COVID-19 Vaccine Issue

Status of adverse reactions after COVID-19 vaccination in the Republic of Korea, February 26, 2021-March 25, 2021

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Abstract

Coronavirus disease (COVID-19) spread throughout the world after first being reported in Wuhan, China in December 2019. As of now (April 6, 2021), there have been around 130,000,000 confirmed cases and 2,850,000 deaths. Countries have employed various strategies to limit the spread of COVID-19, such as patient detection (diagnostic testing), patient and contact management, mask wearing, and social distancing, but due to continued new cases and spread, vaccines have become an important strategy for controlling COVID-19. Various countries invested efforts in developing and procuring COVID-19 vaccines, and on December 8, 2020, COVID-19 vaccination began for the first time in the world in the United Kingdom. However, unintended adverse effects can occur after vaccination, so each country has been evaluating the safety of the vaccines through strengthened monitoring. Monitoring of adverse events following COVID-19 immunization in South Korea is based on the standard monitoring system through which doctors report adverse events according to the Infection Disease Control and Prevention Act, as well as monitoring of individuals who agreed to receive texts to monitor adverse events during their immunization screening.

COVID-19 vaccination began on February 26, 2021 in South Korea, and 773,262 individuals have been vaccinated in the first month (as of March 25, 2021). In total, 10,103 adverse events were reported. More reports of adverse events were made by women than by men, and more adverse events were reported by younger individuals. Almost all (98.8%; 9,982 cases) of the reported adverse events were general symptoms which may occur after vaccination (e.g., muscle aches or headaches). Muscle aches were the most common reported symptoms (60.7%), followed in order by fever (57.6%), headaches (39.2%), and nausea (20.7%).

Only 2.8% (21,433) of the 773,262 individuals who received COVID-19 vaccination agreed to receive texts and responded to them. Of those individuals, 32.9% reported discomfort after vaccination, and younger respondents reported discomfort at a higher proportion. The main symptoms were pain in the injection site (26.9%), muscle aches (23.8%), fatigue (22.5%), headache (19.9%), chills (17.9%), and fever (16.4%).

In South Korea, safe vaccination is promoted through immunization screening, monitoring of adverse events through various methods, rapid response and epidemiological investigations following adverse events, and national vaccine injury compensation program. To return to our daily lives, we should all actively participate in COVID-19 vaccination and monitoring of adverse events after COVID-19 vaccination.

Keywords: COVID-19 vaccination, Adverse events following immunization (AEFI)

Introduction

Coronavirus disease (COVID-19) has spread around the world and continues to be a serious pandemic. Countries are using diverse strategies such as patient detection (diagnostic testing), isolation of patients and their contacts, and social distancing to stop the spread of COVID-19. Among these strategies, limiting the spread of the virus through establishing herd immunity using vaccination is very important.

Several new vaccines to prevent COVID-19 have been developed. Nucleic acid vaccines (mRNA vaccines) that use a new vaccine platform, as well as viral vector vaccines and synthetic antigen vaccines have been developed and adopted by various countries. In South Korea, the Korea AstraZeneca COVID-19 vaccine received approval from Ministry of Food and Drug Safety on February 10, 2021, and vaccination began on February 26. The Comirnaty (Korea Pfizer) vaccine received approval for special import from Ministry of Food and Drug Safety on February 3, 2021, and vaccination began on February 27.

Vaccination is an effective method to prevent infections, but due to the characteristics of biological agents, adverse events can occur following vaccination. The most frequent adverse events identified in clinical trials of COVID-19 vaccines were local reactions such as pain and redness at the site of injection and systemic reactions such as fever, muscle aches, and headaches. Very rarely, anaphylaxis was also reported.

This report analyzed the data reported by doctors for suspected cases of adverse events after COVID-19 vaccination (Korea AstraZeneca COVID-19 vaccine and Comirnaty vaccine [Korea Pfizer]) through the COVID-19 vaccination management system. Moreover, in order to collect safety data for each type of COVID-19 vaccine and to more thoroughly understand potential safety issues regarding adverse events, a survey of possible adverse events from the day of vaccination to 6 weeks after the vaccination (day of vaccination, 3 days post-vaccination, 7 days post-vaccination, and every week until the sixth week post-vaccination) is being conducted with individuals who agreed to receive text messages to monitor adverse events after their COVID-19 vaccination. The data collected so far were analyzed.

Results

1. Reports of adverse events after COVID-19 vaccination

The total number of vaccinations was 773,262 in the first month of COVID-19 vaccination (2/26-3/25). In the same time period, the number of reports of adverse events after COVID-19 vaccination was 10,103. In total, 1.31% of individuals who were vaccinated reported adverse events, of which 9,834 cases were reported after administration of the Korea AstraZeneca COVID-19 vaccine. Twenty-six of these cases were severe or fatal. The proportion of reports of adverse events after vaccination was 13.8 reports per 1,000 vaccinations. The proportion of severe or fatal cases was 0.03 reports per 1,000 vaccinations. After administration of the Comirnaty vaccine, 269 adverse events were reported, corresponding to a proportion of 4.2 reports per 1,000 vaccinations. A daily average of 360 adverse events was reported (Figure 1).

Half of the adverse events (50%; 4,974 cases) were reported on the day of vaccination, 42% (4,275 cases) were reported on the day after vaccination, and cases were reported as long as 21 days after vaccination. The average duration from the day of vaccination to the onset of the adverse events was 1.2 days. In 18% of cases (1,864 cases with adverse events visited a

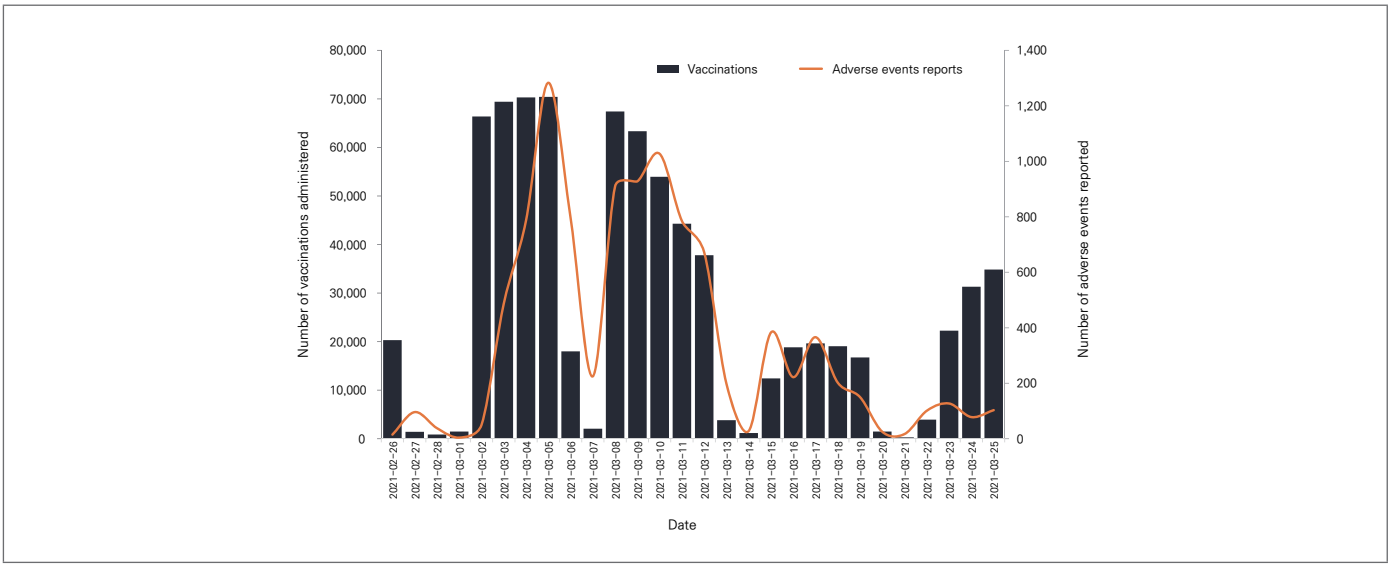

Figure 1. Reported adverse reactions relative to the total number of COVID-19 vaccinations (February 26, 2021–March 25, 2021)

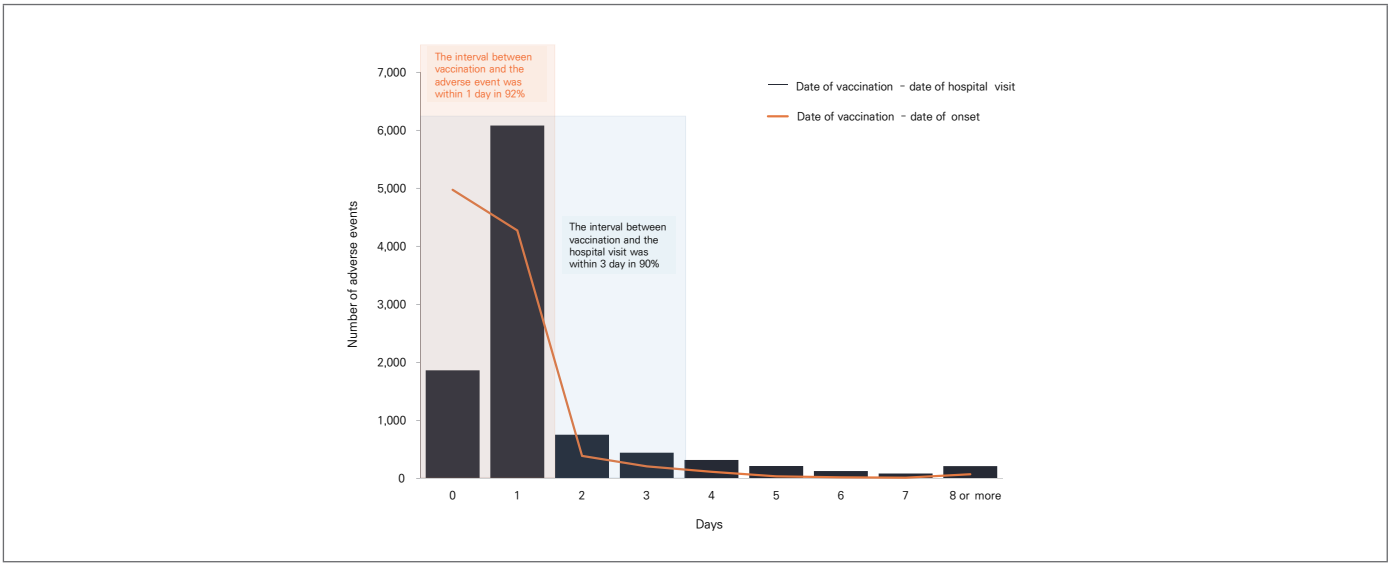

Figure 2. Date of onset of potential adverse reactions after COVID-19 vaccination and date of examination

hospital on the day of vaccination, and 60% (6,082) visited on the day after vaccination. The average duration from the day of vaccination to the hospital visits was 1.67 days. Most cases were examined after adverse events occurred on the day of vaccination or the day after vaccination (Figure 2).

The proportion of reports of adverse reactions relative to the total number of vaccinations was 1.54% among women and 0.76% among men. The number of vaccinations among women was 2.3 times that of vaccinations among men, but the number of adverse reports among women was 4.7 times that among men. By age group, the proportion of reported adverse events was 3.18% in the 20-29 years age group followed by the 30-39 years age group with 1.62%, and the 40-49 years group with 1.10%. In the 50s, 60-64 age group, 65-year-olds and older age groups, they were 0.69%, 0.44%, and 0.02% respectively demonstrating higher proportion of reports of adverse reactions among the younger

Table 1. Reports of potential adverse reactions following COVID-19 vaccination by sex and age

Characteristics		Vaccinations (number)	Adverse events (number)	Proportion of reports (%)
Total		**773,262**	**10,103**	**1.31**
Sex	Male	230,988	1,762	0.76
	Female	542,274	8,341	1.54
Age group	18–29	142,948	4,550	3.18
	30–39	137,323	2,222	1.62
	40–49	145,582	1,601	1.10
	50–59	191,464	1,328	0.69
	60~64	88,171	386	0.44
	65 and above	67,774	16	0.02

Table 2. Reports of potential adverse reactions following COVID-19 vaccination by institution

Characteristics		Vaccinations (number)			Adverse events (number)			Proportion of reports (%)
		Total	Patients or admitted individuals	Employees	Total	Patients or admitted individuals	Employees	
Total		773,262	126,449	646,813	10,103	386	9,717	1.31
Long-term care hospital (less than 65 years old)		238,604	99,550	139,054	2,165	321	1,844	0.91
Long-term care facilities (less than 65 years old)		105,728	15,646	90,082	927	36	891	0.87
COVID-19 first responders		58,583	–	58,583	296	–	296	0.51
Hospitals		305,930	10,885	295,045	6,446	29	6,417	2.11
COVID-19 treatment facilities	First	60,216	–	60,216	269	–	269	0.45
	Second	3,833	–	3,833	0	–	0	–
Others		368	368	–	0	–	0	

population (Table 1).

Vaccination of employees and patients in long-term care hospitals and facilities and COVID-19 first responders started on February 26. Employees of COVID-19 treatment hospitals started to receive vaccinations on February 27, and employees and patients in hospitals started to be vaccinated on March 3. The proportion of reports of adverse events relative to the number of vaccinations was 2.11% in hospitals, 0.91% in long-term care hospitals, 0.87% in long-term care facilities, 0.51% among COVID-19 first responders, and 0.45% in COVID-19 treatment hospitals. Furthermore, 96.2% of the adverse events were reported by employees (Table 2).

Among the reported adverse events (10,103 cases), 98.8% (9,982 cases) were muscle aches, headaches, and others. Eighty percent of general symptom and suspected cases of anaphylaxis were reported by women. Respondents could select more than one adverse reaction to report; 60.7% reported muscle aches, 57.6% reported fever, 39.2% reported headaches, and 20.7% reported nausea (Figure 3).

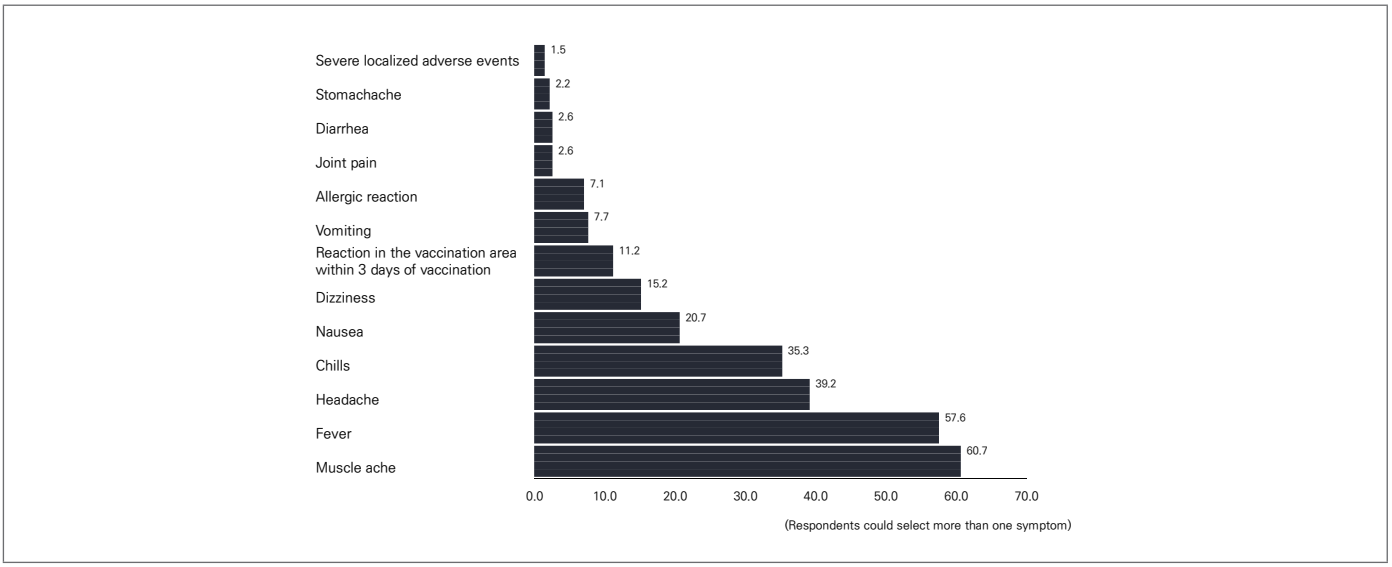

Figure 3. Reports of potential adverse reactions following COVID-19 vaccination by symptom

COVID-19 vaccination first started among admitted individuals and employees in long-term care hospitals and facilities who are vulnerable to COVID-19. Fifteen fatalities from adverse reactions occurred in patients in long-term care hospitals, and one was an employee at a long-term care hospital. The average age of the deceased was 55 years, and the deceased all had underlying conditions, including hypertension (43.8%), neurological diseases (37.5%), cerebral hemorrhage (37.5%), diabetes (31.3%), paralysis (25.0%), and liver disease (12.5%). Autopsies were conducted for eight out of 16 deaths, and the causes of death listed were cardiovascular disease (25.0%), acute respiratory failure (12.5%), and pneumonia, pulmonary thromboembolism, septic shock, and multiple organ failure (6.25% each). The cause of death in the remaining cases (37.5%) was listed as unknown.

Severe cases of adverse events were defined as patients who developed neurological diseases after vaccination or who were hospitalized in intensive care units. In 61.5% of severe cases, the symptoms started within 24 hours of vaccination. Seven cases in employees and six among patients in long-term care hospitals were reported. Most of the patients in long-term care hospitals had underlying conditions such as epilepsy, cerebral hemorrhage, and malignant neoplasms. Five cases of suspected anaphylactic shock were reported. All cases occurred in women, and the reaction occurred within 8.2 minutes on average. All reactions occurred within 10 minutes.

2. Survey of adverse events after COVID-19 vaccination

According to an analysis of the data collected as of March 25 in the survey of adverse events conducted among individuals who received COVID-19 vaccines and who agreed to receive texts to monitor adverse events, 2.8% (21,433) of all vaccinated individuals (773,262) responded. There were more women among all vaccinated individuals (male-to-female ratio=1:2.3), and more women participated in the survey as well (male-to-female ratio=1:3.4). The proportion of participation by age group was 4.4% among those in their 20s, 3.8% among those in their 30s, 3.3% among those in their 40s, 2.2% among those in their 50s, and 0.6% among those 60 and above. There were slight

Table 3. Responses to the survey of potential adverse reactions following COVID-19 vaccination by sex and age

Characteristics		Number of vaccine administered	Number of participants (number, [%])	Proportion of participation (%)
Sex	Male	230,988	4,865 (22.7)	2.1
	Female	542,274	16,568 (77.3)	3.1
Age group	18–29	142,948	6,326 (29.5)	4.4
	30–39	137,323	5,211 (24.3)	3.8
	40–49	145,582	4,795 (22.4)	3.3
	50–59	191,464	4,195 (19.6)	2.2
	60 and above	155,945	906 (4.2)	0.6

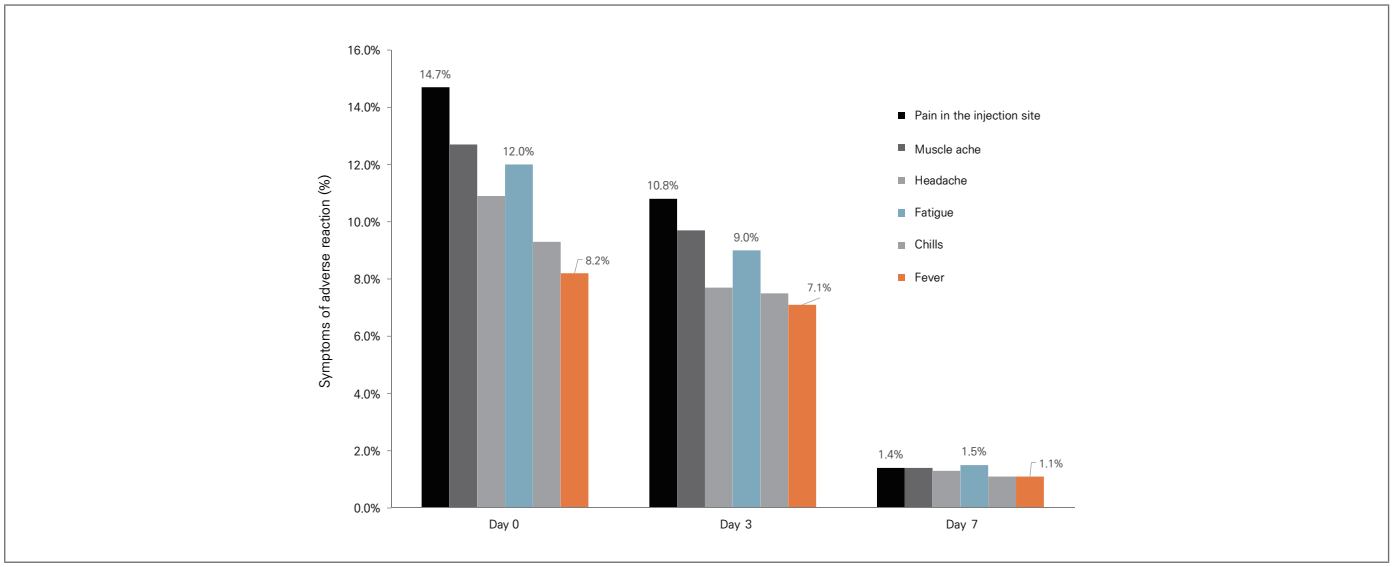

Figure 4. Reported symptoms of adverse reactions after COVID-19 vaccination

differences in the proportion of participation by age (Table 3).

Among those who responded (21,433), 32.9% (7,058) reported discomfort after vaccination. By age group, 10.3% (2,221) of respondents in their 20s, 8.6% (1,836) of respondents in their 30s, 7.1% (1,514) of respondents in their 40s, 5.9% (1,261) of respondents in their 50s, and 226 (1.1%) of respondents in their 60s reported discomfort. Higher proportions of younger respondents reported discomfort.

The common symptoms were pain (26.9%), muscle ache (23.8%), fatigue (22.5%), headache (19.9%), chills (17.9%), fever (16.4%), joint pain (11.2%), nausea (10.1%), and swelling in the injection site (8.0%). Most symptoms were reported on the day of vaccination, and some symptoms continued for 7 days after vaccination (Figure 4). Unlike reports from hospitals, these data are based on the subjective reports of vaccinated individuals, which are different from reports by doctor's reports.

Of the respondents, 14.7% reported pain in the injection site on the day of vaccination, 10.8% on the third day after vaccination, and 1.4% on the seventh day after vaccination. Furthermore, 2.1% of the respondents visited a hospital: 1.3% of the respondents visited as outpatients, 0.7% visited the emergency room, and 0.1% were hospitalized (Figure 4).

Conclusion

It has been 1 month since the administration of the first doses of COVID-19 vaccines started in Republic of Korea. Since vaccination started in certain groups, it is too early to present a comprehensive evaluation of adverse events after vaccination. However, similar to the results of clinical trials and reports from other countries, more than 98% of adverse reactions comprised anticipated localized or systemic adverse events after vaccination.

A limitation is that reports of adverse events by doctors can be an underestimation since those reports are based on individuals who visit hospitals for their symptoms. The results from the survey of adverse events through text messages reflect subjective reports of symptoms by individuals who were not diagnosed by doctors, which can lead to an overestimation of adverse events. The number of reports might increase as a result of the increased public interest in adverse events following newly developed vaccines.

In order to effectively control COVID-19 during the global pandemic, it is very important to establish herd immunity through COVID-19 vaccination. Vaccinations have already started around the world, and more than 100,000,000 individuals have been vaccinated. In most countries, active monitoring of potential adverse events is ongoing. In South Korea, various monitoring and surveys are being conducted to see whether unanticipated health problems are occurring due to COVID-19 vaccination. It is very important that vaccinated individuals actively participate in these efforts.

Acknowledgments

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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