Pediatr Infect Vaccine. 2023 Aug;30(2):73-83
https://doi.org/10.14776/piv.2023.30.e12
pISSN 2384-1079·eISSN 2384-1087

PIV PEDIATRIC INFECTION & VACCINE

Original Article

Viral Load Dynamics After Symptomatic COVID-19 in Children With Underlying Malignancies During the Omicron Wave

Ye Ji Kim,[1,2,3] **Hyun Mi Kang**,[1,2,3] **In Young Yoo**,[4] **Jae Won Yoo**,[1] **Seong Koo Kim**,[1] **Jae Wook Lee**,[1] **Dong Gun Lee**,[2,3,5] **Nack-Gyun Chung**,[1] **Yeon-Joon Park**,[4] **Dae Chul Jeong**,[1] **Bin Cho** [1]

[1]Department of Pediatrics, College of Medicine, The Catholic University of Korea, Seoul, the Republic of Korea
[2]Infection Control Office, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, the Republic of Korea
[3]Vaccine Bio Research Institute, College of Medicine, The Catholic University of Korea, Seoul, the Republic of Korea
[4]Department of Laboratory Medicine, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, the Republic of Korea
[5]Division of Infectious Diseases, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, the Republic of Korea

Received: Jun 14, 2023
Revised: Jul 24, 2023
Accepted: Jul 27, 2023
Published online: Aug 8, 2023

Correspondence to
Hyun Mi Kang
Department of Pediatrics, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, the Republic of Korea.
Email: pedhmk@gmail.com

ORCID iDs
Ye Ji Kim
https://orcid.org/0009-0009-4611-455X
Hyun Mi Kang
https://orcid.org/0000-0003-0513-8407
In Young Yoo
https://orcid.org/0000-0003-1505-846X
Jae Won Yoo
https://orcid.org/0000-0001-7970-1691
Seong Koo Kim
https://orcid.org/0000-0002-1860-3067
Jae Wook Lee
https://orcid.org/0000-0002-0735-0287
Dong Gun Lee
https://orcid.org/0000-0003-4655-0641

ABSTRACT

Purpose: This study aimed to investigate the viral load dynamics in children with underlying malignancies diagnosed with symptomatic coronavirus disease 2019 (COVID-19).
Methods: This was a retrospective longitudinal cohort study of patients <19 years old with underlying hemato-oncologic malignancies that were diagnosed with their first symptomatic severe acute respiratory syndrome coronavirus 2 polymerase chain reaction (PCR)-confirmed COVID-19 infection during March 1 to August 30, 2022. Review of electronic medical records and telephone surveys were undertaken to assess the clinical presentations and transmission route of the patients. Thresholds of negligible likelihood of infectious virus was defined as E gene reverse transcription (RT)-PCR cycle threshold (Ct) value ≥25.
Results: During the 6-month study period, a total of 43 children with 44 episodes of COVID-19 were included. Of the 44 episodes, the median age of the patients included was 8 years old (interquartile range [IQR], 4.9–10.5), and the most common underlying disease was acute lymphoid leukemia (n=30, 68.2%), followed by patients post-hematopoietic stem cell transplantation (n=8, 18.2%). Majority of the patients had mild COVID-19 (n=32, 72.7%), and three patients (7.0%) had severe/critical COVID-19. Furthermore, 2.3% (n=1) died of COVID-19 associated acute respiratory distress syndrome. The largest percentage of the patients showed E gene RT-PCR Ct value ≥25 between 15-21 days (n=13, 39.4%), followed by 22-28 days (n=10, 30.3%). In 15.2% (n=5), E gene RT-PCR Ct value remained <25 beyond 28 days after initial positive PCR. Refractory malignancy status (β, 67.0; 95% confidence interval, 7.0–17.0; P=0.030) was significantly associated with prolonged duration of E gene RT-PCR <25. A patient with prolonged duration of E gene RT-PCR Ct value <25 was suspected to have infectivity shown by the transmission of the virus to his mother at day 86 after his initial positive test.

Nack-Gyun Chung
https://orcid.org/0000-0003-4855-390X
Yeon-Joon Park
https://orcid.org/0000-0003-2182-5821
Dae Chul Jeong
https://orcid.org/0000-0003-0934-817X
Bin Cho
https://orcid.org/0000-0001-6675-695X

Conflict of Interest
No potential conflict of interest relevant to this article was reported.

Author Contributions
Conceptualization: Kang HM; Data curation: Kang HM, Kim YJ; Formal analysis: Kang HM, Kim YJ; Investigation: Kang HM, Kim YJ, Yoo JW, Kim SG, Lee JW, Chung NG, Lee DG, Jeong DC, Cho B; Methodology: Kang HM, Kim YJ, Yoo IY, Park YJ; Supervision: Kim YJ, ; Validation: Kang HM, Kim YJ; Writing - original draft: Kang HM, Kim YJ; Writing - review & editing: Kang HM, Kim YJ, Jeong DC.

Conclusions: Children that acquire symptomatic COVID-19 during refractory malignancy state are at a high risk for prolonged shedding warranting PCR-based transmission precautions in this cohort of patients.

Keywords: Cancer; COVID-19; Children; Viral shedding

INTRODUCTION

Immunocompromised patients are known to shed viruses for a longer period after viral infections such as influenza and norovirus compared to immunocompetent persons.[1,2] Conflicting data have been shown for the shedding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in immunocompromised patients recovering from coronavirus disease 2019 (COVID-19). Although prolonged viral shedding in immunocompromised patients have been reported,[3-5] a study on immunocompromised adults demonstrated delayed polymerase chain reaction (PCR) clearance with older age, multiple comorbidities, and solid organ transplant but not by degree of immunocompromise.[6]

In order to prevent in-hospital transmission of SARS-CoV-2 to vulnerable patients, many hospitals relied on nasopharyngeal real-time PCR assays to detect the viral load in the respiratory tract of COVID-19 confirmed cases and determine whether the viral load is increasing or decreasing to extrapolate potential infectiousness of the shedding virus.[7] Although the presence of SARS-CoV-2 viral RNA alone does not indicate viable virus, a study showed that no viral growth was observed in samples with viral RNA E gene above the cycle threshold (Ct) 24.[8] Furthermore, amounting data shows that although viable virus may persist,[9] infectivity during the recovery stage of COVID-19 is significantly reduced ten days after symptom onset.[10] Therefore, current guidelines for transmission-based precautions of patients with COVID-19 in healthcare settings have been switched from a test-based strategy to a symptom-based approach.[11] Nevertheless, in patients that have severe illness due to COVID-19 or those that have underlying immunocompromising conditions, stricter guidelines for discontinuing transmission based precautions have been recommended.[12]

There remains a paucity of data on the duration of shedding of the SARS-CoV-2 during recovery from COVID-19 in immunocompromised children. However, in children with cancer that require frequent admissions for the ongoing treatment of their underlying disease, positive SARS-CoV-2 PCR results may affect their subsequent treatment plan.[13] Therefore, we aimed to investigate changes in viral load dynamics after symptomatic COVID-19 and time to PCR clearance in children during ongoing treatment for their underlying malignancies.

MATERIALS AND METHODS

1. Study design

This was a retrospective longitudinal cohort study of patients below 19 years old with ongoing treatment for their underlying hemato-oncologic malignancies, that were diagnosed with their first symptomatic COVID-19 during March 1 to August 30, 2022, when the Omicron variant was the dominant circulating strain in South Korea. This study was done at a tertiary referral university hospital's pediatric bone marrow transplant center.

During the study period, the transmission-based precaution protocol at the hospital required all asymptomatic patients admitted to the bone marrow transplant center for any reasons, mainly chemotherapy or hematopoietic stem cell transplantation (HSCT), undergo a nasopharyngeal SARS-CoV-2 reverse transcription (RT)-PCR within 3 days prior to admission. All patients with a fever 38.0°C and above or respiratory symptoms were required a nasopharyngeal SARS-CoV-2 RT-PCR on the day of admission to exclude COVID-19. Patients that were positive for SARS-CoV-2 had a weekly follow up of nasopharyngeal RT-PCR titers until the SARS-CoV-2 E gene Ct value reached ≥25. In those that were asymptomatic, admission was possible after 10 days had passed since the first positive SARS-CoV-2 RT-PCR. All guardians of the patients were required a negative result to stay in the hospital as the patient's caregiver. Both the patient and guardians were unable to leave the wards until discharge. When a switch in guardian was necessary, new in-coming guardians required a negative SARS-CoV-2 RT-PCR results.

2. Data collection

Review of electronic medical records and telephone surveys were undertaken to assess the clinical presentations and transmission routes of the patients. This study was approved by the Institutional Review Board (IRB) of Seoul St. Mary's Hospital (IRB No. KC23RISI0577). Informed consent was waived.

3. SARS-CoV-2 real-time PCR

All SARS-CoV-2 RT-PCR nasopharyngeal swabs were performed by trained medical laboratory technologists. Specimen were obtained as follows: the patient's head was tilted back 70 degrees, and swabs were inserted about 2 cm in the nostril until resistance was met at the nasal midturbinate. The swab was rotated several times against the nasal wall and repeated in the other nostril.

The specimen collected were then sent to the hospital's central laboratory where SARS-CoV-2 RT-PCRs were performed using Real-Q 2019-nCoV Detection Kit (Biosewoom, Seoul, Korea). The RNA-dependent RNA polymerase (RdRp) and E genes were amplified. The positive cut off according to the manufacturer's instruction was <38. The Cts of the E genes were reviewed and analyzed. Thresholds of negligible likelihood of infectivity of the virus was defined as E gene RT-PCR Ct value ≥25 for the analyses of this study.

Patients that had either initial, follow up, and negative (SARS-CoV-2 E gene RT-PCR Ct values >25), or initial and SARS-CoV-2 E gene RT-PCR <25 were included in the analyses for viral load trend.

4. Case definitions

The time to SARS-CoV-2 clearance in this cohort of patients, which was defined as the number of days between first positive SARS-CoV-2 E gene RT-PCR and first SARS-CoV-2 E gene RT-PCR Ct value ≥25, without a subsequent repeat positive PCR. Reinfection was defined as a symptomatic patient with a positive SARS-CoV-2 E gene RT-PCR Ct value ≥90 days after the first episode of COVID-19, who had previously been RT-PCR negative and cleared of all COVID-19 symptoms. COVID-19 disease severity was classified as mild, moderate, severe, and critical, according to the COVID-19 Treatment Guidelines by the National Institute of Health.[14)]

https://doi.org/10.14776/piv.2023.30.e12

5. Statistical analyses

The linear regression model was used in the univariate analyses to identify factors associated with an increased duration of SARS-CoV-2 E gene RT-PCR <25. Variables found to be significant in the univariate analyses were included in the final multivariate linear regression model. A *P*-value of <0.05 was considered statistically significant.

RESULTS

1. Study population

During the 6-month study period, a total of 43 children with 44 episodes of COVID-19 were included. All but one patient received SARS-CoV-2 PCR within 24 hours of symptom onset, and one patient was diagnosed via rapid Ag detection test within 24 hours of symptom onset. The median age of the patients included was 8 years old (interquartile range [IQR], 4.9–11.5), and the most common underlying disease was acute lymphoid leukemia (n=30, 68.2%), followed by patients post-HSCT (n=8, 18.2%). A total 61.4% (n=27) acquired the infection from household transmission, and 34.1% (n=15) of the patients were admitted for the treatment of COVID-19 (**Table 1**).

Table 1. Baseline demographics of the children included in this study (n=44)

Characteristics	No of cases (%)
Sex (male)	32 (72.7)
Age (yr)	8.0 (4.9–11.5)
Underlying disease	
Acute lymphoid leukemia	30 (68.2)
Post-HSCT	8 (18.2)
Solid tumor	4 (9.4)
Acute myeloid leukemia	1 (2.3)
Aplastic anemia	1 (2.3)
Transmission	
Family	27 (61.4)
Unknown	13 (29.5)
In-hospital transmission (during chemotherapy)	4 (9.1)
Admission for COVID-19 treatment	15 (34.1)
Symptoms	
Fever	36 (81.8)
Cough/sputum/rhinorrhea	24 (54.5)
Sore throat	16 (36.4)
GI symptoms*	9 (20.5)
Seizure	1 (2.3)
Reinfection	1 (2.3)
Disease severity	
Mild	32 (72.7)
Moderate	9 (20.5)
Severe/critical	3 (6.8)
Antiviral agents used	6 (13.6)
Mortality	
Directly associated with COVID-19	1 (2.3)
Indirectly associated with COVID-19	2 (4.5)
COVID-19 immunization	1 (2.3)

Values are presented as number (%) or median (interquartile range).
Abbreviations: HSCT, hematopoietic stem cell transplantation; COVID-19, coronavirus disease 2019; GI, gastrointestinal.
*GI symptoms: vomiting/diarrhea.

https://doi.org/10.14776/piv.2023.30.e12

Fever (n=36, 81.8%) and respiratory symptoms including cough, sputum, and rhinorrhea (n=24, 54.5%) were the most common symptoms of COVID-19. Majority of the patients had mild COVID-19 (n=32, 72.7%), and three patients (6.8%) had severe/critical COVID-19. Furthermore, 2.3% (n=1) died of COVID-19 associated acute respiratory distress syndrome, while 2 died due to aggravation of underlying disease due to COVID-19 complications (**Table 1**).

2. SARS-CoV2 RT-PCR analyses

A total 160 E-gene RT-PCR values from 33 patients were included in the viral load trend analyses. The largest percentage of the patients showed E gene RT-PCR Ct value ≥25 between 15–21 days (n=13, 39.4%), followed by 22–28 days (n=10, 30.3%). In 15.2% (n=5), E gene RT-PCR Ct values remained <25 beyond 28 days after initial positive PCRs (**Fig. 1**). Only a cumulative 15.2% (n=5) of the patients achieved SARS-CoV-2 E gene RT-PCR Ct value ≥25 within 14 days, however, reached 84.8% (n=28) by 28 days (**Fig. 2**). One patient showed prolonged duration of positivity beyond 6 months after infection (**Fig. 3**).

A univariate analysis was undertaken to find factors associated with a prolonged duration of E gene RT-PCR <25 (**Table 2**). Post-HSCT (β, 34.9; 95% confidence interval [CI], 7.8–61.9; *P*=0.013), relapse status (β, 41.0; 95% CI, 11.8–70.2; *P*=0.007), and refractory malignancy status (β, 58.1; 95% CI, 27.6–88.6; *P*=0.001) were shown to be associated factors. When adjusting for confounding, a multivariate analysis showed that refractory malignancy status (β, 67.0; 95% CI, 7.0–17.0; *P*=0.030) was found to be significantly associated with a prolonged duration of E gene RT-PCR <25 (**Table 2**, **Fig. 4A**).

A total 24.2% (n=8) patients showed a decrease in E-gene RT-PCR Ct value (increasing viral load) following increasing titers (decreasing viral load) after initial diagnosis. Of these, 37.5% (n=3/8) never reached ≥25 and ended in mortality. Only one patient experienced a decrease below 25 after an increase in titers to 29.5 (**Fig. 4B**, dark gray line).

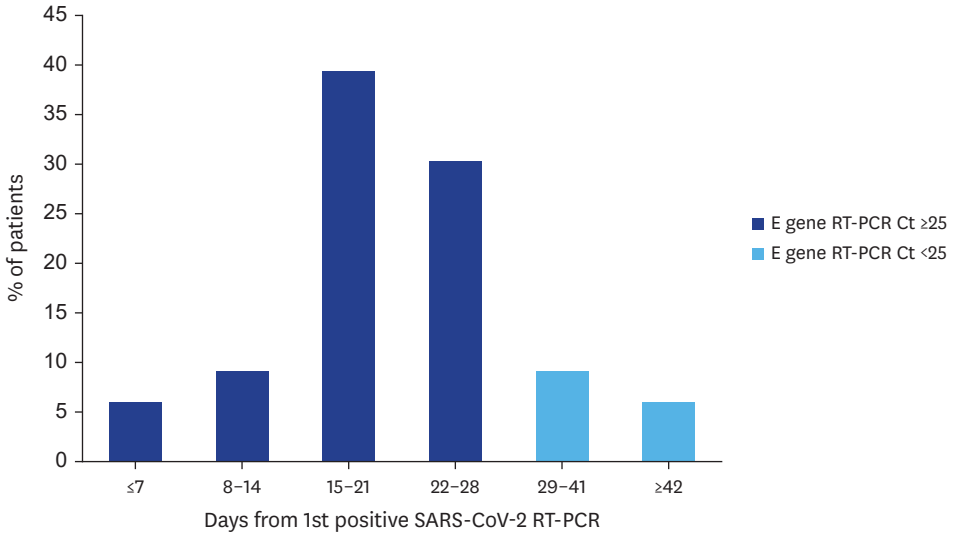

Fig. 1. In the viral load trend analyses, the largest percentage of the patients showed E gene RT-PCR Ct value ≥25 between 15–21 days (n=13, 39.4%), followed by 22–28 days (n=10, 30.3%). In 15.2% (n=5), E gene RT-PCR Ct values remained <25 beyond 28 days after initial positive PCRs.
Abbreviations: RT-PCR, reverse transcription polymerase chain reaction; Ct, cycle threshold; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

https://doi.org/10.14776/piv.2023.30.e12

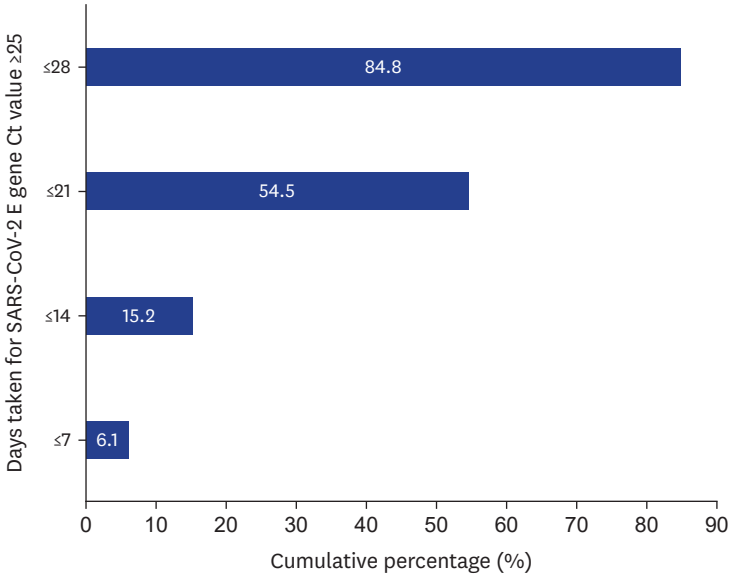

Fig. 2. Cumulative % of patients with SARS-CoV-2 E gene Ct value ≥25. Only a cumulative 15.2% (n=5) of the patients achieved SARS-CoV-2 E gene RT-PCR Ct value ≥25 within 14 days. By 28 days, 84.8% (n=28) achieved SARS-CoV-2 E gene RT-PCR Ct value ≥25.
Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; Ct, cycle threshold; RT-PCR, reverse transcription polymerase chain reaction.

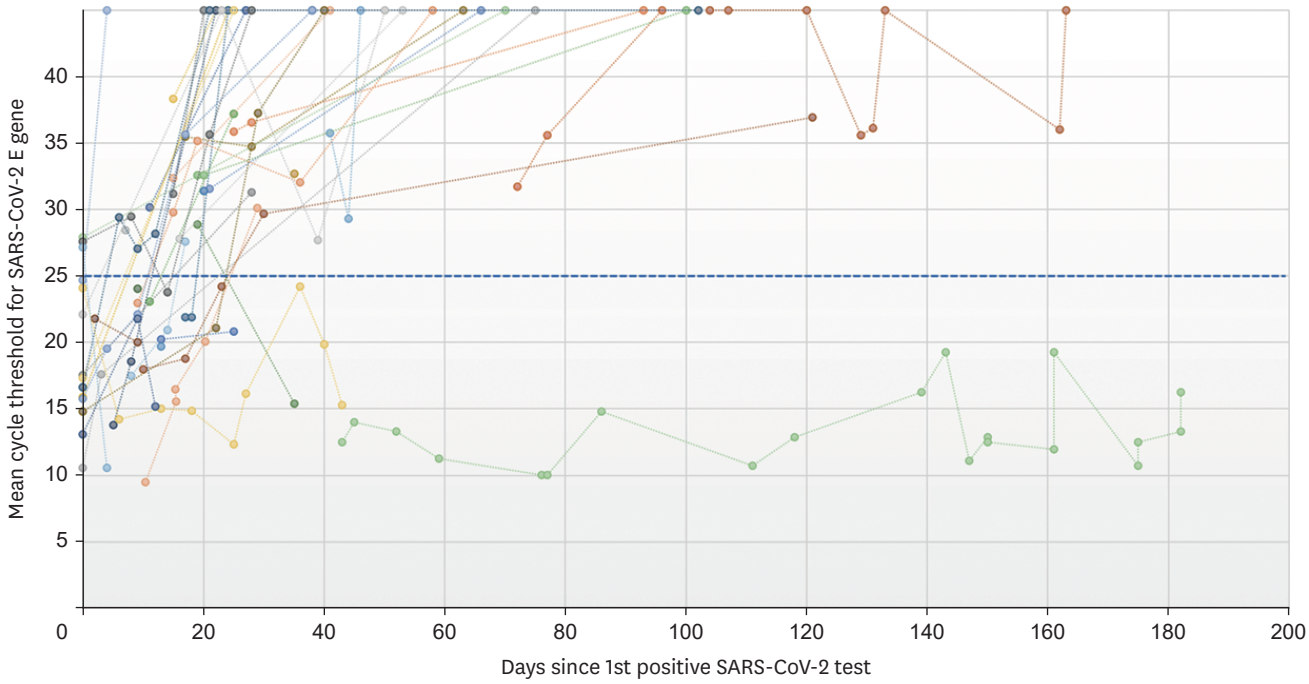

Fig. 3. Viral load trend analyses of the patients included in this study. A total 160 PCR values were included in the viral load trend analyses. The dotted blue line represents SARS-CoV-2 E gene RT-PCR Ct value 25, the thresholds of negligible likelihood of infectious virus.
Abbreviations: PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; Ct, cycle threshold; RT, reverse transcription.

One patient that had a prolonged duration of positivity was suspected to have infectivity shown by the transmission of the virus to his mother (**Fig. 4B**, green line). This patient had an underlying disease of relapsed, refractory acute lymphocytic leukemia after undergoing a second unrelated peripheral blood stem cell transplantation, and was not at a neutropenic

https://doi.org/10.14776/piv.2023.30.e12

Table 2. Univariate and multivariate regression analyses of factors associated with the duration of SARS-CoV-2 E gene RT-PCR <25

Characteristics	Univariable				Multivariable			
	β	95% CI	SE	*P*	β	95% CI	SE	*P*
		Lower, Upper				Lower, Upper		
Sex	−9.7	−31.9, −12.6	10.9	0.381				
Age	1.3	−1.2, 3.7	1.2	0.312				
BMI	−0.6	−3.7, −2.6	1.5	0.713				
Neutropenia at SARS-Co-2 infection	−10.7	−36.1, −14.9	12.4	0.402				
Post-HSCT status	34.9	7.8, 61.9	13.2	0.013	9.1	−43.8, −62.0	25.8	0.780
Relapse status	41.0	11.8, 70.2	14.3	0.007	−18.0	−91.5, −55.5	35.9	0.620
Refractory malignancy status	58.1	27.6, 88.6	14.9	0.001	67.0	7.0, 127.0	29.3	0.030
During ongoing chemotherapy	−14.4	−35.5, −6.8	10.3	0.175				
Antiviral treatment for COVID-19	0.7	−44.4, −45.7	22.0	0.976				
Initial E-gene titer	2.7	−59.9, −65.3	30.7	0.930				
COVID-19 pneumonia	−16.9	−79.2, −45.4	30.5	0.584				

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RT-PCR, reverse transcription polymerase chain reaction; HR, hazard ratio; CI, confidence interval; SE, standard error; BMI, body mass index; HSCT, hematopoietic stem cell transplant; COVID-19, coronavirus disease 2019.

state at initial COVID-19 diagnoses. He had previously been receiving treatment for invasive disseminated aspergillosis in his lungs, fungal abscess in the right cerebellum, and fungal endocarditis in his left ventricle in the preceding year. The patient's mother was negative at admission with the patient, who had an E-gene RT-PCR Ct value of 11.2 which was at day 59 after his initial positive test. The patient's mother remained in the isolation room with the patient to care for him while receiving salvage chemotherapy for his underlying disease. The mother did not have any outside contact because of the hospital's policy at the time. Two weeks into the admission, the mother became symptomatic with a sore throat, fever, and myalgia. A follow up SARS-CoV-2 PCR was positive, and the mother was diagnosed with COVID-19. The patient also underwent follow up testing and was found to have an E-gene RT-PCR Ct value of 14.8 at day 86 after his initial positive test. The patient remained asymptomatic.

DISCUSSION

During the Omicron wave, children with underlying hematologic malignancies diagnosed with symptomatic COVID-19 were included in this study. In this cohort, a total 72.7% had mild disease, 7.0% had severe/critical disease, and the mortality rate directly associated with COVID-19 was 2.30%. This study aimed to understand the viral load dynamics in children with underlying malignancies, and the effects of prolonged viral shedding. It was found that at 14 days after the first positive SARS-CoV-2 PCR, only 15.2% cumulative patients were found to have decreased risk of transmission, shown by E gene RT-PCR Ct value ≥25. A multivariate analysis showed that duration of PCR positivity was significantly associated with patients that acquired SARS-CoV-2 during the refractory malignancy state. Furthermore, 1 patient that had prolonged viral shedding caused transmission to a healthy person between 2–3 months after infection.

Understanding the dynamics of SARS-CoV-2 shedding is important because prolonged shedding caused an increased duration for viral transmission. A systematic review showed that the mean duration of SARS-CoV-2 shedding from the upper respiratory tract is 17 (95% CI, 15.5–18.6) days.[15] A study on immunocompromised persons living with human immunodeficiency virus (HIV) in South Africa showed that the median time to cessation of shedding was 13 days (IQR, 6–25), and in a subset of both HIV and non-HIV patients with high initial SARS-COV-2 viral load, patients with HIV had a longer shedding duration (median, 27 [IQR, 8–43] days) compared non-HIV persons (median, 7 [IQR, 4–13] days).[16]

https://doi.org/10.14776/piv.2023.30.e12

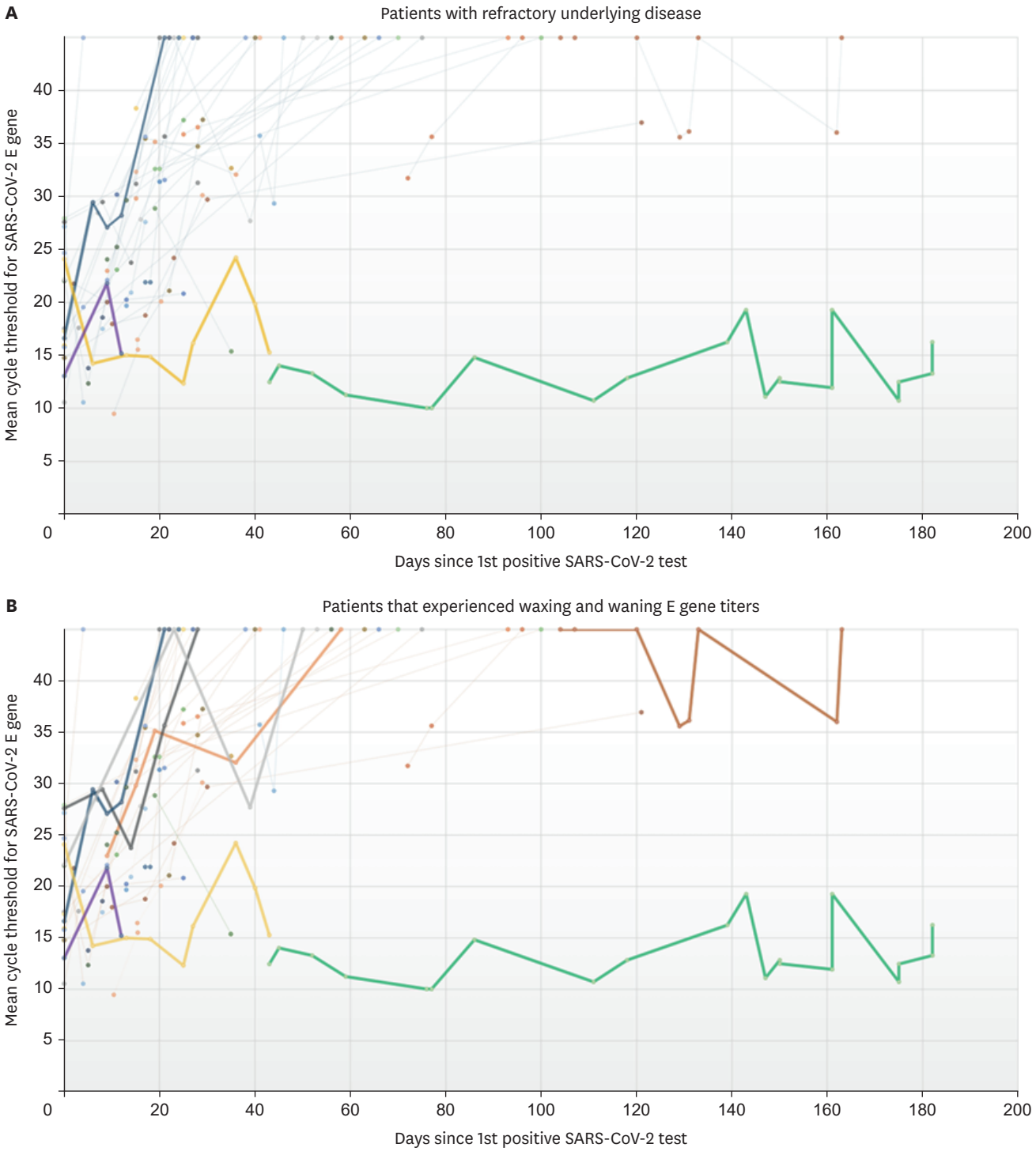

Fig. 4. Viral load trends. (A) Patients that were in the refractory malignancy state. (B) Patients that experienced a decrease in E-gene RT-PCR Ct value following increasing titers after initial diagnosis. Patients with refractory disease showed prolonged E gene positivity. Of the eight patients with waxing and waning E gene titers, 37.5% (n=3/8) never reached ≥25. A dot represents one E gene titer, and a colored line shows longitudinal titers of one patient.
Abbreviations: RT-PCR, reverse transcription polymerase chain reaction; Ct, cycle threshold; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

https://doi.org/10.14776/piv.2023.30.e12

In this study, the median duration of viral shedding was unable to be calculated because the patients were followed up in 4–7 day intervals. However, it was shown that only 54.5% achieved viral clearance by 21 days. Furthermore, 15.2% were still shedding the viral RNA at high viral loads past 28 days.

Although majority of the children with on-going treatment for their underlying malignancies had mild symptomatic COVID-19, the mortality rate due to COVID-19 was 2.3% in this cohort of children. A study using COVID-19 Centers for Disease Control and Prevention (CDC) case surveillance public data showed that the mortality of children below 19 years old wave was 0.1%,[17] showing that the risk of mortality is higher in children with underlying hematologic malignancies, and therefore measures to decrease viral transmission in these children are crucial.

Although viral shedding does not always correlate with the transmission of a viable virus, and many factors are associated with viral transmission and subsequent infection, sufficient studies have shown that high viral loads correlate with infectiousness.[18,19] However, it is known that PCR positivity can overestimate the duration of infectiousness or transmissibility,[20] therefore caution has been advised in PCR-based precautions. Our study showed that a patient with high viral load had the capacity to transmit the SARS-CoV-2 to his mother. Furthermore, our study showed that acquiring the disease during refractory malignancy state was a risk factor for prolonged shedding. Therefore, showing that stricter in-hospital transmission-based precautions are needed in certain cohorts of immunocompromised patients that have a high risk for prolonged shedding. Especially as these patients may transmit the virus to other immunocompromised patients that have a higher risk for SARS-CoV-2 related morbidity and mortality.

There were a few limitations in this study. First, the interval of SARS-CoV-2 RT-PCR testing was different between the patients, and therefore, the exact duration of PCR positivity was uncalculable. Second, only a small number was included in the cohort allowing possible bias in the statistical analyses. Nevertheless, this is the first data on SAR-CoV-2 viral load dynamics in children with malignancies and has important clinical implications in this patient cohort.

To conclude, prolonged viral shedding was observed in children with ongoing treatment for underlying malignancies. Children that acquire symptomatic COVID-19 during refractory malignancy state are at an elevated risk for prolonged shedding. Furthermore, evidence of infectiousness was observed in a patient with prolonged shedding. This warrants stricter transmission-based precautions for patients with refractory malignancies after COVID-19 that require hospitalization and have evidence of prolonged viral shedding.

REFERENCES

1. van der Vries E, Stittelaar KJ, van Amerongen G, Veldhuis Kroeze EJ, de Waal L, Fraaij PL, et al. Prolonged influenza virus shedding and emergence of antiviral resistance in immunocompromised patients and ferrets. PLoS Pathog 2013;9:e1003343.
PUBMED | CROSSREF
2. Haessler S, Granowitz EV. Norovirus gastroenteritis in immunocompromised patients. N Engl J Med 2013;368:971.
PUBMED | CROSSREF

3. Niyonkuru M, Pedersen RM, Assing K, Andersen TE, Skov MN, Johansen IS, et al. Prolonged viral shedding of SARS-CoV-2 in two immunocompromised patients, a case report. BMC Infect Dis 2021;21:743.
PUBMED | CROSSREF
4. Altamirano-Molina M, Pacheco-Modesto I, Amado-Tineo J. Prolonged viral shedding of SARS-CoV-2 in patients with acute leukemia. Hematol Transfus Cell Ther 2022;44:299-300.
PUBMED | CROSSREF
5. Shoji K, Suzuki A, Okamoto M, Tsinda EK, Sugawara N, Sasaki M, et al. Prolonged shedding of infectious viruses with haplotype switches of SARS-CoV-2 in an immunocompromised patient. J Infect Chemother 2022;28:1001-4.
PUBMED | CROSSREF
6. Epstein RL, Sperring H, Hofman M, Lodi S, White LF, Barocas JA, et al. Time to SARS-CoV-2 PCR clearance in immunocompromising conditions: is test-based removal from isolation necessary in severely immunocompromised individuals? Open Forum Infect Dis 2021;8:ofab164.
PUBMED | CROSSREF
7. Puhach O, Meyer B, Eckerle I. SARS-CoV-2 viral load and shedding kinetics. Nat Rev Microbiol 2023;21:147-61.
PUBMED | CROSSREF
8. Bullard J, Dust K, Funk D, Strong JE, Alexander D, Garnett L, et al. Predicting infectious severe acute respiratory syndrome coronavirus 2 from diagnostic samples. Clin Infect Dis 2020;71:2663-6.
PUBMED | CROSSREF
9. Jeong HW, Kim SM, Kim HS, Kim YI, Kim JH, Cho JY, et al. Viable SARS-CoV-2 in various specimens from COVID-19 patients. Clin Microbiol Infect 2020;26:1520-4.
PUBMED | CROSSREF
10. Singanayagam A, Patel M, Charlett A, Lopez Bernal J, Saliba V, Ellis J, et al. Duration of infectiousness and correlation with RT-PCR cycle threshold values in cases of COVID-19, England, January to May 2020. Euro Surveill 2020;25:2001483.
PUBMED | CROSSREF
11. Zapor M. Persistent detection and infectious potential of SARS-CoV-2 virus in clinical specimens from COVID-19 patients. Viruses 2020;12:v12121384.
PUBMED | CROSSREF
12. Reich P, Elward A. Infection prevention during the coronavirus disease 2019 pandemic. Infect Dis Clin North Am 2022;36:15-37.
PUBMED | CROSSREF
13. Węcławek-Tompol J, Zakrzewska Z, Gryniewicz-Kwiatkowska O, Pierlejewski F, Bień E, Zaucha-Prażmo A, et al. COVID-19 in pediatric cancer patients is associated with treatment interruptions but not with short-term mortality: a Polish national study. J Hematol Oncol 2021;14:163.
PUBMED | CROSSREF
14. COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines [Internet]. Bethesda: National Institutes of Health; c2023 [cited 2022 Nov 6]. Available from: https://www.covid19treatmentguidelines.nih.gov/.
15. Cevik M, Tate M, Lloyd O, Maraolo AE, Schafers J, Ho A. SARS-CoV-2, SARS-CoV, and MERS-CoV viral load dynamics, duration of viral shedding, and infectiousness: a systematic review and meta-analysis. Lancet Microbe 2021;2:e13-22.
PUBMED | CROSSREF
16. Meiring S, Tempia S, Bhiman JN, Buys A, Kleynhans J, Makhasi M, et al. Prolonged shedding of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) at high viral loads among hospitalized immunocompromised persons living with human immunodeficiency virus (HIV), South Africa. Clin Infect Dis 2022;75:e144-56.
PUBMED | CROSSREF
17. Tabatabai M, Juarez PD, Matthews-Juarez P, Wilus DM, Ramesh A, Alcendor DJ, et al. An analysis of COVID-19 mortality during the dominancy of Alpha, Delta, and Omicron in the USA. J Prim Care Community Health 2023;14:21501319231170164.
PUBMED | CROSSREF
18. Jones TC, Biele G, Mühlemann B, Veith T, Schneider J, Beheim-Schwarzbach J, et al. Estimating infectiousness throughout SARS-CoV-2 infection course. Science 2021;373:eabi5273.
PUBMED | CROSSREF
19. Marks M, Millat-Martinez P, Ouchi D, Roberts CH, Alemany A, Corbacho-Monné M, et al. Transmission of COVID-19 in 282 clusters in Catalonia, Spain: a cohort study. Lancet Infect Dis 2021;21:629-36.
PUBMED | CROSSREF

20. Johnston C, Hughes H, Lingard S, Hailey S, Healy B. Immunity and infectivity in Covid-19. BMJ 2022;378:e061402.
PUBMED | CROSSREF

요약

목적: 본 연구의 목적은 혈액종양 기저질환으로 치료 중 유증상 코로나바이러스감염증-19(COVID-19)으로 확진 된 소아청소년에서 바이러스 부하(viral load)의 변화를 확인하고자 하였다.

방법: 후향적 종단 코호트연구(retrospective longitudinal cohort study)로, 19세 미만 소아청소년 중 악성 빈혈, 혈액암, 또는 고형암으로 치료 중인 상태에서 2022년 3월 1일부터 8월 30일 사이에 SARS-CoV-2 PCR 양성으로 유증상 코로나바이러스감염증-19가 확진 된 환자를 대상으로 하였다. 환자들의 의무 기록과 전화 문진으로 임상 증상과 전파경로, 그리고 증상의 경과에 대한 자료를 얻었고, 서울성모병원에서 시행했던 SARS-CoV-2 PCR titer 값을 분석하였다. 확진 이후 E gene RT-PCR Ct value ≥25을 전파가능성이 낮은 상태로 정의하였다.

결과: 6개월의 연구 기간 동안 총 43명의 환자에서 44번의 COVID-19 확진 사례가 포함되었다. 환자의 평균 연령은 8세 (interquartile range, 4.9–10.5)였으며, 가장 흔한 기저 질환은 급성 림프구성 백혈병(n=30, 68.2%)이었고, 다음으로 조혈모세포이식 후(n=8, 18.2%) 상태인 환자들이었다. 대부분 경증 COVID-19 (n=32, 72.7%)에 해당이 되었고, 3명의 환자(7.0%)는 중증/위중증 COVID-19에 해당되어 산소 치료를 받았다. 2.3% (n=1)는 COVID-19 관련 급성 호흡곤란 증후군으로 사망하였다. 확진 이후 E gene RT-PCR Ct값이 ≥25을 도달한 시점이 15–21일인 환자는 총 39.4% (n=13)이었고, 22–28일에 도달한 환자는 30.3% (n=10)이었다. 15.2% (n=5)의 환자에서는 확진 후 28일이 지난 시점에서도 Ct값 <25를 유지하였다. E gene Ct값이 <25 장기간 지속되는 위험인자로 난치성 악성 종양 상태(β, 67.0; 95% CI, 7.0–17.0; P=0.030)가 유의한 관련이 있었다. 한 환자는 확진 후 Ct 값이 <25으로 유지되던 중, 확진 후 86일 째 보호자로 상주하던 어머니에게 바이러스를 전파하였다.

결론: 난치성 악성 종양 상태에서 유증상 COVID-19에 확진 되는 경우 바이러스를 장기간 배출 할 수 있기 때문에, 이런 환자군에서는 PCR 기반 바이러스 전파 예방 조치가 도움이 될 수 있다.