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LETTER TO THE EDITOR

The SARS-CoV-2 Omicron Variant Does Not Have Higher Nasal Viral Loads Compared to the Delta Variant in Symptomatic and Asymptomatic Individuals

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Understanding the mechanism of the rapid spread of the SARS-CoV-2 B.1.1.529 (Omicron) variant is of great importance to devising public health interventions. Increased viral load has been reported as one cause of increased infectiousness in prior emergent variants and has been associated with symptomatic versus asymptomatic infections (1). While initial reports have attributed Omicron's exponential growth and increased contagiousness to evasion of humoral memory due to altered spike protein antigens (2, 3), it is unclear to what extent viral load has contributed to its dominance (4, 5). Here, we examine whether symptomatic individuals and asymptomatic carriers infected with Omicron demonstrate differences in viral load by examining the reverse transcriptase PCR (RT-PCR) cycle thresholds (C_T) in sequence-confirmed cases, compared with prior infections with the Alpha and Delta variants of SARS-CoV-2.

Since March 2020, the University of Washington Virology Laboratory has performed approximately one-third of the testing for the state of Washington, with a majority of samples collected at open-access community testing sites throughout the state. Samples were collected using anterior nasal swabs observed by health care professionals and tested on four assays (Roche Cobas 6800, Abbott Alinity m, Panther Hologic Fusion, and a Centers for Disease Control and Prevention (CDC) assay-based lab-developed test [6, 7]). The lowest C_T value output from each platform was chosen as the single representative value. The symptomatic status of the individuals presenting to the testing sites was determined from free-text reasons for seeking testing. Using keywords present in such text responses, we categorized individuals as either symptomatic, exposed, or asymptomatic (see Table S1 in the supplemental material). To control for variations in community-wide viral RNA loads, we restricted our analysis to time periods when the Alpha, Delta, and Omicron variants were increasing in prevalence.

We examined 2001 Alpha samples collected between 1 March and 8 May 2021, 792 Delta samples collected between 1 June and 15 July 2021, and 1,935 Omicron samples collected between 1 December 2021 and 2 January 2022. The median C_T values were 22.0 $\pm$ 4.8 (Alpha), 19.7 $\pm$ 4.8 (Delta), and 20.8 $\pm$ 4.5 (Omicron). Overall, Omicron demonstrated a significantly different C_T distribution compared to both Alpha and Delta (Wilcoxon rank sum test, $P < 2e\text{-}16$).

The Omicron infections did not have higher viral loads than those with Delta when stratified by the major PCR platforms used and by symptomatic versus asymptomatic status (Fig. 1). Consistent with prior reports (4, 5), the symptomatic individuals across each variant had higher viral loads than did the asymptomatic carriers. Within each clinical category examined, the individuals with Omicron did not have higher viral

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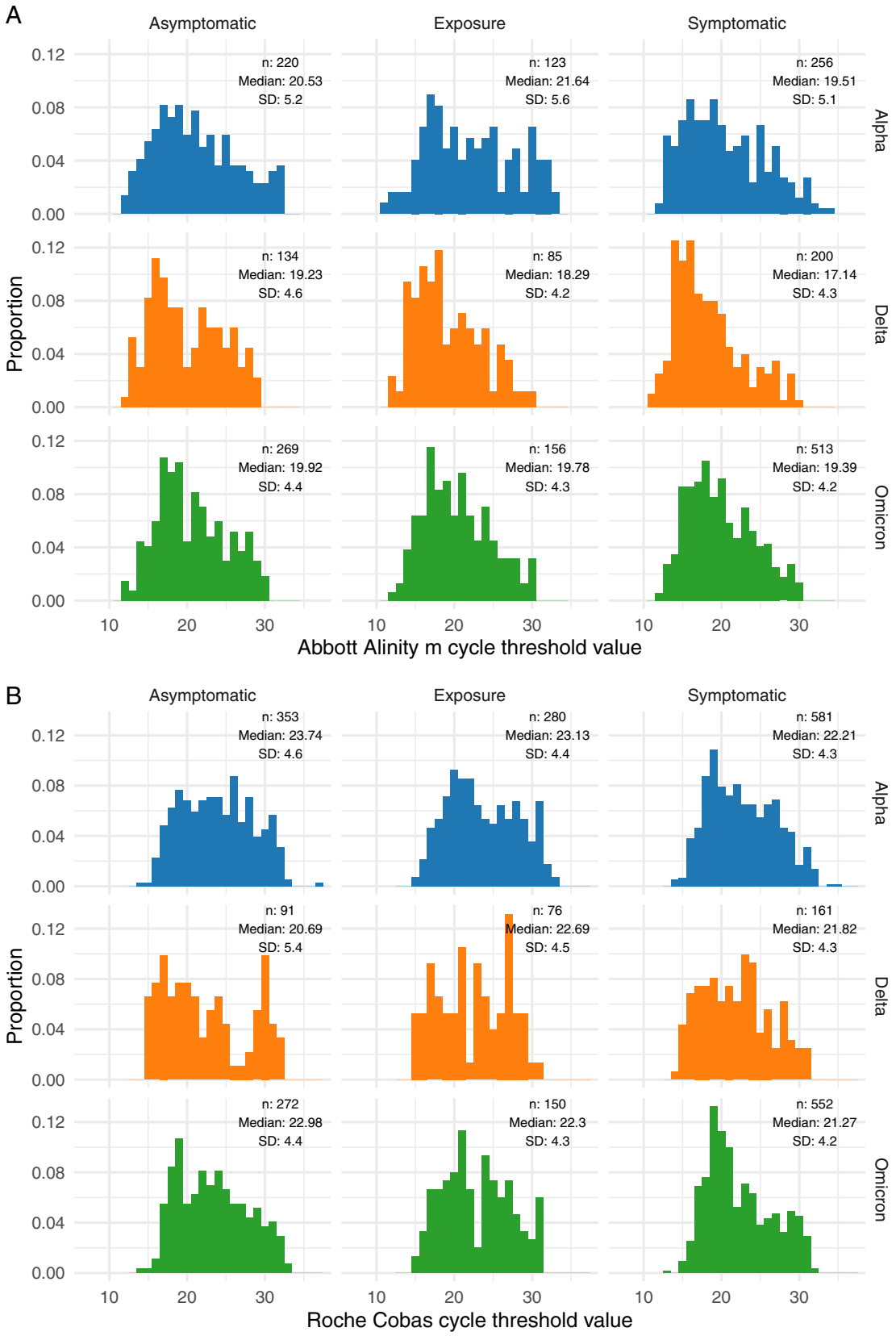

FIG 1 Histogram of RT-PCR cycle threshold distributions among variants, stratified by clinical status and RT-PCR platform. The samples and clinical status are shown for the Abbott Alinity m (A) and Roche cobas (B) platforms.

loads than did those infected with Delta (Wilcoxon rank sum test: symptomatic, $P = 2.7e-6$; asymptomatic, $P = 2.8e-4$; exposure, $P = 0.01$) (Fig. 1). The viral loads from symptomatic individuals measured on the Abbott platform were significantly lower for Omicron versus Delta infections ($P < 0.0001$) but were not significantly different on the Roche platform ($P = 0.29$). The viral loads from asymptomatic individuals trended lower for Omicron infections compared to Delta but were not statistically significant on either the Roche ($P = 0.06$) or Abbott platforms ($P = 0.14$).

Our data suggest that the spread of Omicron is unlikely to be attributed to higher nasal viral loads compared to prior variants. Limitations to this analysis include the lack of stratification by the specific day of symptom onset, lack of longitudinal data to measure the peak viral load, use of C_T as a surrogate for viral load, and restriction of the analysis to only anterior nasal swab viral loads. While recent data suggest that SARS-CoV-2 may be detectable earlier in saliva (8), our data capturing almost 5,000 sequence-confirmed nasal collections across multiple clinical categories and stratified by PCR platform demonstrate that Omicron is not associated with a higher nasal viral load compared to previous variants.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, XLSX file, 0.2 MB.

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