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Evaluation of patients of vaccine side effects after the COVID-19 vaccine

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SUMMARY

OBJECTIVE: Postvaccine side effects were evaluated in patients presenting to our emergency department with complaints of vaccine side effects after taking COVID-19 vaccine, and new unknown side effects ranging from mild complaints to life-threatening risks, and frequency of all side effects were investigated. This study aimed to establish a scientific resource to identify the potential side effects of the vaccine.

METHODS: Patients' demographic information, clinical characteristics, epicrisis reports, COVID-19 disease and vaccination histories, vital values, and blood values were examined. The SPSS 20.0 package program was used for statistical evaluation. $p<0.05$ was considered statistically significant.

RESULTS: Notably, 13.1% of patients presenting to the emergency department started to have complaints after taking Sinovac vaccine, whereas 86.9% of them had complaints after taking BioNTech vaccine. Also, 36.9% of patients stated that they had COVID-19. All patients had a Glasgow coma scale score of 15 during admission. No patient was hospitalized, ventilator was not needed, and all patients were discharged. While the most common presenting complaint to the emergency department after vaccination was fatigue in 29.7%, the most common diagnoses after examination in the emergency department were myalgia in 32.1% and upper respiratory tract infection in 28.6%.

CONCLUSION: Results and conclusions of our study will guide healthcare workers and patients on the side effects of COVID-19 vaccine.

KEYWORDS: COVID-19. Coronavirus. Vaccines.

INTRODUCTION

The WHO declared COVID-19 as a pandemic on March 11, 2020[1]. Since COVID-19 affects people of all ages and has a mortal course with severe clinical pictures even in healthy people, scientists and states aimed to find protective methods to prevent the transmission of the disease. The spread of the disease is prevented in two practices. The first practice consists of general control measures such as mask, interpersonal social distancing of 1.5 m, hand washing, and staying away from non-ventilated areas[1,2]. The second practice consists of developing vaccine suitable for the disease, and thus preventing the transmission of the disease by vaccinating the general population.

The World Health Organization has authorized the use of vaccines for which pharmaceutical companies applied for approval to use and the necessary studies were completed. The effectiveness of vaccines in reducing the mortality and preventing severe diseases in vaccinated people was found to be 99%[3-5]. Nowadays, the vaccines used to combat COVID-19 have been designed to teach the body's immune system to recognize the virus that causes COVID-19 and to destroy the coronavirus in case of facing COVID-19[3,5,6].

In Turkey, two vaccines are mainly used: BioNTech vaccine, which is an mRNA vaccine with a reported efficacy of 95% and efficacy against new variants, and Sinovac vaccine, which is an inactivated vaccine with an efficacy of 50–70% and may require the administration of the third dose due to a decrease in antibody levels 6 months after vaccination administered as two doses[5,7]. Moderna vaccine: Moderna vaccine was produced similar to the BioNTech vaccine; however, its structure surrounding the mRNA is different[8]. Johnson & Johnson vaccine: Adenovirus type 26 is used as a vector in this vaccine[9].

In this study, post-vaccine side effects were evaluated in patients presenting to our emergency department with the complaints of vaccine side effects after the COVID-19 vaccine, and new unknown side effects ranging from mild complaints to life-threatening risks, and the frequency of all side effects

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were investigated. Furthermore, with this study, it is aimed to establish a scientific resource to know the potential side effects in case of vaccine side effects in the vaccinated person.

METHODS

After taking the medical history of 84 patients presenting to the Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Emergency, between October 1, 2021, and December 31, 2021, due to vaccine-related side effects, the patients were examined, their findings were identified, and then the patient files were examined through the automation system and additional information about the patients was obtained. The study was conducted retrospectively, and the data of the patients presenting with the complaint of vaccine adverse effects between the specified dates were obtained from the hospital automation system and the patient examination file. Vaccination information was received from the Ministry of Health's "vaccination" program. The Kolmogorov-Smirnov test was used to analyze the normal distribution of the data. The SPSS 20.0 package program was used for statistical evaluation and necessary tests were performed. The categorical variables were expressed using numbers and percentages. Measurement-based continuous variables were analyzed for normal distribution and presented as median (minimum–maximum) and mean ± standard deviation. In the evaluation of difference between the groups, the level of change was evaluated by the Mann-Whitney U test, and the relationship between the variables was evaluated by Spearman correlation analysis. $p<0.05$ was considered statistically significant. Ethical approval was obtained from the Ministry of Health of the Republic of Turkey and the Ethics Committee of Kahramanmaraş Sütçü İmam University Faculty of Medicine with the resolution number 01 in session 2022/14 on April 26, 2022.

RESULTS

The median age of patients presenting to the emergency department with complaints after taking the COVID-19 vaccine was 36.0, ranging between 18 and 79 years, and 51.2% were female. While body temperatures measured during admission to emergency department were found to be between 35.5 and 39.0°C with median 36.7°C, pulse values were between 53 and 161/min with median 90.0/min, respiratory rates were 92.5±1.9/min, oxygen saturation values were between 92 and 100% with median 97.0%, and systolic blood pressure values were between 95 and 240 mmHg with median 130.0 mmHg. Notably, 31 (36.9%) patients stated that they had COVID-19 (Table 1).

It was determined that 13.1% of the patients presenting to the emergency department due to various complaints after

Table 1. Patient's vital signs, hemogram values, and vaccination-complaint-admission times.

Variable	Variable value	
	Mean ± standard deviation	Median (minimum–maximum value)
Age	37.7±15.5	36.0 (18–79)
Body temperature (°C)	36.8±0.7	36.7 (35.5–39.0)
Pulse/min	92.5±18.9	90.0 (53–161)
Respiratory rate/min	18.0±1.9	18.0 (12–23)
Oxygen saturation (%)	97.1±1.7	97.0 (92–100)
Systolic blood pressure (mmHg)	133.0±21.0	130.0 (95–240)
Hemoglobin (g/dL)		
Female	12.6±1.1	12.7 (10.9–15.3)
Male	13.7±1.1	15.1 (11.2–17.1)
Leukocyte (10^3/mm^3)	8.2±2.8	7.8 (3.6–17.0)
Lymphocyte (10^3/mm^3)	2.0±1.9	1.64 (0.4–14.1)
D-dimer (µg/L)	0.44±0.30	0.36 (0.18–1.57)
Time between vaccination and complaint	1.1±1.2	1.0 (0–4)
Time between vaccination and admission to the emergency department	2.0±1.6	1.0 (0–8)
Time between complaint and admission to the emergency department	0.7±1.4	0.0 (0–8)

vaccination started to have complaints after taking the Sinovac vaccine, while 86.9% of them had complaints after taking the BioNTech vaccine. While 5 patients stated that their complaints occurred after the fourth dose of vaccine, 23 patients indicated that their complaints occurred after the third dose of vaccine, and 40 patients and 16 patients indicated that their complaints occurred after the second dose of vaccine and after the first dose of vaccine, respectively (Table 2).

There was a positive correlation between the age of the patients and the time between vaccination and the onset of complaints. The time between vaccination and the onset of complaints increased as the age of the patients increased (r=0.274, p=0.02). While a weak positive correlation was found between the patients' D-dimer values and age (r=0.319, p=0.003), there was a weak negative correlation with hemoglobin values (r=-0.346, p=0.001). The time of vaccination-complaint and complaint-admission increased as the time between vaccination and admission to the emergency department increased, and the time of complaint-admission decreased as the time of vaccination-complaint increased.

Table 2. Vaccination information, symptoms, diagnosis, and treatment information of the patients.

	n	%
Gender		
Female	43	51.2
Male	41	48.8
Additional disease		
Yes	10	11.9
No	74	88.1
Positive for COVID-19 in the past?		
Yes	31	36.9
No	53	63.1
Hemoglobin value		
Normal and high	70	83.3
Low	14	16.7
Last vaccine		
Sinovac	11	13.1
BioNTech	73	86.9
After which dose of vaccine		
1	16	19.0
2	40	47.6
3	23	27.4
4	5	6.0
Admission complaint		
Fatigue	25	29.7
Joint pain	14	16.6
Fever	13	15.5
Headache	12	14.2
Chest pain	8	9.5
Sore throat	8	9.5
Nausea or vomiting	8	9.5
Shivering	6	7.1
Myalgia	6	7.1
Cough	6	7.1
Stomach ache	6	7.1
Chill	4	4.8
Allergic rash and itching	4	4.8
Dizziness or fainting	4	4.8
Back pain	4	4.8
Dyspnea	4	4.8
Diarrhea	3	3.6
Palpitation	3	3.6
Bone pain	3	3.6
Numbness and pain in the extremities	3	3.6
Axillary swelling	3	3.6
Diagnosis in the emergency department		
Upper respiratory tract infection (URTI)	42	50.1
Myalgia	27	32.1
Acute gastroenteritis	6	7.2
Urticaria	5	6
Angina (chest pain)	5	6
Headache	3	3.6
Arrhythmia	2	2.4
Syncope	2	2.4
Deep vein thrombosis (DVT)	1	1.2
Anaphylaxis	1	1.2
Treatment in the emergency department		
No medication	41	48.8
Diclofenac	19	22.6
Paracetamol	18	21.4
Pheniramine Hydrogen Maleate – Methylprednisolone –Dexketoprofen	2	2.4
Metoclopramide	2	2.4
Ondansetron Hcl	1	1.2
Adrenaline + methylprednisolone	1	1.2

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DISCUSSION

The side effects that occur within the first 48 h after vaccine administration are early side effects. Swelling and pain at the vaccine injection site, fatigue, fever, allergic reactions, and headache are the most common early side effects. It has been reported that severe allergic reactions are mostly found in Pfizer-BioNTech and Moderna vaccines[10]. These vaccines are contraindicated in people who are allergic to any vaccine component. Moreover, in the study of Yoo et al., it was reported that four patients had facial paralysis, two patients had transverse myelitis, and one patient had myocardial infarction[11]. Idiopathic neuralgic amyotrophy that may also occur after COVID-19 was found in one patient after taking Pfizer-BioNTech vaccine[12]. Thrombocytopenia and cerebral venous sinus thrombosis were reported in six cases after Johnson & Johnson's Janssen vaccine[11]. In the evaluations, it was reported that there was a risk of vaccine-induced thrombocytopenia and thrombosis in women under 50 years of age[13]. Most of the vaccine side effects are mild and short term[14]. In our study, similar to other studies, the complaints of the patients presenting to the emergency department due to vaccine side effects were mild, the Glasgow Coma Scale score of all patients was found to be 15, none of the patients were hospitalized, and ventilator was not needed for any of the patients.

In the study of Park et al., fever, myalgia, headache, shivering, injection site redness/pain, urticaria, and itching were the most commonly reported symptoms by patients presenting to the emergency department after taking the COVID-19 vaccine. Anaphylaxis was not found in any patient[15]. When the side effects of our patients after taking the COVID-19 vaccine were examined, chills, shivering, allergic rash or itching, fever, joint/bone pain, fatigue, myalgia, headache, cough, dizziness, syncope, back pain, sore throat, nausea or vomiting, diarrhea, palpitations, chest pain, dyspnea, abdominal pain, numbness, and pain in the extremities were found. In the study of Park et al., intravenous hydration was administered to 68.2% of the patients as parenteral therapy; however, antipyretic and antiemetics were required in 11.5% of the patients. While the mean number of days from vaccination to the emergency department visit was 1.83, 79% of patients came to the emergency department within 2 days. No hospitalization was required for the patients; however, outpatient follow-up was required for 10.2% of the patients, and four patients came to the emergency department at least twice[15].

According to Fertel et al., the mean age of the patients was 57.5 years. They also reported that 70.3% of the patients had a blood test, intravenous (IV) drugs were given to 61.6% of the patients, 45.8% of the patients had a chest X-ray, 20.3% of the patients had a thorax computed tomography, 81% of the patients were discharged, and 17.9% of the patients were hospitalized. The first three main complaints during admission were dyspnea, chest pain, and allergic reaction[16].

All patients included in this study received outpatient treatment, and all patients were discharged. Hemogram and D-dimer examinations of the patients were performed, and blood test results are presented in the "Results" section. The time between patients' vaccination and the onset of complaints was found to be 0–4 days. The time between patients' admission to the emergency department after the onset of post-vaccine side effects was 0–8 days, and it was observed that the date of onset of complaints and the date of admission to the emergency department were the same.

Although data from the studies examining COVID-19 vaccine reactions cover a short time frame, they show that COVID-19 vaccine reactions may also occur with high-risk complaints to the emergency department. The clinician will initiate treatment with an accurate diagnosis by evaluating the side effects of the vaccine and considering it as a trigger for potential severe complications. Most common high-risk side effect complaints and diagnoses associated with the vaccine administration in the past were Guillain-Barré syndrome, febrile convulsions, seizures, anaphylaxis, and meningitis/encephalitis[17].

In Turkey, two types of vaccines are mainly used as COVID-19 vaccine: "Sinovac" and "BioNTech." It was determined that 13.1% of the patients presenting to the emergency department due to various post-vaccine complaints occurred after taking the Sinovac vaccine, while 86.9% of the complaints occurred after taking the BioNTech vaccine. It was found that while the complaints occurred after the fourth dose of vaccine in 5.95% of the patients included in our study, the complaints occurred after the third dose of vaccine in 27.3% of them, the complaints occurred after the second dose of vaccine in 47.6% of them, and the complaints occurred after the first dose of vaccine in 19.04% of them.

There was a positive correlation between the age of the patients and the time between vaccination and the onset of complaints. The time between vaccination and the onset of complaints increased as the age of the patients increased. While a positive correlation was found between the patients' D-dimer values and age, there was a negative correlation with hemoglobin values. The time of vaccination-complaint and complaint-admission increased as the time between vaccination and admission to the emergency department increased. The time of complaint-admission decreased as the time of vaccination-complaint increased (Table 3).

Table 3. COVID-19 histories, vaccine, and additional disease information of patients.

	n	Median (minimum–maximum)	Test p
Gender			
Female	36	1.0 (0–4)	z=-0.748
Male	36	1.0 (0–4)	0.454
Positive for COVID-19 in the past?			
Yes	25	0.0 (0–4)	z=-1.578
No	47	1.0 (0–4)	0.114
Hemoglobin value			
Below normal	12	0.0 (0–3)	z=-1.716
Normal and above	60	1.0 (0–4)	0.086
Last vaccine			
Sinovac	9	1.0 (0–3)	z=-0.321
BioNTech	63	1.0 (0–4)	0.748
Additional disease			
Yes	8	1.0 (0–4)	z=-0.028
No	64	1.0 (0–4)	0.978

In this study, we aimed to ensure that the COVID-19 vaccine side effects are not overlooked, to evaluate the complaints in the best way, and to perform the correct diagnosis and treatment. We hope that our study on vaccine side effects will guide healthcare workers and patients on the side effects of COVID-19 vaccine in the future.

DECLARATION OF INTEREST STATEMENT

Our study was carried out in accordance with the Declaration of Helsinki, and we declare that it complies with the ethical standards of the Republic of Turkey. Ethical approval was obtained from the Ministry of Health of the Republic of Turkey and the Ethics Committee of Kahramanmaraş Sütçü İmam University Faculty of Medicine with the resolution number 1 in session 2022/14 on April 26, 2022.

AUTHORS' CONTRIBUTIONS

MSG: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **AİK:** Conceptualization, Formal Analysis, Methodology, Validation, Visualization, Writing – original draft, Writing –review & editing. **HH:** Data curation, Formal Analysis, Investigation, Project administration, Resources, Writing – original draft, Writing – review & editing. **ÖFK:** Conceptualization, Formal Analysis, Methodology, Validation, Visualization, Writing – review & editing. **YS:** Conceptualization, Formal Analysis, Methodology, Validation, Visualization, Writing – review& editing. **NMB:** Data curation, Formal Analysis, Investigation, Project administration, Resources, Writing – original draft, Writing – review & editing. **YEÇ:** Formal Analysis, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

REFERENCES

1. Gedik MS, Hakkoymaz H, Basan NM. Evaluation of patients diagnosed with COVID-19. Van Sağ Bil Derg. 2020;13(Özel Sayı):19-28. Available from: https://dergipark.org.tr/en/pub/vansaglik/issue/56982/741529
2. Coronavirus Disease 2019. 2022. [cited on April 3, 2022]. Available from: https://covid19.saglik.gov.tr/TR-66300/covid-19-nedir-.html
3. Uzun K. 2022. [cited on April 4, 2022]. Available from: http://www.drkursatuzun.com/wp-content/uploads/2021/08/Covid-19-ve-Asilar.pdf
4. Erdinç Y. COVID-19 Aşıları. Türk Aile Hek Derg. 2020;24(4):227-34. Available from: https://jag.journalagent.com/tahd/pdfs/TAHD-88598-REVIEW_ARTICLE-YAVUZ.pdf
5. Derya SS, Emine EC, Meliz S, Yiğit U, Emel Öykü CU. COVID-19 tanı testleri, tedavisindeki aşılarveilaçlar; güncel durum. Uludağ Üniversitesi Tıp Fakültesi Dergisi. 2021;47(2):295-308. https://doi.org/10.32708/uutfd.957260
6. Coronavirus Disease 2019. 2022. [cited on April 4, 2022]. Available from: https://covid19asi.saglik.gov.tr/TR-77709/covid-19-asisi-uretim-teknolojileri.html
7. Coronavirus Disease 2019. 2022. [cited on April 5, 2022]. Available from: https://covid19asi.saglik.gov.tr/TR-77708/covid-19-asisi-cesitleri.html
8. Baden LR, El Sahyl HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. N Engl J Med. 2021;384(5):403-16. https://doi.org/10.1056/NEJMoa2035389
9. Kaya O. COVID-19 vaccines. Med J SDU. 2021;(ozelsayi-1):31-5.
10. Fix OK, Blumberg EA, Chang KM, Chu J, Chung RT, Goacher EK, et al. American Association for the Study of Liver Diseases expert panel consensus statement: vaccines to prevent coronavirus disease 2019 ınfection in patients with liver disease. Hepatology. 2021;74(2):1049-64. https://doi.org/10.1002/hep.31751
11. Yoo JH. What we do know and do not yet know about COVID-19 vaccines as of the beginning of the year 2021. J Korean Med Sci. 2021;36(6):e54. https://doi.org/10.3346/jkms.2021.36.e54
12. Diaz-Segarra N, Edmond A, Gilbert C, Mckay O, Kloepping C, Yonclas P. Painless idiopathic neuralgic amyotrophy after COVID-19 vaccination: a case report. PM R. 2022;14(7):889-91. https://doi.org/10.1002/pmrj.12619
13. Centers for Disease Control and Prevention. CDC recommends use of Johnson & Johnson's Janssen COVID-19 vaccine resume.

Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/JJUpdate. (Erişimtarihi: 05.04.2022)

14. Lin C, Vasquez-Colon C, Geng-Romos G, Challa C. Implications of anesthesia and vaccination. Paediatr Anaesth. 2021;31(5):531-8. https://doi.org/10.1111/pan.14148
15. Park MJ, Choi YJ, Choi S. Emergency department utilization by in-hospital healthcare workers after COVID-19 vaccination. J Korean Med Sci. 2021;36(27):e196. https://doi.org/10.3346/jkms.2021.36.e196
16. Fertel BS, Milk J, Simon EL, Muir MR, Smalley CM. COVID-19 vaccine adverse reactions bring patients to emergency departments. Am J Emerg Med. 2021;54:302-3. https://doi.org/10.1016/j.ajem.2021.05.013
17. Mesfin YM, Cheng A, Lawrie J, Buttery J. Use of routinely collected electronic healthcare data for postlicensure vaccine safety signal detection: a systematic review. BMJ Glob Health. 2019;4(4):e001065. https://doi.org/10.1136/bmjgh-2018-001065