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Short communication

Comparison of anti-SARS-CoV-2 IgG and IgA antibody responses post complete vaccination, 7 months later and after 3rd dose of the BNT162b2 vaccine in healthy adults

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ABSTRACT

Background: The mRNA Covid-19 vaccine (BNT162b2) is administered in two doses with 21 days interval. On 4th October 2021 European Medicines Agency approved administration of a booster dose in at least 6 months after the second dose for people aged 18 years and older.
Objectives: In the present study we compare the anti-SARS-COV-2 IgG and IgA antibody responses post complete vaccination, 7 months later and after the 3rd (booster) dose of the BNT162B2 vaccine in healthy adults.
Study design: The levels of vaccine IgG and IgA antibodies to SARS-CoV-2 were assessed in serum samples obtained from individuals vaccinated with two doses and a booster of BNT162b2 vaccine. Samples were tested using the SARS-CoV-2 receptor-binding domain (RCB) IgG and IgA semi-quantitative commercial ELISA assay.
Results: The geometric mean of the anti-SARS-COV-2 IgG and IgA antibody level 7 months after vaccination of 90 healthy adults with BNT162B2 vaccine decreased significantly from 12.0 to 5.4 and 5.6 to 2.3, respectively. After the third dose of the same vaccine, the antibody level increased again, to values higher than at the beginning after the second dose.
Conclusions: Significant decrease of antibody levels within a few months after full vaccination could result in the higher risk of SARS-CoV-2 infection, especially when new variants of the virus emerge. The booster could be crucial for protection against new SARS-CoV-2 variants. The antibody level seems to decrease slower in vaccinated individuals with history of COVID-19 and in younger individuals.

1. Background

The COVID-19 vaccination program in Poland was initiated at the end of December 2020, with the Pfizer–BioNTech mRNA vaccine (BNT162b2) administered in two doses with 21 days interval. On 4th October 2021 European Medicines Agency approved administration of a booster dose in at least 6 months after the second dose for people aged 18 years and older. A few days later the administration of the third dose has been started in Poland. By December 2021, 54.8% of the total population were fully vaccinated against COVID-19. 14.7% of the population have received the third dose. Over 75% of doses administered in Poland were BNT162b2 vaccine. The other administered vaccines were mRNA-1273 (Moderna COVID-19 vaccine), Ad26.CoV2-S (COVID-19 Vaccine Janssen) and ChAdOx1-S (COVID-19 vaccine AstraZeneca) [1, 2].

2. Objectives

In the present study we compare the anti-SARS-COV-2 IgG and IgA antibody responses post complete vaccination, 7 months later and after the 3rd dose of the BNT162B2 vaccine in healthy adults, employees of National Institute of Public Health NIH - National Research Institute (NIPH NIH—NRI) in Warsaw, Poland.

3. Study design

The levels of vaccine IgG and IgA antibodies to SARS-CoV-2 were assessed in serum samples obtained twice from 90 individuals (62 women and 28 men) vaccinated with two doses of BNT162b2 vaccine. The first series included serum samples obtained in February 2021, between 10 and 43 days after receiving the second dose of the vaccine (an average of 25 days), while the second series of studies included

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Table 1
Antibody data following administration of two doses of BNT162B2 vaccine, 7 months later and after 3rd dose of BNT162B2 vaccine.

Group of vaccinated individuals (no.)	Class	Positive (%)	GM value	Antibody level			
				<1.1	1.1–5.0	5.1–10	>10
After 2nd dose	IgA	89 (98.9%)	5.6	1 (1.1%)	32 (35.6%)	37 (41.1%)	20 (22.2%)
(90 individuals)	IgG	90 (100%)	12.0	–	–	22 (24.4%)	68 (75.6%)
7 months after 2nd dose (90 individuals)	IgA*	64 (71.1%)	2.3	26 (28.9)	35 (38.9%)	21 (23.3%)	8 (8.9%)
	IgG	90 (100%)	5.4	–	34 (37.8%)	51 (56.7%)	5 (5.6%)
After 3rd dose	IgA	37 (100%)	7.5	–	11 (29,7%)	12 (32.4%)	14 (37.8%)
(37 individuals)	IgG	37 (100%)	11.5	–	–	8 (21.6%)	29 (78.4%)

* $\chi^2 = 25.1; p < 0.05$.

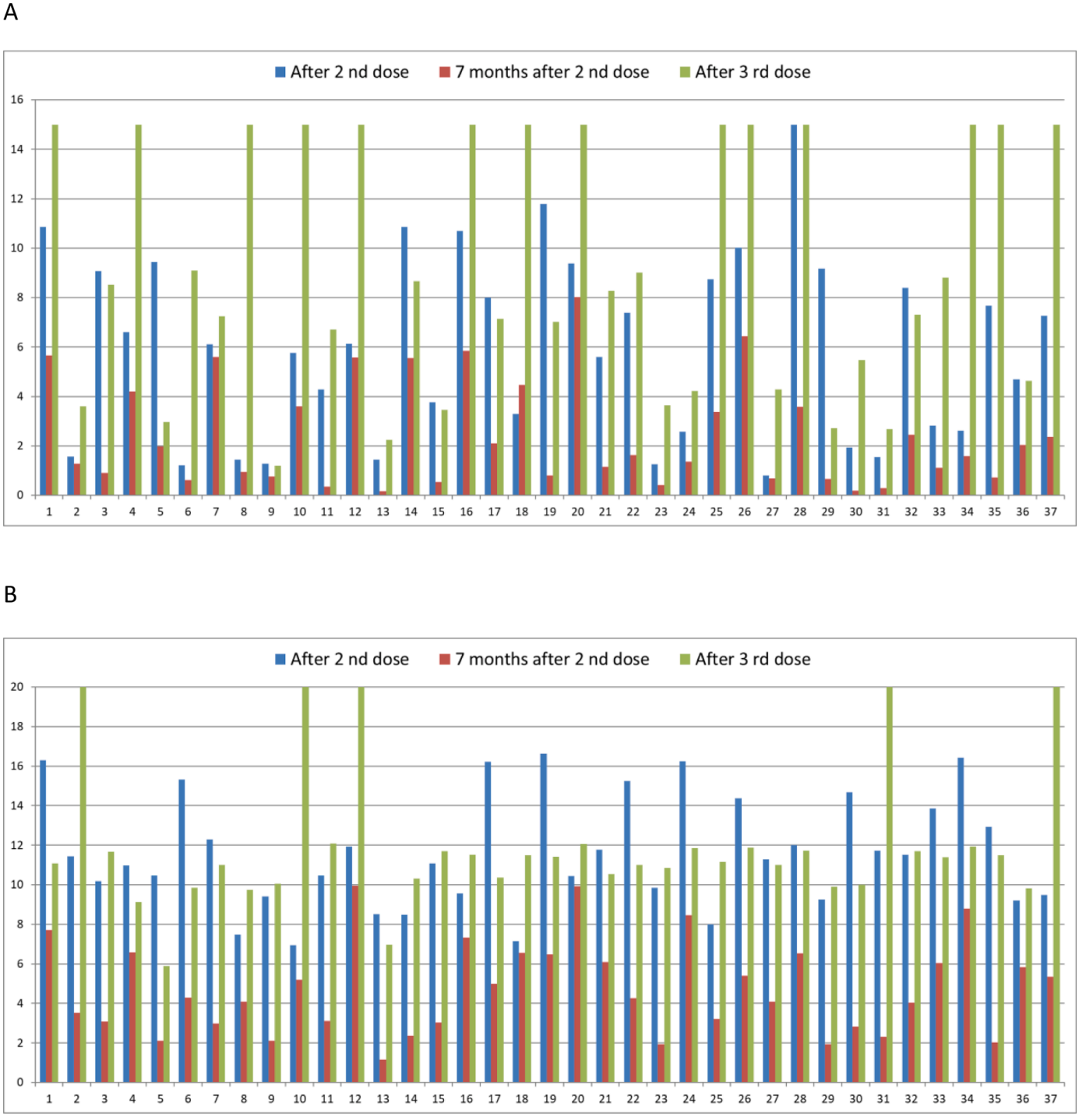

Fig. 1. Levels of IgA and IgG antibodies in serum samples of 37 individuals vaccinated with a booster dose: A – IgA levels, B – IgG levels.

Table 2
The level of IgA and IgG antibodies depending on the gender and age of the individuals.

Group of vaccinated individuals (no.)	Class	Geometric value of antibody level (no. of individuals)			
		Women	Men	<47 years	≥47 years
After 2nd dose (90 individuals)	IgA	5.4 (62)	6.3 (28)	6.2 (45)	4.8 (45)
	IgG	12.2 (62)	11.6 (28)	12.5 (45)	11.5 (45)
7 months after 2nd dose (90 individuals)	IgA	2.4 (62)	2.3 (28)	2.8 (45)	1.9 (45)
	IgG	5.6 (62)	4.9 (28)	6.0 (45)	4.8 (45)
After 3rd dose (37 individuals)	IgA	6,8 (20)	8.4 (17)	8.1 (14)	7.2 (23)
	IgG	11.0 (20)	12.6 (17)	11.5 (14)	11.6 (23)

serum samples obtained on August 2021, between 198 and 231 days after receiving the second dose of the vaccine (an average of 213 days). The age ranged from 25 to 84 years (mean age 48.6 years). Ten individuals had a history of COVID-19 prior to a first dose (four women and 6 men, age 29–55 years). Among the 90 individuals, 37 persons (20 women and 17 men) received the third dose of BNT162b2 vaccine, average 7 months after the second dose. The age ranged from 29 to 78 years (mean age 52.1 years). Sera were obtained an average of 31 days after receiving the third dose of the vaccine (between 15 and 47 days).

Samples were tested using the SARS-CoV-2 receptor-binding domain (RCB) IgG and IgA semi-quantitative commercial ELISA assay (Euroimmun, Germany, cat. EI 2606–9601). The manufacturer assumed a value of ratio <0.8 as a negative result, 0.8 – 1.09 as an equivocal result, and a positive result with a value of ratio ≥ 1.1. The maximum antibody level detected in our study by the test was 15 for IgA and 20 for IgG. Previous studies showed very good sensitivity and specificity of this assay in testing of the Polish population [3,4].

Significance of differences in the frequency of detection of antibodies (values ≥ 1.1 or ≥5.0) depending on period, sex and age group was assessed by the chi-square test of independence using Yates's correction. The differences were considered statistically significant, where the p-value significance levels were lower than $\alpha = 0.05$.

4. Results

An average of 25 days after administration of the second dose of BNT162b2 vaccine only one person had IgA level below the cut-off for positive samples and all the individuals were positive in IgG. After 7 months 28,9% of individuals had IgA levels below positive cut-off of the test ($\chi^2 = 25.1$; $p < 0.05$) (Table 1), whereas IgG level decreased in all individuals, an average decline was 58%, but reminded positive according to the test interpretation (Fig. 1). Statistically significant differences between the two periods were found only when the presence of IgG antibodies was analyzed at the high level ≥5 ($\chi^2 = 38$; $p < 0.05$).

Statistical analysis showed also that the frequency of detecting IgA antibodies at the high level ≥5 a month after full vaccination among employees below the age 47 was significantly higher ($\chi^2 = 3.149$, $p = 0.037$) than in older individuals. There was no such difference in the case of IgG antibodies because in all the serum samples antibodies were detected at the high level ≥5.

However, statistical analysis showed that the rate of decline IgG antibodies between 10 and 42 days and 7 months after receipt of the second dose was higher in the group of older individuals ($\chi^2 = 3.06$, $p = 0.04$). This is in agreement with the recent studies of Grupel et al. [5] and Vassilaki et al. [6], where the anti-Spike-RBD IgGs response was also observed to be more sustained in younger than in older subjects after vaccination with BNT162b2 vaccine. No statistical differences were observed between genders (Table 2). Administration of a booster dose resulted in significant increase of IgA and IgG levels with the geometric mean 7.5 and 11.5, respectively. The statistical analysis showed that IgA antibodies ($\chi^2 = 17.72$; $p < 0.05$) as well as IgG antibodies ($\chi^2 = 24.74$; $p < 0.05$) at the high level ≥5 were detected after a booster dose significantly more often than 7 months after the second dose in the group of 37 subjects. In individuals with previous history of COVID-19 antibody levels were higher and the decrease of the antibody levels in time was slower (Fig. 2). Seven months after the second dose the decrease of IgA level was over 3 times lower in individuals with COVID-19 history than in individuals without COVID-19 history. The IgG level decreased

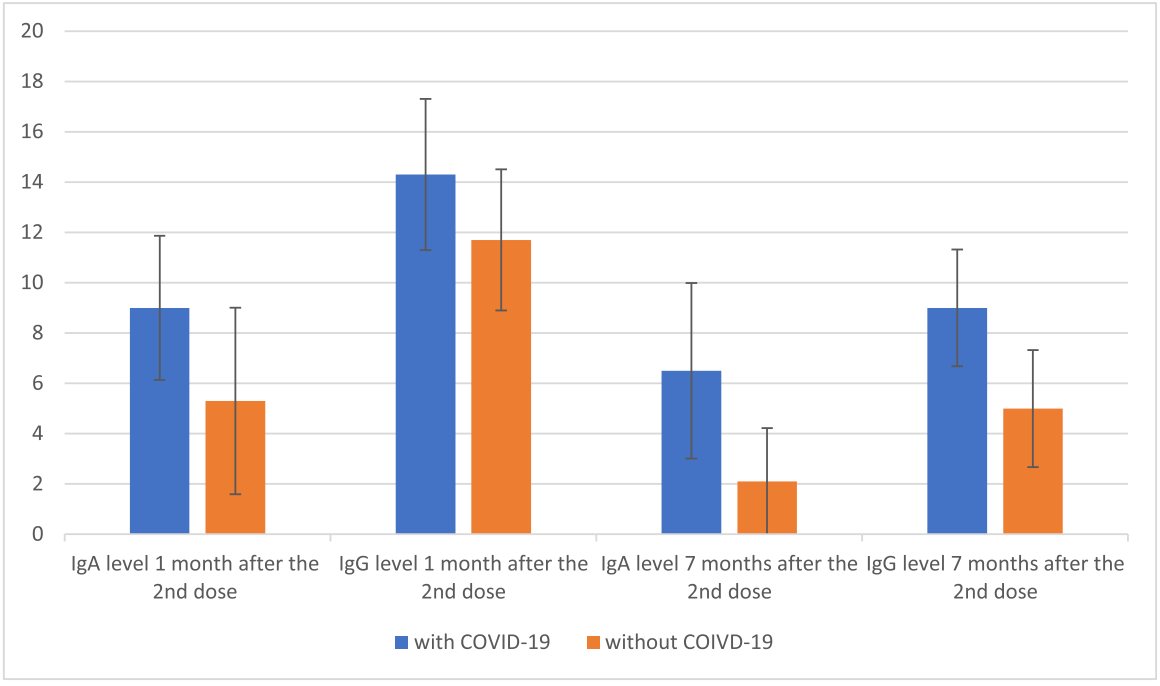

Fig. 2. Geometric mean concentration of RCB IgA and IG antibodies in individuals with COVID-19 history and without the history of COVID-19.

almost 2 times less in those with COVID-19 history. This observation is important because rapid decrease of IgG antibody level was observed in patients with COVID-19 who were not vaccinated [7]. Thus, the vaccination could induce stronger immunological response which lasts longer and could be protective against new SARS-CoV-2 variants.

5. Discussion

In December 2020 Delta (B.1.617.2) variant of SARS-CoV-2 was detected in India for the first time and within a few months it became dominant in most countries. At the same time, the increase in number of COVID-19 cases has been observed in many countries, including countries with high vaccination coverage [8–10]. The increase in death rates is also observed in elderly people whose were vaccinated at the beginning of the vaccination campaign, a few months ago [11,12]. Our results are in agreement with findings that clinical effectiveness of BNT162b2 vaccine decreases over time [11–13]. Tartof et al. [13] revealed that vaccine effectiveness against infections of the Delta variant was 93% during the first month after full vaccination but declined to 53% after 4 months whereas effectiveness against non-Delta variants was 97% during the first month after full vaccination and decreased to 67% after 4 months. The booster vaccination results in antibody level increase which might also increase clinical effectiveness. The data from Israel showed that providing a booster dose of BNT162b2 vaccine 6 months after full vaccination bolsters protection against infection, with a vaccine effectiveness of 89% [14]. In our study, the booster dose of BNT162b2 increased antibody levels to higher levels comparing to the second dose of the base vaccination scheme. However, the rate of decline in the level of antibodies in time after booster is not known, yet and should be monitored.

Antibody responses to S1 protein of SARS-CoV-2 were analyzed not only for Pfizer/BioNTech BNT162b2 vaccine but also for other types of COVID-19 vaccines that are based on different technologies. SARS-CoV-2-spike specific immune responses to Pfizer/BioNTech BNT162b2, Moderna mRNA-1273, Janssen Ad26.COV2.S and Novavax NVX-CoV2373 were examined longitudinally for 6 months by Zhang et al. [15]. In this period, the neutralizing antibody titer hierarchy between the vaccines was: Moderna mRNA-1273 >Pfizer/BioNTech BNT162b2 >Novavax NVX-CoV2373 >Janssen Ad26.COV2.S. The authors concluded that NVX-CoV2373 antibody titers were comparable to that of BNT162b2 and only moderately lower than mRNA 1273. However, in other, much large serological studies ~2-fold higher neutralizing antibody titers were discerned with mRNA-1273 compared to BNT162b2 [16,17].

The main limitation of the study is a limited number of participants, and the results of the study does not represent the total population of Poland. All participants were NIPH NIH—NRI healthy employees and therefore we did not obtained data for younger, older, or immunocompromised individuals. Moreover, we used a semi-quantitative commercial ELISA test that does not allow the determination of the level of antibodies in international units (BAU/ml) according to WHO reference material (NIBSC code: 20/136).

Significant decrease of antibody levels within 7 months after full vaccination with BNT162b2 could result in the higher risk of SARS-CoV-2 infection, especially when new variants of the virus emerge. Administration a booster dose increase antibody level above the level induced and elevated after the second dose both in individuals with negative and positive results in ELISA obtained 7 months after full vaccination. The booster could be crucial for protection against new SARS-CoV-2 variants. The antibody level seems to decrease slower in vaccinated individuals with history of COVID-19 and in younger individuals, but the investigated group was too small to make conclusive observations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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