Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Clinical Microbiology and Infection 28 (2022) 1302–1303

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Letter to the Editor

Omicron (B.1.1.529) SARS-CoV-2 viral load among nasopharyngeal and oral samples compared to other variants of concern and impact on diagnostic testing strategy

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ARTICLE INFO

Article history:
Received 15 February 2022
Received in revised form
19 April 2022
Accepted 25 April 2022
Available online 11 May 2022

Editor: J.M. Hübschen

To the Editor,

With the rapid wave of Omicron (B.1.1.529) SARS-CoV-2 cases detected worldwide and the significant mutation profile of this variant of concern (VOC), questions have been raised about its impact on SARS-CoV-2 tissue tropism and viral load. As Omicron more adeptly replicates in the upper respiratory tract than previous variants [1], it has been proposed that saliva or oral specimens may detect Omicron with greater sensitivity than those from the nasopharynx [2], although evidence for this to date has not included evaluation of nasopharyngeal swabs (NPS). Diagnostic testing recommendations which maximize analytical sensitivity are particularly crucial for patients who may qualify for treatment with monoclonal antibodies and/or antivirals.

To promptly address the question of optimal sample type for Omicron detection, clinical samples received in our laboratory from February 2021 to mid-January 2022 for SARS-CoV-2 diagnostic testing were retrospectively reviewed. Samples included NPS and oral rinses using 5 mL of sterile 0.9% saline (saline gargles [SG]), where patients were instructed to swish and then gargle in their mouth for five seconds each, for a total of three swish/gargle cycles. The saline was then directly emitted into a sterile screw-top container and transported to the laboratory at room temperature. Samples were collected from inpatient hospital wards, long-term care facilities, and community testing centres in British Columbia and Yukon, Canada. SARS-CoV-2 was detected by real-time polymerase chain reaction (RT-PCR, cobas SARS-CoV-2 Test [Roche Molecular Diagnostics, Basel, Switzerland] and LightMix SarbecoV E-gene assay [TIB Molbiol, Berlin, Germany]). Positive SARS-CoV-2 samples underwent VOC SNP testing by RT-PCR (VirSNiP Assays, TIB Molbiol), targeting specific spike protein mutations previously validated by whole-genome sequencing (S371L + E484A for Omicron, P681R for Delta, N501Y + K417T for Gamma, N501Y + K417N for Beta, and N501Y + HV69/70 for Alpha). Mean cycle threshold (Ct) values for the envelope (E) gene and viral load [3] of each VOC and sample type were evaluated using unpaired Student *t* tests (GraphPad Software).

Of 8668 samples, 8312 (95.9%) confirmed as VOC by SNP RT-PCR. Samples were excluded from analysis when sample type was not documented. Beta VOC were excluded due to small sample size (5 NPS, 1 SG). In total, 6456 NPS (1467 Omicron, 2041 Delta, 1777 Gamma, 1171 Alpha) and 1603 SG (164 Omicron, 592 Delta, 504 Gamma, 343 Alpha) were included. There was a statistically significant difference in mean SARS-CoV-2 Ct value between NPS and SG for each VOC ($p < 0.0001$; Omicron 21.37 vs. 25.74, Delta 20.42 vs. 24.59, Gamma 22.00 vs. 25.99, and Alpha 22.59 vs. 25.93), where NPS represented a greater than 10-fold increase in viral load (Fig. 1). Omicron demonstrated comparable viral load to all other VOC for both NPS (mean Ct value 21.37 vs. 21.49; $p = 0.4348$) and SG (mean Ct value 25.74 vs. 25.41; $p = 0.3199$).

In summary, Omicron SARS-CoV-2 viral loads in diagnostic specimens did not differ from those of other VOC. NPS continue to have high analytical sensitivity for RT-PCR. Oral specimens remain an option, particularly when there may be barriers to

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https://doi.org/10.1016/j.cmi.2022.04.022

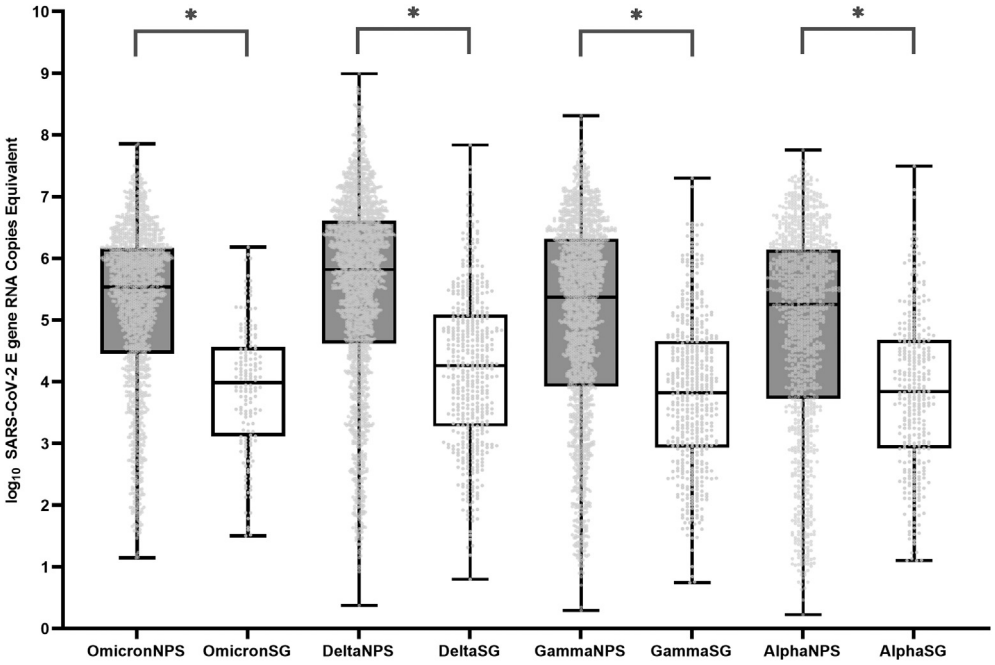

Fig. 1. SARS-CoV-2 viral load in $\log_{10}$ envelope (E) gene RNA copies equivalent for each variant of concern and specimen type. Abbreviations: NPS, nasopharyngeal swab; SG, saline gargle. * denotes statistically significant difference in viral load ($p < 0.0001$).

obtaining NPS, although the lower viral load in oral specimens should be noted and has been described previously in paired samples [4]. This work is consistent with other early findings demonstrating Omicron viral load in nasal and mouth specimens was not significantly higher than other VOC even when accounting for timing of sample collection [5].

Limitations of this analysis include unpaired specimens from different populations, where SG were primarily submitted from community testing centres as opposed to inpatient settings. Furthermore, results were analyzed over an extended period of time (12 months), which may have introduced variability in RT-PCR reagent lots, testing intensity, and changes in the population's vaccination status over time. However, these aspects of the study design were necessary in order to evaluate different VOC which predominated at different time points, and to generate a large sample size. A strength of this analysis is the high number of clinical samples (>8000) that underwent VOC subtyping. Clinical evaluation of each case, including an assessment of the timing of symptom onset in relation to specimen collection, was outside the scope of this study, although the vast majority of specimens presumably were submitted from symptomatic individuals based on local testing criteria. This study did not evaluate the performance of rapid antigen tests using nasal swabs, and the performance characteristics of RT-PCR targeting E gene may differ from rapid antigen tests targeting nucleocapsid protein.

In a rapidly evolving COVID-19 pandemic with a surge of Omicron SARS-CoV-2 cases worldwide and questions about optimal specimen type, these findings may help guide public health response and reassure existing RT-PCR diagnostic testing strategies for clinical management of severe COVID-19.

Transparency declaration

None of the authors has a commercial or other association, financial interest, activity, relationship, or association that might pose a conflict of interest related to this work.

Acknowledgements

We are grateful to Dr. Daniel T. Holmes for statistical analysis support. This work was in part supported by a Public Health Agency of Canada COVID-19 Immunity Task Force COVID-19 Hot Spots Competition Grant (2021-HQ-000120 to MGR, NM, CFL, GR) and Canada Foundation for Innovation Exceptional Opportunities Fund COVID-19 award (to CFL). This study was approved by the Providence Health Care Research Ethics Board (H20-01055).

References

[1] University of Hong Kong. HKUMed finds Omicron SARS-CoV-2 can infect faster and better than Delta in human bronchus but with less severe infection in lung. Available at: https://www.med.hku.hk/en/news/press/20211215-omicron-sars-cov-2-infection. Accessed 18 January 2022.
[2] Marais G, Hsiao N, Iranzadeh A, Doolabh D, Enoch A. Saliva swabs are the preferred sample for Omicron detection. Available at: https://www.medrxiv.org/content/10.1101/2021.12.22.21268246v1.full.pdf. Accessed 18 January 2022.
[3] Kinloch NN, Ritchie G, Dong W, Cobarrubias KD, Sudderuddin H, Lawson T, et al. SARS-CoV-2 RNA quantification using droplet digital RT-PCR. J Mol Diagn 2021;23:907–19.
[4] Williams E, Bond K, Zhang B, Putland M, Williamson DA. Saliva as a noninvasive specimen for detection of SARS-CoV-2. J Clin Microbiol 2020;58. e00776–20.
[5] Hay JA, Kissler SM, Fauver JR, Mack C, Tai CG, Samant RM et al. Viral dynamics and duration of PCR positivity of the SARS-CoV-2 Omicron variant. Available at: https://www.medrxiv.org/content/10.1101/2022.01.13.22269257v1.full.pdf. Accessed 20 January 2022.