perspective. Clin Chem Lab Med. 2003;41(9):1191–8.
14.Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c test in diagnosis and prognosis of diabetic patients. Biomark Insights. 2016;11:95–104.
15. Tran DV, Lyon AW, Higgins TN, Wesenberg JC, Vandergouwe L, Wiley CL, et al. Use of serial patient hemoglobin A1c differences to determine long-term imprecision of immunoassay and highperformance liquid choromatography analyzers. J Diabetes SCI Technol 2009; 3 (3): 424-8.

OP044

INVESTIGATING THE EFFECTS OF BIONTECH AND CORONAVAC VACCINES ON IGG AND IGM LEVELS

Gülşah Alyar[1], Neslihan Yüce[2], Veysel Arslan[4], Nurcan Baygutalp[5], Emine Parlak[6], Ebubekir Bakan[7]

[1]Ataturk University,vocational School of Health Services, Erzurum, Turkey
[2]Bolu Abant Izzet Baysal University, Faculty of Medicine, Department of Biochemistry, Bolu, Turkey
[3]Kutahya Health Sciences University, Department of Fundamental Sciences, Faculty of Engineering and Natural Sciences, Kütahya, Turkey
[4]Bayburt University, Vocational School of Health Services, Bayburt, Turkey
[5]Atatürk University, Faculty of Medicine,department of Medical Biochemistry, Erzurum, Turkey
[6]Ataturk University, Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Erzurum, Turkey
[7]Kafkas University, Faculty of Medicine, Department of Medical Biochemistry, Kars, Turkey

Introduction

Covid-19 (Coronavirus Disease 2019), caused by the SARS-CoV-2 virus, has become a pandemic affecting the entire world by causing severe acute respiratory syndrome [1]. According to data from the World Health Organization (WHO) (as of September 12, 2021), 223 million people worldwide have contracted COVID-19, resulting in 7 million deaths as of November 2023 [2]. In our country, the number of people infected with Covid-19 is 6,590,414, and the total number of deaths due to Covid-19 is 59,170 [3]. Given the high incidence and mortality rates of the disease, in addition to personal hygiene, mask-wearing, and social distancing measures, the development, production, and distribution of safe and effective vaccines are critical to ending the pandemic [4]. The development of vaccines, which is the most promising long-term approach to controlling the pandemic, involved Phase 1, Phase 2, Phase 3, and Phase 4 studies, which are time-consuming. However, these studies were conducted in a relatively short period, resulting in limited data on the immune response following vaccination [5]. Although data on vaccine efficacy has been released by relevant institutions, more studies are needed to determine its effectiveness and duration of protection in real-world settings. The most commonly used vaccine types are mRNA (BNT162b2 and mRNA-1273), adenoviral vector-based (ChAdOx1 nCoV-19, Ad26.CoV2. S, and Gam-COVID-Vac), or inactivated virus (CoronaVac and Sinopharm) vaccines [6]. To date, approximately 13.5 billion doses of vaccine have been administered. According to data from the Ministry of Health (as of September 12, 2021), a total of 101,454,754 doses of vaccine have been administered in our country [3]. During Covid-19 infection, IgM antibodies are formed in the patient's plasma first, followed by IgG antibodies. IgM antibodies typically rise within the first 7–10 days after infection or vaccination and produce a short-term (approximately several weeks) response. This early response is later supported by the production of IgG antibodies, and IgG provides long-term protection. After the 15th day of infection, IgM antibodies can be detected in the majority of patients, and IgG antibodies in 94.2% of them [8]. Our study examined the antibody responses generated by both the Coronavac and Pfizer/BioNTech vaccines. Blood samples were collected from patients before vaccination, 14 days after the first dose, and 14 days after the second dose. IgG and IgM levels were measured to assess differences in the development of immune responses among individuals. The Pfizer/BioNTech vaccine used in our study works by placing the part of the SARS-CoV-2 genome that codes for the spike protein into lipid nanoparticles with an mRNA molecule. In vaccinated individuals, mRNA causes the production

of spike proteins within the cell. Antigen-presenting cells detect these produced antigenic structures and present them to the immune system, causing the development of IgG antibodies against spike proteins (S-receptor-binding domain) [7]. Coronavac is based on the inactivation of SARS-CoV-2 viruses with betapropionyl lactone and enables the production of both IgG (S) and IgG(N) (nucleoprotein-specific) [8].

Materials and Methods

The study was approved by the Atatürk University Faculty of Medicine Clinical Research Ethics Committee (15.04.2021/221 NUMBER: B.30.2.ATA.0.01.00/221) and was conducted in the laboratory of the Department of Medical Biochemistry of Atatürk University Faculty of Medicine in 2021.Volunteers included in the study were enrolled after obtaining informed consent forms. A total of 67 individuals who had received two doses of the COVID-19 vaccine (BioNTech: n=42, CoronaVac: n=25) were included in the study. Blood samples were collected from all volunteers three times: before vaccination, 14 days after the first dose, and 14 days after the second dose. Serum IgG and IgM levels in the samples were measured quantitatively using the ELISA method. (lg G antibody for detection of COVID-19 nucleocapsid spike antigen is scarce, lg M antibody for detection of COVID-19 nucleocapsid spike antigen is scarce LOB (Blank Limit) = 1.9 BAU/mL, LOD (Detection Limit) = 3.2 BAU/mL, LOQ (Quantification Limit) = 24.6 BAU/mL; lg M LOB = 242.2 BAU/mL, LOD = 289.9 BAU/mL, LOQ = 572.4 BAU/mL, Within-run CV% (medium positive) ≈ 10.1% Repeatability (within-run) %CV (medium positive sample) ≈ 4.6%). IgM and IgG levels were measured at baseline (IgG0, IgM0), after the first vaccine (IgG1, IgM1), and after the second vaccine (IgG2, IgM2), and changes in antibody levels over time were determined. IgG and IgM levels measured in two different vaccine groups were compared separately for each biomarker using one-way ANOVA, and significant differences were evaluated using the Tukey post-hoc test.

Results

Following the first dose of vaccination, both vaccines caused an increase in IgG levels, but this increase was not statistically significant. Following the second dose of vaccination, serum IgG levels in individuals who received the CoronaVac and BioNTech vaccines increased to a statistically significant degree compared to baseline (table 1). IgM levels remained unchanged in individuals who received two doses of CoronaVac, while they decreased significantly after the first dose and after the second dose in individuals who received the BioNTech vaccine compared to baseline (table 2).

Discussion

Developing a vaccine, determining its reliability, and evaluating the immune response after vaccination is a lengthy process. However, the global scale of the Covid-19 pandemic, the high transmissibility of the infection, and its mortality rate have necessitated the rapid execution of vaccine studies [9]. Therefore, the immune response generated by vaccines such as BioNTech and Coronavac, which are most commonly used in Covid-19, and the potential effects they cause have been investigated and remain a current research topic [8-9]. In our study, the immune response formed in individuals who received two different Covid-19 vaccines (BioNTech and CoronaVac) was determined by measuring IgG and IgM levels over time to identify changes in antibody levels. The initial finding of our study was that although IgG levels increased after the first dose of both vaccines, this increase was not significant. This result indicates that a single dose of the vaccine does not provide protection. After the second dose, both vaccines elicited a strong IgG response, and IgG levels increased significantly compared to baseline levels. In addition, the BioNTech vaccine elicited a higher IgG antibody response compared to Coronavac. This finding indicates that two doses of vaccine are necessary for a strong and lasting antibody response. Another finding of our study was that IgM levels increased after the first and second doses of the CoronaVac vaccine, but this increase was not significant. The early increase in IgM after CoronaVac indicates the formation of the initial immune response to the vaccine, and its continued high level suggests that the conversion to IgG, which is an indicator of lasting immunity, occurs more slowly in such vaccines. In contrast, IgM levels decreased after the BNT162b2 vaccine, and this decline was considered an indicator that the immune response was maturing and that lasting immunity was developing. High

IgM levels alone are not indicative of protective immunity. However, it can be used as an early biomarker in assessing the vaccine's immunogenicity. IgG antibody levels are more meaningful in assessing long-term protection. A study of 678 people vaccinated with CoronaVac detected titers in all participants 60 days after the second dose of vaccination using a semi-quantitative method [10]. Another study investigated the effect of the CorovaVac vaccine on IgG levels and detected 99.6% IgG antibodies approximately three weeks after the second dose of the vaccine [11]. Studies on SARS-CoV showed that IgM antibody levels increased within the first month in diagnosed patients but decreased significantly between weeks 5 and 11, while IgG antibodies rose to significant levels in the plasma of the vast majority of patients from day 36 onwards and remained high for a long time [12]. A study on SARS-CoV-2 found that antibodies in infected individuals became detectable within 7-50 days after the onset of disease symptoms and reached peak levels an average of 24 days after the symptoms disappeared [13]. According to the results of a similar study on the subject, the antibody level observed 7-21 days after the first dose of the BioNTech vaccine in individuals who had contracted the disease was found to be similar to the antibody level formed after the second dose in those who had not contracted the disease. It has been suggested that the immune response develops rapidly due to the earlier rise of IgG antibodies, which normally rise later, but it has been argued that this needs to be investigated in multicenter studies involving different groups to be validated [14].

Conclusion

Two doses of the vaccine are necessary for a strong and lasting antibody response. The BioNTech vaccine produced a higher IgG response. Completing both doses of the vaccine during outbreaks is important for controlling outbreaks and achieving herd immunity.

References

1.Cao X. COVID-19: immunopathology and its implications for therapy. Nat Rev Immunol 2020;20(5):269-70.

2.int Cw. Who coronavirus (COVID-19) Dashboard. [online]. 2022.

3. https://covid19asi.saglik.gov.tr/

4. Liu YC, Kuo RL, & Shih SR. (2020). COVID-19: The first documented coronavirus pandemic in history. Biomedical journal, 43(4):328-333.

5.Ebinger JE, Fert-Bober J, Printsev I, Wu M, Sun N, Prostko JC, et al. Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2. Nat Med.2021;27(6):981-4.

6. Pascolo, S. (2021). Synthetic messenger RNA-based vaccines: from scorn to hype. Viruses 13(2), 270.

7.Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients with novel coronavirus disease 2019. Clin Infect Dis 2020;71(16):2027-34.

8.Bayram A, Demirbakan H, Günel Karadeniz P, Erdoğan M, Koçer I. Quantitation of antibodies against SARS-CoV-2 spike protein after two doses of CoronaVac in healthcare workers. J Med Virol 2021;93(9):5560-7.

9.Gareayaghi Ng, Dinç HÖ, Özbey D, Akçin R, Daşdemir Fo, Akkus S, et al. COVID-19 Geçiren, CoronaVac ve BNT162b2 Aşı olan Bireylerde Hümoral İmmün Yanıtın Değerlendirilmesi. Harran Üniversitesi Tıp Fakültesi Dergisi 2022;19(3):576-80.

10. Yigit M, Ozkaya-Parlakay A, Cosgun Y et al 2022) Should a third booster dose be scheduled after two doses of

CoronaVac? A single-center experience. J Med Virol 94(1):287-290.

11.Xue J-H, Wang Y-J, Li W, Li Q-L, Xu Q-Y, Niu J-J, et al. Anti–receptor-binding domain immunoglobulin G antibody as a predictor of seropositivity for anti–SARS-CoV-2 neutralizing antibody. Arch Pathol Lab Med 2022;146(7):814-21.

12. Manisty C, Otter AD, Treibel TA et al (2021) Antibody response to first BNT162b2 dose in previously SARS-CoV-2-infected individuals **Lancet** 397(10279):1057-1058.

13. Wajnberg A, Mansour M, Leven E, Bouvier NM, Patel G, Firpo A, et al. Humoral immune response and prolonged PCR positivity in a cohort of 1343 SARS-CoV 2 patients in the New York City region. **medRxiv** 2020-04.

14.Zhou C, Bu G, Sun Y, Ren C, Qu M, Gao Y, et al. Evaluation of serum IgM and IgG antibodies in COVID-19 patients by enzyme linked immunosorbent assay. J Med Virol 2021;93(5):2857-2866.

Tables

Table 1. Comparison of IgG Levels Following CoronaVac and BioNTech Vaccinations

	CoronaVac (Mean± SD)	BNT162b2 (Mean± SD)
lg G0 (IU/mL)	18,7 ± 9,5	34,2 ± 3,6
lg G1 (IU/mL)	(+) 104,3 ± 41,2	(+) 121,4 ± 21,6
lg G2 (IU/mL)	(+) 147,6 ± 61,3	(+) 255,4 ± 81,1
p value		
lg G0 - G1	[a]0,100	[a]0,172
lg G0- G2	[b]<0,001**	[b]<0,000**
lg G1- G2	[c]1,000	[c]0,169

lg G1 and lgG2 levels are presented as the difference from the baseline value (lgG0); (+) indicates an increase, (-) indicates a decrease. Results are expressed as mean ± standard deviation. p-values in the same column are the p-values for the One-Way ANOVA test statistic for Repeated Measures (comparison of time effects in the same column). *: $p<0.05$, **: $p<0.01$. Superscript letters a, b, c represent the p values of the Post-hoc Tukey test results of the One-Way Repeated Measures ANOVA test (comparison of time effects in the same column); a: Comparison of participants' serum IgG levels before vaccination and 14 days after the 1st vaccine, b: Comparison of participants' serum IgG levels before vaccination and 14 days after the second dose, c: Comparison of participants' serum IgG levels 14 days after the first dose and 14 days after the second dose,

Table 2. Comparison of IgM Levels Following CoronaVac and BioNTech Vaccinations

	CoronaVac (Mean± SD)	BioNTech (Mean± SD)
IgM_0 (IU/mL)	7,2 ± 3,1	3,9 ± 0,9
IgM_1 (IU/mL)	(+) 8,3 ± 3,9	(+) 3,3 ± 1,3

	CoronaVac (Mean± SD)	BioNTech (Mean± SD)
IgM_2 (IU/mL)	(+) 9,1 ± 3,3	(+) 2,8 ± 0,7
p değeri		
Ig M0 - M1	[a]1,000	[a]0,009**
Ig M0- M2	[b]1,000	[b]0,009**
Ig M1- M2	[c]1,000	[c]1,000

lgM1 and lgM2 levels are presented as the difference from the baseline value (lgM0); (+) indicates an increase, (-) indicates a decrease. Results are expressed as mean ± standard deviation. p-values in the same column are the p-values for the One-Way ANOVA test statistic for Repeated Measures (comparison of time effects in the same column). *: $p<0.05$, **: $p<0.01$. Superscript letters a,b,c represent the p values of the Post-hoc Tukey test results of the One-Way Repeated Measures ANOVA test (comparison of time effects in the same column); a: Comparison of participants' serum IgM levels before vaccination and 14 days after the 1st dose, b: Comparison of participants' serum IgM levels before vaccination and 14 days after the 2nd dose, c: Comparison of participants' serum IgM levels 14 days after the 1st dose and 14 days after the 2nd dose

Funding source: This study was financially supported by the Coordinator of Scientific Research Projects of Atatürk Üniversity with project number: TKP-2021-9796.

Award Identifier / Grant number: TKP-2021-9796.

Research ethics: This tudy was carried out with the approval of Atatürk University Faculty of Medicine Clinical Research Ethics Committee (15.04.2021/221, B.30.2.ATA.0.01.00/221).

Informed consent: Informed consent was obtained from all individuals included in this study.

Author contributions: All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

Use of Large Language Models, AI and Machine Learning Tools: None declared.

Conflict of interest: The authors state no conflict of interest.

Research funding: This study was supported by Coordinator of Scientific Research Projects of Atatürk Üniversity with project number: TKP-2021-9796.

Data availability: All authors confirm that the raw data for the study are made available by the corresponding author when requested.