

## ABSTRAK

### ANALISIS KADAR INTERLEUKIN-6 (IL-6) DAN PLASMINOGEN ACTIVATOR INHIBITOR-1 (PAI-1), SEBAGAI FAKTOR RESIKO KEJADIAN KEMATIAN PASIEN COVID-19

Yusuf Hakim Aji \*, Nur Farhanah\*\*, Muhammad Hussein Gasem \*\*

\*PPDS-1 Ilmu Penyakit Dalam, Fakultas Kedokteran Universitas Diponegoro / RSUP  
Dr. Kariadi Semarang

\*\*Divisi Penyakit Tropik dan Infeksi Bagian Ilmu Penyakit Dalam, Fakultas  
Kedokteran Universitas Diponegoro Semarang / RSUP Dr. Kariadi Semarang

#### Latar Belakang

COVID -19 menyebabkan komplikasi mematikan berupa kerusakan paru-paru akut yang disebabkan terjadinya badai sitokin. Interleukin-6 (IL-6) dan Plasminogen Activator Inhibitor-1 (PAI-1) adalah dua protein yang berperan penting dalam respons imun dan peradangan. IL-6 merupakan sitokin pro-inflamasi yang diproduksi oleh sel imun, sedangkan PAI-1 adalah protein yang menghambat aktivasi plasmin, enzim yang berperan dalam pemecahan bekuan darah. Tingkat PAI-1 yang tinggi dapat meningkatkan risiko penggumpalan darah, komplikasi serius pada pasien COVID-19. Diduga kuat bahwa IL-6 dan PAI-1 dapat memicu peningkatan sel inflamasi, kerusakan jaringan, dan kematian pada infeksi SARS-CoV-2.

#### Metode

Penelitian *Prospective Cohort* pada pasien COVID-19 yang merupakan bagian dari penelitian payung COVID-19. Penelitian dilaksanakan pada bulan Agustus 2020 hingga Januari 2021 melibatkan 72 subjek yang terinfeksi COVID-19 dengan RT PCR positif yang memenuhi kriteria inklusi.

#### Hasil

Dari 72 sampel penelitian didapatkan 13 subjek meninggal dunia dan 59 subjek bertahan hidup. Penelitian menunjukkan didapatkan perbedaan signifikan tingginya kadar IL-6 ( $p=0,022$ ) terhadap kematian pasien COVID-19, namun kadar PAI-1 ( $p=0,855$ ) tidak menunjukkan perbedaan signifikan dengan kematian pasien COVID-19. Pada penelitian ini menunjukkan nilai kadar IL-6 lebih dari 160 pg/mL dapat digunakan untuk mengidentifikasi pasien dengan faktor risiko kematian, kadar IL-6 dan PAI-1 menunjukkan tidak secara bersama - sama sebagai faktor risiko terhadap kematian COVID-19. Kadar IL-6 paling tinggi pada derajat Kritis COVID-19 (mean 245,9), sedangkan kadar PAI-1 paling tinggi didapatkan pada derajat ringan COVID-

19 (mean 4,4). Rasio PaO<sub>2</sub>/FiO<sub>2</sub> (p=0,023) terbukti kuat sebagai perancu yang mempengaruhi kematian pada penelitian ini.

### **Kesimpulan**

Kadar IL-6 yang tinggi merupakan sebagai faktor risiko kematian COVID-19. Kadar PAI-1 bukan merupakan faktor risiko kematian COVID-19. Rasio PaO<sub>2</sub>/FiO<sub>2</sub> merupakan faktor risiko perancu yang mempengaruhi kematian COVID-19.

**Kata Kunci :** COVID-19, IL-6, PAI-1, Kematian

## ABSTRACT

### ANALYSIS OF RISK FACTORS LEVELS OF INTERLEUKIN-6 (IL-6) AND PLASMINOGEN ACTIVATOR INHIBITOR (PAI-1) WITH MORTALITY OF COVID - 19 PATIENTS

Yusuf Hakim AJi\*, Nur Farhanah\*\*, Muhammad Hussein Gasem \*\*

\*Resident Internal Medicine, Diponegoro University Faculty of Medicine / Dr. Kariadi General Hospital Semarang

\*\*Tropical and Infectious Division of Internal Medicine, Diponegoro University Faculty of Medicine/ Dr. Kariadi General Hospital Semarang

#### Background

COVID-19 causes deadly complications, including acute lung injury caused by cytokine storm. Interleukin-6 (IL-6) and Plasminogen Activator Inhibitor-1 (PAI-1) are two proteins that play important roles in the immune response and inflammation. IL-6 is a pro-inflammatory cytokine produced by immune cells, while PAI-1 is a protein that inhibits the activation of plasmin, an enzyme that plays a role in clot breakdown. High PAI-1 levels can increase the risk of thrombosis, a serious complication in COVID-19 patients. It is thought that IL-6 and PAI-1 may trigger the increase of inflammatory cells, tissue damage, and death in SARS-CoV-2 infection.

#### Methods

Prospective Cohort study in COVID-19 patients which is a part of the COVID-19 joint research. The research was conducted from August 2020 to January 2021 involving 72 subjects with positive RT PCR positive COVID-19 infection who met the inclusion criteria.

#### Results

From the 72 research samples, 13 subjects died and 59 subjects survived. The study showed that a significant difference in IL-6 levels ( $p=0.022$ ) was associated with death in COVID-19 patients, but PAI-1 levels ( $p=0.855$ ) did not show a significant difference with death in COVID-19 patients. In this study, it was shown that a IL-6 level of more than 160 pg/mL can be used to identify patients with a risk factor for death, and that IL-6 and PAI-1 levels do not together act as a risk factor for COVID-19 death. IL-6 levels were highest in the critical stage of COVID-19 (mean 245.9), while PAI-1 levels were highest in the mild stage of COVID-19 (mean 4.4). PaO<sub>2</sub>/FiO<sub>2</sub> ratio ( $p=0.023$ ) was strongly proven as a confounding factor that affects death in this study.

#### Conclusion

High IL-6 levels are a risk factor for COVID-19 mortality. PAI-1 levels are not a risk factor for COVID-19 mortality. PaO<sub>2</sub>/FiO<sub>2</sub> ratio is a confounding risk factor that affects COVID-19 mortality.

**Key words**

COVID-19, Il-6, PAI-1, , Mortality