Vaccine-induced antibody level predicts the clinical course of breakthrough infection of COVID-19 caused by delta and omicron variants: a prospective observational cohort study

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Introduction

Omicron variant virus is spreading rapidly, even in individuals with high vaccination rates. This study aimed to determine the effect of vaccine on clinical course of delta and omicron variant infection. Furthermore, we tried to evaluate the utility of antibody level against spike protein as a predictor of disease course of COVID-19 in vaccinated patients.

Methods

Between December 11, 2021 and February 10, 2022, we performed a prospective observational cohort study in an institution of South Korea. Among adult patients admitted due to COVID-19, individuals with confirmed delta and omicron variant infection were included. Multivariable logistic regression analysis was performed to determine the association between antibody level and clinical course of breakthrough infection in vaccinated patients. The relationship between antibody level and cycle threshold (Ct) values was confirmed using a generalized linear model. We used the antibody titers collected within 7 days of symptom onset or diagnosis and the Ct values tested on days 5-7 days after initial diagnosis.

Results

Of 161 patients with delta and omicron variant infection, 106 vaccinated patients (39 delta and 67 omicron) had available serum samples. The geometric mean titers of antibodies in patients who experienced the fever (≥37.5℃), hypoxia (≤94% of SpO2), pneumonia, C-reactive protein (CRP) elevation (>8 mg/L) or lymphopenia (<1,100 cells/μL) during hospitalization were 1201.5 U/mL, 98.8 U/mL, 774.1 U/mL, 1335.1 U/mL, and 1032.2 U/mL, respectively, which were lower compared with those who did not ($p<0.05$ for all). Increase in antibody level of vaccinated patients with delta and omicron infection was associated with decrease in occurrence of fever (adjusted odds ratio [aOR], 0.23; 95% confidence interval [CI], 0.12-0.51), hypoxia (aOR, 0.23; 95% CI, 0.08-0.7), CRP elevation (aOR, 0.52; 95% CI, 0.29-0.0.94), and lymphopenia (aOR, 0.57; 95% CI, 0.33-0.98) during hospitalization, regardless of virus type or booster vaccination status. Data from 33 patients who had Ct values suitable for analysis showed a positive correlation between antibody levels and Ct values ($p=0.02$).

Conclusions

Antibody levels are predictive of the clinical course of COVID-19 in vaccinated patients with delta and omicron variant infections. Our data highlight the need for concentrated efforts to monitor patients with SARS-CoV-2 infection who are at risk of low antibody levels.

Table and figure

Table 1. Clinical characteristics of patients with SARS-CoV-2 infection according to variant type

Variable	Delta variant (n = 79)	Omicron variant (n = 82)	*p*-value
Demographic data			
Age (years)	58.1 ± 15.7	51.0 ± 21.1	0.017
Female, n (%)	40 (51.3%)	45 (54.9%)	0.590
BMI (kg/m^2)	23.6 ± 3.1	23.7 ± 4.5	0.818
Immunocompromised, n (%)	11 (13.9%)	12 (14.6%)	0.898
CCI ≥ 3, n (%)	39 (49.4%)	28 (34.1%)	0.050
Asymptomatic at diagnosis, n (%)	14 (17.7%)	4 (4.9%)	0.010
Laboratory data (worst results during hospitalisation)			
CRP (mg/L)	47.6 ± 65.8	15.6 ± 23.1	<0.001
Lymphocyte (10^3 cells/uL)	1.1 ± 0.6	1.4 ± 0.6	0.001
IL-6 (pg/mL)	33.8 ± 73.7	9.8 ± 14.6	0.021
D-dimer (mcgFEU/mL)	0.8 ± 1.4	0.6 ± 1.1	0.276
Clinical courses during hospitalisation			
Fever (BT ≥ 37.5 ℃), n (%)	57 (72.2%)	50 (61.7%)	0.161
Time to defervescence (days)	4.6 ± 2.9	3.6 ± 2.3	0.065
Pneumonia[†], n (%)	44 (55.7%)	12 (14.6%)	<0.001
Hypoxia (SpO_2 < 94 %), n (%)	20 (25.3%)	4 (4.9%)	<0.001
Duration of oxygenation (days)	6.6 ± 2.8	4.0 + 0.0	0.002
Treatments			
High flow, n (%)	3 (3.8%)	1 (1.2%)	0.361
Regdanvimab, n (%)	8 (10.1%)	3 (3.7%)	0.104
Remdesivir, n (%)	19 (24.1%)	9 (11.0%)	0.028
Dexamethasone, n (%)	28 (35.4%)	12 (14.6%)	0.002
Antimicrobial agents, n (%)	33 (41.8%)	15 (18.3%)	0.001

Table 2. Association of antibody titres and variables with clinical courses during hospitalisation in vaccinated patients with breakthrough infections caused by delta and omicron variants

	Univariate analysis		Multivariable anaylsis	
	OR (95% CI)	*p*-value	aOR (95% CI)	*p*-value
Fever (BT ≥ 37.5 ℃)	0.25 (0.12–0.52)	<0.001	0.23 (0.11–0.51)	<0.001
Hypoxia (SpO_2 ≥ 94 %)	0.19 (0.07–0.49)	<0.001	0.23 (0.08–0.7)	0.010
Pneumonia	0.43 (0.25–0.74)	0.003	0.53 (0.25–1.11)	0.093
CRP elevation (CRP > 8 mg/L)	0.5 (0.29–0.87)	0.014	0.52 (0.29–0.94)	0.030
Lymphopenia (Lymphocyte < 1,100 cell/uL)	0.51 (0.3–0.84)	0.009	0.57 (0.33–0.98)	0.041

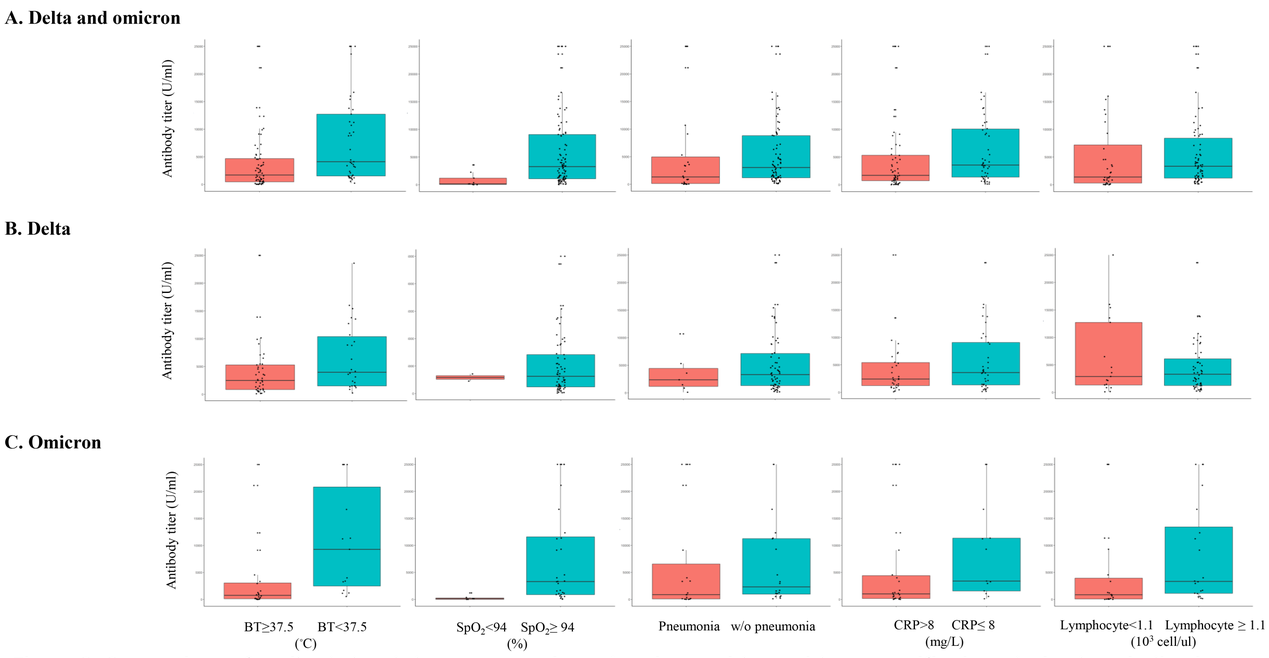

Figure 2. Comparison of antibody levels between vaccinated patients with or without specific signs during hospitalisation
This analysis included 106 patients with delta and omicron variant infections whose serum samples were collected within 7 days of symptom onset or diagnosis. Antibody levels are described as box plots of medians with interquartile ranges.

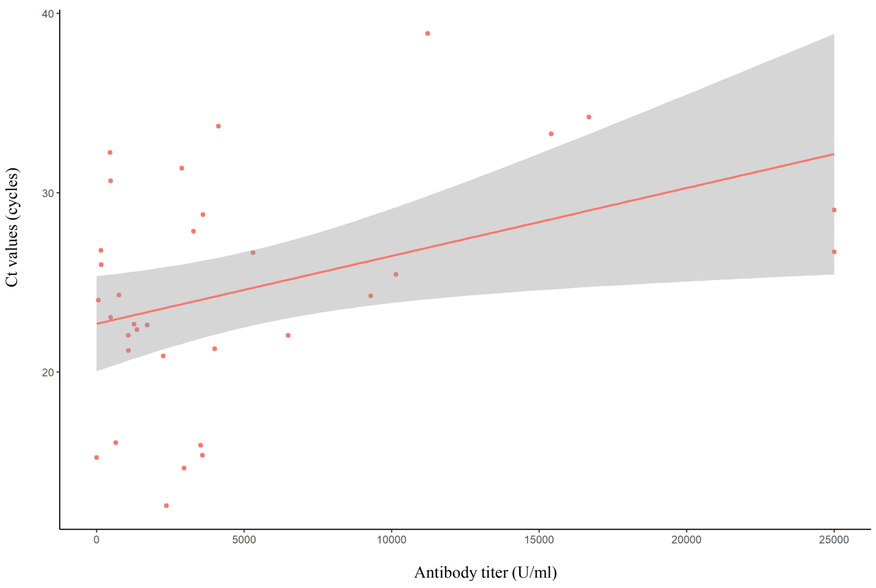

Figure 3. Association of antibody titres and Ct values
Data from 33 patients, with Ct values measured 5–7 days after diagnosis, showed a positive correlation between antibody levels and Ct values (slope: 0.0004, p=0.022)

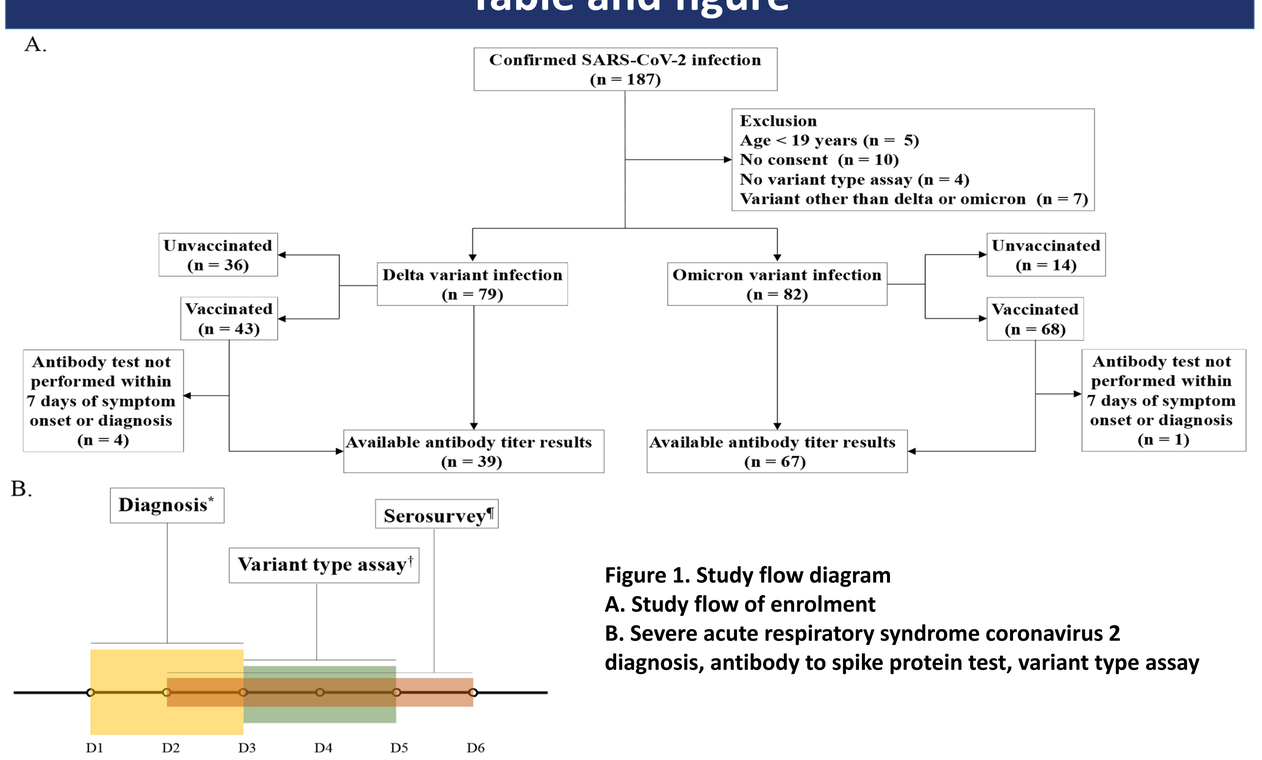

Figure 1. Study flow diagram
A. Study flow of enrolment
B. Severe acute respiratory syndrome coronavirus 2 diagnosis, antibody to spike protein test, variant type assay