Tesis

HUBUNGAN KADAR INTERLEUKIN 6, *PROCALCITONIN*, *C-REACTIVE PROTEIN*, DAN MORTALITAS PADA PASIEN *CORONAVIRUS DISEASE* 2019

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ABSTRAK

Latar Belakang: *Coronavirus Disease* 2019 (COVID-19) memiliki manifestasi klinis beragam dari asimtomatis hingga pneumonia berat dengan gagal nafas sehingga menyebabkan peningkatan morbiditas dan mortalitas. Respons hiperinflamasi yang diinduksi SARS- CoV-2 merupakan penyebab utama keparahan penyakit dan mortalitas pada pasien COVID-19. Disregulasi respons imun, berbagai komorbid dan faktor risiko dapat meningkatkan pelepasan berbagai sitokin proinflamasi seperti interleukin 6. Kadar interleukin 6 yang meningkat merupakan prediktor kuat dan independen untuk risiko mortalitas. Peningkatan kadar interleukin 6 menstimulus pelepasan dan peningkatan protein fase akut lainnya yaitu *procalcitonin*, dan *c-reactive protein* pada pasien COVID-19 terutama derajat berat-kritis. Pemeriksaan kadar penanda inflamasi dan reaktan fase akut saat admisi penting untuk memprediksi mortalitas dan meningkatkan efektifitas terapi sehingga dapat ditatalaksana dengan tepat. Penelitian ini bertujuan untuk menganalisis hubungan kadar interleukin 6, *procalcitonin*, *c- reactive protein* dan mortalitas pada pasien COVID-19 yang dirawat di RSUP Dr. M. Djamil Padang.

Metode: Penelitian analitik potong lintang prospektif dilakukan pada 60 pasien COVID-19 yang dirawat di RSUP Dr. M. Djamil Padang mulai bulan Mei sampai Desember 2021. Pemeriksaan kadar interleukin 6 menggunakan metode ECLIA, *procalcitonin* dengan metode ELFA, sedangkan *c-reactive protein* dengan metode imunokimia fase solid. Analisis bivariat menggunakan uji Mann-Whitney untuk melihat hubungan kadar interleukin 6, *procalcitonin, c -reactive protein* dan mortalitas. Analisis kurva ROC dan nilai AUC digunakan untuk menilai akurasi penanda inflamasi dalam memprediksi mortalitas dan menentukan nilai *cut off* kadar interleukin 6, *procalcitonin*, dan *c-reactive protein* pada pasien COVID-19.

Hasil dan Pembahasan: Rerata usia subjek penelitian yaitu 58,28 (13,07) tahun, dengan perempuan sebanyak 53,3%, dan laki-laki 46,7%. Persentase mortalitas pada pasien COVID-19 adalah 61,7%. Median kadar interleukin 6, *procalcitonin*, dan *c-reactive protein* yaitu 24,55(1,50-4.356,00) pg/mL; 0,43(0,03-200,00) ng/mL; 50,50(5,00-160,00) mg/L secara berurutan. Hubungan antara kadar interleukin 6, *procalcitonin, c -reactive protein* dan mortalitas didapatkan nilai p=0,005; p<0,001, p=0,001, secara berurutan. Nilai AUC berdasarkan kurva ROC pada interleukin 6, *procalcitonin*, dan *c-reactive protein* yaitu 71,6%; 78,8%; dan 75,1% secara berurutan. *Procalcitonin* memiliki nilai AUC yang paling tinggi sehingga paling berperan terhadap mortalitas pada pasien COVID-19. Nilai *cut off* kadar interleukin 6, *procalcitonin*, dan *c-reactive protein* yaitu 21,95 pg/mL; 0,35 ng/mL; dan 43,5 mg/L secara berurutan.

Simpulan: Hasil penelitian ini memperlihatkan terdapat hubungan kadar interleukin 6, *procalcitonin*, *c-reactive protein* dan mortalitas pada pasien COVID-19. *Procalcitonin* merupakan penanda inflamasi yang paling berperan terhadap mortalitas pada pasien COVID-19.

Kata Kunci: interleukin 6, *procalcitonin*, *c-reactive protein*, mortalitas, COVID-19. xii

ASSOCIATION BETWEEN INTERLEUKIN 6, PROCALCITONIN, C-REACTIVE PROTEIN LEVELS AND MORTALITY IN CORONAVIRUS DISEASE 2019 PATIENTS

ABSTRACT

***Background**: Coronavirus Disease 2019 (COVID-19) has various clinical manifestations from asymptomatic to severe pneumonia with respiratory failure, leading to increased morbidity and mortality. The hyperinflammatory response induced by SARS-CoV-2 is the common cause of disease severity and mortality in COVID-19 patients. Dysregulation of the immune response, the presence of various comorbidities, and risk factors can increase the release of proinflammatory cytokines such as interleukin 6. Elevated levels of interleukin 6 are strong and independent predictors of mortality risk. Increased interleukin 6 stimulates other acute-phase proteins, such as procalcitonin, and c-reactive protein of COVID-19 patients, especially severe-critical. Examination of the levels of inflammatory markers and acute phase reactants at admission are necessary to predict mortality and increase the effectiveness of therapy to get appropriate management. This study aims to analyze the association between interleukin 6, procalcitonin, c-reactive protein levels, and mortality in COVID-19 patients treated at Dr. M. Djamil Padang Hospital.*

***Methods**: An prospective cross-sectional analytic study was conducted on 60 treated patients at Dr. M Djamil Padang Hospital from May to December 2021. The quantification of interleukin 6 levels used the ECLIA method, ELFA for procalcitonin, and the solid phase immunochemical method for c-reactive protein. Bivariat analysis using the Mann-Whitney test to evaluated the association between interleukin 6, procalcitonin, c-reactive protein levels, and mortality. To assess the accuracy of inflammatory markers in predicting mortality and determine the cut-off values of interleukin 6, procalcitonin, and c-reactive protein levels in COVID-19 patients used ROC curve analysis and AUC values.*

***Results and Discussion**: The mean age of the subjects was 58.28 (13.07) years, with 53.3% of female and 46,7% of men. The mortality percentage in COVID-19 patients was 61.7%. The median levels of interleukin 6, procalcitonin, and c-reactive protein were 24.55(1.50-4.356.00) pg/mL; 0.43(0.003-200.00)ng/mL; 50.50(5.00-160.00) mg/L, respectively. The association between interleukin 6, procalcitonin, c-reactive protein levels, and mortality obtained p value=0.005; p<0.001, p=0.001, respectively. The AUC values based on the ROC curve for interleukin 6, procalcitonin, and c-reactive protein were 71.6%, 78.8%, and 75.1%, respectively. Procalcitonin has the highest AUC value so it has the most role in mortality related to COVID-19 patients. The cut-off values for interleukin 6, procalcitonin, and c-reactive protein levels were 21.95 pg/mL; 0.35 ng/mL; and 43.5 mg/L, respectively.*

***Conclusion**: The result of this study shows there is an association between interleukin 6, procalcitonin, c-reactive protein levels, and mortality in COVID-19 patients. Procalcitonin is an inflammatory marker that has most role in mortality in COVID-19 patients.*

***Keywords**: interleukin 6, procalcitonin, c-reactive protein, mortality, COVID-19.*