## Association between Serum Biomarkers of Inflammation One Week after ICU Admission and Post-Discharge Mortality in Critically III Patients

Baker Nasser<sup>1</sup>, Alexis Macha<sup>1</sup>, Sikandar Khan<sup>2,3</sup>, Anthony Perkins<sup>4</sup>, Sophia Wang<sup>5</sup>, Peter Conrad<sup>3</sup>, Sarah Seyffert<sup>6</sup>, Courtney Borman<sup>3</sup>, Ammar Athar<sup>3</sup>, Malissa Mulkey<sup>7</sup>, Sujuan Gao<sup>4</sup>, Malaz Boustani<sup>3</sup>, Babar Khan<sup>2,3</sup>

<sup>1</sup>Indiana University School of Medicine; <sup>2</sup>Indiana University School of Medicine Division of Pulmonary, Critical Care, Sleep, and Occupational Medicine; <sup>3</sup>Indiana University Center for Aging Research; <sup>4</sup>Indiana University School of Medicine Department of Biostatistics and Health Data Science; <sup>5</sup>Indiana University School of Medicine Department of Psychiatry; <sup>6</sup>Indiana University School of Medicine Department of Internal Medicine; <sup>7</sup>Indiana University School of Nursing

**Background:** Delirium occurs among up to 80% of critically ill patients and is associated with poor patient outcomes. Levels of serum biomarkers of inflammation and astrocytic and glial activation measured at ICU admission are associated with increased delirium duration, delirium severity, and in-hospital mortality. The utility of measuring biomarkers at later points during ICU stay has not been elucidated.

**Objective:** To determine how serum biomarker levels collected at one week of ICU stay are associated with mortality.

Design: Observational study.

Setting: Three Indianapolis hospitals.

Patients: One hundred seventy-eight critically ill patients.

**Main Results:** The median cohort age was 61 years (IQR 53.5-70.1), 56.2% were female, and 48.3% were African American. The median APACHE II score was 21.0 (IQR 16.0-27.0), and the median Charlson Comorbidity Index score was 3.0 (IQR 1.0-5.0). Approximately 76% were mechanically ventilated; 54% had acute respiratory failure and/or sepsis. Median ICU stay was 13 days (IQR 10.0-22.0).

We analyzed the relationship between serum biomarkers of inflammation (interleukin-1, 6, 8, 10, and tumor necrosis factor  $\alpha$ ), neuroprotection (insulin-like growth factor 1), and astrocytic and glial activation (S-100 $\beta$ ) and mortality 30 days post-discharge. Higher levels only of IL-6 and IL-10 at day 8 of ICU stay were associated with higher odds of death 30 days post-discharge (IL-6 OR: 2.45, 95% CI: 1.49, 4.03, p<0.001; IL-10 OR: 2.07, 95% CI: 1.23, 3.49, p=0.006), while day 1 levels of the same biomarkers were not (IL-6 OR: 1.10, 95% CI: 0.72, 1.70, p=0.662; IL-10 OR: 1.40, 95% CI: 0.88, 2.25, p=0.157).

**Conclusion:** Measuring serum biomarkers of systemic inflammation one week after ICU admission may be more useful than measuring at ICU admission for predicting longer-term outcomes in critically ill patients.