

Is there something novel about SARS-CoV-2 variant transmission kinetics?



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Introduction

- A number of novel SARS-CoV-2 variants have recently been identified that have demonstrated higher viral loads in clinical samples, increased transmissibility, and are potentially associated with more severe disease.¹⁻³
- It has previously been demonstrated that viral shedding occurs for a median of 5-8 days, and in some cases for up to 20 days, after symptom onset. However, the impact of these new variants on viral shedding and kinetics has not been studied.⁴
- A strong relationship has been observed between SARS-CoV-2 RT-PCR cycle threshold (Ct) values and ability to culture virus.⁵⁻⁷ SARS-CoV-2 viral loads of above 6 log₁₀ RNA copies/ml have been independently associated with isolation of virus from respiratory tract specimens.^{4,9}
- Ct values of ≤26 (by Logix Smart RT-PCR) correlate with calculated SARS-CoV-2 viral loads of 6 Log₁₀ copies/ml, while Ct values ≤23 correlate to 7 Log₁₀ copies/ml.⁸
- Concern for transmission of SARS-CoV-2 after 14 days from an asymptomatic patient, and the observation of persistently low Ct values in a few patients during a wave predominated by the B.1.1.7 variant, led to the concern that this variant is associated with longer duration of infectivity.
- We therefore aimed to assess viral kinetics by conducting a retrospective review of all patients with positive naso-oropharyngeal swabs for SARS-CoV-2 by RT-PCR, during the recent wave in our hospitals.

Methodology

- We conducted a retrospective review of all patients who tested positive for SARS-CoV-2 by RT-PCR between 31/11/2020 – 24/02/2021
- Patients with repeat positive swabs were identified.
- Exclusion criteria:
 - Swabs taken within 72hrs of each other.
 - Swabs taken >28 days apart.
 - Occupational Health results.
- As testing is carried out on 3 platforms (Logix Smart, GeneXpert Cepheid, and Alinity M) Ct values for the GeneXpert and Alinity platforms were converted to correlating Ct values on the Logix Smart platform (as this is the most commonly used testing platform in UHW).
- Ct value trends were then determined and results at day 14, 16, and 21 were analysed and stratified according to Ct values ≤23, ≤26, or greater.

Results

- Overall, there were 2,559 people with swabs where SARS-CoV-2 was detected by RT-PCR during the study time period.
- Of these 191 people had multiple positive swabs.
- A further 39 of these were excluded, leaving 152 patients with multiple positive swabs for analysis.
- The average number of swabs for each patient was 3, with a range of 2-8.
- From day 14 onwards, there were 22 patients who had swabs with Ct values of ≤26, including 14 patients with Ct values ≤23.
- From day 16 onwards, this number had reduced to 13 patients with Ct values ≤26, and 9 ≤23.
- At day 21 there were 3 patients with Ct values ≤26, including one with a Ct value of 19, and 22 patients with Ct values >26.
- Of note the patient with a Ct value of 19 at day 21, and also a patient with a Ct value of 19 on a day 19 swab were infected with the B.1.1.7 variant – confirmed by whole-genome sequencing (WGS) in the UCD National Virus Reference Laboratory (NVRL).
- Further WGS results are awaited.

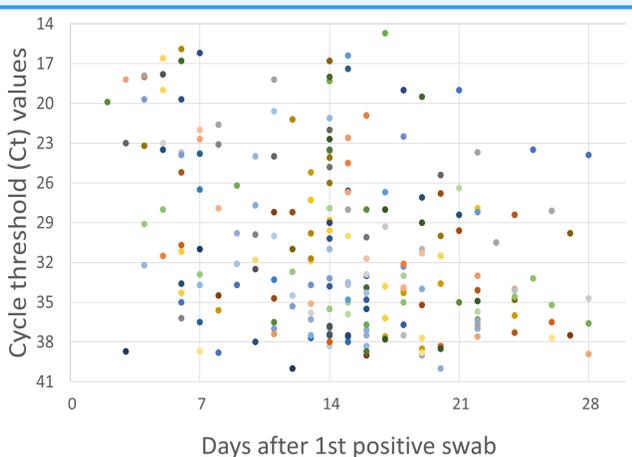


Figure 1: Distribution of Ct values for swabs from day of 1st positive swab (number of patients =152)

| Demographics | N= 152 |
|--------------------------------------|----------|
| Gender | |
| Male | 83 (54%) |
| Female | 69 |
| Location | |
| University Hospital Waterford | 123 |
| St. Luke's General Hospital Kilkenny | 6 |
| South Tipperary General Hospital | 6 |
| Wexford General Hospital | 17 |

Table1: Patient demographics and location

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- The staff of the microbiology laboratory, UHW.

Discussion

- There is evidence to show that where viral loads of >6 Log₁₀ RNA copies/ml are detected, live virus can be cultured, and these patients are considered to be infectious.^{4,7}
- Therefore patients with Ct values of ≤26 may be considered possibly infectious, and patients with Ct values ≤23 are highly likely to be infectious.
- There was a significant number of patients whose Ct values remained below 26 by day 14 and 16, and even 3 patients by day 21.
- This implies that there are a number of patients who are potentially still infectious, but in whom guidelines would allow for de-escalation of infection prevention and control precautions.
- This has important implications for patient and staff safety as these patients may represent an ongoing infection risk.

Limitations

- This study was retrospective in nature.
- There likely existed a selection bias in that patients with severe disease and/or those who were immunocompromised were more likely to undergo repeat testing.
- There were a number of patients in whom repeat testing was not carried out despite low Ct values.
- We were unable to correlate symptom onset or severity of disease to Ct value, as done in previous studies.
- It is, as yet, unclear if all patients with persistently low Ct values were infected with the B.1.1.7 variant, or other novel variants.

Conclusion

- Although this study has a number of limitations, it does raise the question whether new viral mutants, including the now predominant B.1.1.7 mutant, are associated with an alteration in viral kinetics and prolonged viral shedding.
- Further prospective studies are warranted to evaluate this question, and help inform IPC practices and improve patient and staff safety

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