Association of SARS-CoV-2 Genomic Load Trends with Clinical Status in COVID-19:A Retrospective Analysis from an Academic Hospital Center in New York City

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A. BACKGROUND

- At the time of this writing SARS-CoV-2 has caused more than 1 million deaths worldwide.[1]
- The IDSA has emphasized that the ability of a quantitative test for SARS-CoV-2 to be used as a prognostic marker remains a key research question.
- We aimed to examine the **association of SARS-CoV-2 genomic load in sequential nasopharyngeal samples with the clinical status** of patients on the days of testing.
- We used the **Cycle threshold (Ct) value**, the number of amplification cycles needed to yield a positive fluorescent signal in a real-time reverse transcription-polymerase chain reaction test, as a **surrogate for viral load**.

B. METHODS

Study Design:

- We conducted a retrospective cohort study at the NYU Langone Medical Center.
- **Study period:** March 31st- April 10th 2020.
- We evaluated **all patients** who presented to the emergency department during the study period with clinical and radiographic findings of pneumonia and **had 2 or more positive tests for SARS-CoV-2 at least 24h apart**.
- The **qualitative Cepheid Xpert® Xpress SARS-CoV-2 assay** was used for in-house diagnosis of COVID-19.[2]

Outcomes of interest:

- The **main outcome of interest** was the **association of the Ct values among patients with repeat testing** with their **respective Sequential Organ Failure Assessment (SOFA) score,** calculated on the day of the respective positive PCR test.

Statistical analysis:

- A linear mixed-effects regression analysis was performed to account for within-patient variation and adjust for the number of repeat tests performed per patient.
- The model was fitted with the restricted maximum likelihood method given the small sample size.[3]

C. RESULTS

- **42** out of 471 patients who presented to the emergency department with positive swab for SARS-CoV-2 met the inclusion criteria and were **included in the final analysis**.

Number and Timing of Repeat Testing:

- The included patients had **between 1 and 10 positive tests** (median 2; IQR 2-3). 18 patients had at least 3 screenings.
- The **first repeat testing** was performed **at a median of 7 days after the initial swab** (IQR 4-12).

SOFA Score:

- The **median initial SOFA score** of patients was **2** (IQR 2-3).
- SOFA score at the time of repeat testing **decreased by at least 2 points** compared to the initial testing **in 15** patients (35.7%) and **increased by at least 2 points in 4** patients (9.5%).

Patient Characteristics	No. (%) or Median (IQR)
Age (years)	67 (58.0-81.8)
Gender	
Female	13 (31.0%)
Male	29 (69.0%)
Race	
White	19 (45.2%)
African American/Black	3 (7.1%)
Asian	6 (14.3%)
Other/Unknown	14 (33.4%)
BMI	25.4 (22.0-30.2)
Charlson Comorbidity Index	4 (2-5)
Intubation	10 (23.8%)
Death/Discharge to hospice	6 (14.3%)

Footnote: BMI=Body Mass Index, **IQR**=Interquartile Range, **No.**=Number.

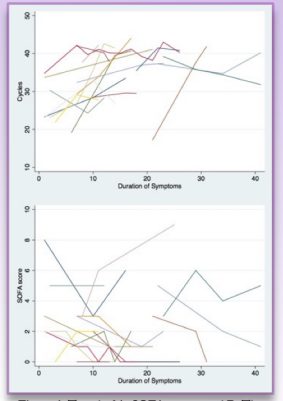

Figure 1. Trend of A. SOFA scores and B. The respective trend of the Ct values of Cepheid Xpert® Xpress SARS-CoV-2 assay among the 18 patients who had at least 3 positive screenings.

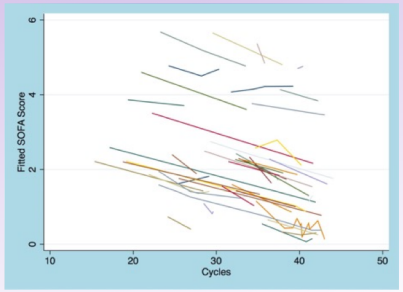

Figure 2. Graph of the fitted SOFA scores based on the Ct values per patient.

C. RESULTS

The mixed-effects linear regression model showed an inverse correlation between the Ct values and patient's change in clinical status. An increase in Ct value by 20 correlated with a decrease in SOFA score by 1 ($p<0.05$). This correlation was adjusted for the duration of symptoms.

D. CONCLUSIONS

- **We showed that in our study cohort improvement in clinical status was associated with a decreasing SARS-CoV-2 genomic** load as reflected by increasing Ct values in sequential RT-PCR nasopharyngeal swabs.
- Even though the increasing Ct values might reflect the natural course of viral replication in the nasopharynx, the observed inverse correlation between the Ct value and the patient's clinical status was adjusted for the duration of symptoms.
- Prospective studies with a pre-specified interval for repeat testing are required to elucidate this further.

E. REFERENCES

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F. ACKNOWLEDGEMENTS

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