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Comparative analysis of antibody responses to BNT162b2, ChAdOx1, and CoronaVac vaccines in the Albanian population over the pandemic years 2021 to 2022

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This repeated cross-sectional study with two independent sample populations compared the antibody response to severe acute respiratory syndrome coronavirus 2 vaccines in Albania in July–August 2021 and 2022. In 2021, it found higher anti-spike-1 seropositivity and antibody levels in fully vaccinated individuals, especially with BNT162b2 and ChAdOx1 and to a lesser degree with CoronaVac. By 2022, all single-dose recipients showed high antibody responses, suggesting natural infection-enhanced immunity. The study indicates a significant evolution in the antibody response to different coronavirus disease 2019 vaccines and suggests that a single vaccine dose, coupled with natural infection, might suffice to maintain adequate immunity levels in an endemic scenario.

Keywords: SARS-CoV2 antibodies, COVID-19 vaccines, Albanian people, Anti-spike-1 immunoglobulin G, Anti-nucleoprotein immunoglobulin G

The rapid development of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines during the coronavirus disease 2019 (COVID-19) pandemic marks a significant milestone in modern biotechnology [1]. It is estimated that at least 18 million lives were saved globally in just the first year of vaccine use [2].

Messenger RNA (mRNA) vaccines, notably, showed high efficacy against COVID-19 infection [3,4]. Despite their success, misinformation and conspiracy theories spread through social media hindered their broader acceptance, particularly among less informed groups [5]. Adenoviral vector vaccines also saw extensive use but faced reduced application due to side effects like venous thrombosis [6]. Traditional vaccines using inactivated viruses were widely administered, but their effectiveness was comparatively lower, notably against Delta and Omicron variants [7,8].

Various studies have compared immune responses to these vaccines at a single point in the pandemic, mainly during 2021 [9-11]. Our research examines the anti-SARS-CoV-2 antibody response in Albania's general population to one or two doses of the primary immunization with these three vaccine types at two-time points: August 2021 and August 2022. This time interval witnessed significant shifts in immune status due to successive pandemic waves and varying viral variants.

This study, employing a repeated cross-sectional approach, assessed the anti-SARSV-CoV-2 antibody response in two independent sample populations during July–August 2021 and 2022. Participants, spanning all age demographics, were randomly

selected from digital registries associated with four primary healthcare centers in Tirana and one in Berat City. These centers cater to approximately 281,600 urban residents. After telephonic consent, enrolled individuals provided blood samples for serological testing and completed standardized questionnaires at the healthcare facilities, providing detailed data about demographics, health status, symptoms, vaccination history, and previous COVID-19 infections. The study's principal variable was the antibody immune response to a primary one-dose or two-dose immunization with BNT162b2, ChAdOx1, and CoronaVac vaccines, evaluated through the presence of anti-spike-1 and anti-nucleoprotein (NCP) SARS-CoV-2 immunoglobulin G (IgG) antibodies. Blood samples underwent serological analysis using two enzyme-linked immunosorbent assay diagnostic kits: IgG anti-S1-SARS-CoV-2 and IgG anti-NCP-SARS-CoV-2 (Euroimmun, Luebeck, Germany). These kits boast sensitivities of 94.4% and 94.6%, and specificities of 99.6% and 99.8%, respectively. The ratio of the samples' optical density, compared to a calibrator (index ratio, IR), was computed following the manufacturer's instructions. The primary endpoints included seropositivity rates (using the 1.1 IR cutoff) and levels of IgG anti-S1-SARS-CoV-2 antibodies in IR units.

Differences in antibody responses were statistically evaluated using the Fisher exact test for categorical variables such as seropositivity rates and the Mann-Whitney test for continuous variables (antibody levels expressed in IR). Data analysis was conducted using MedCalc Statistical Software ver. 20.210 (MedCalc Software Ltd., Ostend, Belgium).

The Albanian Academy of Sciences Ethics Committee approved the study protocol (project number: 33-07-05-2020). All participants provided informed written consent before participation in the study. During July and August of 2021, among the 2,144 individuals included in the study, 713 (33.3%) received at least one dose of the vaccine. Among them, 136 (19.1%) had only received the first dose, while 577 (80.9%) had received both the first and second doses. A year later, in July–August 2022, among all 2,184 studied individuals, 1,210 (55.4%) were vaccinated. Of these, 67 (5.5%) received only one vaccine dose, while 1,143 (94.5%) had received both doses.

In 2021, 309 (43.3%) received the CoronaVac vaccine (Sinovac Biotech Ltd., Beijing, China), 228 (32.0%) the Pfizer vaccine (Pfizer, New York, NY, USA), 160 (22.4%) AstraZeneca (AstraZeneca, Cambridge, UK), and 16 (2.2%) Sputnik (Sputnik V, Moscow, Russia). In 2022, 325 (26.9%) received CoronaVac, 719 (59.4%) Pfizer, 154 (12.7%) AstraZeneca, and 12 (0.08%) Sputnik. All individuals had a minimum interval of 14 days from the last vaccination day. Due to minimal numbers,

Table 1. General characteristics of individuals studied and anti-NCP antibody data classified according to the types of vaccines and vaccine doses in August 2021 and August 2022

Characteristic	CoronaVac			BNT162b2			ChAdOx1		
	One dose	Two doses	p-value	One dose	Two doses	p-value	One dose	Two doses	p-value
No. of individuals									
2021	55	254		20	208		57	103	
2022	15	310		36	683		15	139	
Age (yr)									
2021	58.0 (54.3–60.0)	65.0 (64.9–66.0)		42.5 (38.0–56.8)	49.0 (47.0–50.0)		58,0 (52.0–60.0)	55.0 (51.0–57.0)	
2022	58.0 (44.1–63.5)	65.0 (64.0–67.0)		47.0 (38.8–56.6)	42.0 (40.0–45.0)		47.0 (38.8–56.6)	42.0 (40.0–45.0)	
Sex (female)									
2021	30 (54.5)	132 (52.0)		12 (60.0)	132 (63.5)		34 (59.6)	55 (53.4)	
2022	9 (60.0)	201 (64.8)		20 (55.6)	414 (60.6)		7 (46.6)	87 (62.6)	
Days from vaccination									
2021	18.00 (15.0–28.1)	54.0 (51.0–58.0)		15.0 (5.0–30.7)	46.0 (34.8–76.0)		60.0 (51.9–68.0)	23.0 (19.0–30.0)	
2022	470.0 (218.8–505.8)	343.5 (317.0–371.0)		288.5 (257.8–341.4)	273.0 (260.0–280.0)		347.0 (257.7–407.3)	491.0 (304.9–530.0)	
Anti-NCP-IgG (positivity)									
2021	26 (47.3)	98 (38.6)	0.08123	6 (30.0)	63 (33.2)	1.00	17 (29.8)	30 (29.1)	1.00
2022	12 (80.0)	212 (68.4)	0.407	22 (61.1)	390 (57.1)	0.730	8 (53.3)	95 (68.3)	0.260
NCP-IgG									
2021	0.87 (0.55–2.26)	0.44 (0.39–0.57)	0.0484	0.33 (0.19–1.22)	0.51 (0.42–0.80)	0.5087	0.74 (0.50–0.93)	0.45 (0.30–0.67)	0.1974
2022	2.71 (1.27–4.0)	2.1 (1.82–2.40)	0.2412	1.98 (0.99–2.89)	1.54 (1.32–1.68)	0.1441	1.27 (0.33–3.04)	1.85 (1.53–2.20)	0.2715

Values are presented as number, median (95% confidence interval), or number (%).
NCP, nucleoprotein; IgG, immunoglobulin G.

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this study did not include data on the Sputnik vaccine.

In 2021, 42.0% of vaccinated individuals reported previous COVID-19; in 2022, 56.8% reported having passed the infection ($p<0.0001$). Due to minimal numbers, this study did not include data on the Sputnik vaccine. Detailed data on the number of individuals according to doses for each vaccine studied, the ages and gender of individuals, days from the last vaccine dose, seropositivity, and IgG anti-NCP antibody data are described in Table 1. Fig. 1 graphically presents the seropositivity and IgG anti-S1 antibody levels in the studied individuals in 2021 and Fig. 2 in 2022.

In 2021, as expected in individuals who had received both doses of all three types of vaccines, both seropositivity and antibody levels were higher than in individuals who had received only the first dose. This increase was most noticeable and statistically significant with the Pfizer-BioNTech vaccine (Fig. 1). With this vaccine, the percentage of seropositivity among individuals who had received both doses was 17.8% higher than in the group that had received only the first dose and the antibody level, expressed in IR units, was 2.94 times higher. In the group of individuals who received both doses of the AstraZeneca vaccine, the seropositivity of anti-S1 IgG antibodies was 11.9% higher than in those with only one dose, and their quantitative level was 19% higher. Both these increases were statistically significant. With the CoronaVac vaccine, a statistically significant increase of 16.4% in seropositivity was observed in individuals who had received both doses compared to those with one dose. Still, the antibody level expressed in IR was only 8% higher, a non-significant increase (Fig. 1).

In August 2022, in individuals who received only one dose of all three vaccines, seropositivity and the level of anti-S1 antibodies were similar compared to those who received both doses (Fig. 2). For all three vaccines, both parameters were higher than in 2021 when comparing groups of individuals

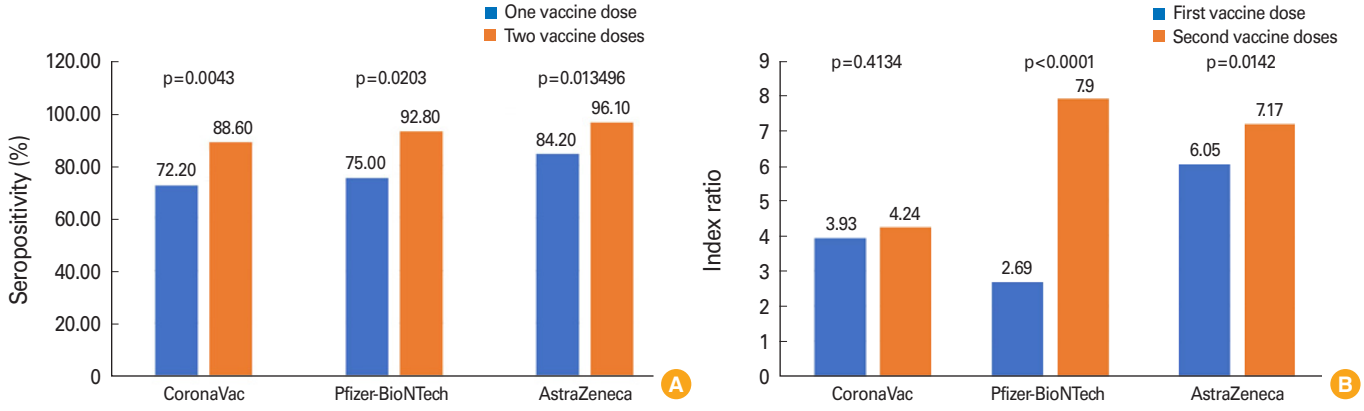

Fig. 1. Anti-spike-1-SARS-CoV-2 seropositivity rates (%) **(A)** and antibody levels (index ratio) **(B)** in individuals with different vaccine types studied in August 2021. Statistical p-values are shown in the boxes above the charts. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

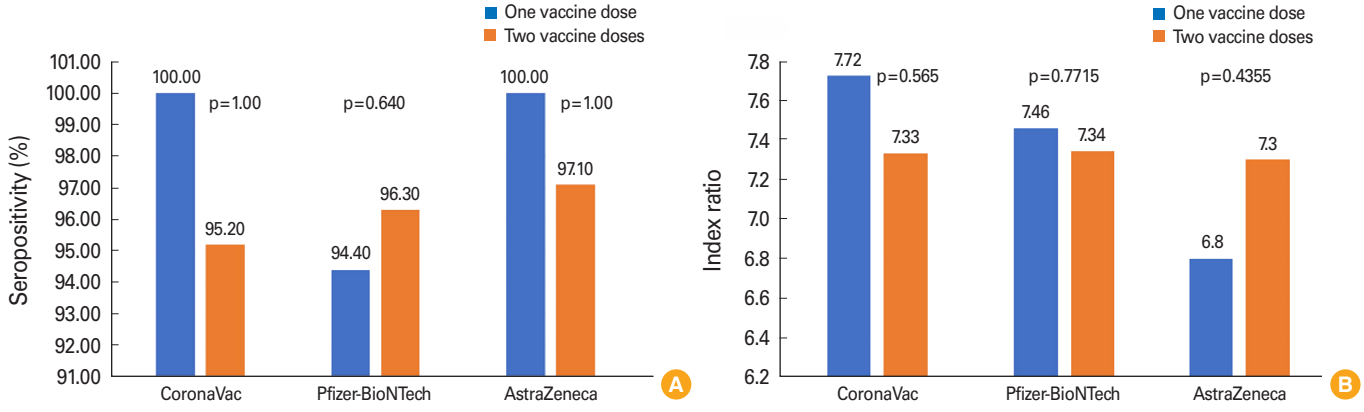

Fig. 2. Anti-spike-1-SARS-CoV-2 seropositivity rates (%) **(A)** and antibody levels (index ratio) **(B)** in individuals with different vaccine types studied in August 2022. Statistical p-values are shown in the boxes above the chart. SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

who had received only one vaccine dose. The exception was the AstraZeneca vaccine, where the increase in the level of anti-S1 antibodies in 2022 did not reach the statistical significance threshold ($p=0.3916$). When comparing groups of individuals who had received both vaccine doses, seropositivity and the level of anti-S1 antibodies did not change significantly between 2021 and 2022, except for the CoronaVac vaccine, with which a significant increase in seropositivity ($p=0.0036$) and antibody levels ($p>0.0001$) was observed in 2022 compared to 2021.

In both years of the study, no significant differences were observed either in seropositivity or in the levels of IgG anti-NCP antibodies among individuals who had received one dose of the vaccine compared to those with two doses. However, in 2022, in all the studied subgroups, there was a considerable increase in both seropositivity (from 66% up to 2.36 times) and the levels of these antibodies (from 72% up to 6.0 times) compared to the year 2021 (Table 1).

The data of our study pinpoint the finding that in August 2021, the highest anti-S1 antibody response was observed in individuals who had received the second dose of the Pfizer-BioNTech mRNA vaccine, followed by the second dose of AstraZeneca adenoviral vector vaccine. CoronaVac's inactivated virus vaccine exhibited the weakest antibody response after the second dose, showing no significant difference from the first.

In August 2022, the situation was quite different regarding seropositivity and anti-S1 antibody levels. In all the individuals studied at this time, no difference was observed in the anti-S1 antibody response, regardless of the type of vaccine received or whether they had received one or both doses of the vaccines administered earlier. The anti-S1 antibody response was at its maximum even in individuals who had only received the first dose of the three vaccine types studied. This strong antibody response corresponds epidemiologically with the absence of COVID-19 epidemic peaks in the Albanian population after August 2022.

Other comparative studies of antibody responses to the Pfizer-BioNTech, AstraZeneca, and CoronaVac vaccines, conducted mainly in 2021, have reached similar conclusions as our study, demonstrating the same hierarchy of antibody response among these three vaccines [7,9,10,12]. However, to our knowledge, no previous study has been repeated in the same population with a 1-year-long dynamic afterward and in the second half of 2022.

In our study, in August 2022, vaccinated individuals reported 14.8% more previous COVID-19 infections compared to August 2021 (not including unreported asymptomatic infections). Also, the levels of anti-NCP antibodies in August 2022 in all studied individuals were significantly higher than in August 2021, demonstrating the important role of concurrent COVID-19 infections during this period. These facts highlight the role of hybrid immunity during the second half of 2022 in maintaining a vigorous response even after a single vaccine dose [13].

Our study has several limitations that should be noticed. The number of people vaccinated with a single vaccine dose is somewhat low, and the interval from vaccination to the serological study is much longer in 2022 than in 2021.

In conclusion, our data confirm that in the current period of an endemic community circulation of the SARS-CoV-2 virus, a single booster dose of any vaccine type could be sufficient to maintain a stable level of immunity in the Albanian population.

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References

1. Barouch DH. COVID-19 vaccines: immunity, variants, boosters. N Engl J Med 2022;387:1011-20.
2. Watson OJ, Barnsley G, Toor J, Hogan AB, Winskill P, Ghani AC. Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. Lancet Infect Dis 2022;22:1293-302.
3. Zhang G, Tang T, Chen Y, Huang X, Liang T. mRNA vaccines in disease prevention and treatment. Signal Transduct Target Ther 2023;8:365.
4. Chavda VP, Soni S, Vora LK, Soni S, Khadela A, Ajabiya J. mRNA-based vaccines and therapeutics for COVID-19 and future pandemics. Vaccines (Basel) 2022;10:2150.
5. Romer D, Jamieson KH. Conspiracy theories as barriers to controlling the spread of COVID-19 in the U.S. Soc Sci Med 2020;263:113356.
6. Guetl K, Raggam RB, Gary T. Thrombotic complications after COVID-19 vaccination: diagnosis and treatment op-

tions. Biomedicines 2022;10:1246.
7. Saure D, O'Ryan M, Torres JP, Zuniga M, Santelices E, Basso LJ. Dynamic IgG seropositivity after rollout of CoronaVac and BNT162b2 COVID-19 vaccines in Chile: a sentinel surveillance study. Lancet Infect Dis 2022;22:56-63.
8. Voko Z, Kiss Z, Surjan G, et al. Effectiveness and waning of protection with different SARS-CoV-2 primary and booster vaccines during the Delta pandemic wave in 2021 in Hungary (HUN-VE 3 Study). Front Immunol 2022;13:919408.
9. Dashdorj NJ, Wirz OF, Roltgen K, et al. Direct comparison of antibody responses to four SARS-CoV-2 vaccines in Mongolia. Cell Host Microbe 2021;29:1738-43.
10. Barin B, Kasap U, Selcuk F, Volkan E, Uluckan O. Comparison of SARS-CoV-2 anti-spike receptor binding domain IgG antibody responses after CoronaVac, BNT162b2, ChAdOx1 COVID-19 vaccines, and a single booster dose: a prospective, longitudinal population-based study. Lancet Microbe 2022;3:e274-83.
11. Ng OT, Marimuthu K, Lim N, et al. Analysis of COVID-19 incidence and severity among adults vaccinated with 2-dose mRNA COVID-19 or inactivated SARS-CoV-2 vaccines with and without boosters in Singapore. JAMA Netw Open 2022;5:e2228900.
12. Liu Y, Sanchez-Ovando S, Carolan L, et al. Comparative B cell and antibody responses induced by adenoviral vectored and mRNA vaccines against COVID-19. medRxiv [Preprint] 2023 Jun 5. https://doi.org/10.1101/2023.06.02.23290871
13. Lasrado N, Barouch DH. SARS-CoV-2 hybrid immunity: the best of both worlds. J Infect Dis 2023;228:1311-3.