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Antibody Response after ChAdOx1 nCoV-19 Vaccination in Patients with Type 2 Diabetes at Vajira Hospital

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ABSTRACT

OBJECTIVE: A question exists as to whether people with diabetes can respond effectively to the COVID-19 vaccine. This study aimed to evaluate antibody response after COVID-19 vaccination in patients with type 2 diabetes.

METHODS: This was a cross-sectional analytical study. Two hundred and twelve type 2 diabetes patients were enrolled after receiving a second dose of the ChAdOx1nCoV-19vaccine 3 months previously. Demographic data, medical history, and blood drawn were collected. Antibodies against receptor binding domain (anti-RBD) was investigated in the laboratory department. Other factors that could affect anti-RBD level, i.e. age, gender, BMI, glycemic control, duration of diabetes, and comorbidity, were collected and analyzed.

RESULTS: Among 212 patients with type 2 diabetes 3 months after receiving a second dose of the ChAdOx1nCoV-19 vaccine, the anti-RBD level mean was 989.56 U/ml. Patients with type 2 diabetes, with or without cardiovascular disease as a comorbidity, had median anti-RBD levels equal to 258 U/ml and 442 U/ml, respectively. The median of anti-RBD levels between groups had statistically significant differences (p-value = 0.021). Age, gender, BMI, duration of diabetes, glycemic control, and other comorbidities showed no statistically significant differences in the median anti-RBD levels.

CONCLUSION: Only patients with type 2 diabetes with cardiovascular disease as a comorbidity showed statistically significant differences in Anti-SARS-CoV-2 response 3 months after receiving a second dose of the ChAdOx1nCoV-19 vaccine. Therefore, patients with diabetes and cardiovascular disease require earlier revaccination to ensure protection against COVID-19 infection.

KEYWORDS: antibodies, chAdOx1 nCoV-19, COVID-19, COVID-19 vaccine, diabetes mellitus type 2

INTRODUCTION

The COVID-19 pandemic has existed in Thailand since early 2020. Previous reports from international sources, including Thailand, have suggested that older adults (over 60 years old) and patients with comorbidities, especially non-communicable diseases (NCDs) such as diabetes mellitus, obesity, hypertension, and heart disease, are in high-risk groups for increased severity of COVID-19 and mortality rates[1]. The most common comorbidities are hypertension, followed by diabetes mellitus and chronic obstructive respiratory disease[2]. COVID-19 patients with comorbidities, such as diabetes mellitus, are more

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likely to develop an increased severity and progression of the disease[3]. It was found that patients with diabetes were linked to higher severity for the effects of COVID-19, such as intensive care unit (ICU) admission, the need for invasive mechanical ventilation, and death[4-5]. Although diabetes mellitus has been associated with an increased risk for COVID-19 complications and severe symptoms, there is inadequate data to indicate whether people with diabetes are more likely to get COVID-19 compared to the general population[6-7].

Recombinant viral vector vaccine (COVID-19 Vaccine AstraZeneca, ChAdOx1 nCoV-19) produces a viral vector vaccine using a genetically engineered virus that cannot cause disease, but encodes coronavirus proteins to safely generate an immune response. Recombinant viral vector vaccine is approved for people aged 18 years or older as well as patients in high-risk groups, such as those with diabetes. ChAdOx1 nCoV-19 vaccination course consists of two separate doses of 0.5 ml each. The second dose should be administered 12-16 weeks after the first dose.

A previous study by Ramasamy et al. found that the factors affecting levels of antibody response in the general population were associated with older age. It was believed that, as people got older, their immune systems would deteriorate and decline[8]. Therefore, the decline of the immune function probably affected the levels of antibody response. According to a recent study by Ali et al. concerning the levels of anti-SARS-CoV-2 IgG and neutralizing antibodies in patients with type 2 diabetes after receiving the BNT162b2 mRNA COVID-19 vaccine compared with people without type 2 diabetes, the results showed that both groups had significantly high levels of antibody response to the vaccine (high titer). However, the results also showed that patients with type 2 diabetes had lower levels of anti-SARS-CoV-2 IgG and neutralizing antibodies than those without type 2 diabetes. Additionally, type 2 diabetes might impact the humoral immune response to the BNT162b2 mRNA vaccine[9].

There is insufficient data on the antibody response of the COVID-19 vaccine in people with diabetes who received the ChAdOx1 nCoV-19 vaccine, which was considered the initial main vaccine in Thailand. Therefore, this study aimed to evaluate the COVID-19 vaccine response in patients with type 2 diabetes who underwent treatment at Vajira Hospital after receiving a second dose of the ChAdOx1 nCoV-19 vaccine for 3 months.

METHODS

The target population comprised patients with type 2 diabetes listed in the medical records or ICD-10 system Codes E110-E119 as reviewed by physicians and those who underwent treatment at the Diabetes Clinic, Division of Endocrinology and Metabolism, Faculty of Medicine Vajira Hospital, Navamindradhiraj University. The participants were patients with type 2 diabetes who received a second dose of the ChAdOx1 nCoV-19 vaccine during a period of 3 months (from September 2021 to January 2022). However, patients infected with COVID-19 before receiving the vaccine and those with pregnancy were excluded.

The quantity of antibodies against the SARS-CoV-2 virus was analyzed using Elecsys Anti-SARS-CoV-2 based on electrochemiluminescence immunoassay "ECLIA," which was a Double-antigen sandwich. The content of the serum used was 12 microliters of serum per time per person. An analysis was performed using Cobas e801 immunoassay analyzers at the laboratory of the Department of Central Laboratory and Blood Bank, Faculty of Medicine Vajira Hospital, in accordance with the manual in the Anti-SARS-CoV-2 test kit. Spike protein was the main antigenic component responsible for inducing the host immune response. Spike protein was the target region of the SARS-CoV-2 virus; this part was used for developing the vaccines available today. After receiving vaccines, the immune

system produced Anti-RBD, which favored the detection of high-affinity antibodies, including IgG.

Nowadays, data from research papers shows that not only can IgG be a neutralizing antibody, but IgM and IgA also have a chance to become neutralizing antibodies. Therefore, manufacturers focused on detecting all high-affinity antibodies, which were suitable for seeking immune response after COVID-19 vaccination.

The results were interpreted based on antibody levels and reported as positive when antibody levels were greater than or equal to 0.80 U/ml., but reported as negative when antibody levels were less than 0.80 U/ml.

This research project was approved by the Institutional Review Board, Faculty of Medicine Vajira Hospital, Navamindradhiraj University (COA No. 170/2564).

STATISTICAL DATA ANALYSIS

Quantitative variables, namely age, height, weight, BMI, duration of diabetes, laboratory test results, HbA1c levels, and antibody level against spike protein receptor binding domain (anti-RBD), were presented in the form of mean and standard deviation or median and IQR, depending on data distribution. T-test independence was used in the analysis with statistical significance when p-value was less than 0.05. Regarding the qualitative variables, namely gender, comorbidity, data about the COVID-19 infection after receiving a COVID-19 vaccine, and side effects after a COVID-19 vaccination, were presented in the form of percentages. Chi-squared test was used to measure the statistical relationships, while SPSS version 21.0 was used for data analysis.

RESULTS

The study included 212 patients with type 2 diabetes who received the ChAdOx1 nCoV-19 vaccine 3 months prior (from September 2021 to January 2022). Most of the participants were women (63.7%). The mean age was 63.27 ± 12.32 years, and most participants were under 70 years old (67.5%). The mean BMI was 26.94 ± 5.30 kg/m^2, and most participants were obese (62.3%). The participants had a median duration of diabetes at 12.5 years [IQR 6 – 20 U/ml], and nearly two-thirds of participants had had diabetes for longer than or equal to 10 years (67.5%). The participants had a median of HbA1c level equal to 7.6 [IQR 6.7 - 8.7 U/ml], and most of them had HbA1c levels higher than or equal to 7.0 (67.9%). The most common comorbidities found were dyslipidemia (81.1%), followed by hypertension (78.8%) and cardiovascular disease (10.4%). (table 1)

Table 1 Baseline characteristics of patients with type 2 diabetes (n = 212)

Characteristics	n	(%)
Gender		
Male	77	(36.3)
Female	135	(63.7)
Age (years), Mean ± SD	63.27 ± 12.32	
<70	143	(67.5)
≥70	69	(32.5)
BMI (kg/m^2), Mean ± SD	26.94 ± 5.30	
<23.0	51	(24.0)
23.0-24.9	29	(13.7)
≥25.0	132	(62.3)
Duration of type 2 diabetes (years), Median [IQR]	12.5	(6 - 20)
<10	69	(32.5)
≥10	143	(67.5)
HbA1c (%), Median [IQR]	7.6	(6.7 - 8.7)
<7.0	68	(32.1)
≥7.0	144	(67.9)

Table 1 Baseline characteristics of patients with type 2 diabetes (n = 212) (continued)

Characteristics	n	(%)
Comorbidity		
Cardiovascular disease	22	(10.4)
Respiratory disease	2	(0.9)
Other comorbidity		
Hypertension	167	(78.8)
Dyslipidemia	172	(81.1)
Chronic kidney disease/ESRD	20	(9.4)
Hypothyroid	17	(8.0)
Old CVA	9	(4.2)
Cancer	3	(1.4)
Thalassemia	1	(0.5)

Data are presented as number (%), mean ± standard deviation or median (interquartile range)
Abbreviations: BMI, body-mass index; HbA1c, glycated hemoglobin; ESRD, end stage renal disease; CVA, cerebrovascular accident

Regarding the antibody level against receptor binding domain (anti-RBD) 3 months after receiving the second dose of the ChAdOx1 nCoV-19 vaccine, it was found that the participants had an antibody level on the average of 989.56 U/ml. The median was 412 U/ml [IQR 196 – 991 U/ml]. (table 2)

According to the analysis, the factors affecting anti-RBD levels in patients with type 2 diabetes were gender, age, BMI, duration of diabetes, HbA1c levels, and comorbidities. The results of the study showed that male and female participants had no statistically significant differences in the median of anti-RBD levels (p-value = 0.427). The median of anti-RBD levels between groups of patients showed no statistically significant differences, specifically among patients with type 2 diabetes aged below 70 years and patients aged 70 years and above; patients with type 2 diabetes having BMI below 23.0 kg/m^2, 23.0-24.9 kg/m^2, and above or equal to 25.0 kg/m^2; patients with type 2 diabetes having diabetes less than 10 years and longer than or equal to 10 years; patients with type 2 diabetes having HbA1c levels below 7.0% and above or equal to 7.0%. The median of anti-RBD levels for patients with type 2 diabetes, with and without cardiovascular disease as a comorbidity, were 258 U/ml [IQR 128 – 438 U/ml] and 442 U/ml [IQR 203 – 1150 U/ml], respectively. The median of anti-RBD levels between groups exhibited statistically significant differences (p-value = 0.021). The median of anti-RBD levels between groups of patients with type 2 diabetes, with and without other comorbidities such as respiratory disease, hypertension, dyslipidemia, chronic kidney disease/ESRD, hypothyroid, old CVA, cancer, and thalassemia, presented no statistically significant differences (p-value = 0.505). (table 3)

Table 2 Antibody level against receptor binding domain (anti-RBD) after COVID-19 vaccination in patients with type 2 diabetes (n = 212)

Antibody level against receptor binding domain (anti-RBD)	U/ml
Mean	989.56
Median	412
SD	1570.37
Minimum	40
Maximum	9645
IQR	196 - 991

Table 3 Factors affecting antibody level against receptor binding domain (anti-RBD)

Characteristics	N	Anti-SARS-CoV-2 Response		P-value
		Median U/ml	[IQR]	
Gender				
Male	77	379	(145 - 1210)	0.427
Female	135	429	(221 - 942)	
Age (years)				
<70	143	464	(220 - 1454)	0.150
≥70	69	368	(130 - 684)	
BMI (kg/m^2)				
<23.0	51	325	(152 - 707)	0.116
23.0-24.9	29	399	(125 - 1051)	
≥25.0	132	462	(208 - 1441)	
Duration of type 2 diabetes (years)				
<10	69	368	(177 - 966)	0.494
≥10	143	429	(204 - 1087)	
HbA1c (%)				
<7.0	68	413	(213 - 908)	0.811
≥7.0	144	406	(188 - 1105)	
Comorbidity				
Cardiovascular disease				
No	190	442	(203 - 1150)	0.021
Yes	22	258	(128 - 438)	
Other comorbidity				
No	204	260	(127 - 1518)	0.505
Yes	8	413	(201 - 988)	

P-value corresponds to the Mann-Whitney U test or the Kruskal-Wallis test
BMI, body-mass index; HbA1c, Glycated hemoglobin; ESRD, End stage renal disease

According to the study results, 29.7% of patients with type 2 diabetes had side effects after receiving the ChAdOx1 nCoV-19 vaccine. In addition, the most common side effect was muscle pain (15.6%). (figure 1)

Regarding the COVID-19 infection rate of patients with diabetes in the third month after receiving the second dose of the ChAdOx1 nCoV-19 vaccine, the results indicated that none of the patients infected with COVID-19 had it in the third month after receiving the ChAdOx1 nCoV-19 vaccine; the COVID-19 infection rate of patients with diabetes in the third month after receiving the ChAdOx1 nCoV-19 vaccine was 0.0%. (figure 1)

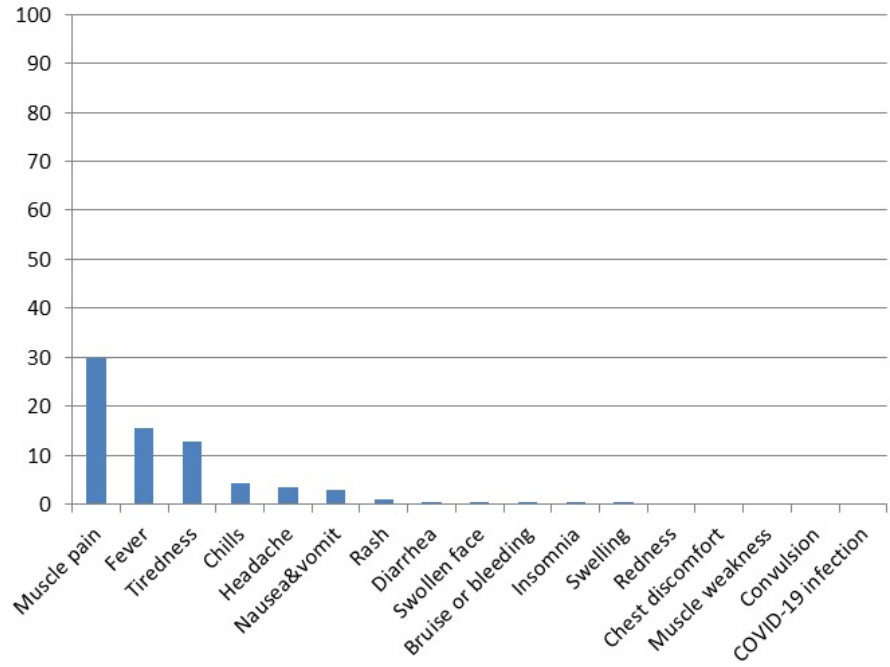

Figure 1

DISCUSSION

There have been many questions and concerns about the effects of vaccination on patients with diabetes. Clinical evidence seems limited only to the immune response after COVID-19 vaccination. Based on this study, analysis of the results of antibody levels against spike protein receptor binding domain (anti-RBD) and factors affecting anti-RBD 3 months after receiving the ChAdOx1 nCoV-19 vaccine in patients with type 2 diabetes were gender, age, BMI, duration of diabetes, HbA1c levels, and other comorbidities. The median of anti-RBD levels between subgroups revealed no statistically significant differences except for cardiovascular disease, in which the median of anti-RBD levels between groups had statistically significant differences. In patients with diabetes, age, gender, BMI, duration of diabetes, HbA1c levels, and other comorbidities had no effect on the anti-RBD level 3 months after receiving a second dose of the ChAdOx1 nCoV-19 vaccine. The results for age, gender, BMI, and hypertension were consistent with the results from the previous cohort study[9]. The previous cohort study indicated that type 2 diabetes had antibody titers (SARSCoV-2-specific IgG and neutralizing antibody responses, following two doses of Pfizer-BioNTech BNT162b2 mRNA vaccine) that were significantly lower than non-diabetics. In contrast, age, gender, BMI, and hypertension did not significantly affect antibody titers. The results of glycemic control (HbA1c levels) were in contrast with an observational study (CAVEAT study) since the observational study reported a lower antibody response to COVID-19 vaccination in people with type 2 diabetes having an HbA1c above 7.0%, compared with normoglycemic individuals and type 2 diabetes patients with good glycemic control[10]. However, the results of this observational study should be interpreted in the context of certain limitations. This was a single-health system study and the participants included in the study received several different vaccines (mRNA-BNT162b2 and mRNA-1273 vaccine, ChAdOx1 nCoV-19 vaccine).

The median of anti-RBD levels in patients with type 2 diabetes, with and without cardiovascular disease as a comorbidity, showed statistically significant differences. Cardiovascular disease might affect the anti-RBD level in patients with diabetes after receiving a second

dose of the ChAdOx1 nCoV-19. These results were consistent with a previous prospective study related to the RBD-IgG level after receiving the BNT162b2 mRNA COVID-19 vaccine in patients with cardiovascular disease (CVD)[11]. The study found that patients with CVD may have a poor humoral response to the BNT162b2 mRNA COVID-19 vaccine. The mechanisms that emphasized the association between CVD and a poor humoral response to the BNT162b2 mRNA COVID-19 vaccine remain unclear. It is possible that the medications used could be associated with a lower humoral response in patients with CVD. Further investigations are required to clarify this issue. However, the results of this prospective study should be interpreted in the context of certain limitations, such as the small sample size, a single-center study approach, and the paucity of long-term data.

In this regard, data from future research studies conducted in Thailand are required. Currently, there is insufficient medical information on the topic, including the use of antibody level testing against spike protein receptor binding domain (anti-RBD), to confirm that antibody detection can prevent COVID-19 infection or serve as a protective antibody. Moreover, further studies are required to clarify how antibody titers potentially affect COVID-19 morbidity.

Regarding the side effects and COVID-19 infection rates of patients with diabetes after receiving the ChAdOx1 nCoV-19 vaccine, the study found that the most common side effect was injection site pain, which was consistent with the current data. On the other hand, no serious side effects from COVID-19 vaccination were detected[12].

Research participants were selected from patients with type 2 diabetes who had undergone treatment at the Endocrinology and Metabolism Clinic, Vajira Hospital and received two doses of the ChAdOx1 nCoV-19 vaccine for 3 months. Data from the database of the E-phis could not be used to represent all patients with diabetes in Thailand. Therefore, the lack of data concerning the non-diabetes population who received two doses of the ChAdOx1 nCoV-19 vaccine for comparing the vaccine response should be addressed. Due to the current situation and the limited quantity of vaccines in Thailand, policies related to exclusively providing the ChAdOx1 nCoV-19 vaccine to high-risk patients with comorbidities such as diabetes were formulated. In contrast, the general population without diabetes has been approved for inactivated COVID-19 vaccination. Moreover, multiple types of COVID-19 vaccines were imported and developed in Thailand during the middle of 2021, contributing to heterologous schedules combining multiple vaccine platforms (e.g. vaccinating a vectored vaccine followed by an mRNA vaccine). In data collection, therefore, there was a small number of participants receiving two doses of the ChAdOx1 nCoV-19 vaccine.

CONCLUSION

Patients with type 2 diabetes and cardiovascular disease as a comorbidity had statistically significant differences in Anti-SARS-CoV-2 responses after receiving a second dose of the ChAdOx1nCoV-19 vaccine for 3 months. Age, gender, BMI, duration of diabetes, HbA1c levels, and other comorbidities had no effect on the Anti-SARS-CoV-2 response. Accordingly, patients with type 2 diabetes and cardiovascular disease are at a high risk for a poor prognosis with COVID-19. Thus, they should be a prioritized group to be vaccinated with a vaccination booster.

CONFLICTS OF INTEREST

The authors declared that the research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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