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Difference of clinical characteristics in patients with reinfection and primary infection variants of SARS-CoV-2: a retrospective study in China

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Abstract

Background The number of patients experiencing re-infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is progressively increasing. In this study, we aimed to explore the differences in clinical characteristics between patients with primary infection and those with re-infection of SARS-CoV-2.

Methods A retrospective data analysis was conducted involving patients diagnosed with coronavirus disease 2019 between April 1, 2023, and June 20, 2023. The patients were categorized into two groups: the observation group, consisting of individuals re-infected with SARS-CoV-2, and the control group, comprising those with primary SARS-CoV-2 infection.

Results A total of 905 (905/1025) patients were included in the study, with 407 in the observation group and 498 in the control group. The top three clinical symptoms in both groups were fever, cough with expectoration, and dizziness with fatigue ($p < 0.001$). The clinical classification of patients in the observation group primarily consisted of non-severe cases ($p < 0.001$). The proportion of hospitalized patients was lower in the observation group than in the control group ($p < 0.001$). The observation group exhibited a shorter clinical symptom recovery time than that did the control group (median, 5 days vs. 7 days, Log rank $p<0.001$, HR = 1.907(95% CI 1.669–2.178).

Conclusions Patients experiencing SARS-CoV-2 re-infection were primarily classified as non-severe cases, with lower proportions of occurrence of severe and rare critical conditions. The severity was milder compared to that in patients with primary SARS-CoV-2 infection.

Keywords SARS-CoV-2, Reinfection, Clinical characteristics, Omicron variant

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Background

Coronavirus disease 2019 (COVID-19), caused by a newly discovered coronavirus in recent years, has emerged as one of the three most severe coronavirus outbreaks, alongside the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and Middle East respiratory syndrome coronavirus in 2012. Since its emergence in late 2019, COVID-19 has rapidly spread worldwide, with the cumulative number of infections exceeding hundreds of millions. With the continuous mutation of coronaviruses [1], the Omicron variant has gained rapid prominence globally since November 2021 [2] and is now the dominant strain in the ongoing pandemic [3]. Previous studies have demonstrated that vaccination can effectively prevent infection with the novel coronavirus; however, vaccine efficacy (VE) can be compromised by the rapid emergence and spread of SARS-CoV-2 variants of concern (VOCs) that could evade neutralizing antibodies and/or cell-mediated immunity [4]. The Omicron variant, notably, exhibits high transmissibility but significantly reduced pathogenicity compared to that of the original strain [5, 6]. Additionally, owing to the mutability of Omicron's antigenic sites, it has a remarkably high capacity for immune evasion, posing a higher risk of reinfection to the population [7]. The study found that the COVID-19 vaccine effectively protects against severe pneumonia caused by the Delta and Omicron variants, but is less effective in preventing Omicron variants from causing SARS-CoV-2 infection [8]. An analysis by the UK Office for National Statistics on COVID-19 cases from July 2020 to November 2022 revealed the highest repeat infection rate at 16.6% [9]. Since December 2022, various regions in China have gradually lifted the isolation treatment policy for individuals infected with SARS-CoV-2.

However, the ongoing spread of SARS-CoV-2 infections has had a severe impact on public health. Understanding the clinical characteristics of SARS-CoV-2 re-infection becomes crucial for adopting effective prevention and treatment strategies.

Hence, in this study, we aimed to elucidate the clinical characteristics of individuals with SARS-CoV-2 re-infection by comparing them with that of those who experienced primary SARS-CoV-2 infection within the same time period.

Methods

Study patients

A retrospective data collection was undertaken, focusing on patients diagnosed with SARS-CoV-re-infection in Wenzhou between April 1, 2023, and June 20, 2023. According to inclusion and exclusion criteria, patients were categorized into two groups based on whether they had experienced SARS-CoV-re-infection. The observation group included patients who had experienced re-infection, whereas the control group consisted of individuals who had experienced primary SARS-CoV-infection. The sample size was determined by using the G*Power software (v3.1.9.7, Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). We used 2-sided testing, effect size = 0.8, α err prob = 0.05, power (1-β err prob) = 0.95,allcocation ratio N2/N1 = 1. The minimum sample size was computed to be 84. The minimum sample size was computed to be 4for each group. Informed consent was obtained from all enrolled patients, who were informed and who voluntarily agreed to participate in the study. This study was approved by the Ethics Committee of Wenzhou Central Hospital of Zhejiang Province (approval number: L2023-03-022) in China (Supplementary Material).

Data collection

Demographic characteristics were collected for the two groups of patients, including age, sex, medical history of underlying diseases, and vaccination history. Additionally, data on clinical classification; clinical symptoms (fever, myalgia, cough expectoration, dizziness, fatigue, loss or reduction of smell and taste, gastrointestinal symptoms [vomiting and diarrhea], chest tightness, shortness of breath, dry throat, sore throat, and sore eyes); laboratory tests (complete blood count and C-reactive protein [CRP] level); and recovery time were collected. This information came from the hospital's electronic medical records.

Selection criteria

Inclusion criteria

(1) Patients diagnosed with SARS-CoV-2 infection within the past week, (2) aged ≥ 18 years, and (3) weight ≥ 40 kg.

Exclusion criteria

(1) Patients with concurrent influenza or other viral infections; (2) those with other serious organic diseases and an expected survival of less than one month; (3) those with acute exacerbation of pulmonary diseases, such as asthma, bronchiectasis, and chronic obstructive pulmonary disease; (4) those who received antiviral medication within the last week prior to enrollment; (5) those suspected or confirmed to have an active systemic infection besides COVID-19; (6) those with known human immunodeficiency virus infection; (7) pregnant or lactating women.

Diagnostic criteria

The diagnosis of SARS-CoV-2 infection was established when patients met both of the following criteria [10]: exhibiting relevant clinical manifestations of

SARS-CoV-2 infection and testing positive on either a COVID-19 nucleic acid test or a COVID-19 antigen test.

Clinical typing

Clinical typing was determined based on the World Health Organization (WHO) severity classification for COVID-19 as follows [11]: (1) Non-severe COVID-19: defined as the absence of any criteria for severe or critical COVID-19. (2) Severe COVID-19: defined by any of the following criteria: oxygen saturation < 90% on room air; signs of pneumonia; signs of severe respiratory distress (in adults, use of the accessory muscle, inability to complete full sentences, respiratory rate > 30 breaths per minute; in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs, including inability to breastfeed or drink, lethargy, convulsions, or reduced level of consciousness). (3) Critical COVID-19: defined by the presence of acute respiratory distress syndrome, sepsis, septic shock, or other conditions requiring life-sustaining therapies, such as mechanical ventilation (invasive or non-invasive) or vasopressor therapy.

Hospitalization criteria

The hospitalization criteria were established based on the clinical management guidelines for COVID-19 provided by the WHO [11] and additional local policies, detailed as follows. Patients meeting any of the following criteria and consenting to hospitalization were eligible:

1. Severe and critical cases.
2. Non-severe cases displaying significant clinical symptoms, especially chest tightness or respiratory distress, necessitating oxygen therapy support.
3. Worsening of pre-existing underlying diseases that could not be managed.

Treatment plan

The treatment plan was based on the dynamic guidelines for pharmacotherapy of COVID-19 published by the WHO, titled "A living WHO guideline on drugs for COVID-19" [12]. The general principles are as follows: for non-severe patients, symptomatic supportive treatment should be provided. Paxlovid is strongly recommended for individuals with high-risk factors who may require hospitalization, whereas molnupiravir, remdesivir, sotrovimab, and casirivimab/imdevimab are weakly recommended. For severe and critical patients, corticosteroids, interleukin (IL)-6 inhibitors, and the Janus kinase inhibitor baricitinib are strongly recommended.

Statistical methods

Data were processed using R.4,3,1 software. The G*Power 3.1.9.7 software was used to estimate the minimum sample size. Normality tests and homogeneity of variance tests were performed for measurement data. Normally distributed data were expressed as mean ± standard deviation ($x \pm s$), whereas non-normally distributed data were presented as median and interquartile range (M[P25, P75]). Comparisons of clinical improvement time were made using Kaplan-Meier method. Count data were described using frequency and percentage. For measurement data that met the normality and homogeneity of variance assumptions, the independent samples t-test was used for between-group comparisons. When these assumptions were not met, a non-parametric statistical test, the Mann–Whitney U test, was used. The between-group comparison of count data was conducted using the chi-squared test. A p-value < 0.05 indicates a statistically significant difference.

Results

General conditions of enrolled patients

In the present study, we initially collected data from a total of 1,025 patients who were diagnosed with SARS-CoV-2 infection in Wenzhou Central Hospital between April 1, 2023, and June 20, 2023. According to the inclusion and exclusion criteria, 120 patients who did not meet the criteria were excluded. Consequently, 905 patients were included in the study, with 407 in the observation group and 498 in the control group. No significant differences in the basic data were observed between the two groups ($p > 0.05$), as presented in Table 1. The comorbidity history of the patients included hypertension (29.1%), diabetes (12.0%), hepatitis B (5.3%), tumor (3.5%), tuberculosis (4.6%), coronary heart disease (13.9%), rheumatic disease (2.4%), and others (4.0%). Vaccination history encompassed any dose of COVID-19 vaccine (including adenovirus vector, inactivated, or recombinant protein vaccines) they had received. According to the Epidemic Control Center data, the prevalent regional epidemic strains of COVID-19 were the Omicron variants, including the XBB series (the most widespread), with its top three subvariants being XBB.1.9, XBB.1.16, and XBB.1.22, and their respective sub-branches. In this study, the intervals between primary SARS-CoV-2 infections and subsequent re-infections varied across the observation group. Specifically, there were 6, 54, 304, 40, 1, 1, and 1 cases of re-infection at intervals of 3, 4, 5, 6, 11, 12, and 14 months, respectively. The average interval length was 5.06 ± 0.877 months, with a median interval of 5 months.

Comparison of clinical symptoms between the two groups

The differences in clinical symptoms between the two patient groups are presented in Table 2. In the observation group, the top three clinical symptoms of SARS-CoV-2 infection were fever (318, 78.1%), cough with

Table 1 Comparison of the demographic characteristics between the two groups of patients ($n = 1,025$)

Feature	Observation group (x ± s)	Control group (x ± s)	t/χ^2	*p* value
Age ¯(years)	54.5 ± 19.6	53.7 ± 18.2	0.630	0.529
Sex			0.008	0.947
Male [number (%)]	199 (48.9%)	242 (48.6%)		
Female [number (%)]	208 (51.1%)	256 (51.4%)		
Medical history of underlying diseases [number (%)]	157 (38.6%)	211 (42.4%)	1.336	0.276
History of one disease	90 (22.1%)	134 (26.7%)		
History of two diseases	45 (11.1%)	52 (10.5%)		
History of three or more diseases	22 (5.4%)	26 (5.2%)		
History of vaccination [number (%)]	340 (83.5%)	432 (86.7%)	1.840	0.187
Adenovirus vector vaccine	280 (68.8%)	351 (70.5%)		
Inactivated vaccine	54 (13.3%)	72 (14.5%)		
Recombinant protein vaccine	6 (1.5%)	9 (1.8%)		

Note: All *p* values > 0.05

expectoration (300, 73.4%), and dizziness with fatigue (188, 46.2%). Similarly, in the control group, the top three clinical symptoms were fever (446, 89.6%), cough with expectoration (338, 67.9%), and dizziness with fatigue (197, 39.6%). The differences in the occurrence rates of clinical symptoms between the two groups were statistically significant ($\chi^2 = 113.537$, $p < 0.001$). In this study, among the patients with fever in the observation ($n = 318$) and control ($n = 446$) groups, the median peak temperatures during the course of illness were 38.3 °C (37.4–40.0 °C) and 39 °C (37.4–40.5 °C), respectively. The difference in peak temperatures between the two groups was statistically significant (t = 14.210, $p < 0.001$).

Comparison of the CT values of COVID-19 nucleic acid between the two groups

Among the 905 enrolled patients, 320 and 585 were diagnosed with positive COVID-19 antigen and positive COVID-19 nucleic acid, respectively. In the observation and control groups, 244 and 341 patients had positive COVID-19 nucleic acid, respectively. The mean CT values of the COVID-19 nucleic acid *N* gene were 28.76 ± 4.93 and 27.49 ± 5.61 in the observation and control groups, respectively. The difference in values for the COVID-19 nucleic acid *N* gene between the two groups was statistically significant (t = 2.542, $p = 0.011$). For the COVID-19 nucleic acid *ORF* gene, the observation and control groups exhibited mean values of 29.46 ± 4.82 and 28.76 ± 4.93, respectively. The difference in values for the COVID-19 nucleic acid *ORF* gene between the two groups was statistically significant (t = 2.480, $p = 0.013$), as shown in Table 2.

Table 2 Comparison of the clinical characteristics between the two groups of patients

Clinical characteristics	Observation group	Control group	t/χ^2	*p* value
Clinical symptoms			113.537	<0.001
Fever [number (%)]	318 (78.1%)	446 (89.6%)	22.229	<0.001
Myalgia [number (%)]	107 (26.3%)	161 (32.3%)	3.919	0.049
Cough with expectoration [number (%)]	300 (73.4%)	338 (67.9%)	3.671	0.055
Dizziness with fatigue [number (%)]	188 (46.2%)	197 (39.6%)	4.032	0.050
Loss or reduced sense of smell and taste [number (%)]]	22 (5.4%)	43 (8.9%)	3.503	0.061
Gastrointestinal symptoms (vomiting, diarrhea) [number (%)]	52(12.8%)	59 (11.8%)	0.180	0.685
Chest tightness and shortness of breath [number (%)]	44 (10.8%)	144 (28.9%)	44.605	<0.001
Dry throat and sore throat [number (%)]	155 (38.1%)	180 (36.1%)	0.361	0.580
Sore eyes [number (%)]	22 (5.4%)	23 (4.6%)	0.294	0.646
Median peak temperature (℃)	38.3 (37.4–40.0)	39.0 (37.4–40.5)	14.210	<0.001
COVID-19 nucleic acid cycle threshold (CT) value				
N gene	28.46 ± 4.69	27.36 ± 5.49	2.542	0.011
ORF1a/b gene	29.19 ± 4.62	28.10 ± 5.62	2.480	0.013
Laboratory tests				
Leukocyte count [$\times 10^9$/L]	5.94 ± 2.19	6.01 ± 2.37	0.321	0.748
C-reactive protein [mg/L]	10.90 ± 11.45	12.21 ± 12.76	1.016	0.310
Clinical classification			115.843	<0.001
Non-severe [number (%)]	344 (84.5%)	307 (61.7%)		
Severe [number (%)]	63 (15.5%)	185 (37.1%)		
Critical [number (%)]	0 (0%)	6 (1.2%)		
Hospitalization [number (%)]	58 (14.3%)	158 (31.7%)	37.644	<0.001

Comparison of laboratory examination indicators between the two patient groups

Among the 905 enrolled patients, 421 (observation group, $n = 136$; control group, $n = 285$) underwent routine blood and/or CRP examinations. The mean leukocyte counts in the observation and control groups were 5.94 ± 2.19 ($\times 10^9$/L) and 6.01 ± 2.37 ($\times 10^9$/L), respectively,

demonstrating no significant difference between the two groups (t = 0.321, $p = 0.748$). Regarding CRP, the observation and control groups exhibited mean values of 10.90 ± 11.45 (mg/L) and 12.21 ± 12.76 (mg/L), respectively, with no significant difference (t = 1.016, $p = 0.310$), as shown in Table 2.

Comparison of severity between the two patient groups

Using the WHO severity classification of COVID-19, the patients were categorized into different groups. In the observation group, out of 407 patients, 344, 63, and 0 were categorized as non-severe, severe, and critical cases, respectively. In contrast, out of 498 patients in the control group, 307, 185, and 6 were categorized as non-severe, severe, and critical cases, respectively. The differences were statistically significant between the two groups ($\chi^2 = 115.843$, $p < 0.001$), as depicted in Fig. 1. Regarding hospitalization, 58 (14.3%) and 158 (31.7%) patients required hospitalization in the observation and control groups, respectively, with statistically significant differences between the two groups ($\chi^2 = 37.644$, $p < 0.001$), as presented in Table 2.

Duration till clinical symptom improvement in the two groups

The treatment plan was guided by the dynamic WHO guidelines for COVID-19 pharmacotherapy, titled "A living WHO guideline on drugs for COVID-19." Patients in both groups received appropriate treatment. The distribution of the duration until clinical symptom improvement for the two groups is illustrated in Fig. 2a and b, respectively. The mortality rate in both groups was at 0. Median time for clinical symptom improvement was 5.00 (4.00,5.00) and 7.0 (7.00,8.00) days for patients in the observation group and the control group, respectively, Log rank $p<0.001$, HR = 1.907(95% CI 1.669–2.178) (Fig. 3).

Discussion

Over time, SARS-CoV-2 has continued to evolve, producing new VOCs. These VOCs, including alpha, beta, gamma, delta, and Omicron, have demonstrated the virus' ability to adapt to its host and evade immune responses, thus reducing the neutralizing efficacy of antibodies [13, 14] and increasing the risk of SARS-CoV-2 re-infection. In late December 2022, China experienced a widespread outbreak of COVID-19, with many individuals contracting the virus. These individuals now face the risk of SARS-CoV-2 re-infection. The present

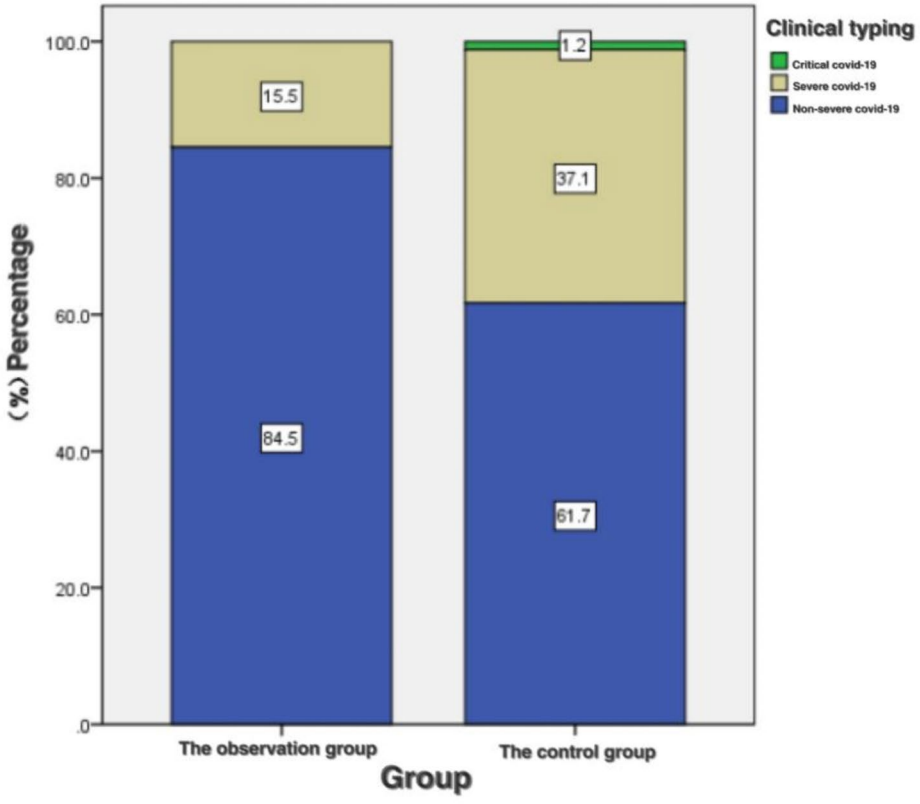

Fig. 1 Proportional distribution of clinical classification in the two groups of patients

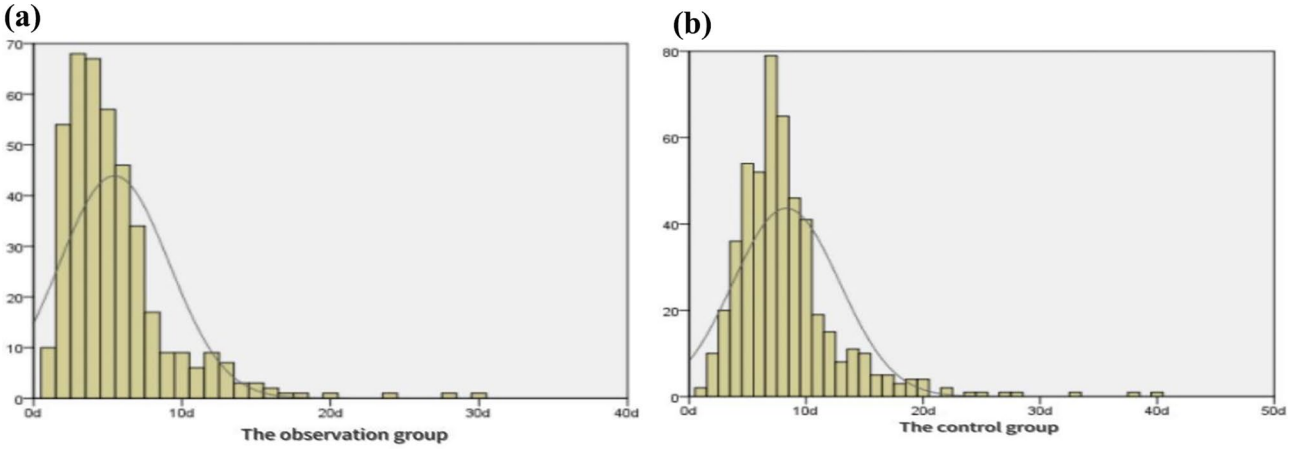

Fig. 2 Distribution of duration (in days) till clinical symptom improvement. (**a**) Distribution of duration (in days) till clinical symptom improvement in the observation group. (**b**) Distribution of duration (in days) till clinical symptom improvement in the control group

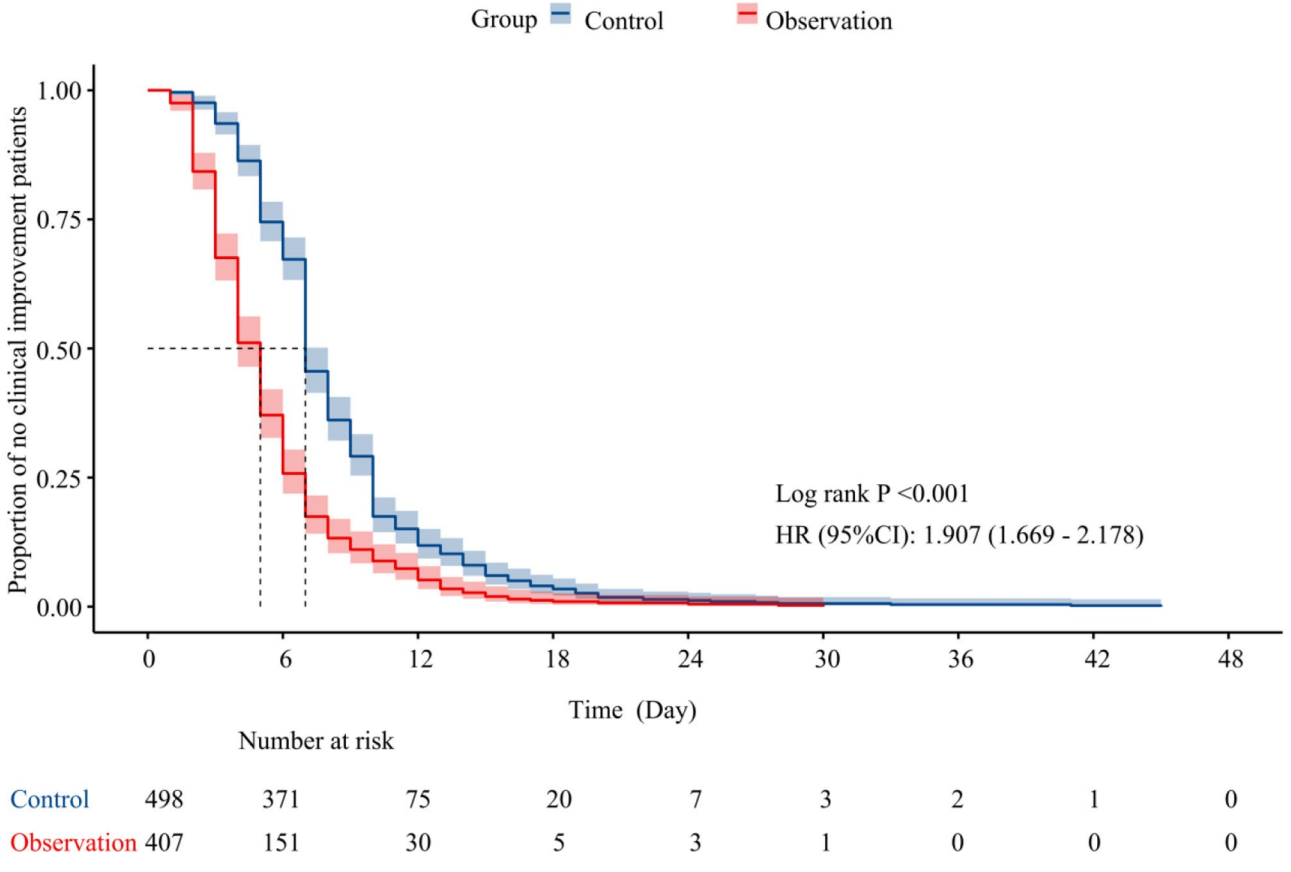

Fig. 3 Kaplan-Meier curve of time for clinical improvement in the observation group and the control group

study aimed to investigate the clinical characteristics of patients with SARS-CoV-2 re-infection by comparing them to those with primary infections during the same period.

In this study, the time interval between SARS-CoV-2 re-infection and the primary infection exceeded 3 months, with the number of re-infections increasing over time. The average interval reached 5.06 ± 0.877 months, with a median of 5 months. This interval is shorter than those reported in other studies (> 200 days) [15, 16], possibly due to differences in study timing. Additionally, variations in circulating strains could have influenced these results. A significant rise in infections was noted in the fourth and fifth months following the primary infection, with a subsequent decline after the 6-month mark. Liew et al. [17] found that nasal antibodies against the

Omicron variant lasted only 3–5 months, potentially contributing to the frequent re-infections with this variant. Limited data were available on infections beyond 6 months, likely because of the short period since the gradual easing of COVID-19 control measures in China, with most included patients experiencing re-infection within 6 months of their primary infection. Consequently, further investigation is necessary to elucidate the dynamics of SARS-CoV-2 re-infection beyond a 6-month interval. Moreover, following the WHO's definition of SARS-CoV-2 re-infection [18], all re-infections in this study occurred more than 3 months after the primary infection, confirming these cases as re-infections rather than COVID-19 viral reactivations.

In this study, the observation group showed proportions of 84.5%, 15.5%, and 0% non-severe, severe, and critical cases in clinical classification, respectively. These proportions were significantly different from those in the control group, which exhibited 61.7% non-severe, 37.1% severe, and 1.2% critical cases. These findings suggest that SARS-CoV-2 re-infection predominantly results in non-severe cases, with a reduced incidence of severe and a rare occurrence of critical cases. Furthermore, a comparison of hospitalization rates between the two groups revealed a notably lower proportion of patients requiring hospitalization due to SARS-CoV-2 re-infection compared to that of those with primary infections. This indicates that the severity of re-infection is generally milder than that of primary infections. However, it is important to acknowledge that this study only included patients who voluntarily sought medical care at the hospital, and many patients with milder symptoms might not have sought hospital care, potentially leading to an underestimation of non-severe cases and an overestimation of severe and critical cases.

When comparing clinical symptoms between two groups, the three most common symptoms were fever, cough with expectoration, and dizziness with fatigue. However, the incidence rates differed between the groups; notably, the observation group exhibited a significantly lower frequency of fever than did the control group. In the SARS-CoV-2 reinfection group, the predominant clinical symptoms remained fever, cough with expectoration, dizziness with fatigue, dry throat, sore throat, and myalgia. Yet, the frequency of fever was reduced in the reinfection group compared to that in the primary infection group. This finding contrasts with previous studies reporting that approximately 85% of patients with SARS-CoV-2 reinfection are asymptomatic [19, 20]. The median highest body temperature for the SARS-CoV-2 re-infection groups was 38.3 °C, which was lower than that observed for the primary SARS-CoV-2 infection group (39.0 °C). This suggests that fever symptoms are less severe in SARS-CoV-2 re-infection patients than in those with primary SARS-CoV-2 infection. The median duration for complete or substantial symptom improvement was 5 and 7 days for patients with re-infection and primary infections, respectively. Consequently, we inferred that patients experiencing SARS-CoV-2 re-infection recover from clinical symptoms at a faster rate than do those with primary infections.

These findings align with those of West [21], who reported milder symptoms and faster recovery in cases of SARS-CoV-2 re-infection. In addition, the COVID-19 Forecasting Team [22] analyzed data from 65 studies across 19 different countries and reported that following a previous infection with the Omicron variant, the antibody levels rapidly decline over time, leading to a rapid decrease in protection against SARS-CoV-2 re-infection. However, protection against severe cases continues for a relatively longer duration. This view aligns with the low proportion of severe and rare critical cases observed in the observation group of the present study. Internationally, scholars hold differing opinions regarding the CT value of COVID-19. Muhammad A [23] argued that the CT value of COVID-19 nucleic acid cannot accurately reflect the viral load in patients. Conversely, John JE, Rabaan AA, and other researchers [24, 25] contend that the CT value of COVID-19 nucleic acid is a reliable indicator for assessing the severity and prognosis of SARS-CoV-2 infection. In this study, the disease in the observation group was less severe than in the control group. A comparison of the CT values of COVID-19 nucleic acid between the two groups showed that the values for the *N* gene and *ORF* gene in the observation group were higher than that of those in the control group, corroborating the perspectives of scholars like John JE and Rabaan AA.

This study had certain limitations. Firstly, this is a retrospective study with limitations in data quality and completeness. This study is limited in terms of patient prognosis. For example, there is a lack of data on the length of stay and need for ICU admission. Future studies will follow up on patient prognosis.The second limitation is that the varied timing of patient visits and COVID-19 nucleic acid sampling could have influenced the accuracy of COVID-19 nucleic acid CT values at specific points after SARS-CoV-2 infection. The third limitation concerns the patient sample, which consisted solely of individuals who voluntarily sought hospital care. Consequently, many patients with relatively mild symptoms who did not seek hospital treatment were excluded, potentially skewing the actual proportion of clinical classifications between the two patient groups studied. The fourth limitation arises from the fact that most study participants were infected or re-infected with SARS-CoV-2 after receiving the COVID-19 vaccine. Although the background section mentions that the COVID-19

vaccine has a diminished preventive effect against Omicron variant strains, this study could not definitively ascertain the vaccine's impact on these strains, as vaccination timing was not considered. Finally, the relationship between Ct values and viral load is still somewhat controversial in global studies, and as this study was single-centre, the conclusions require a larger sample size for further evidence.

Conclusions

Patients experiencing SARS-CoV-2 re-infection are primarily classified as having non-severe conditions, with a low proportion of occurrence of severe and rare critical conditions. Their severity is milder than that of patients experiencing primary SARS-CoV-2 infection. Additionally, the duration till clinical symptom recovery is shorter in patients experiencing re-infection. Furthermore, a lower proportion of these patients require hospitalization.

Abbreviations

COVID-19	Coronavirus disease 2019
CRP	C-reactive protein
CT	Cycle threshold
IL	Interleukin
ORF	Open reading frame
SARS-CoV	Severe acute respiratory syndrome coronavirus
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
VE	Vaccine efficacy
VOCs	Variants of concern
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-10509-1.

Supplementary Material 1

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Author contributions

C.C.Q. and X.G.J. were involved in the conception and design. Q.Z., Y.L.C, X.Q.S., M.Y.Z., L.F.Z, F.C., S.R.X., and L.F.Z. collected the data. X.Q.L. was involved in the analysis and interpretation of the data. Z.R.L., F.C., and S.R.X searched, sorted, and interpreted the relevant literature. C.C.Q., X.Q.L.and J.C.S. were involved in the drafting of the paper, revising it critically for intellectual content. All authors edited and approved the final manuscript and agree to be accountable for all aspects of the work.

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None.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Informed consent was obtained from all enrolled patients, who were duly informed and who voluntarily agreed to participate in the study. This study was approved by the Ethics Committee of Wenzhou Central Hospital of Zhejiang Province (approval number: L2023-03-022) in China.

Consent for publication

Not applicable in this section.

Competing interests

The authors declare no competing interests.

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