

ORIGINAL ARTICLE

Evaluation of Healthcare Workers First Vaccinated with COVID-19 Vaccine in Northwest Syria Observations of Vaccine Side Effects in Emergency Departments

Kuzeybatı Suriye’de COVID-19 Aşısı ile İlk Aşılanan Sağlık Çalışanlarının Değerlendirilmesi: Acil Servislerde Aşı Yan Etkisi Gözlemleri

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ABSTRACT

Aim: In this study, we investigated the adverse effects of the COVID-19 vaccine administered to health workers in northwestern Syria.

Materials and Methods: The study retrospectively analyzed the data of 260 health care workers who received the first dose of COVID-19 vaccine between May 1, 2021, and June 30, 2021, in the northwestern Syria region by searching the Syrian Immunization Group database (SIG) and patient records from hospital or health center emergency departments.

Results: The mean age of health care personnel was 35.86±8.03 years, and 9.6% were women. Of those who participated in the study, 5.8% had comorbid diseases. 109 (42.1%) were vaccinated in hospital emergency departments and 151 (57.9%) in health center emergency departments. It was found that 63.5% (n=165) of those vaccinated experienced adverse reactions to the Oxford/AstraZeneca vaccine. The most common adverse reactions to the vaccine were fever in 128 individuals (49%), fatigue in 89 individuals (55.6%), headache in 54 individuals (20.8%), weakness in 53 individuals (20.4%), joint pain in 50 individuals (19.2%), injection site pain in 47 individuals (18.1%), and muscle pain in 33 individuals (12.7%). The side effects noted were classified as severe, moderate, and mild. Of these, fever 15.4% (n=40), fatigue 11.9% (n=31), and headache 9.6% (n=25) were the most common severe side effects. It was found that 14 (5.4%) individuals required hospitalization and medical treatment due to adverse reactions to the vaccine. When evaluating the side effects observed in hospitalized patients, the most common side effects were fever, chills, muscle pain, joint pain, fatigue, and weakness.

Conclusion: It was concluded that the Oxford/AstraZeneca vaccine administered to health care workers in northwestern Syria had no fatal side effects and that fewer side effects were generally observed in this study compared with the literature. Research on side effects through independent studies will help address global and regional concerns about vaccines.

Keywords: COVID-19 vaccine, emergency medicine, Oxford/AstraZeneca, side effect, Syria

ÖZ

Amaç: Bu çalışmada Kuzeybatı Suriye’de sağlık çalışanlarına uygulanan COVID-19 aşısının yan etkilerinin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Çalışmada 1 Mayıs 2021-30 Haziran 2021 tarihleri arasında Kuzeybatı Suriye Bölgesi’nde birinci doz COVID-19 aşısı olan 260 sağlık çalışanının verileri Syrian Immunization Group (SIG) veri tabanından ve hastanelerin acil servislerinden veya sağlık merkezlerinin acil birimlerinden hasta dosyalarından taranarak retrospektif olarak değerlendirildi.

Bulgular: Sağlık çalışanlarının yaş ortalaması 35.86±8.03 yılı ve %9.6’sı kadındı. Çalışmaya dahil edilenlerin %5.8’i komorbid hastalığa sahiptir ve 109 (%42.1)’u hastanede acil serviste, 151 (%57.9)’i sağlık merkezlerinin acil birimlerinde aşılarını yaptırdı. Aşı olanların %63.5(n=165)’inde Oxford/AstraZeneca aşısının yan etkisi olduğu görüldü. En sık görülen aşı yan etkilerinden ateş 128(%49) kişide, yorgunluk 89(%55.6) kişide, baş ağrısı 54(%20.8) kişide, halsizlik 53(%20.4) kişide, eklem ağrıları 50(%19.2) kişide, aşı yerinde ağrı 47(%18.1) kişide ve kas ağrıları 33(%12.7) kişide tespit edildi. Tespit edilen yan etkiler şiddetli, orta, hafif olarak kendi içinde derecelendirildi. Bunlardan ateş %15.4(n=40), yorgunluk %11.9(n=31) ve baş ağrısı %9.6(n=25) oranlarında olup sırasıyla en sık görülen şiddetli yan etkilerdi. Aşı yan etkileri nedeniyle 14 (%5.4) kişinin tıbbi tedavi desteği almak durumunda kaldığı ve hastaneye yatırılarak tıbbi tedavi desteği aldığı saptandı. Hastaneye yatanlarda görülen yan etkiler değerlendirildiğinde en sık görülen yan etkilerin ateş(n=8), üşüme titreme(n=4), kas ağrıları(n=5), eklem ağrıları(n=4), yorgunluk(n=4) ve halsizlik(n=4) şikayetleri olduğu görüldü.

Sonuç: Kuzeybatı Suriye’de sağlık çalışanlarına uygulanan Oxford/AstraZeneca aşısının ölümcül yan etkilerin görülmediği, bu çalışmada genel olarak literatüre göre daha az yan etki görüldüğü tespit edildi. Bağımsız çalışmalarla yan etkiler üzerine araştırmaların yapılması, küresel ve bölgesel aşı endişelerinin giderilmesine katkı sağlayacaktır.

Anahtar Kelimeler: COVID-19 vaccine, emergency medicine, Oxford/AstraZeneca, side effect, Syria

Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 were made to develop various treatments for the (SARS-CoV-2), which first appeared in China in late disease, supportive care remained the main treatment 2019, was named Coronavirus Disease 2019 (COVID option (2). Governments and healthcare professionals -19) (1). The virus spread rapidly and caused an aimed to prevent the spread of the disease across unprecedented global pandemic. Although attempts society by implementing social restrictions and hygiene



regulations, such as the use of masks, social distancing, travel restrictions, and quarantines (3). However, the epidemic escalated dramatically and caused worldwide socioeconomic damage.

It appears that the solution to the devastating impact of COVID-19 is vaccination. According to calculations, 60-72% of the population must be vaccinated to stop the transmission of the epidemic virus (4). For this reason, an unprecedented vaccine production effort has been initiated worldwide and COVID-19 vaccines have been rapidly produced (2). Although routine vaccine production programs between two and 10 years, COVID-19 vaccines were produced, and clinical trials were completed within a few months (2,4). According to the Milken Institute, 276 COVID-19 vaccines are currently produced or in production worldwide, even though only two years have passed since the discovery of the disease (5).

Studies have shown that rushed vaccine production leads to concerns about vaccines (2, 6). Web-based studies have shown that vaccine concerns are associated with fears of economic crisis (7). Projecting an image of a disease that causes socioeconomic problems creates a global negative trend. Socioeconomic concerns require rapid vaccine production to address these problems. Rapid vaccine production then leads to vaccine fears and a parallel increase in socioeconomic problems. This creates a positive feedback mechanism.

Vaccine side effects have been revealed in studies supported by vaccine manufacturers, and current vaccines are shown to be safe. However, independent studies are required to provide greater confidence (8). It is believed that independent disclosure, from most to least common side effects, will help to reduce concerns about vaccination (9).

In northwestern Syria, COVID-19 vaccination trials for healthcare workers were initiated as a priority. This study aimed to investigate the adverse effects of the COVID-19 vaccine on medical personnel in northwestern Syria.

Materials and Methods

Study Design:

The study retrospectively evaluated 260 healthcare workers who had received the first dose of a COVID-19 vaccine between May 1, 2021, and June 30, 2021, in northwestern Syria. The Oxford/AstraZeneca vaccine was provided by the World Health Organization (WHO) for vaccination in the region. This was organized by the "Syrian Immunization Group (SIG)" under the coordination of the "Assistant Coordination Unit (ACU)", affiliated with WHO (10). Vaccinations were administered in the emergency departments of hospitals, which are part of the humanitarian response in the region, or the emergency departments of primary health centers due to risks posed by adverse

events. Antihistamines, corticosteroids, and adrenaline were used as standard medical treatments depending on the severity of side effects in antiallergic treatments after vaccination if these were deemed necessary by the clinician. Furthermore, if necessary, an inhaler and intravenous support were used. Demographic and clinical data were matched in the SIG database with information from patient files and records of these facilities. The Ethics Committee of Hatay Mustafa Kemal University for Noninterventional Research (meeting date: 26/08/2021, number of decisions: 17), the relevant hospital administrations, and SIG approved the study. In addition, the study was conducted in line with the "Declaration of the World Medical Association on the Ethical Principles of Helsinki".

Patient selection:

Following the completion of these initial vaccination activities, the vaccinated patients in this study were retrospectively evaluated. During the vaccination period, only Oxford/AstraZeneca vaccine was supplied and administered in the region as a COVID-19 vaccine. No other COVID-19 vaccine had been previously used in the region.

Healthcare workers over 18 years of age who had received the first dose of the Oxford/AstraZeneca vaccine in hospital emergency departments or first-level health center emergency units in northwestern Syria were included in this study. People with a history of psychiatric disorders or who did not work in healthcare facilities were not included in the study.

Obtaining data:

Data concerning age, sex, marital status, height, weight, smoking, vaccination date, address, place of residence, branch, known diseases, allergy history, and whether the patient was infected with COVID-19 were obtained from the SIG database and health center patient records. Following this, it was investigated whether the patients experienced side effects of vaccination. If they had, it was researched what they were, how long they lasted, how severe they were, whether the patient was hospitalized due to side effects of vaccination, and whether they suffered from anxiety following vaccination. Data on vaccine side effects were established basing on the statements of those vaccinated from databases and patient records. Up to 24 hours was considered as one day for side effect duration. An additional 24 period was considered as ongoing side effects. For the severity of side effects, records based on patient statements in the form of vaccine side effects categorized as mild, moderate, and severe were used. Those with missing file records were not included in the study.

Statistics:

Statistical analyses of the study were performed using Statistical Package for Social Sciences version 25.0 software for Windows (IBM SPSS Statistics for Windows,

version 21.0. Armonk, NY: IBM Corp., USA). Descriptive statistics of variables were reported as median (min-max) and frequencies were reported as n (%). Fisher exact tests and chi-square tests were used to compare categorical variables.

Results

The study involved 260 healthcare workers in the northwestern region of Syria who were vaccinated with the Oxford/AstraZeneca COVID-19 vaccine. The average age of participants was 35.86±8.03 years. The average height was 173.35±8.41 cm and the average weight was 81.78±13.99 kg. While 79.7% (n=204) lived in the city, fewer of them lived in villages and camps, and 3.5% (n=9) lived in irregular camps, where the most difficult living conditions exist in the region. Among the healthcare workers, 109 (42.1%) were vaccinated in hospital emergency departments and 151 (57.9%) were vaccinated in the emergency units of health centers. Only 3 (1.2%) of vaccinated patients had experienced allergic reactions to known agents. These agents were cigarette smoke, some meals, and diclofenac sodium in the records. It was found that 25.8% (n=67) of participants had previously contracted COVID-19 and 2.3% (n=6) had been hospitalized for COVID-19. 63.5% (n=165) of participants had adverse reactions to the Oxford/AstraZeneca vaccine. While the expected adverse reactions occurred in 162 (62.3%) individuals following the Oxford/AstraZeneca vaccination, 3 (1.2%) employees had a sore throat after vaccination. Additional incidence rates (%) of participants can be found in Figure 1 and Table 1.

Table 1. Data on sex, marital status, comorbidity, and smoking status of health care workers who received the COVID-19 vaccine.

Gender, marital status, comorbidity, and smoking among health professionals		
Gender, n(%)	Male	235(90.4)
	Female	25(9.6)
Marital status, n(%)	Married	227(87.3)
	Single	33(12.7)
Smoking, n (%)	Yes	122(46.7)
	No	138(53.3)
Comorbidity, n(%)	Yes	15(5.8)
	No	245(94.02)

The following adverse reactions to the vaccine were observed in healthcare workers: fever in 128 (49%) subjects, fatigue in 89 (55.6%) subjects, headache in 54 (20.8%) subjects, weakness in 53 (20.4%) subjects, joint pain in 50 (19.2%) subjects, injection site pain in 47 (18.1%) subjects, and muscle pain in 33 (12.7%) subjects. One or more side effects may occur in the same individual. However, no symptoms such as itching, rash on the body, constipation, redness, and swelling of the extremities other than the injection site,

menstrual irregularities, menometrorrhagia, seizures, or palpitations were experienced by subjects. The side effects noted were classified as severe, moderate, and mild. Of these, fever 15.4% (n=40), fatigue 11.9% (n=31), and headache 9.6% (n=25) were the most common severe side effects. The most common side effects observed in patients and their distribution by severity are shown in Figure 2. The least common side effects and their distribution by severity are shown in Figure 3.

The time between the onset of the side effects to the day they ended was assessed. Cough, cold sweat and pallor, and swelling of the mouth and face were the side effects with the longest duration: 8.5, 5, and 4 days, respectively. The minimum, maximum, and median durations of vaccine side effects are shown in Figure 4. Regarding the time of onset of the vaccine side effects, chest pain (median: 2.5 days) and diarrhoea (median: 2 days) were the side effects with the latest onset. Other side effects occurred on the first day.

14 (5.4%) individuals required hospitalization and medical treatment due to adverse reactions to the vaccine. When evaluating the side effects observed in hospitalized patients, the most common side effects were fever (n=8), chills (n=4), muscle pain (n=5), joint pain (n=4), fatigue (n=4), and weakness (n=4). Side effects in hospitalized patients are listed in Table 2.

Table 2. Distribution of symptoms of hospitalized healthcare personnel.

Types of Side Effects	Inpatients with side effects (n=14)
Swelling of the mouth and face	1
Injection site pain	2
Fever	8
Chills/shiver	4
Malaise	4
Fatigue	4
Joint pain	4
Muscle pain	5
Nausea	1
Vomiting	3
Diarrhea	1
Cough	1
Headache	2
Chest pain	2
Cold sweating	1

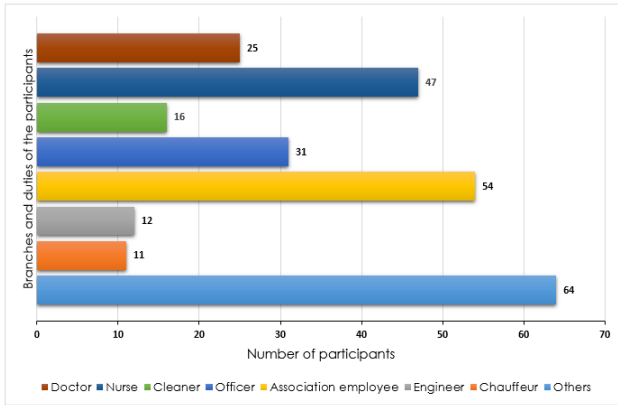


Figure 1. Branches and duties of the participants (n=260)

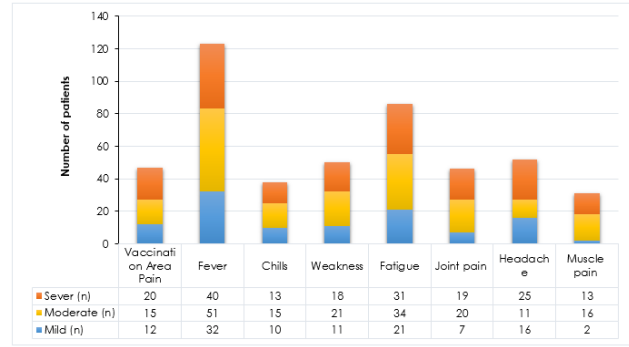


Figure 2. The most common side effects and their distribution by severity

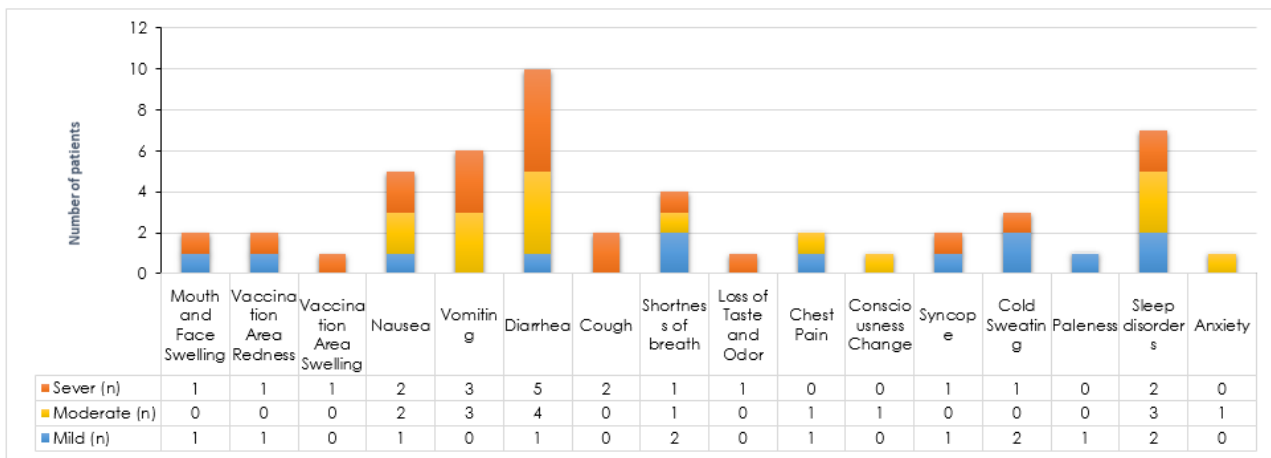


Figure 3. The least common side effects and their distribution by severity

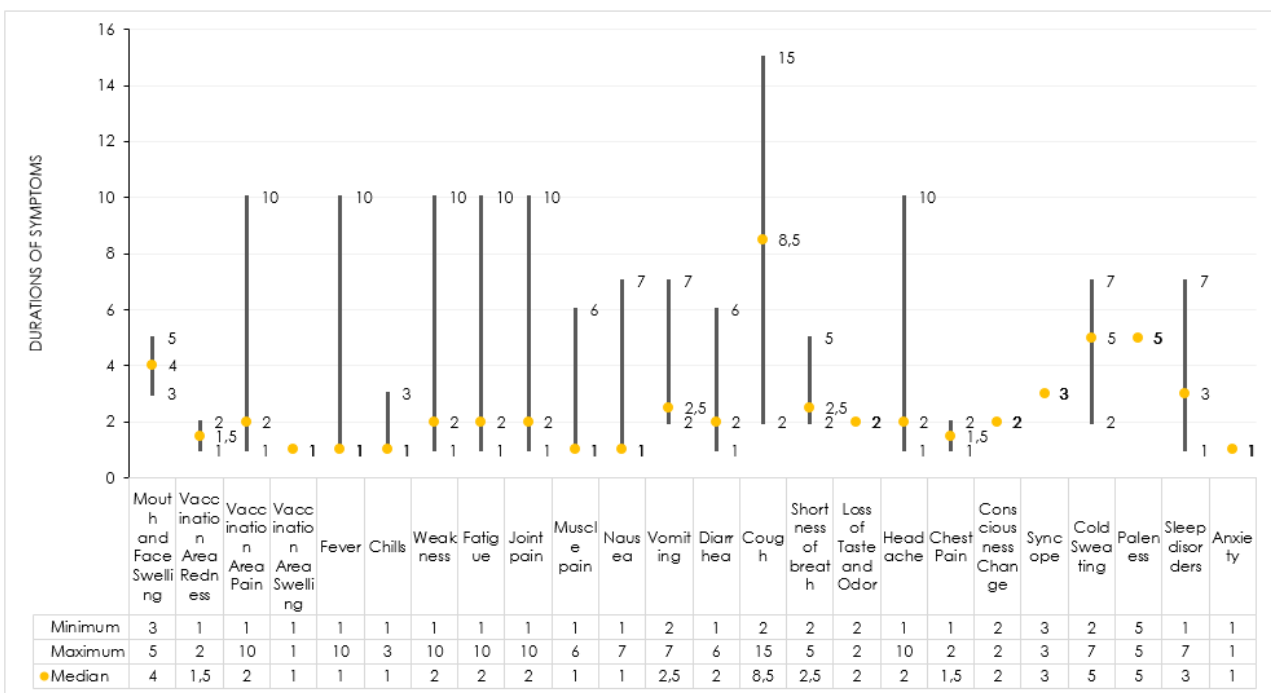


Figure 4. Time distribution of vaccine side effects

Discussion

The first step of vaccination activities in northwestern Syria was to conduct the first vaccination campaign in the region and administer the first dose of the Oxford/AstraZeneca vaccine to health workers with support from the WHO. All healthcare workers in Northwest Syria are targeted to be vaccinated against COVID-19 by providing vaccination teams to all healthcare institutions. Indeed, 25 physicians and 47 nurses and a total of 260 healthcare workers were vaccinated over two months. Studies by Seyhan et al. state that there are more than 4.000 health workers in the northwestern Syria region (11). The number of vaccinated healthcare workers is low despite the high risk. According to the CDC, general concern about vaccines has increased alongside rapid global vaccine production (12). Like other vaccines, the Oxford/AstraZeneca vaccine was developed rapidly but has been proven to be safe in phase studies (13,14,15). Despite this, there have been delays in the administration of the second dose because of the worldwide impact of the negative news about the Oxford/AstraZeneca vaccine (16,17). The total number vaccinated is likely low because participants are the first group to be vaccinated in the region due to worldwide concern about the vaccine and press reports (18).

A study conducted in Poland found that only 3.5% of those who received the Oxford/AstraZeneca vaccine, and 2.5% of those who received the Pfizer-BioNTech vaccine, experienced no side effects (19). A study evaluating adverse reactions in healthcare workers who received the Oxford/AstraZeneca vaccine in Sri Lanka found that at least one adverse reaction was observed in 87.4% of participants (20). This rate is over 90% in studies in Korea (21), over 80% in Iraq and Jordan (22), and over 70% in Ethiopia (23). In this study, 63.5% of participants experienced adverse reactions, which is less than that reported in the literature. Vaccine side effects are common and are evidence that the immune system responds to the vaccine (19). However, severe side effects can be dangerous and provoke anxiety. Concerns about the complications and side effects of COVID-19 vaccines can overshadow the benefits of vaccines, influencing decisions about whether to be vaccinated or not (19). Different cultures and languages express symptoms differently, which may partially explain these differences in the literature. However, differences in study designs and different outcomes may lead to confusion in the population. Clearer information about vaccines through different studies conducted in different countries may increase the effect on vaccine acceptance (24). Countries should conduct risk assessments for their populations and take appropriate action (25). In this study, using data from the pioneering vaccination campaign for healthcare workers in northwestern Syria, it is hypothesized that the low incidence of vaccine adverse events may help to reduce vaccine fear in the region and support evidence-based vaccination policies.

In this study, fever, fatigue, headache, weakness, and joint pain were the most common systemic side effects. Fever, fatigue, and headache were the most common serious side effects. A review of the literature, including the studies by Bae et al. (26), shows that fever, headache, and joint pain were the most common side effects. Fever, headache, and myalgias were reported as the most common symptoms in a study conducted in Nepal (27). Similarly, when data from different parts of the world such as Saudi Arabia, India, Germany, the United States, and England were examined, fever, fatigue, weakness, headache, and joint pain were the most common side effects in those who received the Oxford/AstraZeneca vaccine (26,28-30).

Vaccines may require medical support in patients depending on their side effects (31,32). A review of the literature shows that 0.13% of healthcare workers in Sri Lanka who received the Oxford/AstraZeneca vaccine required hospitalization, while 22.4% required 24-48 hours of rest, and nearly 70% continued to work (20). In a study by Park et al., 9.4% of patients received intravenous treatment due to the first dose of Oxford/AstraZeneca, and 5.3% of patients with Pfizer-BioNTech (25). In a study by Al Bahrani et al., 7% of all participants who were vaccinated with Pfizer-BioNTech and Oxford/AstraZeneca required medical consultation due to adverse effects and 1% were hospitalized (28). This study showed that 5.4% of participants received hospital treatment because of vaccine side effects (fever, chills, muscle and joint pain, fatigue, and weakness). Although the rates of seeking medical support due to vaccine side effects vary, this study supports the finding that the Oxford/AstraZeneca vaccine is safe in terms of side effects, as no patients died or required intensive care.

Although vaccines have many different side effects, fever is a common example of these. In a single-center study by Kim et al., the Pfizer-BioNTech vaccine led to fewer side effects than the Oxford/AstraZeneca vaccine. Furthermore, patients vaccinated with the Oxford/AstraZeneca had to take 9.5 times more medication because of side effects (33). In a study conducted in Korea, fever side effects were observed after each vaccination and were resolved no later than 6 days. However, fever above 39 degrees Celsius was observed in only 12.8% of the subjects enrolled in the study (33). In this study, fever side effects were observed in approximately half of the healthcare workers and high fever was observed in 15% of all participants. While this rate was consistent with the study in Korea, in this study fever side effects were resolved within 2 days.

In a study examining those admitted to the emergency room after vaccination against COVID-19, 85% of patients received treatment within a day of vaccination and 17.9% were hospitalized. Shortness of breath, chest pain, and allergic reactions were the three most common complaints in these emergency admissions (32). Regarding the side effects of the

vaccine, according to the WHO Global Advisory Committee, symptoms can last between 4 and 12 days if those who have severe symptoms after vaccination receive medical treatment (23). Similarly, in the emergency department, almost all adverse reactions occurred on the first day and most of them lasted for a day. However, few of them required medical assistance. In addition, it was found that the median levels of discomfort from coughing and cold sweats lasted an average of 5 days or longer. In a study in Iraq and Jordan, an assessment of the overall duration of side effects found that the median duration of Oxford/AstraZeneca side effects was more than 1.6 days in men and 2.1 days in women (34). The reason for the shorter duration of adverse events in this study may be due to the low female-to-male ratio among study participants and the lower number of severe adverse events.

Regarding serious adverse events that can be life-threatening, complaints of palpitations and dyspnea in the literature are lower in patients with the Oxford/AstraZeneca vaccine than in those with the Pfizer-BioNTech vaccine and are higher than in those with Sinofarm (34). In this study, no side effects such as palpitations were noted in the Oxford/AstraZeneca patients, and only 5 patients suffered from shortness of breath. Reflecting the results of this study, no neurologic side effects were noted in the study by Kim et al. and the rate of thromboembolic events was not higher in patients receiving the Oxford/AstraZeneca or Pfizer-BioNTech vaccines (33). Optimistically, neither thromboembolic status nor serious neurologic symptoms were noted in patients who sought emergency services in northwestern Syria. The rarity of life-threatening serious adverse events in this study supports the safety of the Oxford/AstraZeneca vaccine in terms of adverse events, reflecting previous findings in the literature.

When examining local side effects, the literature found that patients with the Oxford/AstraZeneca vaccine had fewer side effects than patients with the Pfizer-BioNTech vaccine (19). In the study examining Pfizer-BioNTech, Oxford/AstraZeneca, and Sinofarm vaccines involving Iraqis and Jordanians, most local side effects occurred at the first dose in those receiving the Pfizer-BioNTech vaccine. This was followed by the Oxford/AstraZeneca vaccine. The fewest local side effects were reported by those who had the Sinofarm vaccine. When the second dose was studied, all adverse events, including local adverse events, were the lowest in those who received the Oxford/AstraZeneca vaccine (34). In studies conducted in Korea, vaccine local adverse events were noted in 68% of patients who received the Pfizer-BioNTech and Oxford/AstraZeneca vaccines. This rate was the same for both vaccines (26). In Saudi Arabia, these two vaccines were found to cause the same local adverse reactions at the same, but at a higher rate (28). In general, the literature shows that Oxford/AstraZeneca has fewer or similar effects to Pfizer-BioNTech regarding

local side effects. In contrast to the literature, among medical personnel in northwestern Syria, local side effects were noted in nearly 20% of individuals who received the Oxford/AstraZeneca vaccine. In northwestern Syria, people have just emerged from conflict and are living in difficult conditions. This could be partially explained by the difficult socio-economic conditions, high expected side effects of the vaccine, and perceived systemic side effects that make local side effects seem insignificant. These factors may have resulted in lower reported rates of local vaccine side effects in this study than in the literature.

When the allergy history of the participants was examined, very few of them had a history of allergy. Itching, redness on the body, and swelling in the mouth and face were not observed as side effects of the vaccine in the group that participated in the study. In similar studies, these side effects were generally less frequent (34). The absence of a history of allergy may have led to these positive data.

Studies on vaccine side effects that are not life-threatening and uncommon were examined. Insomnia was observed in 8 subjects in a study involving more than 5 thousand health professionals in India and dominated by the Oxford/AstraZeneca vaccine (35). In this study, sleep problems were observed in only 8 subjects. There are limited publications or data in the literature on insomnia after vaccination and further studies are needed to clarify its prevalence.

Conclusion

Mass vaccination is a necessary solution to the COVID-19 pandemic, which is causing global socioeconomic problems and anxiety. People who are forced to live in areas of civil unrest and war do not have access to routine vaccination services. For this reason, emergency services at health centers in the region were tasked with administering vaccines, following up, and managing side effects. Emergency services played a leading role in vaccination, the follow-up of side effects, and the treatment of patients. This study examined the side effects of the Oxford/AstraZeneca vaccine administered to healthcare workers in the emergency departments of healthcare facilities in northwestern Syria. It was found that there were no fatal side effects and generally fewer side effects were observed compared to existing literature. It is believed that this and similar independent studies will help to address global and regional concerns about the vaccine by revealing more data on side effects.

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