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RESEARCH ARTICLE

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Inactivated vaccines prevent severe COVID-19 in patients infected with the Delta variant: A comparative study of the Delta and Alpha variants from China

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Abstract

The Delta variant has gradually replaced the Alpha variant as the major strain of SARS-COV-2 infection worldwide. We extracted the clinical characteristics and outcomes information about 381 hospitalized patients infected with Delta variant and compared them with 856 patients diagnosed with Alpha variant infection in Zhejiang Province. The majority (85.3%) of patients infected with the Delta variant had received inactivated vaccine. The patients' condition was generally mild. Most of them were mild (35.7%) and common (62.7%) types. Only six patients (1.5%) were severe/critical types. During the follow-up period, patients infected with the Delta variant had longer hospital stays than the Alpha variant (24 [21–26] vs. 18 [14–24], $p < 0.001$). In addition, the unvaccinated patients infected with the Delta variant had a higher proportion of severe/critical cases than vaccinated patients (11.11% vs. 0.92%, $p = 0.024$) and a higher usage rate of glucocorticoids (38.89 vs. 14.77%, $p = 0.017$) and antibiotics (55.56% vs. 32.31%, $p = 0.042$) during hospitalization. The vaccine's efficacy against severe COVID-19 did not diminish over time for patients who received two doses of the inactivated vaccine. The disease types and clinical manifestations were generally mild in patients infected with the Delta variant, possibly associated with widespread vaccination with inactivated vaccines in China.

KEYWORDS
Alpha variant, clinical characteristics, Delta variant, SARS-COV-2, vaccine

1 | INTRODUCTION

From its discovery in December 2019 to the present,[1] COVID-19 has affected the world's economy and people's lives worldwide. The mutated strains produced by genetic mutations during the epidemic make the control of COVID-19 even more tricky. In addition to physical measures such as contact isolation and wearing masks, it is recognized at home and abroad that the COVID-19 vaccine is one of the main measures to control the epidemic.[2] Countries worldwide are developing various COVID-19 vaccines, including nucleic acid vaccines, live attenuated vaccines, inactivated virus vaccines, viral vector vaccines, subunit vaccines, and recombinant protein vaccines.[3] In China, five COVID-19 vaccines have been launched, Including the adenovirus vector vaccine that only needs one injection, the inactivated vaccine that requires two injections, and the recombinant protein vaccine that requires three injections, among them the inactivated vaccine CoronaVac (Sinovac Life Sciences) and BBIBP-CorV (Beijing Institute of Biological Products) are currently the most frequently vaccinated vaccine types in China.

Many studies[4–7] have demonstrated the efficacy of inactivated vaccines, and these randomized, double-blind, placebo-controlled clinical trials showed that the inactivated vaccine elicits a strong humoral immune response to SARS-COV-2 infection in healthy people of all ages after two doses and is well tolerated and safe. In this outbreak of the Delta variant in Zhejiang Province, most of the patients have been vaccinated against COVID-19 following the requirements of the Chinese government. To further understand the clinical and epidemiological characteristics of COVID-19 caused by the Delta variants and the effectiveness of inactivated vaccines against the Delta variants, we collected 381 confirmed cases during the current outbreak and compared the clinical characteristics of patients infected with the Alpha variant that broke out in Zhejiang in early 2020, aiming to provide a reference basis for the prevention and control of COVID-19.

2 | METHODS

2.1 | Data sources

This cohort study was conducted among patients diagnosed with COVID-19 according to the Diagnosis and Treatment of COVID-19 of China (seventh edition).[8] The Delta cohort was derived from patients diagnosed with COVID-19 between December 11, 2021, and December 26, 2021, in Zhejiang Province, who were identified as infected with the Delta variant by whole-genome sequencing, and the Alpha cohort was derived from patients diagnosed with COVID-19 in Zhejiang Province between January 17, 2020, and February 7, 2020, who were identified as infected with the Alpha variant by whole-genome sequencing, The Affiliated Hospital of Shaoxing University is the designated treatment hospital for this round of epidemic. All patients infected with the Delta variant were sent to this hospital for hospitalization. The Clinical Research Ethics Committee approved this study of the First Affiliated Hospital of Zhejiang University School of Medicine (No. IIT20220105A). The ethics committee of the designated hospital waived written informed consent and obtained oral consent from the patients, following the ethical guidelines of the Declaration of Helsinki.

2.2 | Procedures

The basic information, epidemiology, laboratory examinations, clinical manifestations, treatments, and prognosis of all patients were extracted from the electronic case database of the Affiliated Hospital of Shaoxing University. The data were entered into a computerized standardized data collection form by several infectious disease physicians specializing in diagnosing and treating COVID-19 and verified by two other experienced clinicians. The follow-up time for outcomes of both groups was 31 days. The Delta cohort was followed until January 10, 2022, and the Alpha cohort was followed until February 16, 2020.

3 | RELATED DEFINITIONS

All confirmed patients met the diagnostic criteria in the Diagnosis and Treatment of COVID-19 of China (Seventh Edition),[8] according to which COVID-19 patients were classified into mild, common, severe, and critical types.

Discharge criteria: (1) temperature returned to normal for more than 3 days; (2) respiratory symptoms improved significantly; (3) the lung imaging absorbed; (4) two consecutive negative nucleic acid tests of respiratory specimens (at least 24 h apart). Those who meet the above conditions can be discharged from the hospital.

Vaccination: based on the information on the home page of the patients' electronic medical records, we extracted the information on the type of vaccine, dose, and time of vaccination. Most of the patients were vaccinated with the inactivated vaccine CoronaVac/BBIBP-CorV. The second dose needs to be completed within 3–8 weeks, and the booster dose can be administered 6 months after the second injection.

3.1 | Statistical analysis

Statistical analysis was performed by SPSS software version 25.0. Continuous measurement data with normal distribution were expressed as mean ± standard deviation, and a *t* test was applied for comparison between groups. Measurement data with non-normal distribution were expressed as median and quartile (Q1–Q3), and the Mann–Whitney *U* test was used for comparison. Categorical variables were expressed as percentages (%) and compared using χ^2 tests, taking the results of Pearson χ^2, continuity correction, or Fisher's exact test as appropriate. Statistical significance was defined as a p value less than 0.05.

The figures were drawn using GraphPad Prism 8.0 software.

4 | RESULTS

4.1 | Comparison of demographic and clinical features

This round of epidemic spread fast. The number of infected people reached nearly 400 in just over 10 days, as shown in Supporting Information: Figure 1. We collected 381 COVID-19 patients as of December 26, 2021, and each patient was identified as infected with the Delta variant by whole-genome sequencing. Among them, 173 (45.4%) were male, and 208 (54.6%) were female, with a median age of 52 (38–61) years, which was older compared to patients infected with the Alpha variant ($p < 0.001$). In the Delta group, 26.8% were ≥60 years, and 7.9% were <18 years, which accounted for a higher proportion than those infected with the Alpha variant ($p < 0.001$). Common clinical manifestations included cough (65.6%), fever (40.9%), expectoration (31.0%), sore throat (22.6%), fatigue (16.3%) and nasal congestion (12.6%), and rare symptoms included muscle

aches (7.3%), headache (6.6%), diarrhea (5.0%), and so forth. Compared with the Alpha variant, the proportion of patients with fever, hemoptysis, nasal congestion, sore throat, muscle pain, nausea/vomiting, and shortness of breath was lower ($p < 0.05$). 122 (32.0%) of the patients infected with the Delta variant carried comorbidities, similar to the Alpha variant (28.3%) (Table 1).

4.2 | Comparison of laboratory tests

After admission, all patients underwent relevant hematological examinations. After statistics, it was found that compared with the Alpha group, the proportion of leukocytes decreased (10.5% vs. 29.2%), INR increased (11.0% vs. 2.8%), transaminase increased (13.6% vs. 19.8%), total bilirubin increased (0.5% vs. 3.5%), serum potassium decreased (17.9% vs. 7.3%), and creatinine increased (0.3% vs. 12.4%) in patients infected with the Delta variant was much lower ($p < 0.01$). However, the proportion of lymphocytes decreased was much higher than that of the Alpha variant (40.9% vs. 17.5%, $p < 0.001$), but there was no difference in the proportion of increased leukocytes and CRP. In addition, 26.0% of patients infected with the Delta variant had elevated blood glucose, and 7.1% had elevated creatine kinase (CK)-MB after admission, but statistical comparisons were not performed due to a lack of data on patients in the Alpha cohort (Table 2).

4.3 | Comparison of clinical treatments and outcomes

Most of the Delta 381 cohort patients were common type (62.7%), 35.7% were mild, and only 6 (1.5%) were severe/critical. The proportion of severe/critical type patients was significantly lower than that of the Alpha cohort (18%), $p < 0.001$. During hospitalization, 65 (17.0%) received glucocorticoid therapy, which was comparable to the Alpha cohort ($p = 0.643$), but the antibiotic usage rate was significantly lower (41.4% vs. 33.9%, $p = 0.013$). In the Delta group, 94.2% received antiviral therapy, almost all patients received Abidol antiviral regimen, and 2 (0.5%) patients underwent invasive mechanical ventilation during hospitalization for progressive disease. Both cohorts were followed up for 31 days, and no patients experienced shock or death during the observation period in the Delta group. As of the follow-up date, 48.6% and 59.8% of the Alpha and Delta cohorts were discharged from the hospital, respectively, with $p < 0.001$. The specific number of daily discharges is shown in Supporting Information: Figure 2. The median length of hospital stay in the Delta cohort was 24 (21–26) days, which was significantly higher than that in the Alpha cohort of 18 (14–24), $p < 0.001$. (Table 3)

4.4 | Comparison between vaccinated and unvaccinated patients infected with the Delta variant

By comparison with the Alpha cohort, we found that the Delta cohort was milder in clinical presentations, abnormal laboratory tests, and

TABLE 1 Comparison of demographic and clinical characteristics between patients infected with the Alpha and Delta variants

Total	Wave 1 ($n = 856$)	Wave 2[a] ($n = 381$)	p Value
Sex			
Male	439 (51.3%)	173 (45.4%)	0.056
Female	417 (48.7%)	208 (54.6%)	0.056
Age (years)	46 (35-56)	52 (38-61)	<0.001
≥60	154 (18.0%)	102 (26.8%)	<0.001
18–59	680 (79.4%)	249 (65.3%)	<0.001
<18	22 (2.6%)	30 (7.9%)	<0.001
Symptoms			
Fever	698 (81.5%)	156 (40.9%)	<0.001
Cough	553 (64.6%)	250 (65.6%)	0.730
Sputum production	290 (33.9%)	118 (31.0%)	0.315
Hemoptysis	14 (1.6%)	0 (0.0%)	0.026
Sore throat	122 (14.3%)	86 (22.6%)	<0.001
Nasal obstruction	50 (5.8%)	48 (12.6%)	<0.001
Muscle ache	96 (11.2%)	28 (7.3%)	0.037
Fatigue	154 (18.0%)	62 (16.3%)	0.463
Diarrhea	65 (7.6%)	19 (5.0%)	0.093
Nausea/vomiting	28 (3.3%)	5 (1.3%)	0.048
Headache	80 (9.3%)	25 (6.6%)	0.105
Shortness of breath	41 (4.8%)	6 (1.6%)	0.006
Comorbidity			
With comorbidities	242 (28.3%)	122 (32.0%)	0.182
Without comorbidity	614 (71.1%)	259 (68.0%)	0.182
Number of comorbidities			
With 1 comorbidity	90 (10.5%)	95 (24.9%)	<0.001
With 2 comorbidities	97 (11.3%)	20 (5.2%)	0.001
With ≥3 comorbidities	55 (6.4%)	7 (1.8%)	0.001
Vaccination against SARS-COV-2			
Unknown	0 (0.0%)	38 (10.0%)	<0.001
No	856 (100%)	18 (4.7%)	<0.001
Yes	0 (0.0%)	325 (85.3%)	<0.001
1 dose	0 (0.0%)	5 (1.3%)	
2 doses	0 (0.0%)	303 (79.5%)	
3 doses	0 (0.0%)	17 (4.5%)	

[a]Wave 1 represents patients infected with the Alpha variant, Wave 2 represents patients infected with the Delta variant. Data are expressed as medians (interquartile ranges, IQR), n (%).

TABLE 2 Comparison of laboratory tests between patients infected with the Alpha and Delta variants

Total	Wave 1[a] (*n* = 856)	Wave 2[b] (*n* = 381)	*p* Value
Leucocytes			
Normal range: 4–10 × 10^9/L[a]; 3.5–9.5 × 10^9/L[b]	4.8 (3.8–6.0)	5.5 (4.3–6.7)	<0.001
<Lower limit of normal	250/856 (29.2%)	40/381 (10.5%)	<0.001
>Upper limit of normal	26/856 (3.0%)	12/381 (3.1%)	0.916
Neutrophils			
Normal range: 2–7 × 10^9/L[a]; 1.8–6.3 × 10^9/L[b]	3.0 (2.3–4.0)	3.3 (2.5–4.5)	0.001
<Lower limit of normal	147/856 (17.2%)	36/381 (9.4%)	<0.001
>Upper limit of normal	46/856 (5.4%)	27/381 (7.1%)	0.238
Lymphocytes			
Normal range: 0.8–4 × 10^9/L; 1.1–3.2 × 10^9/L[b]	1.2 (0.9–1.6)	1.3 (0.9–1.8)	0.002
<Lower limit of normal	150/856 (17.5%)	156/381 (40.9%)	<0.001
Platelets			
Normal range: 83–303 × 10^9/L[a];125–350 × 10^9/L[b]	181.0 (147.0–222.5)	189.0 (153.0–235.0)	0.064
Hemoglobin			
Normal range: 115–170 g/L[a]; 115–150 g/L[b]	138.0 (127.9–150.0)	136.0 (127.0–148.0)	0.302
International normalized ratio			
Normal range: 0.85–1.15	1.01 (0.97–1.08)	1.00 (0.90–1.05)	<0.001
>Upper limit of normal	94/853 (11.0%)	8/289 (2.8%)	<0.001
Albumin			
Normal range: 40–55 g/L	41.2 (38.1–43.6)	41.0 (38.9–44.1)	0.081
<Lower limit of normal	334/853 (39.2%)	154/381 (40.4%)	0.642
Alanine aminotransferase			
Normal range: 9–50 U/L[a]; female 7–40 U/L,[b] male 9–50 U/L[b]	21.8 (15.0–33.0)	17.0 (13.0–28.0)	<0.001
>Upper limit of normal	106/856 (12.4%)	42/381 (11.0%)	0.496
Aspartate aminotransfera			
Normal range: 15–40 U/L[a]; female 13–35 U/L,[b] male 15–40 U/L[b]	25.0 (19.0–32.6)	20.5 (17.0–27.0)	<0.001
>Upper limit of normal	135/856 (15.8%)	38/381 (10.0%)	0.007
Alanine/aspartate aminotransferase elevation	170 (19.8%)	52 (13.6%)	0.009
Total bilirubin			
Normal range: 0–26 μmol/L[a]; 0–23 μmol/L[b]	9.7 (7.0–13.4)	6.6 (4.6–9.0)	<0.001
>Upper limit of normal	30/852 (3.5%)	2/381 (0.5%)	0.002
Serum potassium			
Normal range: 3.5-5.3 mmol/L	3.8 (3.6–4.1)	4.0 (3.7–4.3)	<0.001
<Lower limit of normal	153/856 (17.9)	28/381 (7.3%)	<0.001
Serum sodium			
Normal range: 137–147 mmol/L	138.3 (136.0–140.0)	137.3 (135.7–138.5)	<0.001
<Lower limit of normal	268/856 (31.3%)	168/381 (44.1%)	<0.001
>Upper limit of normal	2/856 (0.2%)	0/381 (0.0%)	1.000

TABLE 2 (Continued)

Total	Wave 1[a] (*n* = 856)	Wave 2[b] (*n* = 381)	*p* Value
Blood urea nitrogen			
Normal range: 3.1–8 mmol/L[a]; 2.5–6 mmol/L[b]	3.8 (3.1–4.6)	4.4 (3.7–5.3)	<0.001
>Upper limit of normal	25/856 (2.9%)	62/381 (16.3%)	<0.001
Serum creatinine			
Normal range: male 57–97 μmol/L[a], 63.6–110.5 μmol/L[b]; female 41–73 μmol/L,[a] 50.4–98.1 μmol/L[b]	66.0 (55.2–77.0)	55.4 (46.1–69.5)	<0.001
>Upper limit of normal	106/855 (12.4%)	1/381 (0.3%)	<0.001
Creatine kinase			
Normal range: 50–310 U/L[a] female 29–168 U/L[b] male 30–200 U/L[b]	70.0 (48.0–107.0)	71.0 (51.0–105.0)	0.863
>Upper limit of normal	38/854 (4.4%)	22/380 (5.8%)	0.312
Creatine kinase-MB			
Normal range: 0–25 U/L[b]	/	15.0 (12.0–19.0)	
>Upper limit of normal	/	27/380 (7.1%)	
Blood glucose			
Normal range: 3.9–6.1 mmol/L[b]	/	5.4 (4.9–6.1)	
>Upper limit of normal	/	99/381 (26.0%)	
C-reactive protein			
Normal range: 0–8 mg/L[a]; 0–6 mg/L[b]	8.4 (2.7–21.2)	7.9 (3.4–17.9)	0.547
>Upper limit of normal	440/854 (51.5%)	219/381 (57.5%)	0.053
Procalcitonin			
Normal range: <0.5 μg/ml[b]			
>Upper limit of normal	/	2/248 (0.8%)	

Note: Data are presented as medians (interquartile ranges, IQR) and *n*/*N* (%).

[a]Wave 1 represents patients infected with the Alpha variant.

[b]Wave 2 represents patients infected with the Delta variant.

clinical outcomes, so we speculated whether this was related to the widespread vaccination with the inactivated vaccine in the Delta cohort. We further divided the patients in the Delta cohort into vaccinated and unvaccinated groups based on vaccination status, with 325 in the vaccinated group and 18 in the unvaccinated group, and another 38 with unknown vaccination history have been censored. We found that the unvaccinated group was dominated by women (83.33%), there was no difference in age and comorbidities between the two groups. There were only three severe/critical type patients among the vaccinated patients, accounting for 0.92%, while the unvaccinated patients accounted for 11.11%, with a statistically significant difference ($p = 0.024$). During hospitalization, the use rates of glucocorticoids (14.77% vs. 38.89%, $p = 0.017$) and antibiotics (32.31% vs. 55.56%, $p = 0.042$) in vaccinated patients were also significantly lower than those in the unvaccinated group. By the end of the observation, 205 (63.08%) of the vaccinated group were discharged from the hospital versus 7 (38.89%) in the unvaccinated group, $p = 0.040$. Nevertheless, there was no difference in the length of hospital stays (24 [20–26] vs. 24 [22–25], $p = 0.700$) and the virus shedding time (22.0 [18.0–25.0] vs. 23.5 [20.0–25.0], $p = 0.370$) between the two groups. In addition, the results of routine laboratory tests are also similar in both groups (Table 4).

4.5 | Comparison of efficacy of inactivated vaccines over time

Among the 325 vaccinated patients, 5 patients received only one dose of the COVID-19 vaccine, 303 completed two doses of inactivated vaccine, and 17 patients completed the booster vaccination. Of the 303 patients who had received two doses of inactivated vaccine, we divided the patients into groups >6 months and ≤6 months after dose 2 according to the time between the second dose and the diagnosis of COVID-19, and compared the epidemiological characteristics, laboratory tests and clinical outcomes between the two groups, of which 69 patients were not included because the

TABLE 3 Comparison of clinical treatments and outcomes between patients infected with the Alpha and Delta variants

Total	Wave 1 (*n* = 856)	Wave 2 (*n* = 381)	*p* Value
Clinical type			
Mild type	50 (5.8%)	136 (35.7%)	<0.001
Ordinary type	652 (76.2%)	239 (62.7%)	<0.001
Severe type	119 (13.9%)	4 (1.0%)	<0.001
Critical type	35 (4.1%)	2 (0.5%)	0.001
Treatment			
Glucocorticoids	137 (16.05)	65 (17.0%)	0.643
Antibiotic treatment	354 (41.4%)	129 (33.9%)	0.013
Anticoronavirus treatment	839 (98.0%)	359 (94.2%)	<0.001
Antivirus regimen			
Interferon-α + Lopinavir/Ritonavir+ Arbidol	330 (38.6%)	0 (0.0%)	
Interferon-α + Lopinavir/Ritonavir	188 (22.0%)	0 (0.0%)	
Interferon-α + Arbidol	52 (6.1%)	0 (0.0%)	
Lopinavir/Ritonavir + Arbidol	90 (10.5%)	0 (0.0%)	
Arbidol	45 (5.3%)	356 (93.4%)	
Interferon-α	45 (5.3%)	0 (0.0%)	
Lopinavir/Ritonavir	71 (8.3%)	0 (0.0%)	
Others	18 (2.1%)	3 (0.8%)	
Mechanical ventilation	29 (3.4%)	2 (0.5%)	0.003
CRRT	2 (0.2%)	0 (0.0%)	0.479
ECOM	9 (1.1%)	0 (0.0%)	0.100
Shock	4 (0.5%)	0 (0.0%)	0.318
Death	1 (0.1%)	0 (0.0%)	1.000
Discharged patient	416 (48.6%)	228 (59.8%)	<0.001
Hospital stays (days)	18 (14–24)	24 (21–26)	<0.001

Note: Wave 1 represents patients infected with the Alpha variant, Wave 2 represents patients infected with the Delta variant. Data are expressed as *n* (%).

Abbreviations: CRRT, continuous renal replacement therapy; ECOM, extracorporeal membrane oxygenation.

vaccination time was unknown. We found no significant differences in baseline characteristics, clinical outcomes, viral shedding time, and laboratory tests between the two groups (Table 5).

5 | DISCUSSION

The data of this study were all from Zhejiang Province, China, and were collected by the same group of doctors, which greatly reduced the data collection errors and provided good comparability. The Delta variant has been studied by many countries. Many data[9–12] show that the Delta variant has strong adaptability to the body, spreads faster, has a relatively high viral load, takes a longer time to cure, and is more likely to develop into severe diseases. Therefore, the threat of the Delta variant to human beings cannot be ignored. After the outbreak in Zhejiang Province, we collected data on COVID-19 patients immediately, striving to describe further the clinical characteristics and outcomes of Chinese Delta variant infection. However, by comparison, we found that the clinical presentation of patients infected with the Delta variant was mild, with symptoms more like a "bad cold." The most common symptoms were fever, cough, sputum, and sore throat, while diarrhea, nausea, vomiting, and other gastrointestinal symptoms were not obvious. As a result, more infected people did not think they had the COVID-19 and continued to go out, thus accelerating the transmission. In our study, the proportion of children and the elderly infected with the Delta variant was much higher than that of Alpha. Therefore, the

TABLE 4 Comparison of laboratory tests, clinical treatments, and outcomes between vaccinated and unvaccinated patients infected with the Delta variants

Variable	Unvaccinated (*n* = 18)	Vaccinated (*n* = 325)	*p* Value
Sex			
Male/female	3 (16.67%)/15 (83.33%)	151 (46.46%)/174 (53.54%)	0.013
Age (years)	56 (22–76)	52 (39–61)	0.535
With/without comorbidities	9 (50.00%)/9 (50.00%)	101 (31.08%)/224 (68.92%)	0.094
Clinical type			
Mild/ordinary type	16 (88.89%)	322 (99.08%)	0.024
Severe/critical type	2 (11.11%)	3 (0.92%)	
Treatment			
Glucocorticoids	7 (38.89%)	48 (14.77%)	0.017
Antibiotic treatment	10 (55.56%)	105 (32.31%)	0.042
Anticoronavirus treatment	13 (72.22%)	311 (95.69%)	<0.001
Mechanical ventilation	1 (5.56%)	1 (0.31%)	0.102
Shock	0 (0.00%)	0 (0.00%)	/
Discharged patient	7 (38.89%)	205 (63.08%)	0.040
Hospital stays (days)	24 (22–25)	24 (20–26)	0.700
Virus shedding time (days)	23.5 (20.0–25.0)	22.0 (18.0–25.0)	0.370
Leucocytes	3.95 (3.20–6.40)	5.50 (4.30–6.80)	0.154
Normal range: $3.5–9.5 \times 10^9$/L			
<Lower limit of normal	3 (16.7%)	33 (10.2%)	0.629
>Upper limit of normal	0 (0.00%)	11 (3.4%)	1.000
Neutrophils	2.66 (2.35–3.20)	3.44 (2.52–4.63)	0.060
Normal range: $1.8–6.3 \times 10^9$/L			
<Lower limit of normal	2 (11.1%)	29 (8.9%)	1.000
>Upper limit of normal	0 (0.0%)	26 (8.0%)	0.429
Lymphocytes	0.98 (0.65–1.50)	1.19 (0.90–1.19)	0.474
Normal range: $1.1–3.2 \times 10^9$/L			
<Lower limit of normal	9 (50.0%)	132 (40.6%)	0.431
Platelets	126.0 (107.0–252.0)	188.0 (153.0–229.0)	0.523
Normal range: $125–350 \times 10^9$/L			
International normalized ratio	1.03 (0.92–1.09)	1.00 (0.91–1.05)	0.530
Normal range: 0.85–1.15			
D-dimer	330.0 (195.0–695.0)	280.0 (140.0–460.0)	0.347
Normal range: 0–550 μg/L			
Albumin	41.0 (37.3–44.4)	41.0 (38.9–44.0)	0.725
Normal range: 40–55 g/L			
Alanine aminotransferase	13.5 (10.0–37.0)	18.0 (13.0–29.5)	0.011
Normal range: female 7–40 U/L; male 9–50 U/L			
>Upper limit of normal	3 (16.7%)	35 (10.8%)	0.696

(Continues)

TABLE 4 (Continued)

Variable	Unvaccinated (*n* = 18)	Vaccinated (*n* = 325)	*p* Value
Aspartate aminotransfera	31.0 (19.0–39.0)	21.0 (17.0–27.0)	0.454
Normal range: female 13–35 U/L; male 15–40 U/L			
>Upper limit of normal	3 (16.7%)	28 (8.6%)	0.461
Alanine/aspartate aminotransferase elevation	3 (16.7%)	42 (12.9%)	0.629
Total bilirubin	5.1 (3.7–9.4)	7.0 (4.9–9.8)	0.347
Normal range: 0–23 μmol/L			
>Upper limit of normal	0 (0.0%)	2 (0.6%)	1.000
Serum potassium	3.82 (3.69–4.34)	3.97 (3.70–4.24)	0.334
Normal range: 3.5–5.3 mmol/L			
Serum sodium	137.6 (137.2–139.1)	137.2 (135.6–138.4)	0.166
Normal range: 137–147 mmol/L			
Blood urea nitrogen	4.86 (4.52–7.36)	4.30 (3.59–5.31)	0.062
Normal range: 2.5–6 mmol/L			
>Upper limit of normal	6 (33.3%)	49 (15.1%)	0.085
Serum creatinine	61.95 (43.05–76.25)	55.40 (46.50–69.40)	0.515
Normal range: male 63.6–110.5 μmol/L, female 50.4–98.1 μmol/L			
Creatine kinase	81.5 (59.5–114.0)	73.0 (51.0–108.0)	0.578
Normal range: female 29–168 U/L; male 30–200 U/L			
Creatine kinase-MB	15.5 (13.0–23.0)	15.0 (12.0–18.0)	0.292
Normal range: 0–25 U/L			
Blood glucose	5.10 (4.49–5.99)	5.55 (4.99–6.42)	0.108
Normal range: 3.9–6.1 mmol/L			
C-reactive protein	3.25 (2.60–16.05)	10.70 (3.90–19.80)	0.089
Normal range: 0–6 mg/L			

Note: Data are presented as medians (interquartile ranges, IQR) and *n* (%).

elderly and children are still vulnerable to the Delta variant and need to be paid more attention.[13,14]

Many previous studies,[15] have shown that COVID-19 often causes liver damage. In a multicenter retrospective study in China,[16] liver enzyme levels were elevated after admission in 28.2% of patients. Data from a prospective study[17] of 217 COVID-19 patients without previous liver diseases showed that 58% of patients observed any liver biochemical abnormality at admission, with 42% having elevated aspartate aminotransferase, 37% elevated gamma-glutamyl-transferase, and 27% elevated alanine aminotransferase. By comparing it to the Alpha group, the proportion of patients with abnormal liver function in the Delta group was significantly lower in our study, which indirectly suggested that the Delta variant had less liver damage. Besides, the Delta cohort had lower rates of abnormalities in other common clinical tests than that of Alpha, which differed from many other studies.[18] Since most patients in the Delta cohort have been vaccinated with inactivated vaccines, we thought it had something to do with the COVID-19 vaccination. By further subgrouping, we found that vaccinated patients did have a lower probability of severe illness and a lower rate of glucocorticoids and antibiotics use, which would explain why the severity of the Delta-infected patients in our study was milder than Alpha (Figure 1).

Before that, A study in Scotland[9] showed that the risk of hospital admission was approximately doubled in those with the Delta variant when compared to the Alpha variant, but COVID-19 vaccines were effective in reducing the risk of SARS-CoV-2 infection and COVID-19 hospitalization in people infected with the Delta variant. In Israel, two doses of mRNA vaccine can reduce symptomatic infections by 94%, related hospitalization by 87%, severe/critical cases by 92%, and the risk of Delta infection by 79%.[19] It can be seen that although the

TABLE 5 Comparison between patients who had been vaccinated for more than 6 months since the second dose and those less than 6 months.

Variable	>6 months after dose 2 (*n* = 42)	≤6 months after dose 2 (*n* = 192)	*p* Value
Sex			
Male	18 (42.86%)	92 (47.92%)	0.552
Female	24 (57.14%)	100 (52.08%)	
Age (years)	52.0 (36.0–63.5)	50.0 (36.0–57.0)	0.23
Comorbidity			
With comorbidities	10 (23.81%)	56 (29.17%)	0.485
Without comorbidities	32 (76.19%)	136 (70.83%)	
Clinical type			
Mild type	14 (33.33%)	70 (36.46%)	0.702
Nonmild type	28 (66.67%)	122 (63.54%)	
Treatment			
Glucocorticoids	8 (19.05%)	26 (13.54%)	0.359
Antibiotic treatment	16 (38.10%)	61 (31.77%)	0.429
Anticoronavirus treatment	42 (100.00%)	182 (94.79%)	0.275
Discharged patient	27 (64.29%)	123 (64.06%)	0.978
Hospital stays (days)	24.0 (21.5–26.0)	24.0 (20.0–26.0)	0.591
Virus shedding time (days)	20.0 (17.0–25.0)	20.0 (9.8–23.0)	0.155
Leucocytes			
Normal range: 3.5–9.5 × 10^9/L	4.95 (3.75–6.85)	5.6 (4.30–6.80)	0.057
<Lower limit of normal	5 (11.90%)	17 (8.85%)	0.748
>Upper limit of normal	0 (0.00%)	7 (3.65%)	0.449
Neutrophils			
Normal range:1.8–6.3 × 10^9/L	3.28 (1.93–4.60)	3.53 (2.57–4.75)	0.376
<Lower limit of normal	6 (14.29%)	12 (6.25%)	0.147
>Upper limit of normal	3 (7.14%)	17 (8.85%)	0.956
Lymphocytes			
Normal range: 1.1–3.2 × 10^9/L	1.08 (0.86–1.61)	1.16 (0.87–1.64)	0.058
<Lower limit of normal	23 (53.49%)	72 (37.50%)	0.039
Platelets			
Normal range: 125–350 × 10^9/L	189.81 ± 43.67	192.13 ± 54.44	0.240
International normalized ratio	1.00 (0.92–1.04)	1.01 (0.90–1.05)	0.736
Normal range: 0.85–1.15			
D-dimer	260.00 (142.50–647.50)	260.00 (147.50–400.00)	0.754
Normal range: 0–550 μg/L			
Albumin	40.15 (38.72-45.53)	40.95 (39.28-44.15)	0.828
Normal range: 40–55 g/L			
Alanine aminotransferase	16.50 (13.00–22.75)	19.00 (14.00–1.00)	0.144
Normal range: female 7–40 U/L; male 9–50 U/L			

(Continues)

TABLE 5 (Continued)

Variable	>6 months after dose 2 (*n* = 42)	≤6 months after dose 2 (*n* = 192)	*p* Value
Aspartate aminotransfera	22.00 (16.25–24.00)	20.00 (17.00–28.00)	0.316
Normal range: female 13–35 U/L; male 15–40 U/L			
Alanine/aspartate aminotransferase elevation	1 (2.38%)	26 (13.54%)	0.074
Total bilirubin	6.95 (3.58–8.65)	7.00 (4.80–9.53)	0.747
Normal range: 0–23 μmol/L			
Serum potassium	3.92 ± 0.35	3.96 ± 0.39	0.09
Normal range: 3.5–5.3 mmol/L			
Serum sodium	136.87 ± 2.18	136.70 ± 2.15	0.265
Normal range: 137–147 mmol/L			
Blood urea nitrogen	4.05 (3.39–4.77)	4.19 (3.59–5.22)	0.696
Normal range: 2.5–6 mmol/L			
Serum creatinine	53.85 (46.73–70.30)	55.90 (46.30–69.08)	0.649
Normal range: male 63.6–110.5 μmol/L, female 50.4–98.1 μmol/L			
Creatine kinase	76.00 (48.25–101.00)	69.50 (49.75–108.50)	0.838
Normal range: female 29–168 U/L; male 30–200 U/L			
Creatine kinase-MB	14.00 (11.00–17.00)	15.00 (12.00–19.00)	0.172
Normal range: 0–25 U/L			
Blood glucose			
Normal range: 3.9–1 mmol/L	5.91 (4.82–6.78)	5.46 (5.00–6.16)	0.317
>Upper limit of normal	12 (28.57%)	46 (23.96%)	0.531
C-reactive protein			
Normal range: 0–6 mg/L	9.90 (4.55–18.18)	11.40 (3.75–24.55)	0.647
>Upper limit of normal	27 (64.29%)	112 (58.33%)	0.477

Note: Data are presented as medians (interquartile ranges, IQR), mean ± standard deviation, and *n* (%).

Delta variant exhibits partial immune escape,[20] the vaccine still has a protective effect against the Delta variant, which is consistent with the conclusion of our article. The prevention and control measures against the SARS-CoV-2 outbreaks in China, such as wearing masks, maintaining social distancing, limiting social activities, and regionally locking down communities, have been proven effective.[21] Besides, broad, community-wide vaccination of all eligible individuals is a critical component of mitigation strategies to protect populations from SARS-CoV-2 infection and severe COVID-19 illness. As of February 1, 2022, China vaccinated more than 3 billion doses of inactivated vaccines, striving to achieve a universal immunization barrier.

The findings in this report were subject to at least the following limitations. Studies have shown[22] that the Delta variant had a higher viral load than the historical variants. Although we found longer hospital stays in the Delta cohort, there was no comparative viral load analysis between the two. In our study, 26.0% of patients infected with the Delta variant had elevated blood glucose on admission. Elevated blood glucose is an independent risk factor for the progression of non-severe/critical cases of COVID-19 to severe/critical cases or death,[23] and good glycemic control (3.9–10.0 mmol/L) in COVID-19 patients with diabetes can significantly reduce the incidence of serious adverse outcome events and death.[24] Therefore, the blood glucose level is an important point in treating COVID-19. However, because the data of the Alpha cohort came from multiple centers, the number of cases surged in the early stage of the outbreak, and due to various reasons, such as the shortage of medical resources, many patients lacked blood glucose data, so they could not be statistically compared with the Delta cohort. In addition, although we grouped the Delta cohort according to the vaccination status for comparative analysis, due to the large disparity in numbers, it tends to lead to large statistical errors, and a larger sample size is required for relevant verification in the future.

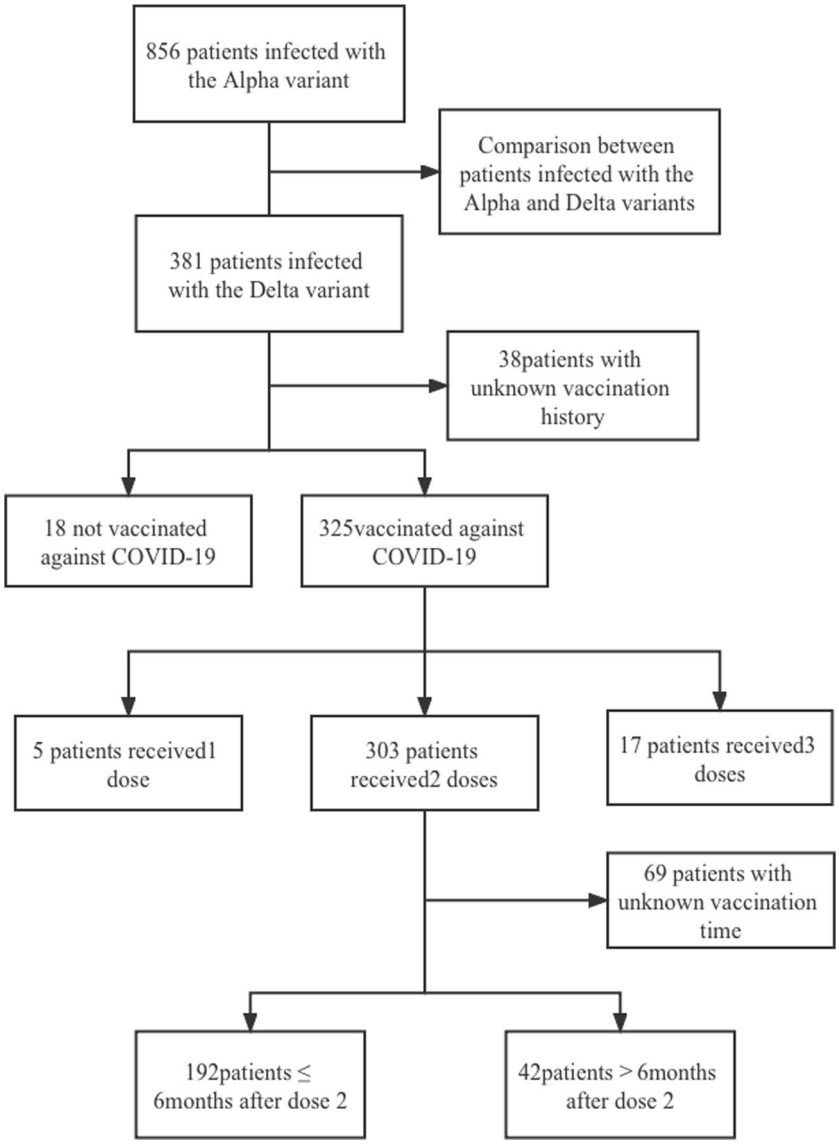

FIGURE 1 Study profile. When comparing the characteristics of the vaccinated and unvaccinated cohorts in the Delta group, 38 patients were not included because of the unknown history of COVID-19 vaccination. Of the vaccinated patients, 303 received two doses of the inactivated COVID-19 vaccine, and when comparing vaccine efficacy over time, 69 patients were not included due to a lack of information on the timing of vaccination

AUTHOR CONTRIBUTIONS

Chanyuan Ye designed the study and drafted the manuscript; Yida Yang supervised the whole study process; Yan Lv, Wei Kuang, Lisha Yang, Jueqing Gu, Yingfeng Lu, Feng Ding, and Huajiang Shen participated in the collection of data. Yida Yang reviewed the manuscript before submission. All authors scrutinized the manuscript and approved the final version for publication.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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