



INTISARI

Latar belakang : Pasien COVID-19 berat memiliki respon imun berlebihan sehingga badai sitokin dan *Systemic Inflammatory Response Syndrome* (SIRS) dapat terjadi. Respon inflamasi sistemik berlebihan dapat menyebabkan terjadinya jejas endotel sistemik dan hiperkoagulasi sehingga terjadi makrotrombosis dan mikrotrombosis sistemik. D-dimer dilepaskan ketika plasmin dan enzim fibrinolitik memecah fibrin sebagai bentuk proses trombosis endovaskuler. Oleh karena itu, penilaian konsentrasi D-dimer dalam sirkulasi merupakan tes yang sensitif untuk mendiagnosis status trombosis (termasuk emboli paru dan *disseminated intravascular coagulation* (DIC)) serta prediksi terhadap kejadian mortalitas.

Tujuan : Menilai hubungan kadar awal D-Dimer terhadap kejadian mortalitas pasien COVID-19.

Metode : Metode studi observasional kohort retrospektif dilakukan dengan mengambil data sekunder dari rekam medis pasien terkonfirmasi COVID-19 yang dirawat di RSUP dr. Sardjito pada Maret – Desember 2020 yang dilakukan pemeriksaan D-Dimer selama perawatan. Data kadar D-dimer saat admisi dan kejadian mortalitas dikumpulkan untuk menghitung *cut-off* optimal menggunakan kurva ROC. Hubungan antara kadar D-dimer dengan mortalitas dianalisis menggunakan *chi-square test*. Analisis multivariat dilakukan dengan regresi logistik untuk mengontrol efek perancu variabel lain. Kaplan Meier dan *Cox Regression* digunakan untuk mengetahui kesintasan subjek berdasarkan nilai D-dimer. Pengujian dinyatakan signifikan apabila $p < 0,05$.

Hasil : Berdasarkan kurva ROC, *cut-off point* D-dimer admisi senilai 669 ng/ml memiliki sensitivitas 71,2% dan spesifitas 62,2%. Pasien dengan D-dimer admisi ≥ 669 ng/ml memiliki hubungan signifikan terhadap terjadinya mortalitas ($p=0,000$). Analisis multivariat menunjukkan bahwa D-dimer tetap memiliki hubungan signifikan terhadap mortalitas (OR 3,269; CI 1,655 – 6,457; $p=0,001$), dengan faktor perancu usia ($p=0,000$) dan indeks massa tubuh ($p=0,017$). Berdasarkan Kaplan Meier, didapatkan waktu kesintasan kelompok D-dimer admisi ≥ 669 ng/ml lebih singkat (25,84 hari) dibandingkan D-dimer admisi < 669 ng/ml (37,98 hari) ($p = 0,000$). Analisis *cox regression* menunjukkan D-dimer saat admisi merupakan variabel yang signifikan berpengaruh terhadap kesintasan pasien COVID-19 ($p = 0,004$; HR: 2,323; 95% CI: 1,301-4,147), dengan umur ($p = 0,000$) dan BMI ($p=0,032$) sebagai faktor perancu.

Kesimpulan : Kadar awal D-dimer ≥ 669 ng/mL berhubungan positif dengan tingkat mortalitas. Tingkat mortalitas pasien COVID-19 dengan kadar D-dimer admisi ≥ 669 ng/mL sebesar 3 kali lipat, dengan usia dan BMI sebagai faktor perancu.

Kata Kunci: COVID-19, D-Dimer, Koagulopati, Trombosis, Mortalitas



ABSTRACT

Background : *In severe COVID-19 infection, the immune response can be exaggerated and cause a systemic cytokine storm that triggers systemic inflammatory response syndrome (SIRS). Excessive systemic inflammatory response can lead to systemic endothelial injury (endotheliopathy) and a hypercoagulable state that increases the risk of systemic macrothrombosis and microthrombosis. D-dimers are released when plasmin, a fibrinolytic enzyme, breaks down fibrin and is a reflection of the endovascular thrombosis process. Assessment of circulating D-dimer concentrations is a sensitive test for diagnosing thrombotic status (including pulmonary embolism and DIC) and predicting mortality event in patient contracted with covid-19.*

Aim: *Assessing D-Dimer levels on admission correlation towards mortality case in COVID-19 patients.*

Methods : *The study was design used a retrospective cohort observational study method by taking secondary data from the medical records of COVID-19 confirmed patients treated at Dr. Sardjito from March to December 2020 who underwent D-Dimer testing during therapy.. D-Dimer levels on admission and death events were collected to calculate the optimum cutoff using receiver operating characteristics curves (ROC). Using the chi-square test, we investigated the association between D-dimer levels and mortality A multivariate analysis with logistic regression was conducted to compensate for the confounding effects of other factors. In addition to Kaplan Meier and Cox Regression, the D-dimer value was analyzed to measure the subject's survival. Two-tailed P values <0.05 were considered statistically significant.*

Result : *Based on the ROC curve, the D-dimer admission cut-off point of 669 ng/ml had a sensitivity of 71.2% and a specificity of 62.2%. Patients with D-dimer levels ≥ 669 ng/ml at admission had a higher risk of mortality ($p=0,000$). Despite the confounding effects of age ($p=0,000$) and body mass index ($p=0.017$), multivariate analysis revealed a significant association between D-dimer and mortality (OR 3,269; CI 1,651 – 6,457; $p=0.001$). According to Kaplan Meier, the D-dimer ≥ 669 ng/ml group had a shorter survival time (25.84 days) than the D-dimer < 669 ng/ml group (37.98 days) ($p = 0.000$). Cox regression analysis revealed that D-dimer at admission was a significant predictor of survival in COVID-19 patients ($p = 0.004$; HR: 2.323; 95% CI: 1.301-4,147), with age ($p = 0.000$) and BMI ($p=0,032$) as confounding variables*

Conclusion : *Initial D-dimer level ≥ 669 ng/mL significantly related to mortality rate in patient contracted to Covid 19. D-dimer ≥ 669 ng/mL increase three-fold to mortality level, with age and BMI as a counfounding factor.*

Keywords: *COVID-19, D-Dimer, Coagulopathy, Thrombosis, Mortality*