Medical Science Journal for Advance Research


Vol. 5, No.1, March 2024
*e*-ISSN: 2774-4892

# Evaluation of Humoral Immunogenicity in Diabetes Patients Six Months Post-Second Dose: Comparative Analysis of BNT162b2, ChAdOx1 nCoV-19, and BBIBP-CorV Vaccines

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## ABSTRACT

***Background:*** *Diabetes mellitus patients are usually considered a high risk population for SARS – COV2 infection and shown blunted immune responses when vaccinated with different types of vaccines.* ***Aims:*** *The study aimed to compare the humoral immune response at one to six months post the second dose of BNT162b2, ChAdOx1 nCoV-19, and BBIBP-CorV vaccine in diabetes people. The humoral immune response was assessed by determining SARS-CoV-2 Spike IgG antibodies, and SARS-CoV-2 Neutralization Antibody inhibition %.* ***Materials and methods:*** *A total of 180 participants with diabetes were eligible for analysis. chemiluminescent immunoassay (CLI) quantify SARS-COV-2 spike protein IgG antibody and Enzyme linked immunoassay (ELISA) was used to SARS-CoV-2 Neutralization Antibody inhibition % at most during the six months after the second dose of vaccination.* ***Results:*** *BNT162b2 vaccine induce a highest levels of anti-S IgG antibody and NAB IH5% (25.66±1.67 AU\mL, 76.32±11.6% respectively), followed by ChAdOx1 nCoV-19 (11.53±2.11 AU\Ml, 69.62±14.53 % respectively) and BBIBP-CorV (51.32±11.6 AU\Ml, 7.84±2.41 % respectively) ($p<0.001$) after six months post second dose of vaccination. The impaired antibodies response by BBIBP-CorV vaccine suggests that the vaccine may be less effective in generating a robust immune response in diabetes patients. Furthermore, Sex, Age, and duration were significantly correlated with levels of antibodies.* ***Conclusions:*** *The long-term humoral immunogenicity of several COVID-19 vaccinations in individuals with diabetes is clarified by this study. After six months, BNT162b2 exhibited better humoral immune responses followed by ChAdOx1nCoV-19 and BBIBP-CorV vaccines. Sex, age, and duration after vaccination were correlated with IgG antibody levels and NAB-IH%. These results emphasize the significance of taking into account the type of vaccine and the patients' long-term immune responses when developing an effective COVID-19 immunization strategy.*

***Keywords:*** *Covid-19 vaccine, Diabetes, SARS-COV2, Neutralization antibody, Humoral response.*

**Article Information**

Received: January 16, 2024; Revised: February 21, 2024; Online: March , 2024


https://doi.org/10.46966/msjar.v5i1.169

## INTRODUCTION

Covid-19 has a negative influence on human health, quality of life, and the world economy (1).The prognosis has been poorer for older persons and individual of any age with underlying medical disorders including diabetes mellitus and hypertension. (2). Diabetes mellitus was considered as autonomous risk factor for complications and death during 2002–2003 outbreak of Severe acute respiratory syndrome (SARS-CoV-1) and SARS-COV-2 (3)(4). Angiotensin-converting enzyme 2 (ACE-2), a metallopeptidase, is the physiological receptor for COVID-19, expressed in all tissues and involved in the pathogenesis of the SARS-CoV-2 virus (5).

The SARS-CoV-2 virus is believed to have entered islets cells through ACE-2 receptors, causing pancreatic islet cell damage that impairs beta cell insulin output and resulting in new-onset diabetes or a decline in prior glycemic control (6). The adjusted odds ratios (ORs) for hospitalization (3.90 for T1DM vs. 3.36 for T2DM), severity of disease (3.35 vs. 3.42) and in-hospital mortality (3.51 vs. 2.02) were comparable between patients with T1DM and those with T2DM (7). Although the causes of COVID-19 severity in individuals with diabetes mellitus are complicated, metabolic disorders, such as T2DM, are often characterized by persistent, systemic low-grade inflammation (8). Increased cytokine and inflammatory mediator production is responsible for both the increased insulin resistance and the hyperglycemia that results (Ceriello, 2020). Individuals who are obese or have T2DM already have abnormalities in their adaptive immune system (B and T lymphocytes). These alterations include T cells that express fewer co-stimulatory molecules (CD69, CD28, CD40 ligand) or the interleukin-12 receptor, which leads to a decrease in interferon and granzyme B production in comparison to individuals who do not have T2DM (9). Furthermore, glycated hemoglobin (HbA1c), which measures glycemic control prior to hospital admission, has not always been linked to better results in DM patients treated for COVID-19 (10). A significant step in primary prevention of infections is timely and appropriate vaccination. Since 202, Several vaccine types have been released thus far, including mRNA vaccines such as Pfizer (BNT162b2)(10), and vector-based vaccinations such as AZD1222 (ChAdOx1) (11), and inactivated virus(12). The extent of antibodies against the targeted virus depends up on the type of vaccine and the type of induced antibodies, where neutralizing antibodies embody those conferring protection (13). As the impact of different vaccines on the immune system varies, considering both cellular and humoral immunity is crucial. Few research have examined the COVID-19 vaccine's long-term immunological response to yet. (14–16). A recent publication reviewed the available data on duration of vaccine effectiveness, which was assessed to decrease by about 20-30% within 6 months (17). In this prospective study, We compared the sero-status of diabetes participants and serum level of anti-spike IgG antibody and neutralizing antibody of participants who were administered BNT162b2, ChAdOx1 nCoV-19, and BBIBP-CorV vaccine. Furthermore, we looked at whether age and sex had an impact on the antibody response to vaccines.

## MATERIAL AND METHODS

All blood samples were collected from diabetes-people (n=180) after a 6-months-second-dose of three types of COVID-19 vaccines BNT162b2, ChAdOx1 nCoV-19 and BBIBP-CorV. Participants who did not exhibit any signs of previous SARS-CoV-2 infection and who received two doses of the vaccination 60 days apart. Three groups of participants were selected from Al-Sadder Medical City /

 

Al-Najaf Center for Diabetes and Endocrine, 60 individuals vaccinated with BNT162b2, 60 individuals vaccinated with ChAdOx1 nCoV-19 and 60 individuals vaccinated with BBIBP-CorV) and matched sex. Participants who received the vaccination and had a history of COVID-19 infection or laboratory confirmation of it using reverse transcription polymerase chain reactions were excluded. The serum samples were tested with assay designed to measure SARS-COV-2 spike protein IgG antibody using chemiluminescent immunoassay (CLI) CLIA/China and SARS-CoV-2 Neutralization Antibody inhibition% (NAB-IH%) (Elabscience, China, Cat Number: E-EL-H0108 ) using quantitative enzyme linked immunoassay (ELISA) .

## STATISTICAL ANALYSIS

The SPSS program 26.0 statistical software was used for performing all statistical analysis. Data were expressed as mean±SD and P-values <0.05 were considered statistically significant. The Pearson correlation coefficient (r) was used to explore potential correlation between age with SARS-COV2 spike protein IgG AU/ML and IH % Neutralizing antibody.

## RESULT

A total 180 serum samples were included and analyzed. Mean age 45.03 ±12.23, 44.12±13.01, 45±11.41 years for diabetes participant vaccinated with vaccines BNT162b2, ChAdOx1 nCoV-19 and BBIBP-CorV respectively.

Distinct variations in the levels of antibodies were noted among individuals who were administered different vaccines, as delineated in table 1. Analysis of the SARS-Cov2 IgG antibodies and neutralizing antibodies % based on types of vaccines showed that all three types of vaccines elected robust level of antibodies at the first month post vaccination. Mean IgG antibody levels 25.66±1.67 AU\mL and 15.84±3.01AU\mL for BNT162b2, 23.37±1.56 AU\mL and 11.53±2.11AU\mL for ChAdOx1nCoV-19, and 19.66±1.67AU\mL and 7.84±2.41AU\mL for BBIBP-CorV vaccination group after the one and six months after the second dose, Figure 1a . High neutralizing antibodies inhibition % (NAB%) were seen after one and six months of the second dose of BNT162b2, (85.74±13.2 and 76.32±11.6), followed by ChAdOx1nCoV-19 (85.35±12.29 and 69.62±14.53), then BBIBP-CorV (75.22±13.2 and 51.32±11.6), Figure 1b.

Mean IgG-Ab levels at the 30 day from administration the second dose of BNT162b2, ChAdOx1nCoV-19, and BBIBP-CorV vaccines for males were (22.45±1.99, 20.35±0.98, and 16.21±2.03 AU\ml) respectively ($p < 0.05$) and females were (28.87±1.35, 26.39±2.14, and 23.11±1.31 AU\ml) respectively ($p < 0.05$). At the six-month interval subsequent to the administration of the second vaccine dose, male subjects exhibited mean antibody concentrations of (11.98±2.78 10.08±1.75, and 5.67±1.89 AU/ml) for the BNT162b2, ChAdOx1nCoV-19, and BBIBP-CorV respectively ($p < 0.05$). This discrepancy was statistically significant ($p < 0.05$). Similarly, compression of the three vaccinated groups' antibody levels in females revealed that 19.7±3.24, 12.98±2.47, and 10.01±2.93 AU/ml, respectively ($p < 0.05$). Additionally, there was a statistically significant decrease in Ab levels pertaining to participant sex between two time periods. Table1, Figure 2a.

The comparison strength of the NAB-IH % at 30 days against three types of vaccines in males were 86.41±12.3 %, 83.89±9.31%, and 74.21±12.51%, ($p < 0.05$), while the female were (89.07±14.1%, 86.81±15.27%, and 76.23±13.89%) for BNT162b2, ChAdOx1nCoV-19, and BBIBP-CorV respectively, $p < 0.05$. In contrast, at the six-month mark subsequent to the administration of the second vaccination dose among male

participants, neutralizing antibody percentages exhibited no significant deviation for BNT162b2 and ChAdOx1nCoV-19, while a notable decrease was observed for BBIBP-CorV (72.03±11.3% 65.93±13.27%, and 47.30±12.24%, respectively; p < 0.01). Females were revealed a significant difference for BNT162b2 and ChAdOx1nCoV-19 as compared with BBIBP-CorV (80.61±11.9 %, 73.31±15.79%, and 55.34±10.96%, p < 0.01), Table1, Figure 2b.

Figure 2b: Neutralizing antibodies inhibition % at the 30 day and six months after the second dose of vaccines according to sex. * p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.

Table 2 illustrates that in a model of age, there was a significant variation in IgG antibody levels between two time points with respect to participant age for each of the three vaccination groups. After analyzing Ab levels by age groups, a significant increase of measured Ab levels was reported for BNT162b2 and ChAdOx1nCoV-19 (in age categories < 40 years, p < 0.05) at the 30 day then gradual decline in Ab levels at six months after the second dose. Significant differences were reported for BNT162b2 by age groups < 50 years (p < 0.01), ChAdOx1nCoV-19 (age groups < 40 years, p < 0.01), and BBIBP-CorV (age groups < 50 years, p < 0.01), Table 2a.

Although most vaccinated subjects developed significant levels of NAB IH% at 30 day and at 6 months of second dose post vaccination (Table-1), such levels varied greatly from one vaccine to another according to age categories as noted in table – 3. Participant with age less than 60 years showed a significant level of NAB IH% at 30 day post vaccination with three different types of vaccines. In contract, six months after second dose of vaccination, All age groups less than 70 showed a significant level of NAB IH% among three types of vaccines.

In addition, we found a positive t correlation was seen between titter of SARS-COV-2 spike protein IgG AU/ML and IH % Neutralizing antibody in all types of vaccines, also titter of SARS-COV-2 spike protein IgG AU/ML and IH % Neutralizing antibody to Sinopharm vaccine revealed significant negative correlation with age (rs=0.645**p-0.001, rs= -0.505**p-0.004), table 3.

**Table 1. Levels of Anti-spike IgG antibodies and neutralizing antibodies inhibition % on 30 days and six months after the administration of the second dose of vaccine, stratified by sex and age groups of participants.**

| Characters | n. | % | Anti-spike IgG antibodies (AU\ml) | | | SARS-CoV-2 neutralization antibodies% | | |
|---|---|---|---|---|---|---|---|---|
| | | | At the 30 day after the second dose | At the six months after the second dose | P-value | At the 30 day after the second dose | At the six months after the second dose | P-value |
| | | | mean±SD | mean±SD | | mean±SD | mean±SD | |
| **BNT162b2 vaccines (N=60)** | | | | | | | | |
| **Total** | **60** | **100** | **25.66±1.67** | **15.84±3.01** | **0.01** | **85.74±13.2** | **76.32±11.6** | **0.05** |
| **sex** | | | | | | | | |
| **Male** | **18** | **30** | **22.45±1.99** | **11.98±2.78** | **0.05** | **86.41±12.3** | **72.03±11.3** | **0.05** |
| **Female** | **42** | **70** | **28.87±1.35** | **19.7±3.24** | **0.01** | **89.07±14.1** | **80.61±11.9** | **0.05** |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Age groups** | | | | | | | | |
| **20-29** | **8** | **13.3** | **34.85±1.08** | **20.41±2.69** | **0.05** | **91.65±9.45** | **83.11±7.11** | **0.05** |
| **30-39** | **7** | **11.7** | **29.88±1.77** | **20.73±2.87** | **0.05** | **89.2±8.01** | **83.41±6.98** | **0.06** |
| **40-49** | **9** | **15** | **28.83±1.93** | **17.92±3.94** | **0.01** | **84.36±8.23** | **79.92±14.88** | **0.08** |
| **50-59** | **15** | **25** | **24.12±1.39** | **18.56±2.89** | **0.062** | **84.02±14.96** | **73.98±12.68** | **0.05** |
| **60-69** | **15** | **25** | **18.96±1.42** | **12.85±2.78** | **0.06** | **82.98±19.76** | **69.52±14.01** | **0.01** |
| **≥ 70** | **6** | **10** | **17.32±2.43** | **7.57±3.78** | **0.01** | **82.23±18.79** | **67.78±13.94** | **0.01** |
| **ChAdOx1nCoV-19 vaccines(N=60)** | | | | | | | | |
| **Total** | **60** | **100** | **23.37±1.56** | **11.53±2.11** | **0.01** | **85.35±12.29** | **69.62±14.53** | **0.01** |
| **sex** | | | | | | | | |
| **Male** | **28** | **46.7** | **20.35±0.98** | **10.08±1.75** | **0.01** | **83.89±9.31** | **65.93±13.27** | **0.05** |
| **Female** | **32** | **53.3** | **26.39±2.14** | **12.98±2.47** | **0.01** | **86.81±15.27** | **73.31±15.79** | **0.05** |
| **Age groups** | | | | | | | | |
| **20-29** | **13** | **21.7** | **30.15±1.38** | **21.14±1.36** | **0.05** | **90.23±11.39** | **75.12±13.74** | **0.01** |
| **30-39** | **17** | **28.3** | **27.91±1.09** | **17.32±2.19** | **0.05** | **90.04±10.54** | **76.25±12.81** | **0.01** |
| **40-49** | **9** | **31.7** | **24.72±1.21** | **13.09±2.81** | **0.05** | **83.76±11.23** | **74.98±13.66** | **0.05** |
| **50-59** | **11** | **18.3** | **20.21±2.09** | **9.13±2.02** | **0.01** | **82.64±12.98** | **64.70±13.62** | **0.01** |
| **60-69** | **7** | **11.7** | **17.71±2.33** | **4.11±1.36** | **0.001** | **82.31±12.39** | **65.81±13.21** | **0.001** |
| **≥ 70** | **3** | **5** | **17.13±1.26** | **4.39±1.92** | **0.001** | **83.12±15.21** | **59.86±12.58** | **0.001** |
| **BBIBP-CorV vaccines(N=60)** | | | | | | | | |
| **Total** | **60** | **100** | **19.66±1.67** | **7.84±2.41** | **0.001** | **75.22±13.2** | **51.32±11.6** | **0.001** |
| **sex** | | | | | | | | |
| **Male** | **23** | **38.33** | **16.21±2.03** | **5.67±1.89** | **0.01** | **74.21±12.51** | **47.30±12.24** | **0.001** |
| **Female** | **37** | **61.67** | **23.11±1.31** | **10.01±2.93** | **0.01** | **76.23±13.89** | **55.34±10.96** | **0.001** |
| **Age groups** | | | | | | | | |
| **20-29** | **11** | **18.3** | **23.90±1.85** | **12.53±2.59** | **0.01** | **82.43±14.57** | **62.35±12.30** | **0.001** |
| **30-39** | **15** | **25** | **23.81±1.48** | **10.78±2.19** | **0.01** | **83.12±12.57** | **57.39±11.86** | **0.001** |
| **40-49** | **8** | **13.3** | **20.89±2.89** | **10.49±2.41** | **0.05** | **73.24±13.82** | **52.49±10.73** | **0.001** |
| **50-59** | **13** | **21.7** | **18.9±1.23** | **7.80±1.83** | **0.05** | **74.17±11.91** | **53.69±11.56** | **0.001** |
| **60-69** | **9** | **15** | **15.22±1.31** | **3.41±1.25** | **0.01** | **70.76±13.64** | **46.28±11.73** | **0.001** |
| **≥ 70** | **4** | **6.7** | **15.24±1.22** | **3.91±1.85** | **0.01** | **67.90±12.96** | **35.72±11.42** | **0.001** |

*** p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.**

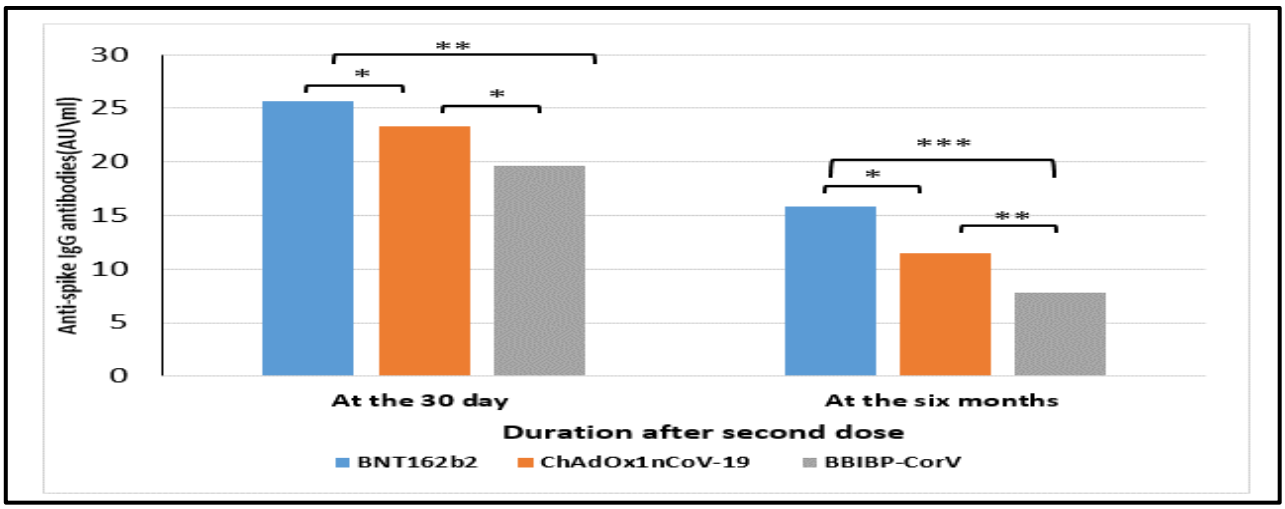


**Figure 1a: Anti-spike IgG antibodies(AU\ml) level at the 30 day and six months after the second dose of vaccines. * p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.**

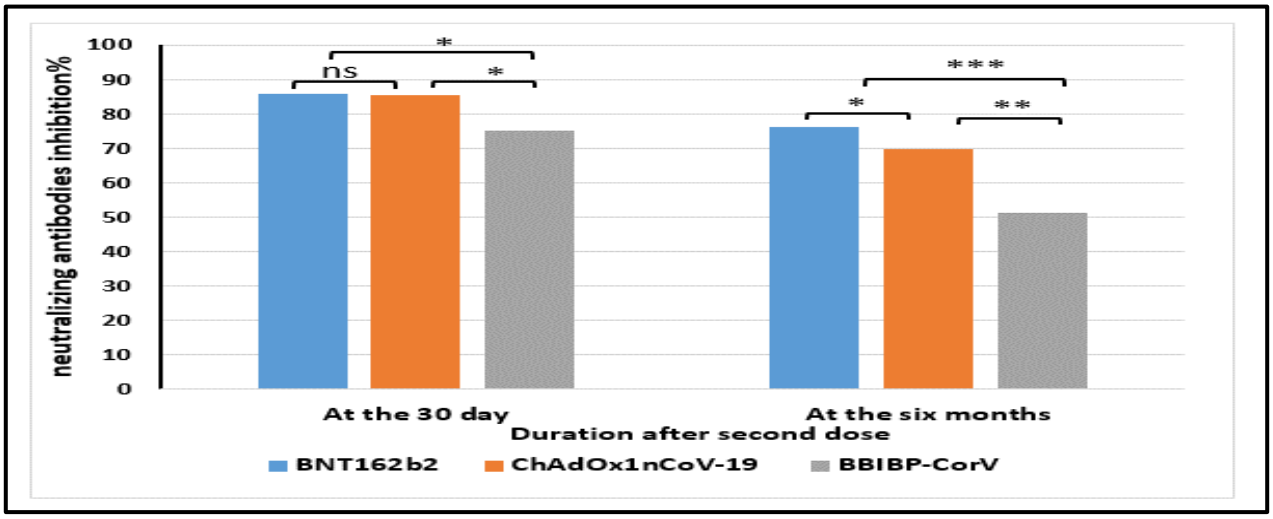


**Figure 1b: Neutralizing antibodies inhibition % at the 30 day and six months after the second dose of vaccines. * p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.**

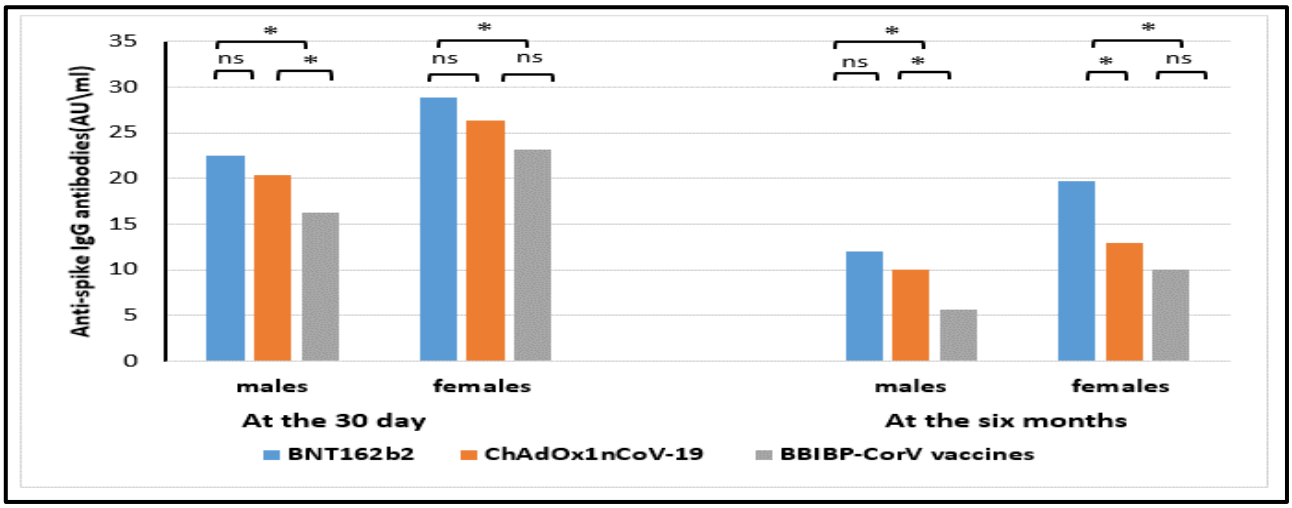


**Figure 2a: Anti-spike IgG antibodies(AU\ml) level at the 30 day and six months after the second dose of vaccines. * p < 0.05, ns=not significant.**

 

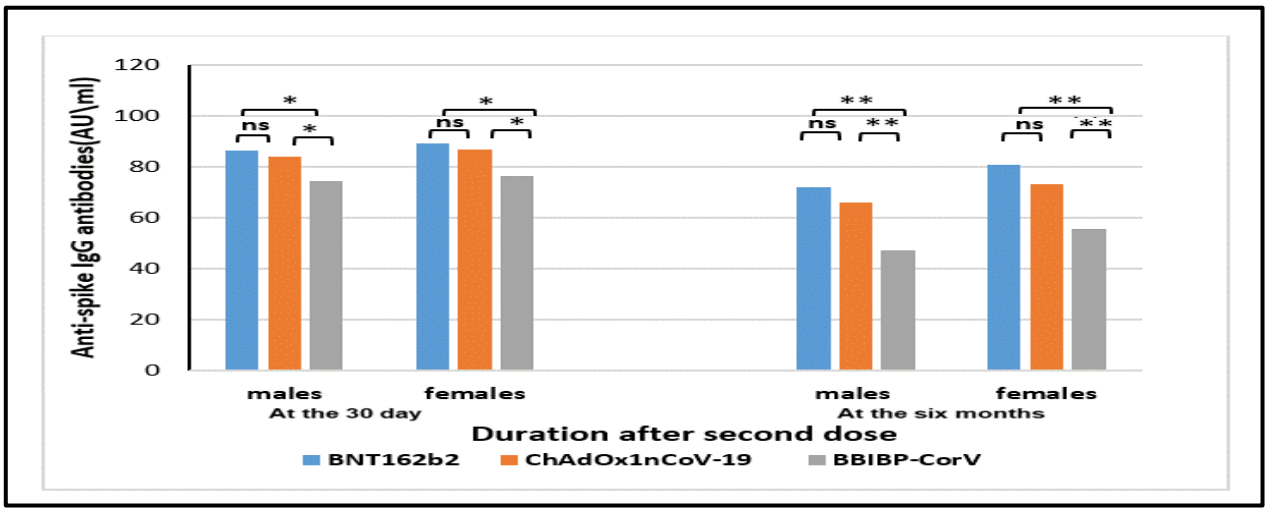


**Figure 2b: Neutralizing antibodies inhibition % at the 30 day and six months after the second dose of vaccines according to sex. * p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.**

**Table 2a: Levels of Anti-spike IgG antibodies on 30 days and six months after the administration of the second dose of vaccine, stratified by age groups of participants.**

| Age groups | BNT162b2 | ChAdOx1nCoV-19 | BBIBP-CorV | p-value |
|---|---|---|---|---|
| At 30 day | | | | |
| 20-29 | 34.85±1.08 | 30.15±1.38 | 23.90±1.85 | 0.05 |
| 30-39 | 29.88±1.77 | 27.91±1.09 | 23.81±1.48 | 0.05 |
| 40-49 | 28.83±1.93 | 24.72±1.21 | 20.89±2.89 | 0.05 |
| 50-59 | 24.12±1.39 | 20.21±2.09 | 18.9±1.23 | 0.02 |
| 60-69 | 18.96±1.42 | 17.71±2.33 | 15.22±1.31 | 0.3 |
| ≥ 70 | 17.32±2.43 | 17.13±1.26 | 15.24±1.22 | 0.42 |
| At 6 months | | | | |
| 20-29 | 20.41±2.69 | 21.14±1.36 | 12.53±2.59 | 0.01 |
| 30-39 | 20.73±2.87 | 17.32±2.19 | 10.78±2.19 | 0.05 |
| 40-49 | 17.92±3.94 | 13.09±2.81 | 10.49±2.41 | 0.05 |
| 50-59 | 18.56±2.89 | 9.13±2.02 | 7.80±1.83 | 0.01 |
| 60-69 | 12.85±2.78 | 4.11±1.36 | 3.41±1.25 | 0.05 |
| ≥ 70 | 7.57±3.78 | 4.39±1.92 | 3.91±1.85 | 0.22 |

*** p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.**

**Table 2b : Neutralizing antibodies inhibition % at the 30 day and six months after the second dose of vaccines stratified by age groups of participants.**

| Age groups | BNT162b2 | ChAdOx1nCoV-19 | BBIBP-CorV | p-value |
|---|---|---|---|---|
| At 30 day | | | | |
| 20-29 | 91.65±9.45 | 90.23±11.39 | 82.43±14.57 | 0.84 |
| 30-39 | 89.2±8.01 | 90.04±10.54 | 83.12±12.57 | 0.61 |
| 40-49 | 84.36±8.23 | 83.76±11.23 | 73.24±13.82 | 0.05 |
| 50-59 | 84.02±14.96 | 82.64±12.98 | 74.17±11.91 | 0.02 |
| 60-69 | 82.98±19.76 | 82.31±12.39 | 70.76±13.64 | 0.05 |
| ≥ 70 | 82.23±18.79 | 83.12±15.21 | 67.90±12.96 | 0.05 |
| At 6 months | | | | |
| 20-29 | 83.11±7.11 | 75.12±13.74 | 62.35±12.30 | 0.05 |
| 30-39 | 83.41±6.98 | 76.25±12.81 | 57.39±11.86 | 0.05 |
| 40-49 | 79.92±14.88 | 74.98±13.66 | 52.49±10.73 | 0.05 |
| 50-59 | 73.98±12.68 | 64.70±13.62 | 53.69±11.56 | 0.01 |
| 60-69 | 69.52±14.01 | 65.81±13.21 | 46.28±11.73 | 0.001 |
| ≥ 70 | 67.78±13.94 | 59.86±12.58 | 35.72±11.42 | 0.001 |

*** p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.**

**Table 3: Spearman correlation determining relationship of age with SARS-COV2 spike protein IgG AU/ML and IH % Neutralizing antibody.**

| | Types of vaccines | Correlation Coefficient(rs) SARS-COV2 spike protein IgG AU/ML | Correlation Coefficient(rs) Neutralizing antibody IH % | Age year |
|---|---|---|---|---|
| SARS-COV2 spike protein IgG AU/ML | BNT162b2 | 1 | rs = 0.871** p- 0.001 | rs = - 0.326 p - 0.079 |
| Neutralizing antibody IH % | | rs = 0.871** p- 0.001 | 1 | rs = - 0.424 p- 0.8 |
| Age year | | rs=-0.326 p-0.079 | rs = - 0.424 p-0.8 | 1 |
| SARS-COV2 spike protein IgG AU/ML | ChAdOx1nCoV-19 | 1 | rs = 0.792** p- 0.001 | rs = 0.-227 p- 0.228 |
| Neutralizing antibody IH % | | rs =0.792** p- 0.001 | 1 | rs = 0.043 p- 0.02 |
| Age year | | rs=0.-227 p-0.228 | rs=0.043 p-0.02 | 1 |
| SARS-COV2 spike protein IgG AU/ML | BBIBP-CorV | 1 | rs = 0.61** p- 0.001 | rs = - 0.645** p- 0.001 |
| Neutralizing antibody IH % | | rs = 0.61** p- 0.0.001 | 1 | rs = - 0.505** p- 0.004 |
| Age year | | rs = - 0.645** p- 0.001 | rs = -0.505** p- 0.004 | 1 |
| *** p < 0.05, ** p < 0.01, *** p < 0.001, ns=not significant.** | | | | |

## DISCUSSION

The current study assessed 180 diabetic participants, aged 20 to 85, for SARS-CoV-2-specific IgG and neutralizing antibody IH% responses after receiving the second doses of the BNT162b2, ChAdOx1 nCoV-19, and BBIBP-CorV vaccine. Age, sex, and duration after the second dose were also involved. Our research on the particular vaccine kinds and the amount of time after the second dosage shows that the group vaccinated with BNT162b2 had the greatest mean value, followed by ChAdOx1 nCoV-19 and BBIBP-CorV (Figure 1a-b). Resent study suggest that the BNT162b2 mRNA vaccine is effective in eliciting a strong immune response of both anti-SARS-CoV-2 IgG and NAbs in patients with T2DM(18). BNT162b2 mRNA vaccine exhibited more robust antibody response , characterized by higher levels of IgG antibody and neutralizing antibodies comparing to inactivated COVID-19 vaccine in diabetic patients (19) . All vaccines group, the females had significantly higher anti-S antibody levels and neutralizing antibody IH% than the males (Figure 2a-b).

Both the anti-S antibody titer and neutralization antibody IH% tend to decrease as six months after doses, age increased, irrespective of vaccine type (Table 2a-b). Khoury *et al.* (2021) observed that BNT162b2 vaccination recipients older than 50 years had lower antibody titers than younger patients(20) . Furthermore, females had greater titers than men among the subjects who were older. HCWs under 46 who received the BNT162b2 vaccination had IgG concentrations that were 1.34–1.57 times greater than those of older individuals (21). Fujigaki *et al.* (2022) demonstrated that following second dose of BNT162b2, the IgG titer of females (263.6 ± 158.0 U/mL) was considerably greater than that of males (209.9 ± 137.6 U/mL)(22). Overall, several biological, hormonal, genetic, and behavioral factors may be involved in the greater antibody titers seen in female participants across all COVID-19 vaccine groups in the study.

The study concluded that the humoral immune response to COVID-19 vaccination in individuals with diabetes is influenced by age, with older individuals exhibiting a weaker response compared to younger individuals(23). According to our research, a COVID-19 vaccination's humoral immune response is significantly influenced by age. This is consistent with other research that demonstrates older individuals not only show a faster waning of antibodies but also a lower antibody response to various vaccines (24) . Although the protective levels of neutralizing Abs have not yet been established, it is already recognized that these levels are useful indicators of vaccination effectiveness, herd and individual immunity beside the virus, and the resilience of humoral immune response. A gradual decline in Ab titers or levels could be interpreted as a sign of less than ideal defense against SARS-CoV-2 infection (25). Therefore, evaluating post-vaccination titers/levels can aid in improving current vaccination tactics and providing a better understanding of the vaccine's long-term efficacy (26).

Numerous investigations have documented a noteworthy association between the identified concentrations of anti-S Abs and the serum neutralizing activity assessed using neutralization assays. The observed connection indicates that these tests have significant promise for the measurable prediction of neutralizing antibodies titers and the assessment of the degree and duration of protection (27,28).

Our study has several limitations, including the small size of participants consequently, particularly when it comes to the proportion of

males and females, makes it challenging to get greater connections between the defined categories. The individuals that infected with COVID-19 after second dose, diabetic patients with malignancy or chemotherapy, presence of chronic disease individuals that vaccinated with different second dose were excluded.

## CONCLUSION

This long-term assessment showed that diabetic individuals who had the BNT162b2, ChAdOx1nCoV-19, and BBIBP-CorV vaccinations had decreased in SARS-CoV-2 anti Spike IgG and Neutralizing antibody IH% at six months after vaccination, but BNT162b2 had slightly declined levels of SARS-CoV-2 anti Spike IgG and Neutralizing antibody IH%. Regarding sex, Females have a high humoral immune response than males. In comparison of age categories, the diabetic individuals who were younger had a higher mean Ab level and Neutralizing antibody IH% after receiving the BNT162b2 vaccination compared to those who were older. Ultimately, more extensive research is necessary to ascertain the level of the SARS-CoV-2 specific Ab following the third dosage at the subsequent time points and to get a deeper comprehension of the correlation between the drop in Ab and the efficiency of the vaccine.

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