

## Hubungan antara IL-6, IL-10, TNF- dengan Acute Kidney Injury pada Pasien Covid-19 Derajat Sedang dan Berat = The Relationship between IL-6, IL-10, TNF- with AKI in Moderate and Severe Covid-19 Patients

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### Abstrak

Latar Belakang: Acute Kidney Injury pada COVID-19 merupakan komplikasi penting dan dikaitkan dengan peningkatan risiko kematian diduga diperantarai kondisi inflamasi dan disregulasi imun, baik di awal maupun selama perawatan. Tujuan: Untuk mengetahui hubungan antara IL-6, IL-10, TNF- dengan AKI dan memprediksi perburukan hematuria, dan kejadian AKI Metode: Studi potong lintang dan prospektif kohort melibatkan 43 pasien COVID-19 derajat sedang dan berat yang dirawat di Rumah Sakit Pertamina Pusat di Jakarta, Indonesia dari bulan November 2020 hingga Januari 2021. Selama observasi dilakukan pemeriksaan darah lengkap, serum kreatinin, urinalisis, kadar IL-6, IL-10, TNF- pada hari pertama dan hari ketujuh pengobatan atau sebelum hari ketujuh jika pasien meninggal atau dipulangkan, dan perubahannya di analisis. Insiden AKI ditentukan ketika perubahan serum kreatinin dan urin output memenuhi kriteria pedoman Kidney Disease Improving Global Outcomes. Uji korelasi dilakukan terhadap peningkatan sitokin dengan perubahan hematuria dan kreatinin. Uji Wilcoxon dilakukan untuk mengetahui perbedaan kadar sitokin diantara status albuminuria. Selanjutnya dilakukan uji Receiver Operator Characteristic untuk melihat kemampuan prediksi IL-6, IL-10, TNF- terhadap perburukan hematuria dan kejadian AKI, menggunakan AUC minimal 0,7 dengan batas bawah IK 95% lebih dari 0,5 dan nilai  $p < 0,05$  Hasil: Terdapat korelasi antara peningkatan kadar serum IL-10 dengan perubahan serum kreatinin ( $r = -0,343$ ;  $p = 0,024$ ) tetapi tidak pada perubahan IL-6 dan TNF-a. Perubahan hematuria tidak berkorelasi dengan peningkatan ketiga kadar sitokin. Juga tidak ada perbedaan dalam kadar sitokin di antara kelompok albuminuria. Kadar serum TNF- dihari pertama perawatan dapat memprediksi AKI pada hari ke tujuh, AUC 85%;  $p = 0,045$  (IK 0,737-0,963), tetapi tidak dapat memprediksi perburukan hematuria Kesimpulan: Terdapat korelasi antara peningkatan IL-10 dengan perubahan serum kreatinin. TNF-! pada hari pertama perawatan dapat memprediksi kejadian AKI di hari ketujuh perawatan pasien COVID-19 derajat sedang dan berat.

.....Background: Acute Kidney Injury is an important complication and is associated with increased risk of death in COVID-19 due to inflammatory conditions and immune dysregulation, both at the beginning and during treatment. Aim: To determine the relationship between IL-6, IL-10, TNF- with AKI and their ability to predict the worsening of hematuria, and the incidence of AKI. Methods: 43 moderate and severe COVID-19 patients treated from November 2020 to January 2021 at Pertamina Central Hospital in Jakarta, Indonesia were included in this cross-sectional and prospective cohort study. During observation, tests including complete blood count, serum creatinine, urinalysis, levels of IL-6, IL-10 and TNF- were performed on the first and seventh day of treatment, or before day 7 if the patient died or was discharged, and the changes were analyzed. The incidence of AKI is determined when changes in serum creatinine and urine output meet the criteria in the Kidney Disease Improving Global Outcomes guidelines. Correlation test was performed on increased cytokines with changes in hematuria and creatinine. Wilcoxon test was performed to obtain differences in cytokine levels among albuminuria status. Receiver Operator Characteristic test was then

carried out to see the predictive ability of IL-6, IL-10, TNF- $\alpha$  on the worsening of hematuria and the incidence of AKI. Results: There was a correlation between increased serum IL-10 levels with changes in serum creatinine ( $r = -0.343$ ;  $p = 0.024$ ), but not in IL-6 and TNF- $\alpha$  levels. On the other hand, changes in hematuria did not correlate with an increase in the levels of the three cytokines. There was also no significant difference in the levels of cytokines among albuminuria groups. Serum TNF- $\alpha$  levels on the first day of treatment were able to predict AKI on the seventh day (AUC 85%;  $p = 0.045$ ; 95% CI 0.737-0.963), but did not predict the worsening of hematuria. Conclusion: There was a correlation between increased serum IL-10 with changes in serum creatinine. TNF- $\alpha$  on the first day of treatment can predict the incidence of AKI on the seventh day of treatment for moderate and severe COVID-19 patients.