Detection of Higher Cycle Threshold Values in Culturable SARS-CoV-2 Omicron BA.1 Sublineage Compared with Pre-Omicron Variant Specimens — San Francisco Bay Area, California, July 2021—March 2022

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Introduction

Although CDC and others do not recommend attempting to correlate Ct values from SARS-CoV-2 RT-PCT tests, with the amount of infectious virus in the original specimen (1,2), low Ct values are sometimes used as surrogate markers for infectiousness in clinical, public health, or research settings without access to virus culture (1).

However, the consistency in reliability of this practice across SARS-CoV-2 variants remains uncertain because Omicron-specific data on infectious virus shedding, including its relationship with RNA levels, are limited.

Methods

Nasal specimens were collected daily for 2 weeks after symptoms onset from non-hospitalized participants infected with SARS-CoV-2 pre-Omicron variants or Omicron BA.1 sublineage(**Table**).

Real Time RT-PCR was used to generate ***Ct values*** as a measure of viral RNA load (*E* and *N* genes).

Presence of ***culturable SARS-CoV-2 virus*** in nasal samples (as a proxy for infectiouness) was measured in cell culture (BSL3 facility).

Findings were compared between specimens from participants infected with ***pre-Omicron variants*** and those infected with the ***Omicron BA.1 sublineage***.

Observations

Culturable virus was detected in specimens from a ***similar percentage of participants*** in both variant groups (Omicron = 76%; pre-Omicron = 71%), a similar percentage of total specimens (Omicron = 26%; pre-Omicron: 30%), and was detected for a ***similar duration*** following onset (**Table**).

Ct values were ***significantly higher in Omicron specimens than pre-Omicron*** (Ct difference = 5.77, p<0.001).This difference was observed as early as day 3 after onset through day 8 after onset (**Fig 1**).

When ***stratified by age group or vaccination status*** (**Fig 2**), ***virus-positive Omicron*** specimens were associated with ***higher*** E-specific ***Ct values*** than were virus-positive pre-Omicron specimens

Conclusions

Ct values likely ***do not provide*** a consistent ***proxy for infectiousness across SARS-CoV-2 variant***s.

Table : Characteristics of participants infected with SARS-CoV-2 pre-Omicron variants or Omicron BA.1 sublineage and nasal specimens evaluated for viral RNA and infectious virus

Participant and specimen	No. (%) Pre-Omicron	No. (%) Omicron	Change in *E*-specific Ct value between pre-Omicron and Omicron variants
All participants (N = 124)	107 (100)	17 (100)	—
Adults aged ≥18 yrs	92 (86)	9 (53)	—
Fully vaccinated*	35 (33)	10 (59)	—
Symptomatic†	100 (93)	16 (94)	—
Culturable virus detected	76 (71)	13 (76)	—
All specimens (N = 1,147)	998 (100)	149 (100)	4.45§
RNA-positive specimens¶	539 (53)	72 (48)	3.90§
Virus-positive specimens¶	298 (30)	39 (26)	5.77§
Median duration of virus detection after onset, days (IQR)	6 (5–8)	6 (5–8)	—
Median interval from onset to specimen collection, days (IQR)	8 (6–11)	8 (6–11)	

Abbreviations: Ct = cycle threshold; *E* = envelope gene. p<0.001

* Fully vaccinated participants were defined as those who had received all recommended doses of a Food and Drug Administration–authorized or approved primary vaccine series (2 mRNA vaccine doses or a single dose of Johnson and Johnson/Janssen vaccine) ≥14 days before either symptom onset or enrollment (whichever occurred earlier).

FIGURE 1 : Omicron BA.1 and pre-Omicron E-specific Ct values among nasal specimens with culturable virus

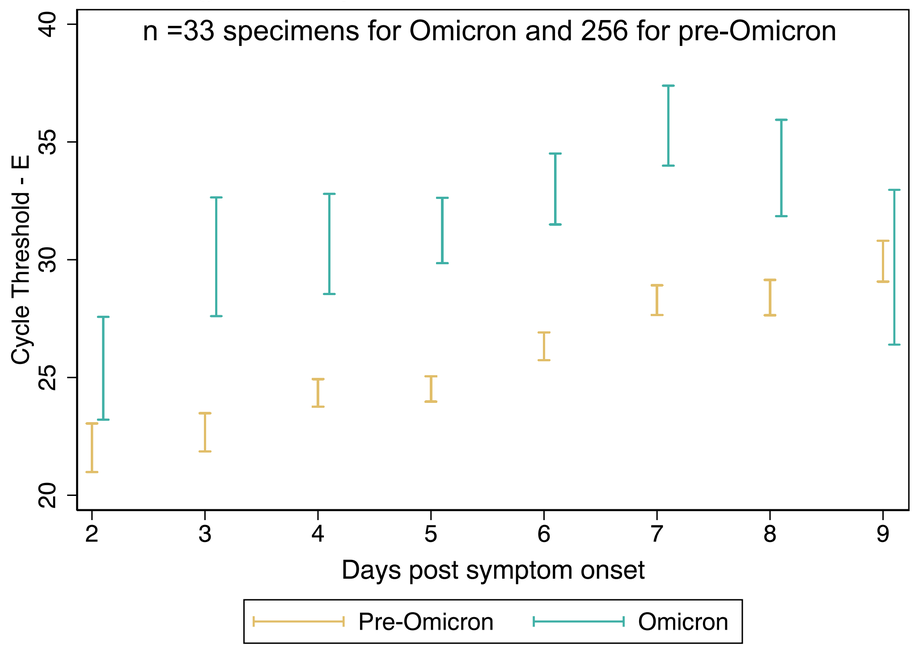
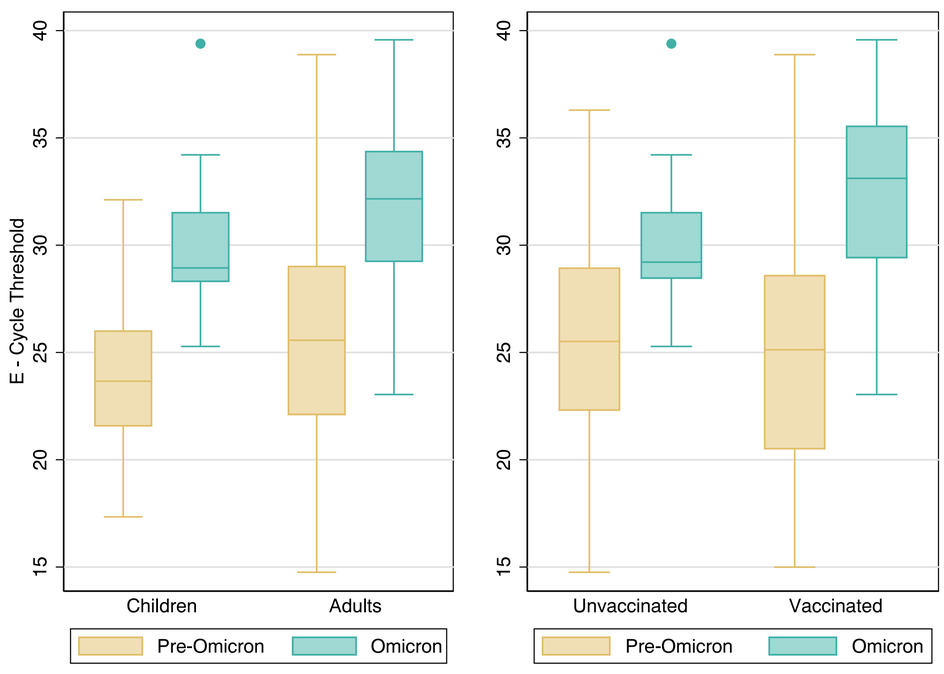


FIGURE 2 : Omicron BA.1 and pre-Omicron E-specific Ct values among nasal specimens with culturable virus by age group and by primary COVID-19 vaccination status



¶ Adult (aged ≥18 years): 21 Omicron and 273 pre-Omicron specimens included. Children (aged <18 years): 18 Omicron and 25 pre-Omicron specimens included

** Fully vaccinated: 18 Omicron and 81 pre-Omicron specimens included. Unvaccinated: 21 Omicron and 217 pre-Omicron specimens included.

References :

1. CDC. Frequently asked questions about coronavirus (COVID-19) for laboratories. Atlanta, GA: US Department of Health and Human Services, CDC; 2021.

2.Binnicker MJ. Can testing predict SARS-CoV-2 infectivity? The potential for certain methods to be surrogates for replication-competent virus. J Clin Microbiol 2021;59:e0046921 10.1128/JCM.00469-21.