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Brief Report

Adverse events of the Pfizer-BioNTech COVID-19 vaccine in Korean children and adolescents aged 5 to 17 years

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ABSTRACT

Objectives: This study aimed to identify potential safety signals and adverse events following the primary Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccination series among children and adolescents aged 5 to 17 years in the Republic of Korea.
Methods: Adverse events reported through the COVID-19 vaccination management system (CVMS, a web-based passive vaccine safety surveillance system) and adverse events and health conditions collected from a text message-based survey were analyzed.
Results: A total of 14,786 adverse events among 5 to 17-year-old children and adolescents were reported in the CVMS; 14,334 (96.9%) were non-serious and 452 (3.1%) were serious, including 125 suspected cases of acute cardiovascular injury and 101 suspected cases of anaphylaxis. The overall reporting rate was lower in 5 to 11-year-old children (64.5 per 100,000 doses) than in 12 to 17-year-old adolescents (300.5 per 100,000 doses). The text message survey identified that local and systemic adverse events after either dose were reported less frequently in 5 to 11-year-old children than in 12 to 17-year-old adolescents ($p < 0.001$). The most commonly reported adverse events were pain at the injection site, myalgia, headache, and fatigue/tiredness.
Conclusion: The overall results are consistent with the results of controlled trials; serious adverse events were extremely rare among 5 to 17-year-old children and adolescents following Pfizer-BioNTech COVID-19 vaccination. Adverse events were less frequent in children aged 5 to 11 years than in adolescents aged 12 to 17 years.

Keywords: Adolescent; Child; COVID-19; Safety; Vaccination; Vaccines

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Introduction

In the Republic of Korea (ROK), only the Pfizer-BioNTech (BNT-162b2) messenger RNA (mRNA) coronavirus disease 2019 (COVID-19) vaccine has been authorized for use in persons

aged ≥5 years based on safety and efficacy data from controlled trials organized in the United States (US) by the Korea Ministry of Food and Drug Safety [1–3]. The Pfizer-BioNTech COVID-19 vaccine (30 μg, 0.3 mL each) was initially authorized for use in persons aged ≥16 years on March 5, 2021 [4], and expanded to include adolescents aged ≥12 years on July 16, 2021 [5]. The use of the Pfizer-BioNTech COVID-19 vaccine (10 μg, 0.2 mL each) for children aged 5 to 11 years was authorized on February 23, 2022 [6].

Since then, the Pfizer-BioNTech vaccine has been nationally distributed to adolescents aged 16 to 17 years starting on October 18, 2021, and to adolescents aged 12 to 15 years starting on November 1, 2021, following a decision by the Korea Advisory Committee on Immunization Practices (KACIP) in 2021 [7,8]. Following the KACIP in 2022, the Pfizer-BioNTech vaccine was offered to children aged 5 to 11 years starting on March 31, 2022, with the recommendation of an 8-week interval between the 2 doses based on findings that showed increased safety and efficacy with the extended interval [9–12].

To monitor adverse events following immunization (AEFIs) and identify potential safety signals for further evaluation, the Korea Disease Control and Prevention Agency (KDCA) manages the COVID-19 vaccination management system (CVMS, a web-based passive vaccine safety surveillance system), in which doctors and forensic pathologists can report AEFIs regardless of a causal association between events and vaccines as per the Infectious Disease Control and Prevention Act [13]. The KDCA also operates a text message-based vaccine safety surveillance system that surveys adverse events and health conditions following COVID-19 vaccination for particular populations who consent to receive text message surveys through smartphones on the day of their first vaccination [13].

This study aimed to identify potential safety signals and adverse events following the primary series of Pfizer-BioNTech vaccination, including dose 1 and dose 2, for children and adolescents aged 5 to 17 years in the ROK. This study analyzed data on adverse events reported in the CVMS and the text message-based vaccine safety surveillance system.

Materials and Methods

COVID-19 Vaccination Management System

From March 5, 2021 to July 2, 2022, in total, 4,995,280 primary doses of the Pfizer-BioNTech vaccination series were administered to children and adolescents aged 5 to 17 years in the ROK, and 14,786 adverse events after vaccination were reported to the CVMS. Data on an additional dose (dose 3), vaccines other than the Pfizer-BioNTech vaccine for children aged 5 to 11 years (10 μg) and adolescents aged 12 to 17 years (30 μg), and vaccination that occurred abroad and before authorization for use in children and adolescents in the ROK were excluded. Adverse events reported in the CVMS were divided into non-serious and serious events in accordance with the Guidelines for Adverse Events Following COVID-19 Immunization [13]. Non-serious events included common symptoms such as redness, pain, and swelling at the injection site, myalgia, fever, headache, chills, and others. The following adverse events were classified as serious: death, anaphylaxis, adverse events of special interest (AESIs), intensive care unit admission, life-threatening events, permanent disability or sequelae, and others. The characteristics of adverse events reported in the CVMS among 5 to 17-year-old children and adolescents were analyzed by sex, age group, and vaccine dose. The types of symptoms and signs were presented in descending order of the number of cases reported as adverse events. The events do not indicate medically confirmed diagnoses, as adverse events reported to the CVMS are suspected cases.

Text Message-Based Vaccine Safety Surveillance System

Text messages were sent to parents or guardians of children and adolescents aged 5 to 17 years in the ROK who received the primary series of the Pfizer-BioNTech vaccine, on a daily basis until day 7 post-vaccination to investigate adverse events and health conditions. A total of 10,398 adolescents aged 12 to 17 years from December 13, 2021 to January 26, 2022, and 1,025 children aged 5 to 11 years from March 31 to June 20, 2022, were enrolled in the text message-based surveillance system. The surveys asked questions about experiences of local and systemic adverse events, limits to normal daily activities, and visits to medical facilities following vaccination. The respondents were able to report multiple adverse events on each day. The characteristics of respondents were described by sex and age, and adverse events and health conditions reported at least once during days 0 to 7 following vaccination were assessed by vaccine doses and age groups. All variables were examined using the chi-square or Fisher exact test as appropriate to compare adverse events and health conditions between age groups and vaccine doses. A p-value <0.05 indicated statistical significance.

SAS ver. 9.4 (SAS Institute, Cary, NC, USA) was used to conduct all analyses. The passive surveillance activity was conducted and authorized by the KDCA; the study was not subject to institutional review board approval under government regulations. The study of the text message-based surveillance was exempted from review by the Public Institutional

Review Board designated by the Korea Ministry of Health and Welfare (No: P01-202206-01-033).

Results

Adverse Events Reported in the COVID-19 Vaccination Management System

From March 5, 2021 to July 2, 2022, the CVMS confirmed a total of 14,786 adverse events among children and adolescents aged 5 to 17 years after primary doses of the Pfizer-BioNTech vaccination series (Table 1); 14,334 (96.9%) were non-serious and 452 (3.1%) were serious. Serious adverse events included death (5, 0.0%), suspected anaphylaxis (101, 0.7%) and major adverse events including AESIs for COVID-19 vaccines (346, 2.3%). During the study period, 4,995,280 doses were administered to children and adolescents aged 5 to 17 years, and the overall reporting rate per 100,000 doses administered was 296.0 (dose 1, 270.0; dose 2, 323.3). The reporting rate per 100,000 doses after the primary vaccination series by sex was 283.6 in males and 309.2 in females. The reporting rate per 100,000 doses was lower in children aged 5 to 11 years (64.5/100,000 doses) than in adolescents aged 12 to 17 years (300.5/100,000 doses). Among non-serious adverse events, the most commonly reported symptoms based on the reporting rate per 100,000 doses were headache (75.4/100,000 doses), chest pain (68.4/100,000 doses), myalgia (43.1/100,000 doses), dizziness (41.3/100,000 doses), and nausea (36.9/100,000 doses) (Table 2). Among serious adverse events, acute cardiovascular injury including myocarditis/pericarditis (2.5/100,000 doses) had the highest reporting rate per 100,000 doses, followed by anaphylaxis, including anaphylactoid reactions (2.0/100,000 doses), convulsions or seizures (1.0/100,000 doses), acute paralysis (0.8/100,000 doses), and vaccine-associated enhanced disease (0.8/100,000 doses).

Adverse Events Collected in the Text Message-Based Vaccine Safety Surveillance System

From December 13, 2021 to June 20, 2022, the total number of children and adolescents aged 5 to 17 years enrolled in at least 1 text message survey on days 0 to 7 following Pfizer-BioNTech COVID-19 vaccination was 11,414 after dose 1

Table 1. Characteristics of adverse events reported to the CVMS among children and adolescents aged 5 to 17 years after Pfizer-BioNTech COVID-19 vaccination, Republic of Korea, March 5, 2021 to July 2, 2022

Variable	No. of doses administered	Adverse events (n = 14,786)[a]					
		Total	Non-serious adverse events[b]	Serious adverse events[c]			
				Sub-total	Death	Anaphylaxis	Others[d]
Total	4,995,280	14,786 (296.0)	14,334 (287.0)	452 (9.0)	5 (0.1)	101 (2.0)	346 (6.9)
Dose 1	2,555,595	6,899 (270.0)	6,659 (260.6)	240 (9.4)	0	82 (3.2)	158 (6.2)
Dose 2	2,439,685	7,887 (323.3)	7,675 (314.6)	212 (8.7)	5 (0.2)	19 (0.8)	188 (7.7)
Sex							
Male	2,568,739	7,284 (283.6)	7,028 (273.6)	256 (10.0)	3 (0.1)	46 (1.8)	207 (8.1)
Dose 1	1,314,670	3,329 (253.2)	3,199 (243.3)	130 (9.9)	0	36 (2.7)	94 (7.2)
Dose 2	1,254,069	3,955 (315.4)	3,829 (305.3)	126 (10.0)	3 (0.2)	10 (0.8)	113 (9.0)
Female	2,426,541	7,502 (309.2)	7,306 (301.1)	196 (8.1)	2 (0.1)	55 (2.3)	139 (5.7)
Dose 1	1,240,925	3,570 (287.7)	3,460 (278.8)	110 (8.9)	0	46 (3.7)	64 (5.2)
Dose 2	1,185,616	3,932 (331.6)	3,846 (324.4)	86 (7.3)	2 (0.2)	9 (0.8)	75 (6.3)
Age (y)							
5–11	94,518	61 (64.5)	59 (62.4)	2 (2.1)	0	1 (1.1)	1 (1.1)
Dose 1	58,636	47 (80.2)	45 (76.7)	2 (3.4)	0	1 (1.7)	1 (1.7)
Dose 2	35,882	14 (39.0)	14 (39.0)	0	0	0	0
12–17	4,900,762	14,725 (300.5)	14,275 (291.3)	450 (9.2)	5 (0.1)	100 (2.0)	345 (7.0)
Dose 1	2,496,959	6,852 (274.4)	6,614 (264.9)	238 (9.5)	0	81 (3.2)	157 (6.3)
Dose 2	2,403,803	7,873 (327.5)	7,661 (318.7)	212 (8.8)	5 (0.2)	19 (0.8)	188 (7.8)

Data are presented as n (per 100,000): the reporting rate of adverse events per 100,000 doses administered.
CVMS, COVID-19 vaccination management system; COVID-19, coronavirus disease 2019.
[a]Data were based on suspected adverse events following COVID-19 vaccination reported by medical institutions or doctors. The results do not indicate medically confirmed diagnoses or causality between the events and the vaccines. [b]Non-serious adverse events include common symptoms such as redness at the injection site, pain, swelling, myalgia, fever, headache, chills, and others. [c]Serious adverse events include the following: death, suspected anaphylaxis, and others. [d]Others include major adverse events including adverse events of special interest, intensive care unit admission, life-threatening events, permanent disability or sequelae, and others.

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Table 2. Types of symptoms and signs reported to the CVMS among children and adolescents aged 5 to 17 years after Pfizer-BioNTech COVID-19 vaccination, Republic of Korea, March 5, 2021 to July 2, 2022

Symptoms and signs (n = 14,786)[a]	Case (per 100,000)
Non-serious adverse events (n = 14,334)	
Headache	3,765 (75.4)
Chest pain	3,417 (68.4)
Myalgia	2,152 (43.1)
Dizziness	2,065 (41.3)
Nausea	1,843 (36.9)
Fever	1,550 (31.0)
Allergic reactions	918 (18.4)
Vomiting	889 (17.8)
Abdominal pain	872 (17.5)
Chills	848 (17.0)
Pain, redness, or swelling at the injection site within 3 days after	541 (10.8)
Diarrhea	526 (10.5)
Lymphadenitis	447 (8.9)
Abnormal uterine bleeding	140 (2.8)
Cellulitis	71 (1.4)
Arthritis	59 (1.2)
Dyspnea[b]	46 (0.9)
Severe local adverse events	33 (0.7)
Itching[b]	13 (0.3)
Abscess at the injection site	2 (< 0.1)
Systemic disseminated Bacillus Calmette-Guerin infection	1 (< 0.1)
Severe adverse events (n = 452) including reports of death	
Acute cardiovascular injury[c]	125 (2.5)
Anaphylaxis[d]	101 (2.0)
Convulsions or seizures	49 (1.0)
Acute paralysis	42 (0.8)
Vaccine-associated enhanced disease	42 (0.8)
Acute respiratory distress syndrome	18 (0.4)
Encephalopathy or encephalitis	17 (0.3)
Thrombocytopenia	7 (0.1)
Thrombocytopenic purpura	6 (0.1)
Osteitis or osteomyelitis	5 (0.1)
Anosmia or ageusia	5 (0.1)
Erythema multiforme	5 (0.1)
Coagulation disorder	4 (0.1)
Acute kidney injury	4 (0.1)
Single organ cutaneous vasculitis	3 (0.1)
Multisystem inflammatory syndrome	3 (0.1)
Acute liver injury	3 (0.1)
Thrombosis	3 (0.1)
Meningitis	2 (< 0.1)
Guillain-Barre syndrome	2 (< 0.1)
Myelitis	1 (< 0.1)
Capillary leak syndrome	1 (< 0.1)
Chilblains	1 (< 0.1)

Data are presented as n (per 100,000): the reporting rate of adverse events per 100,000 doses administered.
CVMS, COVID-19 vaccination management system; COVID-19, coronavirus disease 2019.
[a]Data were based on suspected adverse events following COVID-19 vaccination reported by medical institutions or doctors. The results do not indicate medically confirmed diagnoses or causality between the events and the vaccines. [b]These were reported from March 10, 2022. [c]Acute cardiovascular injury includes myocarditis, pericarditis, and others. [d]Anaphylaxis includes anaphylactoid reactions.

(male, 47.0%; female, 53.0%), and 3,688 after dose 2 (male, 46.8%; female, 53.2%) (Table 3). The number of respondents by age group was 1,025 (9.0%) after dose 1 and 541 (14.7%) after dose 2 among 5 to 11-year-old children, and 10,389 (91.0%) after dose 1 and 3,147 (85.3%) after dose 2 among 12 to 17-year-old adolescents respectively. During the week after either dose, local adverse events were reported more frequently than systemic adverse events in both age groups. The reporting rate of local adverse events after dose 1 was 32.8% in 5 to 11-year-old children and 48.2% in 12 to 17-year-old adolescents ($p < 0.001$) (Figure 1; Table 4). After dose 2, the reporting rate of local adverse events was 27.4% in 5 to 11-year-old children and 53.1% in 12 to 17-year-old adolescents ($p < 0.001$). For systemic adverse events after dose 1, 26.8% of 5 to 11-year-old children and 41.9% of 12 to 17-year-old adolescents responded ($p < 0.001$), and the reporting rate after dose 2 was 22.4% for 5 to 11-year-old children and 52.5% for 12 to 17-year-old adolescents ($p < 0.001$). The most frequently reported local adverse events were pain at the injection site and swelling, and the most commonly reported systemic adverse events were myalgia, headache, and fatigue or tiredness among both age groups after either dose (Table 4). Symptoms were most frequently reported during days 0 to 1, but were least frequently reported or disappeared during days 6 to 7 post-

Table 3. Characteristics of children and adolescents aged 5 to 17 years who completed at least 1 text message-based survey on days 0 to 7 following Pfizer-BioNTech COVID-19 vaccination, Republic of Korea, December 13, 2021 to June 20, 2022

Characteristic	Dose 1 (n = 11,414)	Dose 2 (n = 3,688)
Sex		
Male	5,367 (47.0)	1,727 (46.8)
Female	6,047 (53.0)	1,961 (53.2)
Age (y)		
5–11	1,025 (9.0)	541 (14.7)
5	66 (0.6)	38 (1.0)
6	90 (0.8)	47 (1.3)
7	122 (1.1)	52 (1.4)
8	125 (1.1)	71 (1.9)
9	160 (1.4)	86 (2.3)
10	197 (1.7)	115 (3.1)
11	265 (2.3)	132 (3.6)
12–17	10,389 (91.0)	3,147 (85.3)
12	1,948 (17.1)	639 (17.3)
13	2,432 (21.3)	766 (20.8)
14	1,857 (16.3)	584 (15.8)
15	2,672 (23.4)	755 (20.5)
16	864 (7.6)	247 (6.7)
17	616 (5.4)	156 (4.2)

Data are presented as n (%).
COVID-19, coronavirus disease 2019.

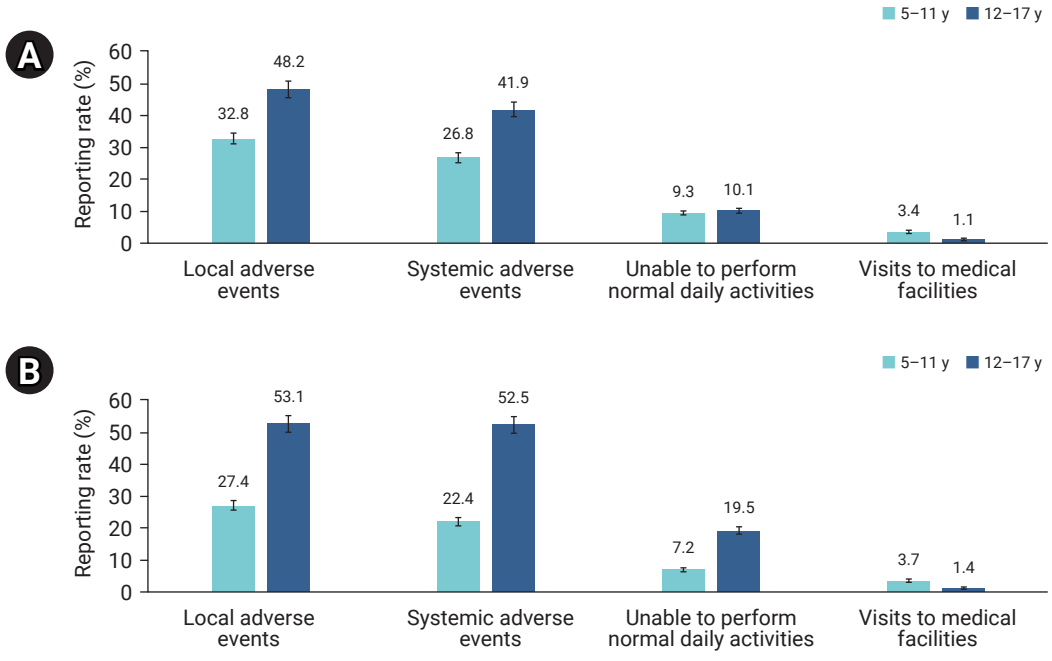

Figure 1. Adverse events and health conditions reported among children and adolescents aged 5 to 17 years following Pfizer-BioNTech coronavirus disease 2019 vaccination, Republic of Korea, December 13, 2021 to June 20, 2022. Values represent the percentage of respondents who reported adverse events and health conditions at least once during days 0 to 7 post-vaccination. (A) Dose 1. (B) Dose 2.
5–11 y, children aged 5–11 years; 12–17 y, adolescents aged 12–17 years.

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Table 4. Adverse events and health conditions reported among children and adolescents aged 5 to 17 years following Pfizer-BioNTech COVID-19 vaccination, Republic of Korea, December 13, 2021 to June 20, 2022

Events[a]	Dose 1 (n = 11,414)			Dose 2 (n = 3,688)		
	5–11 y (n = 1,025)	12–17 y (n = 10,389)	p-value[c]	5–11 y (n = 541)	12–17 y (n = 3,147)	p-value[c]
Local adverse events	336 (32.8)	5,009 (48.2)	< 0.001	148 (27.4)	1,672 (53.1)	< 0.001
Pain	309 (30.1)	4,612 (44.4)	< 0.001	133 (24.6)	1,546 (49.1)	< 0.001
Redness	17 (1.7)	234 (2.3)	0.216	11 (2.0)	108 (3.4)	0.089
Swelling	58 (5.7)	973 (9.4)	< 0.001	29 (5.4)	371 (11.8)	< 0.001
Itching	30 (2.9)	276 (2.7)	0.609	11 (2.0)	107 (3.4)	0.095
Urticaria	5 (0.5)	51 (0.5)	1	1 (0.2)	14 (0.4)	0.712
Others	42 (4.1)	592 (5.7)	0.033	25 (4.6)	195 (6.2)	0.153
Systemic adverse events	275 (26.8)	4,351 (41.9)	< 0.001	121 (22.4)	1,651 (52.5)	< 0.001
Fever	94 (9.2)	797 (7.7)	0.088	48 (8.9)	723 (23.0)	< 0.001
Chills	55 (5.4)	596 (5.7)	0.625	21 (3.9)	452 (14.4)	< 0.001
Headache	97 (9.5)	1,717 (16.5)	< 0.001	40 (7.4)	999 (31.7)	< 0.001
Joint pain	15 (1.5)	266 (2.6)	0.031	3 (0.6)	181 (5.8)	< 0.001
Myalgia	132 (12.9)	2,474 (23.8)	< 0.001	48 (8.9)	865 (27.5)	< 0.001
Fatigue or tiredness	95 (9.3)	2,091 (20.1)	< 0.001	45 (8.3)	892 (28.3)	< 0.001
Nausea	37 (3.6)	680 (6.5)	< 0.001	14 (2.6)	322 (10.2)	< 0.001
Vomiting	13 (1.3)	47 (0.5)	0.001	5 (0.9)	28 (0.9)	0.809
Diarrhea	16 (1.6)	224 (2.2)	0.205	6 (1.1)	81 (2.6)	0.038
Abdominal pain	20 (2.0)	379 (3.6)	0.005	10 (1.8)	171 (5.4)	< 0.001
Rash	3 (0.3)	35 (0.3)	1	0	16 (0.5)	0.151
Armpit tenderness	30 (2.9)	412 (4.0)	0.1	20 (3.7)	327 (10.4)	< 0.001
Chest pain[b]	8 (0.8)	-	-	6 (1.1)	-	-
Heart palpitations[b]	4 (0.4)	-	-	1 (0.2)	-	-
Others	42 (4.1)	523 (5.0)	0.187	19 (3.5)	180 (5.7)	0.036
Unable to perform normal daily activities	95 (9.3)	1,052 (10.1)	0.384	39 (7.2)	613 (19.5)	< 0.001
Visits to medical facilities	35 (3.4)	116 (1.1)	< 0.001	20 (3.7)	44 (1.4)	< 0.001
Emergency department visit	0	18 (0.2)	0.399	0	7 (0.2)	0.603
Hospitalization	0	2 (0)	1	1 (0.2)	0	0.147
Clinic visit	35 (3.4)	100 (1.0)	< 0.001	19 (3.5)	39 (1.2)	< 0.001

Data are presented as n (%): the percentage of respondents who reported adverse events and health conditions at least once during days 0 to 7 post-vaccination.

COVID-19, coronavirus disease 2019.

[a]Events reported by respondents who completed at least 1 text message-based survey on days 0 to 7. Respondents were able to report multiple adverse events on each day. [b]These were additionally investigated only for children aged 5 to 11 years.[c]Chi-square or Fisher exact test as appropriate.

vaccination. Almost one-tenth of 5 to 17-year-old children and adolescents responded that they were unable to perform their normal daily activities after dose 1 (p = 0.384), and this percentage after dose 2 was 7.2% in 5 to 11-year-old children and 19.5% in 12 to 17-year-old adolescents (p < 0.001) (Figure 1; Table 4). Approximately 1.1% to 3.7% of 5 to 17-year-old children and adolescents visited medical facilities during days 0 to 7 after either dose. In addition, in the 5 to 11-year-old group, none of the local and adverse events showed statistically significant differences between the 2 doses except for pain (p = 0.02) and myalgia (p = 0.018), while among 12 to 17-year-old group, all dose 1 and dose 2 comparisons were statistically significant except for urticaria, diarrhea, and rash (Table S1).

Discussion

Regarding the adverse events reported in the CVMS among children and adolescents aged 5 to 17 years after Pfizer-BioNTech COVID-19 vaccination, 96.9% were non-serious and 3.1% were serious. These proportions are similar to those in the safety data from the Vaccine Adverse Event Reporting System in the US; the great majority of adverse events were non-serious (5 to 11-year-old group, 97.4%; 12 to

17-year-old group, 90.7%), and serious adverse events were rare (5 to 11-year-old group, 2.6%; 12 to 17-year-old group, 9.3%) [14,15].

The serious adverse events reported in the CVMS included 125 suspected cases of acute cardiovascular injury, 101 suspected cases of anaphylaxis, and 5 deaths. Reviewing 101 suspected cases of anaphylaxis, the number of cases was 1 in 5 to 11-year-old children (1.0%) and 100 in 12 to 17-year-old adolescents (99.0%). The number of cases was greater after dose 1 (82, 81.2%) than after dose 2 (19, 18.8%), but similar between males (46, 45.5%) and females (55, 54.5%). Other studies also found that anaphylaxis cases were reported more frequently after dose 1 than after dose 2, highlighting the significance of closely monitoring people who receive a first dose of the COVID-19 vaccine [16–18]. Furthermore, among 125 suspected cases of acute cardiovascular injury, the number of suspected myocarditis/pericarditis reports was 103; 1 case (1.0%) was in a 5 to 11-year-old, and 102 cases (99.0%) were in 12 to 17-year-old adolescents. Similar to previous findings [19–22], these cases were more frequent after dose 2 (67, 65.0%) than after dose 1 (36, 35.0%), and in males (79, 76.7%) than in females (24, 23.3%). However, since all adverse events reported in the CVMS are suspected cases, these events do not indicate medically confirmed diagnoses; therefore, a follow-up study will be required to medically confirm major suspected cases of serious adverse events for further evaluation, such as causality assessment between events and vaccines. Until now, none of the death reports has been assessed to be associated with vaccination based on medical records and epidemiological investigation results through an initial review conducted by provincial rapid response teams.

The highest risk of myocarditis/pericarditis was observed in males aged 18 to 25 after dose 2 of the mRNA COVID-19 vaccine [19], and the reporting rate for mRNA-based COVID-19 vaccine-associated myocarditis appeared highest among males aged 12 to 29 years [20]. However, myocarditis/pericarditis cases following mRNA COVID-19 vaccination are rare among adolescents, and patients can recover quickly if treated well [23]. One study found no increased incidence of myocarditis/pericarditis after COVID-19 vaccination compared to other standard immunizations such as smallpox and influenza vaccines [22]. Furthermore, verified cases of myocarditis were rare among children aged 5 to 11 years after Pfizer-BioNTech vaccination in the US vaccine surveillance systems [24,25], and no cases of myocarditis were reported among 3,082 trial participants of the same age with 0 to 7 days of follow-up after dose 2 [26]. In this respect, the benefits of COVID-19 vaccination for children and adolescents aged 5 to 17 years are considered to outweigh the known and potential risks [27–30]; thus, this study does not support actions to exclude 5 to 17-year-old children and adolescents from vaccination and recommend that adverse events after COVID-19 vaccination should continue to be closely monitored to respond and provide additional information on COVID-19 vaccine safety, considering the limited information available in early safety monitoring [31].

The results of the text message survey on adverse events and health conditions for children and adolescents aged 5 to 17 years following the primary Pfizer-BioNTech COVID-19 vaccination series are similar to the safety data reported in the v-safe system [14,15,24] and controlled trials [1,2] among those in the US; local adverse events were more common than systemic adverse events following either dose, and the majority of symptoms were mild, without major safety issues, and disappeared within a few days after vaccination. Moreover, injection site pain was the most common local adverse event, and fatigue, headache, and myalgia were the most common systemic adverse events in v-safe and controlled trials.

According to the v-safe data [14,15], local (dose 1, 54.9%; dose 2, 56.8%) and systemic adverse events (dose 1, 35.3%; dose 2, 41.0%) among 5 to 11-year-old children were less frequently reported than local (dose 1, 62.7% to 63.9%; dose 2, 62.4% to 64.4%) and systemic adverse events (dose 1, 48.9% to 55.7%; dose 2, 63.4% to 69.9%) among 12 to 17-year-old adolescents. This trend is consistent with the results of the text message survey in this study; local and systemic adverse events were lower in children aged 5 to 11 years than in adolescents aged 12 to 17 years. However, this might be affected by the difference in the dose administered between children (10 μg) and adolescents (30 μg) [14] and the number of respondents enrolled in the surveys; thus, these figures should be compared with caution.

This study has some limitations. First, the data were based on suspected adverse events following COVID-19 vaccination, and the events were not medically confirmed for an accurate diagnosis; thus, the results do not indicate causality. Second, as adverse events reported to the CVMS are based on individuals who visit medical facilities, the reports are subject to underreporting. Third, since text message surveys merely relied on self-reported responses, the number of adverse events reported might have been overestimated due to the likelihood of responding by parents or guardians. Fourth, as the text messages were sent during a particular period, the findings cannot be generalized to the entire child and adolescent population in the ROK. Nevertheless, the key strength of this study, as far as we know, is that this is the first study on COVID-19 vaccine safety among children

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and adolescents aged 5 to 17 years in real-world settings in the ROK based on national vaccine safety surveillance data. This study found consistent safety information on the Pfizer-BioNTech COVID-19 vaccine with controlled trials; serious adverse events following vaccination were extremely rare, with no major safety issues among children and adolescents aged 5 to 17 years.

Supplementary Material

Table S1. Comparisons of adverse events and health conditions between vaccine doses among children and adolescents aged 5 to 17 years following Pfizer-BioNTech COVID-19 vaccination, Republic of Korea, December 13, 2021 to June 20, 2022. Supplementary data are available at https://doi.org/10.24171/j.phrp.2022.0233.

Notes

Ethics Approval

The passive surveillance activity was conducted and authorized by the public health authority; the study was not subject to the institutional review board approval under government regulations. The study of text message-based surveillance was exempted from review by the Public Institutional Review Board designated by the Korea Ministry of Health and Welfare (No: P01-202206-01-033).

Conflicts of Interest

The authors have no conflicts of interest to declare.

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None.

Availability of Data

The data used in this study are protected under the Personal Information Protection Act.

Authors' Contributions

Conceptualization: SK, SYS, YKL, EC; Data curation: SK, YH, DSL; Formal analysis: SK, YH, DSL; Investigation: SK, YH; Methodology: all authors; Validation: SK, SYS, YKL; Visualization: SK, YH; Writing–original draft: SK, YKL; Writing–review & editing: all authors.

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References

1. Walter EB, Talaat KR, Sabharwal C, et al. Evaluation of the BNT162b2 Covid-19 vaccine in children 5 to 11 years of age. N Engl J Med 2022;386:35–46.
2. Frenck RW Jr, Klein NP, Kitchin N, et al. Safety, immunogenicity, and efficacy of the BNT162b2 Covid-19 vaccine in adolescents. N Engl J Med 2021;385:239–50.
3. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603–15.
4. Ministry of Food and Drug Safety (MFDS). Press release: authorization for the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) [Internet]. Cheongju: MFDS; 2021 [cited 2022 Jul 7]. Available from: https://www.mfds.go.kr/brd/m_99/view.do?seq=45117&srchFr=&srchTo=&srchWord=&srchTp=&itm_seq_1=0&itm_seq_2=0&multi_itm_seq=0&company_cd=&company_nm=&page=1. Korean.
5. Ministry of Food and Drug Safety (MFDS). Press release: age expansion to use of the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) [Internet]. Cheongju: MFDS; 2021 [cited 2022 Jul 7]. Available from: https://www.mfds.go.kr/brd/m_99/view.do?seq=45566&srchFr=&srchTo=&srchWord=접종+연령+확대&srchTp=0&itm_seq_1=0&itm_seq_2=0&multi_itm_seq=0&company_cd=&company_nm=&Data_stts_gubun=C9999&page=1. Korean.
6. Ministry of Food and Drug Safety (MFDS). Press release: authorization for the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) for children aged 5 to 11 years old [Internet]. Cheongju: MFDS; 2022 [cited 2022 Jul 7]. Available from: https://nedrug.mfds.go.kr/bbs/119/201. Korean.
7. Korea Disease Control and Prevention Agency (KDCA). Press releases: adolescents aged 16-17 years vaccination (October 18, 2021, regular briefing) [Internet]. Cheongju: KDCA; 2021 [cited 2022 Oct 12). Available from: https://www.kdca.go.kr/board/board.es?mid=a20501020000&bid=0015&list_no=717277&cg_code=C01&act=view&nPage=1. Korean.
8. Korea Disease Control and Prevention Agency (KDCA). Press releases: adolescents aged 12-17 years vaccination (August 30, 2021, regular briefing) [Internet]. Cheongju: KDCA; 2021 [cited 2022 Oct 12). Available from: https://www.kdca.go.kr/board/board.es?mid=a20501020000&bid=0015&list_no=716707&cg_code=C0&act=view&nPage=11. Korean.
9. Korea Disease Control and Prevention Agency (KDCA). Press releases: children aged 5-11 years vaccination (March 24, 2022, regular briefing) [Internet]. Cheongju: KDCA; 2021 [cited 2022 Oct 12). Available from: https://www.kdca.go.kr/board/board.es?mid=a20501010000&bid=0015&list_no=719074&cg_code=&act=view&nPage=1. Korean.
10. Korea Disease Control and Prevention Agency (KDCA). Press release: initiation of primary series vaccination for children (5–11 years old) and additional vaccination for adolescents (12–17 years old) [Internet]. Cheongju: KDCA; 2022 [cited 2022 Jul 7]. Available from: https://www.kdca.go.kr/board/board.es?mid=a20501010000&bid=0015&list_no=718990&cg_code=&act=view&nPage=1. Korean.
11. Payne RP, Longet S, Austin JA, et al. Immunogenicity of standard and extended dosing intervals of BNT162b2 mRNA vaccine. Cell 2021;184:5699–714.e11.
12. Buchan SA, Seo CY, Johnson C, et al. Epidemiology of myocarditis and pericarditis following mRNA vaccination by vaccine product, schedule, and interdose interval among adolescents and adults in Ontario, Canada. JAMA Netw Open 2022;5:e2218505.
13. Korea Disease Control and Prevention Agency (KDCA). Guideline for adverse events following COVID-19 immunization [Internet]. 2nd ed.

Cheongju: KDCA; 2021 [cited 2022 Jul 7]. Available from: https://www.kdca.go.kr/upload_comm/syview/doc.html?fn=163463647072000.pdf&rs=/upload_comm/docu/0019. Korean.
14. Hause AM, Shay DK, Klein NP, et al. Safety of COVID-19 vaccination in United States children ages 5 to 11 years. Pediatrics 2022;150:e2022057313.
15. Hause AM, Gee J, Baggs J, et al. COVID-19 vaccine safety in adolescents aged 12-17 years: United States, December 14, 2020-July 16, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1053–8.
16. Hwang I, Park K, Kim TE, et al. COVID-19 vaccine safety monitoring in Republic of Korea from February 26, 2021 to October 31, 2021. Osong Public Health Res Perspect 2021;12:396–402.
17. Shimabukuro TT, Cole M, Su JR. Reports of anaphylaxis after receipt of mRNA COVID-19 vaccines in the US-December 14, 2020-January 18, 2021. JAMA 2021;325:1101–2.
18. Bian S, Li L, Wang Z, et al. Allergic reactions after the administration of COVID-19 vaccines. Front Public Health 2022;10:878081.
19. Wong HL, Hu M, Zhou CK, et al. Risk of myocarditis and pericarditis after the COVID-19 mRNA vaccination in the USA: a cohort study in claims databases. Lancet 2022;399:2191–9.
20. Oster ME, Shay DK, Su JR, et al. Myocarditis cases reported after mRNA-based COVID-19 vaccination in the US from December 2020 to August 2021. JAMA 2022;327:331–40.
21. Lv M, Luo X, Shen Q, et al. Safety, Immunogenicity, and efficacy of COVID-19 vaccines in children and adolescents: a systematic review. Vaccines (Basel) 2021;9:1102.
22. Ling RR, Ramanathan K, Tan FL, et al. Myopericarditis following COVID-19 vaccination and non-COVID-19 vaccination: a systematic review and meta-analysis. Lancet Respir Med 2022;10:679–88.
23. Centers for Disease Control and Prevention (CDC). COVID-19: myocarditis and pericarditis after mRNA COVID-19 vaccination [Internet]. Atlanta, GA: CDC; 2021 [cited 2022 Jul 25]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html.
24. Hause AM, Baggs J, Marquez P, et al. COVID-19 vaccine safety in children aged 5-11 years: United States, November 3-December 19, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1755–60.
25. Su JR. Adverse events among children ages 5-11 years after COVID-19 vaccination: updates from v-safe and the Vaccine Adverse Event Reporting System (VAERS) [Internet]. Atlanta, GA: CDC; 2021 [cited 2022 Jul 7]. Available from: https://stacks.cdc.gov/view/cdc/112668.
26. Food and Drug Administration (FDA). Comirnaty and Pfizer-BioNTech COVID-19 vaccine [Internet]. Silver Spring, MD: FDA; 2021 [cited 2022 Jul 7]. Available from: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine.
27. Woodworth KR, Moulia D, Collins JP, et al. The advisory committee on immunization practices' interim recommendation for use of Pfizer-BioNTech COVID-19 vaccine in children aged 5-11 years: United States, November 2021. MMWR Morb Mortal Wkly Rep 2021;70:1579–83.
28. Gargano JW, Wallace M, Hadler SC, et al. Use of mRNA COVID-19 vaccine after reports of myocarditis among vaccine recipients: update from the advisory committee on immunization practices: United States, June 2021. MMWR Morb Mortal Wkly Rep 2021;70:977–82.
29. Wise J. Covid-19: should we be worried about reports of myocarditis and pericarditis after mRNA vaccines? BMJ 2021;373:n1635.
30. Saxena S, Skirrow H, Wighton K. Should the UK vaccinate children and adolescents against COVID-19? BMJ 2021;374:n1866.
31. Ryan M, Montgomery J. Myopericarditis after COVID-19 vaccination: unexpected but not unprecedented. Lancet Respir Med 2022;10:625–5.

https://doi.org/10.24171/j.phrp.2022.0233