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Research article

Viral load dynamics of SARS-CoV-2 in the moderately symptomatic COVID-19 patients in Dak Lak, Viet Nam, 2021

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Abstract: COVID-19 vaccines reduce infection, disease severity, and death by SARS-CoV-2 by reducing viral load. This study aimed to evaluate the change of cycle threshold (Ct) value in COVID-19 patients and investigate factors related to the Ct value change on the 3rd (D3), 7th (D7), 10th (D10), and 14th (D14) day after hospital admission in Dak Lak in 2021. Nasopharyngeal swabs and serum samples were obtained from 251 COVID-19 patients. Samples were collected on D3, D7, D10, and D14 after hospital admission and tested for SARS-CoV-2 by real-time RT-PCR tests. Ct values were categorized as *high viral load*, *moderate viral*, and *low viral load*. Electrochemiluminescence immunoassay was used to estimate the anti-SARS-CoV-2 antibodies. The results demonstrated that vaccinated individuals against COVID-19 have a faster rate of hospital discharge than the unvaccinated group, most clearly on D10. The Ct change on D10 of vaccinated individuals was statistically significantly higher (1.35 times) than of unvaccinated individuals ($P < 0.01$). The mean Ct values of unvaccinated individuals on D3, D7, D10, and D14 were lower than that of vaccinated individuals. However, there was a statistically significant increase in Ct of vaccinated individuals compared to unvaccinated individuals only on D10 and D14 ($P < 0.03$). The percentage of Ct value ≥ 30 and negative of vaccinated persons on D7 (60.9%) was similar to that of unvaccinated persons on D10 (59.4%) ($P > 0.05$). Vaccinated individuals at hospital admission with Ct ≤ 20 on D1 had a statistically significant decline in viral load on D10 and D14, 1.55 and 1.30 times higher compared to unvaccinated individuals ($P < 0.05$). The percentage of Ct ≥ 30 was significantly higher in males than females,

especially on D7 and D14 with PR = 1.26 and 1.11 ($P < 0.05$). In conclusion, individuals vaccinated against COVID-19 had reduced transmission by a significant decline in viral load and recovered faster than unvaccinated individuals.

Keywords: COVID-19; Dak Lak; real-time RT-PCR; cycle threshold

1. Introduction

In early December 2019, pneumonia with an unknown etiology was reported among a cluster of patients in a hospital in Wuhan, Hubei Province, China. Similar to the outbreak of SARS in 2003, this disease could develop into pneumonia and respiratory failure [1]. One month later, the World Health Organization (WHO) declared COVID-19, the disease caused by a novel coronavirus (2019-nCoV), a Public Health Emergency of International Concern [2]. The 2019-nCoV was officially called SARS-CoV-2, and the disease was named COVID-19. Since then, SARS-CoV-2 spread around the world, causing a prolonged pandemic with a high mortality rate. By October 31, 2021, the World Health Organization (WHO) reported more than 246 million confirmed cases and nearly 5 million deaths globally [3]. COVID-19 vaccination was found to be effective in reducing household transmission of the alpha variant (B.1.1.7) by 40–50% [4]; infected, vaccinated individuals had a lower viral load in the upper respiratory tract (URT) than unvaccinated individuals, indicative of reduced infectiousness [5–7].

But how do viral load dynamics [indirectly determined by cycle threshold (Ct) in real-time PCR] differ in vaccinated and unvaccinated people? To evaluate the infectiousness of an individual, Ct values are used as an indirect marker of the viral load. One hypothesized mechanism is that viral loads observed in people infected with SARS-CoV-2 after vaccination are lower than those among unvaccinated people, and the viral load is associated with the likelihood of infection in contacts. However, the absence of a reported difference in viral loads between vaccinated and unvaccinated infected people calls into question whether vaccination controls the spread of the disease as effectively as it controls transmissibility with increasing vaccination coverage.

During the period of the COVID-19 pandemic in Vietnam in 2020–2021, the Ministry of Health (MOH) issued Decision No. 3416/QD-BYT dated July 14, 2021, to promulgate the criteria for the classification of the risk of people infected with SARS-CoV-2 divided into three floors for treatment. On the first floor, COVID-19-infected people presented no symptoms or mild symptoms and should be isolated and tested on the 10th day; if the Ct value was ≥30, then they could be transferred to the home for isolation to reduce the medical burden [8]. However, this decision had not yet mentioned COVID-19 vaccines. Therefore, COVID-19 patients who were treated on the first floor were required to wait up to 10 days for testing (by real-time RT-PCR) whether they could be transferred home for required isolation or not. In addition, the Vietnamese Dak Lak province conducted a mass vaccination campaign against COVID-19 in October 2021; at the same time, the COVID-19 pandemic was spreading quickly with hundreds of cases daily in this region [8].

This study aimed to evaluate the change of Ct value in COVID-19 patients and investigate some factors related to this change on the 3rd, 7th, 10th, and 14th day after hospital admission at two field hospitals in Dak Lak, Vietnam in 2021.

2. Materials and methods

2.1. Study design and population

A cross-sectional study was conducted on 251 patients from November 2021 to March 2022 in two field hospitals in Dak Lak province. Patients infected with SARS-CoV-2 for the first time were admitted to the field hospitals on the first day (called first floor). Data was collected by convenience sampling. All patients were interviewed by questionnaire on the first day of admission (D1), and samples of the nasopharyngeal swabs were collected on D3, D7, D10, and D14 to determine the change of viral load via Ct value. In addition, serum samples were collected on D7 and D14 to determine the SARS-CoV-2 antibody levels of patients with COVID-19.

2.2. Exclusion criteria

Subjects who met any of the following criteria were disqualified from entering the study: (1) immunodeficiency disorders, (2) pregnant women, and (3) persons who had confirmed previous COVID-19 infection.

2.3. Sample size calculation

The sample size was calculated using the single proportion sample size formula:

$$n = \frac{\left(Z^2 \frac{\alpha}{2} p(1-p)\right)}{\mathrm{d}^2}$$

where n is the sample size; Zα/2 is the statistic corresponding to the level of confidence, assumed to be 1.96 (when α = 0.05); d is precision (5%), and p is the estimated prevalence of COVID-19 patients with Ct value ≥ 30 (86% on the D14). The minimum sample size was 251.

2.4. Laboratory procedures

All cases were diagnosed as COVID-19 based on RT-PCR tests of nasopharyngeal samples. The nasopharyngeal samples were transferred to a viral transport media immediately after collection and transported to the COVID-19 laboratory of the Institute of Hygiene and Epidemiology of Tay Nguyen for testing. The RT-PCR tests were conducted using the SuperScript™ III Platinum™ One-Step qRT-PCR Kit (catalog number: 11732020). RT-PCR was conducted on Applied Biosystems (Foster City, CA). The assay used targeted the E target gene according to the Charité-Berlin protocol. If positive, the sample was confirmed by RdRP and N genes. The E gene Ct value was reported and used in this study. Ct values > 40 were considered negative. Ct values from 17 to 24, from 24 to 31, and from 31 to 38 were categorized as *high viral load*, *moderate viral load*, and *low viral load*, respectively. Electrochemiluminescence immunoassay (ECLIA) was used to detect antibodies against RDB-S of SARS-COV-2 with a cutoff ≥ 0.8 U/mL considered as positive by Elecsys ® Anti-SARS-CoV-2 S (Roche/Germany).

2.5. Statistical analysis

The data are expressed as mean ± standard deviation (SD). Prevalence rates and Ct value means and 95% confidence intervals (CIs) were calculated. The comparisons of participant characteristics and rate of Ct ≥ 30 difference between groups were performed using Chi-square for 2 × 2 tables, while the Yates test was used when at least one cell had an expected frequency lower than 5. The mean value of the Ct value between the groups was examined by two-way ANOVA. A test probability of 5% and a two-sided interval was considered statistically significant. Categorical variables were reported as frequencies and percentages. Statistics were performed using SPSS version 22 (IBM, USA).

3. Results

3.1. Epidemiological data of the study population

In total, 251 COVID-19 patients (136 males and 115 females) were included in the study. The majority of patients were 18–49 years old (80.08%); males represented 54.18% of the entire study population. Kinh represented a majority of the cohort (64.68%). Only 16.33% of patients were vaccinated with two doses of the COVID-19 vaccine (Table 1).

Table 1. Characteristics of COVID-19 patients in Dak Lak.

Characteristics	N	%
Age		
<18	5	1.99
18–49	201	80.08
≥50	45	17.93
Gender		
Male	136	54.18
Female	115	45.82
Ethnicity		
Kinh	163	64.68
Ethnic minorities	89	35.32
Vaccinated history with COVID-19		
One dose	177	70.52
Two doses	41	16.33
Unvaccinated	33	13.15
Total	251	100

3.2. Change of Ct values according to characteristics

The vaccinated group had a faster rate of hospital discharge than the unvaccinated group, most clearly observed on D10. The change of Ct value on D10 with Ct value ≥ 30 of the vaccinated group was statistically significantly higher (1.35 times) than the unvaccinated group (95% CI: 1.00–1.81) ($P < 0.01$). The discharge rate of persons vaccinated against COVID-19 on D7 (60.9%) was slightly higher than that of the unvaccinated persons on D10 (59.4%). Similarly, the comparison between persons who received one and two doses of the vaccine showed that the rate of the increasing Ct was

significantly faster in persons with two doses of vaccine [PR = 1.2 (95% CI: 1.07–1.35) ($P < 0.05$)] (Table 2).

Table 2. Ct value change at different time points (patients with Ct ≥ 30 and negative).

Date	D3		D7		D10		D14	
Parameter	Case/n*	(%)	Case/n*	(%)	Case/n*	(%)	Case/n*	(%)
Vaccinated against COVID-19	83/218	38.1	131/215	60.9	172/215	80.0	186/204	91.2
Unvaccinated against COVID-19	9/33	27.3	17/33	51.5	19/32	59.4	26/32	81.3
P	0.23		0.19		<0.01		0.08	
PR (95% CI)					1.35 (1.00–1.81)			
2 doses	16/41	39.0	27/41	65.9	38/41	92.7	38/40	95.0
1 dose	67/177	37.9	104/174	59.8	134/174	77.0	148/164	90.2
P	0.90		0.47		0.02		0.52	
PR (95% CI)					1.2 (1.07–1.35)			

Note: n*: Sample size of each group according to the different time. *P*: Probability; PR: Prevalence Ratio; 95% CI: 95% Confidence Interval.

The mean Ct values of vaccinated individuals on D3, D7, D10, and D14 were 23.6 (± 6.4); 26.4 (± 5.9); 29.0 (± 5.2), and 30.9 (± 4.1); Ct values of unvaccinated individuals were 21.6 (± 6.9); 25.7 (± 6.1); 25.5 (± 5.7), and 27.8 (± 4.3). There was a statistically significant difference in mean Ct values between vaccinated and unvaccinated individuals on D10 and D14 ($P < 0.05$) (Table 3).

Table 3. Mean Ct value at different times (negative cases not included) (average mean of Ct (± SD)).

Time	D3	D7	D10	D14
Vaccinated against COVID-19	23.6 (± 6.4)	26.4 (± 5.9)	29.0 (± 5.2)	30.9 (± 4.1)
Unvaccinated against COVID-19	21.6 (± 6.9)	25.7 (± 6.1)	25.5 (± 5.7)	27.8 (± 4.3)
P	0.13	0.56	0.01	0.03
1 dose	23.6 (± 6.1)	26.4 (± 5.6)	28.4 (± 5.3)	30.7 (± 4.9)
2 doses	23.5 (± 7.3)	26.6 (± 6.8)	32.1 (± 3.1)	32.2 (± 3.5)
P	0.87	0.88	<0.01	0.46

Note: *P*: Probability; SD: Standard deviation.

The international classification of the Ct value on D1 showed that the percentage of Ct ≥ 30 in vaccinated individuals is always higher than that of the unvaccinated individuals at any time point, although the Ct value at the time of hospital admission may be different (≤ 24; 24–30; 31–37, and >37). No significant difference between times was found ($P > 0.05$). However, for individuals with Ct < 24 at D1, there was a statistically significant difference in the percentage of Ct ≥ 30 in the vaccinated group (higher by 1.42 times) compared with the unvaccinated group on D10 ($p < 0.05$). Vaccinated patients who were admitted to the hospital with Ct ≤ 20 on D1 had a statistically significant decline in viral load (Ct ≥ 30) on D10 and D14; it was higher by 1.55 and 1.3 times, respectively, compared with unvaccinated patients ($P < 0.05$). The ratio of Ct ≥ 30, according to subclinical characteristics such as SARS-CoV-2 antibodies and leukocytosis at testing time points, presented no significant differences ($P > 0.05$) (Table 4).

Table 4. Ct value change according to the Ct value at the first day (D1).

Ct value at D1	COVID-19 vaccine	Ct ≥ 30 and negative							
		D3		D7		D10		D14	
		Case/n*	(%)	Case/n*	(%)	Case/n*	(%)	Case/n*	(%)
<24	Vaccinated	48/158	30.4	92/155	59.4	127/156	81.4	135/151	89.4
	Unvaccinated	2/21	9.5	11/21	52.4	12/21	57.1	16/20	80.0
	P	0.08		0.54		0.01		0.39	
	PR (95% CI)					1.42 (0.98–2.08)			
24–30	Vaccinated	16/27	59.3	19/27	70.4	20/27	74.1	25/25	100
	Unvaccinated	4/7	57.1	3/7	42.9	4/6	66.7	6/7	85.7
	P	0.74		0.36		0.89		0.49	
31–37	Vaccinated	7/9	77.8	7/9	77.8	8/9	88.9	6/6	100
	Unvaccinated	2/2	100	2/2	100	2/2	100	2/2	100
	P	0.78		0.78		0.39		0.56	
Antigen rapid testing	Vaccinated	12/24	50.0	13/24	54.2	17/23	73.9	20/22	90.9
	Unvaccinated	1/3	33.3	1/3	33.3	1/3	33.3	2/3	66.7
	P	0.94		0.95		0.44		0.79	
<20	Vaccinated	39/132	29.5	74/129	57.4	107/130	82.3	113/126	89.7
	Unvaccinated	1/17	5.9	9/17	52.9	9/17	52.9	11/16	68.8
	P	0.07		0.7		0.01		0.048	
	PR (95% CI)					1.55 (0.99–2.45)		1.30 (0.93–1.81)	

Note: n*: Sample size of each group according to the different times. *P*: Probability; PR: Prevalence Ratio; 95% CI: 95% Confidence Interval.

There was no statistically significant difference in Ct value ≥ 30 according to age group and ethnicity during the first 10 days of hospital admission ($P > 0.05$). The percentage of the Kinh group with a Ct value ≥ 30 was significantly higher than that of the ethnic minority group on D14, with PR = 1.11 (95% CI: 0.99–1.20) ($P < 0.05$). The percentage of Ct ≥ 30 was significantly higher in males than females at the time of testing, especially on D7 and D14 with PR = 1.26 (95% CI: 1.02–1.56) and 1.11 (95% CI: 1.01–1.21) ($P < 0.05$) (Table 5).

The percentage of positive antibodies against SARS-CoV-2 at D7 in the vaccinated group (80.7%) was significantly higher (1.5 times) compared to the unvaccinated group (53.3%) at D10 with Ct ≥ 30 ($P < 0.05$). Similarity, a significant difference in the percentage of positive antibodies at D14 was found between the vaccinated and unvaccinated groups at D3, D7, and D10 with Ct ≥ 30 ($P < 0.05$). However, there was no statistically significant difference in the percentage of positive antibodies between the vaccinated and unvaccinated groups at D14 with Ct ≥ 30 ($P > 0.05$). There was no significant difference in the ratio of Ct ≥ 30 according to the count of leukocytosis at testing time ($P > 0.05$) (Table 6).

Table 5. Ct value change according to epidemiological characteristics.

Characteristics		Ct ≥ 30 and negative							
		D3		D7		D10		D14	
		Case/n*	(%)	Case/n*	(%)	Case/n*	(%)	Case/n*	(%)
Age	<18	2/6	33.3	3/6	50.0	4/6	66.7	4/5	80.0
	18–50	78/200	39.0	123/199	61.8	155/197	78.7	176/191	92.1
	>50	12/45	26.7	22/43	51.2	32/44	72.7	32/40	80.0
	P	0.2		0.34		0.62		0.07	
Gender	Male	53/136	39.0	89/135	65.9	109/134	81.3	122/130	93.8
	Female	39/115	33.9	59/113	52.2	82/113	72.6	90/106	84.9
	P	0.41		0.03		0.1		0.03	
	PR (95% CI)			1.26 (1.02–1.56)				1.11 (1.01–1.21)	
Ethnicity	Kinh	57/163	35.0	95/160	59.4	129/150	86.0	141/152	92.8
	Ethnic minority	35/88	39.8	53/88	60.2	62/88	70.5	71/84	84.5
	P	0.45		0.9		0.055		0.045	
	PR (95% CI)							1.11 (0.99–1.21)	

Note: n*: Sample size of each group according to the different times. *P*: Probability; PR: Prevalence Ratio; 95% CI: 95% Confidence Interval.

Table 6. RT-PCR cycle threshold (Ct) change according to epidemiological characteristics.

Subclinical indicators	Covid-19 vaccination	Ct ≥ 30 and negative							
		D3		D7		D10		D14	
		Case/n*	(%)	Case/n*	(%)	Case/n*	(%)	Case/n*	(%)
Positive antibodies against SARS-CoV-2 at D7	Vaccinated	74/199	37.2	121/198	61.1	159/197	80.7	171/189	90.5
	Unvaccinated	5/16	31.3	7/16	43.8	8/15	53.3	14/16	87.5
	P	0.6		0.17		0.012		0.95	
	PR (95% CI)					1.51 (0.94–2.44)			
Positive antibodies against SARS-CoV-2 at D14	Vaccinated	50/129	38.8	78/129	60.5	100/128	78.1	115/129	89.1
	Unvaccinated	0/10	0.0	1/10	10.0	3/9	33.3	8/10	80.0
	P	0.03		<0.01		<0.01		0.32	
	PR (95% CI)			6.05 (0.94–39.0)		2.34 (0.93–5.93)			
White blood cell count (>8000) at D3	Vaccinated	10/26	38.5	17/26	65.4	22/26	84.6	21/26	80.8
	Unvaccinated	½	50.0	½	50.0	0/2	0.0	½	50.0
	P	0.67		0.67		0.06		0.32	

Note: n*: Sample size of each group according to the different times. *P*: Probability; PR: Prevalence Ratio; 95% CI: 95% Confidence Interval.

4. Discussion and conclusions

This study was conducted during the fourth wave of the COVID-19 pandemic in Vietnam (starting from April 27, 2022) with a high confirmed number of cases, multiple sources of transmission, circulating virus variants (including SARS-CoV-2 Delta variant), and all ages being affected. At that time, Vietnam was accelerating vaccination coverage nationwide [9].

This work evaluated COVID-19 patients, most being 18–49 years old (80.08%) and female. The percentage of ethnic minorities (35.32%) was quite high compared to the general ethnic minority rate of the population in Dak Lak (31.3%). At the time of the study, most people who received treatment had received 1–2 doses of the vaccine (86.85%). Our results show that vaccinated individuals have a faster rate of hospital discharge than unvaccinated individuals, most visible on D10. The change of Ct value on D10 (with Ct value ≥ 30) was significantly higher (1.35 times) in the vaccinated than the unvaccinated groups ($P < 0.01$). It is also important to note that the discharge rate of the vaccinated group on D7 was 60.90% higher than that of the unvaccinated group on D10 (59.40%). This finding provides support to counsel the Vietnam MOH to reduce the testing time for COVID-19 patients who have been vaccinated against COVID-19 from D10 to D7, as previously required [8]. Similarly, the comparison between individuals who received 1 and 2 doses of the vaccine showed a faster increasing rate of Ct in the group with 2 doses of vaccine, mostly obvious on D10 with PR = 1.2 and $P < 0.05$. This finding is a confirmation of the effectiveness of COVID-19 vaccination; the vaccine leads to rapidly reduced viral load (Ct value) and, therefore, a significant decrease in the quarantine time from 10 to 7 days. The majority of vaccinated persons only required quarantine time between D7 and D10 (the percentage with Ct value ≥ 30 was from 60.9% to 80.0%). Our results are consistent with a study on 142 COVID-19 patients in Shanghai in April 2022, in which vaccinated individuals had a significantly shorter time to achieve a Ct value >35 (median was 12.6 ± 3.4 days) than unvaccinated patients (14.8 ± 4.7 days) [10]. Our findings also agree with a study in Seoul, Korea that showed that the viral load reduced faster in the full-dose vaccinated group than in the incomplete and unvaccinated groups (after D4, D8, and D10) [11]. These results are also in accordance with previous studies on hemodialysis patients in Singapore, in which the median time to become negative was 24 days for the vaccinated group and 32 days for the unvaccinated group [12]. A study in the United Kingdom also showed that individuals who received two doses of the COVID-19 vaccine had an 88% reduction in the number of cases with Ct < 30 (95% CI: 80–93%, $P < 0.001$) compared to unvaccinated individuals and a 91% reduction (95% CI = 85–94%; $P < 0.001$) compared to individuals with one dose of the vaccine after 21 days [12].

The mean Ct values on D3, D7, D10, and D14 were 23.6, 26.4, 29.0, and 30.9, respectively, for vaccinated individuals, and 21.6, 25.7, 25.5, and 27.8, respectively, for unvaccinated individuals. These findings demonstrate that the mean Ct value of vaccinated individuals is lower than that of the unvaccinated individuals on D3 and D7. However, there was a statistically higher Ct in vaccinated individuals on D10 and D14 ($P < 0.03$). This means that the vaccinated individuals recovered faster. These results are consistent with previous studies [13–15], while disagreeing with a previous study in California, USA, conducted on 869 individuals, which showed no significant differences in the mean Ct value between vaccinated and unvaccinated persons [16]. When considering the international classification of Ct value on D1 [17], the percentage of Ct ≥ 30 in the vaccinated group was always higher than in the unvaccinated group, although the Ct value at the time of hospital admission may be different (≤ 24; 24–30; 31–37, and > 37). No significant differences between times were found ($P > 0.05$). However, for individuals with Ct < 24 at D1, there was a statistically significant difference in the percentage of Ct ≥ 30 in the vaccinated group (higher by 1.42 times) compared with the unvaccinated group on D10 ($P < 0.05$). These viral dynamics may explain epidemiologic studies showing reduced transmission from vaccinated individuals [18]. One important unanswered question is what proportion of infections are due to transmission from asymptomatic individuals.

Our analysis at different Ct intervals found that vaccinated patients who were admitted to the hospital with Ct ≤ 20 on D1 had a statistically significant decline in viral load (Ct ≥ 30) on D10 and D14; this was higher from 1.55 to 1.30 times compared with unvaccinated individuals ($P < 0.05$). Our results are consistent with previous studies by Pritchard et al. (2021) [12], Acharya et al. (2022) [13], and Wu et al. (2022) [16]. These findings demonstrate that vaccinated individuals have a faster reduction in viral load than unvaccinated individuals. Our study showed there was no statistically significant difference in Ct value ≥ 30 according to age group and ethnicity during the first 10 days of disease ($P > 0.05$). The percentage of Kinh individuals with Ct value ≥ 30 was significantly higher than the ethnic minority group on D14 (PR = 1.11; $P < 0.05$). The percentage of Ct ≥ 30 was significantly higher in males than females, meaning that the COVID-19 recovery rate was significantly faster in men, especially on D7 and D14 with PR = 1.26 and 1.11 ($P< 0.05$). These findings are in accordance with previous studies in the United States, in which ethnic minorities were 1.2–3.18 times more likely to have infection, hospitalization, and mortality than White persons ($P < 0.05$) [15,19]. Some studies found a higher risk of hospitalization among Asian or Pacific Islander and Latino persons [20], while others found no difference in risk [21]. Our study results agree with a study from the United Kingdom that showed Asian women had an 11% higher risk of death than Asian men [22].

The ratio of Ct ≥ 30 according to subclinical characteristics such as SARS-CoV-2 antibodies and leukocytosis was not significantly different at different testing time points ($p > 0.05$). In other words, the subclinical indicators of the asymptomatic or mildly symptomatic COVID-19 patients were not related to the rate of increase in Ct value (decline of viral load) at the different testing time points. These results are in accordance with a study in Iran showing no relationship between the Ct value and SARS-CoV-2 antibodies ($P > 0.05$) [23,24]. A study on COVID-19 patients in Turkey showed that the number of white blood cells (after 1–3 days of infection) was statistically significantly lower in patients with a high viral load (low Ct value ≤ 25) ($P < 0.001$) [25].

In conclusion, this study revealed the effectiveness of COVID-19 vaccination to rapidly reduce the viral load and, as a consequence, to reduce infection, transmission, disease severity, and death by COVID-19.

Author contributions

Chien Chinh Vien: conceived the idea and designed the study; Tuan Van Le, Van Tuyet Thi Nguyen, Thang Nghia Hoang, Phila Nay: collected the data; Chien Chinh Vien, Tuan Van Le, Thang Nghia Hoang: analyzed the data and drafted the manuscript. All authors commented the paper and approved the final manuscript.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Ethics approval of research and informed consent

This study was approved by the Ethical Committee of Tay Nguyen Institute of Hygiene and Epidemiology, Vietnam (Approval number: 07/CN-VTN, dated 15th November 2021). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. All participants had provided written informed consent and assent, as appropriate, prior to study enrollment.

Conflict of interest

The authors declare no conflict of interest.

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