

Profil Sitokin Pro- dan Anti-Inflamasi Saluran Napas Atas untuk Memprediksi Tingkat Keparahan COVID-19 = Profile of Pro- and Anti-Inflammatory Cytokines in Upper Respiratory Tract to Predict Severity of COVID-19

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Abstrak

Latar Belakang: Coronavirus disease 2019 (COVID-19) adalah penyakit infeksi saluran pernapasan yang pertama kali ditemukan di Wuhan. Sejak ditetapkan sebagai pandemi oleh WHO hingga 3 Juli 2021 terdapat sebanyak 183.098.615 kasus terkonfirmasi positif COVID-19 dengan jumlah kematian sebesar 3.964.145 kasus di seluruh dunia. Secara etiologi COVID-19 disebabkan oleh varian coronavirus baru yang dikenal sebagai SARS-CoV-2. Individu yang terinfeksi SARS-CoV-2 sebagian besar mengalami gejala ringan atau asimtomatis. Namun, pada sebagian orang dengan usia lanjut dan mengidap penyakit komorbid manifestasi gejala berat lebih sering ditemui. Salah satu faktor yang berkaitan terhadap manifestasi COVID-19 adalah respons imun host. Molekul sitokin merupakan protein yang berperan untuk mengaktifkan mekanisme perlawanannya terhadap virus. Pengetahuan tentang profil imunitas yang diperantarai oleh sitokin dari saluran napas atas masih sangat sedikit sekali yang dipelajari. Penentuan biomarker yang dapat dijadikan penanda keparahan juga perlu untuk diketahui.

Metode: Sampel swab NP diperoleh dari pasien terkonfirmasi positif COVID-19. Subjek dibagi menjadi 2 kategori berdasarkan manifestasi COVID-19 gejala ringan dan berat. Kadar sitokin (pg/ml) IL-2, IL-4, IL-10, IL-13, IL-17A, dan GMCSF dianalisis dari sampel swab NP menggunakan Luminex® assay.

Hasil: Faktor demografi seperti usia ($p=0,024$) dan komorbid ($p=0,017$) secara signifikan berperan dalam menentukan keparahan gejala pada pasien COVID-19. Kadar (pg/ml) IL-2, IL-4, IL-10, IL-13, IL-17A, dan GMCSF antara kedua kelompok pasien COVID-19 gejala ringan dan berat tidak berbeda signifikan. Namun demikian, terdapat kecenderungan bahwa kadar (pg/ml) IL-2, IL-4, IL-13, dan GMCSF meningkat pada kelompok pasien COVID-19 gejala berat. Sedangkan, kadar (pg/ml) IL-10 dan IL-17A cenderung menurun pada pasien COVID-19 yang bergejala berat. Selain itu, rasio antara IL-2/IL-10 secara signifikan ($p=0,004$) lebih tinggi pada pasien COVID-19 gejala berat. Sebanyak 65,7% pasien COVID-19 dengan gejala berat memiliki nilai rasio IL-2/IL-10 yang tinggi.

Kesimpulan: Kadar sitokin (pg/ml) IL-2, IL-4, IL-10, IL-13, IL-17A dan kemungkinan GMCSF (pg/ml) dari sampel swab NP dapat terdeteksi menggunakan Luminex® assay. Rasio kadar sitokin IL-2/IL-10 dapat dijadikan sebagai kandidat biomarker keparahan infeksi COVID-19 di masa mendatang.

.....Background: Coronavirus disease 2019 (COVID-19) is a respiratory tract infectious disease. Since the outbreak in Wuhan, COVID-19 was declared as a pandemic by WHO. Data from July 3rd, 2021, showed that there have been 183,098,615 confirmed positive cases of COVID-19 with a death toll of 3,964,145 worldwide. Etiologically COVID-19 is caused by the new coronavirus known as SARS-CoV-2. The majority of people infected with SARS-CoV-2 experience mild symptoms or even are asymptomatic. However, for some people with older age and having comorbid diseases, severe manifestations are very common. Host immune response is one of the factors which affect disease severity. Playing a vital role in activating the immune system against viruses, cytokine protein can also contribute to the severity. Currently,

very little is known about the profile of cytokine-mediated immunity from the upper respiratory tract. This research is aimed to find a potential candidate of biomarkers to predict severity in the early phase of COVID-19 infections.

Methods: NP swab samples were obtained from patients who were positively confirmed for COVID-19. Subjects were divided into 2 categories based on the manifestation as mild or severe symptoms of COVID-19. Cytokine levels (pg/ml) of IL-2, IL-4, IL-10, IL-13, IL-17A, and GMCSF were analyzed from NP swab samples using Luminex® assay.

Results: Demographic factors such as age ($p=0.024$) and comorbidities ($p=0.017$) significantly played a role in determining severity of COVID-19 patients. The levels (pg/ml) of IL-2, IL-4, IL-10, IL-13, IL-17A, and GMCSF between the two groups of patients with mild and severe COVID-19 symptoms were not significantly different. However, there was a tendency that the levels (pg/ml) of IL-2, IL-4, IL-13, and GMCSF to increase in the group of patients with severe COVID-19 symptoms. Meanwhile, levels (pg/ml) of IL-10 and IL-17A tend to decrease in COVID-19 patients with severe symptoms. In addition, the ratio of IL-2/IL-10 was significantly ($p=0.004$) higher in severe COVID-19 patients. A total of 65.7% of COVID-19 patients with severe symptoms had high values of IL-2/IL-10 ratio.

Conclusion: Cytokine levels (pg/ml) of IL-2, IL-4, IL-10, IL-13, IL-17A, and GMCSF from NP swab samples can be detected using the Luminex® assay. The ratio of IL-2/IL-10 cytokine levels can be used as a biomarker candidate to predict severity for COVID-19 infection in the future.