

Faktor-Faktor yang Memengaruhi Long COVID dan Kelelahan pada Penyintas COVID-19 yang Pernah Dirawat Inap di Beberapa Rumah Sakit di Palembang

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Abstrak

Latar Belakang: Long COVID adalah kondisi pasca infeksi SARS-CoV-2 yang ditandai oleh gejala yang bertahan ≥ 2 bulan, dengan kelelahan sebagai keluhan utama. Di Indonesia, tercatat sekitar 1.400 kasus COVID-19 aktif, dan berpotensi mengalami long COVID. Meskipun kelelahan umum terjadi, faktor risiko dan biomarker yang mendasarinya, baik pada long COVID maupun COVID-19 secara umum, belum sepenuhnya dipahami. Interleukin-6 (IL-6) diduga berperan dalam mekanisme kelelahan, tetapi hubungan antara varian virus SARS-CoV-2, kadar IL-6, dan gejala kelelahan masih belum jelas. **Metode:** Penelitian ini merupakan studi kohort ambispektif yang melibatkan pasien dewasa yang dirawat inap ≥ 5 hari karena COVID-19. Data klinis, demografis, dan riwayat vaksinasi diperoleh dari rekam medis. Gejala kelelahan dinilai menggunakan kuesioner Fatigue Assessment Scale (FAS), sedangkan long COVID dinilai melalui kuesioner terstruktur. Analisis regresi Cox digunakan untuk mengidentifikasi faktor risiko. IL-6 diukur dengan metode ELISA, dan analisis in-silico dilakukan untuk menilai hubungan mutasi ssRNA terhadap binding affinity TLR8 dan kadar IL-6. **Hasil:** Sebanyak 257 pasien terlibat dalam penelitian, dengan 30 subjek diambil darahnya untuk pemeriksaan IL-6. Enam faktor risiko ditemukan terkait dengan long COVID, yaitu riwayat kelelahan akut saat dirawat, penyakit ginjal kronis, status PCR positif saat keluar RS, trombositosis, status vaksinasi, dan kebiasaan olahraga. Eritrositopenia dan terapi oksigen berkorelasi dengan kelelahan long COVID, sedangkan kelelahan akut dan kebiasaan olahraga memengaruhi kelelahan COVID-19 umum. Varian Delta meningkatkan risiko long COVID namun menurunkan risiko kelelahan, dan kadar IL-6 tinggi berhubungan dengan kelelahan setelah dikendalikan oleh variabel confounding. Selain itu, ditemukan secara in-silico perbedaan skor binding affinity yang disebabkan mutasi pada ssRNA memengaruhi kadar IL-6 subjek. **Kesimpulan:** Long COVID, kelelahan long COVID dan kelelahan COVID-19 umum dipengaruhi oleh kombinasi faktor klinis, perilaku, dan varian virus. IL-6 berperan penting dalam patogenesis kelelahan, dengan kemungkinan pengaruh mutasi virus terhadap disregulasi imun. **Kata kunci:** coronavirus disease 2019, faktor risiko, interleukin 6, long COVID, penyintas COVID-19.

Background: Long COVID is a post-infection condition following SARS-CoV-2 infection characterized by symptoms lasting ≥ 2 months, with fatigue being the major complaint. In Indonesia, around 1,400 active COVID-19 cases have been recorded. These individuals have the potential to develop long COVID. Although fatigue is common, the underlying risk factors and biomarkers both in long COVID and in COVID-19 generally are not yet fully understood. Interleukin-6 (IL-6) is suspected to play a role in the mechanism of fatigue, but the relationship between SARS-CoV-2 variants, IL-6 levels, and fatigue symptoms remains unclear. **Methods:** This was an ambispective cohort study involving adult patients hospitalized for ≥ 5 days due to COVID-19. Clinical, demographic, and vaccination history data were collected from medical records. Fatigue status was assessed using the Fatigue Assessment Scale (FAS), and long COVID was evaluated through a structured questionnaire. Cox regression analysis was used to identify risk factors. IL-6 was measured using ELISA,

and in-silico analysis was performed to assess the relationship ssRNA mutations based its binding affinity to TLR8. The binding affinity score was compared to IL-6 levels. Results: A total of 257 patients participated in the study, with blood samples for IL-6 testing collected from 30 subjects. Six risk factors were found to be associated with long COVID: history of acute fatigue during hospitalization, chronic kidney disease, PCR-positive status at hospital discharge, thrombocytosis, vaccination status, and exercise habits. Erythrocytopenia and oxygen therapy were correlated with long COVID fatigue, while acute fatigue and exercise habits influenced general COVID-19-related fatigue. After controlling for confounding variables, the Delta variant increased the risk of long COVID but had the lower risk of fatigue, and high IL-6 levels were associated with fatigue. Additionally, in-silico findings showed that mutations in ssRNA altered TLR8 binding affinity scores, which influenced IL-6 levels in subjects. Conclusion: Long COVID, long COVID fatigue, and general COVID-19-related fatigue are influenced by a combination of clinical, behavioral, and viral variant factors. IL-6 plays an important role in the pathogenesis of fatigue, with possible viral mutation effects contributing to immune dysregulation. Keywords: coronavirus disease 2019, COVID-19 survivors, interleukin 6, long COVID, risk factors.</div>