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Immunogenicity of the ChAdOx1 nCoV-19 vaccine in patients with hematologic malignancies

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Purpose: The present study aimed to study the immunogenicity of the ChAdOx1 nCoV-19 vaccine in patients with hematologic malignancies.

Materials and Methods: This prospective cohort study of hematology patients aimed to evaluate their antibody levels against the receptor-binding domain of the severe acute respiratory syndrome coronavirus 2 spike protein and seroconversion rates following two doses of the ChAdOx1 nCoV-19 vaccine. Between June and July 2021, we enrolled 61 patients and included 44 patients in our analysis. Antibody levels were assessed 8 and 4 weeks after the first and second injections, respectively, and compared with those of a healthy group.

Results: Eight weeks after the first dose, the geometric mean antibody level was 1.02 binding antibody units (BAU)/mL in the patient group and 37.91 BAU/mL in the healthy volunteer group ($p<0.01$). Four weeks after the second dose, the geometric mean antibody level was 9.44 BAU/mL in patients and 641.6 BAU/mL in healthy volunteers ($p<0.01$). The seroconversion rates 8 weeks after the first dose were 27.27% and 98.86% in the patient and healthy volunteer groups, respectively ($p<0.001$). The seroconversion rate 4 weeks after the second dose was 47.73% in patients and 100% in healthy volunteers. Factors leading to lower seroconversion rates were rituximab therapy ($p=0.002$), steroid therapy ($p<0.001$), and ongoing chemotherapy ($p=0.048$). Factors that decreased antibody levels were hematologic cancer ($p<0.001$), ongoing chemotherapy ($p=0.004$), rituximab ($p<0.001$), steroid use ($p<0.001$), and absolute lymphocyte count $<1,000/mm^3$ ($p=0.009$).

Conclusion: Immune responses were impaired in individuals with hematologic malignancies, particularly patients undergoing ongoing therapy and B-cell-depleting therapy. Additional vaccinations should be considered for these patients, and further investigated.

Keywords: ChAdOx1 nCoV-19 vaccine, SARS-CoV-2 virus, COVID-19 vaccine, COVID-19 virus

Introduction

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a major pandemic disease that, as of April 2022, has led to 500 million infections and more than 6 million deaths worldwide [1]. Patients with hematologic malignancies are reported to have a high mortality rate, ranging from 13.8% to 39% [2]. The use of immune-compromising and immunosuppressive therapies on patients with hematologic cancer might lead to severe and life-threatening infections. Vaccines against SARS-CoV2 have been effective in preventing COVID-19,

particularly severe cases of the disease [3-6]; however, the diminished efficacy of SARS-CoV-2 vaccines in patients with hematologic cancer is a concern. Some studies have shown lower seroconversion rates and antibody concentrations in patients with cancer, especially patients with hematologic malignancies [7-14].

We aimed to identify the antibody responses and factors that suppress immunogenicity, in patients with hematologic malignancies after receiving the ChAdOx1 nCoV-19 vaccine.

Materials and Methods

Study design

This was a prospective cohort study that enrolled adult patients aged >18 years with hematologic malignancies who were untreated, receiving ongoing treatment, or had completed treatment within 1 year before enrollment at Chulabhorn Hospital. Participants had received two doses of the ChAdOx1 nCoV-19 vaccine, 12 weeks apart, after completing a paper questionnaire about their baseline demographics, medical history, vaccination information, and postvaccine symptoms. Additional clinical data from the medical records were reviewed. The enrollment started on June 10 and ended on July 12, 2021.

The control group comprised healthy volunteers who were healthcare providers from our institution with no comorbidities. The Stata program was used to match the hematology patients with the healthy volunteers by sex and age (±5 years) in a 1:2 ratio.

Serum antibody levels were tested before the first injection of the ChAdOx1 nCoV-19 vaccine, and at 8 and 16 weeks after the first dose. Antibody testing was performed from June 10 until November 1, 2021.

This prospective cohort study was approved by the approval by the Human Research Ethics Committee of Chulabhorn Research Institute (approval no., 056/2564). Inform consent was obtained from all individual participants included in the study.

Antibody assays

Elecsys Anti-SARS-CoV-2 S (Elecsys-S) (Roche Diagnostics International AG, Rotkreuz, Switzerland) serum antibody assays were used to measure levels of antibodies against the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein at Chulabhorn Hospital. The results were interpreted as positive (≥0.8 U/mL) or negative (<0.8 U/mL) on the basis of the international standard for anti-SARS-CoV-2 immunoglobulin titers developed by the World Health Organization [15]. Elec-

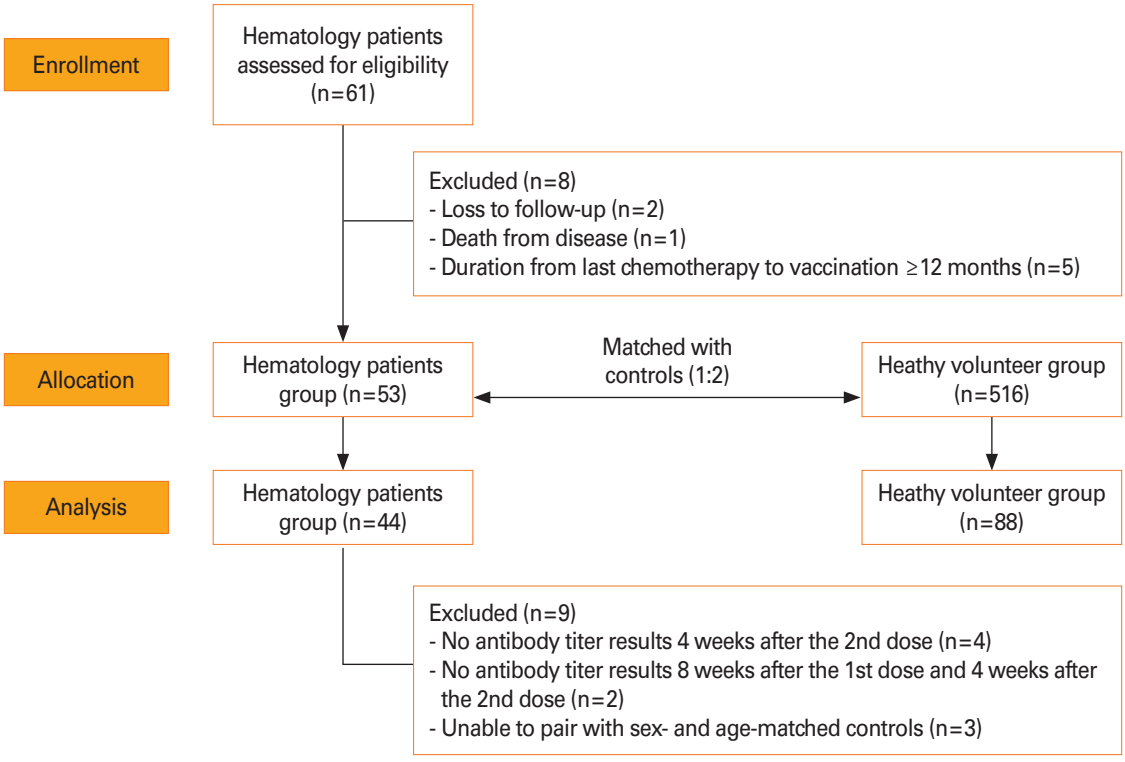

Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) flow diagram.

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sys-S units were converted to binding antibody units (BAU) using the following equation [16]: Elecsys-S U=0.972×BAU.

Statistical analysis

Statistical analyses were performed using Stata/SE ver. 16.1 (Stata Corp., College Station, TX, USA). A p-value of <0.05 was considered statistically significant. Comparisons of anti-RBD antibody levels between the hematology patient group and healthy volunteer group were conducted using linear regression. Logistic regression was used to compare the seroconversion rates between the hematology patient group and healthy volunteer group, and perform univariate and multivariate analyses.

Table 1. Baseline demographic data

Characteristic	Hematology patients (n=44)	Healthy volunteers (n=88)
Age (yr)	64 (60.5–72.5)	64 (61–69)
≥60	35 (79.55)	73 (82.95)
<60	9 (20.45)	15 (17.05)
Sex		
Female	19 (43.18)	38 (43.18)
Male	25 (56.82)	50 (56.82)
Malignancy		
Hematologic cancer patients	34 (77.27)	
Patients with benign diseases	10 (22.73)	
Disease status		
Progressive disease	1 (2.27)	
Stable disease	8 (18.18)	
Partial response/partial metabolic response	13 (29.55)	
Complete response/complete metabolic response	9 (20.45)	
Not assessed	13 (29.55)	
Chemotherapy		
Ongoing chemotherapy	26 (59)	
Previous chemotherapy	9 (20.5)	
No chemotherapy	9 (20.5)	
Rituximab therapy		
Rituximab	16 (36.36)	
No rituximab	28 (63.64)	
Steroid therapy		
Steroids	26 (59.09)	
No steroids	18 (40.91)	
Absolute neutrophil count at day 0		
<1,500/mm^3	4 (9.09)	
>1,500/mm^3	40 (90.91)	
Absolute lymphocyte count at day 0		
<1,000/mm^3	8 (18.18)	
>1,000/mm^3	36 (81.82)	

Values are presented as median (interquartile range) or number (%).

Study endpoints

The primary endpoints were the concentrations (BAU/mL) of anti-RBD antibodies in patients with hematologic malignancies compared with healthy volunteers at 8 weeks after the first dose of the vaccination and 4 weeks after the second dose of the vaccination.

The secondary endpoints were the seroconversion rates at 8 weeks after the first dose of the vaccination and 4 weeks after the second dose of the vaccination in patients with hematologic malignancies compared with healthy volunteers, and the factors influencing antibody responses, namely the type of malignancy, disease status, type of chemotherapy or immunosuppressive therapy, timing of treatment, absolute neutrophil count before vaccination, and absolute lymphocyte count (ALC) before vaccination.

Results

Patient characteristics

Between June 10 and July 12, 2021, 61 patients were enrolled.

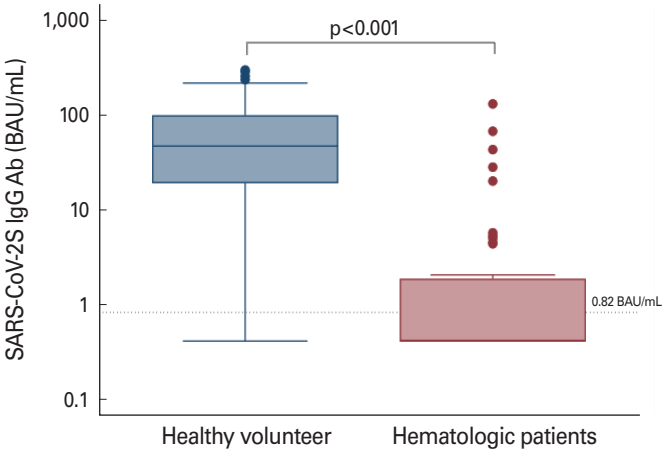

Fig. 2. Antibody concentrations at 8 weeks after first-dose ChAdOx1 nCoV-19 vaccination of hematology patients compared with healthy volunteers. The geometric mean antibody (Ab) level was 1.02 binding antibody units (BAU)/mL (95% confidence interval [CI], 0.62–1.66) in the hematology patient group and 37.91 BAU/mL (95% CI, 28.73–50.02) in the healthy volunteer group (p<0.01). Box plots show the severe acute respiratory syndrome coronavirus 2 spike (SARS-CoV-2S) immunoglobulin G (IgG) Ab concentrations (BAU/mL); the lower endpoints of the boxes represent the 25th percentiles, the upper endpoints represent the 75th percentiles, and the dots represent the outliers. The dotted line is the determined cut-off value for seropositivity (Ab level ≥0.8 U/mL or ≥0.82 BAU/mL). Elecsys-S units were converted to BAU using the following equation: Elecsys-S U=0.972×BAU[16].

Five participants were excluded because they had finished treatment more than 1 year previously, two patients were lost to follow-up after the first dose, and one patient died from the disease after the first vaccination dose. A total of 53 patients were administered two doses of the vaccine, and 44 patients were included in the analysis (four patients had no antibody titer results at 4 weeks after the second dose, two patients had no antibody titer results at 8 weeks after the first dose and 4 weeks after the second dose, and three patients could not be matched to individuals in the healthy volunteer group of equal age and sex). Fig. 1 shows the CONSORT flow diagram of the study. Table 1 summarizes the baseline demographics, cancer history, and therapy history of the study cohort.

Immunogenicity of the ChAdOx1 nCoV-19 vaccine

We analyzed the concentrations of anti-RBD targeting the SARS-CoV-2 spike protein. For comparison, we included data from the same assays of healthy volunteers without cancer. At 8 weeks after the first vaccine injection, the mean antibody level in the hematology patient group was 1.02 BAU/mL (geometric mean; 95% confidence interval [CI], 0.62–1.66), while that of the healthy volunteer group was 37.91 BAU/mL (geometric mean; 95% CI, 28.73–50.02) ($p<0.01$) (Figs. 2, 3). At 4 weeks after the second vaccine, the mean antibody level in the hematology patient group was 9.44 BAU/mL (geometric mean; 95% CI, 3.33–28.49), while that of the healthy volunteer group was 641.6 BAU/mL (geometric mean; 95% CI, 511.16–805.34) ($p<0.01$) (Figs. 3, 4).

Seroconversion rate

The participants' results were interpreted as positive or negative using cut-off anti-RBD antibody levels of ≥0.8 U/mL and <0.8 U/mL, respectively. The seroconversion rate at 8 weeks after the first dose of the vaccine in the hematology patient group was 27.27% (12 of 44 participants) compared with that of the healthy volunteer group, which was 98.86% (87 of 88 participants) ($p<0.001$). At 4 weeks after vaccination, the seroconversion rate of the hematology patients was 47.73% (21 of 44 participants), while that of the healthy volunteers was

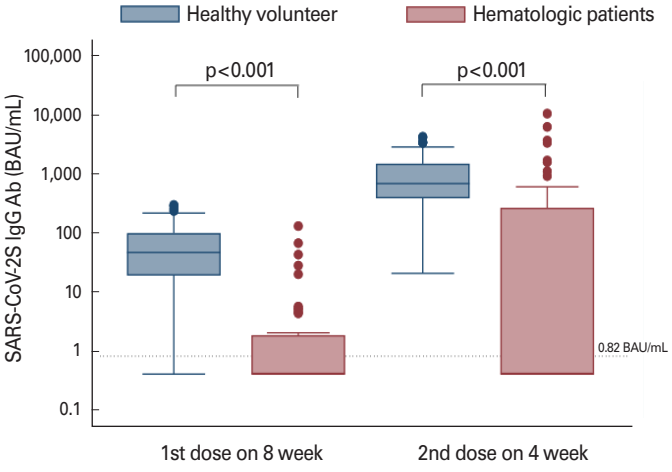

Fig. 3. Antibody concentrations at 8 weeks after first-dose and 4 weeks after second-dose ChAdOx1 nCoV-19 vaccination of hematology patients compared with healthy volunteers. At 8 weeks after the first vaccine injection, the geometric mean antibody level was 1.02 binding antibody (Ab) units (BAU)/mL (95% confidence interval [CI], 0.62–1.66) in the hematology patient group and 37.91 BAU/mL (95% CI, 28.73–50.02) in the healthy volunteer group ($p<0.01$). At 4 weeks after the second vaccine, the geometric mean Ab level was 9.44 BAU/mL (95% CI, 3.33–28.49) in in the hematology patient group and 641.6 BAU/mL (95% CI, 511.16–805.34) in the healthy volunteer group ($p<0.01$). Box plots show the severe acute respiratory syndrome coronavirus 2 spike (SARS-CoV-2S) immunoglobulin G (IgG) Ab concentrations (BAU/mL); the lower endpoints of the boxes represent the 25th percentiles, the upper endpoints represent the 75th percentiles, and the dots represent the outliers. The dotted line is the determined cut-off value for seropositivity (Ab level ≥0.8 U/mL or ≥0.82 BAU/mL). Elecsys-S units were converted to BAU using the following equation: Elecsys-S U=0.972×BAU[16].

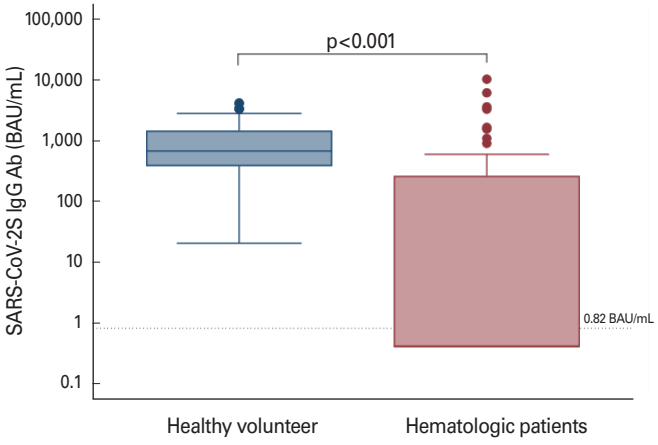

Fig. 4. Antibody concentrations at 4 weeks after second-dose ChAdOx1 nCoV-19 vaccination of hematology patients compared with healthy volunteers. The geometric mean antibody (Ab) level was 9.44 binding antibody units (BAU)/mL (95% confidence interval [CI], 3.33–28.49) in the hematology patient group and 641.6 BAU/mL (95% CI, 511.16–805.34) in the healthy volunteer group ($p<0.01$). Box plots show the severe acute respiratory syndrome coronavirus 2 spike (SARS-CoV-2S) immunoglobulin G (IgG) Ab concentrations (BAU/mL); the lower endpoints of the boxes represent the 25th percentiles, the upper endpoints represent the 75th percentiles, and the dots represent the outliers. The dotted line is the determined cut-off value for seropositivity (Ab level ≥0.8 U/mL or ≥0.82 BAU/mL). Elecsys-S units were converted to BAU using the following equation: Elecsys-S U=0.972×BAU[16].

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100% (88 of 88 participants).

Univariate analysis of data from 8 weeks after the first dose of the vaccine showed that patients with hematologic cancer, including lymphoma, multiple myeloma, and leukemia, had a seroconversion rate of 17.6% (six of 34 participants), which was lower than the 60% (six of 10 participants) of patients with benign hematologic diseases, including myelodysplastic syndrome, myeloproliferative disorders, immune thrombocytopenia on steroid therapy, and Langerhans cell histiocytosis (p=0.013). The seroconversion rates of rituximab treatment and no rituximab treatment subgroups were 6.25% (one of 16 participants) and 60.7% (17 of 28 participants), respectively (p=0.039). Furthermore, patients on steroids had a lower seroconversion rate, i.e., 7.7% (two of 26 participants), than those without steroid use, i.e., 55.5% (10 of 18 participants) (p=0.02).

We analyzed the factors affecting the seroconversion rate of participants at 4 weeks after the second dose of the vaccine. The seroconversion rate was 12.5% (two of 16 participants) in patients receiving rituximab therapy and 67.8% (19 of 28 participants) in patients not receiving rituximab therapy (p=0.002). The seroconversion rate in patients receiving steroid therapy was 23.1% (six of 26 participants), while that in patients not receiving steroid therapy was 83.3% (15 of 18 participants) (p<0.001). Moreover, patients with ongoing chemotherapy tended to have a decreased seroconversion rate compared with patients who did not receive chemotherapy before the vaccine (p=0.048) (Table 2).

The influencing factors leading to a decrease in antibody levels after complete vaccination were hematologic cancer, receiving chemotherapy before vaccination, rituximab and steroid use, and an ALC of <1,000/mm^3. A comparison of patients with cancer and patients with benign diseases showed significantly different antibody levels: the geometric mean

Table 2. Univariate and multivariate analyses of factors affecting the seroconversion rate at 4 weeks after complete vaccination

Variable	Total	Antibody level		Univariate		Multivariate	
		<0.8 U/mL	≥0.8 U/mL	OR (95% CI)	p-value	OR (95% CI)	p-value
Age (yr)							
≥60	35 (79.55)	18 (78.26)	17 (80.95)	Ref			
<60	9 (20.45)	5 (21.74)	4 (19.05)	0.85 (0.19–3.69)	0.825		
Sex							
Female	19 (43.18)	12 (52.17)	7 (33.33)	Ref			
Male	25 (56.82)	11 (47.83)	14 (66.67)	2.18 (0.64–7.40)	0.211		
Malignancy							
Hematologic cancer	34 (77.27)	23 (100.00)	11 (52.38)	Ref			
Benign diseases	10 (22.73)	0	10 (47.62)	-	-		
Chemotherapy history							
Ongoing chemotherapy	26 (59.09)	14 (60.87)	12 (57.14)	Ref		Ref	
Previous chemotherapy	9 (20.45)	8 (34.78)	1 (4.76)	0.15 (0.02–1.34)	0.089	0.18 (0.01–2.43)	0.198
No previous chemotherapy	9 (20.45)	1 (4.35)	8 (38.10)	9.33 (1.02–85.70)	**0.048**	5.88 (0.36–96.39)	0.214
Rituximab therapy							
Rituximab	16 (36.36)	14 (60.87)	2 (9.52)	Ref		Ref	
No rituximab	28 (63.64)	9 (39.13)	19 (90.48)	14.78 (2.75–79.33)	**0.002**	8.36 (1.22–57.51)	**0.031**
Steroid therapy							
Steroids	26 (59.09)	20 (86.96)	6 (28.57)	Ref		Ref	
No steroids	18 (40.91)	3 (13.04)	15 (71.43)	16.67 (3.58–77.68)	**<0.001**	7.21 (1.23–42.32)	**0.029**
ANC at injection day							
<1,500/mm^3	9 (34.62)	5 (35.71)	4 (33.33)	Ref			
>1,500/mm^3	17 (65.38)	9 (64.29)	8 (66.67)	1.11 (0.22–5.63)	0.899		
ALC at injection day							
<1,000/mm^3	6 (23.08)	5 (35.71)	1 (8.33)	Ref.			
>1,000/mm^3	20 (76.92)	9 (64.29)	11 (91.67)	6.11 (0.60–62.23)	0.126		

Values are presented as number (%) or OR (95% CI), unless otherwise stated. The bold type is considered statistically significant (p<0.05).
OR, odds ratio; CI, confidence interval; ALC, absolute lymphocyte count; ANC, absolute neutrophil count; Ref, reference.

antibody level in the benign group was 392.44 BAU/mL, while that in the cancer group was 3.16 BAU/mL ($p<0.001$). The mean antibody level was higher in patients who did not receive chemotherapy before the vaccination than in those who were receiving ongoing chemotherapy (281.10 BAU/mL versus 6.31 BAU/mL, respectively; $p=0.04$). Moreover, patients who received chemotherapy with rituximab showed a diminished mean antibody level, at 0.64 BAU/mL, while patients who did not receive rituximab had an antibody level of 43.93 BAU/mL ($p<0.01$). Similarly, the mean antibody level of patients on steroid therapy was 1.29 BAU/mL, which was lower than that of patients who were not on steroids, 168.04 BAU/mL ($p<0.01$). The mean antibody level of patients with an ALC of <1,000/mm^3 was decreased to 0.53 BAU/mL compared with 17.95 BAU/mL in patients with an ALC of >1,000/mm^3 ($p=0.009$) (Table 3).

Multivariate analysis revealed that the factors associated with a decreased seroconversion rate were rituximab exposure ($p=0.031$) and steroid use ($p=0.029$) (Table 2). Similarly, the factor associated with a diminished antibody level was rituximab treatment ($p=0.013$) (Table 3).

SARS-CoV-2 infection

We followed up the hematology patient group for 6 months after the completion of the vaccination course. Only one of 44 hematology patients who was a non-responder developed SARS-CoV-2 infection within 6 months after vaccination. The healthy volunteer group was not followed up regarding the infection rate.

Adverse effects

In the hematology patient group, only four of 44 patients reported adverse effects after the first dose of the vaccine, and all were mild or moderate. One patient had an injection site

Table 3. Univariate and multivariate analyses of factors affecting the mean antibody levels at 4 weeks after complete vaccination

Variable	Antibody level (BAU/mL), geometric mean (95% CI))	Univariate		Multivariate	
		Geometric ratio (95% CI)	p-value	Geometric ratio (95% CI)	p-value
Age (yr)					
≥60	9.27 (2.70–31.81)	Ref			
<60	10.23 (0.47–223.16)	1.10 (0.06–19.68)	0.946		
Sex					
Female	20.90 (4.39–99.56)	Ref			
Male	3.33 (0.70–15.77)	6.27 (0.74–52.96)	0.090		
Malignancy					
Hematologic cancer	3.16 (0.99–10.14)	Ref		Ref	
Benign diseases	392.44 (138.61–1111.12)	124.07 (28.43–541.50)	**<0.001**	3.37 (0.16–73.02)	0.429
Chemotherapy history					
Ongoing chemotherapy	6.31 (1.69–23.57)	Ref		Ref	
Previous chemotherapy	1.03 (0.12–8.46)	0.16 (0.02–1.52)	0.108	0.56 (0.10–3.24)	0.504
No previous chemotherapy	281.10 (21.96–3597.52)	44.56 (3.50–568.11)	**0.004**	6.53 (0.46–93.43)	0.162
Rituximab therapy					
Rituximab	0.64 (0.33–1.25)	Ref		Ref	
No rituximab	43.93 (10.62–181.69)	68.19 (14.69–316.49)	**<0.001**	9.94 (1.66–59.57)	**0.013**
Steroid therapy					
Steroids	1.29 (0.48–3.46)	Ref		Ref	
No steroids	168.04 (35.57–793.82)	130.18 (22.25–761.77)	**<0.001**	10.84 (0.49–238.21)	0.127
ANC at injection day					
<1,500	5.49 (0.04–671.19)	Ref			
>1,500	9.99 (3.05–32.77)	0.88 (0.03–25.67)	0.937		
ALC at injection day					
<1,000	0.53 (0.29–0.96)	Ref			
>1,000	17.95 (5.12–63.01)	23.62 (2.37–234.88)	**0.009**		

The bold type is considered statistically significant ($p<0.05$).
BAU, binding antibody units; CI, confidence interval; ALC, absolute lymphocyte count; ANC, absolute neutrophil count; Ref, reference.

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reaction, one had a headache, one had fatigue, and one had myalgia. No serious adverse events were reported (Table 4, Fig. 5). In the healthy volunteer group, nine participants experienced severe adverse effects, 12 experienced moderate adverse effects, and 30 experienced mild adverse effects (Table 5, Fig. 6).

Table 4. Adverse effects affecting hematology patients after their 1st dose of the AstraZeneca vaccine

Symptoms	Mild	Moderate	Severe	Total
Injection site reaction	0	1 (2.27)	0	1 (2.27)
Fever	0	0	0	0
Headache	0	1 (2.27)	0	1 (2.27)
Fatigue	1 (2.27)	0	0	1 (2.27)
Myalgia	1 (2.27)	0	0	1 (2.27)
Nausea/vomiting	0	0	0	0
Diarrhea	0	0	0	0
Rash	0	0	0	0
Other	0	0	0	0

Values are presented as number (%).

Table 5. Adverse effects affecting healthy volunteers after their 1st dose of the AstraZeneca vaccine

Symptoms	Mild	Moderate	Severe	Total
Injection site reaction	4 (4.55)	0	1 (1.14)	5 (5.68)
Fever	5 (5.68)	2 (2.27)	3 (3.41)	10 (11.36)
Headache	4 (4.55)	3 (3.41)	1 (1.14)	8 (9.09)
Fatigue	3 (3.41)	4 (4.55)	1 (1.14)	8 (9.09)
Myalgia	5 (5.68)	2 (2.27)	2 (2.27)	9 (10.23)
Nausea/vomiting	4 (4.55)	1 (1.14)	0	5 (5.68)
Diarrhea	3 (3.41)	0	0	3 (3.41)
Rash	1 (1.14)	0	0	1 (1.14)
Other	1 (1.14)	0	1 (1.14)	2 (2.27)

Values are presented as number (%).

Table 6. Adverse effects affecting hematology patients after their 2nd dose of the AstraZeneca vaccine

Symptoms	Mild	Moderate	Severe	Total
Injection site reaction	1 (2.27)	0	0	1 (2.27)
Fever	1 (2.27)	1 (2.27)	0	2 (4.55)
Headache	1 (2.27)	0	0	1 (2.27)
Fatigue	1 (2.27)	0	0	1 (2.27)
Myalgia	0	0	0	0
Nausea/vomiting	0	0	0	0
Diarrhea	0	0	0	0
Rash	0	0	0	0
Other	0	0	0	0

Values are presented as number (%).

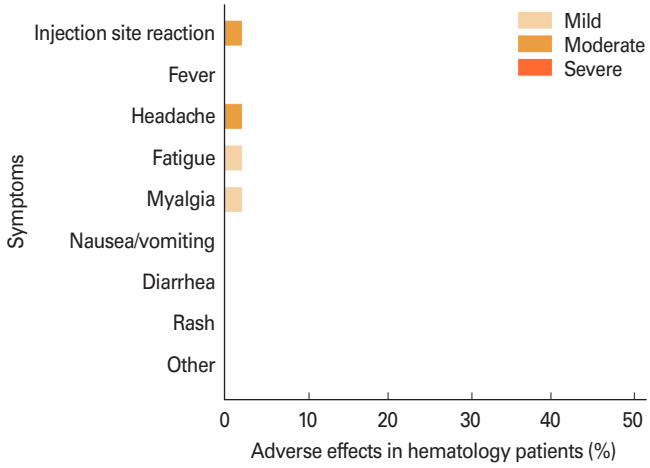

Fig. 5. Adverse effects affecting hematology patients after their 1st dose of the Astra Zeneca vaccine.

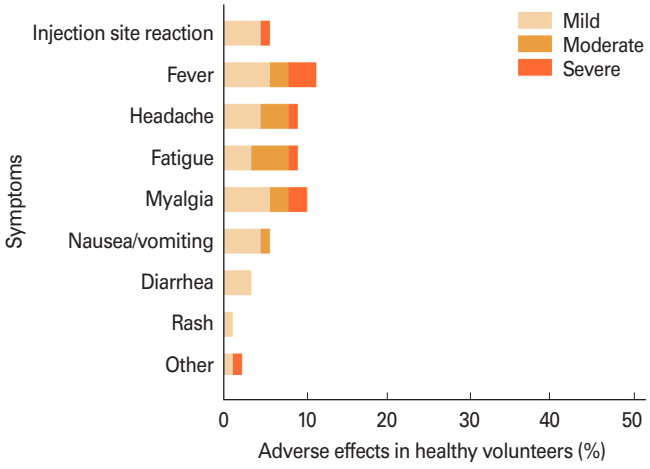

Fig. 6. Adverse effects affecting healthy volunteers after their 1st dose of the Astra Zeneca vaccine.

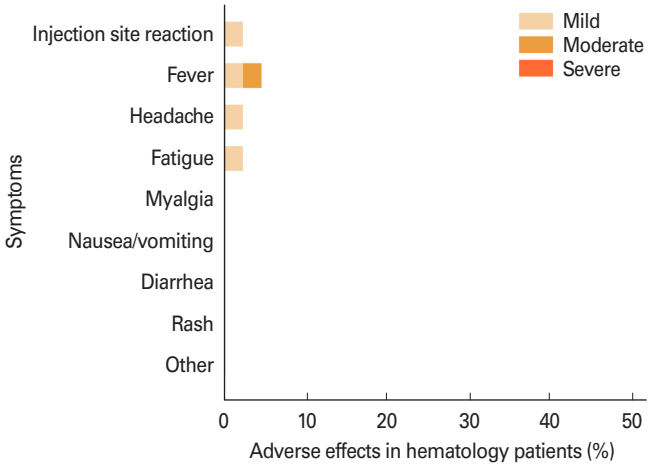

Fig. 7. Adverse effects affecting hematology patients after their 2nd dose of the Astra Zeneca vaccine.

Table 7. Adverse effects affecting healthy volunteer after their 2nd dose of the AstraZeneca vaccine

Symptoms	Mild	Moderate	Severe	Total
Injection site reaction	2 (2.27)	0	0	2 (2.27)
Fever	2 (2.27)	1 (1.14)	0	3 (3.41)
Headache	1 (1.14)	2 (2.27)	0	3 (3.41)
Fatigue	1 (1.14)	1 (1.14)	0	2 (2.27)
Myalgia	0	0	0	0
Nausea/vomiting	3 (3.41)	0	0	3 (3.41)
Diarrhea	2 (2.27)	0	0	2 (2.27)
Rash	1 (1.14)	0	0	1 (1.14)
Other	0	1 (1.14)	0	1 (1.14)

Values are presented as number (%).

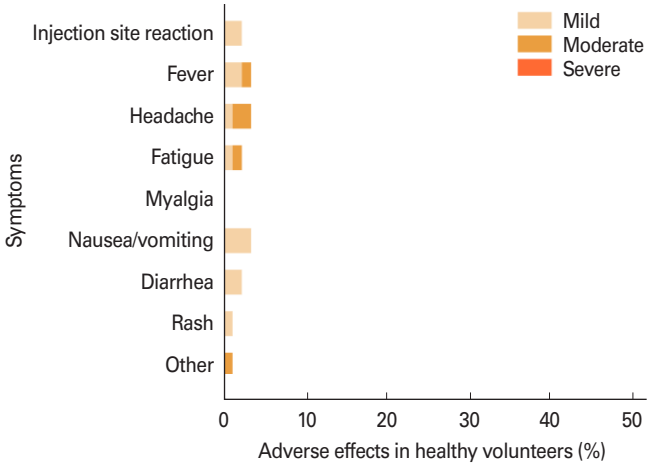

Fig. 8. Adverse effects affecting healthy volunteers after their 2nd dose of the Astra Zeneca vaccine.

After the second dose of the vaccine, the hematology patients group reported no serious adverse effects, while one patient had a moderate adverse effect and three patients had mild adverse effects (Table 6, Fig. 7). In the healthy volunteer group, there were no severe adverse effects reported after the second dose of the vaccine, and the numbers of mild and moderate adverse effects were decreased compared with after the first dose (Table 7, Fig. 8).

Discussion

SARS-CoV-2 infections adversely affect patients with hematologic cancer, resulting in high rates of morbidity and mortality [1]. Our study demonstrated the lower immunogenicity and seropositivity in these patients compared with healthy controls after COVID-19 vaccination, as suggested in past studies [7-14]. Moreover, patients with hematologic cancer had a lower seroconversion rate after COVID-19 vaccination, particularly patients who received anti-CD20 therapy [7,8,11,12]. A previous study of patients who received the BNT162b2, messenger RNA (mRNA)-1273, or Ad26.COV2.S vaccine demonstrated the significantly lower seroconversion rates of patients who underwent anti-CD20 therapies ($p=0.0001$) [7]. This study supports the observation of a reduced seroconversion rate in those with hematological malignancies compared with healthy people, especially patients on anti-CD20 therapy ($p=0.002$) or steroids ($p<0.001$). Another study observed that concordant receipt of corticosteroids is associated with lower antibody concentrations ($p=0.003$) and tends to be associated with lower neutralization titers ($p=0.09$) [14].

Our study showed that the ALC of patients on the day of injection affected the level of immunogenicity ($p=0.009$). Similarly, a study observed that lymphopenia (ALC <1,000/μL), as measured at the last clinical visit before vaccination (median, 6 days prior; interquartile range, 19 days), is associated with lower antibody concentrations ($p=0.01$) but not lower neutralization titers [14].

The limitations of our study were that we only investigated the levels of anti-spike immunoglobulin G antibodies specific to the RBD of the spike protein and did not collect data on the levels of SARS-CoV-2-specific T cell responses or virus neutralization. Second, our study observed responses to the ChAdOx1 nCoV-19 vaccine, but recent data have shown the higher efficacy of mRNA COVID-19 vaccines, even in patients with cancer [14]. However, mRNA vaccines, including BNT162b2 and mRNA-1273, were not widely available at the time of our study. Lastly, our study observed small groups of participants; thus, studies with more participants are needed for validation.

In conclusion, the immune responses of hematology patients after COVID-19 vaccination, particularly those receiving active therapy or B-cell-depleting therapy, are modest compared with those of healthy people. The use of booster or additional vaccinations to raise the immunogenicity of hematology patients should be considered, and this needs to be addressed in more studies.

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