

Analisis Respons Immunopatologi Lokal pada Pneumonia Berat yang Mengalami Kematian Akibat Gagal Ekstubasi: Kajian Khusus Peran sTREM, Makrofag Alveolar, IL-6, IL-17, CD4, Treg Foxp3+, Surfactant Protein-A, Caspase-3 = Analysis of Local Immunopathology Responses in Severe Pneumonia with Mortality due to Extubation Failure: Focus on sTREM, Alveolar Macrophage, IL-6, IL-17, CD4, Foxp3+ Tregs, Surfactant Protein-A, and Caspase-3

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Abstrak

Pneumonia merupakan penyebab kedua terbanyak perawatan di rumah sakit yaitu 600,000 pasien setiap tahun di dunia dengan mortalitas tinggi pada pneumonia berat (50%). Di Indonesia, mortalitas community-acquired pneumonia (CAP) CURB skor 3 tinggi (60,8%) dengan penyebab tersering gagal ekstubasi. Immunopatologi lokal yang mendasari kegagalan ekstubasi belum diketahui dengan pasti. Oleh karena itu diperlukan penelitian untuk menganalisis respons imunopatologi lokal pada pneumonia berat yang mengalami kematian akibat gagal ekstubasi.

Penelitian ini merupakan studi kohort prospektif pada pasien pneumonia berat yang masuk instalasi gawat darurat (IGD) dan intensive care unit (ICU) RS dr. Cipto Mangunkusumo pada bulan November 2020–Januari 2021. Pasien yang memenuhi kriteria penelitian diambil sebagai subjek dengan consecutive sampling. Dilakukan pengambilan cairan bronchoalveolar lavage (BAL) untuk pemeriksaan sTREM, makrofag alveolar, IL-6, IL-17, CD4, Treg Foxp3+, surfactant protein-A, dan caspase-3. Status ekstubasi dievaluasi pada hari ke-20 dan mortalitas pada hari ke-28. Data dianalisis dengan uji Mann-Whitney dan uji t tidak berpasangan sedangkan hubungan antar parameter dianalisis dengan uji Fisher.

Terdapat 40 pasien pneumonia berat yang menjadi subjek penelitian saat pandemi COVID-19. Proporsi cedera paru berat 70% di paru kanan, proporsi gagal ekstubasi hari ke-20 sebanyak 80% dan mortalitas hari ke-28 adalah 75%. Kadar CD4 paru kanan lebih rendah secara bermakna dibandingkan paru kiri (uji Mann Whitney, $p = 0,003$). Kadar CD4 cedera paru berat lebih rendah pada pasien gagal ekstubasi (uji Mann Whitney, $p = 0,010$) dan status mortalitas (uji Mann Whitney, $p = 0,004$). Terdapat perbedaan bermakna pada makrofag alveolar fungsional, IL-6, dan CD4; namun tidak ada perbedaan bermakna pada kadar sTREM, IL-17, Treg Foxp3+, jumlah makrofag alveolar, surfactant protein-A, dan caspase-3 terhadap keberhasilan ekstubasi. Disimpulkan gagal ekstubasi dan mortalitas berhubungan dengan kadar CD4 rendah cairan BAL di cedera paru berat. Keberhasilan ekstubasi berhubungan dengan makrofag alveolar fungsional rendah, kadar IL-6 rendah, dan kadar CD4 tinggi di cedera paru berat.

.....Pneumonia is the second leading cause for hospitalization with 600,000 patients annually and mortality rate. In Indonesia, community-acquired pneumonia (CAP) with high CURB score represents 60,8% of mortality due to extubation failure. The explanation of severe pneumonia pathophysiology that underlying immunopathology causing extubation failure is still insufficient. Therefore, the analysis of lungs' local immunopathology in severe pneumonia patients with mortality due to extubation failure is required.

This is a prospective cohort study. Subject recruitments were conducted in the resuscitation emergency unit (REU) and intensive care unit (ICU) ward, Cipto Mangunkusumo Hospital, from November 2020 to January 2021. Bronchoalveolar lavage fluid (BALF) was performed to investigate sTREM, alveolar macrophage (amount and functional), IL-6, IL-17, CD4, Foxp3+ Tregs, surfactant protein-A, and caspase-3. Data was analyzed using Mann-Whitney and unpaired t test, while fisher test was used to analyze parameter associations.

A total of 40 severe pneumonia patients were enrolled as the study subjects during COVID-19 pandemic. Study results showed the proportion of severe lung injury was 70% in the right lung, the proportion of 20-days extubation failure was 80%, and the 28-days mortality rate was 75%. Levels of CD4 BAL in the right was lower than the left lung ($p = 0,003$). There was a significant difference of CD4 BAL on 20-days extubation (Mann Whitney test, $p = 0,010$) and 28-days mortality (Mann Whitney test, $p = 0,004$). There were an association of functional alveolar macrophage, IL-6, and CD4 in severely affected lungs with extubation success; There were no association of sTREM, IL-17, Foxp3+ Tregs, amount and functional alveolar macrophage, surfactant protein-A, dan caspase-3 in severely affected lungs with extubation success. In summary, extubation failure and mortality are associated with low BALF CD4 in severely affected lungs. Extubation success is associated with low functional alveolar macrophage, low IL-6, and high CD4 levels in severe pneumonia patients.