Clinical Features of Imported Chinese COVID-19 Patients Following Chinese Inactivated Vaccines Injection Abroad

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Research Article

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Abstract

Background Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination has been demonstrated as an effective way to reduce the risk of coronavirus disease 2019 (COVID-19), and only a few vaccinees suffered from SARS-CoV-2 infection. However, limited data concerning the clinical features of these vaccinees infected with SARS-CoV-2 can be identified.

Methods We retrospectively collected and analyzed epidemiological and clinical characteristics data of the imported COVID-19 cases who received Chinese inactivated vaccines abroad. Data were extracted from electronic medical records from a designated hospital in the Shaanxi Province of China between March 22 and May 17, 2021.

Results Totally, 46 confirmed SARS-CoV-2 infection patients were enrolled. The mean age was 40.5 years (range 20-61), 41 (89.1%) are male. Eighteen (39.1%) patients were from Pakistan. Fourteen (30.4%) patients had at least one comorbidity. Forty (87.0%) and 6 cases were fully vaccinated and partly vaccinated. The time interval between vaccination and infection was 88 days (IQR, 33-123), 31 (67.4%) and 15 (32.6%) were asymptomatic and symptomatic cases, respectively. Fever (3/46, 6.5%) was the most common symptom; however, none had a body temperature higher than 38.0°C, and no severe case was observed. Notably, the rate of SARS-CoV-2 shedding discontinuation at 7 days after hospitalization in asymptomatic cases was higher than symptomatic one (93.5% vs 40%, $P < 0.0001$).

Conclusions Individuals who received Chinese inactivated vaccines abroad remain have the probability to be infected with SARS-CoV-2, but all the vaccinees infected with SARS-CoV-2 were asymptomatic or had mild symptoms with favorable clinical outcomes.

Introduction

As of May 23, 2021, the coronavirus disease 2019 (COVID-19) pandemic has caused more than 166 million cases and 3.4 million deaths worldwide, including more than 600,000 cases and 10,000 deaths per day after April 2021[1]. Unfortunately, the numbers of both infected patients and fatalities are still growing, and no special efficient drugs are clinically approved. Although social distance, quarantine, isolation and lockdown restrictions were effective in limiting the infection and spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in a short period, they are not the long-term solution. The absence of immunity in the population leaves them susceptible to further waves of SARS-CoV-2 infection. Effective and safe vaccines are urgently needed for the global epidemic control of COVID-19. To date, several vaccine types, such as RNA vaccines, inactivated vaccines, adenovirus-vectored vaccines, protein subunit vaccines, and virus-like particle vaccines, have been developed or approved to be used urgently [2–6]. And these vaccines have shown favorable safety and tolerability. They induced high neutralizing antibodies levels against SARS-CoV-2 in the phase 1/2 trials and were highly effective in the prevention of both asymptomatic and symptomatic SARS-CoV-2 infection in phase 3 clinical trials and real-world study [7–15]. However, the production of neutralizing antibodies cannot completely protect individuals from the SARS-CoV-2 infection, especially with the emergence of mutant virus strains, vaccine breakthrough infection has been reported [16].

China has well-controlled the epidemic of COVID-19 from May 2020, and the focus of epidemic prevention and control has been on the management of imported cases since that time. As an important city in Northwest China, the city of Xi'an is one of the key entry sites for international flights, facing the pressure of huge imported infection cases. The Chinese government requires all immigrants to undergo routine nasal swabs nucleic acid screening, which has allowed for the detection of asymptomatic and symptomatic SARS-CoV-2 infections, including individuals who completed vaccination. Currently, China has five vaccines, including three inactivated vaccines, one adenovirus-vectored vaccine and one recombinant protein vaccine, which have been approved to carry out phase 1/2/3 clinical studies in China, Brazil, Chile, Middle East countries, Pakistan and Turkey. They have been widely licensed in more than 80 countries worldwide. Further, the Chinese government has developed strategies to speed up vaccination, and there is more than 700 million doses of vaccine have been delivered as of June 4 in China.

A recent double-blind, randomized, phase 3 study performed in four Middle East countries has revealed that two inactivated SARS-CoV-2 vaccinations produced by the China National Biotech Group Company Limited significantly reduced the risk of symptomatic COVID-19 in adults [17]. In this study, a total of 47 symptomatic COVID-19 cases and 26 asymptomatic cases were identified among 25440 participants who received two doses of vaccines. However, the detailed clinical characteristics of these symptomatic and asymptomatic COVID-19 cases after injection of inactivated COVID-19 vaccines are rare to date. The current study intends to fill this knowledge gap from a unique aspect of imported Chinese COVID-19 cases who injected the Chinese inactivated COVID-19 vaccines in the Middle East and other countries.

Methods

Study design and participants

The Chinese government stipulates all passengers abroad entering China mainland, including Xi'an City, should conduct pharyngeal swab nucleic acid screening and should be centralized quarantined and (or) treated in a designated hospital, and The Eighth Hospital of Xi'an City is the only location in Shaanxi Province. This retrospective, single center, observational study included consecutive hospitalized patients receiving at least one dose vaccine who were confirmed SARS-CoV-2 infection between March 22 and May 17, 2021, in The Eighth Hospital of Xi'an City, Shaanxi Province, China.

As the most important port of entry in Northwest China, Xi'an City has continued to have imported cases. Passengers with positive results of SARS-CoV-2 RNA in the first screening were sent to our hospital for isolation, and the second specimens were then sent to the Centers for Disease Control and Prevention of Shaanxi Province or Xi'an City for reconfirmation. SARS-CoV-2 infection was diagnosed based on two times positive SARS-CoV-2 in the throat swab specimens from the upper respiratory tract with or without positive SARS-CoV-2 IgM and/or IgG according to new coronavirus pneumonia prevention and control program (8th Edition) in China [18]. All patients received the third SARS-CoV-2 RNA tests 7 days after hospitalization. The diagnostic reagents of RT-PCR were provided by the four companies (Beijing Applied Biological Technology, Shanghai Zhijiang Biotechnology, Shanghai BioGerm Medical Biotechnology and Shanghai Huirui Biotechnology). The procedures of specimen pretreatment, RNA extraction, RT-PCR reaction conditions and results interpretation were strictly followed the manufacturers' instructions.

Asymptomatic infection was defined as an individual with laboratory-confirmed SARS-CoV-2 infection who reported no fever and no respiratory symptoms, as well as normal chest CT findings [18]. Symptomatic infection was defined as an individual with laboratory-confirmed SARS-CoV-2 infection who reported symptom or abnormal Chest CT findings [18]. Full vaccination was defined as an individual who has been received the second dose of vaccine for more than 14 days. For patients who only received one dose of the vaccine, received two doses of the vaccine in one time or completed the second dose of vaccine for less than 14 days were defined as partly vaccinated. The time interval of vaccination to infection was defined as the period between the last dose of vaccination to confirmed SARS-CoV-2 infection.

Data Collection

Data were extracted from the electronic medical records by pre-designed case report form. We extracted the vaccination, demographic, epidemiological, clinical, laboratory, management, and outcome data of patients. We directly communicated to patients if data were missing from the records or clarification was needed. All data were checked by two physicians.

Statistical analysis

Data are presented as the mean and standard deviation or median (interquartile range, IQR) for continuous variables and as absolute and relative frequencies for categorical variables. The data in two groups were compared using Student *t*-test, Mann-Whitney U test, χ^2 test, or Fisher's exact probability method, as appropriate. Analyses were carried out using SPSS statistical software, version 18.0 (IBM, Chicago, IL, USA). A *p*-value of < 0.05 was set as the threshold for statistical significance.

Ethics Approval

The protocol of this retrospective multicenter study was in compliance with the Helsinki Declaration and was approved by the Institutional Review Board of The Eighth Hospital of Xi'an City, Xi'an Jiaotong University. The study was exempted from the requirement for informed consent because of the retrospective design and deidentified individuals.

Results

Demographics and clinical characteristics at baseline

Totally, 46 consecutively vaccinated patients were included and analyzed in this study. The mean age was 40.5 years (range 20–61), 41 (89.1%) are male. All patients have exposed to COVID-19 family members or patients. Forty-five patients were imported cases, and the remained one was health care worker in our hospital and was the first reported COVID-19 patient after vaccination in China. Eighteen (39.1%) of them from Pakistan, followed by Sudan, United Arab Emirates, Uzbekistan, Serbia, Tajikistan, Kyrgyzstan and Nigeria (Table 1, Table S1). Fourteen (30.4%) patients had at least one comorbidity, including hypertension, diabetes, respiratory system diseases, etc. (Tables 1, 2).

Table 1
Baseline characteristics of patients with SARS-CoV-2 infection after vaccination

Demographic and clinical features	Overall patients (N = 46)
Sex, male	41/46 (89.1%)
Age, years	40.5 ± 9.8
Chinese Han ethnicity	46/46 (100%)
BMI	24.3 ± 2.7
Smoking	13/46 (28.3%)
Vaccination	
Fully vaccinated	40/46 (87%)
Partly vaccinated	6/46 (13%)
The time interval of vaccination to infection	88 (33–123)
Expose to COVID-19 family members or patients	46/46 (100%)
Source countries of imported cases (n, %) (N = 45)	
Pakistan	18/46 (39.1%)
Sudan	10/46 (21.7%)
United Arab Emirates	9/46 (19.6%)
Uzbekistan	3/46 (6.6%)
Others (Serbia/Tajikistan/Kyrgyzstan/Nigeria)	5/46 (10.9%)
Chronic comorbidity	
Hypertension	6/46 (13%)
Diabetes	3/46 (6.6%)
Respiratory diseases	3/46 (6.6%)
Gastrointestinal diseases	2/46 (4.4%)
Sinusitis	2/46 (4.4%)
Signs and symptoms	
Fever, ≥ 37.3°C	3/46 (6.6%)
≥ 38.0°C	0/46 (0%)
Cough	3/46 (6.6%)
Dry cough	1/46 (2.2%)
Productive cough	2/46 (4.4%)
Fatigue	2/46 (4.4%)
Pharyngalgia	1/46 (2.2%)
Headache	1/46 (2.2%)
Myalgia	1/46 (2.2%)
Shortness of breath	0/46 (0%)
Note: Data are presented as the mean ± SD or median (IQR), n (%) or n/N (%),	
BMI: body mass index CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; ULN: upper limit of normal.	

Demographic and clinical features	Overall patients (N = 46)
Anorexia	0/46 (0%)
Diarrhoea	0/46 (0%)
≥two above-mentioned signs or symptoms	4/46 (8.8%)
Laboratory testing	
ALT (U/L; normal range 0–41)	6/46 (13.0%), 24.5 ± 12.8
AST (U/L; normal range 0–37)	11/46 (23.9%), 29.2 ± 19.2
LDH (U/L; normal range 115–220)	4/46 (8.8%), 170.9 ± 45.1
Creatine kinase (U/L; normal range 24–190)	3/46 (6.5%), 123.8 ± 170.1
CRP (mg/L; normal range 0–8)	6/46 (13.0%), 4.8 ± 5.6
ESR (mm/h; normal range 0–15)	18/46 (39.1%), 18.6 ± 17.5
D-dimer (mg/L; normal range 0–0.4)	0/46 (0%), 0.15 ± 0.18
Increased procalcitonin	2/46 (4.4%)
Chest CT findings	
Normal	32/46 (69.6%)
Unilateral pneumonia	6/46 (13.0%)
Bilateral pneumonia	8/46 (17.4%)
Multiple mottling and ground-glass opacity	7/46 (15.2%)
Pleural effusion	0/46 (0%)
Remission time of imaging abnormalities (days, N = 14)	7 (6–8)
SARS-CoV-2 shedding period (Negative on 7th day)	35/46 (76.1%)
Note: Data are presented as the mean ± SD or median (IQR), n (%) or n/N (%),	
BMI: body mass index CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; ULN: upper limit of normal.	

Table 2
Demographic and clinical characteristics of SARS-CoV-2 patients with fully and partly vaccinated

Demographic and clinical features	Fully vaccinated (n = 40)	Partly vaccinated (n = 6)	P value
Sex, male	37 (80.4%)	4 (66.7%)	0.12
Age, years	41 (34–48)	38 (30–51)	0.995
BMI	24.3 ± 2.7	24.1 ± 3.4	0.977
Smoking	11 (27.5%)	2 (33.3%)	1.000
Symptomatic infection	13 (32.5%)	2 (33.3%)	1.000
The time interval of vaccination to infection	66 (30–108)	228 (165–256)	0.000
At least one comorbidity	11 (27.5%)	3 (50%)	0.521
At least one sign or symptom	6 (15%)	1 (16.7%)	1.000
Increased ALT	5 (12.5%)	1 (16.7%)	1.000
Increased AST	9 (22.5%)	2 (3.3%)	0.947
Increased LDH	3 (7.5%)	1 (16.7%)	0.440
Increased creatine kinase	3 (7.5%)	0 (0%)	1.000
Increased CRP	5 (12.5%)	1 (16.7%)	1.000
Increased ESR	15 (37.5%)	3 (5%)	0.891
Increased procalcitonin	1 (2.5%)	1 (16.7%)	0.246
Abnormal Chest CT findings	12 (35.7%)	2 (33.3%)	1.000
Virus shedding period (Negative on 7th day)	31/40 (77.5%)	4/6 (66.7%)	0.947
Note: Data are presented as the mean ± SD or median (IQR), n (%) or n/N (%), BMI: body mass index CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; ULN: upper limit of normal.			

Table S2

Demographic and clinical characteristics of asymptomatic and symptomatic SARS-CoV-2 infections after vaccination

Demographic and clinical features	Asymptomatic infection (n = 31)	Symptomatic infection (n = 15)	p value
Sex, male	28 (90.3%)	13 (86.7%)	1.000
Age, years	42 (34–47)	36 (33–53)	0.319
BMI	24.3 ± 2.7	24.3 ± 2.9	0.979
Smoking	11 (35.5%)	2 (13.3%)	0.224
Fully vaccinated	27 (87.1%)	13 (86.7%)	1.000
The time interval of vaccination to infection	65 (30–123)	98 (57–153)	0.555
At least one comorbidity	9 (29.0%)	5 (33.3%)	1.000
At least one sign or symptom	0 (%)	7 (46.7%)	0.001
Increased ALT (> ULN)	2 (6.5%)	4 (26.7%)	0.149
Increased AST (> ULN)	6 (19.4%)	5 (33.3%)	0.501
Increased LDH (> ULN)	3 (9.7%)	1 (6.7%)	1.000
Increased creatine kinase (> ULN)	1 (3.2%)	2 (13.3%)	0.244
Increased CRP (> ULN)	3 (9.7%)	3 (20%)	0.612
Increased ESR (> ULN)	10 (32.3%)	8 (53.3%)	0.170
Increased procalcitonin	1 (3.2%)	1 (6.7%)	1.000
Abnormal Chest CT findings	0 (%)	14 (93.3%)	0.000
Virus shedding period (Negative on 7th day)	29/31 (93.5%)	6/15 (40%)	0.000
Note: Data are presented as the mean ± SD or median (IQR), n (%) or n/N (%).			
BMI: body mass index CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; ULN: upper limit of normal.			

All patients received inactivated vaccines, 23 (50%) cases with SARS-CoV-2 Vaccine (Vero Cell) (China National Pharmaceutical Group, Beijing, China), 13 (28.3%) cases with CoronaVac (Sinovac Life Sciences, Beijing, China) and 10 (21.7%) with BIBP-CorV (Beijing Institute of Biological Products, Beijing, China). Forty (87.0%) patients were fully vaccinated, the remaining six patients were partly vaccinated. With the exception of the longer interval between vaccination and infection, no significant differences in the sex, age, BMI, smoking, the rate of symptomatic infection, laboratory testing, chest CT findings and SARS-CoV-2 shedding period were found between the patients who were fully and partly vaccinated (Table 2). The time interval between vaccination and infection was 88 days (IQR, 33–123), 23 (50%) patients infected SARS-CoV-2 more than 90 days after the vaccination, and six patients infected after more than 210 days of vaccination (Fig. 1).

Of the 46 patients, 31 (67.4%) and 15 (32.6%) were asymptomatic and symptomatic infection, respectively. In addition to the symptoms and chest CT findings, which are two important indicators to distinguish the asymptomatic and symptomatic infections, no difference was observed in demographic and clinical characteristics in both groups. Notably, the SARS-CoV-2 shedding period was shorter in asymptomatic cases (Table S2). Of the 15 patients with symptomatic infection, all were mild or moderate COVID-19. Fever (3/46, 6.5%) was the most common symptom; however, none of them higher than 38.0°C, followed by cough (3/46, 6.5%), fatigue (2/46, 4.3%), myalgia (1/46, 2.2%), pharyngalgia (1/46, 2.2%), headache (1/46, 2.2%). Four patients had at least two above-mentioned symptoms; no patient presented shortness of breath (Table 1).

Laboratory Characteristics

On admission, 6 (13.0%) and 11 (23.9%) patients had elevated levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), respectively. Six (13.0%) patients had abnormal myocardial zymogram included the elevations of lactate dehydrogenase (LDH) and creatine kinase in 4 and 3 patients, respectively. Eighteen (39.1%) and 6 (13.0%) patients had erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) exceeding the upper limit of the normal range, respectively. Only 2 (4.3%) patients had increased procalcitonin and no patient with increased D-dimer (Table 1).

Radiological Characteristics

Of the 46 confirmed cases, 14 (93.3%) of the 15 symptomatic infections had pneumonia manifestation on CT examination on admission. For the 14 patients who had pneumonia imaging findings, 6 (42.9%) cases had unilateral pneumonia, 8 (57.1%) had bilateral pneumonia, 7 (50.0%) had multiple mottling and ground-glass opacity, and no patient had pleural effusion (Table 1). The median remission time of abnormal chest imaging was 7 days (IQR, 6–8). And the representative chest CT images of one mild and one 'most severe' patients with moderate COVID-19 were presented in Fig. 2.

Treatment And Prognosis

For the management of the patients, all received combination antiviral treatment with Arbidol Hydrochloride Tablets (200 mg every 8 hours, orally for 10 days) and interferon α (2 times every 24 hours, aerosol inhalation for 7–10 days). For the 15 symptomatic infections, additional traditional Chinese herbal medicine Lianhua Qingwen granules were prescribed for 5–10 days, and two patients have given Cefixime and Cefoperazone treatment for 3 and 5 days, respectively. One patient received Methylprednisolone at a dose of 40mg for 7 days, and none needed intravenous immunoglobulin therapy. Four (8.8%) patients received low-flow nasal cannula for 2–3 days; no patient required non-invasive ventilation or high-flow nasal cannula. No patients developed severe illnesses or needed ICU care, or died. And all patients have recovered uneventfully.

Discussion

Currently, the phase 3 trial concerning the efficacy of two Chinese inactivated SARS-CoV-2 vaccines on symptomatic COVID-19 infection in adults has been released on May 26, 2021, and found that 72.8% (95% CI, 58.1%-82.4%) of vaccinees in WIV04 vaccine group and 78.1% (95% CI, 64.8%-86.3%) of vaccinees in HB02 vaccine group acquired immunity against COVID-19 during a median (range) follow-up duration of 77 (1-121) days [17]. Notably, 26 vaccinees were identified as symptomatic COVID-19 after WIV04 vaccine injections, 21 vaccinees were identified as symptomatic COVID-19 after HB02 vaccine injections, the corresponding incidence rate (per 1000 person-years) was 12.1 (95% CI, 8.3–17.8) in the WIV04 group, and 9.8 (95% CI, 6.4–15.0) in the HB02 group. Additionally, a total of 26 asymptomatic cases of COVID-19 were diagnosed 14 days following the second dose (16 in the WIV04 group, 10 in the HB02 group) [17]. However, no study reported detailed information of clinical manifestations and prognosis of patients after Chinese inactivated vaccination. To the best of our knowledge, the current study is the first observational cohort to investigate Chinese imported COVID-19 patients after injection of Chinese inactivated vaccines abroad. Our results showed that the vaccine protection could last at least 8–9 months. The vaccinated patients infected with SARS-CoV-2 experienced slighter clinical manifestations when historically compared with previous local COVID-19 cases in early 2020 [19, 20]. Furthermore, our results were different with the previous study included non-vaccinated patients that showed imported cases were more severe than local cases [21].

In the current study, more than two-thirds of patients were asymptomatic infection, and for symptomatic infections, all of their symptoms were mild, no patient presented fever more than 38.0°C, shortness of breath or required high-flow nasal cannula, despite four patients received low-flow nasal cannula due to slightly reduced oxygenation. All symptomatic infections were diagnosed as mild or moderate COVID-19, and no cases were severe, required ICU care or death. Furthermore, the SARS-CoV-2 shedding period was short, and 76% of patients with negative SARS-CoV-2 on the seventh day of hospitalization. The chest CT abnormalities of symptomatic infection patients were also mild, 7 (46.7%) of them only unilateral lung involvement or no abnormalities. Although one patient was given glucocorticoid treatment for chest CT imaging progress with decreased blood oxygenation after hospitalization, the median time of imaging recovery was only 7 days.

Vaccinations have shown to be highly effective in preventing SARS-CoV-2 infections, COVID-19-related hospitalizations, severe diseases, and death [10, 15]. The latest evidence indicated that no severe COVID-19 cases were identified after receiving the Chinese inactivated vaccines, which means an efficacy of 100% against severe COVID-19 [17]. Previous studies showed that chronic

comorbidity and high BMI were the risk factors of severe COVID-19, requiring ICU care or death [20, 22]. In the current study, no severe COVID-19 cases were identified. Furthermore, the chronic comorbidity and high BMI did not present any risk to contribute the individuals to develop to symptomatic infection other than asymptomatic infection. Additionally, the SARS-CoV-2 shedding period was not different in patients with or without chronic comorbidity or high BMI. These results suggest that even people with a high risk of exacerbation before SARS-CoV-2 infection, such as chronic comorbidity or high BMI, may benefit more from vaccination. Since vaccines, especially inactivated vaccines, are safe and well-tolerated, priority should be given to these high-risk population.

Immunization after infection can obtain the same protection as vaccination, with up to 90% protection against reinfection [7, 9, 10, 23]. The risk of SARS-CoV-2 infection after vaccination always have an overall higher probability of exposure to SARS-CoV-2, such as health care workers or individuals who closely contact with COVID-19 patients [9, 12]. All the patients in our study closely contacted with COVID-19 cases, suggesting that social distance and masks are still needed to prevent infection even after vaccination. More than two-thirds of the patients were asymptomatic infection, so it further emphasized the need for consecutive testing of the population who were fully vaccinated and exposed to confirmed COVID-19 patients. Furthermore, strengthening the management of these asymptomatic infections is also an important measure to prevent the spread of SARS-CoV-2 and then control the COVID-19 pandemic.

The durability of the vaccine-induced immunity protection against infection remains unknown because too little time has elapsed since the start of the vaccination campaign. Studies showed that robust neutralizing antibodies against SARS-CoV-2 re-infection in previous COVID-19 patients could maintain up to 6–12 months [23–26]. In the current study, the median interval between vaccination and infection was 88 days, and more than 210 days in 6 patients, including 4 partly vaccinated patients, a fully vaccinated individual who received inactivated vaccine may obtain longer-term immune protection. These results were similar or better than the previous reports that showed a protective effect of the vaccine might persist after 6 months of full vaccination [10, 14]. The decrease of neutralizing antibody titer may be one of the reasons for infection after vaccination; further dynamic monitoring studies are needed.

The current study has several limitations. First, only 46 cases were retrospectively included in this single center hampered us to observe potential severe COVID-19 cases among vaccinee. However, according to the latest Chinese inactivated vaccine study abroad, no severe case was identified among 25440 participants who injected the Chinese inactivated vaccines; therefore, it is normal that we did not observe any severe case in the current study. Second, these early vaccinees were all Chinese Han adults aged 18–59 years; our case series do not include the patients aged more than 60 or less than 18. Future studies need to assess the risk of post-vaccination SARS-CoV-2 infection and the disease severity in various populations, including older people and children, as well as ethnic and geographical diversity. Third, potential sources of bias may exist in this study since these imported cases from 8 countries distributed in Asia, Africa and Europe. However, they were all Chinese Han population and used inactivated vaccine may largest extent offset this deviation. Fourth, concerns have emerged regarding the breakthrough infections implies that the virus broke through a protective barrier provided by the vaccine [16, 27]. We had not performed the examination of the SARS-CoV-2 sequences and neutralizing antibody titers, thus we cannot clarify the infection due to suboptimal immune responses to the vaccines or breakthrough infections with SARS-CoV-2 variants, especially 59% patients from West Asia and South Asia where the mutant virus strain is high prevalence. Despite these limitations, our findings are important in understanding and filling the gap of the clinical characteristics in a significant number of Chinese COVID-19 patients who received Chinese inactivated vaccines abroad because there only 73 asymptomatic and symptomatic cases among 25440 participants who injected the Chinese inactivated vaccines according to the latest study [17].

In conclusion, our study indicated a potential risk of SARS-CoV-2 infections even after successful vaccination with Chinese inactivated vaccines. However, most patients present no clinical symptoms or clinically mild symptomatic COVID-19, and a shorter SARS-CoV-2 shedding period when compared to the patients in early 2020 in our previous study [20]. These observations in no way undermine the importance of the urgent efforts to vaccinate the population. Instead, it emphasizes the importance of vaccines in reducing the severity of the disease, and meanwhile, supports maintaining social distance and wearing masks to reduce the risk of reinfection even after vaccination in current circumstances.

Abbreviations

COVID-19, Coronavirus disease 2019; SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; IQR, interquartile range; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; ULN upper limit of normal.

Declarations

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Not applicable.

Authors' contributions

YLG, FPJ, and QLZ designed the study, and YLG and FPJ had full access to all data in the study. JWL, NJ, YZ, YC, WNJ, YL, WS, MY, WHH, LM, YX, YLG and FPJ collected the epidemiological and clinical data. JWL, NJ, QLZ, YZ, YL, LZ and FPJ analysis the data. JWL, FPJ and QLZ drafted the manuscript. YLG, LZ and FPJ revised the final manuscript. All authors reviewed and approved the final version of this manuscript.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

The protocol of this retrospective multicenter study was in compliance with the Helsinki Declaration and was approved by the Institutional Review Board of The Eighth Hospital of Xi'an City, Xi'an Jiaotong University. The study was exempted from the requirement for informed consent because of the retrospective design and deidentified individuals.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

The time interval between vaccination and infection in patients with SARS-CoV-2 infection. Patient number color in red was symptomatic infection and number in black was asymptomatic infection. * Patient with partly vaccinated.

Figure 2

Representative chest CT images of two confirmed COVID-19 patients. A 34-years-old male with mild COVID-19. (A) Chest CT images showing right lung small patchy shadows on admission. (B) The chest imaging alleviated on the third day after admission. (C) Chest CT images complete remission 7 days after admission. A 30-years-old male with moderate COVID-19. (D) Chest CT images showing bilateral ground-glass opacity and patchy shadows on admission. (E) The chest imaging was aggravated, accompanied by vascular shadow and bronchiectasis in the focus on the third day after admission. (F) Chest CT images showing bilateral ground-glass opacity and patchy shadows was improved and the inflammatory exudation was absorbed 20 days after admission.

Supplementary Files

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- [IDOPSupplementarytable10608Final.xlsx](#)