COVID-19 Special Report 2

Analysis of transmission period among patients with 501Y.V1 in Republic of Korea

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Abstract

After being confirmed as 501Y.V1 on September 20, 2020, about 125 countries have confirmed the 501Y.V1, and the recent COVID-19 pandemic in Brazil has become serious due to the 501Y.V3[1]. A total of 330 Variant of Concern (VOCs) were confirmed by April 5, after the first case was confirmed in Republic of Korea in December 2020. Since January 2, 2021, the Central Disease Control Headquarters has been managing VOCs and suspects by applying "the enhanced case management guidelines" to prevent the inflow and spread of variant in Korea. Therefore, we decided to derive an appropriate isolation period based on scientific grounds for analysis, which accounts for guidance on discharging patients with 501Y.V1 in Korea.

Except for factors such as severe/critical, death, etc. that may affect the transmission period; 501Y.V1 group was selected for 78 and Non-501Y.V1 group for 311 (May, 2020). Further analysis was conducted on 522 501Y.V1 and 522 Non-501Y.V1 group (May, 2020) including 211 unconfirmed C_t values in Polymerase Chain Reaction (PCR) tests during isolation, 851 Non-501Y.V1 group (April, 2020) to comprised the difference between the period of PCR negative conversion. The distribution of C_t values in PCR tests was similar during isolation between the 501Y.V1 group and the Non-501Y.V1 group (May, 2020), and within five days of symptoms or confirmed date, 10 samples with C_t value (RdRp) below 24.68 were negative, and the remaining 30 samples were negative.

In addition, the median was 30 days for 501Y.V1 group, 33 days for non-501Y.V1 group (April, 2020) and 26 days for non-501Y.V1 group (May, 2020) with differences in the distribution of infection routes. The difference in period of PCR negative conversion is expected to take into account the impact of patient characteristics (such as underlying disease and age) according to infection routes rather than infection with COVID-19 variant.

The analysis is meaningful in that it has been able to lay the groundwork for clinical-based guidance on discharging patients as a way to manage patients with the 501Y.V1 by confirming that transmission period of the 501Y.V1 is no different from the COVID-19. In the future, it is necessary to establish a scientific evidence-based strategy to respond to VOCs by continuously analyzing the epidemiological and clinical information of patients with 501Y.V2., 501Y.V3. as well as from the 501Y.V1.

Keywords: Covid-19, Variant of Concern (VOC), 501Y.V1, Transmission period

Introduction

It has been a year since coronavirus disease 2019 (COVID-19) pandemic began, and the world is facing another rise in cases due to variants of COVID-19. After the 501Y.V1 (originating from the United Kingdom) was confirmed on September 20, 2020, 501Y.V1 has been confirmed in approximately 125 countries, and the recent addition of 501Y.V3 (originating from Brazil) has further exacerbated the situation [1]. Since the first detection of 501Y.V1 in Republic of Korea (hereafter, Korea) during quarantine in December 2020, as of April 27, 2021, 535 cases of variants of concern (VOCs) have been confirmed.

To prevent the inflow and spread of variants in Korea, since January 2, 2021, the Central Disease Control Headquarters (CDCH) has been managing VOCs and suspected cases using the Enhanced Case Management Guidelines. According to the strengthened management plan, confirmed patients from abroad are isolated and controlled in a single room, and additional test-based guidance is required for confirmed or suspected cases of VOCs, as these patients are only discharged after two consecutive negative polymerase chain reaction (PCR) tests.

However, the mandatory enforcement of the test-based guidance on discharging patients has inevitably lengthened the isolation period for confirmed and suspected cases of VOCs. This has led to increased financial instability and psychological suffering for patients and less efficiency in the use of medical resources.

Hence, by analyzing the length of the transmission period of 501Y.V1, which is the most common VOC in Korea, the aim of this study was to derive an appropriate end isolation period and establish scientific evidence-based guidance for discharging patients.

Methods

This research aimed to verify the differences in the length of transmission period between 501Y.V1 and non-501Y.V1 by comparing the timing of PCR-negative conversion along with the C_t value distribution of the PCR tests and culture tests during isolation. A cohort study was conducted from December 28, 2020 to March 15, 2021 on 178 patients who have been confirmed with 501Y.V1. R was used to conduct frequency analysis and cross-analysis(using the chi-square test) to compare epidemiological characteristics. A Kaplan Meier survival curve was constructed and the log-rank test was used to analyze the length of transmission period, and the C_t value distribution of the specimens during isolation was analyzed using a scatter plot.

1. Subjects of analysis

A. 501Y.V1 Group

Between December 28, 2020 and March 15, 2021, there were a total of 178 confirmed cases of 501Y.V1 in Korea. The C_t value of the PCR test during isolation could be confirmed for all patients. To exclude factors that could affect the length of transmission period, the following subjects were excluded from the study: 7 patients who were in severe/critical condition or died; 30 patients who did not complete the isolation treatment; and 63 patients who were discharged according to the clinical-based guidance for discharging patients. Hence, 501Y.V1 group consisted of a total of 78 patients, who were then further divided into symptomatic (54 patients) and asymptomatic (24 patients) groups prior to analysis.

B. Non-501Y.V1 Group

Two separate groups were formed for the non-501Y.V1

group according to the aim of the analysis. First, to compare the timing of PCR-negative conversion, the C_t value distribution of the PCR tests, and culture tests between the 501Y.V1 group and non-501Y.V1 group, the research subjects for the non-501Y.V1 group were chosen among patients confirmed to have COVID-19 prior to September 20, 2020—and specifically, those who were confirmed in May 2020 when the GH type virus, which is currently predominant in Korea, was detected. In total, there were 728 confirmed cases of COVID-19 in Korea between May 1, 2020 and May 31, 2020 (based on the date of confirmation). Among those confirmed cases, the following subjects were excluded: 211 patients who had missing values because the C_t values of the PCR tests were unconfirmed during isolation; 10 patients who were in severe/critical condition or died; and 196 patients who were discharged according to the clinical progress-based guidance on discharging patients. There were a total of 311 patients in the non-501Y.V1 group, which were further divided into symptomatic (201 patients) and asymptomatic (110 patients) groups to analyze the C_t distribution pattern of PCR tests and PCR-negative conversion during isolation.

Second, to compare differences in the timing of PCR-negative conversion according to the infection route, patients infected outbreaks at hospitals/nursing homes in April 2020, and those infected in May 2020, when regional group outbreaks were common, were considered as the non-501Y.V1 groups for comparisons. There were 886 patients who were confirmed with COVID-19 in Korea between April 1, 2020 and April 30, 2020 (based on the confirmation date). To eliminate factors that may affect transmission period, the following subjects were excluded: 27 patients who were in severe/critical condition or died, and 8 patients who were discharged according to the clinical progress-based guidance on discharging patients. Hence, the first non-501Y.V1 group (May 2020) was composed of 522 patients (including 211 patients whose C_t values of PCR tests during isolation were unconfirmed) and the second non-501Y.V1 group (April 2020) was composed of 851 patients. The timing of PCR-negative conversion was analyzed in both groups.

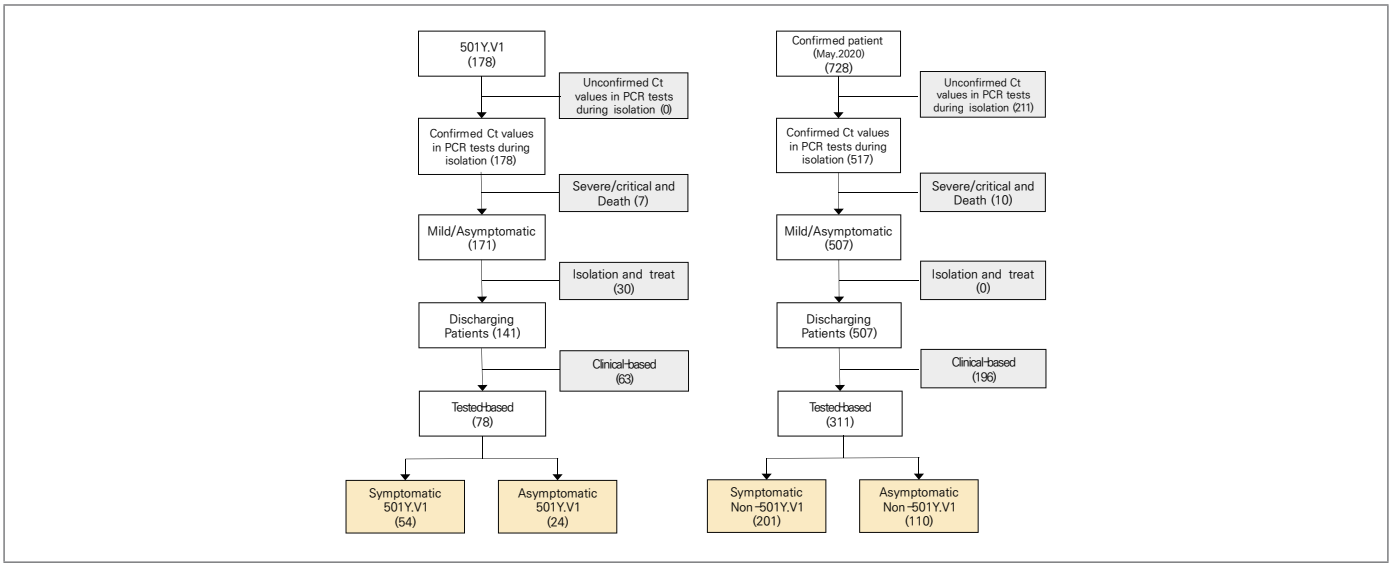

Figure 1. Classification of group for 501Y.V1 and non-501Y.V1

Table 1. Epidemiological characteristics of symptomatic 501Y.V1 and non-501Y.V1

Unit: n (%)

	Total	501Y.V1	Non-501Y.V1 (May, 2020)	*p*-value*
Total	255 (100.0%)	54 (100.0%)	201 (100.0%)	
Gender				
Male	179 (70.2%)	36 (66.7%)	143 (71.1%)	0.523
Female	76 (29.8%)	18 (33.3%)	58 (28.9%)	
Age group (yrs)				
0-9	7 (2.7%)	1 (1.9%)	6 (3.0%)	0.002
10-19	28 (11.0%)	1 (1.9%)	27 (13.4%)	
20-29	87 (34.1%)	13 (24.1%)	74 (36.8%)	
30-39	46 (18.0%)	9 (16.7%)	37 (18.4%)	
40-49	39 (15.3%)	17 (31.5%)	22 (10.9%)	
50-59	28 (11.0%)	8 (14.8%)	20 (10.0%)	
60-69	16 (6.3%)	3 (5.6%)	13 (6.5%)	
70-79	3 (1.2%)	1 (1.9%)	2 (1.0%)	
80+	1 (0.4%)	1 (1.9%)	0 (0.0%)	
Nationality				
Koreans	244 (95.7%)	46 (85.2%)	198 (98.5%)	0.000
Foreigners	11 (4.3%)	8 (14.8%)	3 (1.5%)	
Route of infection and detection				
Imported cases	74 (29.0%)	48 (88.9%)	26 (12.9%)	0.000
Imported cases realated	4 (1.6%)	4 (7.4%)	0 (0.0%)	
Nursing hospital/facilities related	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Religion related	136 (53.3%)	2 (3.7%)	134 (66.7%)	
Contact with confirmed cases	2 (0.8%)	0 (0.0%)	2 (1.0%)	
Under investigation (unclassified)	6 (2.4%)	0 (0.0%)	6 (3.0%)	

* χ^2 test

Table 2. Epidemiological characteristics of asymptomatic 501Y.V1 and non-501Y.V1

Unit: n (%)

	Total	501Y.V1	Non-501Y.V1 (May, 2020)	*p*-value*
Total	134 (100.0%)	24 (100.0%)	110 (100.0%)	
Gender				
Male	85 (63.4%)	14 (58.3%)	71 (64.5%)	0.566
Female	49 (36.6%)	10 (41.7%)	39 (35.5%)	
Age group (yrs)				
0-9	4 (3.0%)	2 (8.3%)	2 (1.8%)	0.089
10-19	13 (9.7%)	3 (12.5%)	10 (9.1%)	
20-29	39 (29.1%)	5 (20.8%)	34 (30.9%)	
30-39	26 (19.4%)	8 (33.3%)	18 (16.4%)	
40-49	18 (13.4%)	0 (0.0%)	18 (16.4%)	
50-59	18 (13.4%)	3 (12.5%)	15 (13.6%)	
60-69	11 (8.2%)	3 (12.5%)	8 (7.3%)	
70-79	5 (3.7%)	0 (0.0%)	5 (4.5%)	
80+	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Nationality				
Koreans	113 (84.3%)	11 (45.8%)	102 (92.7%)	0.000
Foreigners	21 (15.7%)	13 (54.2%)	8 (7.3%)	
Route of infection and detection				
Imported cases	57 (42.5%)	19 (79.2%)	38 (34.5%)	0.000
Imported cases realated	4 (3.0%)	3 (12.5%)	1 (0.9%)	
Nursing hospital/facilities related	2 (1.5%)	0 (0.0%)	2 (1.8%)	
Religion related	61 (45.5%)	2 (8.3%)	59 (53.6%)	
Contact with confirmed cases	0 (0.0%)	0 (0.0%)	0 (0.0%)	
Under investigation (unclassified)	10 (7.5%)	0 (0.0%)	10 (9.1%)	

* χ^2 test

Table 3. Epidemiological characteristics of symptomatic 501Y.V1 and non-501Y.V1 (April, May 2020)

Unit: n (%)

	Total	501Y.V1	Non-501Y.V1 (April, 2020)	Non-501Y.V1 (May, 2020)
Total	**1,020 (100.0%)**	**54 (100.0%)**	**643 (100.0%)**	**323 (100.0%)**
Gender				
Male	533 (52.3%)	36 (66.7%)	285 (44.3%)	212 (65.6%)
Female	487 (47.7%)	18 (33.3%)	358 (55.7%)	111 (34.4%)
Age group (yrs)				
0-9	19 (1.9%)	1 (1.9%)	9 (1.4%)	9 (2.8%)
10-19	95 (9.3%)	1 (1.9%)	57 (8.9%)	37 (11.5%)
20-29	347 (34.0%)	13 (24.1%)	222 (34.5%)	112 (34.7%)
30-39	181 (17.7%)	9 (16.7%)	107 (16.6%)	65 (20.1%)
40-49	132 (12.9%)	17 (31.5%)	75 (11.7%)	40 (12.4%)
50-59	109 (10.7%)	8 (14.8%)	70 (10.9%)	31 (9.6%)
60-69	84 (8.2%)	3 (5.6%)	61 (9.5%)	20 (6.2%)
70-79	33 (3.2%)	1 (1.9%)	24 (3.7%)	8 (2.5%)
80+	20 (2.0%)	1 (1.9%)	18 (2.8%)	1 (0.3%)
Nationality				
Koreans	925 (90.7%)	46 (85.2%)	585 (91.0%)	294 (91.0%)
Foreigners	95 (9.3%)	8 (14.8%)	58 (9.0%)	29 (9.0%)
Route of infection and detection				
Imported cases	507 (49.7%)	48 (88.9%)	381 (59.3%)	78 (24.1%)
Imported cases realated	61 (6.0%)	4 (7.4%)	57 (8.9%)	0 (0.0%)
Nursing hospital/facilities related	100 (9.8%)	0 (0.0%)	100 (15.6%)	0 (0.0%)
Religion related	284 (27.8%)	2 (3.7%)	60 (9.3%)	222 (68.7%)
Contact with confirmed cases	31 (3.0%)	0 (0.0%)	27 (4.2%)	4 (1.2%)
Under investigation (unclassified)	37 (3.6%)	0 (0.0%)	18 (2.8%)	19 (5.9%)

Table 4. Epidemiological characteristics of asymptomatic 501Y.V1 and non-501Y.V1 (April, May 2020)

Unit: n (%)

	Total	501Y.V1	Non-501Y.V1 (April, 2020)	Non-501Y.V1 (May, 2020)
Total	**431 (100.0%)**	**24 (100.0%)**	**208 (100.0%)**	**199 (100.0%)**
Gender				
Male	192 (44.5%)	14 (58.3%)	107 (51.4%)	71 (35.7%)
Female	150 (34.8%)	10 (41.7%)	101 (48.6%)	39 (19.6%)
Age group (yrs)				
0-9	23 (5.3%)	2 (8.3%)	14 (6.7%)	7 (3.5%)
10-19	34 (7.9%)	3 (12.5%)	14 (6.7%)	17 (8.5%)
20-29	118 (27.4%)	5 (20.8%)	51 (24.5%)	62 (31.2%)
30-39	68 (15.8%)	8 (33.3%)	25 (12.0%)	35 (17.6%)
40-49	54 (12.5%)	0 (0.0%)	27 (13.0%)	27 (13.6%)
50-59	44 (10.2%)	3 (12.5%)	19 (9.1%)	22 (11.1%)
60-69	51 (11.8%)	3 (12.5%)	31 (14.9%)	17 (8.5%)
70-79	27 (6.3%)	0 (0.0%)	19 (9.1%)	8 (4.0%)
80+	12 (2.8%)	0 (0.0%)	8 (3.8%)	4 (2.0%)
Nationality				
Koreans	364 (84.5%)	11 (45.8%)	193 (92.8%)	160 (80.4%)
Foreigners	67 (15.5%)	13 (54.2%)	15 (7.2%)	39 (19.6%)
Route of infection and detection				
Imported cases	224 (52.0%)	19 (79.2%)	110 (52.9%)	95 (47.7%)
Imported cases realated	15 (3.5%)	3 (12.5%)	11 (5.3%)	1 (0.5%)
Nursing hospital/facilities related	71 (16.5%)	0 (0.0%)	69 (33.2%)	2 (1.0%)
Religion related	90 (20.9%)	2 (8.3%)	8 (3.8%)	80 (40.2%)
Contact with confirmed cases	5 (1.2%)	0 (0.0%)	3 (1.4%)	2 (1.0%)
Under investigation (unclassified)	26 (6.0%)	0 (0.0%)	7 (3.4%)	19 (9.5%)

Results

1. Distribution of C_t values

When comparing the C_t value distributions in the PCR tests during isolation between symptomatic and asymptomatic patients, no significant difference was found in the distribution of the 1,176 C_t values from the 255 symptomatic patients and the 559 C_t values from the 134 asymptomatic patients.

2. Comparison of the timing of PCR-negative conversion

The timing of PCR-negative conversion of patients infected with 501Y.V1 or non-501Y.V1 was compared between symptomatic and asymptomatic groups. In symptomatic patients, 501Y.V1 had a longer interval until PCR-negative conversion, with 31.5 days compared to the 29 days for non-501Y.V1 patients (p=0.026). However, there were no significant differences between the two groups in asymptomatic patients (p=0.33), with 501Y.V1 patients requiring 23 days and non-501Y.V1 patients requiring 21 days.

Furthermore, in order to evaluate the effect of the selection method for the non-501Y.V1 group, confirmed cases in April 2020 were also included in the analysis of the timing of PCR-negative

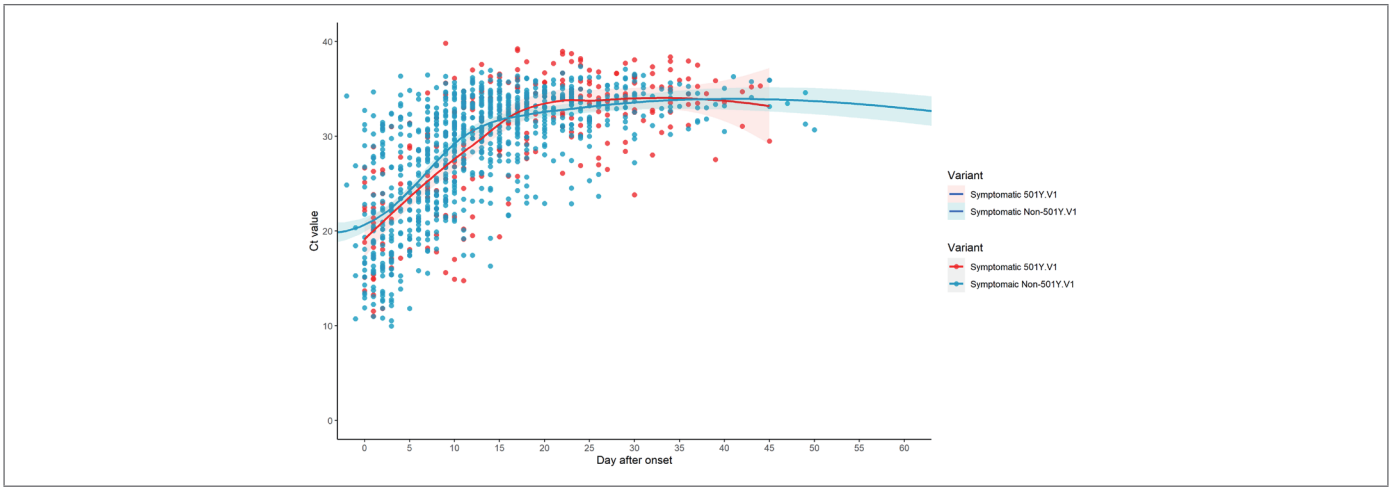

Figure 2. The distribution of C_t values between the 501Y.V1 and the Non-501Y.V1 (May, 2020)

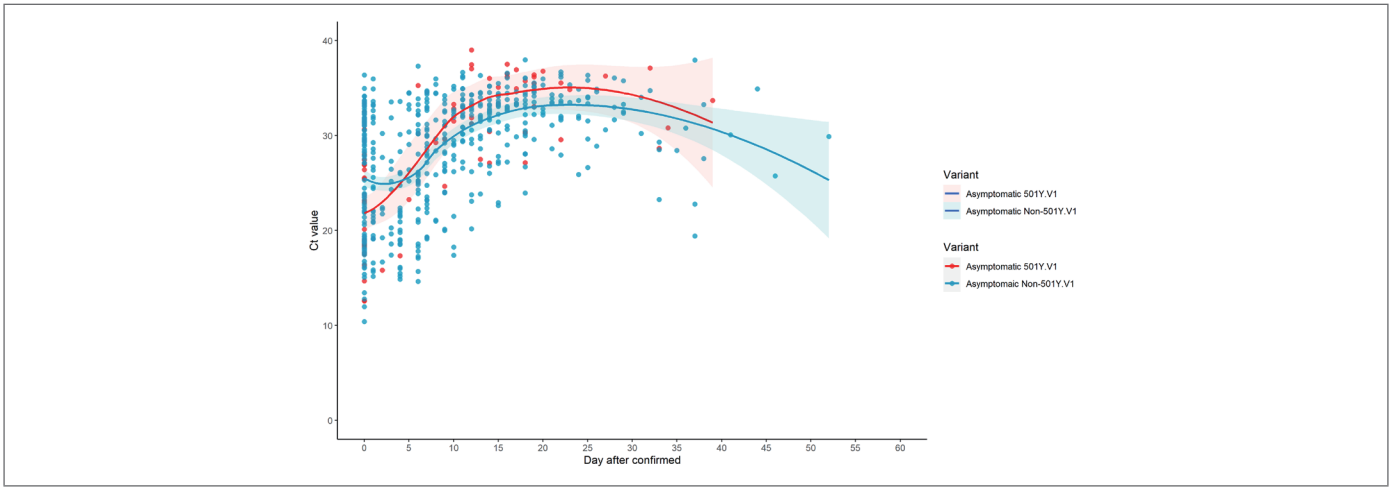

Figure 3. The distribution of C_t values between the 501Y.V1 and the Non-501Y.V1 (May, 2020)

conversion. The median interval until PCR-negative conversion was 30 days for the 501Y.V1 group, 33 days for the non-501Y.V1 group (April 2020), and 26 days for the other non-501Y.V1 group (May 2020). Because the infections in the April 2020 non-501Y.V1 group largely occurred in group outbreaks at hospital or nursing homes in old age groups and many of the patients, the age group of the patients was high and many of the patients were in the high-risk group with underlying diseases, explaining the long interval until PCR negative conversion. In contrast, the infections in the May 2020 non-501Y.V1 group largely occurred in regional group outbreaks; therefore, this group comprised relatively young patients, fewer of whom were at risk, and had the shortest interval until PCR-negative conversion. The differences in the timing of PCR-negative conversion appear to be more heavily affected by patient characteristics (such as underlying disease and age) and infection route, rather than the variant type.

A. Culture test results

Culture tests were conducted on 77 positive PCR samples from 33 patients infected with 501Y.V1. Of the tested samples, 31 cases within 9 days of confirmation or onset of symptoms that had C_t values lower than 26.73 demonstrated positive culture tests, while the remaining 46 samples were all negative.

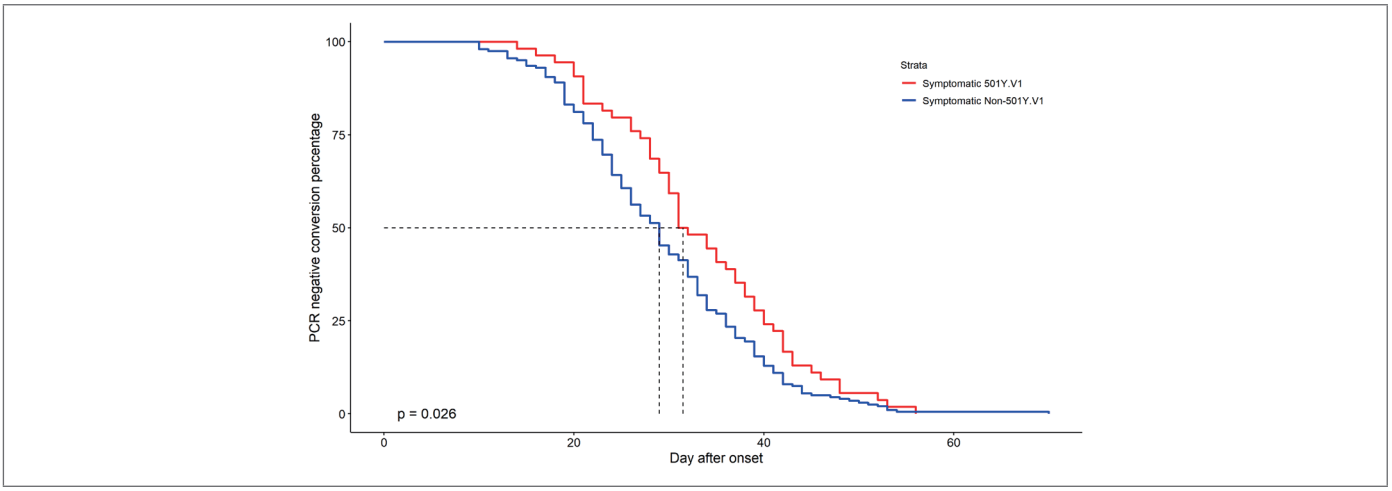

Figure 4. Survival curve between the symptomatic 501Y.V1 and the Non-501Y.V1 (May, 2020)

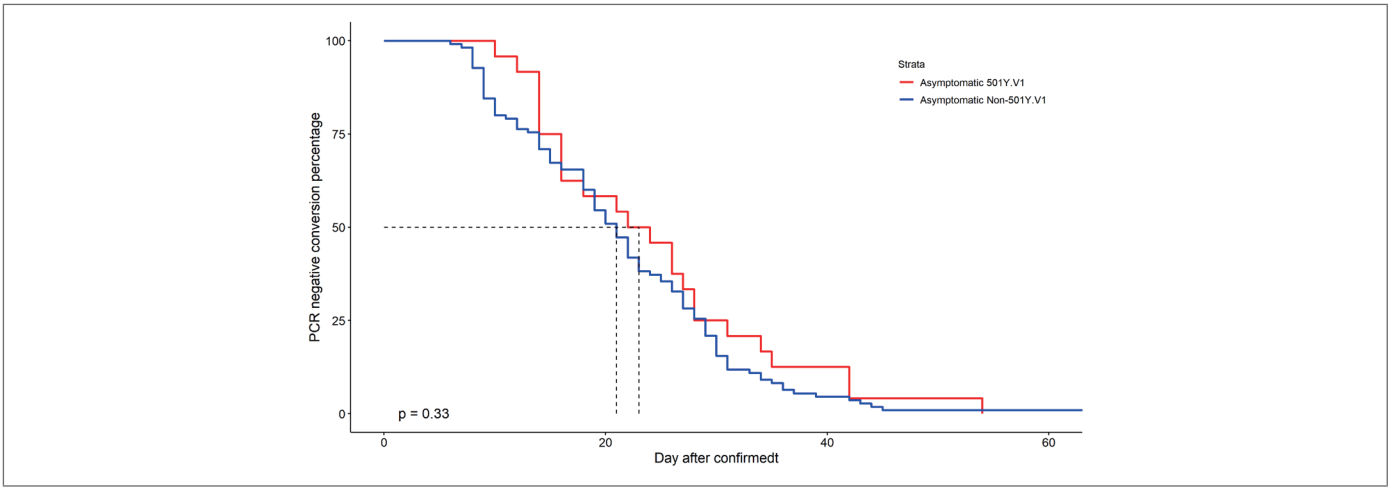

Figure 5. Survival curve between the asymptomatic 501Y.V1 and the Non-501Y.V1 (May, 2020)

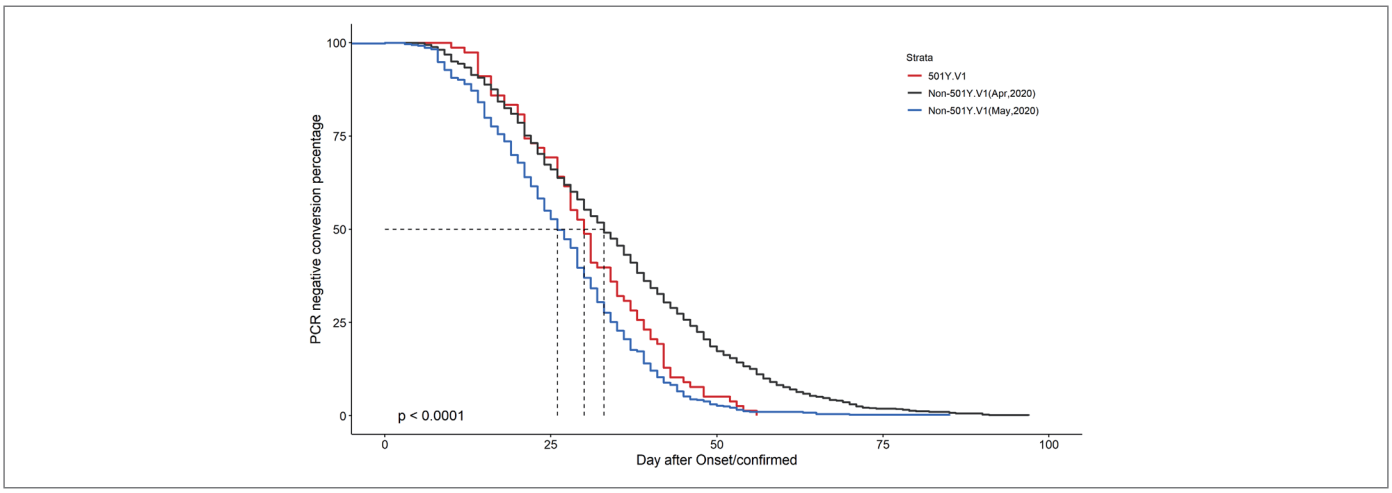

Figure 6. Survival curve between the 501Y.V1 and the Non-501Y.V1 (Apr, May)

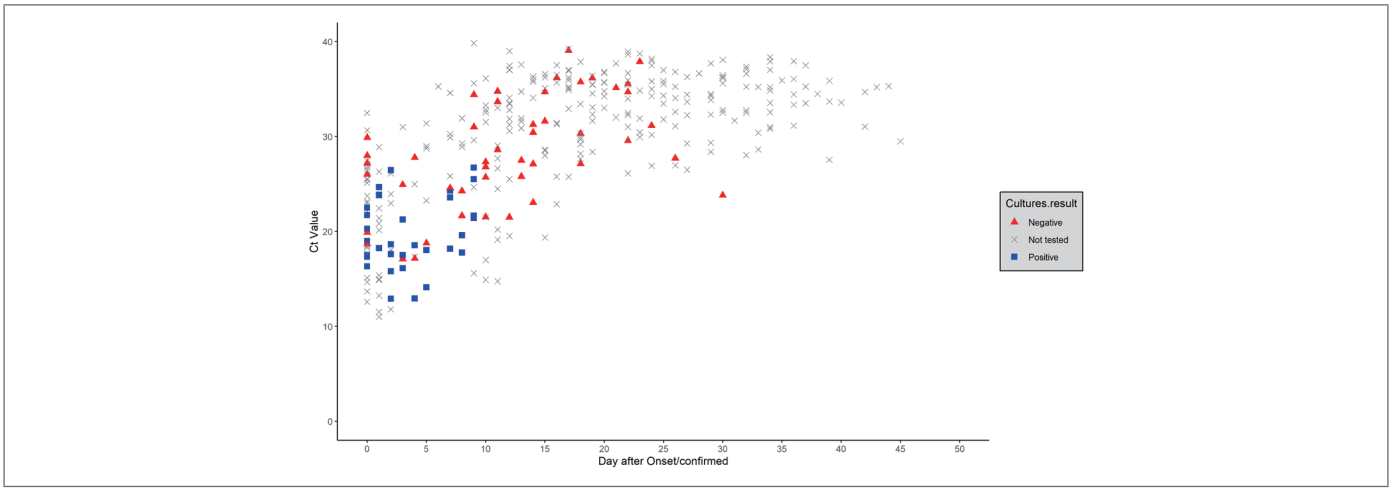

Figure 7. The distribution of C_t values and culture result between the 501Y.V1 (including clinical-based Guidance on discharging patients, Severe/critical)

* Positive 31 patients and negative 46 patients

Conclusion

After cases of pneumonia with an unknown cause were first announced in Wuhan, Hubei Province, China on December 31, 2019, the global COVID-19 pandemic has been continuing for over a year. Despite tremendous efforts, the pandemic still continues due to the emergence of variant viruses. 501Y.V1, for example, has demonstrated increased transmission rates (1.5 times) and fatality [1,2] and has caused another surge of cases in many nations. Hence, many nations around the world have taken drastic measures to prevent a resurgence of COVID-19 such as closing borders. In South Korea, enhanced case management guidelines have been applied to prevent all variants of the virus from entering the country.

As a preemptive measure, mandatory test-based guidance on discharging patients has been applied for patients with variants to manage the virus conservatively. However, this analysis confirmed that transmission period of 501Y.V1 has only a negligible difference compared to that of the existing SARS-CoV-2 virus, and therefore provides a meaningful basis for

clinical-based discharge guidelines regarding 501Y.V1 patients. There still is a need for continued research regarding VOCs. Hence, epidemiological and clinical information regarding patients infected with other variants, such as 501Y.V2, 501Y.V3, must be analyzed to establish patient management strategies for cases of COVID-19 variants in Korea.

Acknowledgments

Conflict of Interest

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

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Submitted: April 23, 2021; **Revised:** April 26, 2021; **Accepted:** April 27, 2021

① What was known?

After the first confirmed case in Korea in December 2020, 178 cases of 501Y.V1 have been confirmed as of March 15, 2021. Since January 2, 2021, the Central Disease Control Headquarters(CDCH) has applied the Enhanced Case Management Guidelines to confirmed and suspected cases of VOCs to prevent the inflow and further spread of variants in Korea.

② What does this study add?

The 501Y.V1 group and the non-501Y.V1 group (May 2020) both had similar distributions of C_t values from PCR tests. Culture tests showed positive results for 31 samples that were taken within 9 days of symptom onset in patients with a C_t value below 26.73, but they showed negative results for the remaining 46 samples. In addition, the 501Y.V1 group and the two non-501Y.V1 groups, which had different infection routes (April 2020, May 2020), had intervals of negative PCR conversion of 30 days, 33 days (April 2020), and 26 days (May 2020), respectively. Hence, it seems necessary to prioritize patient characteristics (such as underlying disease and age) resulting from the infection route over variant type when considering the timing of negative PCR conversion.

③ What are the implications?

By confirming that there were no significant differences in transmission period between the 501Y.V1 variant and the existing SARS-CoV-2 virus, this study provides the basis for the establishment of clinical-based discharge guidelines as a method of patient care. In the future, analysis of epidemiological and clinical information of patients infected with other variants, such as 501Y.V2, 501Y.V3, should be continued to establish scientific evidence-based patient management strategies for variant cases domestically.

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This article has been translated from the Public Health Weekly Report (PHWR) volume 14, Number 18, 2021.