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Evaluation of post-vaccination antibody response of biochemical analysis in SARS-CoV-2 inactivated vaccine strategy

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ABSTRACT

Introduction: The importance of academic equipment in biochemical and microbiological evaluations of SARS-CoV-2 is increased. In this context, different techniques have been developed in the diagnosis and treatment of COVID-19 disease as qRT-PCR, rapid antigen tests and vaccine technology. The first known example of vaccine technology is the CoronaVac (Sinovac, China) inactivated vaccine throughout pandemic. In the presented study, the sensitivity of CoronaVac in the community would be positively increased and this data would be strengthened. In addition, antibody sensitivity of the CoronaVac between two doses, as well as the hemogram and biochemical analyzes were evaluated. The focus will be on increasing the sensitivity of the society to the vaccine.

Materials and methods: The immunoglobulin, biochemical analyzes, hemogram, and iron-iron binding capacities were evaluated after vaccinated person in a vaccine administration center in Istanbul, Türkiye.

Results: RBDIgG level was significantly higher after second dose ($p<0.05$). Mon#, Bas#, IMG#, Mon, Hgb, MCH, MCHC, RDWCV, RDWSD, and PDW levels were higher at 28th day. RBDIgG, Fe, WBC, Neu#, Lym#, Eos#, and PLT levels were higher at 42nd day. All other parameter means were higher at 56th day. RBDIgG, Fe, WBC, RDWCV, RDWSD and PDW differences between 28th and 42nd days were significant ($p<0.05$). RBDIgG, HCT, MCV, MCH, MCHC, and RDWCV differences between 28th and 56th days were statistically significant ($p<0.05$). RBDIgG, MCV and MCH differences between 42nd and 56th days were statistically significant ($p<0.05$).

Discussion and conclusion: The 60 volunteers in our study were laboratory, emergency service staffes and hospital personnel working at high risk of COVID-19. There was no differentiation in blood values related to the vaccine. It has been shown as an example of the phase-1 and the side effects of the CoronaVac, were also evaluated, and all our volunteers were followed for 60 days, and no possible serious side effects were observed. In groups with statistical significance in blood results, a vaccine related observation is not clearly revealed. We see that CoronaVac vaccine offers a positive confidence interval in antibody responses after the 2nd dose. These data are great importance in terms of better monitoring of the data by the anti-vaccine groups in Türkiye. It is beneficial to remove the vaccine mistrust against the anti-vaccination and pave the way for social immunization. This study contributes to the accuracy of the ministry and the vaccination strategy implemented in Türkiye. The result of this study provides preliminary information for the studies that will result from the application of the 3rd and 4th dose of vaccines.

Keywords: SARS-CoV-2, coronavirus, CoronaVac, inactivated vaccine, hemogram, biochemical analysis

INTRODUCTION

Throughout history, although there are many pandemics situation at all over the world, three types of coronaviruses have affected humanity since the early 21st century. These are severe acute respiratory syndrome coronavirus (SARS-CoV-1), which emerged in Guangdong in 2003, China, while the Middle East respiratory syndrome coronavirus (MERS) emerged in Saudi Arabia in 2012. Moreover nowadays, new version of the coronavirus family, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first reported in the Wuhan City of China in December 2019 and spread all over the world rapidly [1]. The major structural form of the SARS-CoV-2 is RNA virus involving a 30 kb genome with 14 open reading frames encoded by the spike protein (S), nucleocapsid protein (N), a

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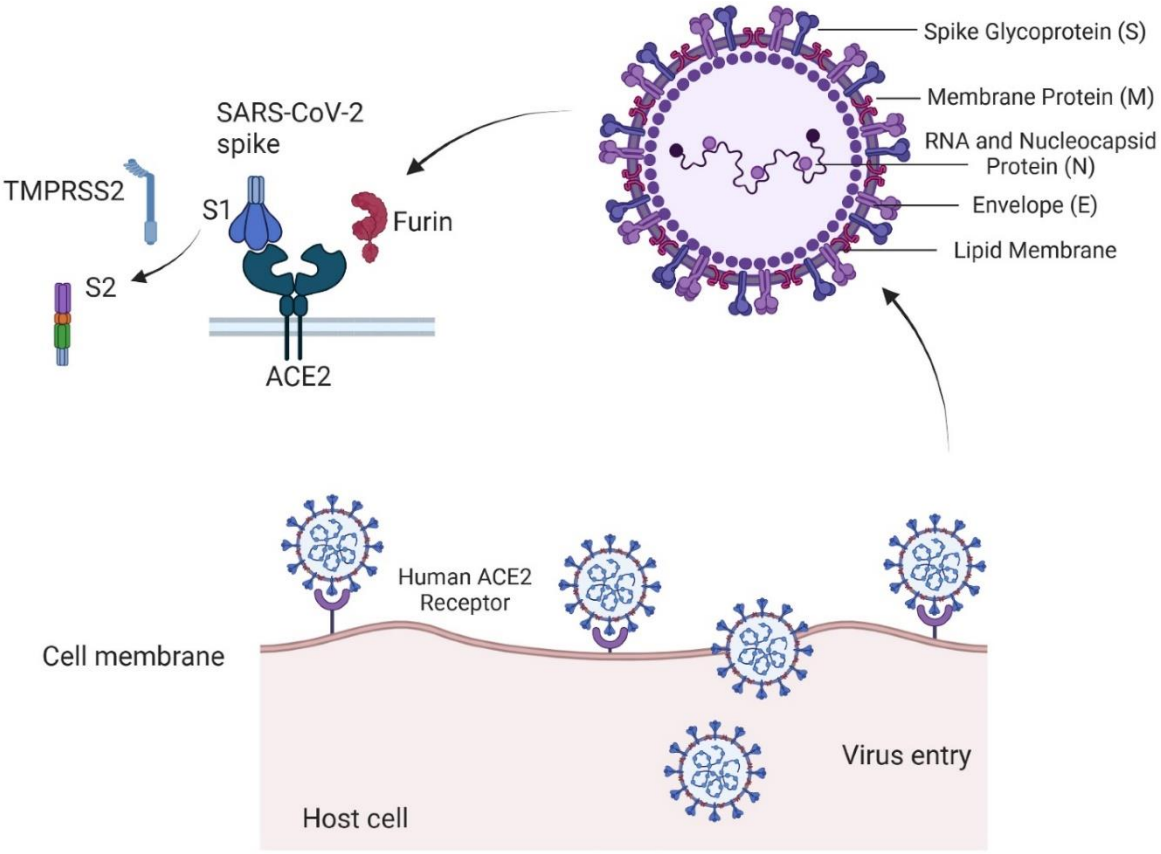

Figure 1. General structure of SARS-CoV-2, the spike protein and the ACE2 receptor. ACE2: Angiotensin converting enzyme-2; CD: connector domain; CH: central helix; CT: C-terminal domain; FP: fusion peptide; HR1: heptad repeat 1; HR2: heptad repeat 2; NTD: N terminal area; RBD: receptor-binding domain; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; SD1: subdomain 1; SD2: subdomain 2; TM: transmembrane region [3]. (Source: Authors, designed via BioRender).

small membrane protein (SM) and membrane glycoprotein (M) with an additional membrane glycoprotein (HE) [4]. The SARS-CoV-2 is enveloped positively single-stranded large RNA beta coronavirus that infects not only humans but also a widely of animals [5, 6]. This enveloped virus fastened on host angiotensin-converting enzyme 2 (ACE2) receptor in order to infects respiratory cells [7] (See **Figure 1**). This receptor is a membrane-bound aminopeptidase, which takes a role as putative receptor within the cell [8, 9]. Moreover, it is mainly located in type II alveolar cells of the lung but also placed in various extrapulmonary sites across the aerodigestive tract, involving the mucosa of the oral cavity within the body [10]. Although there are many prevention strategies such as physical distancing and wearing mask in current pandemic process, these strategies will paradoxically cause to lack of people's immune response against SARS-CoV-2 [11, 12]. According to the R0 value (2.5-3.5) of SARS-CoV-2, which is the causative agent of COVID-19 disease, 60-72% of the population should be immune to prevent the spread of the virus [13]. Thus, it is thought that world will not return normal state up to successfully implemented a global vaccination program [14].

With the COVID-19 pandemic and spread all over the world, vaccine studies have been started by many centers rapidly. One of them is the inactivated CoronaVac vaccine of Sinovac Company (Sinovac Life Sciences Co., Ltd., China). The inactive vaccines are one of the traditional vaccines and obtained using inactivated pathogens. They have different types known as subunit, toxoid and conjugated vaccines. With our research is aimed to increase the confidence of the society in the vaccine with the data obtained as a result of this research, retrospectively. With the presented study, it will contribute to the COVID-19 vaccination data in terms of being an example for the phase-1 clinical studies on vaccine applications in our country (Türkiye), and because of this study, the analyzes of the whole blood hemogram, antibody, iron and iron binding capacity of the vaccine were examined in a random population. The study was consisting of people who have had the CoronaVac SARS-CoV-2 inactivated vaccine. The age scale for the volunteers who are given the first dose varies between 20-65. Since the parameters we looked at were not gender dependent, the whole blood hemogram, iron, iron binding and antibody effect values of the vaccine were examined on a random population who voluntarily applied to the study after being vaccinated. For this reason, it is the only criterion for the volunteer to have the COVID-19 vaccine. Since the statistical analysis of the study will be made according to the population formed by the volunteers to participate in the study, no other criteria are required. Methodologies such as macro-ELISA, ECLIA or micro ELISA methods, autoanalyzer's and complete blood count (CBC) methods were used, and statistical data of analysis results were calculated [15]. The first volunteer was recruited on April 15, 2021, and the last volunteer on June 15, 2021.

MATERIALS AND METHODS

This study is accomplished in the Department of the Biochemistry Laboratory (University of Health Sciences Kanuni Sultan Suleyman Training and Research Hospital). The study

group consisted of volunteers between the ages of 18-64, including hospital staff and their relatives, and the average age of the total volunteers was 37 (standard deviation [SD]: 10.21), the mean age for women was 38 (SD: 9.96) and males was 35 (SD: 10.93). Experiments were carried out by ignoring these factors and not depending on age and gender while calculating the statistics of the parameters created. The study period lasted about two months, and the first volunteer was included in the study on April 15, 2021, and the last volunteer on June 15, 2021.

Only blood samples were taken from the volunteers. These samples were examined in different time periods as 14th and 28th days in their clinical studies as stated in the literature. For us to analyze the results correctly, the samples were studied immediately. Because total of three samples were taken from the participants on the 28th day after the first vaccination, and on the 14th and 28th days after the second vaccination [16].

After the ethics committee approval, volunteers who did not exceed 28 days after the first dose of vaccine were collected and plasma samples were taken on the 28th day after the first vaccine. Volunteers included in the study are of different ages and genders and do not require any special criteria. The screening study in this direction is not carried out on a special group or on a special criterion. These people consist of volunteers who participated in the vaccine application initiated by the Republic of Turkish Ministry of Health at their own request and were shot CoronaVac inactivated vaccine. We collected blood from these volunteers with two tubes and hemogram tubes in only three different time periods and evaluated the data obtained from this blood in accordance with the criteria and statistics in the phase-1 of clinical studies.

This study was the first dose of vaccine and was administered on a population of 60 informed volunteer participants [17]. Volunteers, who were given the 1st dose of COVID-19 vaccine, were drawn from two tubes of hemogram on the 28th day after the first day they were vaccinated. Later on, the 14th day after the 2nd dose of the COVID-19 vaccine, blood was drawn in two tubes of hemogram, and on the 28th day, blood was taken from the volunteers in two hemogram tubes. Thus, blood was collected in two tubes of hemogram in each time period, in three different time periods (1st dose–28 days, 2nd dose–14th day and 2nd dose–28th day) blood was drawn in the hemogram tube. All the following parameters were examined (**Table 1**):

1. Antibody level in serum (RBD IgG)
2. Iron binding level in serum (UIBC)
3. Iron level (FE) in the serum
4. Complete blood count (hemogram) in the plasma.

The relationships between the parameters presented in **Table 1** and their values in three different time periods (28 days after the 1st dose, 14th day after the 2nd dose, 28 days after the 2nd dose) were examined. These values were created in the form of a table in Excel, and it was checked for each person how these data changed or did not change.

Statistical Methods

Scale parameters were described with means and SDs. Kolmogorov Smirnov test was used for normality distribution of parameters. Since 28th day was after first dose, and 42nd and 56th days were after second dose, two group differences (first and second dose) were evaluated by Mann-Whitney U test for non-normally distributed parameters, and independent samples t-test for normally distributed parameters. In paired sample comparisons, Wilcoxon signed rank test was used for non-normally distributed parameters, and paired samples t-test for normally distributed parameters. All analysis were performed at SPSS 17.0 for Windows at 95% confidence interval with 0.05 significance level.

Table 1. Complete blood count hemogram parameters

Parameter	Unit
White blood cell (WBC)	10^3/µL
Neutrophil (Neu)	10^3/µL
Lymphocyte (Lym)	10^3/µL
Monocytes (Mon)	10^3/µL
Eosinophil (Eos)	10^3/µL
Basophil (Bas)	10^3/µL
Immature granulocyte (IMG)	10^3/µL
Neutrophil (Neu)	%
Lymphocyte (Lym)	%
Monocytes (Mon)	%
Eosinophil (Eos)	%
Basophil (Bas)	%
Immature granulocyte (IMG)	%
Erythrocyte (RBC)	10^6/µL
Hemoglobin (HGB)	g/dL
Hematocrit (HCT)	%
Mean corpuscular volume (MCV)	fL
Mean corpuscular hemoglobin (MCH)	pg
Mean corpuscular hemoglobin concentration (MCHC)	g/dL
Red cell distribution width corpuscular volume (RDW-CV)	%
Red cell distribution width standard deviation (RDW-SD)	fL
Platelets, T (PLT)	10^3/µL
Mean platelet volume (MPV)	fL
Thrombocyte distribution width (PDW)	fL
Procalcitonin (PCT)	%
Platelet large cell (P-LCC)	10^9/L
Platelet large cell ratio (P-LCR)	%
Nucleated red blood cells (NRBC)	10^3/µL
Nucleated red blood cells/White blood cell (NRBC/WBC)	%
Unsaturated iron binding capacity (UIBC)	µg/dL
Iron (FE)	ml/ng
*Receptor-binding domain immunoglobulin G (RBDIgG)	COI=1

Note. *COI<1→Negative–COI>/=→Positive

RESULTS

RBD IgG level was significantly higher after second dose ($p<0.05$). MCHC level was significantly higher after first dose ($p<0.05$). Other clinical parameter differences were insignificant between first and second doses ($p>0.05$) (**Table 2**).

Mon, Bas, IMG, Mon, Hgb, MCH, MCHC, RDWCV, RDWSD, and PDW levels were higher at 28th day. RBDIgG, Fe, WBC, Neu, Lym, Eos, and PLT levels were higher at 42nd day. All other parameter means were higher at 56th day (**Table 3**).

RBDIgG, Fe, WBC, RDWCV, RDWSD and PDW differences between 28th and 42nd days were statistically significant ($p<0.05$). RBDIgG, HCT, MCV, MCH, MCHC, and RDWCV differences between 28th and 56th days were statistically significant ($p<0.05$). RBDIgG, MCV and MCH differences between 42nd and 56th days were statistically significant ($p<0.05$) (**Table 4**).

Table 2. Clinical parameters & difference results between 1st & 2nd dose (n=60)

Parameters (unit)	FD (Mean±SD)	SD (Mean±SD)	p-value
RBDIgG (COI=1)	1.68±2.52	**8.56±2.68**	**0.000[a]**
UIBC (µg/dL)	264.04±67.43	263.98±63.96	0.996[b]
FE (ml/ng)	73.54±28.39	79.44±35.27	0.262[b]
WBC (10^3uL)	7.17±1.67	7.46±1.79	0.287[b]
Neu (10^3uL)	4.42±1.32	4.58±1.44	0.456[b]
Lym (10^3uL)	2.18±0.53	2.29±0.57	0.343[a]
Mon (10^3uL)	0.46±0.40	0.41±0.14	0.966[a]
Eos (10^3uL)	0.14±0.14	0.16±0.18	0.891[a]
Bas (10^3uL)	0.03±0.02	0.03±0.01	0.861[a]
IMG (10^3uL)	0.01±0.01	0.01±0.01	0.794[a]
Neu (%)	60.85±7.24	60.61±7.99	0.847[b]
Lym (%)	30.99±6.41	31.32±6.88	0.757[b]
Mon (%)	5.66±1.25	5.57±1.31	0.659[b]
Eos (%)	2.08±2.29	2.16±2.43	0.873[a]
Bas (%)	0.39±0.24	0.38±0.22	0.999[a]
IMG (%)	0.13±0.10	0.13±0.12	0.713[a]
RBC (10^6uL)	4.74±0.58	4.72±0.50	0.854[b]
HGB (gdL)	13.72±1.63	13.62±1.37	0.971[a]
HCT (%)	40.57±4.86	40.57±3.73	0.488[a]
MCV (fL)	86.14±6.19	86.34±5.98	0.686[a]
MCH (pg)	29.17±2.42	28.99±2.35	0.629[a]
MCHC (gdL)	**33.82±0.69**	33.56±0.86	**0.039[b]**
RDWCV (%)	13.48±1.27	13.26±0.99	0.259[a]
RDWSD (fL)	41.70±3.13	41.16±2.15	0.176[b]
PLT (10^3uL)	261.40±57.71	264.20±59.10	0.763[b]
MPV (fL)	10.00±1.11	10.01±1.18	0.944[b]
PDW (fL)	16.26±0.43	16.19±0.38	0.267[b]
PCT (%)	0.26±0.05	0.26±0.05	0.750[b]
PLCC (10^9L)	68.07±18.37	68.25±20.41	0.954[b]
PLCR (%)	26.84±7.70	26.75±8.44	0.944[b]

Note. FD: 1st dose (28th day); SD: 2nd dose (42nd & 56th days); [a]Mann-Whitney U test, & [b]Independent samples t-test

Table 3. Clinical parameter means at 28th, 42nd, & 56th days

Parameters (unit)	28th day	42nd day	56th day
RBDIgG (COI=1)	1.68±2.52	**8.79±2.46**	8.33±2.88
UIBC (µg/dL)	264.04±67.43	262.48±63.93	**265.48±64.48**
FE (ml/ng)	73.54±28.39	**81.32±37.79**	77.55±32.77
WBC (10^3uL)	7.17±1.67	**7.60±1.74**	7.32±1.84
Neu (10^3uL)	4.42±1.32	**4.69±1.45**	4.48±1.42
Lym (10^3uL)	2.18±0.53	**2.32±0.57**	2.25±0.57
Mon (10^3uL)	**0.46±0.40**	0.42±0.13	0.41±0.15
Eos (10^3uL)	0.14±0.14	**0.16±0.20**	0.15±0.15
Bas (10^3uL)	**0.03±0.02**	0.03±0.01	**0.03±0.02**
IMG (10^3uL)	0.01±0.01	0.01±0.01	0.01±0.01
Neu (%)	**60.85±7.24**	60.72±8.77	60.51±7.20
Lym (%)	30.99±6.41	31.21±7.17	**31.42±6.64**
Mon (%)	**5.66±1.25**	5.58±1.42	5.57±1.19
Eos (%)	2.08±2.29	**2.19±2.72**	2.14±2.12
Bas (%)	0.39±0.24	0.37±0.21	**0.40±0.22**
IMG (%)	0.13±0.10	0.12±0.09	**0.14±0.15**
RBC (10^6uL)	4.74±0.58	4.69±0.47	**4.75±0.53**
HGB (gdL)	**13.72±1.63**	13.62±1.30	13.63±1.45
HCT (%)	40.57±4.86	40.28±3.48	**40.87±3.97**
MCV (fL)	86.14±6.19	86.19±5.98	**86.48±6.02**
MCH (pg)	**29.17±2.42**	29.13±2.32	28.84±2.39
MCHC (gdL)	**33.82±0.69**	33.79±0.85	33.33±0.80
RDWCV (%)	**13.48±1.27**	13.28±0.98	13.24±1.00
RDWSD (fL)	**41.70±3.13**	41.09±2.18	41.23±2.13
PLT (10^3uL)	261.40±57.71	**268.32±58.60**	260.08±59.79
MPV (fL)	10.00±1.11	9.94±1.17	**10.09±1.20**
PDW (fL)	**16.26±0.43**	16.18±0.37	16.20±0.39
PCT (%)	0.26±0.05	0.26±0.05	**0.26±0.06**
PLCC (10^9L)	68.07±18.37	68.13±19.21	**68.36±21.70**
PLCR (%)	26.84±7.70	26.32±8.34	**27.17±8.60**

Table 4. Clinical parameter differences between different day pairs (p-values)

Parameters (unit)	28^{th}-42^{nd} days	28^{th}-56^{th} days	42^{nd}-56^{th} days
RBDIgG (COI=1)	**0.000[a]**	**0.000[a]**	**0.000[a]**
UIBC (µg/dL)	0.786[b]	0.711[b]	0.564[b]
FE (ml/ng)	**0.045[b]**	0.245[b]	0.364[b]
WBC (10^3uL)	**0.026[b]**	0.473[b]	0.118[b]
Neu (10^3uL)	0.088[b]	0.719[b]	0.148[b]
Lym (10^3uL)	0.109[a]	0.375[a]	0.254[a]
Mon (10^3uL)	0.600[a]	0.352[a]	0.713[a]
Eos (10^3uL)	0.936[a]	0.933[a]	0.536[a]
Bas (10^3uL)	0.538[a]	0.884[a]	0.229[a]
IMG (10^3uL)	0.861[a]	0.739[a]	0.535[a]
Neu (%)	0.888[b]	0.642[b]	0.806[b]
Lym (%)	0.795[b]	0.494[b]	0.782[b]
Mon (%)	0.620[b]	0.445[b]	0.894[b]
Eos (%)	0.423[a]	0.819[a]	0.753[a]
Bas (%)	0.389[a]	0.688[a]	0.207[a]
IMG (%)	0.565[a]	0.931[a]	0.374[a]
RBC (10^6uL)	0.373[b]	0.807[b]	0.092[b]
HGB (gdL)	0.870[a]	0.571[a]	0.312[a]
HCT (%)	0.883[a]	**0.046[a]**	0.205[a]
MCV (fL)	0.408[a]	**0.005[a]**	0.075[a]
MCH (pg)	0.686[a]	**0.000[a]**	**0.000[a]**
MCHC (gdL)	0.656[b]	**0.000[b]**	**0.000[b]**
RDWCV (%)	**0.001[a]**	**0.001[a]**	0.178[a]
RDWSD (fL)	**0.026[b]**	0.086[b]	0.229[b]
PLT (10^3uL)	0.292[b]	0.828[b]	0.171[b]
MPV (fL)	0.391[b]	0.290[b]	0.086[b]
PDW (fL)	**0.040[b]**	0.137[b]	0.586[b]
PCT (%)	0.425[b]	0.913[b]	0.469[b]
PLCC (10^9L)	0.968[b]	0.843[b]	0.901[b]
PLCR (%)	0.299[b]	0.552[b]	0.144[b]

Note. [a]Wilcoxon signed rank test & [b]Paired samples t-test

DISCUSSION AND CONCLUSION

WHO has declared a pandemic phenomenon at March 11,2020 and the preparation of vaccines against COVID-19 have mainly considered at the whole world [18, 19]. Among many different variations, it is difficult to predict which type of immune response and hence the vaccine will be more effective. Therefore, traditional vaccines from the past to the present have come to the fore again. There are big differences between traditional vaccine development and the development of these vaccines under the pressure of a widespread epidemic phenomena. The inactive vaccines are one of the traditional vaccines. Inactivated vaccines often contain disease-causing organisms or pathogenic proteins that are weakened or inactivated to stimulate the body's immune response. In this vaccine strategy more stable than live attenuated vaccines. The short-term immune memory is main limitation for it, which requires the vaccination at higher amounts of vaccines or the inactivated microorganism combination with an adjuvant. The resulting immune response is not directed only with the S protein of SARS-CoV-2, but also many other SARS-CoV-2 antigens. Although the induced response is generally weaker in attenuated viruses, the vaccine is easier to handle, cheaper [20, 21]. The inactive vaccine of CoronaVac response is evaluated in this paper with the analysis of antibody level in blood (RBD IgG), iron binding level in blood (UIBC), iron level (FE) in the blood and complete blood count hemogram. However, there were some limitations in this study.

We aimed to evaluate of effectivity of phase-1 of vaccine application among 60 people (between 18-59 years). The main reason why the number of samples is limited to 60 is due to the budget cost in this study. Another limitation of the study is that it was conducted in a single center.

Considering the data in the presented study, comparing to the countries of the world and European countries, the rapid progress of the vaccination process in our country in the COVID-19 global epidemic pandemic has necessitated the continuous study of the phases of clinical trials in our research centers. In order to help increase the new and updated data on the vaccine, to eliminate the vaccine opposition with the results, this research study was aimed to be evaluated by examining the clinical research processes as a phase-1 clinical trial. For this reason, according to the "Turkish Medical Association (TTB) COVID-19 six month evaluation report", (International Clinical Trials 230 Registry Platform (ICTRP), and (glossary of terms used in EU) referred to under the title of Stages of clinical trials on page 229. According to the Clinical Trials Register sources, "Phases of clinical trials:", under the title, "A clinical trial is any research study that prospectively assigns human participants or groups of people to one or more health-related interventions to evaluate their effects on health outcomes." definition has been made [17, 22]. According to this definition, "Phase-1 studies constitute the first phase of a clinical trial. Rather than treating or preventing any disease, it is the researched stage to determine whether the researched product is safe to be taken by humans (for example, to determine a safe dose range, to determine the side effects of the doses in this range, to examine it in detail by observing it in a minimum number of patients). The number of people invited to this stage is very small; typically between 20-80 people, with about 30 people. It usually includes healthy volunteers or

sometimes patients." It has been expressed as. Thus, in this study 60 random people was evaluated.

After the second dose of the vaccination process, RBDIgG level was significantly higher than first dose while MCHC level was significantly higher after first dose. On the other hand, Mon, Bas, IMG, Mon, Hgb, MCH, MCHC, RDWCV, RDWSD, and PDW levels were higher at 28th day. RBDIgG, Fe, WBC, Neu, Lym, Eos, and PLT levels were higher at 42nd day, which are important data for the understanding of the vaccination results after as the days go by. As evidence of the optimum results we have obtained, in the literature recommended to administer the CoronaVac vaccine in two doses, 28 days apart, in order to be effective [15]. In the phase-1 study in which CoronaVac vaccine was administered to individuals aged 18-59 years, seroconversion rates were found to be 46% and 50% with 0.5 mL vaccine containing 3 µg and 6 µg of inactivated virus 14 days after the vaccine, and 83% and 79% after 28 days, respectively in literature. In the phase-2 study, seroconversion rates were found to be 92% and 98%, and 97% and 100% after 28 days, respectively, with 0.5 mL vaccine containing 3 µg and 6 µg of inactivated virus 14 days after the vaccine [15]. In the phase-1 study in which CoronaVac vaccine was administered to individuals over 60 years of age, seroconversion rates were found to be 100% and 95.7% with 0.5 mL vaccine containing 3 µg and 6 µg of inactivated virus 28 days after the vaccine, respectively, and 98% and 99% in the phase-2 study [23].

The CoronaVac vaccine is currently only approved by China, and the vaccine has been approved for emergency use by 20 countries, including Türkiye. It started as of January 14, 2021, in Türkiye and all health workers who want to be vaccinated in a short time have been vaccinated [24].

Moreover, for inactivated vaccine studies that have started to be implemented in Türkiye, only antibody tests were subjected. The 60 volunteers in our study were mostly COVID-19, laboratory, emergency service staffs and hospital personnel working at high risk of COVID-19. Addition to [24], hemogram, iron and iron binding capacities were added to the evaluation of antibody responses in the study. There was no significant differentiation in blood values related to the vaccine. It has been shown as an example of the phase-1 and the side effects of the Chinese vaccine, inactivated CoronaVac vaccine, were also evaluated, and all our volunteers were followed for 60 days, and no possible serious side effects were observed. In groups with statistical significance in blood results, a vaccine-related observation is not clearly revealed. We see that CoronaVac vaccine offers a positive confidence interval in antibody responses after the 2nd dose. These data are of great importance in terms of better monitoring of the data by the anti-vaccine groups in Türkiye. It is beneficial to remove the vaccine mistrust against the anti-vaccination and pave the way for social immunization. The result of this study provides preliminary information for the studies that will result from the application of the 3rd dose CoronaVac or BioNTech vaccine. Blood results and antibody results can be shown as a source for the vaccine studies to be carried out for the 3rd and 4th dose vaccination applied in Türkiye.

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Ethical statement: This study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. This study protocol was reviewed and approved by Ethics Committee of Kanuni Sultan Suleyman Training and Research Hospital No: 2021.03.102, Subject No: KAEK/2021.03.102 Date: 25.03.2021-09:17-E-80929729-000-5611 and Republic of Türkiye, Ministry of Health, COVID-19 Scientific Research Studies Approval No: YakupArtik-2021-02-28T17_23_27.

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Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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