RESEARCH ARTICLE

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

Chanyuan Ye1 | Yan Lv1 | Wei Kuang1 | Lisha Yang1 | Yingfeng Lu1 | Jueqing Gu1 | Feng Ding2 | Huajiang Shen2 | Yida Yang1

1State Key Laboratory for Diagnosis and Treatment of Infectious Diseases, Department of Infectious Diseases, National Clinical Research Center for Infectious Diseases, National Medical Center for Infectious Diseases, Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China

2Department of Infectious Diseases, Affiliated Hospital of Shaoxing University, Shaoxing, Zhejiang, China

Correspondence
Yida Yang, Department of Infection Disease, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Rd., Hangzhou City 310003, China. Email: yidayang65@zju.edu.cn

Funding information
National Health Commission Scientific Research Foundation of China; Shaoxing Science and Technology Project

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, 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. 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. 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\textsuperscript{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).\textsuperscript{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),\textsuperscript{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 \( \chi^2 \) tests, taking the results of Pearson \( \chi^2 \), 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

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

| Total | Wave 1 (n = 856) | Wave 2* (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)** |                  |                   |                |
| ≥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         |
| **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%)         |                |

*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

|                      | Wave 1<sup>a</sup> (n = 856) | Wave 2<sup>b</sup> (n = 381) | p Value |
|----------------------|-------------------------------|-------------------------------|---------|
| **Leucocytes**       |                               |                               |         |
| Normal range: 4–10 × 10<sup>9</sup>/L<sup>a</sup>; 3.5–9.5 × 10<sup>9</sup>/L<sup>b</sup> | 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<sup>9</sup>/L<sup>a</sup>; 1.8–6.3 × 10<sup>9</sup>/L<sup>b</sup> | 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<sup>9</sup>/L<sup>a</sup>; 1.1–3.2 × 10<sup>9</sup>/L<sup>b</sup> | 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<sup>9</sup>/L<sup>a</sup>; 125–350 × 10<sup>9</sup>/L<sup>b</sup> | 181.0 (147.0–222.5) | 189.0 (153.0–235.0) | 0.064   |
| **Hemoglobin**       |                               |                               |         |
| Normal range: 115–170 g/L<sup>a</sup>; 115–150 g/L<sup>b</sup> | 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<sup>a</sup>; female 7–40 U/L<sup>b</sup>; male 9–50 U/L<sup>b</sup> | 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 aminotransferase** |                            |                               |         |
| Normal range: 15–40 U/L<sup>a</sup>; female 13–35 U/L<sup>b</sup>; male 15–40 U/L<sup>b</sup> | 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<sup>a</sup>; 0–23 μmol/L<sup>b</sup> | 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   |
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

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**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$^b$; 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 57.97–110.5 μmol/L$^b$, female 41.73–98.1 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$^b$ 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**                                               | /                      | 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**                                               | 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.*
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).

## 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 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** | | | 0.643 |
| 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** | | | 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** | | | <0.001 |
| Hospital stays (days) | 416 (48.6%) | 228 (59.8%) | <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.
| 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%) |                      | 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 × 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 × 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 × 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 × 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)
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 study17 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 Scotland9 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 4 (Continued)

| Variable                        | Unvaccinated (n = 18) | Vaccinated (n = 325) | p Value |
|---------------------------------|-----------------------|----------------------|---------|
| Aspartate aminotransferase      | 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 (%).
| 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 × 10⁹/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 × 10⁹/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 × 10⁹/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 × 10⁹/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   |
| 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 |                 |                                 |         |
Delta variant exhibits partial immune escape, 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. 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 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, 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. 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.

### TABLE 5 (Continued)

| Variable                                | >6 months after dose 2 (n = 42) | ≤6 months after dose 2 (n = 192) | p Value |
|-----------------------------------------|---------------------------------|---------------------------------|---------|
| Aspartate aminotransfera                |                                 |                                 |         |
| Normal range: female 13–35 U/L; male 15–40 U/L | 22.00 (16.25–24.00)                      | 20.00 (17.00–28.00)                      | 0.316   |
| 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                           | 5.91 (4.82–6.78)                 | 5.46 (5.00–6.16)                 | 0.317   |
| Normal range: 3.9–1 mmol/L             |                                 |                                 |         |
| >Upper limit of normal                  | 12 (28.57%)                      | 46 (23.96%)                      | 0.531   |
| C-reactive protein                      | 9.90 (4.55–18.18)                | 11.40 (3.75–24.55)               | 0.647   |
| Normal range: 0–6 mg/L                  |                                 |                                 |         |
| >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 (%).
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.

ACKNOWLEDGMENT
We thank the Affiliated Hospital of Shaoxing University for its support and salute every medical worker contributing to epidemic prevention and control. This study was supported by the National Health Commission Scientific Research Foundation of China (WKJ-ZJ-2111) and Shaoxing Science and Technology Project (2020A13102).

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.

ORCID
Yida Yang  http://orcid.org/0000-0002-9673-0969

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**SUPPORTING INFORMATION**

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

**How to cite this article:** Ye C, Lv Y, Kuang W, et al. Inactivated vaccines prevent severe COVID-19 in patients infected with the Delta variant: a comparative study of the Delta and Alpha variants from China. *J Med Virol.* 2022;94:3613-3624. doi:10.1002/jmv.27759