



Short-term safety profile of COVID-19 vaccination in children and adolescents with underlying medical conditions: a prospective cohort study

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Purpose: This article was to collect data on the safety of coronavirus disease 2019 (COVID-19) vaccines in children with underlying medical conditions.

Methods: We constructed a prospective cohort of children and adolescents aged 5 to 19 years who had received at least one dose of COVID-19 vaccine. Patients diagnosed with and treated for chronic kidney disease, autoimmune disease, or other chronic conditions at the Seoul National University Children's Hospital were recruited from June to December 2022. A mobile survey questionnaire was sent to their guardians. The presence of adverse events on the day (day 0), 3 weeks (day 21), and 6 months (day 180) after the 1st dose of COVID-19 vaccine was recorded by the guardians.

Results: A total of 73 children participated. The median age was 14 years, and 64.4% of the patients were male. On the day of immunization, 65.8% of the patients reported at least one adverse event. Pain at the injection site, fatigue, headache, arthralgia, and myalgia were the most common symptoms. The prevalence of adverse events decreased over time (65.8% on day 0, 27.4% between days 0 and 21, and 24.6% between days 21 and 180). Severe acute respiratory syndrome coronavirus 2 infection after the 1st dose occurred in 17 patients (23.3%) and one of the patients (5.88%) was hospitalized due to infection.

Conclusions: Adverse events after COVID-19 vaccination were generally mild in children and adolescents with underlying medical conditions. Our findings provide evidence for the safety of COVID-19 vaccination in the vulnerable pediatric population.

Keywords: Adolescent; Child; COVID-19; Safety; SARS-CoV-2

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Introduction

Since the emergence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic at the end of 2019, the greatest burden of SARS-CoV-2 infection in terms of severe morbidity and mortality remains among older people and those with underlying medical conditions [1]. Compared to adults, SARS-CoV-2 is known to cause less severe infections and lower fatalities in children and adolescents. Many children and adolescents remain susceptible to SARS-CoV-2 infection and can transmit the virus to others. Their risk of infection and transmission is higher with increasing age [2]. Compared to the adult population with high coronavirus disease 2019 (COVID-19) immunity, children and adolescents account for an increasing proportion of COVID-19 cases [3]. Thus, COVID-19 vaccination in children and adolescents could prevent the disease and contribute to the development of herd immunity. In addition, although children and adolescents generally experience milder infections than adults, severe morbidity and mortality can occur in this population, especially in those with comorbidities [4]. Given the interrupted educational and social development of young children and adolescents during the pandemic, increasing the uptake of COVID-19 vaccination in children and adolescents, especially those with underlying medical conditions, is important.

Children and adolescents with underlying medical conditions are at a greater risk for many infections, some of which are vaccine-preventable. Several clinical trials have supported the favorable immune response, effectiveness, and safety profiles of COVID-19 vaccines in healthy children and adolescents and those with underlying medical conditions [5,6]. Prior reports on the safety of COVID-19 vaccination among children were limited by the small number of selected underlying diseases and inability to detect adverse events in children at multiple time points after vaccination [7]. In the current study, we aimed to collect all the data on the safety of available COVID-19 vaccines to guide healthcare workers and families in vaccinating the younger population (5–19 years old) with underlying medical conditions.

Methods

To obtain information about adverse events following COVID-19 vaccination among children and adolescents with underlying diseases, we constructed a prospective cohort of children and

adolescents between the ages of 5 and 19 years who received at least one dose of the COVID-19 vaccine. In the Republic of Korea, the mass COVID-19 vaccination program started for 12 to 17 years in November 2021 and for 5 to 12 years in March 2022. We recruited patients who had been diagnosed and treated for chronic kidney disease (CKD), autoimmune disease, or other chronic conditions at the pediatric nephrology and pediatric rheumatology divisions of the Seoul National University Children's Hospital from June to December 2022. CKD in children and adolescents is defined as the presence of structural or functional kidney damage that persists over a minimum period of 3 months [8]. We identified children and adolescents with autoimmune diseases including type I diabetes, juvenile idiopathic arthritis, and systemic lupus erythematosus. After obtaining informed consent from the child and one of their parents, we sent a text of the mobile link to the guardian to complete the survey. Those whose parents refused to participate in the study, could not understand Korean, or did not have CKD, autoimmune diseases, or other chronic conditions were excluded.

A survey containing 27 questions was developed ([Supplement Material 1](#), available online) based on a study protocol for the safety of COVID-19 vaccines [9]. We collected baseline information on the children's age, sex, birth weight, preterm birth, age and education of parents, underlying medical condition, and current medication. Local adverse events after COVID-19 vaccination were pain at the injection site, edema, and redness at the injection site. Systemic events included fever, nausea and vomiting, headache, arthralgia, myalgia, fatigue, general allergic reactions (urticaria, rash, facial or hand edema, etc.), and others. We identified individuals who experienced at least one of the following adverse events: outpatient visits due to adverse reactions and hospitalization due to adverse reactions. The presence of adverse events on the day (day 0), 3 weeks (day 21), and 6 months (day 180) after the 1st dose of COVID-19 vaccination was recorded by the guardians.

Results

The characteristics of the participants are presented in [Table 1](#). Participants were aged 5 to 19 years and 64.4% (47/73) of them were boys and 35.6% (26/73) of them were girls. The mean birth weight was 3.08 ± 0.66 kg and nine were preterm births (12.5%). Parents were aged 47.3 and 44.6 years on average, and the majority were college or university graduates. Fifty-four (74.0%)

Table 1. Characteristics of study participants (n=73)

Variable	Study population
Age	
5–11 yr	11 (15.1)
12–19 yr	62 (84.9)
Sex	
Boys	47 (64.4)
Girls	26 (35.6)
Birth weight (kg)	3.08±0.66
Preterm birth (<37 wk)	9 (12.5)
Completion of routine pediatric immunization	72 (98.6)
Parental age (yr)	
Father	47.3±4.66
Mother	44.6±3.74
Parental highest education	
Father	
High school or lower	22 (30.1)
College/university or higher	51 (69.7)
Mother	
High school or lower	23 (31.5)
College/university or higher	50 (68.5)
Underlying medical condition	
Chronic kidney disease	54 (74.0)
Autoimmune disease	10 (13.7)
Other medical conditions ^{a)}	9 (12.3)
Current medication	
Immunosuppressant	12 (16.4)
Anti-inflammatory agent	8 (11.0)
Others ^{b)}	45 (61.6)
No medication	8 (11.0)

Values are presented as number (%) or mean±standard deviation.

^{a)}Included congenital heart disease and solid organ transplantation.

^{b)}Included antihypertensive drugs, insulin, etc.

children and adolescents had CKD patients and 10 (13.7%) had autoimmune disease. The majority of the children and adolescents were taking medications at the time of the survey.

Participants received their first dose of COVID-19 vaccination between January 13, 2021, and July 25, 2022. The adverse events after the 1st dose of COVID-19 in the study population are shown in Table 2. On the day of 1st dose, 65.8% (n=48) of patients reported at least one adverse event. Pain at the injection site, fatigue, headache, arthralgia, and myalgia were the most common symptoms observed on day 0. The prevalence of adverse event decreased over time (65.8% on day 0, 27.4% between days 0 and 21, and 24.6% between days 21 and 180).

All children and adolescents in the cohort, except one (98.6%) received 2nd dose of COVID-19 vaccination (Table 3). Almost one-third (n=26, 36.1%) reported that they completed their third dose during the study period. SARS-CoV-2 infection after the 1st dose occurred in 17 (23.3%) and one of the patients (1/17, 5.88%) was hospitalized due to infection. Of the 17 patients, 13 patients had kidney disease, 11 patients were taking immunosuppressive medications, and two patients had no medication. One patient with a history of kidney transplantation, underlying heart disease, and receiving regular immunosuppressive medication was hospitalized for one day due to an unknown adverse event following the COVID-19 vaccination. The parent did not specify the adverse event as the reason for hospital admission.

Table 2. Adverse event after the 1st dose of COVID-19 in the study population

Adverse events and management	Day 0 (n=73)	Day 21 (n=73)	Day 180 (n=57)
Adverse events			
Pain at injection site	32 (43.8)	11 (15.1)	9 (15.8)
Edema, redness at injection site	12 (16.4)	4 (5.48)	6 (10.5)
Fever	23 (31.5)	8 (11.0)	11 (19.3)
Nausea and vomiting	4 (5.48)	2 (2.74)	5 (8.77)
Headache, arthralgia, and myalgia	24 (32.9)	12 (16.4)	11 (19.3)
Fatigue	25 (34.2)	9 (12.3)	10 (17.5)
General allergic reaction (urticaria, rash, facial or hand edema, etc.)	2 (2.74)	1 (1.37)	3 (5.26)
Others	5 (6.85)	4 (5.48)	8 (14.0)
Any symptom	48 (65.8)	20 (27.4)	14 (24.6)
Management			
Outpatients visit due to adverse reaction	5 (6.85)	2 (2.74) ^{a)}	7 (9.58) ^{a)}
Hospitalization due to adverse reaction	0	0	0

Values are presented as number (%).

Day 0, day of the 1st coronavirus disease 2019 (COVID-19) vaccination; Day 21, 3 weeks after COVID-19 vaccination; Day 180, 6 months after COVID-19 vaccination.

^{a)}Two patients had reported repeated outpatient visits on within days 0, 21, and 180.

Table 3. COVID-19 immunization dose and SARS-CoV-2 infection after immunization

Outcome	Frequency (%)
COVID-19 immunization	
First dose	73 (100)
Second dose	72 (98.6)
Third dose	26 (36.1)
SARS-CoV-2 infection after the 1st dose	17 (23.3)
Hospitalization from COVID-19 infection	1 (5.88) ^{a)}
ICU administration from COVID-19 infection	0

COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; ICU, intensive care unit.

^{a)}Proportion was calculated by dividing the number of cases of SARS-CoV-2 infection.

Discussion

In this prospective cohort study, we observed tolerable outcomes after COVID-19 vaccination in children and adolescents with underlying medical conditions. Within 6 months of 1st dose of COVID-19 vaccination, 65.8% reported at least one mild-to-moderate adverse event. While one patient was hospitalized due to SARS-CoV-2 infection, none of the study participants experienced adverse events requiring hospitalization due to COVID-19 vaccination. Our findings support the safety of COVID-19 vaccination in high-risk children and adolescents.

Despite the greater need for COVID-19 vaccination in children with underlying medical conditions [7], the number of safety studies in this population has been limited. In a clinical trial of the BNT162b2 COVID-19 vaccine, the immune response was stronger in 12- to 15-year-old recipients than in young adults [5]. Given that autoimmune disease is associated with a high risk of drug allergy [10], the risk of adverse events after vaccination may be higher in patients with autoimmune disease. We observed no evidence of a higher risk of severe adverse events following COVID-19 vaccination among children with autoimmune diseases, which is consistent with previous studies [6,11].

Several studies conducted in the UK [12-14] have shown that children with kidney disease have a lower risk of becoming ill with COVID-19 infection compared to adult patients with CKD [15]. However, CKD patients may be more vulnerable to infection and severe disease due to their CKD condition and the use of immunosuppressive agents [16-18]. Approximately 0.50% of children in the US have CKD, and up to 1.50% of patients with CKD are hospitalized due to COVID-19, with kidney disease be-

ing the strongest predictor of hospitalization [19,20]. However, a recent study published in the US showed that two-thirds of parents were hesitant to allow administration of COVID-19 vaccines to their children with kidney disease or hypertension [21]. This highlights the importance of providing more information to parents and caregivers regarding the benefits and harms of vaccination in this population.

This study has limitations that require caution when interpreting the findings. Firstly, our study population may not be representative of all children with underlying medical conditions. The heterogeneity of underlying disease in our study population also limits the generalizability of our findings. Given the generally low prevalence of CKD or autoimmune disease in children, our findings would contribute to the pool of vaccinated pediatric patients to construct a body of evidence for COVID-19 vaccine safety. Secondly, we could not assess vaccine effectiveness in the population. Furthermore, this study did not stratify the kidney disease patients according to their glomerular filtration rate, whether they were on dialysis or had a kidney transplant. Additionally, the results of this study were based on self-reported surveys which could limit the accuracy and completeness of the data. Considering that the risk-benefit profile is critical for the attitude toward COVID-19 vaccination in the pediatric population, acquiring a safety profile in each specific underlying disease group with more detailed clinical information would be necessary in future studies.

In conclusion, this study suggests that the COVID-19 vaccination is safe for children and adolescents with underlying medical conditions. Adverse events after COVID-19 vaccination in children with underlying medical conditions, including CKD and autoimmune diseases, were tolerated. Our findings provide evidence for the safety of COVID-19 vaccination in the vulnerable pediatric population.

Ethical statements

The study protocol was reviewed and approved by the Institutional Review Board of the Seoul National University Hospital (IRB No. 2205-034-1323). Informed consent was obtained.

Conflicts of interest

Seung-Ah Choe received research funding from SK Bioscience. Hee Gyung Kang is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation,

or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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