunakan dalam praktik klinis sehari-hari. Endokan merupakan proteoglikan yang diproduksi oleh sel endotel yang teraktivasi. Studi pada pasien sepsis dan Coronavirus Disease-19 (COVID-19) memperlihatkan bahwa kadar protein ini dapat digunakan sebagai penanda disfungsi endotel dan faktor prognostik infeksi berat. Penelitian ini bertujuan untuk mengevaluasi endokan sebagai penanda kebocoran plasma pada infeksi DBD. Metode: Penelitian ini dilakukan secara kohort retrospektif menggunakan data sekunder dari penelitian International Study on Biomarkers and Gene Expression Patterns in Patients with Dengue Virus Infection (INVEST) yang diambil pada tahun 2010-2011 di RS Cipto Mangunkusumo, Jakarta. Endokan diperiksa menggunakan teknik ELISA. Uji diagnostik kebocoran plasma dilakukan menggunakan ultrasonografi (USG) sebagai baku emas. Nilai titik potong endokan sebagai penanda kebocoran plasma dilakukan menggunakan kurva Receiver Operating Characteristic (ROC). Uji korelasi dilakukan terhadap nilai hematokrit, delta hematokrit, dan albumin dengan endokan. Analisis data dilakukan dengan menggunakan GraphPad Prism versi 5.0 untuk Windows dan Statistical Package for the Social Sciences (SPSS) versi 28. Hasil: Terdapat 64 pasien yang memenuhi kriteria inklusi dan eksklusi dan terdiri atas 31 pasien demam dengue (DD) dan 33 pasien demam berdarah dengue (DBD). Terdapat perbedaan bermakna untuk parameter endokan, albumin, trombosit dan nilai delta hematokrit antara kelompok DD dan DBD. Didapatkan area under the curve (AUC) 0,83 (95% interval kepercayaan: 0,73-0,93). Endokan dengan nilai titik potong 1,63 ng/mL dapat digunakan sebagai penanda kebocoran plasma, dengan angka sensitivitas 66,7%, spesifisitas 90,3%, nilai prediksi positif (NPP) 88%, dan nilai prediksi negatif (NPN) 71,8%. Terdapat korelasi negatif antara nilai endokan dan albumin pada fase kritis infeksi dengue ( $r: -0,4; p: 0,001$ ). Tidak terdapat korelasi antara kadar endokan fase kritis dengan hematokrit ( $r: 0,12; P=0,36$ ) dan delta hematokrit ( $r: 0,16; P=0,21$ ). Kesimpulan: Endokan dengan nilai titik potong 1,63 ng/mL memberikan angka sensitivitas 66,7%, spesifisitas 90,3%, NPP 88%, dan NPN 71,8 sebagai penanda kebocoran plasma. Terdapat korelasi negatif antara nilai endokan dan albumin pada fase kritis infeksi dengue.

.....Background: Dengue is one of the most important infectious diseases in tropical and subtropical countries. This disease is caused by dengue virus (DENV). Plasma leakage is one of the most important clinical manifestations of severe dengue. However, there are shortcomings of various diagnostic methods that have been recommended by WHO to be used in daily clinical practice. Endocan is a proteoglycan produced by activated endothelial cells. Studies in patients with sepsis and Coronavirus Disease-19 (COVID-19) showed that endocan levels can be used as a marker of endothelial cell dysfunction and prognostic factors for severe disease. This study aims to evaluate endocan as a marker of plasma leakage in

dengue infection. Methods: The design of this study was retrospective cohort. Secondary data from the International Study on Biomarkers and Gene Expression Patterns in Patients with Dengue Virus Infection (INVEST) that was performed from 2010-2011 at Cipto Mangunkusumo Hospital, Jakarta were used. Endocan levels were determined with ELISA test. Plasma leakage diagnosis was performed with ultrasonography (USG) as the gold standard. Receiver Operating Characteristic (ROC) curve was performed to determine endocan cut-off level to detect plasma leakage. Correlation tests were performed on hematocrit, delta hematocrit, and albumin levels with endocan. Data analyses were performed with GraphPad Prism versi 5.0 for Windows and SPSS version 28. Results: 64 patients fulfilled the inclusion and exclusion criteria. There were 31 patients with dengue fever (DF) and 33 patients with dengue hemorrhagic fever (DHF). We observed significant differences of endocan, thrombocyte, hematocrit, delta hematocrit, and albumin levels between DF and DHF patients. The area under the curve (AUC) was 0.83 ((95% confidence interval (CI): 0.73-0.93). Endocan with a cut off value of 1.63 ng/mL can be used as a marker for plasma leakage with a sensitivity of 66.7%, a specificity of 90.3%, a positive predictive value (PPV) of 88%, and a negative predictive value (NPV) of 71.8%. There was a negative correlation between endocan and albumin levels in the critical phase of dengue ( $r: -0,4; p: 0,001$ ). There was no significant correlation ( $r: 0.12; P=0.36$ ) between the endocan and hematocrit values in the critical phase of dengue infection and the critical phase values of endocan with delta hematocrit ( $r: 0.16; P=0.21$ ). Conclusion: Endocan with a cut point value of 1.63 ng/mL can be used as a marker for plasma leakage with a sensitivity value of 66.7%, a specificity of 90.3%, a PPV of 88%, and a NPV of 71.8%. There was a negative correlation between endocan and albumin values in the critical phase of dengue infection.