Clinical Characteristics of COVID-19 Patients’ Postvaccination

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Abstract

To investigate the clinical characteristic of domestic coronavirus disease 2019 (COVID-19) patients after vaccination campaign conducted in China. According to vaccination status and months from first vaccine dose to infection detection, patients were divided into unvaccinated, <3 months, 3–6 months, and >6 months groups. The information of demographic and clinical characteristics, laboratory and thoracic computed tomography (CT) findings, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid and IgM, IgG antibodies was retrospectively collected. Therapeutic approaches, temperature-normalizing and viral shedding times, outcomes were also summarized. SARS-CoV-2 antibody levels were further analyzed based on the other following variables: time from second vaccine dose to infection, vaccine dose, the interval from the first to the second dose, and vaccine brand. Among 208 COVID-19 patients, 13 (6.28%) were unvaccinated. No significant differences in demographic and clinical characteristics, laboratory and CT findings, and SARS-CoV-2 nucleic acid loads were detected between groups (all \( p > 0.05 \)). In comparison with the unvaccinated group, the median SARS-CoV-2 IgG levels were noticeably increased in those vaccinated groups (0.603 in unvaccinated, 15.925 in <3 months, 14.04 in 3–6 months, and 4.94 in >6 months, respectively, \( p < 0.05 \)). However, SARS-CoV-2 IgG levels were not altered between groups divided based on the other variables. Vaccination does not affect the clinical characteristics in COVID-19 patients. COVID-19 patients with vaccination have high SARS-CoV-2 IgG levels. Underscore the necessity of rapid implementation of vaccination campaigns can be speculated.

Keywords: COVID-19, SARS-CoV-2, vaccination, clinical characteristic, IgG

Introduction

CORONAVIRUS DISEASE 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in a global pandemic and affected millions of people around the world. There is still no definitely effective therapeutic approach against SARS-CoV-2. Quarantine and other physical protective measurements might be useful temporarily, but they cannot protect the individual in the future. Vaccination against SARS-CoV-2 is
| Variable                              | Total (n = 208) | Unvaccinated (n = 13) | <3 months (n = 116) | 3–6 months (n = 68) | >6 months (n = 11) | p       |
|--------------------------------------|----------------|-----------------------|---------------------|---------------------|-------------------|---------|
| **Age, years**                       |                |                       |                     |                     |                   | >0.05   |
|                                      | 41.0 (34.0–48.0)| 43.0 (32.0–60.5)      | 40.5 (34.0–49.0)    | 41.0 (34.0–47.0)    | 36.0 (31.0–48.0)  | >0.05   |
| **Gender, n (%)**                    |                |                       |                     |                     |                   | >0.05   |
| Male                                 | 101 (48.6)     | 9 (69.2)              | 57 (49.1)           | 31 (45.6)           | 4 (36.4)          |         |
| Female                               | 107 (51.4)     | 4 (30.8)              | 59 (50.9)           | 37 (45.4)           | 7 (63.6)          |         |
| **Body mass index, kg/m^2**          | 23.36 (20.92–25.40) | 22.5 (20.05–24.95) | 23.44 (21.42–25.35) | 22.92 (20.72–25.26) | 23.80 (19.68–26.0) | >0.05   |
| **Comorbidities, n (%)**             |                |                       |                     |                     |                   |         |
| Hypertension                         | 25 (12.0)      | 1 (7.7)               | 15 (12.9)           | 8 (11.8)            | 1 (9.1)           | >0.05   |
| Cardiovascular or cerebrovascular    | 3 (1.4)        | 1 (7.7)               | 2 (1.7)             | 0 (0.0)             | 0 (0.0)           | >0.05   |
| Cardiovascular or cerebrovascular    | 10 (4.8)       | 0 (0.0)               | 5 (4.3)             | 5 (7.4)             | 0 (0.0)           | >0.05   |
| Cardiovascular or cerebrovascular    | 2 (1.0)        | 1 (7.7)               | 1 (0.9)             | 0 (0.0)             | 0 (0.0)           | >0.05   |
| Hypertension                         | 5 (2.4)        | 0 (0.0)               | 4 (3.4)             | 1 (1.5)             | 0 (0.0)           | >0.05   |
| **Symptom**                          |                |                       |                     |                     |                   | >0.05   |
| Fever                                | 93 (44.7)      | 5 (38.5)              | 46 (39.7)           | 35 (51.5)           | 7 (63.6)          | >0.05   |
| Cough with or without sputum         | 103 (49.5)     | 10 (76.9)             | 55 (47.4)           | 35 (51.5)           | 3 (27.3)          | >0.05   |
| Fatigue                              | 39 (18.8)      | 2 (15.4)              | 20 (17.2)           | 17 (25.0)           | 0 (0.0)           | >0.05   |
| Chest tightness or dysnea            | 12 (5.8)       | 1 (7.7)               | 6 (5.2)             | 5 (7.4)             | 0 (0.0)           | >0.05   |
| Anosmia or ageusia                   | 34 (16.3)      | 4 (30.8)              | 18 (15.5)           | 17 (25.0)           | 0 (0.0)           | >0.05   |
| Throat pain or discomfort            | 88 (42.3)      | 5 (38.5)              | 54 (46.6)           | 26 (38.2)           | 3 (27.3)          | >0.05   |
| Myalgia                              | 28 (13.5)      | 1 (7.7)               | 13 (16.2)           | 11 (16.2)           | 3 (13.5)          | >0.05   |
| Temperature, °C                      | 36.8 (36.4–37.3)| 36.7 (36.5–37.0)      | 36.7 (36.3–37.1)    | 37.0 (36.4–37.5)    | 36.8 (36.5–38.4)  | >0.05   |
| Heart rate, beats/minutes            | 92.0 (81.3–102.8)| 97.0 (79.0–105.5)     | 92.5 (85.3–100.8)   | 90.0 (78.0–104.8)   | 93.0 (88.0–109.0) | >0.05   |
| Respiratory rate, breaths/minutes    | 20.0 (19.0–21.0)| 20.0 (18.0–20.0)      | 20.0 (19.0–21.0)    | 20.0 (19.0–21.0)    | 20.0 (20.0–22.0)  | >0.05   |
| Systolic blood pressure, mmHg        | 126.0 (114.0–135.8)| 128.0 (122.0–141.5) | 124.5 (114.0–133.0) | 127.5 (112.0–135.8) | 127.0 (115.0–145.0) | >0.05   |
| Diastolic blood pressure, mmHg       | 85.0 (78.0–92.0)| 84.0 (79.5–93.5)      | 85.0 (79.0–92.0)    | 85.0 (77.0–92.0)    | 87.0 (75.0–95.0)  | >0.05   |
| Pulse oxygen saturation at rest, %   | 98.0 (97.3–99.0)| 98.0 (97.5–98.0)      | 98.0 (98.0–98.8)    | 98.0 (97.0–98.0)    | 98.0 (97.0–98.0)  | >0.05   |
| Pulse oxygen saturation during exertion, % | 98.0 (97.0–98.0) | 98.0 (96.5–98.0)     | 98.0 (97.0–98.0)    | 97.0 (96.0–98.0)    | 98.0 (97.0–98.0)  | >0.05   |
| First vaccine dose to infection detection, days | 78.0 (52.0–109.0) | - | 75.0 (54.5–77.0) | 109.0 (105.0–133.0) | 237.0 (199.0–261.0) | <0.001 |
| Second vaccine dose to infection detection, days | 49.0 (22.0–74.0) | - | 24.0 (17.0–33.5) | 77.0 (63.0–92.0) | 195.0 (161.0–229.0) | <0.001 |
| Interval between first and second vaccine dose, days | 38.0 (25.0–47.0) | - | 29.0 (22.5–45.0) | 42.0 (30.0–48.0)* | 41.0 (35.0–48.0) | <0.05   |
| Illness onset or positive SARS-CoV-2 nucleic acid to hospital admission, days | 2.0 (1.0–3.0) | 2.0 (1.0–4.5) | 2.0 (1.0–2.0) | 2.0 (1.0–3.0) | 2.0 (0.5–3.0) | >0.05   |
| Vaccine typeb                         |                |                       |                     |                     |                   | <0.001  |
| Sinovac                              | 98 (47.1)      | -                     | 63 (54.3)           | 33 (48.5)           | 2 (18.2)          |         |
| Sinopharm                            | 43 (20.7)      | -                     | 22 (19.0)           | 14 (20.6)           | 7 (63.6)          |         |
| Sinovac and Sinopharm                | 30 (14.4)      | -                     | 18 (15.5)           | 12 (17.6)           | 0 (0.0)           |         |
| Ad5-nCoV                             | 5 (2.4)        | -                     | 3 (2.6)             | 2 (2.9)             | 0 (0.0)           |         |
| Unknown                               | 19 (9.1)       | -                     | 10 (8.6)            | 7 (10.3)            | 2 (18.2)          |         |

*p* <0.01 when compared with <3 months group.

a*p* <0.01 when compared with <3 months group.

bSinovac: Sinovac COVID-19 vaccine (Vero Cell), inactivated, Sinovac Life Sciences Co., Ltd. Sinopharm: Sinopharm (Vero Cell)-inactivated, COVID-19 Vaccine, Beijing Institute of Biological Products Co., Ltd. Ad5-nCoV: recombinant COVID-19 vaccine, adenovirus type-5 vector-based COVID-19 vaccine, CanSino Biologics, Inc.
the leading strategy to change the current situation of the COVID-19 pandemic. Extremely strict policies have been undertaken against the spread of COVID-19 in China. Vaccination has also been approved, and the national immunization campaign has been conducted since the late 2020. The efficacy of all vaccines is ~70%; the mRNA vaccines have even up to 95% protective rate against COVID-19 (1,2,8).

Bichara et al. reported that the efficacy of the first vaccine was up to 70% in Brazil, but decreased with age. The emergence of major new variants has raised concerns regarding their efficacy. In such strictly controlled circumstances, there are limited COVID-19 cases originating from the general population in China’s mainland. In September 2021, however, there was a local clustering occurrence of domestic COVID-19 in Xiamen city, Fujian province. Here, we analyzed the clinical characteristics of these COVID-19 patients, who received one or two doses of SARS-CoV-2 vaccination.

Methods

Study population

Adult patients (age ≥18 years) with laboratory-confirmed and symptomatic COVID-19 who received treatment uniformly in Xiamen COVID-19 Designated hospital were enrolled in our retrospective analysis. All patients were admitted to the hospital between September 12, 2021 and October 3, 2021. According to the lengths from first vaccine dose to infection detection, patients were divided into the following four groups: unvaccinated group, <3 months, 3–6 months, and >6 months. The diagnosis criteria and severity of COVID-19 were assessed according to the New Coronavirus Pneumonia Prevention and Control Program published by the Chinese National Health Commission (version 8) (4). The written consents from all patients were waived due to the retrospective nature of the study, and the study was approved by the Institutional Ethics Committee of the hospital.

Data collection

The demographic, clinical, and laboratory characteristics, and computed tomography (CT) features were gathered from eligible patients at hospital admission. In brief, the following demographic and clinical information was extracted from medical records: age, gender, body mass index (BMI), medical history, comorbidities, symptoms, vital signs, pulse oxygen saturation (SpO2, %) at rest and exertion, regarding vaccine inoculation and the first and second dose date, vaccine brand, etc. Laboratory findings, white blood cell (WBC), lymphocyte count, hemoglobin (HB), platelet (PLT) count, albumin, creatine kinase (CK), CK-MB, and D-dimer, were detected.

Meanwhile, data of liver and renal functions and inflammatory biomarkers, total bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (Cr), C-reactive protein (CRP), and interleukin-6 (IL-6) were also collected. SARS-CoV-2 nucleic acid from nasopharyngeal swab samples was obtained and amplified by using real-time reverse transcriptase-polymerase chain reaction. The cycle threshold (Ct) values for SARS-CoV-2 open reading frame 1ab (ORF1ab) and nucleocapsid gene (N gene) were recorded. In addition, thoracic CT scans were conducted in all patients.

Two researchers reviewed the thoracic CT features and scored independently. The CT score was based on the following semiquantitative criteria (5): each lobar involvement of both lungs was classified as 0—none (0%), 1—minimal (1–25%), 2—mild (26–50%), 3—moderate (51–75%), or 4—severe (76–100%). Finally, a total score of 0–20 for the five lobes was summarized. Serum SARS-CoV-2 IgM and IgG antibodies were quantified by using enzyme-linked immunosorbent assay, recorded, and analyzed based on the time from the first or second vaccine dose to infection detection, vaccine dose, the interval from the first to the second dose, and vaccine brand.

The therapeutic approaches, temperature-normalizing time, viral shedding time, and outcomes were also obtained. Viral shedding time was defined as the length from the first positive SARS-CoV-2 nucleic acid of the nasopharyngeal swab to two continuous negative results at ~24h intervals (4). Two researchers reviewed the data collection independently for verifying the accuracy.

Data statistical analysis

Binary/categorical variables were presented as numbers (percentage) and compared using the chi-square test or Fisher’s exact test; while continuous variables were presented as medians (interquartile ranges) and compared using the Kruskal–Wallis test. Statistical significance was confirmed if p-value was <0.05. Statistical analyses and figure depiction were performed by using the IBM SPSS Statistics software 23.0 (SPSS, Inc., Chicago, IL).

Results

Demographic, clinical characteristics, and disease severity

A total of 208 COVID-19 cases were enrolled in our analysis. The median age was 41.0 (34.0–48.0); 48.6% (101/208)
was male. Among them, 13 (6.25%) cases were unvaccinated. As outlined in Table 1, after grouping based on months from first vaccine dose to infection detection, we found that underlying comorbidities between groups were similar. No statistical differences in COVID-19-relevant symptoms, vital signs, SP\textsubscript{O2} at rest and during exertion, and BMI were observed among groups. The median lengths from the first and second vaccine doses to infection detection were 78 (52–109) and 49 (22–74) days, respectively.

There was a median of 38 (25–47) days apart from the first to second vaccine dose. The interval days between the first and second vaccine doses were significantly higher in the 3–6 months group than in the <3 months groups [42 (30–48) vs. 29 (22.5–45), \(p<0.01\)]. Nearly half (47.1\%) of the cases received Sinovac-inactivated vaccine, 20.7\% cases inoculated Sinopharm-inactivated vaccine; only 5 (2.4\%) cases received one dose recombinant vaccine (adenovirus type-5 vector-based COVID-19 vaccine, Ad5-nCoV) (Table 2).

According to the COVID-19 severity criteria (4), the proportions are 17.8\% (37/208) of mild type, 78.4\% (163/208) of moderate type, and 3.8\% (8/208) of severe type; no patient was defined as critical type at hospital admission. Although no mild type in the unvaccinated group, the disease severity did not differ between these groups based on vaccination status (Table 2).

**Laboratory findings, SARS-CoV-2 nucleic acid Ct value, and thoracic CT features**

As summarized in Table 3, there was no significant difference in blood routine test (WBC, lymphocytes count, HB, and PLT), liver and renal functions (ALT, AST, and Cr), CK, CK-MB, LDH, D-dimer, as well as inflammatory biomarkers (CRP, IL-6) between groups. As compared with unvaccinated patients, both the SARS-CoV-2 ORF1ab and \(N\) genes were not noticeably decreased in patients who received vaccination at different times (\(p<0.05\)) (Fig. 1). Regarding CT imaging features, the majority of patients had ground-glass opacity (95.9\%) and bilateral lung involvement (85.4\%); few of patients with consolidation were observed (17.0\%); the CT appearances were also not different across the groups according to the vaccination status (Table 4).

**SARS-CoV-2 IgM and IgG antibody levels**

When grouped based on the time from the first vaccine dose to infection detection, the IgM levels in <3 months group were markedly higher than those in the unvaccinated group (\(p<0.05\)); while IgM levels were decreased in patients who received the first vaccination dose >6 months when compared with those who received in <3 months (\(p<0.001\)) and 3–6 months (\(p<0.05\)). When compared with unvaccinated patients, the IgM levels were also increased in patients who received second vaccine dose <1 month (\(p<0.01\) vs. <0.5-month group; \(p<0.05\) vs. 0.5–1 month group) before infection detection. When compared with unvaccinated patients, dramatically higher levels of IgG were detected in all vaccinated patients, despite the length of time from vaccination to infection detection (all \(p<0.05\)).

Although median IgG levels dropped to 4.94 in those who had the time from the first dose vaccine to infection >6 months, the statistical difference remained when compared with unvaccinated patients (\(p<0.05\)). Despite low levels in the Ad5-

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### Table 3. Comparison of Laboratory Findings of COVID-19 Patients Between Groups Based on Months from First Vaccine Dose to Infection Detection

| Variable                        | Total (n = 208) | <3 months (n = 68) | 3–6 months (n = 60) | >6 months (n = 70) | \(p\)     |
|---------------------------------|-----------------|-------------------|---------------------|-------------------|---------|
| White blood cell count \(\times10^9/\text{L}\) | 5.27 (4.39–6.68) | 5.26 (4.43–6.66) | 5.28 (4.26–6.83) | 5.50 (4.34–7.56) | \(>0.05\) |
| Hemoglobin, g/L                 | 136.0 (127.0–148.5) | 135.0 (126.3–148.5) | 139.0 (127.0–148.5) | 132.0 (128.0–150.0) | \(>0.05\) |
| Platelet count, \(\times10^9/\text{L}\) | 206.0 (155.0–230.0) | 200.0 (150.0–233.0) | 206.0 (155.0–233.0) | 216.0 (197.0–234.0) | \(>0.05\) |
| Albumin, g/L                    | 41.5 (39.0–43.8)  | 42.0 (40.0–44.0)  | 41.0 (36.0–43.0)  | 42.0 (36.0–43.0)  | \(>0.05\) |
| Aspartate aminotransferase, U/L | 23.0 (19.0–27.0)  | 23.0 (19.0–27.0)  | 22.5 (19.0–26.0)  | 23.0 (18.0–28.0)  | \(>0.05\) |
| Creatinine, \(\mu\text{mol}/\text{L}\) | 70.0 (59.0–85.0)  | 75.0 (59.0–85.0)  | 70.5 (59.0–83.8)  | 70.0 (59.0–83.8)  | \(>0.05\) |
| CK, U/L                         | 84.0 (62.3–115.0) | 84.0 (62.3–115.0) | 83.5 (66.3–114.5) | 85.0 (66.3–114.5) | \(>0.05\) |
| CK-MB, U/L                      | 9.0 (5.3–13.0)   | 9.0 (5.3–13.0)    | 10.0 (6.0–13.0)   | 8.0 (5.0–11.0)    | \(>0.05\) |
| Lactate dehydrogenase, U/L      | 42.0 (36.0–43.0) | 42.0 (36.0–43.0) | 42.0 (36.0–43.0) | 42.0 (36.0–43.0) | \(>0.05\) |
| C reactive protein, mg/L        | 5.36 (1.91–12.44) | 5.96 (1.91–12.13) | 5.96 (1.91–12.13) | 5.96 (1.91–12.13) | \(>0.05\) |
| Interleukin-6, pg/mL            | 3.26 (1.50–8.46) | 3.26 (1.50–8.46)  | 3.26 (1.50–8.46)  | 3.26 (1.50–8.46)  | \(>0.05\) |

All data are presented as median IQR. CK, creatine kinase; IQR, interquartile range.
nCoV group, the overall IgG levels did not reach statistical
difference between groups, which were subdivided by either
vaccine dose or brand. All the results regarding SARS-CoV-2
IgM and IgG antibody levels are outlined in Table 5.

Therapeutic approaches, temperature-normalizing
time, viral shedding time, and outcome

Table 6 illustrates that 100.0% of patients received Chi-
inese traditional medicine at the early 7 days of infection
detection according to the abovementioned Control Pro-
gram (4) in China. No patients received any kind of
antivirus agents in our study. All the nonmild disease pa-
tients with abnormal thoracic CT features were asked
to take a prone position. As a result, all the patients
(171, 82.2%) with moderate and severe disease assumed
the awake prone position as long as they can (median 12 h
per day).

TABLE 4. COMPARISON OF CT IMAGE RESULTS OF COVID-19 PATIENTS BETWEEN GROUPS BASED ON MONTHS FROM FIRST VACCINE DOSE TO INFECTION DETECTION

| Variable               | Total (n=171) | Unvaccinated (n=13) | <3 months (n=96) | 3–6 months (n=55) | >6 months (n=7) | p   |
|------------------------|--------------|---------------------|------------------|-------------------|----------------|-----|
| Ground-glass opacity   | 164 (95.9)   | 13 (100.0)          | 91 (94.8)        | 53 (96.4)         | 7 (100.0)      | >0.05|
| Consolidation          | 29 (17.0)    | 1 (7.7)             | 15 (15.6)        | 12 (21.8)         | 1 (14.3)       | >0.05|
| Bilateral lung involve | 146 (85.4)   | 11 (84.6)           | 81 (84.4)        | 48 (87.3)         | 6 (85.7)       | >0.05|
| CT score               | 5.0 (2.0–8.0)| 7.0 (3.5–8.5)       | 5.0 (3.0–8.0)    | 5.0 (2.0–9.0)     | 2.0 (0.0–9.0)  | >0.05|

Patients who have abnormalities on CT imaging, namely moderate, severe, and critically ill cases, were included in this analysis.

CT, computed tomography.
### Table 5. SARS-CoV-2 IgM and IgG Levels on the Basis of Different Variables

| Months from first vaccine dose to infection detection (n=195) | Months from second vaccine dose to infection detection (n=187) | Weeks from first to second vaccine dose (n=187) |
|---|---|---|
| | <3 months (n=116) | 3–6 months (n=68) | >6 months (n=11) | <0.5 month (n=25) | 0.5–1 month (n=32) | 1–2 months (n=44) | 2–3 months (n=38) | >3 months (n=20) | <3 weeks (n=51) | 3–8 weeks (n=144) | >8 weeks (n=12) |
| **IgM** | | | | | | | | | | | | |
| Unvaccinated (n=13) | 0.070 (0.047–0.210) | 0.220 (0.120–0.540) | 0.155 (0.099–0.358) | 0.054 (0.024–0.078) | 0.270 (0.171–0.960) | 0.180 (0.120–0.562) | 0.165 (0.095–0.318) | 0.145 (0.100–0.259) | 0.083 (0.055–0.256) | 0.140 (0.110–0.289) | 0.170 (0.100–0.500) | 0.210 (0.067–0.339) |
| IgG (n=28) | 0.063 (0.021–0.615) | 15.925 (5.040–47.034) | 14.040 (4.318–48.878) | 4.940 (0.689–21.440) | 23.470 (6.939–83.220) | 18.620 (4.620–67.269) | 10.000 (4.275–51.777) | 12.720 (4.573–48.799) | 12.240 (1.654–44.807) | 14.270 (3.026–34.960) | 15.680 (4.560–48.660) | 12.095 (3.227–31.320) |
| **IgG** | | | | | | | | | | | | |
| Unvaccinated (n=25) | 0.120 (0.070–0.235) | 0.150 (0.100–0.485) | 0.150 (0.098–0.298) | 0.220 (0.139–2.332) | 0.230 (0.090–0.562) | 0.230 (0.110–0.485) | 0.230 (0.139–2.332) | 0.230 (0.090–0.562) | 0.230 (0.110–0.485) | 0.230 (0.139–2.332) | 0.230 (0.090–0.562) |
| Vaccine brand (n=195) | | | | | | | | | | | | |
| One dose (n=8) | 0.206 (0.110–0.485) | 0.150 (0.071–0.660) | 0.150 (0.098–0.298) | 0.220 (0.139–2.332) | 0.230 (0.090–0.562) | 0.230 (0.110–0.485) | 0.230 (0.139–2.332) | 0.230 (0.090–0.562) | 0.230 (0.110–0.485) | 0.230 (0.139–2.332) | 0.230 (0.090–0.562) |
| Two doses (n=187) | 0.170 (0.100–0.399) | 15.925 (5.040–47.034) | 14.040 (4.318–48.878) | 4.940 (0.689–21.440) | 23.470 (6.939–83.220) | 18.620 (4.620–67.269) | 10.000 (4.275–51.777) | 12.720 (4.573–48.799) | 12.240 (1.654–44.807) | 14.270 (3.026–34.960) | 15.680 (4.560–48.660) | 12.095 (3.227–31.320) |

*p < 0.05, when compared with unvaccinated group; **p < 0.01, when compared with unvaccinated group and >3 months group; ***p < 0.001, when compared with unvaccinated group; *p < 0.05, when compared with unvaccinated group; "p < 0.05, when compared with unvaccinated group.

### Table 6. Therapeutic Approaches, Temperature-Normalizing Time, and Viral Shedding Time of COVID-19 Patients Between Groups Based on Months from First Vaccine Dose to Infection Detection

| Variable | Total (n=208) | Unvaccinated (n=13) | <3 months (n=116) | 3–6 months (n=68) | >6 months (n=11) | p |
|---|---|---|---|---|---|---|
| Therapeutic approaches | | | | | | |
| Chinese traditional medicine, n (%) | 208 (100.0) | 13 (100.0) | 116 (100.0) | 68 (100.0) | 11 (100.0) | >0.05 |
| Awake prone position, n (%) | 171 (82.2) | 13 (100.0) | 96 (82.8) | 55 (80.9) | 7 (63.6) | >0.05 |
| Awake prone position time, hours/per day | 12.0 (12.0–13.0) | 12.0 (12.0–12.5) | 12.0 (12.0–13.0) | 12.0 (12.0–13.0) | 12.0 (12.0–14.0) | >0.05 |
| Low molecular heparin, n (%) | 95 (45.7) | 8 (61.5) | 49 (42.2) | 34 (50.0) | 4 (36.4) | >0.05 |
| Thymosin z1, n (%) | 22 (10.6) | 1 (7.7) | 10 (8.6) | 7 (10.3) | 3 (27.3) | >0.05 |
| Glucocorticoids, n (%)b | 10 (4.8) | 1 (7.7) | 3 (2.6) | 5 (7.4) | 1 (9.1) | >0.05 |
| Neutralizing antibodies injection, n (%) | 24 (11.5) | 4 (30.8) | 9 (7.8) | 8 (11.8) | 3 (27.3) | >0.05 |
| Oxygen supplement, n (%) | 26 (12.5) | 2 (15.4) | 12 (10.3) | 11 (16.2) | 1 (9.1) | >0.05 |
| Nasal cannula, n (%) | 12 (5.8) | 1 (7.7) | 6 (5.2) | 5 (7.4) | 0 (0.0) | >0.05 |
| High-flow oxygen therapy, n (%) | 10 (4.8) | 1 (7.7) | 1 (2.6) | 5 (7.4) | 1 (9.1) | >0.05 |
| Noninvasive ventilation, n (%) | 3 (1.4) | 0 (0.0) | 2 (1.7) | 1 (1.5) | 0 (0.0) | >0.05 |
| Temperature-normalizing time, days | 4.0 (2.0–5.0) | 3.0 (1.3–5.5) | 4.0 (1.0–6.0) | 3.0 (1.5–5.0) | 4.0 (3.0–6.0) | >0.05 |
| Viral shedding time, days | 21.0 (15.0–28.0) | 25.5 (19.5–34.0) | 20.0 (14.0–26.0) | 23.0 (15.0–28.0) | 28.0 (12.0–32.0) | >0.05 |

aAccording to the New Coronavirus Pneumonia Prevention and Control Program published by the Chinese National Health Commission (version 8).
bDexamethasone or methylprednisolone.
acid Ct value regardless of the vaccination status. No critically ill case was found and the number of severe case was also low in COVID-19 patients with vaccination. The SARS-CoV-2 IgG antibody levels were elevated in vaccinated patients at hospital admission. It has been speculated that SARS-CoV-2 vaccination fails to stop the disease occurrence, but it inhibits the disease severity from mild or moderate to the severe or critical.

Compared with SARS-CoV-2 wild-type strains, several variants of concern (VOCs), recently, have emerged and been associated with increased transmissibility, evasion of immunity from infection. The top 3 VOCs were B.1.1.7, B.1.351, and B.1.617.2 (7,9). The last one, B.1.617.2, also known as the Delta variant and first reported in India (10), is now rapidly becoming the dominant strain in several countries owing to its extreme infectiousness.

One study (7) conducted in Singapore concluded that the Delta variant is tightly correlated with elevated disease severity, higher viral load, and longer viral shedding time; 18 patients with the Delta variant infection who were pre-vaccinated had only mild illness, and no one developed pneumonia and required oxygen supplement in their study. In Guangzhou, China, Wang and associates (11) reported that infection with the Delta VOCs had a markedly increased transmissibility, viral loads, and risk of disease progression. For well-controlled COVID-19 pandemic, SARS-CoV-2 vaccine was widely used in the last less than a year.

The most commonly used COVID-19 vaccines globally are inactivated, mRNA, and adenovirus-vector vaccines. Most of the vaccine recipients in China took inactivated vaccine (Vero Cell) inoculation. The inactivated vaccine brands, including Sinovac and Sinopharm, were widely used. As mentioned above, the overall protective efficacy of the vaccine against SARS-CoV-2 infection is ~70% (1,3). Although the vaccination campaign was widely conducted, there are limited data on the clinical manifestations of domestic COVID-19 caused by the Delta VOCs in China. Qiu and coworkers (12) reported 75 imported COVID-19 cases (20 cases vaccinated, 55 cases unvaccinated) in Chengdu, China, demonstrating no differences in virus load, inflammatory biomarkers, and lymphocyte subtypes. Asymptomatic and mild infections were more in vaccinated recipients.

Furthermore, SARS-CoV-2 serum antibodies of IgM and IgG were significantly higher in vaccinated patients. The authors concluded that when the vaccinated person is exposed to the virus, the body can enhance neutralizing antibodies of IgM and IgG, which can protect against SARS-CoV-2 infection, reducing clinical symptoms and inhibiting the disease severity. All the COVID-19 patients originated from domestic China rather than imported in this study.

The results showed that the ratio of severe to critical disease in vaccinated patients was lower in this study than the ratio observed in the early 2020 of Hubei province in our previous study (13). All unvaccinated patients were moderate, no mild disease. But 17.8% of the vaccinated patients had mild disease. No differences in clinical presentation, laboratory findings, virus nucleic acid load, and CT features between the groups based on vaccination status were observed.

The SARS-CoV-2 antibodies, both IgM and IgG, were noticeably increased in vaccinated recipients despite the length of inoculation to infection detection. A total of 11 patients in the >6 months group had a median of 237 days from the first dose to illness onset (the longest one was 266 days). The IgG seems to be slightly decreased in this group, but it remained to be statistically significant as compared with unvaccinated patients. The interval of the first and second dose, vaccination frequency, and vaccine brand appear to have no effect on the IgG levels.

The strength of this study was that some vaccinated patients (11 cases in >6 months) had the vaccination over half years apart from the disease onset, but the vaccine protective efficacy remained since the SARS-CoV-2 IgG antibody levels were higher than those in the unvaccinated patients. The results of this study were consistent with those of the previous studies (7,12) showing the protective efficacy of vaccination against severe disease due to the emerging Delta VOCs, underscoring the necessity of rapid implementation of the vaccination campaign.

The previous study had proved that vaccines induce neutralizing antibodies and block the viral receptor binding domain from binding to the angiotensin-converting enzyme 2 receptors. Against the emerging VOCs, such as the Delta variant, although vaccine showed a reduction in its efficacy, it still protected the patients as human proper T cell can rapidly respond to the virus spike protein when prevaccinated (2,6). The results of this study may be explained by the abovementioned mechanism.

Our study is subject to several limitations. First, since the vaccine campaign is spreading, only a small number of people are currently unvaccinated in China. Only 13 cases (6.25%) were unvaccinated in our study population, which may partly interfere with the interpretation of our conclusion. Second, the SARS-CoV-2 RNA sequencing and VOCs determination were not conducted in this study; we only postulated that the infection might be caused by the Delta variant based on the previous reports (11) in China and the results of VOCs analysis (7) around the world. Third, some important parameters, such as artery gas analysis and T lymphocyte subset, were not detected and analyzed.

In conclusion, this study found that SARS-CoV-2 IgM and IgG antibodies were elevated in vaccinated recipients despite the time of inoculation. It can be speculated that vaccination cannot completely prevent infection by the SARS-CoV-2 Delta variant, but it can protect against disease severity.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Xiamen COVID-19 Designated hospital, China.

Availability of Data and Material

All data generated or analyzed during this study are included in this published article.

Authors’ Contributions

X.-B.Z. and H.-Q.Z contributed to conception and design. S.-J.Y., Y.L., and L.-L.C performed collection and assembly of data. X.-B.Z., Y.-L.Z., and H.-Q.Z performed data analysis and interpretation. All authors contributed to article writing and final approval of the article.
Author Disclosure Statement

No competing financial interests exist.

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