

# The immunomodulation of SARS-COV-2 infection on the production of cytokines by peripheral blood mononuclear cells and neutrophils in COVID-19 ICU patients.

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## Abstract

COVID-19 pandemic is spreading globally with a worrying mortality rate. Unique medical features of severe COVID-19 include neutrophilia, cytokine storm, acute respiratory distress syndrome, and severe inflammatory syndrome. Here, we propose investigating the influence of SARS-CoV-2 infection on the cytokines profile of peripheral blood mononuclear cells (PBMC) and neutrophils in COVID-19 patients. This study examines PBMC and neutrophils as a potential source of immunopathologic complications for severely ill COVID-19 patients or as an immunomodulation target for SARS-CoV-2 infection. Neutrophils and PBMC were separated by density gradient sedimentation and stimulated with mitogen. Culture supernatants from 89 COVID-19 patients and 89 sex and age-matched healthy control (HC) were stimulated evaluated for levels of Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF), interferon (IFN)- $\alpha$ , IFN- $\gamma$ , interleukin (IL)-2, -4, -5, -6, -9, -10, -12, -17A, and tumor necrosis factor (TNF)- $\alpha$  using anti-cytokine antibody MACSPlex capture beads. The PBMC cytokine profiles showed significantly lower mean values of GM-CSF, IFN- $\gamma$ , IL-6, IL-9, IL-10, IL-17A, and TNF- $\alpha$  ( $p < 0.0001$ ) for COVID-19 patients compared to HC. In contrast, COVID-19 patients showed higher mean levels of PBMC cytokine values for IL-2 ( $p < 0.001$ ) and IL-5 ( $p < 0.01$ ). As for neutrophils, COVID-19 patients showed significantly lower mean values in the levels of GM-CSF, IFN- $\gamma$ , IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-17A, IL-12, TNF- $\alpha$  ( $p < 0.0001$ ), and IFN- $\alpha$  ( $p < 0.01$ ). The Th1:Th2 cytokine ratios revealed a lower inflammatory cytokine for 12 out of 24 combinations in COVID-19 ICU patients, suggesting downregulation of the cell-mediated immunity by SARS-CoV-2 infection for both the PBMC and neutrophils. Our finding may also indicate the source of raised serum cytokine levels (GM-CSF, IFN- $\alpha$ , IFN- $\gamma$ , IL-4, IL-6, IL-9, IL-10, IL-17A, IL-12, and TNF- $\alpha$ ) documented by previous studies in COVID-19 patients are not from PBMC or neutrophils but maybe from another cell type. We also detected a significant increase in the cytokine levels of IL-2 and IL-5 by PBMC, which may indicate that PBMC do play a part in the elevated IL-2 and IL-5 serum levels in COVID-19 patients. In conclusion, data collected for the cytokine profiles and Th1:Th2 cytokine ratios suggest that SARS-CoV-2 infection brings about an immunomodulatory effect on PBMC and neutrophils.

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## Biography:

Dr. Sahar Essa is a virologist who completed her Ph.D. at Warwick University, United Kingdom. In addition to teaching, Dr. Essa is professionally involved in medical research. She is mainly interested in viral immunopathology. Her experience in detecting and evaluating cytokine responses in virally infected

patients. She has published papers in reputed journals and recently collaborated with her colleagues and submitted conducted grants to investigate the cell-mediated immune responses during viral infections.