The imaging and clinical characteristics of patients with immune breakthrough Omicron-variant infected patients, Tianjin China: Is the vaccine effective?

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Research Article

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Abstract

Background

The protective effect of the inactivated vaccine against the omicron variant of COVID-19 is unclear. The purpose of this study was to investigate the protective effect of different vaccination status on omicron infection.

Methods

In this retrospective study, we analyzed patients over 14 years old, and were diagnosed with immune breakthrough Omicron-variant infection between December 2021 and February 2022 in Tianjin, China, as well as data from several previous study infected by other types of SARS-CoV-2. The data were subdivided into three groups: patients with fully, partially and unvaccine. Differences of clinical and imaging characteristics were compared based on the different vaccination status using Pearson Chi-square test, Fisher's accuracy test and non-parametric test. All of the data were also compared with other types of SARS-CoV-2. Logistic regression and mediation effect analysis were used to assess the association between vaccination status and pneumonia progression during hospitalization.

Results

Among the 314 cases of immune breakthrough Omicron-variant infected patients, 21(7%) patients were unvaccinated, 134 (43%) were partially vaccinated, and 159 (50%) were full vaccinated. Among fully vaccinated patients, the proportion of patients with positive CT findings (32%) and CT score 2 (6%) was significantly lower than that of partially vaccinated (46%, 14%) and unvaccinated patients (67%, 19%) ($P < 0.05$). CT score by vaccination status are similar between Omicron and other types, only partially vaccinated group of Omicron infected patients show lower CT score than other types infected patients ($P = 0.005$). Increased age and lower IgG levels were associated with the risk of disease progression. IgG level had a complete mediating effect between vaccination status/ days after vaccination and disease progression.

Conclusion

The inactivated vaccine provided similar protection against Omicron infection of SARS-CoV-2, compared to the patients who received other types vaccines. Compared with partially vaccinated and unvaccinated patients, fully vaccinated patients had a higher CT negative rate and a lower rate of severe pneumonia. Vaccination status and days after vaccination affect disease progression through IgG levels.

Introduction

Since the first case was reported in late 2019, the original SARS-CoV-2, the Beta, and the Delta variants caused multiple waves of infection that have swept more than 200 countries and territories around the world[1]. The outbreak of SARS-CoV-2 declared a global health emergency by the World Health Organization. The current global epidemiology of SARS-CoV-2 is characterized by the global dominance of the Omicron variant. As of early March 2022, the number of confirmed cases worldwide exceeds 433 million and total deaths exceed 5.9 million (1.3%), have led to a horrible medical and economic disaster for the world[2].

For the clinical and imaging features of the Coronavirus Disease 2019 (COVID-19) patients, multiple previous studies have reported that there are differences in imaging findings among patients with different clinical types and stages[3, 4]. Omicron mutation causes mild clinical symptoms than Delta, but CT features have not been reported in Omicron infection. There was little knowledge about the similarities and differences of clinical and imaging characters among different variants of SARS-CoV-2.

Vaccines are the most important tools in controlling the spread of SARS-COV-2. Now, multiple SARS-COV-2 vaccines such as inactivated vaccine, recombinant protein vaccine, adenovirus vector vaccine, DNA vaccine and RNA vaccine have been developed, and these vaccines achieved up to 95% vaccine efficacy (VE) in clinical trials[5, 6]. However, the variations of the virushas reduced VE to varying degrees. The VE of ChAdOx1 nCoV-19 vaccine against the B.1.351 variant declined from 89.3–21.9% in a phase 3 trial[7], In another cohort study, VE for the inactivated vaccine against the B.1.617.2 (Delta) variant dropped to 51.8%[8]. The B.1.1.529 variant (Omicron) discovered in South Africa in November 2021, it's spike proteins has more than 50 mutations, of which the virus' spike protein has 26–35 amino acids that are different from the original SARS-CoV-2 virus or the Delta[9], has been shown to be highly contagious, and can neutralize antibodies produced by previous infections or vaccines[10]. Because the Omicron variant carry more mutations, it significantly reduced the VE of vaccines, even though vaccination can reduce the severity of the disease and mortality rates[11]. The study about the values of vaccines on the clinical and imaging characters needs further study.

Since December 2021, there have been Omicron-variant related outbreaks in Tianjin, China, most patients are immune breakthrough. Breakthrough infection is defined as a positive test of SARS-CoV-2 in the vaccinated person more than 14 days after completion of vaccination. According to China's COVID-19 Diagnosis and Treatment Protocol (Ninth Edition), positive computed tomography (CT) findings determine the need for hospitalization[12]. Besides, chest CT is an important tool in evaluating the severity of pneumonia. The purpose of this study was: first, to compare the clinical and radiographic characteristics of patients infected with SARS-COV-2 Omicron variant, with those patients with other types of SARS-COV-2 infection. Second, to investigate the value of different vaccination status on the appearances and difference of imaging features and laboratory results among patients, and compare with Omicron variant immune breakthrough patients. And finally, the progress of chest CT manifestations during hospitalization was compared to determine the effect of vaccination on preventing the progression of pneumonia.

Methods And Materials

Study population

430 COVID-19 patients confirmed in Tianjin Haihe Hospital and Tianjin First Central Hospital between 2021.12 and 2022.2.2 were confirmed according to COVID-19 Diagnosis and Treatment Protocol (Ninth Edition) of the National Health Commission of the People's Republic of China. Inclusion criteria include the following: (1) Native Omicron variant infected; (2) Age over 14 years; (3) Chest CT examination was performed; (4) Complete clinical data are available. Patients with other inflammatory lung infections were excluded. All of them were followed up until they were discharged from hospital. The criteria for discharge include the following: (1) The patient's temperature returned to normal for more than 3 days; (2) The patient's respiratory symptoms improved significantly; (3) Chest imaging showed marked improvement in acute exudative lesions; (4) Negative nucleic acid tests of sputum, nasopharyngeal swabs and other respiratory specimens for 2 consecutive times (sampling intervals of at least 24 hours)[12]. Other types of SARS-COV-2 cases came from a published research that included chest CT images as well as general clinical information. In this multicenter retrospective study, with the approval of the ethics committee, the patient informed unification is abandon. The work flow show in Figure 1.

Figure 1. Workflow of the study

CT Scan protocol

Two different CT scanners were used to scan 314 patients. including Siemens Go-Top and Toshiba Canon 64-slice CT scanner, both the two scanners was used with the following parameters: 1.0mm section thickness, 5mm gap, 120kV tube voltage and adaptive tube current. The patient was examined in supine position, range was from the apex of the lung to the lower margin of the diaphragm.

After admission, CT examination is determined by the clinician according to the clinical situation. All of 314 cases completed their chest CT scans within 3 days after their initial symptoms or nucleic acid test results are positive. We follow up patients until they are discharged. The CT images were displayed with standard lung (window width, 1000 to 2000 HU; window level −700 to – 500 HU) and mediastinal (window width 300 to 400 HU; window level 30 to 50 HU) for save and view.

Imaging studies and analysis

Chest CT scan results of each patient during hospitalization were obtained including information of baseline, negative to positive, peak lesion and discharged CT data of each patient. All CT images were evaluated by two radiologists with 5 and 10 years of experience, respectively, without knowing the clinical data and consensus was reached through discussion when differences arise. The severity and image characteristics of pneumonia in all examinations were analyzed. The severity was graded according to the affected area between 0 to 2. No significantly involved was 0, less than 25% involved was 1, more than 25% involved was 2. The morphological features include stripe, consolidation, ground-glass opacity(GGO), thickened pleura, crazy paving sign, bronchiolitis. Standard vocabulary for chest imaging based on Fleischner Society reports[13]. GGO referred to an area of increased attenuation that did not obscure the underlying pulmonary vessels or bronchi and was classified as round or patchy· Consolidation referred to an area of increased attenuation in the lung that obscured the underlying pulmonary vessels. Crazy paving sign was defined as an irregular line or band with a high-attenuation pattern. Bronchiolitis was defined as tree-in-bud sign, central lobular nodules and thickening of bronchiole wall. Distribution characteristics include subpleural, peribronchovascular, and diffuse. (Figure 2)

Figure 2. Chest CT findings of COVID-19 pneumonia on axial images. (A) GGO; (B) Consolidation; (C) Crazy-paving pattern; (D) Interlobular and/or intralobular septal thickening; (E) Subpleural lines; (F) bronchiolitis.

Clinical and laboratory data

All of the electronic medical records were reviewed. Patient demographics (including age and gender), height and weight were used for calculating body mass index (BMI), the initial symptoms (including fever, cough, myalgia, sore throat, loss of sensory, weak, rhinorrhea), previous comorbidities, (including diabetes, hypertension, heart cerebrovascular disease, chronic lung disease), vaccination characteristics (including the type of vaccine, dose, the time interval between the last vaccination and infection) were recored. Unvaccinated individuals were defined as those who tested positive for COVID-19 by reverse transcription-polymerase chain reaction (RT-PCR), had no record of COVID-19 vaccination, or were diagnosed with COVID-19 <14 days after receiving the first dose of vaccine. Partially vaccinated individuals were defined as those who tested positive for COVID-19 by RT-PCR ≥14 days after receiving the first or second dose of vaccine and prior to receiving the third dose. Fully vaccinated individuals were defined as having tested positive for COVID-19 by RT-PCR ≥14 days after the third dose of vaccine. Laboratory tests obtained within 1 day of the corresponding date of the chest CT scan were recorded. Including blood routine examination (white blood cell count,

lymphocyte count, neutrophil count, blood platelet count) inflammatory markers (C-reactive protein, erythrocyte sedimentation rate, procalcitonin and interleukin-6) and antibody (IgM, IgG).

To compare the imaging findings and clinical characteristics of the immune breakthrough, we compared them with a published multicenter research that included 761 patients from July to August 2021[14]. But the study did not mention the type of SARS-CoV-2.

Statistical analysis

SPSS (SPSS, IBM SPSS Statistics, Armonk, New York, USA) were used for statistical analysis. The classification variables are expressed by frequency and percentage, statistical assessment of differences between groups was performed using Pearson Chi-square test or Fisher's exact test (sex, comorbidities, smoking history, symptoms, laboratory findings, three-point scales of CT scores and vaccination characteristics). Continuous variables are represented by mean and standard deviation if they follow a normal distribution, non-normally distributed continuous variables are represented by median and inter-quartile range, Mann-Whitney U and Kruskal-Wallis H test were used for comparison between groups. Associations between vaccination status and clinical factors were assessed using a multivariate logistic retrospective analysis. The relationship between vaccine characteristics, IgG levels and disease progression was tested by mediating effect model. P<0.05 on both sides was considered statistically significant.

Results

Patient vaccination status and breakthrough infections

Regarding vaccination status among the 314 patients, 21(6.6%) were unvaccinated, 136 (42.6%) were partially vaccinated and 159 (50.8%) were fully vaccinated. Time between final vaccination and diagnosis was 127 ± 80 days. About the type of vaccine, most(242,77%) received the inactivated vaccine, followed by 49 (16.1%) received the adenovirusvector vaccine, 2 (0.6%) received the recombinant vaccine. Of the patients with breakthrough infection, 94 (70.4%) received the inactivated vaccine, 17 (14.7%) received the adenovirusvector vaccine, and 2 (1.7%) received the recombinant vaccine.

Proportions of chest CT scores and imaging features by vaccination status

Chest CT examination results of 314 patients over 14 years old were shown in Table 1. About patients who had a score 0, 7 (33.3%) were unvaccinated patients, 72 (53.7%) were partially vaccinated patients, and 108 (67.9%) were fully vaccinated patients. The proportion of score 0 CT scans was higher in the fully vaccinated group than in the unvaccinated group (*P*=0.024). Among patients with CT scores 1, the proportion of patients in the unvaccinated group was higher than that in the partial vaccinated group and the fully vaccinated group, but the difference was not statistically significant (P=0.091). Among patients with CT scores 2, the proportion of unvaccinated patients and partially vaccinated patients was significantly higher than that of fully vaccinated patients (P=0.038).

Table 1. CT scores and imaging features by vaccination status

	Unvaccinated	Partially vaccinated	Fully vaccinated	*P* value
Morphological feature				
Subpleural lines	21.4% (3/14)	25.8% (16/62)	20.8% (11/53)	0.872
Consolidation	71.4% (10/14)	61.3% (38/62)	50.9%(27/53)	0.302
GGO	92.2% (13/14)	95.2% (59/62)	94.3% (50/53)	0.869
Thickened pleura	42.9% (6/14)	22.6%□14/62□	22.6%□12/53)	0.264
Crazy paving sign	50.0% (7/14)	38.7% (24/62)	32.1% (17/53)	0.441
Distribution				
Subpleural	92.9% (13/14)	87.1% (54/62)	90.6% (48/53)	0.981
Peribronchovascular	0% (0/14)	6.5% (4/62)	3.8% (2/53)	
Diffuse	7.1% (1/14)	6.5% (4/62)	5.7% (3/53)	
CT score				
0	33%□7/21)a	54% (72/134)a	68% (108/159)b	0.024
1	48% (10/21)	32% (43/134)	26% (41/159)	0.091
2	19% (4/21)a	14% (19/134) a	6% (10/159)b	0.038

Note. GGO= ground-glass opacity. Each subscript indicates a subset of the vaccination status categories, and at the 0.05 level, the column proportions of these categories do not differ significantly from each other.

Clinical characteristics and laboratory data by vaccination status

Baseline clinical characteristics by vaccination status are presented in Table 2. The mean age between different vaccination status grouop are similar (P=0.063). The proportion of patients with at least one comorbidities was higher in the unvaccinated(11, 52.4%) group than in the fully vaccinated(38, 23.9%) group (P=0.023). In detail, diabetes and chronic lung disease were higher in unvaccinated group. The length of hospital stay in the three groups were similar(P=0.080).

Table 2
Clinical Characteristics and Laboratory examination of patients by Vaccination Status

Parameter	Unvaccinated	Partially vaccinated	Fully vaccinated	*P* value
Age	56 ± 20	45 ± 16	45 ± 13	0.063
Gender				0.191
Male	28.6% (6/21)	40.2% (54/134)	47.2% (75/159)	
Female	71.4% (15/21)	59.8% (80/134)	52.8% (84/159)	
BMI	24.34 (23.73, 26.35)	24.97 (22.16, 27.43)	25.56 (22.59, 28.4)	0.248
Comorbidities	52.4% (11/21)$_a$	27.6% (37/134)$_{a,b}$	23.9% (38/159)$_b$	0.023
Hypertension	33.3% (7/21)	17.9% (24/134)	22.6% (36/159)	0.235
Diabetes	38.1% (8/21))$_a$	14.2% (19/134)$_b$	4.4% (7/159)$_c$	< 0.001
Heart cerebrovascular disease	14.3% (3/21)	8.2% (11/134)	7.5% (12/159)	0.574
Chronic lung disease	14.3% (3/21)$_a$	0.7% (1/134)$_b$	0% (0/159)$_b$	< 0.001
Smoking	19.0% (4/21)	19.4% (26/134)	10.1% (16/159)	0.066
Initial symptoms	81% (17/21)	81.3% (109/134)	85.5% (136/159)	0.599
Fever	23.8% (5/21)	28.4% (38/134)	31.4% (50/159)	0.706
Cough	33.3% 7/21)	47.8% (64/134)	51.6% (82/159)	0.278
Rhinorrhea	14.3% (3/21)	14.2% (19/134)	14.5% (23/159)	0.998
Sore throat	28.6% (6/21)$_a$	50.7% (68/135)$_{a,b}$	57.9% (92/159)$_b$	0.033
Myalgia	9.5% (2/21)	7.5% (10/135)	6.9% (11/159)	0.908
Loss of sensory	0% (0/21)	0.7% (1/134)	3.1% (5/159)	0.393
Weak	9.5% (2/21)	6.7% (9/134)	8.8% (14/159)	0.776
Length of hospital stay (day)	13 (12, 15)	13 (12,15)	12 (11,14)	0.080
Inflammatory marks				
CRP(>5.0mg/L)	52.4% (11/21)$_{a,b}$	34.3% (46/134)$_b$	48.4% (77/159)$_a$	0.033
IL-6(>7.0pg/mL)	71.4% (15/21)	46% (57/134)	46.4% (71/159)	0.090
Antibody				
IgG(S/CO)	1.07 ± 3.89$_a$	43 ± 69.31$_b$	52.1 ± 55.6$_c$	< 0.001
IgM(S/CO)	0.10 ± .010$_a$	0.50 ± 1.38$_b$	0.73 ± 1.61$_c$	< 0.001
Blood routine				
WBC count > 10,000/μl	33.3% (7/21)$_a$	19.4% (26/134)$_{a,b}$	11.9% (19/159)$_b$	0.026
Neutrophil count < 2000/μl	42.9% (9/21)$_a$	22.4% (30/134)$_{a,b}$	12.6% (20/159)$_b$	0.002

Parameter	Unvaccinated	Partially vaccinated	Fully vaccinated	*P* value
Lymphocyte count < 1000/μl	52.4% (11/21)$_a$	29.1% (39/134)$_{a, b}$	20.8% (33/159)$_b$	0.006
Platelet count < 150,000/μl	33.3% (7/21)$_a$	9.0% (12/134)$_b$	7.5% (12/159)$_b$	0.002
LDH (> 250U/L)	9.5% (2/21)	1.5% (2/134)	2.6% (4/159)	0.102

Note. CRP = C-reactive protein, IL-6 = interleukin-6, LDH = Lactate dehydrogenase. Each subscript indicates a subset of the vaccination status categories, and at the 0.05 level, the column proportions of these categories do not differ significantly from each other.

Laboratory tests showed that there were statistically significant differences in abnormal percentages of white blood cell count, neutrophil count, lymphocyte count and platelet count among the unvaccinated group and fully vaccinated (P<0.05), low platelet count rate in fully vaccinated group and partially vaccinated group was lower than that in unvaccinated group (P=0.002). For the Inflammatory marks, C-reactive protein (CRP) elevation was more common in the unvaccinated group and the fully vaccinated group (P=0.033), IL-6 elevation shows a similar level between three groups, the difference was not significant(P=0.09). In the antibody indices, The IgM and IgG level of the fully and partial vaccinated groups was significantly higher than that of the unvaccinated group and unvaccinated group(P<0.001).

Table 2. Clinical Characteristics and Laboratory examination of patients by Vaccination Status is in this area

Proportions of chest CT scores by vaccination status and virus type

Compared with previous studies on the imaging performance of patients with immune breakthrough in Table 3, CT scores in the unvaccinated group and fully vaccinated group were similar in Omicron and other type variant. In partially vaccinated group, the proportion of patients with negative CT performance in this study (54%) was larger than that in other type variant (30%), the proportion of patients with CT score 1 in Omicron variant (32%) was less than that in other type (53%) (P=0.005), and the proportion of patients with CT score 2 showed no significant different[14](Figure 3).

Table 3. The CT score by Vaccination Status between different virus type

CT score	Unvaccinated		*P* value	Partially vaccinated		*P* value	Fully vaccinated		*P* value
	Omicron	Other type		Omicron	Other type		Omicron	Other type	
0	33%7/21)	22% (71/326)	0.257	54% (72/134)a	30% (19/64)b	0.005	68% (108/159)	59% (13/22)	0.688
1	48% (10/21)	64% (209/326)		32% (43/134)a	53% (34/64)b		26% (41/159)	32% (7/22)	
2	19% (4/21)	14% (46/326)		14% (19/134)	17% (11/64)		6% (10/159)	9% (2/22)	

Note. Data on other types of COVID-19 are from published paper[14]. Each subscript indicates a subset of the virus type categories, and at the 0.05 level, the column proportions of these categories do not differ significantly from each other.

Figure 3. CT scores grade of the patients that underwent chest CT during hospitalization by vaccination status between Omicron and other type infection.

Clinical characteristics and laboratory examination by vaccination status and virus type

The demographics and baseline clinical characteristics and laboratory examination of by vaccination status between Omicron and other varian are presented in Table 4. In Partially vaccinated patients, a higher proportion of women were infected with Omicron (59.7%) than other type (47.2%) (P=0.044). Among unvaccinated patients, a higher proportion of Omicron infected patients (52.4%) had at least one comorbidities than pther type infected patients (26.2%) (P=0.008). While among partially and fully vaccinated patients, the proportion of omicron infected patients with at least one comorbidities (27.6%, 23.9%) was lower than the other types (57.5%, 55.3%) (p<0.001).

Table 4
Clinical Characteristics by Vaccination Status between different virus type

Parameter	Unvaccinated		*P* value	Partially vaccinated		*P* value	Fully vaccinated		*P* value
	Omicron	Other type		Omicron	Other type		Omicron	Other type	
Age (years)	56 ± 20	43 ± 15	-	45 ± 17	59 ± 14	-	45 ± 13	65 ± 18	-
Sex									
Male	28.6% (6/21)	47.9% (281/587)	0.082	40.3% (54/134)	52.8% (67/127)	0.044	47.2% (75/159)	59.6% (28/47)	0.135
Female	71.4% (15/21)	52.1% (306/587)		59.7% (80/134)	47.2% 60/127)		52.8% (84/159)	40.4% (19/47)	
Smoking history	19% (4/21)	21.8% (128/587)	0.763	19.4% (26/134)	16.5% (21/127)	0.547	10.1% (16/159)	12.8% (6/47)	0.598
Comorbidities									
Any comorbidities	52.4% (11/21)	26.2% (154/587)	0.008	27.6% (37/134)	57.5% (73/127)	< 0.001	23.9% (38/159)	55.3% (26/47)	< 0.001
Hypertension	33.3% (7/21)	16.2% (95/587)	0.039	17.9% (24/134)	44.1% (56/127)	< 0.001	22.6% (36/159)	38.3% (18/47)	0.032
Diabetes	38.1% (8/21)	9.7% (57/587)	< 0.001	14.2% (19/134)	26.8% (34/127)	0.011	4.4% (7/159)	19,1% (9/47)	0.001
Cardiovascular disease	14.3% (3/21)	3.4% (20/587)	0.01	8.2% (11/134)	8.7% (11/127)	0.895	7.5% (12/159)	21.3% (10/47)	0.007
Initial laboratory findings									
WBC count > 10,000/μl	9.5% (2/21)	2.9% (17/587)	0.137	0.7% (1/134)	1.6% (2/127)	0.53	3.8% (6/159)	0% (0/47)	0.207
Lymphocyte count < 1000/μl	52.3% (11/21)	23.3% (137/587)	0.02	14.9% (39/134)	18.9% (24/127)	0.054	20.7% (33/159)	27.7% (13/47)	0.318
Platelet count < 150,000/μl	33.3% (7/21)	17.5% (103/587)	0.081	8.9% (12/134)	22.8% (29/127)	0.002	7.5% (12/159)	14.9% (7/47)	0.151
LDH > 250 U/L	9.5% (2/21)	41.2% (242/587)	0.004	1.5% (2/134)	48.8% (62/127)	< 0.001	2.5% (4/159)	34% (16/47)	< 0.001
CRP > 50 mg/L	4.8% (1/21)	11% (63/587)	0.331	0% (0/134)	13.4% (17/127)	< 0.001	0.6% (1/159)	17% (8/47)	< 0.001
Clinical outcomes									
Length of hospital stay	13.4 ± 3.6	10.1 ± 30.8	-	13.4 ± 3.2	11.5 ± 4.8	-	12.7 ± 3.3	12.2 ± 5.8	-

Note. Data on other types of COVID-19 are from published paper[14]. CRP = C-reactive protein, IL-6 = interleukin-6, LDH = Lactate dehydrogenase.

About laboratory findings, with the exception of unvaccinated patients, the proportion of CRP elevation in partially vaccinated and fully vaccinated omicron patients was significantly lower than that in other types of patients(P<0.001).

The proportion of lactate dehydrogenase (LDH) increase under different vaccination status was significantly lower in omicron infection than in other types of infection(P<0.05). The proportion of patients with reduced lymphocyte counts in unvaccinated omicron infected patients(52.3%) was significantly higher than that of other types infections(23.3%) (P=0.02). The platelet count reduction rate of partially vaccinated omicron infected patients(8.9%) was lower than that of other types of patients(22.8%) (P=0.002).

Table 4. Clinical Characteristics by Vaccination Status between different virus type is in this area

The relationship between vaccination and antibody and changes of CT findings

We analyzed the CT scores of all examinations during hospitalization, the vaccination status and antibody were compared according to the progress of CT findings in Table S1 and Figure S1. After adjusted odds ratios for disease progression are summarized in Table 5. Adjusted multivariate analysis showed older age and low IgG levels are associated with an increased risk of disease progression (Figure 4).

Table 5. Odds Ratios for progression of disease

Parameter	OR	*P* value
Vaccination status		
Unvaccinated	Reference	
Partially vaccinated	1.37 (0.05-36.78)	0.853
Fully vaccinated	1.05 (0.04-25.54)	0.977
Age	1.04 (1.01-1,06)	0.002
BMI (>24)	2.03 (1.06-3.89)	0.032
Comorbidities		
Diabetes	0.90 (0.31-2.60)	0.842
Heart cerebrovascular disease	1.82 (0.58-5.7)	0.303
Days after vaccination (day)	1.00 (1.00-1.01)	0.77
Inflammatory marks		
IL-6（>7.0pg/mL）	1.75 (0.95-3.22)	0.074
Antibody		
IgG（S/CO）	0.91 (0.95-0.98)	<0.001
IgM（S/CO）	1.29 (0.97-1.72)	0.082
Blood routine		
Lymphopenia (<0.8x109g/L)	1.82 (0.78-4.25)	0.163

Note. BMI= body mass index, IL-6 = interleukin- 6, OR = odds ratio. Data in parentheses are 95% confidence intervals. The analysis was performed using a logistic regression model.

Figure 4. Clinical and laboratory parameters related to disease progression, 0: no progression, 1: progression. (A) The relationship between age and disease progression. (B)The relationship between IgG levels and disease progression.

The days after vaccination was inversely correlated with serum IgG levels (β=-0.0338, P<0.001), was positively correlated with disease progression (r=0.0006, P=0.7621), also negatively correlated with positive IgG level (=-0.1612, P<0.001). With the extension of inoculation time, the mediating effect of serum IgG increased the chance of disease progression. There was a positive correlation between vaccination status and serum IgG level (β=-0.0337, P<0.001), was negatively correlated with disease progression (r=0.0882, P=0.693), also negatively correlated with positive IgG level (=17.437, P=0.002). The dose of vaccinations increased and the serum IgG mediated effect reduced the rate of disease progression (Figure 5).

Figure 5. Mediating role of IgG in the relationship between vaccination characteristics and disease progression. (A) DAYS: days after vaccination; RESULT: progression of disease. IgG level had a complete mediating effect between days after vaccination and disease progression (=-0.1612). (B) DOSE: vaccination Status. RESULT: progression of disease. IgG level had a complete mediating effect between vaccination status and disease progression (=17.4347).

Discussion

There have been no studies on the imaging manifestations of omicron infection in immunobreakthrough patient, we have investigated the clinical and radiographic features of hospitalized COVID-19 Omicron variant patients in a multicenter cohort. Summarizing our findings were as follows:1) The CT positive rate and 2 points rate of fully vaccinated patients were lower than those of partially vaccinated and unvaccinated patients. 2) The progress of CT signs is related to inoculation and IgG concentration.The concentration of IgG is related to the number of vaccine doses and time of vaccination. The more vaccines, the better the immune status, and the better disease of patient.3) In these 314 cases of omicron infection,CT positive rates were similar to other types of COVID-19 infection, and the proportion of laboratory abnormalities was significantly lower than other types of COVID-19 infection. The results demonstrated that the better immune status in our omicron infected after vaccination could protect the body from suffering severe pneumonia.

In this study, CT positivity of fully vaccinated patients with 3 doses was significantly lower than that of partially vaccinated patients and unvaccinated patients (P = 0.024), and the proportion of CT score 2 in fully vaccinated patients was significantly lower than that of partially vaccinated patients and unvaccinated patients (P = 0.038), CT findings were closely related to pathology, indicating that the lung injury of the patient in fully vaccinated patients were mild[15], revealed the protection of vaccination in body immune status. Previous studies have reported inadequate protection against omicron with two doses of the mRNA vaccine, but a third dose can reduce morbidity and disease severity in the population[11]. [16, 17]In another study, a third dose of the homologous or heterologous vaccine, in addition to two inactivated doses, increased levels of neutralizing antibodies[18]. Reductions in white blood cell count, neutrophil count, lymphocyte count, and platelet count were more common in the unvaccinated group than in the fully vaccinated group.Laboratory tests indicated higher IgG levels in fully vaccinated patients, suggesting the protective effect of the vaccine against the Omicron variant[19]. Combined with laboratory and imaging findings, complete vaccination is protective against disease progression in COVID-19 patients.

The observed differences in clinical characteristics may reflect differences in vaccination priorities based on consideration of potential comorbidities. According to China's vaccination guidelines during the study period, chronic diseases such as hypertension and diabetes need to be well controlled by drugs before vaccination[20]. These basic diseases are common in the elderly. Therefore, in our study, the proportion of elderly patients with fully vaccination group was low. Among patients with diabetes and hypertension, multivariate analysis showed that the risk of positive CT findings was lower in fully vaccinated patients than in partially vaccinated patients.

After adjusting for demographic and clinical characteristics at admission, as well as several laboratory biomarkers, low IgG concentrations were independently associated with a higher risk of disease progression. Vaccine status and after vaccination influence disease progression through IgG levels. IgG concentration was correlated with vaccination status and time of infection from vaccination distance. Pawlowski et al. showed in a previous study that the 14-day hospitalization rate, ICU admission rate and mortality rate of infection cases after vaccination were lower than those in the unvaccinated group[21]. After vaccination, the antibody titer peaked at 28 days after vaccination, but decreased by 34% at 90 days and by 64% at 180 days[22]. The third dose of the vaccine increases the antibody titer and maintains the antibody response for a longer time[23]. It is important to note that age and overweight are significant predictors of disease progression in COVID-19 patients, even those with breakthrough infections.

In a previous multicenter study, 761 breakout infections involving both mRNA and adenovirus vaccines were reported, and the distribution of CT scores across vaccination Settings was similar to that in this study[14]. Omicron's CT performance was superior to other types of infection only in partially vaccinated patients, which may be due to different definitions of partially vaccinated patients in our research, about inactivated vaccine patients, the partially vaccinated group included patients who received one and two injections, compared with mRNA vaccine and adenovirus vaccine, partial vaccinators are given one shot, this may result in the low CT positive rate and CT score 1 of partially vaccinated patients with inactivated vaccine.

In our research, the imaging manifestations, including morphological characteristics and distribution characteristics, of hospitalized patients with omicron infection showed no significant difference from those of the other types COVID-19 infection, but the range of involvement was significantly lower than previous studies, and the positive CT manifestations were significantly lower than those of non-Omicron infection in previous study[24].The percentage of laboratory abnormalities in omicron infected patients was also lower than in other types infected patients, the levels of CRP, LDH, procalcitonin (PCT) and interleukin 6 (IL-6) were significantly lower than those in non-omicron infection, previous studies have proved that elevated IL-6, CRP and LDH levels are indicators of poor prognosis in COVID-19 patients[25, 26], the elevation of PCT usually indicates severe transformation. Lan et al. found a correlation between laboratory abnormalities and radiographic abnormalities[27], but the sample size of the study was small, may have an impact on the conclusions drawn.

Our findings are consistent with recent research on the relationship between vaccination and disease severity in COVID-19 patients. There are several limitations that warrant mention. First, among the partially vaccinated patients, no distinction was made between those who received one dose and those who received two doses, the small sample size of unvaccinated patients may affect the statistical results. Second, most of the patients received inactivated vaccines, there was no comparison of the effectiveness of the different types of vaccines. Third, CT score only includes the relationship with the lesion area and does not consider the difference in lesion density, which may lead to inaccurate estimation of pneumonia severity.

Conclusion

The inactivated vaccine provided similar protection against Omicron infection of SARS-CoV-2, compared to the patients who received other types vaccines. Compared with those who were not vaccinated and those who received one or two doses of vaccine, 3 dose vaccinated patients had a higher CT negative rate and a lower rate of severe pneumonia. Vaccination status and days after vaccination affect disease progression through IgG levels. Our study found that inactivated vaccination reduced patient symptoms, inhibited pneumonia progression, increased dose dose, and protected

Abbreviations

COVID-19
Coronavirus Disease 2019
VE
vaccine efficacy
CT
computed tomography
GGO
ground-glass opacity
BMI
body mass index
RT-PCR
reverse transcription-polymerase chain reaction
CRP
C-reactive protein
LDH
lactate dehydrogenase
PCT
procalcitonin
IL-6
interleukin 6.

Declarations

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Authors' contributions

W. S. and Z.H.X. take responsibility for the content of the manuscript, including the data and analysis. J.Q.C., L.W., W.S. and Z.H.X contributed to the design and conception of the study; J.Q.C. and L.W. contributed to data collection; Z.Y., X.D.J. and H.W. contributed to data analysis and interpretation; J.Q.C. drafted the manuscript; and S.X., W.S., Z.H.X, X.H.G., G.F.G. and H.Y.W. contributed to revising it critically for important intellectual content. J.Q.C. and W.L. are contributed equally to this work and should be considered co-first authors. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

Institutional Review Board approval was obtained by the Ethics Review Committee of Tianjin First Central Hospital (No. 2022N127KY) and Haihe Hospital Ethics Committee (No. 2020HHKT-008).

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Figures

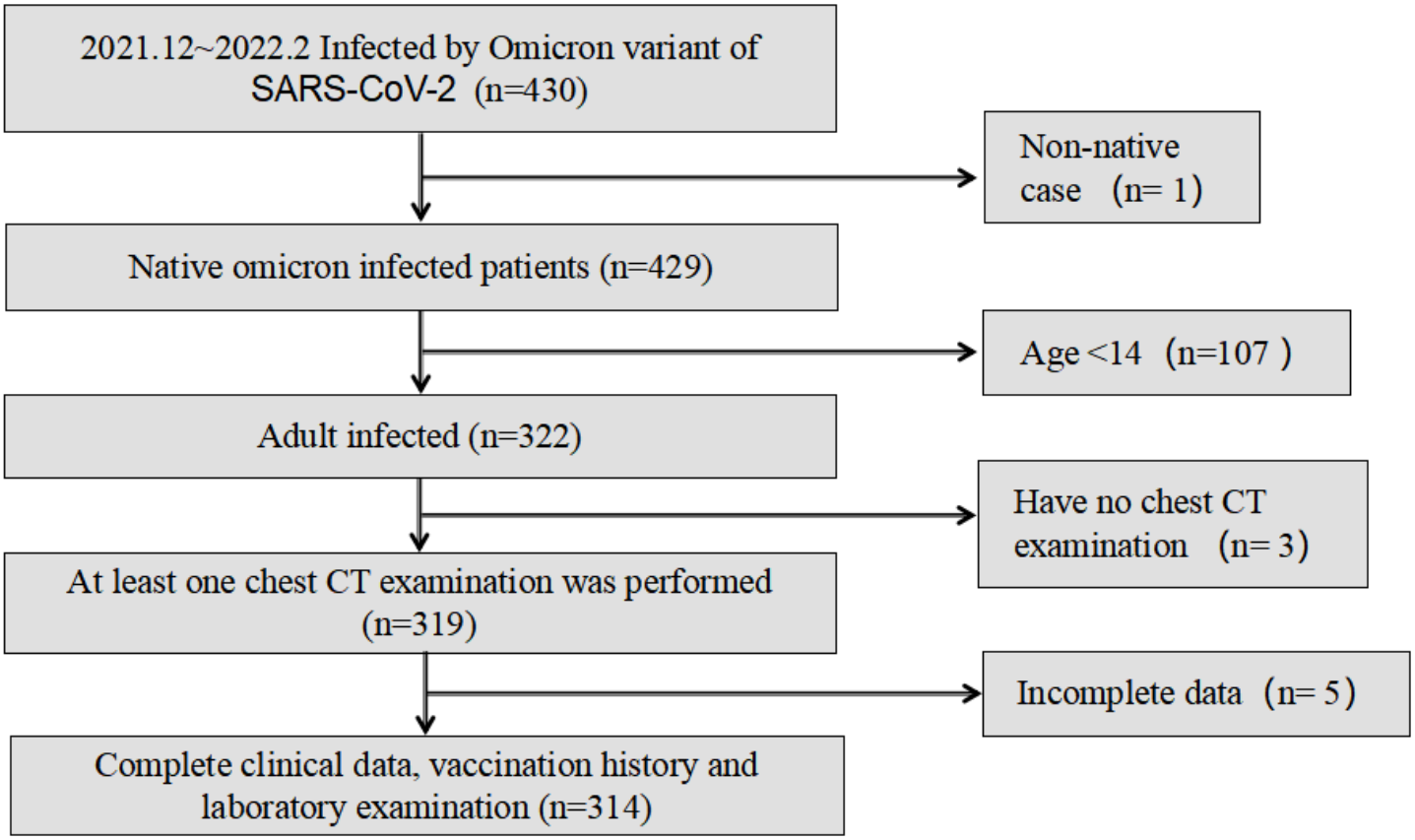

Figure 1

Workflow of the study

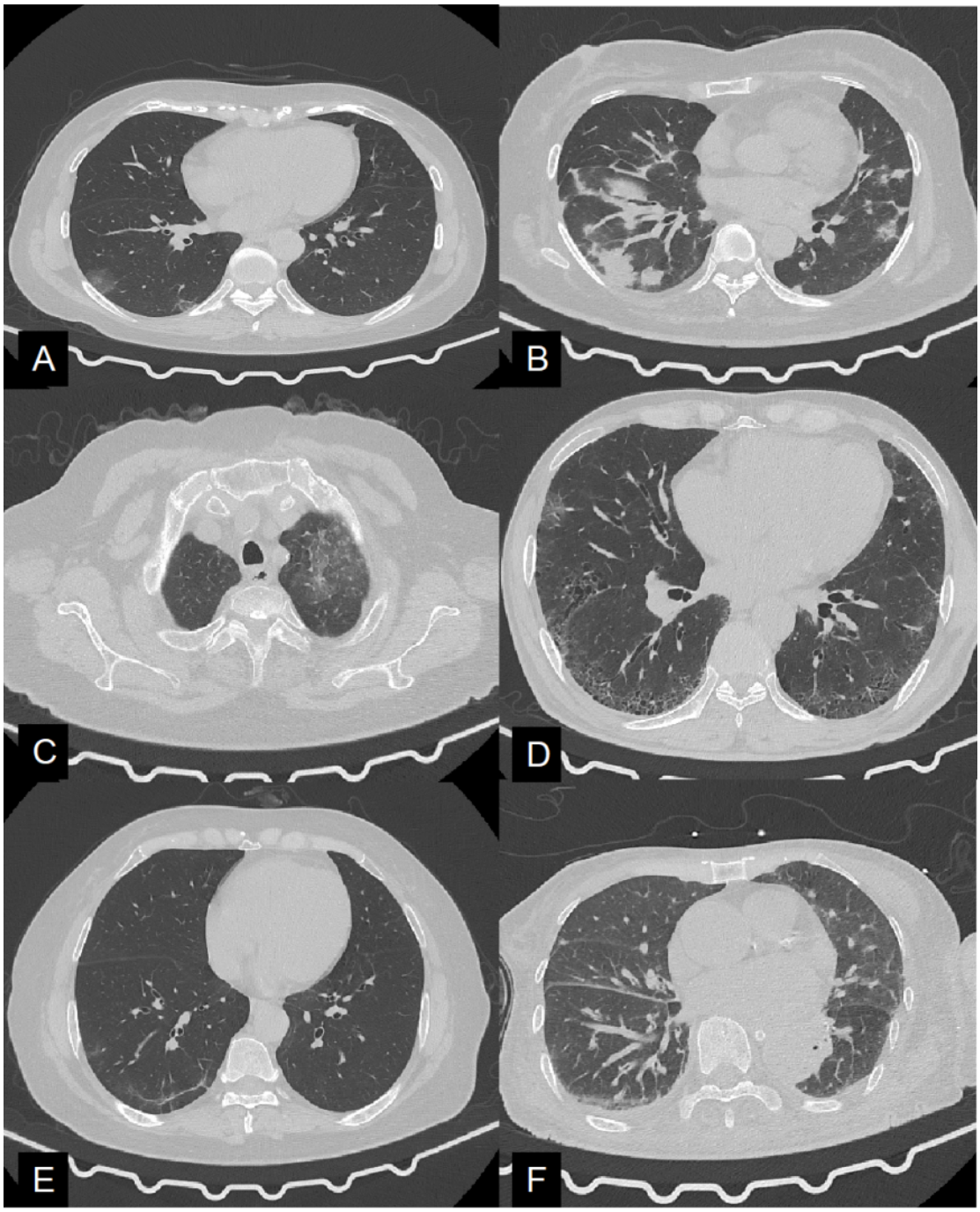

Figure 2

Chest CT findings of COVID-19 pneumonia on axial images. (A) GGO; (B) Consolidation; (C) Crazy-paving pattern; (D) Interlobular and/or intralobular septal thickening; (E) Subpleural lines; (F) bronchiolitis.

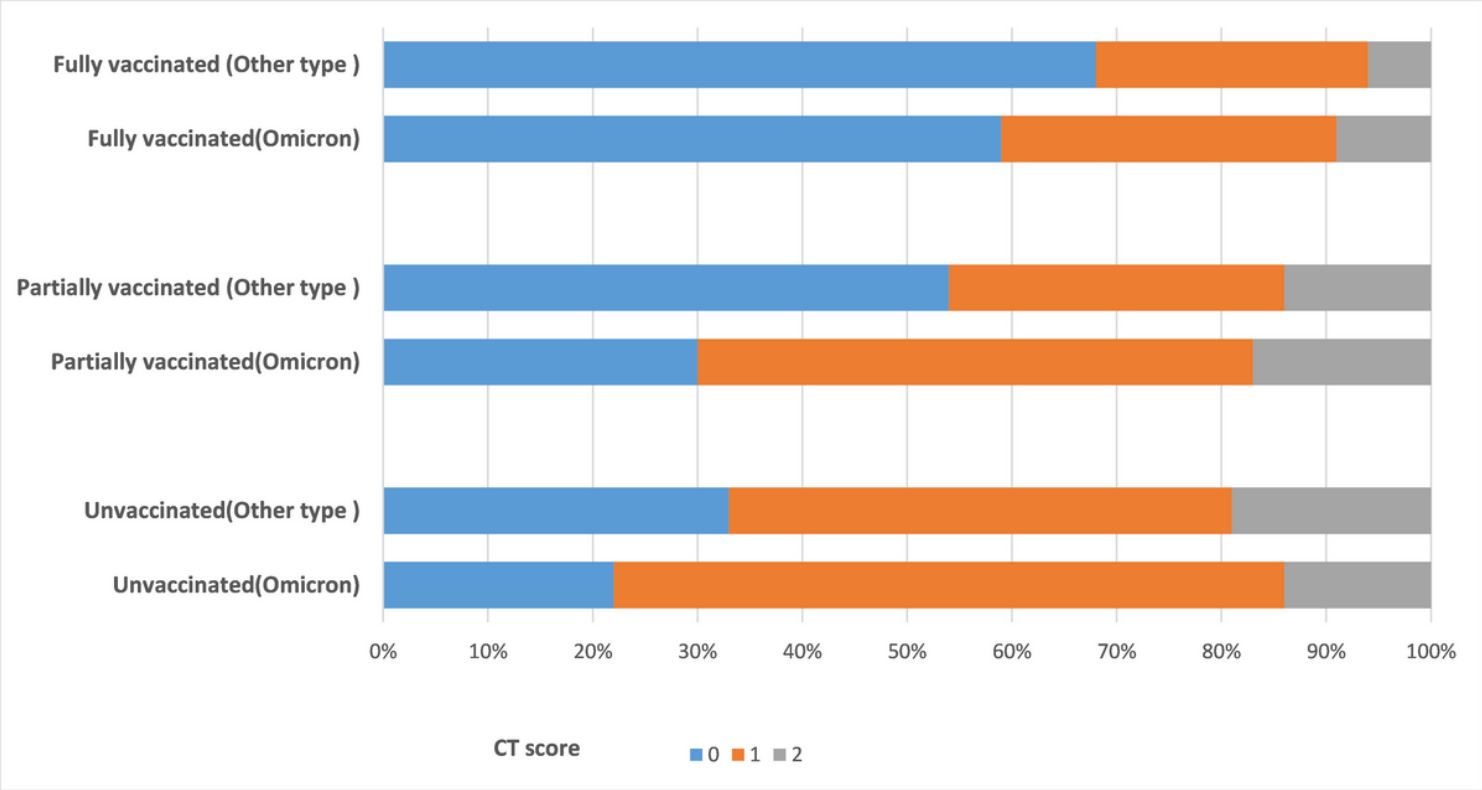

Figure 3

CT scores grade of the patients that underwent chest CT during hospitalization by vaccination status between Omicron and other type infection.

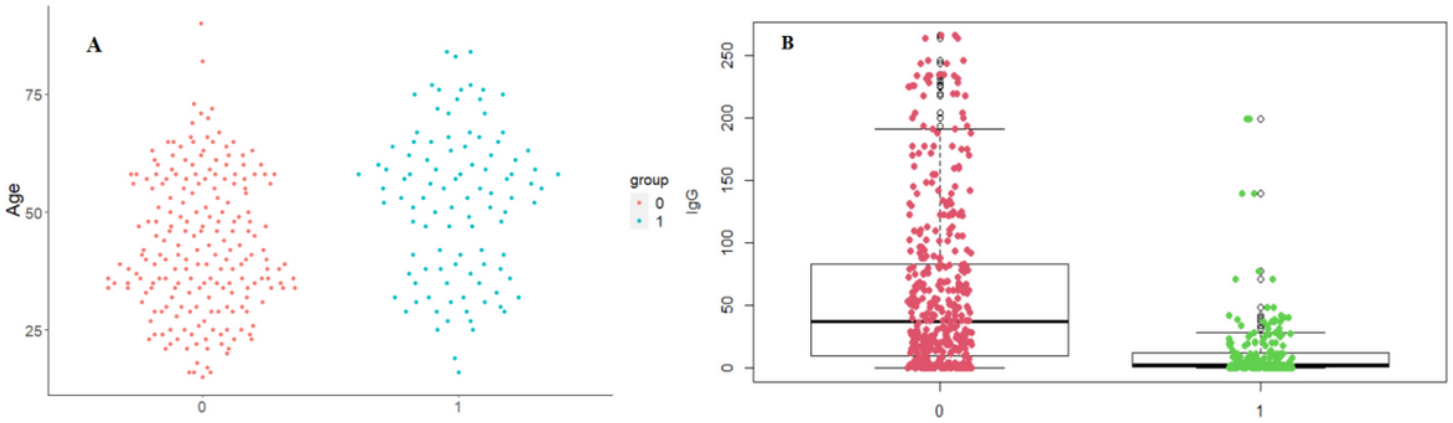

Figure 4

Clinical and laboratory parameters related to disease progression, 0: no progression, 1: progression. (A) The relationship between age and disease progression. (B)The relationship between IgG levels and disease progression.

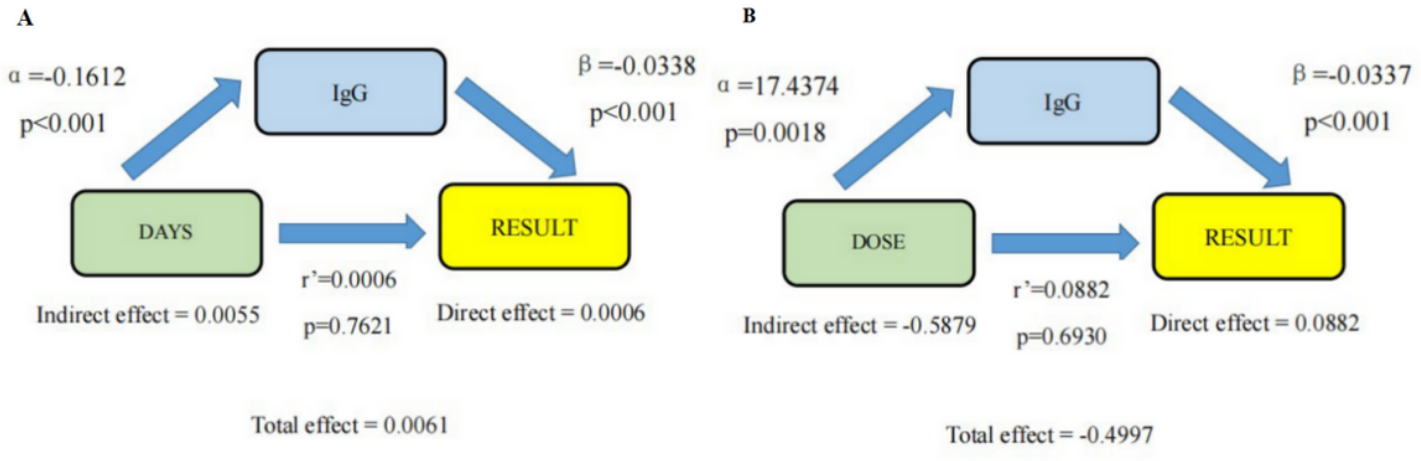

Figure 5

Mediating role of IgG in the relationship between vaccination characteristics and disease progression. (A) DAYS: days after vaccination; RESULT: progression of disease. IgG level had a complete mediating effect between days after vaccination and disease progression (=-0.1612). (B) DOSE: vaccination Status. RESULT: progression of disease. IgG level had a complete mediating effect between vaccination status and disease progression (=17.4347).

Supplementary Files

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