Know-C19
Knowledge Hub for COVID-19
A policy, health response and implementation Hub

Technical Brief 3.1 | 28 March 2020

Viral Dynamics in Upper Respiratory Tract Specimens of patients with COVID-19

Question

What is the pattern of viral dynamics/viral shedding in upper respiratory tract (URT) specimens of patients with COVID 19? i.e. is the sensitivity of PCR testing on URT swabs likely to change during the disease course

Answer

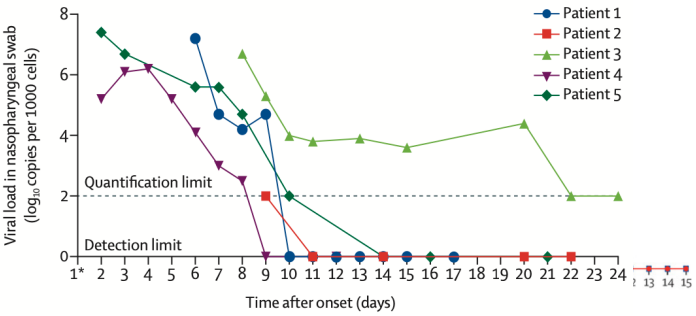
Simple URT samples are recognized to have a significant false negative rate for COVID-19 (requiring repeat sampling when the clinical suspicion is high), however the current literature on viral dynamics does not suggest that low viral load is the reason for false negatives early in the course of disease

Background

Nucleic acid testing using real time PCR is the current method of choice for detection of SARS-CoV2.[1] Nasopharyngeal and oropharyngeal swabs are most frequently collected. RT PCR results on swab specimens are frequently only qualitative, however an estimate of viral load/quantification is often possible through analysis of the Ct (cycle threshold) value. Higher viral loads are inversely related to Ct value, and may be used to estimate the number of RNA copies per µL.

Literature Review

There are a number of publications that address this question by reporting on serial URT (upper respiratory tract) sampling throughout the clinical course of infection in a cohort of patients. A generally consistent finding is that high viral loads (low Ct values) are detected early in the course of illness, soon after symptom onset, resembling the pattern seen in influenza virus, but in contrast to SARS-CoV, which is noted to peak at about 10 days after onset).[2,3] The viral load generally decreases over time (see below: left [3]) before coming negative. An earlier study on 2 patients from China noted a peak viral load in throat swabs around day 5-6 after symptom onset (below right).[4]



1 https:// www.health.gov.au/sites/default/files/documents/2020/03/phln-guidance-on-laboratory-testing-for-sars-cov-2-the-virus-that-causes-covid-19.pdf
2 Zou L, Ruan F, Huang M, Liang L, Huang H, Hong Z, Yu J, Kang M, Song Y, Xia J, Guo Q. SARS-CoV-2 viral load in upper respiratory specimens of infected patients. New England Journal of Medicine. 2020 Mar 19;382(12):1177-9.
3 Lescure et al. Clinical and virological data of the first cases of COVID-19 in Europe: a case series. Lancet Infect Dis. 2020 Mar 27. https://doi.org/10.1016/S1473-3099(20)30200-0
4 Pan Y, Zhang D, Yang P, Poon LL, Wang Q. Viral load of SARS-CoV-2 in clinical samples. The Lancet Infectious Diseases. 2020 Feb 24.

Burnet Institute
Medical Research. Practical Action.

An observation in a recent French study, [3] was that of the 3 patients with a severe or critical outcome, there were two different courses observed. In two of the patients, there was a biphasic evolution starting with a mild presentation, followed by a respiratory worsening in the second week of illness. This clinical pattern has been observed in previous cohorts,[5] however the notable finding was that SARS CoV-2 was no longer detected in the URT in one patient and at very low levels in the other (potentially suggesting an immunologically mediated process). The findings in the third patient with critical disease, were of persistent and high viral excretion in URT samples (combined with PCR positivity in other body fluids). This pattern has also been observed in critically unwell patients in China.[2]

Of note, a number of publications report that viral loads detected in asymptomatic patients to be similar/comparable to symptomatic patients.[2,6] However other studies have noted higher viral loads to be associated with more severe cases of disease.[7]

Conclusions

In general, these findings are consistent with the reports of transmission early in the course of infection. **Simple URT samples are recognized to have a significant false negative rate for COVID-19 (requiring repeat sampling when the clinical suspicion is high), however the current literature on viral dynamics does not suggest that low viral load is the reason for false negatives early in the course of disease.** Alternate reasons may be variability due to sampling method, or the absence of virus in the upper respiratory tract in some cases.

An issue largely not addressed is whether viral load as detected by RT-PCR correlates with live virus, as opposed to just detection of RNA (due to the difficulty in culturing virus) and hence transmissibility.

5 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497–506.
6 Kimball A, Hatfield KM, Arons M, et al. Asymptomatic and Presymptomatic SARS-CoV-2 Infections in Residents of a Long-Term Care Skilled Nursing Facility — King County, Washington, March 2020. MMWR Morb Mortal Wkly Rep. ePub: 27 March 2020
7 Liu Y, Yan LM, Wan L, Xiang TX, Le A, Liu JM, Peiris M, Poon LL, Zhang W. Viral dynamics in mild and severe cases of COVID-19. The Lancet Infectious Diseases. 2020 Mar 19.