(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 5, Issue 2, Page No: 652-660
March-April 2022

IJMSCR

Adverse Events of COVID-19 Vaccine in Thai Adolescents Aged 12-18: A Cross-Sectional Survey Study

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Type of Publication: Original Research Paper
Conflicts of Interest: Nil

Abstract:

Background: The coronavirus disease 2019 (Covid-19) has affected millions of people in a worldwide pandemic. Safe vaccines are needed urgently. Still, vaccines for COVID-19 in adolescents carry little knowledge of safety.

Objective: To evaluate adverse events of the Covid-19 vaccine in Thai adolescents aged 12-18 years.

Materials and methods: This was a cross-sectional study and data were collected between October 9, 2021, and December 2, 2021. It was an online survey in the format of Google Forms and adverse events were collected following immunization and within 3 days after the receipt of the vaccine.

Results: A total of 3,132 responses were received. The median participant age was 16 years (IQR 14, 17), 58.2% were female, and 8.4% had underlying medical conditions. Overall, 99.9% received the mRNA Covid-19 vaccine (Pfizer-BioNTech) and 71.3% received the first dose. At least one of the adverse events was reported in 37.4% of the participants. Systemic adverse events were common and the most frequent were muscle pain (22.9%), headache (12.8%), and fever (12.6%). Local adverse events were less common, with 6.5% reported pain, redness, or swelling at the injection site. Compared to the first dose, fever and headache were more common after the second dose.

Conclusions: The covid-19 vaccine in adolescents had a favorable safety profile.

Keywords: Covid-19 vaccine, adverse events, adolescent

Introduction

The novel coronavirus SARS-CoV-2 was reported firstly as an epidemic in the Hubei Province of Wuhan, China in December of 2019 and was officially declared a pandemic and nominated as Covid-19 by the World Health Organization on March 11, 2020. (1) A total of 456 million confirmed cases and 6 million fatalities due to COVID-19 have been reported globally. (2, 3) Early studies showed the transmission rate and the severe consequence is high in the elderly, healthcare workers, and people with comorbidities. (4,5) However, recent studies revealed the virus largely spread the children and adolescents. Not only increased the risk of severe disease and life-threatening complications in children and adolescents, but Covid-19 also cause the negative consequences of the pandemic with restrictions on academic and social activities leading to isolation,

depression, and obesity. (6-8) Due to the reopening of schools, the transmission is increased, and the spread appeared to be more rapid in secondary schools. (9) Vaccines are one of the most significant preventive measures for bringing the Covid-19 pandemic under control. The clinical trials have shown the high effectiveness of vaccines protection against Covid-19 infection, severe-critical disease, hospital admission, and death. (10-13) However, most of the COVID-19 vaccines are approved for use in people over 18 years and the evidence in adolescents or children is limited. (13,14) On May 10, 2021, the U.S. Food and Drug Administration (FDA) issued an emergency use authorization for the mRNA vaccine in adolescents 12-15 years that previous authorization had been issued for persons starting at 16 years of age. (15)

The Royal College of Pediatricians of Thailand & Pediatric Society has recommended vaccination for children aged 12-18 since September 2021 (16) and the mRNA Covid-19 vaccine (Pfizer-BioNTech) was the first COVID-19 vaccine approved for Thai adolescents and fully licensed for ages 12 and over in Thailand on 24 June 2021. (17) Apart from the efficacy, one of the important factors of vaccine acceptance is the safety of vaccines. However, vaccines for COVID-19 in adolescents carry little knowledge of safety due to most of the early RCTs involving adult subjects over 18 years. Therefore, the objective of this study was to evaluate adverse events of the Covid-19 vaccine in Thai adolescents aged 12-18 years.

Materials and methods:

This was a cross-sectional study and data were collected between October 9 and December 2, 2021. The survey was voluntary and online in the format of Google Forms. The invitation was distributed to social media groups and those receiving vaccination at Hospital also were invited directly.

The objective of this study was to estimate adverse events after Covid-19 vaccination in adolescents aged 12-18 years. The participants were advised to collect data of adverse events occurring within the first 3 days after vaccination. The survey was developed based on the literature review of the safety results of the Covid-19 vaccine. (10,13,18-21) A preliminary version of the survey was reviewed by an expert and a researcher in the tertiary hospital to validate its content. The survey contained 2 sections: demographic characteristic data and adverse events following the Covid-19 vaccine. The response to the demographic data consisted of age, sex, and underlying medical conditions. The adverse events were specific to local and systemic symptoms that occurred within 3 days after vaccination. Local symptoms included pain, swelling, and redness at the injection site. Systemic symptoms included muscle pain, headache, fever, fatigue, weakness, nausea and vomiting, diarrhea, chest tightness, palpitation, shortness of breath, petechiae, and ecchymosis.

Ethical consideration:

This study used anonymous data and no personnel data were collected. All participations were voluntary. The invitation stated the objectives of the survey and asked for informed consent for published data. Respondents were consenting to participate in the study through the act of answering, submitting the questionnaire, and marking the checkbox to allow their information to be published.

Statistical analysis:

Descriptive analysis was used to summarize the demographic characteristics and adverse events related to the Covid-19 vaccine and are presented as frequencies and percentages. The Chi-square test was used to estimate the unadjusted association of participant characteristics (age, sex, underlying medical conditions, Covid-19 vaccine dose, and type of vaccine) and adverse events. Multivariate logistic regression was performed to identify predictors of adverse events. Statistical analysis was performed using the R program, and a p-value less than 0.05 was considered statistically significant.

Results:

A total of 3,132 respondents answered the survey between October 9, and December 2, 2021. The clinical characteristics of the participants are presented in Table 1. The median age was 16 years (IQR 14, 17), 58.2% were female, and 8.4% had underlying medical conditions.

Overall, 99.9% received the mRNA Covid-19 vaccine (Pfizer-BioNTech) and 71.3% received the first dose. At least one of the adverse events was reported in 37.4% of the participants. Systemic adverse events were common and the most frequent

were muscle pain (22.9%), headache (12.8%), and fever (12.6%). Local adverse events were less common, with 6.5% reported pain, redness, or swelling at the injection site (Table 2).

Compared to the first dose, fever and headache were more common after the second dose (Table 3).

Table 4 showed the potential characteristics associated with at least 1 of the reported adverse events. Multivariate regression analysis showed that older adolescents (16-18 years), those who were male, and those without underlying medical conditions were associated with adverse events (Table 5).

Discussion:

In this study, we collected the data of adverse events that occurred within 3 days following the vaccination because the prior studies showed that almost 95% of the adverse events following immunization occurred within three days after vaccination and generally peaked by day 2. (21, 22)

The report of at least one of the adverse events observed in the present study was 37.3%. Systemic adverse events were common and the most frequent were muscle pain (22.9%), headache (12.8%), and fever (12.6%). Local adverse events were less common, with 6.5% reporting pain, redness, or swelling at the injection site. These community-based results were less common than in the clinical trial report that studied the efficacy and safety of the mRNA Covid-19 vaccine compared to the placebo in participants 12-25 years of age. (23) They found injection-site pain in 79-86%, fatigue in 60-66%, headache in 55-65%, muscle pain in 24-41%, and fever in 7-20% of the participants. Possible explanations for the inconsistency might be from the difference in the study setting (clinical trial and community data) and the study sample (age).

Although, systemic adverse events including muscle pain, headache, and fever were the most common in this study, however, they were classified as nonserious adverse events. (22)

Compared to the first dose, fever and headache were more common after the second dose, with this result was consistent with the report of the prior study. (23)

Other reported systemic adverse events in our study including nausea, vomiting, diarrhea, chest tightness, shortness of breath, palpitation, petechiae, and ecchymosis were reported in small numbers after both the first and the second vaccine dose.

The present study had several limitations. Firstly, it was a self-reported online survey which might be some information bias such as misunderstanding of the definition of each adverse event in the questionnaire. Secondly, the accuracy of data may not be comparable with the clinical trials as lack of an unvaccinated comparison group. Thirdly, there might be some selection bias from the restrictions to only participants who could have internet access. However, in the emergency situation, this information would help parents and adolescents in consideration of vaccines to fight against the Covid-19 pandemic.

Conclusion:

The covid-19 vaccine in adolescents had a favorable safety profile.

Table 1: Baseline characteristics of the participants

Variables	**N (%)**
Age (years) median	16 (IQR 14,17)
Age group (years)	
12-15	1,249 (39.9)
16-18	1,883 (60.1)
Sex	
Male	1,310 (41.8)
Female	1,822 (58.2)
Underlying medical conditions	
No	2,870 (91.6)
Yes	262 (8.4)
Vaccination	
First vaccine dose	2,232 (71.3)
Second vaccine dose	900 (28.7)
Covid-19 vaccine	
mRNA Covid-19 vaccine (Pfizer-BioNTech)	3,128 (99.9)
BBIBP-CorV Covid-19 vaccine (Sinopharm)	4 (0.1)
Adverse events	
No	1,963 (62.7)
Yes	1,170 (37.4)

Table 2: Adverse events within 3 days following vaccination (N=3,132)

Adverse events	**N (%)**
No	1,963 (62.7)
Yes	1,169 (37.3)

- Muscle pain	719 (23.0)
- Headache	402 (12.8)
- Fever	393 (12.5)
- Fatigue	211 (6.7)
- Pain, redness, or swelling at the injection site	213 (6.8)
- Muscle weakness	100 (3.2)
- Nausea or vomiting	63 (2.0)
- Diarrhea	60 (1.9)
- Chest tightness	50 (1.6)
- Palpitation	23 (0.7)
- Shortness of breath	33 (1.1)
- Petechiae	12 (0.4)
- Ecchymosis	11 (0.4)

Table 3: Adverse events in the first and the second dose vaccine

Adverse events	**The first dose** (N=2,232) N (%)	**The second dose** (N=900) N (%)	P-value
At least 1 of the adverse events	813 (36.4)	356 (39.6)	0.1
- Muscle pain	508 (22.8)	211 (23.4)	0.7
- Headache	266 (11.9)	136 (15.1)	0.018*
- Fever	211 (9.5)	182 (20.2)	< 0.001*
- Fatigue	152 (6.8)	59 (6.6)	0.8
- Pain, redness, or swelling at the injection site	162 (7.3)	51 (5.7)	0.1

- Muscle weakness	70 (3.1)	30 (3.3)	0.8
- Nausea or vomiting	43 (1.9)	20 (2.2)	0.6
- Diarrhea	42 (1.9)	18 (2.0)	0.9
- Chest tightness	33 (1.5)	17 (1.9)	0.5
- Palpitation	29 (1.3)	5 (0.6)	0.1
- Shortness of breath	23 (1.0)	10 (1.1)	0.9
- Petechiae	11 (0.5)	1 (0.1)	0.2
- Ecchymosis	9 (0.4)	2 (0.2)	0.6

Table 4: Reported adverse events by participant characteristics

Characteristics	**No adverse events** N (%) N=1,984	**Reported adverse events*** N (%) N=1,148	**P-value**
Age group (years)			
12-15	746 (37.6)	503 (43.8)	< 0.001
16-18	1,238 (62.4)	645 (56.2)	
Sex			
Female	1,066 (53.7)	756 (65.9)	< 0.001
Male	918 (46.3)	392 (34.1)	
Underlying medical conditions			
No	1,852 (93.3)	1,018 (88.7)	< 0.001
Yes	132 (6.7)	130 (11.3)	
Vaccination			
First vaccine dose	1,435 (72.3)	797 (69.4)	0.09
Second vaccine dose	549 (27.7)	351 (30.6)	

Covid-19 vaccine			
mRNA Covid-19 vaccine (Pfizer-BioNTech)	1,982 (99.9)	797 (99.8)	0.97
BBIBP-CorV Covid-19 vaccine (Sinopharm)	2 (0.1)	2 (0.2)	

* Reported adverse events defined as at least 1 adverse event that occurred included pain, swelling, and redness at the injection site, muscle pain, headache, fever, fatigue, weakness, nausea and vomiting, diarrhea, chest tightness, palpitation, shortness of breath, petechiae, and ecchymosis

Table 5: Multivariate analysis for participant characteristics associated with adverse events

Characteristics	**Reported adverse events**	
	OR (95% CI)	**P-value**
Age group (years)		
12-15	0.77 (0.7,0.9)	< 0.001
16-18	1	
Sex		
Female	0.6 (0.5,0.7)	< 0.001
Male	1	
Underlying medical conditions		
No	1.86 (1.4, 2.4)	< 0.001
Yes	1	

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