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Research Article

Post-vaccination Comparative Studies of the Dynamics of Antibodies Neutralizing the SARS-CoV-2 Virus During Vaccination with Various Vaccines in Kazakhstan

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Abstract

Post-vaccination measurement of the level of antibodies neutralizing the SARS-CoV-2 virus (NA) in blood serum is a marker for monitoring the effectiveness of immunity formation [1,2]. In 4 groups of 462 patients, a comparative study of the neutralizing effectiveness of antibodies was carried out with single and double administration of CoronaVac brand vaccines (SynoVac), VeroCell (Sinofarm), Sputnik-V (GamCovidVac) and domestically produced QazVac (QazCovid-in). Of the 462 vaccinated subjects examined for NA, 46 recovered from COVID-19 and 416 were not infected with the SARS CoV-2 virus. The latter were included in the present study. In 34 (8.2%) patients, threshold values of NA were not found in the blood serum after vaccination. The Chinese-made vaccines Vero-Cell and the Kazakhstani manufacturer QazCovid (Research Institute for Biological Safety of the Ministry of Education and Science of the Republic of Kazakhstan) had practically the same indicators of post-vaccination immunogenicity.

Keywords: Vaccines; CoronaVac (SynoVac); VeroCell (Sinofarm); Sputnik-V (GamCovidVac); QazVac (QazCovid-in); SARS-CoV-2 IgG Neutralizing Antibodies; Quantitatively; Coronavirus-19

Introduction

Vaccination of the population is a serious problem for the country's healthcare system. The formation of herd antiviral immunity in the presence of many mutated strains of the SARS-CoV-2 virus that can avoid it becomes a serious obstacle to achieving vaccination goals.

Levels of circulating antibodies (titers) can be used as indicators of the effectiveness of vaccination in infectious diseases [3,4].

The World Health Organization (WHO) has developed a standard for the use of antibodies to SARS-CoV-2 [5,6]. It was developed on the basis of the collected serological pool of convalescent plasma

and is recommended for the detection of neutralizing antibodies to the SARS-CoV-2 virus. The standard allows you to determine the levels of antibodies that are necessary to assess the effectiveness of vaccines and the formation of post-vaccination immunity.

It has been shown that a certain percentage of patients do not produce antibodies after the end of the vaccination course [7]. It was found that the immune response induced by vaccines was low in the elderly [8].

Evaluation of the level of post-vaccination antibodies will help identify individuals who may not develop antibodies or may not have an "adequate" immune response, and provide them with appropriate recommendations for improving immunity.

The aim of the study is a comparative assessment of the dynamics of the neutralizing effectiveness of antibodies to the SARS-CoV-2 virus induced by 4 vaccines from different manufacturers.

Material and Methods

Existing methods for testing SARS CoV2 for antibodies of the IgG and IgM classes do not allow the selection and testing of only neutralizing antibodies, so all antigen-binding antibodies are measured. A new testing method, SARS CoV2 Neutralizing Ab, is a technology that selects and tests specific virus neutralizing antibodies [8-13]. A neutralizing antibody is an antibody that protects the body from a viral infection by binding to the antigenic protein of the virus when the virus enters the body. Therefore, a neutralizing antibody is an antibody that neutralizes a virus by binding to the virus. Qualitative determination of neutralizing antibodies against SARS-CoV-2 is achieved using enzyme-linked immunosorbent assay (ELISA). The R-FIND SARS-CoV-2 Neutralizing Antibody ELISA Kit is a one-step immunoassay kit with incubation in a monoclonal antibody reagent. The human receptor protein ACE2, previously coated on polystyrene microwells, can specifically recognize the HRP-conjugated RBD (protein-binding protein) of the virus. Protein-protein interaction between RBD-HRP and the human ACE2 protein can be suppressed by SARS-CoV-2 neutralizing antibodies against RBD. Testing of the neutralizing antibodies that will be produced after vaccination will make it easier to monitor the effectiveness of vaccination and the treatment process after a viral infection.

All vaccines of various manufacturers and brands: CoronaVac (SynoVac); VeroCell (Sinofarm): Sputnik-V (GamCovidVac) and QazVac (QazCovid-in) were administered twice in medical organizations in Almaty in compliance with the established indications and intervals specified in their instructions.

Venous blood serum samples of 462 patients from 5 city polyclinics in Almaty and the City Clinical Infectious Diseases Hospital named after M.A. Zhekenova were transported in containers with temperature sensors to the Medical Partners Corean laboratory on the day of sampling for 4 hours.

Sample preparation and quality control for immunochemiluminescent studies were carried out according to the SG Medical reagent instructions "R-FIND SARS-CoV-2 Neutralizing Antibody ELISA". The study of samples was carried out on a BioTek 800 TS rider from plastic microplates at a wavelength of 450 nm.

The interpretation was made according to the manufacturer's instructions according to the following table.

Results interpretation

Measured value	Result	Interpretation
S.I ≥ 30%	Positive	Neutralizing Ab for SARS CoV-2 are detected
S.I < 30%	Negative	Neutralizing Ab for SARS CoV-2 are not detected

Table a

Statistical analysis of the study materials was carried out using the IBM PS Imago PRO software (SPSS Statistics, v. 26). The normality of the distribution of quantitative traits in the samples was determined by the Kruskal-Wallis test.

With a normal distribution of quantitative characteristics, hypotheses about the equality of means in two samples were tested using the Student's t-test, assuming equal or unequal variances, depending on the results obtained. Mean, standard deviation, Levine's test for equality of variances, t-test for equality of means (mean (two-tailed), mean difference, root mean square difference), 95% confidence interval are given.

With a significant deviation of the distribution of the trait from the normal distribution, to assess the differences between the samples (according to the Kruskal-Wallis test, asymptotic values), the nonparametric Mann-Whitney U-test was used with the calculation of the average ranks, the sum of the ranks, the Mann-Whitney U tests, the Wilcoxon W test, the asymptotic value (two-sided).

When considering qualitative features, contingency tables were used. To analyze the contingency tables, Pearson's $\chi 2$ test, Fisher's exact two-sided test, and regression analysis were used.

Research results

Table 1 presents data on quantitative data on the distribution of people who have recovered from and have not been ill with COVID-19 in the process of participating in the Vaccination Program in Almaty in 2021.

In the group who received a double dose of the Chinese CoronaVac vaccine (manufactured by SynoVac), there were 70 people, of whom 8 people recovered from COVID-19, 5 men and 3 women, the remaining 62 vaccinated had no history of indications of COVID-19 (Table 1).

The Chinese vaccine manufactured by Sinofarm Vero-Cell was administered twice to 119 patients, of which 17 people (8 men and 9 women) recovered from COVID-19. Kazakhstan vaccine QazVac was received by 113 persons. Of these, 37 men and 61 women were not ill with COVID-19 - 98 patients, but 15 people (5 men and 10 women) recovered from COVID-19. The Russian vaccine Sputnik-V (GamCovidVac) was administered to 159 patients, of whom only 4 women recovered.

In total, 461 people took part at the beginning of the study, of which 44 participants who recovered from COVID-19 were transferred to another group of studies. One subject withdrew due to a violation of the vaccination schedule.

Among the participants of the Vaccination Program, women accounted for 278 subjects (60.3%), men - 183 (39.7%). Among women, 26 participants underwent CVI, there were 18 men. The number of recovered COVID-19 in the group vaccinated with Sputnik-V was only 4 women (Table 1).

Vaccine **Men** **Female**			**Gender**		**Total**
CoronoVac	COVID-19	No	27	35	62 (88,6%)
		Yes	5	3	8 (11,4%)
	Total		32 (45,7%)	38 (54,3%)	70
Vero-Cell	COVID-19	No	37	65	102 (85,7%)
		Yes	8	9	17 (14,3%)
	Total		45 (37,8%)	74 (62,2%)	119
QazVac	COVID-19	No	37	61	98 (86,7%)
		Yes	5	10	15 (13,3%)
	Total		42 (37,2%)	71 (62,8%)	113
Sputnik-V	COVID-19	No	64	91	155 (97,5%)
		Yes	0	4	4 (2,5%)
	Total		64 (40,3%)	95(59,7%)	159
Total	COVID-19	No	165	252	417 (90,5%)
		Yes	18	26	44 (9,5%)
	Total		183 (39,7%)	278 (60,3%)	461

Table 1: Characteristics of vaccinated persons among residents of the city of Almaty in relation to COVID-19 and gender.

Table 2 shows the distribution of all vaccinated individuals, including those who recovered, by age categories.

COVID-19 Men Female			Gender		Bcero
No	Age category	18-29	43	51	94
		30-59	92	141	233
		60 and older	30	60	90
	Total		165	252	417
Yes	Age category	18-29	2	5	7
		30-59	13	15	28
		60 and older	3	6	9
	Total		18	26	44
Total	Age category	18-29	45	56	101
		30-59	105	156	261
		60 and older	33	66	99
	Total		183	278	461

Table 2: Characteristics of vaccinated persons by age, depending on the gender of residents of Almaty.

The average age of those who had COVID-19 was 47.02 ± 15.48, and that of healthy people was 45.05 ± 16.89 (years), no significant differences were found in this trait ($p > 0.05$).

No differences were found in the distribution of vaccinated individuals by age categories among those who had COVID-19 and healthy individuals ($p > 0.05$).

Characteristics of vaccinated individuals in terms of NA production depending on the gender of Almaty residents is presented in table 3. A negative result for neutralizing antibodies was detected in 22 (7.9%) women and 12 (6.6%) men, which amounted to 34 (7.4%) of the subject of the total number vaccinated with various vaccines. A positive result for neutralizing antibodies was detected in 256 (92.1%) women and 171 (93.4%) men in the study groups.

Vaccine	NA	NO YES NA Men	Gender		Total
			Female		
CoronoVac	NA	NO	3	2	5
	YES NA	29	36	65	
	Total	32	38	70	
Vero-Cell	NA	NO	3	6	9
	YES NA	42	68	110	
	Total	45	74	119	
QazVac	NA	NO NA	5	8	13
	YES NA	37	63	100	

	Total	42	71	113	
Sputnik-V	NA	NO NA	1	6	7
	YES NA	63	89	152	
	Total	64	95	159	
Total	NA	NO NA	12 (6,6%)	22 (7,9%)	34 (7,4%)
	YES NA	171 (93,4%)	256 (92,1%)	427 (93,6%)	
	Total	183 (39,7%	278 (61,3%)	461	

Table 3: Characteristics of vaccinated individuals in terms of NA (Neutralizing Antibodies) production, depending on the gender of residents of Almaty.

Table 4 and Figure 1 show the age distribution of vaccinated residents of Almaty with a positive and negative result of the study in the blood serum NA (Neutralizing Antibodies).

Vaccine 18-29 30-59			**Age**			**Total**	**p**
			60 ≥				
CoronoVac	NA	NO NA	1	2	2	5	0,232
		YES NA	21	36	8	65	
	Total		22	38	10	70	
Vero-Cell	NA	NO NA	0	4	5	9	0,021
		YES NA	22	68	20	110	
	Total		22	72	25	119	
QazVac	NA	NO NA	2	7	4	13	0,804
		YES NA	20	57	23	100	
	Total		22	64	27	113	
Sputnik-V	NA	NO NA	2	5	0	7	0,329
		YES NA	33	82	37	152	
	Total		35	87	37	159	
Total	NA	NO NA	5	18	11	34	0,225
		YES NA	96	243	88	427	
	Total		101(21.9%)	261(56,6%)	99(21.5%)	461	

Table 4: Age distribution of vaccinated residents of Almaty with a positive and negative result of the study in blood serum NA (Neutralizing Antibodies).

Note: p - comparison was made on the production of antibodies between age categories within each group vaccinated with different vaccines.

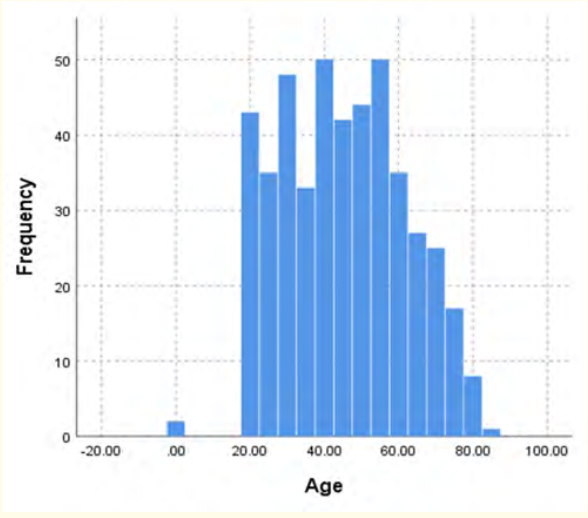

Figure 1: Age distribution of vaccinated individuals with a positive and negative result of the study in the blood serum level of NA (Neutralizing Antibodies).

The largest number of vaccinated persons is in the age group of 30-59 years - 261 vaccinated (56.6%). Among them, the percentage of negative results of determining neutralizing antibodies is high - 6.9%, while in the age categories 18-29 and 60 and older, the percentage of negative results is 4.9% and 11.1%, respectively, of the number vaccinated in these groups. The production of neutralizing antibodies was significantly significant in the age category from 30 to 59 years among those vaccinated with the VeroCell vaccine, in comparison with other age categories ($p = 0.021$). Table 4 shows that in terms of the level of NA among those vaccinated with vaccines CoronoVac, QazVac, Sputnik-V, no differences were found by age categories ($p > 0.05$).

Table 5 shows the characteristics of healthy individuals who responded to vaccination with NA (Neutralizing Antibodies) products.

Vaccine		Age			Total
		18-29	30-59	60≥	
Gender	Men	5	13	6	24
	Female	14	17	2	33
Total		19	30	8	57
Gender	Men	10	20	4	34
	Female	10	37	12	59
Total		20	57	16	93
Gender	Men	8	21	4	33
	Female	9	30	15	54
Total		17	51	19	87
Gender	Men	17	36	10	63
	Female	16	43	26	85
Total		33	79	36	148
Gender	Men	40	90	24	154
	Female	49	127	55	231
Total		89 (23.1%)	217 (56,4%)	79 (20,5%)	385

Table 5: Characteristics by age and sex of healthy individuals vaccinated with various vaccines with positive results of NA (Neutralizing Antibodies) in the blood.

According to the age category, women in the age groups of 30-59 and 60 and older prevailed among those vaccinated with various vaccines. The largest number of vaccinated was in the age range of 30-59 years (56.4%).

Table 6 shows the distribution of healthy vaccinated individuals who responded to vaccination with the production of specific neutralizing antibodies by study period.

Vaccine 18-29 30-59			Age category		Total
CoronoVac	Gender	Men	5	0	5
		Female	2	1	3
	Total		7	1	8
Vero-Cell	Gender	Men	1	6	7
		Female	1	8	9
	Total		2	14	16
QazVac	Gender	Men	1	4	5
		Female	3	7	10
	Total		4	11	15
Sputnik-V	Gender	Men		1	1
		Female		4	4
	Total			5	5
Total	Gender	Men	7	11	18
		Female	6	20	26
	Total		13 (29,5%)	31 (70,5%)	44

Table 6: Distribution of healthy vaccinated individuals who responded to vaccination with NA (Neutralizing Antibodies) products, by study period.

Table 7 and Figure 2 present the results of determining the level of neutralizing antibodies on days 21, 22-42 and 43-235 in vaccinated individuals.

Vaccine 0-21 day		Time			Total n = 461
		22-42 day	43-235 day		
QazVac	N	16	75	24	115
	Positive rate (%)	100,00	77,33	75,00	80,00
	Mean ± SD (% inhibition)	72,55 ± 19,92	81,44 ± 18,70	73,51 ± 24,16	78,34 ± 20,25
p value		0,025			
Sputnik-V	N	52	74	32	158
	Positive rate (%)	98,08	91,89	90,63	93,67
	Mean ± SD (% inhibition)	84,77 ± 20,07	85,48 ± 16,28	86,30 ± 16,60	85,40 ± 17,62
p value		0,016*	0,006***		
Vero-Cell	N	46	71	1	118
	Positive rate (%)	84,78	73,24	-	77,12
	Mean ± SD (% inhibition)	81,92 ± 16,52	79,43 ± 17,52		80,50 ± 17,11
p value			0,046		
CoronoVac	N	10	23	37	70
	Positive rate (%)	90,00	95,65	64,86	78,57
	Mean ± SD (% inhibition)	86,04 ± 12,40	83,81 ± 21,56	74,85 ± 24,31	80,27 ± 21,89
p value		0,049**			
QazVac	N	16	75	24	115
	Positive rate (%)	100,00	77,33	75,00	80,00
	Mean ± SD (% inhibition)	72,55 ± 19,92	81,44 ± 18,70	73,51 ± 24,16	78,34 ± 20,25
p value (between time periods)		0,174	0,716	0,545	0,181

Table 7: Dynamics of the level of neutralizing antibodies in all vaccinated individuals with various brands of vaccines.

* Between Vero-Cell and Sputnik-V.

** CoronoVac and QazVac.

*** Vero-Cell and Sputnik-V.

Table 7 shows that the highest concentration of neutralizing antibodies is observed in those vaccinated with the Chinese-made vaccine Sinovac-CoronaVac. On the 21st day, the average levels of antibodies were 86.04 ± 12.40, by 22-42 days the level of antibodies remained and amounted to 83.8 ± 21.56. On days 43-235 from the start of vaccination, the level of antibodies in the serum of the subjects decreased to 74.85 ± 24.31. In terms of blood NA (neutralizing antibodies) levels, this vaccine had significant differences in comparison with the domestic vaccine QazVac in the period of 0-21 days (p = 0.049) and in the second observation period of 22-42 days with the Vero-Cell vaccine (p = 0.046).

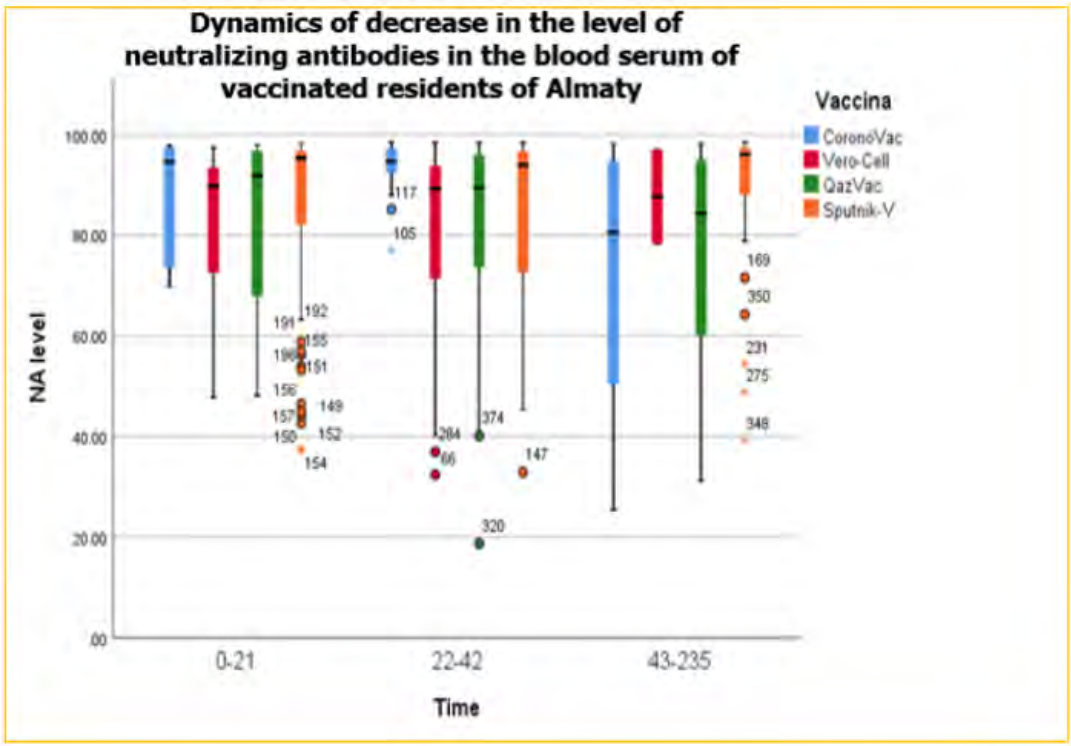

Figure 2: Dynamics of the level of neutralizing antibodies in the blood serum of residents of Almaty vaccinated with vaccines from various manufacturers.

In second place in terms of the ability to induce NA (neutralizing antibodies) production to the SARS-CoV-2 virus is the Russian-made vaccine Sputnik-V. In the dynamics of observation, there was an increase in the level of antibodies from 84.77 ± 20.7 on the 21st day of observation to 86.30 ± 16.60 in the blood serum of the subjects of this group at 43-235 days of observation (table 8). In comparison with the domestic QazVac vaccine and the Vero-Cell vaccine, in the first observation period, the production of antibodies in the Russian vaccine was significantly higher (p = 0.025; p = 0.006, respectively), and also in comparison with the Chinese-made Vero-Cell vaccine in the second period (p = 0.006).

Figure 2 shows graphically the dynamics of changes in the level of neutralizing antibodies, depending on the formation of post-vaccination immunity to various vaccines. Vaccines of Chinese production Vero-Cell and Kazakhstani manufacturer QazCovid (Research Institute of Biological Safety of the Ministry of Education and Science of the Republic of Kazakhstan) in the dynamics of observation had almost the same levels of NA in the blood of vaccinated (Table 7, Figure 2).

Table 8 shows the level of neutralizing antibodies in vaccinated individuals who have had COVID-19.

Vaccine	n	Mean	p
CoronoVac	8	81,35 ± 20.69	> 0.05
Vero-Cell	16	73,96 ± 30,29	
QazVac	15	80,91 ± 24.57	
Sputnik-V	5	81,52 ± 27.02	
Total	44	81,52 ± 27.02	

Table 8: Average level of neutralizing antibodies in vaccinated individuals who have had COVID-19.

p - is an indicator of the significance of differences between the compared groups of vaccinated

Analysis of the obtained results and their discussion

The results of the dynamics of the level of NA (neutralizing antibodies) were distributed over the periods of the study according to the vaccination programs into three groups: 3 weeks (0-21 days) after vaccination; 6 weeks (22-42 days); and 6 weeks (43-235 days) or more after vaccination. A positive result for neutralizing antibodies was detected in 257 (92.1%) women and 171 (93.4%) men in the study groups. According to the study, it can be concluded that after the introduction of two doses of vaccines from different manufacturers, a stable humoral immune response is formed.

In 34 (8.2%) of 461 vaccinated subjects from the city of Almaty, threshold values of NA (neutralizing antibodies) were not found in the blood serum after vaccination. It is natural that in the population there are 34 individuals (8.2%) in whom vaccination does not cause the production of specific neutralizing antibodies, demonstrated in numerous reports [14-18].

For unknown reasons, in some cases, vaccination may not induce a protective immune response in some of the vaccinated individuals. This phenomenon is most commonly associated with attenuated live virus vaccines, but can occur with any type of vaccine [19-23].

Statistical analysis showed that the Chinese-made vaccine Sinovac-CoronaVac had a higher mean NA (neutralizing antibodies) level compared to the domestic vaccine QazVac in the period of 3-21 days ($p = 0.049$) and in the second observation period of 22-42 days - from the Vero-Cell vaccine ($p = 0.046$); in comparison with the domestic vaccine QazVac and the vaccine Vero-Cell in the first observation period on days 3-21, the average value of the NA (neutralizing antibodies) level in the blood of the Russian Sputnik-V vaccine was significantly higher ($p = 0.025$; $p = 0.006$, respectively), and also in compared with the Vero-Cell vaccine - in the second period of 22-42 days ($p = 0.006$).

As a result of observing a group of subjects 22-42 days after vaccination, the indicators of the formation of neutralizing antibodies by the vaccine were in the following order: Sinovac, Sputnik, QazCovid and Vero-Cell. In addition, vaccinated subjects at 43-235 days showed statistically non-significant differences. However, during this follow-up period, the level of neutralizing antibodies persists longer after vaccination with Sputnik-V compared to other vaccines.

Vaccines manufactured by Chinese manufacturer Vero-Cell and Kazakh manufacturer QazCovid (Research Institute of Biological Safety of the Ministry of Education and Science of the Republic of Kazakhstan) had practically the same indicators of post-vaccination immunogenicity in the dynamics of monitoring the level of NA in the blood of vaccinated residents of Almaty.

The mean NA level in vaccinated individuals with CVI was 84.59 ± 19.42% and was significantly higher than the mean NA level in vaccinated healthy individuals, which was 76.56 ± 25.71% ($p = 0.014$).

Conflict of Interest

The authors declare no conflict of interest.

Ethics Statement

This study was approved by the ethics committee of the Kazakh National Center for Dermatovenereology and Infectious Diseases of the Ministry of Health of the Republic of Kazakhstan (No. 2/2564), and written informed consent was obtained from all participants.

Authors' Contribution

- BekshinZh.M.: The supervisor who developed this study, the concept and design of the study, scientific editing, reviewed and edited the manuscript.
- Rysuly M.: Data collection, analysis and interpretation, text writing, material processing, bibliography design, illustrations preparation.
- Abishev A.T.: Data analysis and interpretation, material processing.
- Akhmetova G.K.: Performed statistical analysis and provided data analysis and visualization.
- Sadvakas A.S.: Final preparation of the manuscript.

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Data Availability Statement

Supporting data is available in the article.

Bibliography

1. Evaluation of COVID-19 vaccine effectiveness. WHO, Interim Guidance. 17 March (2021): 60.

2. Plotkin SA and Gilbert PB. "Nomenclature for immune correlates of protection after vaccination". *Clinical Infectious Diseases* 54.11 (2012): 1615-1617.

3. Fei Xiang., *et al*. "Antibody Detection and Dynamic Characteristics in Patients with COVID-19". *Clinical Infectious Diseases*, ciaa461.

4. Takahashi T and Iwasaki A. "Sex differences in immune responses". *Science* 371.6527 (2021): 347-348.

5. Thailand Food and Drug Administration. Summary of Product Characteristic CoronaVac (2021).

6. Zhang Y., *et al*. "Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial". *Lancet Infectious Diseases* 21.2 (2021): 181-192.

7. Voysey M., *et al*. "Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARSCoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK". *Lancet* 397.10269 (2021): 99-111.

8. Thompson MG., *et al*. "Prevention and Attenuation of Covid-19 with the BNT162b2 and mRNA-1273 Vaccines. *The New England Journal of Medicine* 385.4 (2021): 320-329.

9. Al Kaabi N., *et al*. "Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults: A Randomized Clinical Trial". *JAMA* 1 (2021): 32635-32645.

10. Yan ZP., *et al*. "COVID-19 Vaccines: A Review of the Safety and Efficacy of Current Clinical Trials". *Pharmaceuticals (Basel)* 14.5 (2021): 406.

11. Madhi SA., *et al*. "Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant". *The New England Journal of Medicine* 384.20 (2021): 1885-1898.

12. Pan H., *et al*. "Immunogenicity and safety of a third dose, and immune persistence of CoronaVac vaccine in healthy adults aged 18-59 years: interim results from a double-blind, randomized, placebo-controlled phase 2 clinical trial". *medRxiv* (2021).

13. Sterlin D., *et al*. "IgA dominates the early neutralizing antibody response to SARS-CoV-2". *Science Translational Medicine* 13.577 (2021).

14. Madhi SA., *et al*. "Efficacy of the ChAdOx1 nCoV-19 Covid-19 Vaccine against the B.1.351 Variant". *The New England Journal of Medicine* (2021).

15. Rossman H., *et al*. "COVID-19 dynamics after a national immunization program in Israel". *Nature Medicine* (2021).

16. Dejnirattisai W., *et al*. "Antibody evasion by the P.1 strain of SARS-CoV-2". *Cell* (2021).

17. Yuan M., *et al*. "Recognition of the SARS-CoV-2 receptor binding domain by neutralizing antibodies". *Biochemical and Biophysical Research Communications* 538 (2021): 192-203.

18. Greaney AJ., *et al*. "The SARS-CoV-2 mRNA-1273 vaccine elicits more RBD-focused neutralization, but with broader antibody binding within the RBD". *bioRxiv* (2021).

19. Abu-Raddad LJ., *et al*. "Pfizer-BioNTech mRNA BNT162b2 Covid-19 vaccine protection against variants of concern after one versus two doses". *Journal of Travel Medicine* (2021).

20. Earle KA., *et al*. "Evidence for antibody as a protective correlate for COVID-19 vaccines". *medRxiv* (2021): 2021.03.17.20200246.

21. Khoury DS., *et al*. "Neutralizing antibody levels are highly predictive of immune protection from symptomatic SARS-CoV-2 infection". *Nature Medicine* (2021).

22. Craig Fenwickhttps., *et al*. "Changes in SARS-CoV-2 Spike versus Nucleoprotein Antibody Responses Impact the Estimates of Infections in Population-Based Seroprevalence Studies". *Journal of Virology* 95.3 (2021): e01828-20.

23. Zhao J., *et al*. "Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019". *Clinical Infectious Diseases* (2019).