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Standardized Measurement of SARS-CoV-2 Viral Load Over Time in Respiratory Compartments and in Response to Remdesivir Treatment

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Introduction

- SARS-CoV-2 has infected over 500 million people worldwide and has caused more than 6 million deaths.
- Clinicians do not have access to a standardized measurement of SARS-CoV-2 viral load (VL) that allows for reliable comparison across different clinical specimens and assays.
- Reliable VL measurement across different respiratory specimens, over time, and in response to treatments could also be a powerful tool for clinicians to assess response to treatments and prevent further infections.

Methods

- From Dec 2020 to May 2022, patients hospitalized with COVID-19, with or without Remdesivir (RDV) treatment, were enrolled at The Miriam Hospital and Rhode Island Hospital in Providence, RI.
- Serial respiratory samples [nasal (NA), nasopharyngeal (NP), oropharyngeal (OP), and saliva (SA)] were collected across a maximum of three visits during hospitalization.
  - Among participants who received RDV, baseline specimens were pre-RDV exposure.
- SARS-CoV-2 VL was quantified using the ChromaCode HDPCR™ assay, calibrated to the first World Health Organization (WHO) International Standard (IS).
- Using R version 4.1.2, linear mixed effects models were used to analyze inter-compartmental VL differences at enrollment, over time between 1st and last specimens, and with/without RDV exposure.

Results

- Among 43 participants [mean age 61 years (range 22-89); 58% male, 42% female; 74% white, 14% black; 14% Hispanic; mean length of hospitalization 5 days (range 1-17)], a total of 91 NA, 46 NP, 72 OP, and 91 SA samples were collected.
- Specimens were collected on mean hospital days 1 (range 0-3, Visit 1), 2 (range 1-8, Visit 2), and 4 (range 3-7, Visit 3) for all participants.
- Mean $\log_{10}$VLs ($\log_{10}$IU/mL) differed between compartments at visit 1 (NA 5.3, NP 6.4, OP 4.3, SA 5.9, p<0.0001); **(Fig 1A)**.
- NA, NP, and SA compartments significantly decreased over time (p<0.0001); OP also decreased over time but was not statistically significant (p=0.058); **(Fig 1B, Fig 1C)**.

Figure 1: SARS-CoV-2 viral load ($\log_{10}$IU/mL) across the four sample types and over time: visit 1 (left), visit 2 (middle), and visit 3 (right).

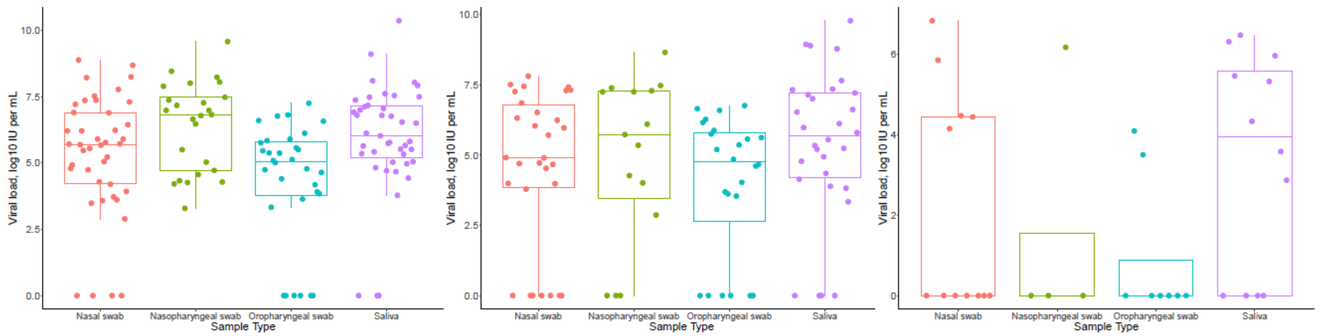


Figure 1A: Visit 1 | Figure 1B: Visit 2 | Figure 1C: Visit 3

Figure 2: Change in viral load over time for each sample type (A=NA, B=NP, C=OP, D=SA) collected since hospitalization among patients who did (blue) and did not (pink) receive RDV.

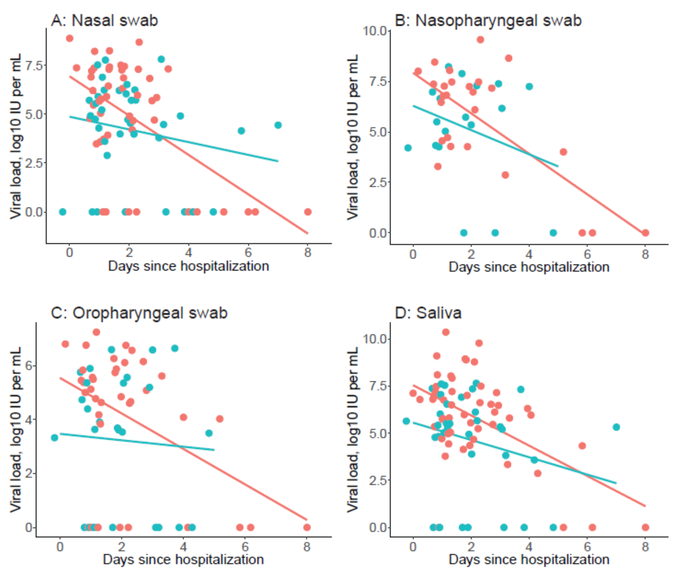
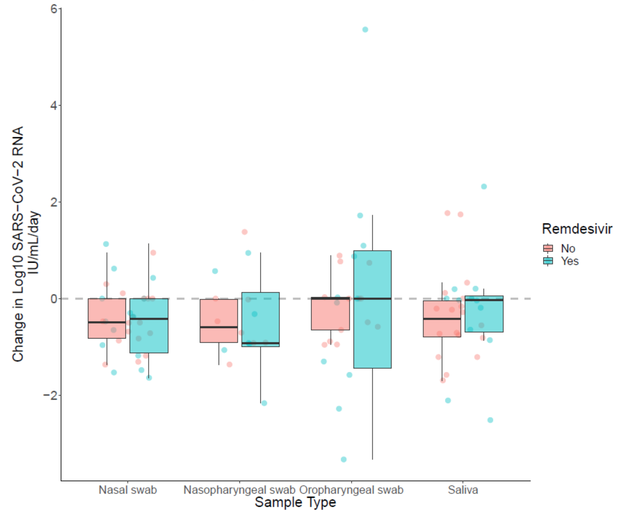


Figure 3: Rate change in viral load between visit 1 and last available specimen for each sample type (NA, NP, OP, SA) among patients who did (blue) and did not (pink) receive RDV.



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Results Cont'd

- Seventeen (40%) participants received RDV; mean hospital day of initial RDV dose was hospital day #1 (range day 0-4); mean length of RDV treatment was 4 days (range 1-5).
- Among patients treated/not treated with RDV:
  - Baseline VL at visit 1 was higher in those not treated with RDV (p=0.03).
  - Change in $\log_{10}$VL over time for each sample type collected since hospitalization was not statistically different **(Fig 2)**.
  - Overall rate change in $\log_{10}$VL between first and last specimens was not statistically different between compartments **(Fig 3)**.

Discussion

- Respiratory inter-compartmental SARS-CoV-2 VL differences were successfully measured using a standardized assay calibrated to the WHO IS, suggesting potential relevance of the sampled location to clinical assessments.
- Use of standardized VL measurements quantified in IU/mL will advance measurement compared to using cycle threshold (Ct) values from qualitative assays; will allow for accurate VL comparisons across compartments and assay types; and will improve assessment of COVID-19 treatments.
- RDV did not appear to accelerate viral decay; yet there were limitations in our ability to detect differences between persons who did/did not receive RDV:
  - Collection of viral RNA from respiratory specimens is dependent upon collection technique; this may introduce sampling variability and not reflect true differences in VL.
  - Baseline VL differed between the two groups.
  - Serial assessments occurred over a short period of time (one week).
  - Positive quantitative VL results may persist beyond infectiousness and not be indicative of transmissibility.

Acknowledgements

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