

## Developing topics

# Quantification of neurological blood-based biomarkers in critically ill patients with COVID-19

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**Abstract**

**Background:** Multiple neurological manifestations of COVID-19 have been reported such as headache, anosmia, ischemic stroke, and cerebral hemorrhages. Objective characterization of the acute neurological damage in critically ill patients with COVID-19 has not yet been reported.

**Method:** We performed a prospective observational study of plasma brain biomarkers in critically ill patients with respiratory failure that were diagnosed with (COVID-19) or without (ICU control) COVID-19. Demographics, co-morbidities, daily clinical physiologic and laboratory data were collected. Plasma samples were drawn for measurement of neurofilament-light chain (NF-L), total tau (t-tau), ubiquitin carboxy-terminal hydrolase L1 (UCH-L1), and glial fibrillary acidic protein (GFAP). The primary neurological outcome was delirium as defined by the intensive care delirium screening checklist (ICDSC, scale 1 - 8). Associations between brain biomarkers and markers of respiratory failure of COVID-19 were analyzed.

**Result:** 27 patients with COVID-19 and 19 ICU controls were enrolled. The concentration of plasma GFAP, UCH-L1 and NF-L levels was higher in both groups compared to healthy controls. Compared to ICU controls, patients with COVID-19 had significantly higher GFAP (272 [150-555] pg/ml vs 118 [78.5-168] pg/ml,  $p=0.0009$ ). In patients with COVID-19, GFAP ( $\rho=0.5115$ ,  $p=0.0064$ ), UCH-L1 ( $\rho=0.4056$ ,  $p=0.0358$ ) and NF-L ( $\rho=0.6223$ ,  $p=0.0005$ ) were positively correlated with the ICDSC score and were higher in patients diagnosed with delirium (ICDSC  $\geq 4$ ) in the COVID-19 group but not ICU controls. There were no associations between PaO<sub>2</sub>/FiO<sub>2</sub> or diagnosis of ARDS and plasma concentration of GFAP, t-tau, UCH-L1, or NF-L in patients with COVID-19.

**Conclusion:** Plasma GFAP is 2-fold higher in critically ill patients with COVID-19 compared to ICU controls, and higher concentrations of GFAP, UCH-L1 and NF-L are associated with delirium specifically in patients with COVID-19.