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ASSOCIATION BETWEEN INTERLEUKIN-6 AND MORTALITY IN SEVERE AND CRITICAL COVID-19 PATIENTS
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ABSTRACT

Background: Severe and critical coronavirus disease 2019 (COVID-19) are associated with systemic hyperinflammation, organ dysfunction, and high mortality. Interleukin-6 (IL-6) is a major pro-inflammatory cytokine involved in cytokine storm and may serve as a prognostic biomarker in patients with severe COVID-19.

Objective: To determine the association between serum IL-6 levels and 14-day mortality among patients with severe and critical COVID-19.

Methods: This retrospective cohort study included adult patients with severe or critical COVID-19 admitted to Dr. Sardjito General Hospital, Yogyakarta, between May and October 2021. Patients with a history of IL-6 inhibitor therapy were excluded. A total of 136 complete medical records were analyzed. The optimal IL-6 cutoff value for predicting mortality was determined using receiver operating characteristic analysis. Differences in mortality proportions were assessed using the chi-square test, and the strength of association was expressed as an odds ratio (OR) with a 95% confidence interval (CI).

Results: The mean age of the patients was 56.08 ± 14.05 years, and 63.2% were male. Of the participants, 104 (76.4%) had severe COVID-19 and 32 (23.6%) had critical COVID-19. The overall 14-day mortality rate was 83.1%. The optimal IL-6 cutoff value was 31.92 pg/mL, with a sensitivity of 80.5% and specificity of 69.6%. Mortality occurred in 91 of 98 patients (92.9%) with IL-6 levels above 31.92 pg/mL, compared with 22 of 38 patients (57.9%) with IL-6 levels at or below the cutoff. Elevated IL-6 levels were significantly associated with mortality ($\chi^2 = 23.82$; $p < 0.001$; OR 9.46; 95% CI 3.47–25.77).

Conclusion: Serum IL-6 levels above 31.92 pg/mL were significantly associated with higher 14-day mortality among patients with severe and critical COVID-19. IL-6 may serve as a useful prognostic biomarker for early risk stratification in this population.

Keywords: COVID-19, interleukin-6, mortality, cytokine storm, prognostic biomarker.

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ABSTRAK

Latar Belakang: Penyakit coronavirus 2019 (COVID-19) yang berat dan kritis dikaitkan dengan hiperinflamasi sistemik, disfungsi organ, dan angka kematian yang tinggi. Interleukin-6 (IL-6) merupakan sitokin pro-inflamasi utama yang berperan dalam badai sitokin dan dapat berfungsi sebagai biomarker prognostik pada pasien dengan COVID-19 berat.

Tujuan: Untuk menentukan hubungan antara kadar IL-6 serum dan mortalitas 14 hari pada pasien COVID-19 derajat berat dan kritis.

Metode Penelitian: Studi kohort retrospektif ini melibatkan pasien dewasa dengan COVID-19 derajat berat atau kritis yang dirawat di RSUP Dr. Sardjito, Yogyakarta, antara bulan Mei dan Oktober 2021. Pasien dengan riwayat terapi penghambat IL-6 tidak disertakan dalam penelitian ini. Sebanyak 136 rekam medis lengkap dianalisis. Nilai ambang batas (cut-off) IL-6 yang optimal untuk memprediksi mortalitas ditentukan menggunakan analisis *receiver operating characteristic*. Perbedaan proporsi mortalitas dinilai menggunakan uji *chi-square*, dan kekuatan asosiasi dinyatakan sebagai *odds ratio* (OR) dengan interval kepercayaan (CI) 95%.

Hasil: Rata-rata usia pasien adalah 56,08 ± 14,05 tahun, dan 63,2% di antaranya berjenis kelamin laki-laki. Dari seluruh partisipan, 104 orang (76,4%) menderita COVID-19 berat dan 32 orang (23,6%) menderita COVID-19 kritis. Angka kematian keseluruhan dalam 14 hari adalah 83,1%. Nilai ambang batas IL-6 yang optimal adalah 31,92 pg/mL, dengan sensitivitas 80,5% dan spesifisitas 69,6%. Kematian terjadi pada 91 dari 98 pasien (92,9%) dengan kadar IL-6 di atas 31,92 pg/mL, dibandingkan dengan 22 dari 38 pasien (57,9%) dengan kadar IL-6 pada atau di bawah nilai ambang batas tersebut. Kadar IL-6 yang tinggi berhubungan secara signifikan dengan kematian ($\chi^2 = 23,82$; $p < 0,001$; OR 9,46; IK 95% 3,47–25,77).

Kesimpulan: Kadar IL-6 serum di atas 31,92 pg/mL berhubungan secara signifikan dengan angka kematian 14 hari yang lebih tinggi pada pasien COVID-19 derajat berat dan kritis. IL-6 dapat menjadi biomarker prognostik yang bermanfaat untuk stratifikasi risiko dini pada populasi ini.

Kata Kunci: COVID-19, interleukin-6, mortality, cytokine storm, prognostic biomarker.