

Infants Younger Than 6 Months Infected With SARS-CoV-2 Show the Highest Respiratory Viral Loads

Chi-Ching Kao[†], Yung-Po Liaw^{*}

Chi-Ching Kao

School of Medicine, Chung-Shan Medical University, Taichung, Taiwan

splendia1008@gmail.com

*Corresponding Author:

Yung-Po Liaw, PhD, ORCID: 0000-0003-2046-4964

Department of Public Health and Institute of Public Health, Chung Shan Medical University, Taichung 40201, Taiwan

Department of Medical Imaging, Chung Shan Medical University Hospital, Taichung, Taiwan

Medical Imaging and Big Data Center, Chung Shan Medical University Hospital, Taichung, Taiwan

Chung Shan Medical University No. 110, Sec. 1, Jianguo N. Rd., South District, Taichung City 40201, Taiwan, (TEL) +886 4 36097222 #11838 or +886 4 36097501, (FAX) No Fax

liawyp@csmu.edu.tw

Author contributions: C.C.K. drafted the manuscript. Y.P.L. critically revised the manuscript.

Funding sources: None

Potential conflicts of interest: All No reported conflicts of interest.

Key words: SARS-CoV-2, COVID-19, infant, viral load result, infections

To the Editor:

We read with great interest the article by Ochoa et al. on the role of infants in spreading SARS-CoV-2 infection [1]. Based on their findings, they concluded that children younger than 6 months old displayed higher SARS-CoV-2 loads with less severe presentation compared to other age groups[1]. . Although this article provided insights into coronavirus disease 2019 (COVID-19), the findings on the accuracy of ORF1ab Cycle Threshold (Ct) might be compromised due to other predictor variables.

To begin with, there is uncertainty regarding the accuracy of Reverse Transcriptase polymerase chain reaction (RT-PCR) using nasopharyngeal specimens, when viral loads are low; in such situations we recommend supplemental fecal specimen testing to be performed [2].

In addition, the time between COVID-19 infection and PCR testing may affect the PCR test results. For instance, it has been suggested that the later an infected individual is tested after symptom onset, the less likely the test is positive [3]. Early sampling within seven days of symptom onset can decrease the false-negative rate of RT-PCR [4]. In this study, the final tests used to determine viral loads may not be as precise since the samples may have been collected at a different time. The observed ORF1ab Ct may be underestimated. Therefore, we recommend that measures such as testing before washing in the morning may increase diagnostic accuracy in patients with low viral loads during latent infection stages [5].

Finally, although some potential influencing factors have been excluded in this study [1], other predictive variables, such as laboratory data including CCL5 expression, may lead to potential confounding bias. For example, previous studies showed that COVID-19 patients had upregulated innate immunity genes, which were directly associated with SARS-CoV-2 load. [6] In this regard, subgroup analysis of genes would greatly reduce potential confounding bias. Therefore, we suggest genetic testing data of mucosal biomarkers be included in future studies.

In conclusion, several factors that may influence the accuracy of viral load detection should be considered in future studies. For instance, reference fecal sample testing in addition to nasopharyngeal specimens for RT-PCR tests should be included. Likewise, genetic testing , such as CCL5 expression, should be considered as a predictor variable and stratified in further analyses. Lastly, strategies to enhance diagnostic accuracy of PCR tests in latent infection should be considered.

References:

1. Ochoa, V., et al. (2021). "Infants younger than 6 months old infected by SARS-CoV-2 show the highest respiratory viral loads." *J Infect Dis* **2021**; 1537-6613.
2. Park, S. K., et al. (2021). "Detection of SARS-CoV-2 in Fecal Samples From Patients With Asymptomatic and Mild COVID-19 in Korea." *Clin Gastroenterol Hepatol* 19(7): 1387-1394.e1382.
3. Wikramaratna, P. S., et al. (2020). "Estimating the false-negative test probability of SARS-CoV-2 by RT-PCR." *Euro Surveill* **25**(50).
4. İşlek, A. and M. K. Balcı (2021). "Analysis of Factors Causing False-Negative Real-Time Polymerase Chain Reaction Results in Oropharyngeal and Nasopharyngeal Swabs of Patients With COVID-19." *Ear Nose Throat J*: 145561321996621.
5. Liu, M., et al. (2020). "Value of swab types and collection time on SARS-COV-2 detection using RT-PCR assay." *J Virol Methods* **286**: 113974.
6. Pérez-García, F., et al. (2021). "High SARS-CoV-2 viral load and low CCL5 expression levels in the upper respiratory tract are associated with COVID-19 severity." *J Infect Dis* **2021**: 1537-6613.

Accepted Manuscript