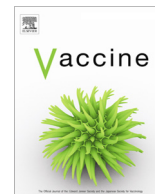




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Short communication

Safety and effectiveness of BNT162b2 mRNA Covid-19 vaccine in adolescents



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ABSTRACT

In South Korea, all 12th grade students (high school seniors) were offered BNT162b2 vaccine starting July 19, 2021; while 10th–11th grade students were not eligible. We conducted a nationwide retrospective cohort study to determine the safety and effectiveness of BNT162b2 mRNA Covid-19 vaccine in adolescents against SARS-CoV-2 infection. Among 444,313 persons who received the first dose of vaccine, reporting rate for myocarditis and/or pericarditis was 1.8 per 100,000 (95% C.I. 0.8–3.5) among first-dose recipients and 4.3 per 100,000 (95% C.I. 2.6–6.7) in second-dose recipients. Vaccine effectiveness against symptomatic/asymptomatic SARS-CoV-2 infection 14 days post-first dose vaccination was 91.1% (95% C.I. 89.6–92.5), and 14 days post-second dose was 99.1% (95% C.I. 98.5–99.5). In this retrospective cohort study, BNT162b2 vaccination was safe and was associated with a significantly lower risk of SARS-CoV-2 infection, suggesting that vaccination in adolescent may reduce the burden of Covid-19.

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1. Introduction

Children and adolescents appear to have milder form of coronavirus disease 2019 (Covid-2019) than adults but remain at risk for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection across all ages [1]. Since its development and licensure, the Covid-19 vaccine studies have been conducted mainly in adults, and data on adolescent population is relatively scarce. Although high immunogenicity and efficacy in adolescents had been reported in controlled trials, data to inform the vaccine safety and effectiveness in the real-world setting are limited [2].

In South Korea, Covid-19 vaccination was initially prioritized for older adults and healthcare workers, with subsequent rollout to younger population.[3] As Covid-19 vaccine distribution continued, all 12th grade students (high school seniors) were offered BNT162b2 mRNA Covid-19 vaccine starting July 19, 2021; while 10th and 11th grade students were not eligible to receive the vaccines. This Covid-19 vaccination program targeting the 12th grade

students provide a unique opportunity to study the real-world impact of vaccination program in adolescents.

2. Methods

We conducted a retrospective cohort study within the Korean education system, a three-year high school system, from 10th grade to 12th grade (around 16–18 years of age). We linked the student Covid-19 confirmed case reports from the Ministry of Education and immunization registry from the Korea Disease Control and Prevention Agency, to determine the effectiveness of BNT162b2 mRNA Covid-19 vaccine in adolescents against SARS-CoV-2 infection (both symptomatic and asymptomatic). Korean education system has a three-year high school system, from 10th grade to 12th grade (around age 16–18 years of age). Laboratory testing, epidemiologic investigation, and surveillance practices did not change over the course of vaccination campaign.

Passive surveillance for adverse events was conducted through the medical facilities across the country, in accordance with COVID-19 Vaccination Adverse Events Management Guideline [4]. Anyone, including vaccine recipients and health care providers, were encouraged to report a suspected adverse event following immunization to the government. Serious adverse events were

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defined as cases with diagnoses of myocarditis and/or pericarditis, anaphylaxis reaction, convulsion/seizure, acute paralysis, encephalopathy/encephalitis, thrombocytopenia, Guillain-Barre syndrome, and any other diagnosis deemed by doctors that require close medical attention. History of hospitalization due to the symptoms following immunizations were recorded. All other adverse events were classified as nonserious adverse event. The presence of adverse events was monitored between the first and the second dose of BNT162b2 mRNA Covid-19 vaccines (post-first dose), and 30 days following the second dose (post-second dose).

Daily number of COVID-19 polymerase-chain-reaction (PCR) confirmed cases were obtained, and incidence per 100,000 was calculated per respective grades. Weekly incidence rate ratio was compared between the 10th–11th grade students vs. 12th grade students. We estimated vaccine effectiveness by calculating the reduction in cases in vaccinated students (≥ 14 -day post 1st dose and ≥ 14 -days post 2nd dose vaccination) to unvaccinated students. Weekly Covid-19 vaccination coverage rate (%) was derived from the national immunization registry.

This study was conducted as a legally mandated public health investigation under the authority of the Korean Infectious Diseases Control and Prevention Act (No. 12,444 and No. 13,392) and was not research that was subject to institutional review board approval; therefore, written informed consent was not required.

3. Results

The vaccination campaign targeted 45,4876 12th grade high school students across the country (out of 1,299,965 total high school students), reaching 82.2% of one-dose vaccine coverage rate during the first 2 weeks, and 95.4% of two-dose vaccine coverage rate within the next 3 weeks.

Among 444,313 persons who received the first dose of BNT162b2 vaccine, 1,287 (0.29%) reported to have adverse events, while 2,694/442,025 (0.61%) of second-dose recipients had reported the events (Table 1). Among the first-dose recipients and the second-dose recipients, 37 (0.01%) and 57 (0.01%) serious adverse events were reported, respectively. The reporting rate for myocarditis and/or pericarditis was the most common serious adverse event reported, with 1.8 per 100,000 (95% C.I. 0.8–3.5) among first-dose recipients and 4.3 per 100,000 (95% C.I. 2.6–6.7) in second-dose recipients (Fig. 1). Other adverse events include anaphylaxis reaction (1.6–2.3 per 100,000), convulsion (0.7–1.1 per 100,000), seizure (0.7–1.1 per 100,000), and acute paralysis (0.9 per 100,000).

Following the 12th grade student vaccination program, there was a decrease in 12th grade student cases (Fig. 2A), from 3.73 per 100,000 (95% C.I. 3.47–4.00) during 30–31st week to 2.35 per 100,000 (95% C.I. 2.08–2.63) during 32–33rd week, to 1.39 per 100,000 (95% C.I. 1.12–1.66) after 34–35th week (Fig. 2B). The incidence of 10–11th grade students increased from 2.78 per 100,000 (95% C.I. 2.69–2.88) during 30–31st week to 3.34 per 100,000 (95% C.I. 3.02–3.87) during 32–33rd week to 4.80 per 100,000

(95% C.I. 4.60–5.00) after 34–35th week. Incidence rate ratio for 12th grade students vs. 10–11th grade students has decreased from 1.34 (95% C.I. 1.29–1.39) during 30–31st week to 0.29 (95% C.I. 0.24–0.33) after 34–35th week. Vaccine effectiveness against symptomatic/asymptomatic SARS-CoV-2 infection ≥ 14 days post-first dose vaccination was 91.1% (95% C.I. 89.6–92.5), and ≥ 14 days post-second dose vaccination in adolescent was 99.1% (95% C.I. 98.5–99.5) (Table 2).

4. Discussion

Among adolescents, receipt of the BNT162b2 vaccine was safe, and was associated with a lower risk of laboratory-confirmed Covid-19 in South Korea. The rate of serious adverse events was low in both vaccination doses, and no potentially vaccine-associated deaths were identified. Our data on safety of BNT162b2 vaccine in adolescents were strengthened by study from Israel, which showed the risk of myocarditis for 16–19 years of age within 21 days of vaccination to be 1.34 per 100,000 (first dose) and 15.07 per 100,000 (second dose) [5]. In the U.S., myocarditis/pericarditis rates were around 12 cases per million doses of second-dose mRNA vaccine among individuals 12–39 years of age [6].

Our finding extends previous clinical trial data on 2,260 adolescent aged 12–15 years resulting vaccine efficacy of 100% (95% C.I., 75.3–100) [2]. Evidence among adolescents on vaccine effectiveness against Covid-19 in real-world settings are limited. A nationwide retrospective cohort study from Israel on vaccine effectiveness of BNT162b2 in adolescents during SARS-CoV-2 delta variant outbreak showed 91.5% (95% CI 88.2–93.9%) post two-dose vaccination [7]. In a test-negative, case-control study at U.S. pediatric hospitals, the effectiveness of 2 doses of BNT162b2 against Covid-19 hospitalization in children and adolescents aged 12–18 years was 93% (95% CI, 83–97) [8]. Note that the BNT162b2 mRNA vaccine was effective against PCR-confirmed SARS-CoV-2 infection in Korean adolescents, despite the B.1.617.2 (delta) variant emerged as the predominant strain in the country [9]. The schools reopened for the fall semester after 34th week, albeit showing continued reduction in cases among 12th grade students. Our finding complements other reported estimates of the effectiveness of the BNT162b2 mRNA vaccine [10–12], and it confirms that the public health impact in adolescents.

Study limitations include possible confounded result because our estimates are unadjusted because of the lack of demographic data for individual cases. 10–11th grade students might be more prone to present for testing than 12th grade students because of concerns about their vulnerability. However, SARS-CoV-2 testing was offered to all suspected persons regardless of presence of symptoms or vaccination status.

As of November 13, 2021, >75% of Korean adult population aged 18 years and older were fully vaccinated against Covid-19, while the vaccination is now open to children and adolescents aged 12 years and older. In this retrospective cohort study of high school students in South Korea, BNT162b2 mRNA vaccination was safe

Table 1
Safety profile of BNT162b2 by number of doses in high school students following a nationwide 12th grade students vaccination campaign in Korea.

Variables	First dose		Second dose		Total	
	No.	(%)	No.	(%)	No.	(%)
Total vaccinations	444,313		442,025		886,338	
Adverse event reports	1287	(0.29)	2694	(0.61)	3981	(0.45)
Nonserious adverse event	1250	(0.28)	2637	(0.60)	3887	(0.44)
Serious adverse event	37	(0.01)	57	(0.01)	94	(0.01)
Hospitalization	36	(0.01)	71	(0.02)	107	(0.01)

* Patients in the “nonserious adverse event” and “serious adverse event” are mutually exclusive, whereas patients in the “hospitalization” are mutually inclusive with the aforementioned groups.

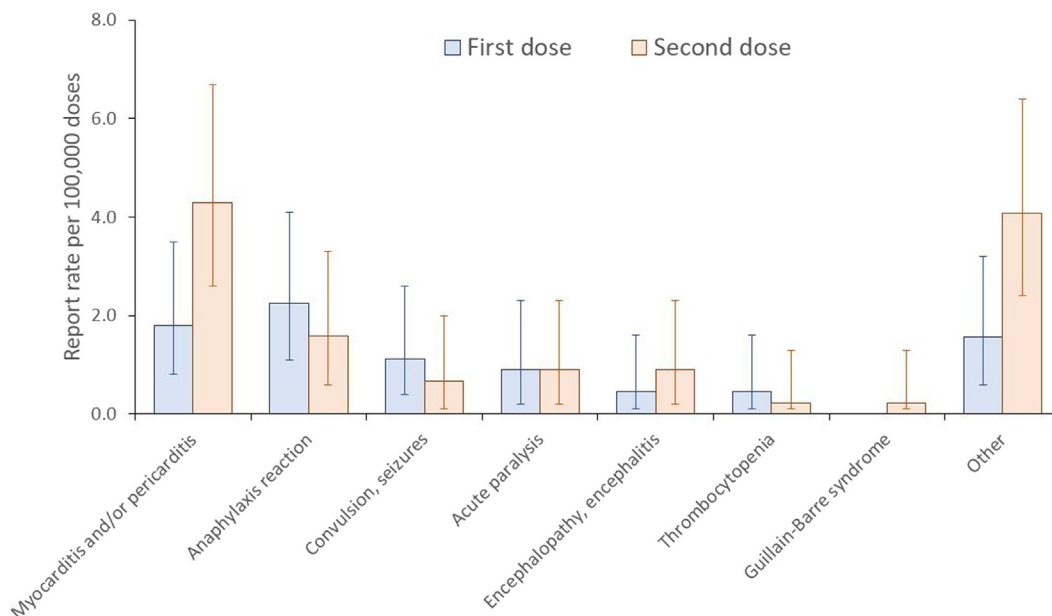


Fig. 1. Report rate of serious adverse events following BNT162b2 by number of doses in high school students following a nationwide 12th grade students vaccination campaign in Korea. * Others (mutually inclusive with other adverse events): chest pain, dyspnea, chest discomfort.

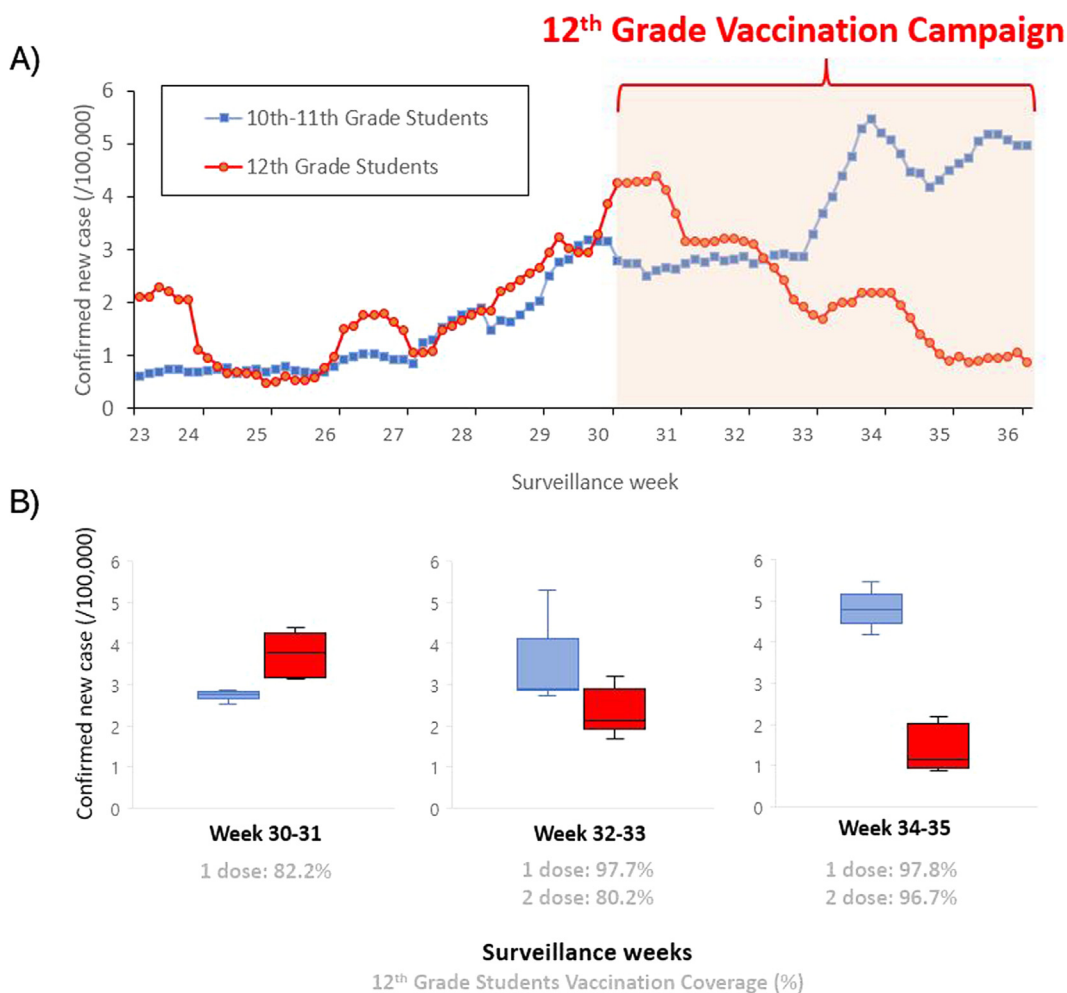


Fig. 2. A) Daily laboratory-confirmed SARS-CoV-2 infections among high school students following a nationwide 12th grade students vaccination campaign in Korea; B) Bi-weekly laboratory-confirmed SARS-CoV-2 infections and vaccination coverage rate.

Table 2
Effectiveness of BNT162b2 vaccine against SARS-CoV-2 infection in high school students following a nationwide 12th grade students vaccination campaign in Korea.

Vaccine Status	High school students			Vaccine Effectiveness	
	Case	Total	Attack Rate (%)	V.E. %	(95% C.I.)
No vaccine	3,358	863,341	(0.39)		
One dose vaccination (post 14 days)	153	444,322	(0.03)	91.1	(89.6–92.5)
Two doses vaccination (post 14 days)	15	439,079	(0.01)	99.1	(98.5–99.5)

and was associated with a significantly lower risk of SARS-CoV-2 infection. Our finding suggests that vaccination in children and adolescent may reduce the burden of Covid-19 in the community.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disclaimers

The opinions expressed by authors contributing to this journal do not necessarily reflect the opinions of the Korea Disease Control and Prevention Agency, Ministry of Education, or the institutions with which the authors are affiliated.

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