Characteristics and Risk Factors of Prolonged Viable Virus Shedding in Immunocompromised Patients with COVID-19: A Prospective Cohort Study

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BACKGROUND

Immunocompromised patients with COVID-19 tend to shed viable virus for a prolonged period. Therefore, for moderately or severely immunocompromised patients with COVID-19, CDC recommends an isolation period of at least 20 days and ending isolation. However, data on viral kinetics and risk factors for prolonged viral shedding in these patients are limited.

METHODS

From February 1, 2022 to April 1, 2022, we collected weekly saliva samples from immunocompromised patients with COVID-19 admitted to the Asan Medical Center, tertiary hospital located in Seoul, South Korea. Saliva samples were collected until 12 weeks after diagnosis or discharge. Genomic and subgenomic RNAs were measured, and virus culture was performed. Realtime RT-PCR was then performed to identify SARS-CoV-2 variants.

Figure 1A.

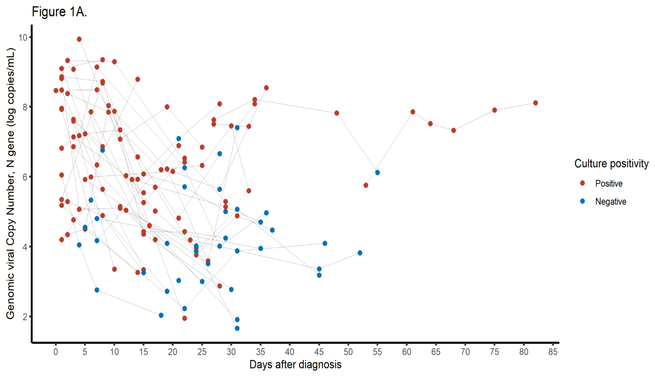
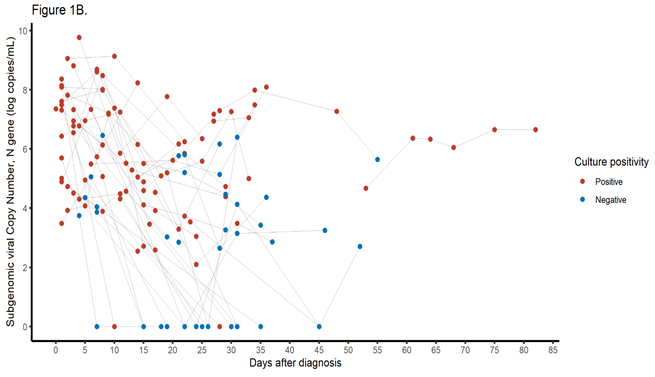


Figure 1B.



Immunocompromised patients with COVID-19 shed viable virus for **median 4 weeks.**

B-cell depleting therapy **increases the risk of prolonged viable viral shedding.**

Vaccination shortens the viable virus shedding in immunocompromised patients.

RESULTS

- A total of 41 patients were enrolled; 29 (70%) were receiving chemotherapy against hematologic malignancies and the remaining 12 (30%) had undergone solid organ transplantation.
- Of 142 saliva samples from the 41 patients, 102 (72%) gave positive results (Figure 1A & 1B).
- Realtime RT-PCR revealed that 7 (17%) were infected with Omicron BA.1, and 33 (80%) with Omicron BA.2.
- The **median duration of viable virus shedding was 4 weeks (IQR 3–6)** (Figure 2).
- Patients undergoing **B-cell depleting therapy shed viable virus for longer** than the comparator (median not reached, p=0.01 in log-rank test: Figure 3).
- Multivariable analysis showed **that 3-dose or more vaccination** (HR 0.33, 95% CI 0.12 – 0.93, p = 0.04) and **B-cell depleting therapy** (HR 12.50, 95% CI 2.44 – 100.00, p = 0.003) independently affected viable virus shedding period of SARS-CoV-2 (Table 1).

Figure 2.

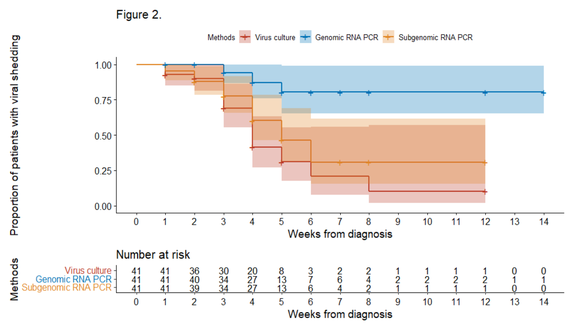
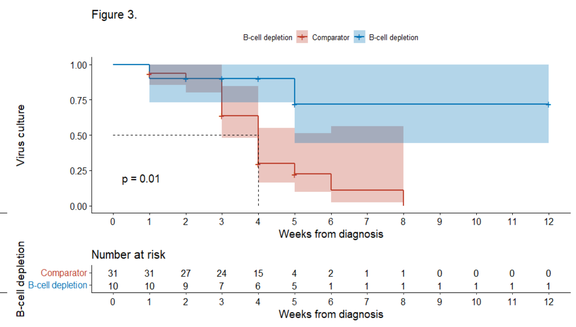


Figure 3.



CONCLUSIONS

- Immunocompromised patients with COVID-19 shed viable virus for median 4 weeks.
- B-cell depleting therapy increases the risk of prolonged viable viral shedding, while completion of a primary vaccine series reduces this risk.

ADDITIONAL KEY INFORMATION

- More specific way tests for assessing viable virus shedding, such as RAT or subgenomic RNA PCR is ungently needed.
- Further studies are needed on the efficacy of vaccination and monoclonal antibody therapy as pre-exposure prophylaxis on viable virus shedding in immunocompromised patients.

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Table 1. Multivariable analysis of viable virus shedding

Characteristic	Multivariable analysis		
	aHR	95% CI	P- value
Less than 3-dose	Reference		
3-dose or more	0.33	0.12 – 0.93	0.04
B-cell depleting therapy			
Comparator	Reference		
B-cell depletion	12.5	2.44 – 100.00	0.003