

INTISARI

HUBUNGAN KADAR INTERLEUKIN-6 SAAT RAWAT INAP DENGAN KEJADIAN MORTALITAS PASIEN COVID-19 DENGAN PENYAKIT PENYERTA KARDIOVASKULAR DI RSUP DR. SARDJITO

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Latar Belakang: *Corona Virus Disease 2019* (COVID-19) adalah penyakit yang disebabkan oleh *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) yang telah menginfeksi lebih dari 400 juta orang dengan tingkat mortalitas 2,3%. Mortalitas meningkat pada pasien yang memiliki penyakit penyerta salah satunya penyakit kardiovaskular. Interleukin-6 merupakan salah satu penanda biologis inflamasi yang memiliki hubungan dalam penilaian luaran COVID-19. Peningkatan IL-6 berhubungan dengan tingkat keparahan inflamasi dan risiko trombotik akibat COVID-19. Pada pasien dengan penyakit kardiovaskular, kadar IL-6 meningkat dibandingkan dengan tanpa penyakit kardiovaskular dan berhubungan dengan luaran dan prognosis.

Tujuan: Mengetahui hubungan kadar IL-6 yang tinggi saat perawatan dengan mortalitas pasien COVID-19 dengan penyakit penyerta kardiovaskular di RSUP Dr. Sardjito.

Metode Penelitian: Observasi analisis ini dilakukan secara kohort retrospektif menggunakan data sekunder rekam medis di RSUP Dr. Sardjito sejak Maret 2020 – Mei 2022 pada populasi COVID-19 dengan penyakit penyerta kardiovaskular. Dilakukan pengambilan data karakteristik dasar, hasil swab COVID-19, penyakit penyerta kardiovaskular, dan kadar IL-6. Interleukin-6 diukur dengan metode *Enzym-Linked Immunosorbent Assay* (ELISA) di Laboratorium RSUP Dr. Sardjito. Dilakukan analisis menentukan *cut-off* IL-6 dan menilai hubungannya dengan mortalitas saat rawat inap.

Hasil: Seratus pasien COVID-19 dengan penyakit penyerta kardiovaskular diinklusi dalam penelitian (70 pasien laki-laki). Didapatkan 63 (63%) subjek meninggal dan 37 (37%) subjek tidak meninggal dengan usia pasien pada kelompok meninggal lebih tua (65 (57-74) tahun vs 58 (45-65) tahun, $p = 0,002$). Pasien yang meninggal memiliki kadar IL-6 yang lebih tinggi dibandingkan yang tidak meninggal (75,78 (37,19 – 169,50) pg/ml vs 31,81 (9,89-71,65) pg/ml, $p = 0,001$). *Cut-off* IL-6 optimal memprediksi mortalitas adalah 36,25 pg/ml dengan *area under the curve* (AUC) 0,70 (0,605 – 0,812) sensitivitas 77,8% dan spesifisitas 59,5%, nilai prediksi positif 76,5% dan nilai prediksi negatif 61,1%. Kadar IL-6 $\geq 36,25$ pg/ml berhubungan dengan peningkatan mortalitas saat rawat inap (OR 4,678, IK 95% 1,713 – 12,778, $p = 0,003$).

Simpulan: Kadar IL-6 tinggi ($\geq 36,25$ pg/ml) merupakan faktor independen terhadap peningkatan mortalitas saat rawat inap pasien COVID-19 dengan penyakit penyerta kardiovaskular. Risiko peningkatan mortalitas paling tinggi pada pasien usia lanjut (≥ 65 tahun) dan kadar IL-6 tinggi ($\geq 36,25$ pg/ml).

Kata Kunci: COVID-19, interleukin-6, mortalitas, penyakit kardiovaskular

ABSTRACT

ASSOCIATION OF INTERLEUKIN-6 WITH MORTALITY IN COVID-19 PATIENT WITH CARDIOVASCULAR DISEASE IN RSUP DR. SARDJITO

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Background: Corona Virus Disease 2019 (COVID-19) is caused by *severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) has infected more than 400 millions people with case fatality rate 2,3%. Mortality increased in patient with comorbidity cardiovascular disease. Interleukin-6 is the inflammatory which has been positively correlated with outcome and prognosis of COVID-19 patient. Increasing IL-6 associated with inflammation severity and thrombosis risk. Patient had cardiovascular diseases has higher IL-6 level and correlate with prognosis of the COVID-19.

Aim: This study aimed to assess the association between increasing IL-6 concentration with mortality in COVID-19 patient with cardiovascular diseases.

Research Methods: Analytical observational study with a cohort retrospective design were conducted using secondary data from medical record in RSUP Dr. Sardjito since March 2020 - May 2022 in population of COVID-19 with cardiovascular disease. Patients baseline characteristics, COVID-19 nasal swab examination, cardiovascular disease and IL-6 level were collected. Interleukin-6 was quantified using Enzym-Linked Immunosorbent Assay (ELISA) method in RSUP Dr Sardjito laboratorium. Analyzing and detemining IL-6 cut off was performed and assessing the association with mortality.

Results: Hundred patients diagnosed with COVID-19 with cardiovascular disease were included in the study (70 patients were male). Sixty three (63%) patients were not survive and 37 (37%) patients were survive with older age patients in non-survive group (65 (57-74) years vs 58 (45-65) years, $p = 0,002$). Patients who died had higher IL-6 compare to survive group (75,78 (37,19 – 169,50) pg/ml vs 31,81 (9,89-71,65) pg/ml, $p = 0,001$). The optimal cut-off value of IL-6 level for predicting mortality was 32,65 pg/ml with area under the curve (AUC) 0,70 (0,605 – 0,812) with sensitivity of 77,8% and spesificity of 59,5%, positive predictive value and negative predictive value were 76,5% and 61,1%, respectively. IL-6 level $\geq 36,25$ pg/ml was associated with increasing in-hospital mortality rate (OR 4,678, CI 95% 1,713 – 12,778, $p = 0,003$)

Conclusion: IL-6 level ($\geq 36,25$ p/ml) was the independence factor to predict in-hospital mortality in COVID-19 patient with cardiovascular disease. Mortality increased in older age (≥ 65 years old) and high IL-6 level ($\geq 36,25$ pg/ml).

Keywords: COVID-19, interleukin-6, mortality, cardiovascular disease