Association Between SARS-CoV-2 Viral Load and Patient Symptoms and Clinical Outcomes Using Digital Droplet PCR

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BACKGROUND

- Association between nasopharyngeal (NP) SARS-CoV-2 viral load and clinical outcomes has been heavily investigated:
  - Majority of studies utilize qualitative reverse transcription PCR (RT-qPCR assays)
  - Results are conflicting
- Utility of determining SARS-CoV-2 viral load:
  - Optimization of early treatment eligibility
  - Transmission prevention
  - Prognostication
  - Determining efficacy of novel treatments
- **Droplet digital PCR (dd-PCR)** is a newer, quantitative PCR technology that is **more sensitive, specific, and repeatable** than RT-qPCR

RT-qPCR	dd-PCR
Relative quantification via comparison of cycle threshold value to standard curves	**Absolute quantification** via analysis of thousands of individual PCR reactions

STUDY GOAL: To explore associations between SARS-CoV-2 viral load and patient symptoms, demographics and clinical outcomes in COVID-19 utilizing dd-PCR

METHODS

- The remnants of NP swabs positive for SARS-CoV-2 were collected between November 2020 and September 2021
- Viral load was determined via BioRad's One-Step RT-ddPCR
- Chart review was performed extracting demographic and clinical details for each individual

Nasopharyngeal viral load was predictive of symptomatic disease and in-hospital mortality.

Early viral control may prevent progression of disease.

Table 1: Descriptive characteristics of cohort

Characteristic	Description
Age	50.2 (+/- 17.1)
Male	86.6% (604)
Hispanic/Latino	23.6% (158)
Comorbidities	
DM2	17.4% (121)
CAD	7.9% (55)
HTN	33.8% (236)
Hemodialysis	0.4% (3)
Prior SOT	0.4% (3)
COPD/Asthma	9.2% (64)
BMI	29.76 (+/-6.1)
Any Immuno-suppression	4.2% (29)
Laboratory Values	
Peak CRP	7.09 (2.58 – 14.62)
Peak CPK	167.0 (67.5-325.5)
Peak D-dimer	0.94 (0.51-1.63)
Peak Ferritin	717 (332-1475)
Absolute Lymphocytes (nadir)	0.90 (0.60 – 1.43)

Figure 1: Histogram of Viral Loads

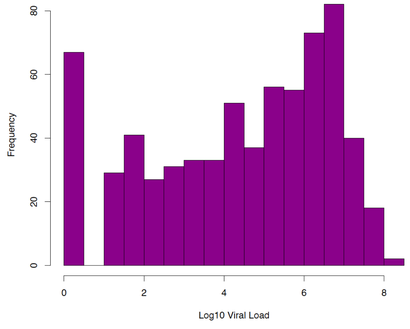


Figure 2: Scatterplot of Log 10 SARS-CoV-2 viral load vs days between onset of symptoms and test collection

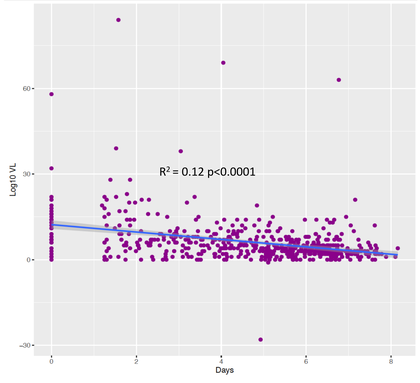


Figure 3: Viral Load vs. Presence of Fever

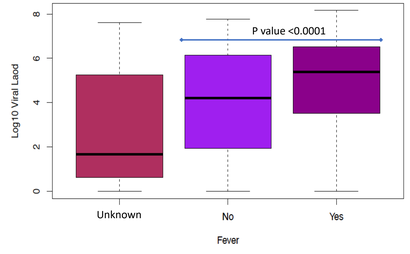
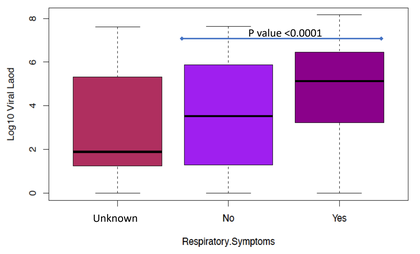


Figure 4: Viral Load vs. Presence of Respiratory Symptoms



RESULTS

- Total of 698 veterans included (Table 1)
  - 76.3% (n=529) were unvaccinated at diagnosis
- Strong correlation observed between Log 10 viral load and time of onset of symptoms (Figure 2)
- In univariate analyses, Log 10 viral load associated with fever, respiratory symptoms, gastrointestinal symptoms, and headache (Figures 3-5)
- In univariate analyses, Log 10 viral load associated with death during hospital admission (Figure 7)
- In multivariate analyses, when adjusting for days between symptom onset and sampling, wave of the epidemic (Delta vs pre-Delta), and risk factors (e.g. diabetes mellitus, coronary artery disease, immunosuppression), viral load was still predictive of death during admission

Figure 5: Viral Load vs. Presence of Gastrointestinal symptoms

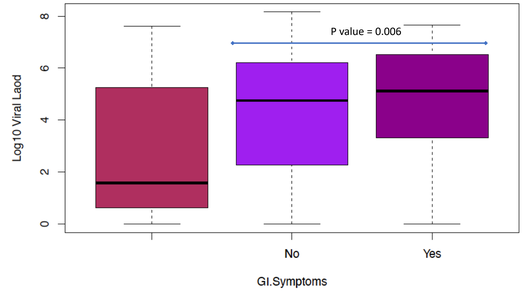


Figure 6: Viral Load vs. Presence of Headache

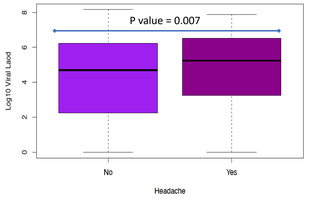
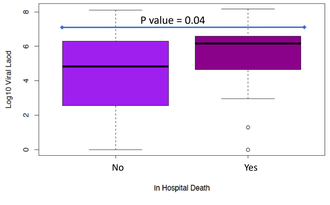


Figure 7: Viral Load vs. Death During Admission



FINANCIAL SUPPORT

Generous grant from Gilead Sciences, Inc.