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LETTER TO THE EDITOR

Cycle Threshold and SARS-CoV-2 Infectivity

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ABSTRACT

The ability of the cycle threshold to inform the infectivity of SARS-CoV-2 polymerase chain reaction (PCR)-positive individuals remains controversial. Berengua et al. have recently reported that in immunocompetent individuals SARS-CoV-2 infectivity lasts < 15 days and that Ct value > 27 indicates low probability for infectivity. This important study, however, comes with several caveats. The authors performed a single cell culture for each sample. Additionally, cycle threshold values and corresponding viral loads differ between variants. During the study period at least four strains were prevalent in Europe, yet the authors do not provide information regarding the isolated strains. Lastly, this hospital-based study seems to involve sampling bias. The findings of Berengua et al. may be leveraged to guide clinical decision in SARS-CoV-2 PCR-positive convalescing candidates for organ donation or transplantation.

Keywords: SARS-COV-2, Cycle Threshold, Infectivity, Viral culture

EDITORIAL

Suitability of SARS-CoV-2 polymerase chain reaction (PCR)-positive convalescing candidates for organ donation or transplantation is unknown, and despite recommendations to the contrary, the Cycle Threshold (Ct) is leveraged by many transplant infections disease clinicians to discriminate active viral replication and transmissibility from prolonged non-infectious shedding of viral genome.[1,2] Based on viral-culture of PCR-positive samples, Berengua et al. contributes clinically important knowledge that in immunocompetent individuals SARS-CoV-2 infectivity lasts < 15 days from symptom onset, and that Ct value > 27 indicates low probability (3.1%) for infectivity.[3] We salute the authors on this important investigation, and would like to highlight several points.

First, the authors performed a single cell culture for each of the 100 samples. However, in a much larger study and using a similar cell culture, SARS-CoV-2 was isolated in 6% of 3790 PCR-positive specimens in two subsequent subcultures performed weekly, but not in the primary culture.[4] Thus, Berengua et al. may have underestimated the true probability of culture positivity.

Second, Ct values and corresponding viral loads differ between SARS-CoV-2 variants.[5] At the study period at least four strains were prevalent in Europe, namely the wild–type, Alpha, Beta, and Gamma. The authors do not provide any information regarding the isolated strains.

Lastly, all 100 consecutive PCR-positive samples were collected over 200 days in a hospital setting. The average of a single PCR-positive sample every two days appears to be unusually low for a hospital setting; total number of specimens, however, is not provided. Additionally, hospital samples constitute a significant sampling bias which limit inference to the general population for infection control purposes. Providing the reader with the reason for COVID-19 testing for these 100 samples will be helpful. Likewise, the authors included a morbidly obese diabetic patient, and a 101-year-old man among the six immunocompromised patients with infectivity beyond 14 days. A detailed delineation of what constitutes immunodeficiency regarding prolonged SARS-CoV-2 transmissibility is exceedingly important, but is neither provided nor justified.

While we appreciate the authors' outstanding work, addressing these points would further strengthen their findings.

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