SARS-CoV-2 RNAEMIA AS A BIOMARKER OF LOWER RESPIRATORY VIRAL LOAD IN COVID-19

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BACKGROUND

- Plasma SARS-CoV-2 RNA (vRNA) levels (RNAemia) are significantly associated with COVID-19 severity indices and predict adverse clinical outcomes in hospitalized patients [Jacobs 2021, Fajnzylber 2020, Hagman 2020, Hogan 2020, Prebensen 2020, Veyer 2020].
- We and others have recently shown that detectable RNAemia can indicate presence of virions in plasma (i.e. true viremia) [Jacobs 2021, VanCleemput 2021].
- Lower respiratory tract (LRT) infection by SARS-CoV-2 can lead to pneumonia and acute respiratory distress syndrome (ARDS), which is the most common cause of COVID-19 mortality [Ketcham 2021].
- Viral RNA levels in LRT secretions have been shown to be associated with COVID-19 outcome [Buetti 2020, Chen 2021].
- The relationship between LRT and plasma vRNA is not well defined.

METHODS

- Observational cohort study
  - Hospitalized patients with COVID-19 prospectively enrolled from three UPMC hospitals April 2020 to May 2021.
  - Critically ill patients 18-90 years of age diagnosed with SARS-CoV-2 infection and who were intubated and mechanically ventilated for acute hypoxemic respiratory failure due to COVID-19 pneumonia.
- We performed qRT-PCR for SARS-CoV-2 N on total RNA extracted from 0.5-1.0 mL plasma or 150 uL ETA collected on enrollment day (Day 1 – baseline) and on Days 5 and 10 during hospitalization.

Plasma viral RNA (vRNA) measurement may offer a practical surrogate of lower respiratory tract (LRT) vRNA burden in critically ill patients, especially early in severe disease.

RESULTS

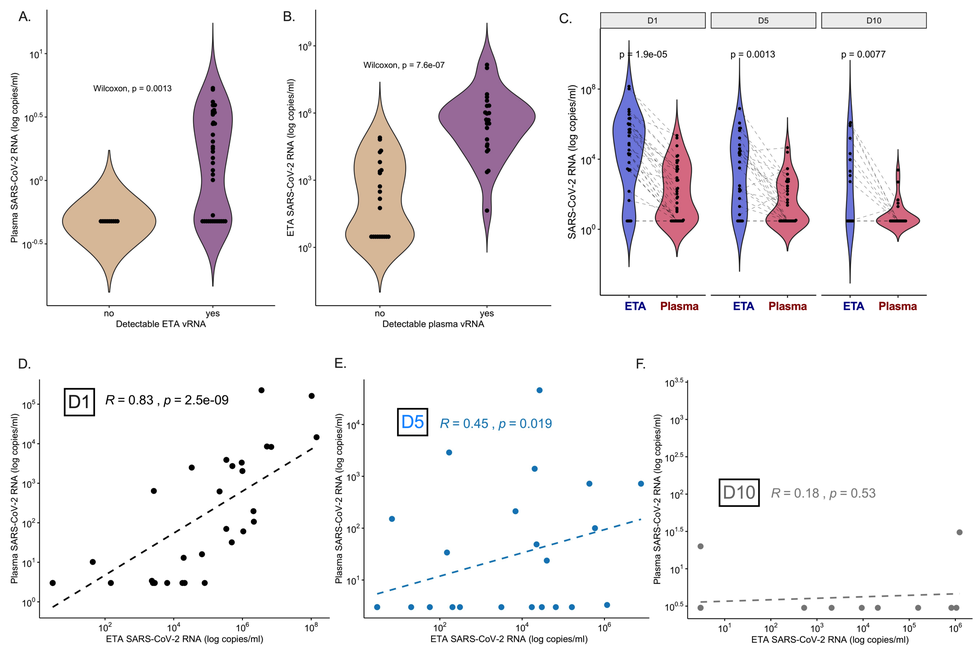

Figure 1. Plasma SARS-CoV-2 viral RNA levels reflect lower respiratory tract viral RNA levels. (A) Plasma vRNA levels in first available sample pair separated by non-detectable (left) or detectable (right) ETA vRNA. (B) ETA vRNA levels in first available sample pair separated by non-detectable (left) or detectable (right) plasma vRNA. (C) ETA and plasma vRNA levels by day of sampling (D-F): Scatter plots of paired ETA and plasma SARS-CoV-2 RNA levels stratified by sampling day

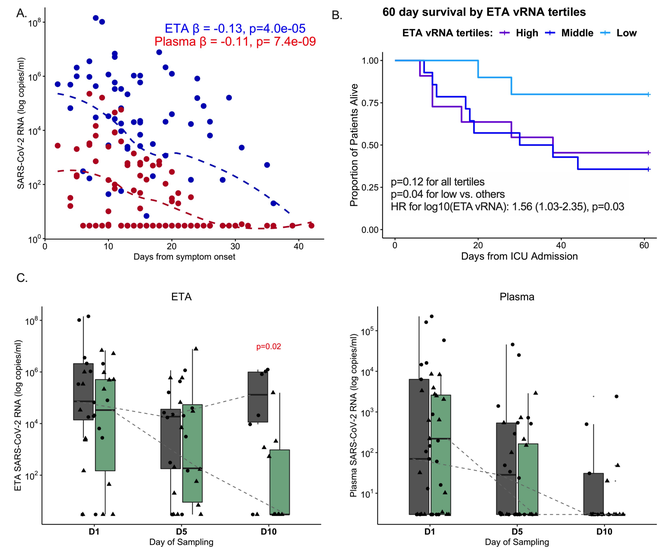

Figure 2. Plasma and lower respiratory tract SARS-CoV-2 viral levels exhibit similar temporal decline although persistently elevated RNA levels in lower respiratory tract samples are associated with increased mortality. (A) Scatterplot of reported days from COVID-19 symptom onset (x-axis) and viral RNA (vRNA) levels (log10-transformed) in ETA (blue) and plasma (red) samples. (B) 60-day survival by ETA vRNA tertiles among patient samples obtained within the first six days of ICU admission: low tertile<4,844; middle 4,482-490,922; high> 490,922 copies/ml. (C and D) ETA and plasma vRNA levels by sampling day and comparing non-survivors (dark gray) and survivors (light green).

CONCLUSIONS

- SARS-CoV-2 viral RNA levels in plasma and LRT secretions are strongly correlated in patients with severe COVID-19 early after ICU admission.
- LRT and plasma vRNA decrease over time, and in parallel, with higher levels and prolonged detection of LRT vRNA in non-survivors compared to survivors.
- Our data implicate plasma vRNA as an indicator of lung SARS-CoV-2 infection and suggests that plasma vRNA may be a useful biomarker for LRT viral burden.

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