Infection Control & Hospital Epidemiology (2025), **46**, 99–101
doi:10.1017/ice.2024.188

SHEA

Concise Communication

Comparative quantification of varicella-zoster virus in air, pharyngeal swabs, and vesicle content in patients with varicella, disseminated zoster, and localized herpes zoster

Kei Yamamoto MD[1], Maki Nagashima MT[1], Motoko Ishida MT[1], Masayuki Ota MD[1], Yuichi Katanami MD, MSc[1], Ryoko Adachi B.Pharm[2], Ayako Shigeno B.Pharm[2], Takeshi Tamaki MD, PhD[3] and Norio Ohmagari PhD MD, MSc[1]

[1]Diseases Control and Prevention Center, National Center for Global Health and Medicine, Tokyo, Japan, [2]Department of Pharmacy, National Center for Global Health and Medicine, Tokyo, Japan and [3]Department of Dermatology, National Center for Global Health and Medicine, Tokyo, Japan

Abstract

We evaluated the viral load of varicella-zoster virus (VZV) in ambient air, vesicle, and pharyngeal swabs in VZV-infected patients. Of 46 cases, 6 had VZV detected in indoor air samples from patient rooms. Results suggest an association between viral load in the pharyngeal swab and indoor air.

(Received 30 May 2024; accepted 8 October 2024; electronically published 15 November 2024)

Introduction

Varicella-zoster virus (VZV) is known to spread by the airborne route, underscoring the importance of effective containment measures for primary varicella (VA) and immunosuppressed patients with disseminated or localized zoster.[1] Airborne precautions are not considered necessary for immunocompetent patients with localized herpes zoster (HZ), although nosocomial cases of secondary varicella without direct contact with HZ lesions have been reported.[2,3] VZV has been isolated from the air or air filters of hospital rooms of such patients,[4–6] although there are no reports on VZV viral in room air with quantitative evaluation and comparison of VZV disease types. Therefore, we aimed to evaluate the concentration of VZV in hospital isolation rooms of patients with VZV infection.

Methods

This single-center, prospective, observational study was conducted from November 1, 2015, to July 31, 2018. Hospitalized patients admitted to a private room with VA, disseminated herpes zoster (DZ), or HZ, as suspected by dermatology, internal medicine, or infectious disease physicians, were included. The ambient air inside ("inside air") and outside ("outside air") of the patients' rooms was collected. At least 1 pharyngeal and vesicular swab was collected for quantitative polymerase chain reaction (PCR) for VZV (Supplemental Material). Patients who had taken antivirals for VZV >5 days or in whom VZV was not detected from vesicles or pharyngeal swabs were excluded.

Corresponding author: Kei Yamamoto; Email: kyamamoto@hosp.ncgm.go.jp

Cite this article: Yamamoto K, Nagashima M, Ishida M, *et al.* Comparative quantification of varicella-zoster virus in air, pharyngeal swabs, and vesicle content in patients with varicella, disseminated zoster, and localized herpes zoster. *Infect Control Hosp Epidemiol* 2025. 46: 99–101, doi: 10.1017/ice.2024.188

This study was approved by the Research Ethics Committee of the National Center for Global Health and Medicine (NCGM-G-001822-02).

We obtained written informed consent and clinical information from the clinical review (Supplemental Material). DZ was defined as a case of HZ with skin lesions on 3 or more adjacent or 2 nonadjacent dermatomes or a generalized rash due to VZV infection in a patient with a history of VA.

Statistical analysis

Characteristics of study patients were compared using the Mann–Whitney test for continuous variables and Fisher's exact test for categorical variables. For multiple comparisons, P values were corrected using the Benjamini–Hochberg method. Statistical significance was set at $P < .05$. All analyses were performed using R software (version 4.3.0, R Development Core Team 2023).

Results

One hundred six patients had VZV infection, with 120 excluded mainly owing to lack of private room or having received antivirals for >5 days (Supplemental Figure S1). Forty-six patients were included (Table 1). All vesicular swab VZV PCR tests were positive, with no difference in median viral load among the 3 disease types (Table 1). Twenty-four cases (57.1%) had positive pharyngeal swabs, including 100% of VA patients (7/7) and 33.3% of those with HZ (6/18) ($P = .016$). The median pharyngeal viral load for VA was significantly higher than that for DZ or HZ ($P = .047$, $P = .002$, respectively). Although 2 DZ cases (4.0%) were VZV PCR-positive upon testing outside air samples, neither was in a negative pressure room; in 1 case, the virus was not detected in the inside air. Although the viral load in pharyngeal secretions tended to decrease over time from the appearance of skin lesions or

Table 1. Characteristics of study patients

	All	Varicella	Disseminated zoster	Localized herpes zoster
N	46	7	18	21
Age, years, median, interquartile range (IQR)	64.5 (42.5–74.0)	28.0 (26.0–38.5) *1, *2	68.0 (51.5–74.0) *1	72.0 (61.0–77.0) *2
Sex (male), n (%)	21 (45.7)	4 (57.1)	10 (55.6)	7 (33.3)
Negative pressure room, n (%)	2 (4.3)	0 (0.0)	2 (11.1)	0 (0.0)
Immunization (live-attenuated VZV vaccine), n (%)	4 (8.7)	3 (42.9) *1	1 (5.6)	0 (0.0) *1
Underlying diseases, n (%)	25 (54.3)	1 (14.3)	10 (55.6)	14 (66.7)
Solid cancer (active), n	4	0	1	3
Solid cancer (inactive), n	1	0	0	1
Hematological malignancy, n	1	0	1	0
Bone marrow transplantation, n	2	0	2	0
Solid organ transplantation, n	1	0	1	0
Collagen disease, n	9	0	3	6
Diabetes mellitus, n	6	0	4	2
Others, n	7	1	2	44
Immunosuppressive agents, n (%) (including low-dose oral corticosteroids and methotrexate)	16 (34.8)	1 (14.3)	6 (33.3)	9 (42.9)
Initial symptom: Rash (%)	17 (37.0)	2 (28.6)	6 (33.3)	9 (42.9)
Initial symptom: Pain (%)	33 (71.7)	1 (14.3) *1, *2	15 (83.3) *1	17 (81.0) *2
Initial symptom: Fever (%)	6 (13.0)	5 (71.4) *1, *2	0 (0.0) *1	1 (4.8) *2
WBC (/μL), median (IQR)	5515.0 (4435.0–7012.5)	4270.0 (3560.0–5005.0) *1, *2	6000.0 (4947.5–7785.0) *1	5930.0 (4950.0–7610.0) *2
ANC (/μL), median (IQR)	3650.8 (2721.8–5146.7)	2509.9 (2042.9–3029.2) *1, *2	4236.9 (2964.6–5746.0) *1	3950.1 (2772.9–5229.3) *2
ALC (/μL), median (IQR)	1175.3 (852.5–1614.2)	940.8 (759.9–1311.2)	1166.4 (810.0–1702.4)	1332.9 (990.2–1523.0)
Prior antiviral agents, n (%)	40 (87.0)	3 (42.9) *1, *2	17 (94.4) *1	20 (95.2) *2
Median time between onset of rash and sampling, days, median (IQR)	4.0 (3.0–5.0)	3.0 (1.5–4.0)	4.0 (3.2–5.8)	5.0 (3.0–6.0)
Median time between initiating antiviral agents and sampling, days IQR)	2.0 (2.0–4.0)	1.0 (1.0–2.0) *1, *2	3.0 (2.0–4.0) *1	3.0 (2.0–4.0) *2
Vesicular swabs: positive rate, % (n/N)	100 (45/45)	100 (6/6)	100 (18/18)	100 (21/21)
median viral load, $\log_{10}$ copies/test (IQR)	7.6 (6.1–7.9)	7.8 (7.2–7.9)	7.6 (7.1–7.9)	7.3 (5.3–7.8)
Pharyngeal swabs: positive rate, % (n/N)	57.1 (24/42)	100 (7/7) *1	64.7 (11/17)	33.3 (6/18) *1
median viral load, $\log_{10}$ copies/test (IQR) †	1.3 (0–3.7)	4.6 (3.6–5.2) *1, *2	1.5 (0–4.3) *1, *3	0 (0–1.6) *2, *3
Inside air: positive rate, % (n/N)	13.0 (6/46)	42.9 (3/7)	11.1 (2/18)	4.8 (1/21)
median viral load, $\log_{10}$ copies/test (IQR) †	0 (0–0)	0 (0–1.5)	0 (0–0)	0 (0–0)
PCR-positive rate in the outside air, % (n/N)	4.3 (2/46)	0 (0/7)	11.1 (2/18)	0 (0/21)

Note. VZV, varicella zoster virus; WBC, white blood count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; PCR, polymerase chain reaction.
*1,*2,*3: significant difference ($P < 0.05$) by pairwise comparison adjusted by Benjamini–Hochberg procedure. The number reflects paired items.
†"log0" is a value that does not exist, but for convenience, less than 1 copy/test was replaced by "0."

starting antivirals, no clear trend was observed for vesicular content (Supplemental Figures S2 and S3).

A PCR test of the inside air was positive for 6 patients (range, 0.7–3.1 $\log_{10}$ copies/test) (Table 1). Although the small number of VZV cases with VZV detected in inside air did not result in significant differences, VA had the highest positivity rate, followed by DZ and HZ. There were no significant differences in underlying disease or immunosuppressant use between those with and without VZV detected in the inside air. Those with VZV detected in the inside air were more likely to have not received antivirals at sampling, to have been on antivirals for fewer days, or to have lower white blood cell counts (Supplementary Table S1a). When VA was excluded, although no significant difference was observed owing to the sample size, a similar trend was observed (Supplemental Table S1b). VZV DNA was detected in room air in 5 (20.8%) of the 24 pharyngeal PCR-positive cases and none (0%) of 18 pharyngeal PCR-negative cases. VZV was detected in 2 (4.3%) of 46 samples of air outside the patient room (Table 1). A receiver operating characteristic curve was used to examine pharyngeal swab viral load to identify positive VZV PCR of indoor air, revealing an area under the curve (AUC) of 0.89 (95% CI 0.78–0.99, Figure 1).

No hospital-acquired symptomatic VA occurred during the study.

https://doi.org/10.1017/ice.2024.188 Published online by Cambridge University Press

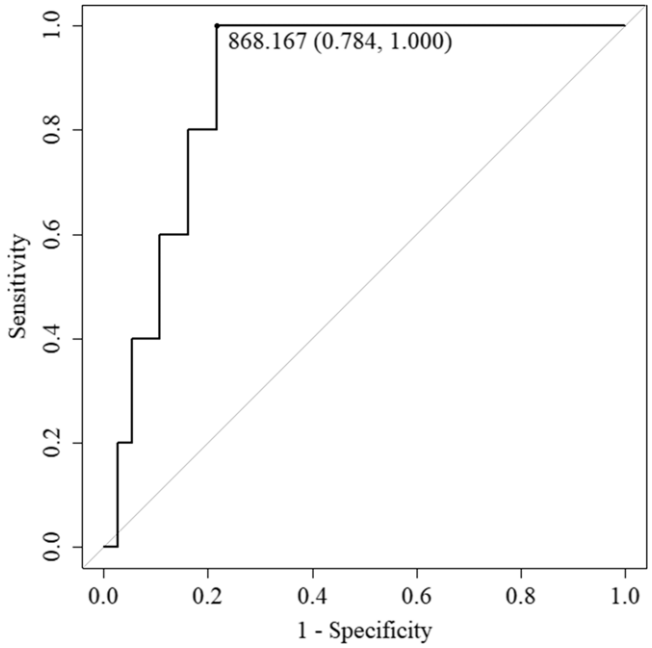

Figure 1. ROC curve demonstrating the varicella-zoster viral load of pharyngeal secretions used to detect the varicella-zoster virus in the air inside the room. AUC 0.89 (95% CI 0.78–0.99). Youden's index showed a cutoff value of 2.9 $\log_{10}$ copies/test with a sensitivity of 0.78 and a specificity of 1.00. ROC, receiver operating characteristic.

Discussion

In this study, VZV viral nucleic acids were detected in the air inside the room of 13% of patients with VZV infection, with VA having the highest positive percentage (43%), followed by DZ (11%) and HZ (5%). Although only 4.3% of patients were placed in negative pressure rooms, 95% of the PCR results for air outside the rooms were negative. VZV was detected in pharyngeal swabs in 31.6%–100% of cases. This was similar to the previously reported detection rate in VA (60%–100%)[7,8] and HZ (5%–100%), depending on the phase of the disease.[4,9,10]

VZV infection transmission is airborne and via contact, with airborne transmission involving viral shedding from the respiratory tract. This study supports this, showing a high pharyngeal PCR positivity rate in patients with VA, who are assumed to be the most infectious. However, in patients with HZ without a high pharyngeal PCR positivity rate, some cases of secondary varicella without direct contact with HZ lesions have been reported.[2,3] VZV has been isolated from air samples collected by cellulose filters or air purifier filters in patients with VA, DZ, and HZ in the rooms.[4–6] Because the positivity rate of VZV in air filters was decreased by covering the vesicles with a hydrocolloid dressing, VZV from vesicles was thought to contribute to airborne transmission.[5] In this study, although the viral load of the vesicular content did not significantly correlate with that of the air in the room, the condition of the vesicles was not constant; for example, some were dried, some were numerous, and some were few. The volume of the swab samples was unstable. Therefore, it may be less meaningful to quantify the amount of VZV within vesicles to assess the risk of airborne transmission.

Although VZV was also detected in the air inside the patient rooms, the positivity rate was lower than that of previous studies.[4,6] In a previous study, VZV was detected by swabbing air purifier filters after 24 hours of use.[4] It is difficult to compare the quantitative differences among the 3 disease types of VZV in air using this method. Sawyer et al collected air samples at various suction rates and times but did not describe the amount of air collected.[6] Therefore, it was difficult to compare the detection rates of viruses in the air for each disease in this report. Another limitation was that the appropriate amount of air to be collected for assessing infectivity remains unknown. Further studies are needed to ascertain the appropriate amount of air and confirm that differences in disease types are related to differences in the number of viral particles in the air. In addition to PCR, it is also desirable to examine the relationship with infectiousness using viral culture. The small sample of patients with VA was also a limitation.

This study suggests VZV detection in indoor air was associated with VZV disease type and viral load in pharyngeal swabs.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/ice.2024.188.

Acknowledgments. We would like to express our deep appreciation to Mr. Fukano and Ms. Takeuchi of the Department of Academic-Industrial Partnerships Promotion, Center for Clinical Sciences, National Center, for their advice in conducting real-time PCR and to all the medical staff who treated the patients.

Financial support. This work was supported by grants from the National Center for Global Health and Medicine (27-6001).

Competing interests. K.Y. reports that he has received research grants from Fujirebio Inc., Canon Medical Systems Corp., Sanyo Chemical Industries Ltd., CarbGeM Inc., Sysmex Corp., and Toyobo Co. Ltd. outside the submitted work. The remaining authors report no conflicts of interest relevant to this article.

References

1. Siegel JD, Rhinehart E, Jackson M, Chiarello L; Health care infection control practices advisory committee. 2007 guideline for isolation precautions: preventing transmission of infectious agents in health care settings. *Am J Infect Control* 2007;35:S65–S164.
2. Viner K, Perella D, Lopez A, *et al.* Transmission of varicella zoster virus from individuals with herpes zoster or varicella in school and day care settings. *J Infect Dis* 2012;205:1336–1341.
3. Cholongitas E, Ilonidis G. Transmission of varicella-zoster virus originating from a patient with localized herpes zoster: Implications for infection control? *Am J Infect Control* 2010;38:669–670.
4. Suzuki K, Yoshikawa T, Tomitaka A, Suzuki K, Matsunaga K, Asano Y. Detection of varicella-zoster virus DNA in throat swabs of patients with herpes zoster and on air purifier filters. *J Med Virol* 2002;66:567–570.
5. Suzuki K, Yoshikawa T, Tomitaka A, Matsunaga K, Asano Y. Detection of aerosolized varicella-zoster virus DNA in patients with localized herpes zoster. *J Infect Dis* 2004;189:1009–1012.
6. Sawyer MH, Chamberlin CJ, Wu YN, Aintablian N, Wallace MR. Detection of varicella-zoster virus DNA in air samples from hospital rooms. *J Infect Dis* 1994;169:91–94.
7. Sawyer MH, Wu YN, Chamberlin CJ, *et al.* Detection of varicella-zoster virus DNA in the oropharynx and blood of patients with varicella. *J Infect Dis* 1992;166:885–888.
8. Leung J, Harpaz R, Baughman AL, *et al.* Evaluation of laboratory methods for diagnosis of varicella. *Clin Infect Dis* 2010;51:23–32.
9. Mehta SK, Tyring SK, Gilden DH, *et al.* Varicella-zoster virus in the saliva of patients with herpes zoster. *J Infect Dis* 2008;197:654–657.
10. Yamakawa K, Hamada M, Takeda T. Different real-time PCR assays could lead to a different result of detection of varicella-zoster virus in facial palsy. *J Virol Methods* 2007;139:227–229.