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Association of clinical characteristics and vaccines with risk of persistently viral clearance in patients infected with SARS-CoV-2 Omicron variant in Shanghai, China☆

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ABSTRACT

Importance: The global COVID-19 pandemic does not appear to end in the near future. Currently, limited data are available on the risk factors for delayed viral clearance in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant infection.
Objective: This study aimed to investigate the association of clinical characteristics and vaccination with prolonged viral clearance.
Methods: This retrospective cohort included 16,985 patients who had contracted the SARS-CoV-2 Omicron variant between April 5 and May 30, 2022, in Shanghai, China, and had mild or no symptoms. The patients were admitted to the quarantine venue at the Shanghai New International Expo Center.
Results: Of the 16,985 participants, the occurrence of viral clearance was ≤8 and > 8 days in 11,009 (64.8 %) and 5976 (35.2 %) participants, respectively. Risk factors related to patients who remained persistently polymerase chain reaction (PCR)-positive were sex (Male, odds ratio [OR] 1.221, $p < 0.001$), older age (35–49, OR 1.389, $p < 0.001$; 50–64, OR 1.659, $p < 0.001$; ≥65, OR 2.139, $p < 0.001$), presence of symptoms (OR 1.093, $p = 0.030$), number of vaccinations (two doses, OR 0.753, $p < 0.001$; three doses, OR 0.797, $p < 0.001$; four doses, OR 0.543, $p < 0.001$), and cycle threshold (Ct) value for ORF1ab gene at diagnosis (25–35, OR 0.235, $p < 0.001$; >35, OR 0.079, $p < 0.001$). The lower rates of increase in Ct values were observed in the later viral

☆ The study was approved by the Longhua Hospital, Shanghai University of Traditional Chinese Medicine Ethical Review Authority (2022LCSY026) and registered in the Chinese Clinical Trial Registry (ChiCTR2200060472).

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shedding group than in the early viral shedding group for ORF1ab ($\beta = -0.791$, $p < 0.001$) and N genes ($\beta = -0.825$, $p < 0.001$).
Conclusion: Prolonged SARS-CoV-2 RNA detection and higher viral concentrations were associated with factors such as male sex, older age, symptomatic status, and fewer doses of vaccination in patients admitted to Shanghai Makeshift Hospital between April 5 and May 30, 2022.

1. Introduction

Considering its current status, the global COVID-19 pandemic does not appear to end in the near future. The World Health Organization reported 5,987,880 cases with 24,258 deaths from January 3, 2020, to August 16, 2022, in China [1]. In late February 2022, a new wave of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron infections rapidly emerged in Shanghai, China. Following appearance of Omicron, ballooning incidence exposed a greater rate of transmission than the previously dominant variant, which is known to exhibit immune evasion [2]. According to the Shanghai Municipal Health Commission, from April 1 to June 1, 2022, asymptomatic and mildly symptomatic infections played a substantial role in the challenge of controlling the COVID-19 pandemic. These clinical types led to increased mobility and reduced disease awareness [3]. Although most cases are not severe, the high transmissibility of the Omicron variant places a huge burden on healthcare resources. The Chinese government imposed strict bans to lock down the city of Shanghai from April 1 to June 1, 2022, to suppress the outburst of Omicron cases [3].

The duration of viral clearance is usually ≥20 days in the early days of the outbreak [4]. Recent research has indicated a shorter nucleic acid conversion time since the dominance of the Omicron variant BA.2 [5,6]. Although the viral load of SARS-CoV-2 has decreased since disease onset, the period of viral clearance may vary among patients. Viral clearance is an important aspect because it has been linked to an increased risk of transmissibility. However, little is known about factors associated with prolonged viral clearance in patients infected with this variant. There have been some reports on risk factors that influence the persistence of SARS-CoV-2 RNA shedding [7–9]. In a recent study of 142 patients with SARS-CoV-2 Omicron variant infection from March 4 to 30, 2022 in China, vaccination was found to be a protective factor against shorter viral shedding time in these patients [10]. Herein, the effect of SARS-CoV-2 vaccines on viral clearance time was investigated. However, limited clinical and virological data were available.

According to the latest research that enrolled 1377 participants older than 60 years in 2022, the median Omicron viral clearance time was nine days [11]. Our previous studies showed that the median negative conversion time for nucleic acids was no more than 8 days [12–14]. Hence, we defined the cutoff point for prolonged viral clearance as >8 days. Herein, we conducted a large study to evaluate the association of clinical characteristics and number of vaccinations with the risk predictors of prolonged viral clearance and higher viral load in the Shanghai New International Expo Center Makeshift Hospital during the Omicron outbreak.

2. Materials and METHODS

2.1. Study design and population

We performed a retrospective study to evaluate the potential risk factors for prolonged viral clearance. This retrospective study was carried out from April 5 to May 30, 2022, at the Shanghai New International Expo Center, the largest quarantine venue in Shanghai, which had up to 15,000 beds and isolated more than 40,000 patients with Omicron variants during outbreaks. The whole-genome targeted sequencing technology results obtained from the Shanghai Center for Disease Control and Prevention revealed that the Omicron variant BA.2 was the dominant variant in the COVID-19 outbreak in Shanghai since March 2022 [3,15–17].

We collected data from electronic medical records. Baseline demographic and health information, symptoms, vaccination history, number of vaccinations, comorbidities, vaccine manufacturer, and reverse transcription quantitative polymerase chain reaction (RT-qPCR) cycle threshold (Ct) values were collected from the inpatients.

All inpatients with COVID-19 reported in electronic medical records were included in this retrospective study. The clinical diagnosis of the confirmed cases was based on nucleic acid detection in nasopharyngeal and oropharyngeal samples by RT-qPCR using a SARS-CoV-2 RNA detection kit (BioGerm Medical Technology Co., Ltd, Shanghai, China). All patients were retested daily after diagnosis. Patients were considered to be in virologic remission based on consecutive RT-PCR tests (Ct values > 35) with an interval of at least 24 h. The viral clearance time was defined as the time from a positive nucleic acid test to two consecutive negative nucleic acid tests at an interval of 24 h.

2.2. Procedures

We included data from all Shanghai New International Expo Center inpatients confirmed by RT-qPCR between April 5 and May 30, 2022. Patients with COVID-19 who underwent consecutive RT-PCR tests ≤2 days after admission were excluded from this study. Patients who were transferred to another hospital during hospitalization were also excluded. This study involved two key steps. First, a logistic regression model was used to assess the potential risk of prolonged viral shedding. We defined cohorts that included a comparator of patients with early viral shedding (≤8 days) and later viral shedding (>8 days). We developed a generalized estimating equation (GEE) model to estimate the relative Ct value patterns that varied according to viral shedding since admission to the hospital.

2.3. Statistical analysis

We compared the characteristics of all inpatients infected with Omicron variants according to the duration of viral shedding (≤8 days vs. >8 days). Categorical measures are presented as frequencies with percentages. Continuous variables are described using medians with interquartile ranges (IQR). The chi-square test was used to compare categorical variables between the later and early viral clearance groups. Differences in continuous variables between the later and early viral clearance groups were assessed using the Mann–Whitney *U* test.

Univariate and multivariable binary logistic regression models were used to quantify the strength of the association between age, sex, comorbidities, hypertension, diabetes, coronary heart disease, arrhythmia, chronic gastropathy, chronic liver disease, vaccination status, number of vaccines, vaccine manufacturers, symptoms, and persistent viral clearance in the later vs. early clearance groups. We used backward stepwise elimination (with a threshold of $P < 0.05$) to select covariates for inclusion in the final models.

A GEE was used to examine the main effects, time effects, and interactions in the Ct values of the ORF1ab and N genes over time. We adopted a first-order autoregressive covariance as the working covariance structure for the GEE estimation of the primary outcome. All results are presented as 95 % confidence intervals. All analyses were performed using SPSS version 25.0 (IBM SPSS Statistics for Windows).

2.4. Ethics

The study was approved by the Longhua Hospital, Shanghai University of Traditional Chinese Medicine Ethical Review Authority (2022LCSY026) and registered in the Chinese Clinical Trial Registry (ChiCTR2200060472). All methods were performed in accordance with relevant regulations and the Declaration of Helsinki. The need for informed consent from the patients was waived by the research ethics board because of the fully anonymized individual data and the retrospective nature of the study.

3. Result

3.1. Baseline characteristics

A flow diagram summarizing the selection of enrolled patients is shown in Fig. 1. Of the 16,985 participants, the occurrence of viral clearance was ≤8 and > 8 days in 11,009 (64.8 %) and 5976 (35.2 %) participants, respectively. The demographic characteristics of the patients are shown in Table 1. A total of 10,132 (59.7 %) patients were male and 6853 (40.3 %) were female. The median age of the patients was 46 years (IQR: 32–56 years). A total of 188 (1.1 %) patients returned from abroad, and 2762 (16.3 %) had comorbidities. The most common comorbidities were hypertension (11.3 %), diabetes (4.9 %), coronary heart disease (2.1 %), and arrhythmias (1.7 %). In total, 12,604 (74.2 %) patients received one or more doses of the vaccine: 3.3 % received one dose, 28.8 % received two doses, 40.9 % received three doses, and 1.2 % received four or more doses. The vaccines were produced by Sinovac Biotech Co. Ltd. (49.3 %), China National Pharmaceutical Group Co. Ltd. (22.6 %), CanSino Biologics Inc. (1.7 %), and Anhui Zhifei Longcom Biopharmaceuticals (0.6 %).

The patients who reported any of the health conditions selected for this study are shown in Table 2. Among the 4269 (25.1 %) participants who reported one or more symptoms of COVID-19, the most commonly reported symptoms were cough (20.9 %), sputum production (10.6 %), fatigue (6.6 %), fever (6.0 %), muscle soreness (5.1 %), sore throat (1.6 %), nasal congestion (0.5 %), headache (0.6 %), and runny nose (0.6 %). The median Ct values of the sequenced ORF1ab and N genes were 27.12 and 26.54 cycles,

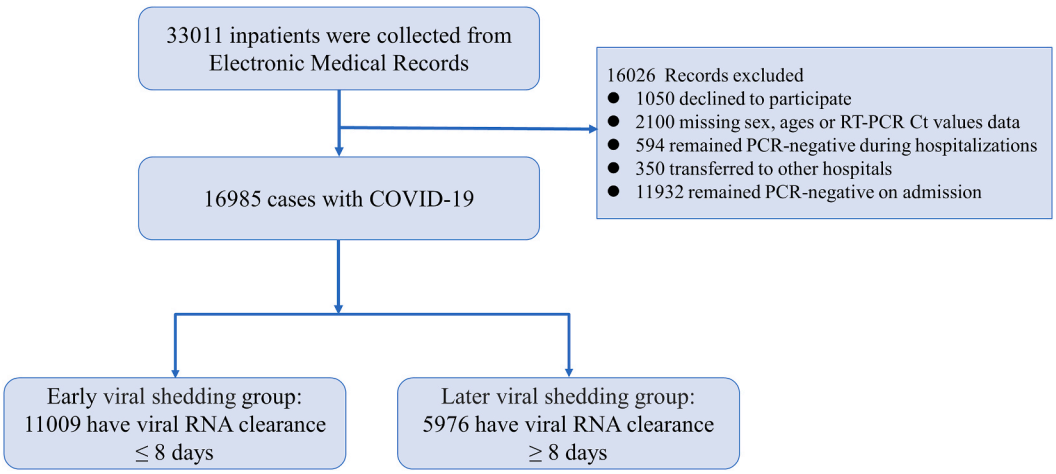

Fig. 1. Trial profile describing the selection of participants in the study. Abbreviations: COVID-19, coronavirus disease 2019; RT-PCR: real-time reverse transcriptase-polymerase chain reaction; Ct: circle threshold.

Table 1
Demographics and baseline characteristics of patients with the SARS-CoV-2 omicron variant Shanghai April 1-June 15, 2022.

Characteristic	All patients	>8 days	≤8 days	*P* value
Overall, n (%)	16,985 (100)	5976 (35.2)	11,009 (64.8)	
Sex				
Male, n (%)	10,132 (59.7)	3684 (61.6)	6448 (58.6)	<0.001
Female, n (%)	6853 (40.3)	2292 (38.4)	4561 (41.4)	
Ages, medium (IQR)	46 (32–56)	49 (35–59)	43 (30–55)	<0.001
0-19, n (%)	1167 (6.9)	282 (4.7)	885 (8.0)	<0.05
20-34, n (%)	4034 (23.8)	1132 (18.9)	2902 (26.4)	<0.05
35-49, n (%)	4628 (27.2)	1599 (26.8)	3029 (27.5)	>0.05
50-64, n (%)	5269 (31.0)	2098 (35.1)	3171 (28.8)	<0.05
≥65, n (%)	1887 (11.1)	865 (14.5)	1022 (9.3)	<0.05
Comes back from abroad, n (%)	188 (1.1)	53 (0.9)	135 (1.2)	0.043
Comorbidity, n (%)				
Any, n (%)	2762 (16.3)	1140 (19.1)	1622 (14.7)	<0.001
Hypertension, n (%)	1924 (11.3)	817 (13.7)	1107 (10.1)	<0.001
Diabetes, n (%)	829 (4.9)	353 (5.9)	476 (4.3)	<0.001
Coronary heart disease, n (%)	361 (2.1)	143 (2.4)	218 (2.0)	0.075
Congestive heart failure, n (%)	109 (0.6)	41 (0.7)	68 (0.6)	0.594
Stroke, n (%)	138 (0.8)	57 (1.0)	81 (0.7)	0.131
Kidney disease, n (%)	33 (0.2)	15 (0.3)	18 (0.2)	0.216
Cancer, n (%)	41 (0.2)	19 (0.3)	22 (0.2)	0.134
Arrhythmia, n (%)	296 (1.7)	123 (2.1)	173 (1.6)	0.021
Thrombotic diseases, n (%)	174 (1.0)	66 (1.1)	108 (1.0)	0.446
Rhinitis, n (%)	33 (0.2)	20 (0.2)	13 (0.2)	0.612
Thyroid diseases, n (%)	58 (0.3)	16 (0.3)	42 (0.4)	0.225
Chronic lung disease	29 (0.2)	11 (0.2)	18 (0.2)	0.757
Bronchitis, n (%)	27 (0.2)	5 (0.1)	22 (0.2)	0.070
Chronic liver disease, n (%)	60 (0.4)	28 (0.5)	32 (0.3)	0.062
Allergy, n (%)	613 (3.6)	213 (3.6)	400 (3.6)	0.818
Vaccination, n (%)	12,604 (74.2)	4249 (71.1)	8355 (75.9)	<0.001
No. of vaccination				<0.001
Unvaccinated, n (%)	4381 (25.8)	1727 (28.9)	2654 (24.1)	
Received 1 dose of vaccine, n (%)	568 (3.3)	211 (3.5)	357 (3.2)	>0.05
Completed 2 doses of vaccine, n (%)	4885 (28.8)	1555 (26.0)	3330 (30.2)	<0.05
Completed 3 doses of vaccine, n (%)	6951 (40.9)	2431 (40.7)	4520 (41.1)	>0.05
Completed ≥4 doses of vaccine, n (%)	200 (1.2)	52 (0.9)	148 (1.3)	<0.05
Vaccine manufacturer, n (%)				<0.001
Sinovac Biotech Co., Ltd.	8368 (49.3)	2847 (47.6)	5521 (50.1)	<0.05
China National Pharmaceutical Group Co., Ltd.	3841 (22.6)	1267 (21.2)	2574 (23.4)	<0.05
CanSino Biologics Inc	286 (1.7)	91 (1.5)	195 (1.8)	>0.05
Anhui Zhifei Longcom Biopharmaceutical	109 (0.6)	44 (0.7)	65 (0.6)	>0.05

Abbreviations: IQR, interquartile range; Ct, cycle threshold; ORF 1 ab gene, open reading frame 1 ab; N gene, nucleocapsid protein (N) gene.

respectively.

Of the 16,985 patients, 64.8 % and 35.2 % had early (≤8 days) and later viral clearance (>8 days), respectively. A higher proportion of older age (median age, 49 vs. 43 years), male sex (61.6 % vs. 58.6 %), comorbidities (19.1 % vs. 14.7 %), and fewer vaccination doses (71.1 % vs. 75.9 %) were observed in the later viral clearance group than in the early viral clearance group.

3.2. Predictors of prolonged viral clearance

Risk factors associated with patients who remained persistently PCR-positive were sex (Male, odds ratio [OR] 1.221, $p < 0.001$), older age (35–49, OR 1.389, $p < 0.001$; 50–64, OR 1.659, $p < 0.001$; and ≥65, OR 2.139, $p < 0.001$), presence of symptoms (OR 1.093, $p = 0.030$), number of vaccinations (two doses, OR 0.753, $p < 0.001$; three doses, OR 0.797, $p < 0.001$; and four doses, OR 0.543, $p < 0.001$) and Ct value at diagnosis (ORF1ab gene, 25–35, OR 0.235, $p < 0.001$; >35, OR 0.079, $p < 0.001$) (Table 3).

3.3. Risk factors associated with higher viral load

The Ct values for the sequenced N and ORF1ab genes showed an upward trend as the duration since diagnosis increased. Moreover, the later viral shedding group exhibited a slower rate of increase in Ct values for both ORF1ab ($\beta = -0.791$, $p < 0.001$) and N genes ($\beta = -0.825$, $p < 0.001$) compared to the early viral shedding group (Table 4).

4. Discussion

This retrospective study was conducted to identify several risk factors associated with prolonged RT-PCR positivity in patients with the SARS-CoV-2 Omicron variant in Shanghai. We found that the median duration from diagnosis to RNA clearance was 8 days, which

Table 2
Clinical features of the patients with SARS-CoV-2 Omicron variant.

Characteristic	All patients	>8 days	≤8 days	*P* value
Overall, n (%)	16,985 (100)	5976 (35.2)	11,009 (64.8)	
Initial symptoms, n (%)				0.482
Asymptomatic	12,716 (74.9)	4455 (74.5)	8261 (75.0)	
Symptomatic	4269 (25.1)	1521 (25.5)	2748 (25.0)	
Muscle soreness, n (%)	869 (5.1)	408 (6.8)	461 (4.2)	<0.001
Sputum production, n (%)	1798 (10.6)	565 (9.5)	1233 (11.2)	<0.001
Fever, n (%)	1018 (6.0)	465 (7.8)	553 (5.0)	<0.001
Fatigue, n (%)	1113 (6.6)	454 (7.6)	659 (6.0)	<0.001
Cough, n (%)	3548 (20.9)	1165 (19.5)	2383 (21.6)	0.001
Running nose, n (%)	99 (0.6)	22 (0.4)	77 (0.7)	0.007
Nasal congestion, n (%)	78 (0.5)	12 (0.2)	66 (0.6)	0.101
Sore throat, n (%)	268 (1.6)	116 (1.9)	152 (1.4)	0.005
Headaches, n (%)	103 (0.6)	50 (0.8)	53 (0.5)	0.004
Ct value for ORF1ab gene at diagnosis, medium (IQR)	27.12 (22.87–31.57)	23.62 (20.73–27.45)	29.11 (25.06–32.69)	<0.001
Ct value < 25, n (%)	6273 (36.9)	3572 (59.8)	2701 (24.5)	<0.05
25≥ Ct value ≤ 35, n (%)	10,006 (58.9)	2338 (39.1)	7668 (69.7)	<0.05
35 > Ct value ≤ 40, n (%)	701 (4.1)	66 (1.1)	635 (5.8)	<0.05
Ct value > 40, n (%)	2 (0.0)	0 (0)	2 (0.0)	<0.05
Ct value for N gene at diagnosis, medium (IQR)	26.54 (22.22–31.13)	23.11 (20.15–27.06)	28.55 (24.29–32.22)	<0.001
Ct value < 25, n (%)	6928 (40.8)	3787 (63.4)	3141 (28.5)	<0.05
25≥ Ct value ≤ 35, n (%)	9591 (56.5)	2071 (34.7)	7520 (68.3)	<0.05
35 > Ct value ≤ 40, n (%)	114 (0.7)	10 (0.2)	104 (0.9)	<0.05
Ct value > 40, n (%)	352 (2.1)	108 (1.8)	244 (2.2)	<0.05
Viral clearance duration, medium (IQR)	6 (5–8)	9 (8–11)	5 (4–6)	<0.001

Abbreviations: IQR, interquartile range; Ct, cycle threshold; ORF 1 ab gene, open reading frame 1 ab; N gene, nucleocapsid protein (N) gene.

Table 3
Independent predictors of persistently PCR-positive patients identified by multivariate logistic regression models logistic regression.

	Multivariate	
	OR (95 % CI)	*P* value
Sex		
Female	1 (ref)	
Male	1.221 (1.138–1.310)	<0.001
Ages		<0.001
0–19	1 (ref)	
20–34	1.040 (0.885–1.222)	0.633
35–49	1.389 (1.185–1.628)	<0.001
50–64	1.659 (1.416–1.944)	<0.001
≥65	2.139 (1.788–2.558)	<0.001
No comorbidity	1 (ref)	
Any comorbidity	1.058 (0.960–1.165)	0.255
Asymptomatic	1 (ref)	
Symptomatic	1.093 (1.009–1.185)	0.030
The number of vaccination		<0.001
Not vaccinated	1 (ref)	
Received 1 dose of vaccine	0.973 (0.800–1.184)	0.787
Completed 2 doses of vaccine	0.753 (0.686–0.827)	<0.001
Completed ≥3 doses of vaccine	0.797 (0.731–0.869)	<0.001
Completed ≥4 doses of vaccine	0.543 (0.385–0.766)	<0.001
Ct value for ORF1ab gene at diagnosis		<0.001
Ct value < 25	1 (ref)	
25≥ Ct value ≤ 35	0.235 (0.220–0.252)	<0.001
35 > Ct value	0.079 (0.061–0.102)	<0.001

Abbreviations: OR, Odds Ratio; ORF 1 ab gene, open reading frame 1 ab; N gene, nucleocapsid protein (N) gene; CI, confidence interval.

was shorter than previously reported (median, 14 days) [18,19]. We classified patients based on their length of stay; 25.05 % (9498) of patients required more than 8 days to achieve a negative viral RNA test result. Male sex, older age, symptomatic status, presence of comorbidities, and fewer vaccination doses were identified as independent risk factors for prolonged RT-PCR positivity. Consistent with previous studies, we found that prolonged RNA shedding was associated with male sex, older age, presence of symptoms, and comorbidities [7,20,21]. Risk predictors for longer viral shedding remain controversial [8,22]. Gonzalez et al. [8] did not find differences in nucleic acid conversion time between younger and older age groups. Another study showed that the presence or absence of

Table 4
Generalized estimating equation analysis of the association of Ct values with a prolonged viral shedding.

	ORF1ab gene			N gene		
	β (SE)	95 % CI	*P* value	B (SE)	95 % CI	*P* value
Groups						
≤8 days	1 (ref)			1 (ref)		
>8 days	−7.522 (0.0552)	−7.630–7.414	<0.001	−7.709 (0.0584)	−7.824–7.595	<0.001
Time	1.997 (0.0138)	1.970–2.024	<0.001	1.992 (0.0145)	1.963–2.020	<0.001
Group × time	−0.791 (0.0190)	−0.828–0.753	<0.001	−0.825 (0.0203)	−0.865–0.785	<0.001

Adjusted for sex, ages, comorbidities, symptoms, the doses of vaccination. Abbreviations: OR, Odds Ratio; ORF 1 ab gene, open reading frame 1 ab; N gene, nucleocapsid protein (N) gene; CI, confidence interval.

clinical symptoms was not a risk predictor for persistent viral detection [23]. Older patients may have more disease symptoms and comorbidities at admission owing to an unhealthy lifestyle and impaired immune function [7,24].

This study also found that male patients usually had a longer duration of viral RNA shedding than female patients with COVID-19. Our results are consistent with recent research, including 113 symptomatic patients from two hospitals outside Wuhan, which showed that the median duration of SARS-CoV-2 RNA clearance was 15 days vs. 18.5 days in the female and male groups, respectively [7]. Another epidemiological report included 44,672 confirmed cases in China, and the results showed a case fatality rate of 2.8 % in males and 1.7 % in female [25]. Differences in immune system responses and the steroid hormone milieu may be major contributing factors to viral RNA shedding and disease severity [26,27]. Because many immune genes exist on the X chromosome, the XX and XY genetic constituents could also trigger stronger immune responses to pathogens. Estrogen in females can strengthen the immune reaction, whereas testosterone secreted by the testes can weaken the immune reaction [28].

This study indicated that unvaccinated patients had a longer viral shedding time than vaccinated patients, which is consistent with previous studies [29,30]. An observational study included a total of 361 participants with confirmed SARS-CoV-2 Omicron BA.2.2 and revealed that unvaccinated patients exhibited a longer viral shedding time than vaccinated patients in our study [38 (43.18 %) vs. 18 (19.57 %)]. Furthermore, Public Health England reported that COVID-19 vaccination with BNT162b2 or AZD1222 could be effective against death and hospitalization [31]. Notably, our study observed that at least two doses resulted in a shorter viral shedding time than in once-vaccinated or unvaccinated patients. The Omicron variant has a large number of mutations (>50 mutations) and has a high capacity for immune escape; hence, infected cells cannot be recognized and destroyed, resulting in major vaccines being less effective against Omicron [32]. This observation demonstrates the efficacy of the booster-dose vaccine against Omicron SARS-CoV-2 variants. Similarly, an ongoing, multicenter, prospective cohort, including 35,768 participants in the United Kingdom, investigated vaccine effectiveness and showed that two doses of the BNT162b2 vaccine were related to high short-term protection against SARS-CoV-2 infection [33]. This protection waned significantly after 6 months. However, Wu et al. [10] found that a three-dose booster vaccination did not attenuate the target Ct value compared with a two-dose primary vaccination. Munro et al. [34] conducted a multicenter, blinded, phase 2, randomized controlled trial to investigate the effectiveness of four-dose boosters against COVID-19. The peak responses in humoral and cellular immunity following the administration of the fourth dose of the COVID-19 mRNA vaccine were comparable to, and potentially even superior to, those observed after the third dose.

Higher Ct values are associated with lower viral loads. Bullard et al. [35] found that the infectivity of SARS-CoV-2 was only observed for RT-PCR Ct values of <24 in vitro. Previous data from outpatient settings demonstrated that Ct values were similar between symptomatic and asymptomatic COVID-19 patients [36]. We observed that increased Ct values of the ORF1ab and N genes were associated with viral shedding, and prolonged positive patients had lower Ct values and slower rates of increase than patients with early viral shedding. Several other studies also reported no significant difference in viral load depending on the presence of accompanying symptoms [37]. Patients who were vaccinated showed significantly higher Ct values for the ORF1ab increase rate than those who were unvaccinated with viral clearance. This difference was also observed in the Ct values of the N genes.

This study had few limitations. First, our study was limited to a single institute, and the participants were of Chinese ethnicity. Although the sample size of 16,985 is relatively large, our findings cannot be generalized until a larger survey involving multiple institutes reaches the same conclusion as our study did. Second, because this was a retrospective single-center study, there may have been a selection bias. Third, the duration of viral clearance was not correlated with the transmissibility of the disease.

Herein, prolonged SARS-CoV-2 RNA detection within the Shanghai Makeshift Hospital from April 5 to May 30, 2022, was associated with male sex, older age, presence of symptoms, fewer doses of vaccine, and Ct value at diagnosis.

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Author contributions

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Data availability statement

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e23256.

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