COVID-19 vaccine safety and side effects in children aged 5-11 years: a cross-sectional study

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ABSTRACT

Introduction: The COVID-19 pandemic has prompted a global drive for vaccination, including children. Despite the urgency, understanding the safety and side effects remains crucial. Our study aimed to evaluate the safety of the Pfizer-BioNTech (BNT162b2) vaccine in children by determining the proportion of vaccinated children who experienced side effects and identifying factors associated with post-vaccination side effects.

Materials and Methods: A cross-sectional study was conducted among children who received the COVID-19 vaccine between 3 February and 8 May 2022. Data were collected using a self-administered questionnaire filled out by the parent or legal guardian.

Results: The mean age of the study participants was 9 years old and 43.1% were males. Out of the 195 participants in the study, 62 (31.8%) reported side effects after vaccination. The most frequently reported side effects were pain at the injection site (29.7%, n=58), fever (15.9%, n=31), localised inflammation (10.8%, n=21) and arthralgia/myalgia (9.2%, n=18). There were no reported severe adverse events such as anaphylaxis or myocarditis. Most side effects occurred within the first two days post-vaccination. There was a higher proportion of side effects among children with underlying co-morbidities. No significant differences were observed based on age, weight, ethnicity and the presence of allergies, or the use of premedication.

Conclusion: The BNT162b2 vaccine was generally well-tolerated in children, with most side effects being mild and self-limiting. These findings support the safety of the COVID-19 vaccine and would guide healthcare professionals, parents and policy-makers in making informed decisions about COVID-19 vaccination, especially among high-risk groups.

KEYWORDS:
COVID-19, SARS-CoV-2, vaccine, adverse effects, children

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) pandemic has significantly impacted global health, prompting the rapid development and distribution of effective vaccines. The initial vaccination efforts targeted the adult population due to their higher risk for severe disease. However, the importance of including the paediatric population in these efforts quickly became evident as part of the broader strategy to emerge from the pandemic.

Despite their general resilience, children remain susceptible to infection, often through household contacts or school settings.[1,2] Although children often experience milder forms of COVID-19,[3,4] there are instances where it can lead to severe outcomes, including the need for hospitalisation, admission to the intensive care unit and mechanical ventilation.[5-7] Additionally, they are at risk for serious post-infectious complications, such as multi-system inflammatory syndrome (MIS-C) or long COVID.[8-10] The impact of COVID-19 extends beyond health, causing disruptions to children's social interactions, school attendance and potentially affecting long-term cognitive and social development.[11] Therefore, COVID-19 vaccination plays an important role in safeguarding children against infection.

Healthcare stakeholders across the world have implemented extensive safety monitoring efforts to ensure a favourable risk-to-benefit ratio for COVID-19 vaccines. The Pfizer-BioNTech BNT162b2 vaccine, in particular, has demonstrated promising safety and efficacy in phase 2/3 clinical trials involving adolescent and younger children.[12] The safety and efficacy of the vaccine have been further demonstrated by real-world data and its broad use worldwide.[13] Malaysia initiated the National COVID-19 Immunisation Program for children aged 5-11 years (PICKids) on February 3, 2022. In this program, eligible children received two doses of Pfizer-BioNTech's Comirnaty, spaced 8 weeks apart.[14] During the period of the study, the Pfizer-BioNTech BNT162b2 was the sole vaccine approved and available for administration in the eligible paediatric population.

A detailed understanding of vaccine adverse effects is vital, as it provides healthcare professionals, parents and policymakers with the necessary information to make informed decisions about paediatric COVID-19 vaccination. There is a need to publish local data on the safety of the COVID-19 vaccine in children, where differences in ethnicity, genetic composition and environmental factors could influence the occurrences and manifestations of side effects. Therefore, we aim to evaluate the safety of the COVID-19 vaccine in children by determining the proportion of vaccinated children who experienced side effects and identify factors associated with these post-vaccination side effects.

This article was accepted: 25 October 2023
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Table I: Baseline characteristics of the study population

Baseline characteristics	Total, N=195
Age in years, mean (SD)	9 (2.0)
Weight in kilograms, mean (SD)	28.9 (10.5)
Gender	
Male	84 (43.1%)
Female	111(56.9%)
Ethnicity	
• Malay	156 (80.0%)
• Chinese	29 (14.9%)
• Indian	10 (5.1%)
Comorbidities[a]	
• None	148 (75.9)
• Respiratory	26 (13.3)
• Prematurity	11 (5.6)
• Cardiovascular	6 (3.1)
• Neurological	3 (1.5)
• Genetic	3 (1.5)
• Others	12 (6.2)
Allergy historya	
• None	155 (79.5)
• Dust	23 (11.8)
• Seafood	16 (8.2)
• Pet	11 (5.6)
• Egg	9 (4.6)
• Dairy	8 (4.1)
• Medication	7 (3.6)
• Nuts	6 (3.1)
• Others	11 (5.6)

[a]A subject may have more than one of the following subcategories

Table II: Comparison of side effects after the first or second dose of Pfizer-BioNTech (Comirnaty) vaccine

Side effect	Either dose, n (%)	First dose, n (%)	Second dose, n (%)	p-value
Any side effect	62 (31.8)	41 (21.0)	56 (28.7)	0.079[a]
Pain at injection site	58 (29.7)	40 (20.5)	51 (26.2)	0.396[b]
Fever	31 (15.9)	15 (7.7)	26 (13.3)	0.332[a]
Inflammation/redness	21 (10.8)	13 (6.7)	19 (9.7)	0.818[a]
Arthralgia/myalgia	18 (9.2)	11 (5.6)	16 (8.2)	0.850[a]
Malaise	13 (6.7)	9 (4.6)	12 (6.2)	0.951[a]
Headache	13 (6.7)	7 (3.6)	12 (6.2)	0.593[a]
Pruritus	5 (2.6)	0	5 (2.6)	-
Chills	4 (2.1)	3 (1.5)	3 (1.5)	0.695[b]
Nausea/vomiting	3 (1.5)	2 (1.0)	1 (0.5)	0.572[b]
Rash	3 (1.5)	0	3 (1.5)	-
Dyspnea	2 (1.0)	1 (0.5)	1 (0.5)	1.0[b]
Chest pain	1 (0.5)	0	1 (0.5)	-
Insomnia	1 (0.5)	0	1 (0.5)	-
Diarrhea	1 (0.5)	0	1 (0.5)	-
Lymphadenopathy	1 (0.5)	0	1 (0.5)	-
Inconsolable crying	0	0	0	-
Anaphylaxis	0	0	0	-
Myocarditis	0	0	0	-

[a]Chi-squared tests, [b]Fisher-exact tests.

MATERIALS AND METHODS

We invited a total of 516 children of hospital staff members from Hospital Tuanku Ja'afar Seremban to participate in this cross-sectional study. This group was selected because the hospital's designated vaccination centre specifically catered to these children. The children received two doses of the Pfizer Comirnaty® vaccine (BNT162b2) between 3 February and 8 May 2022 at the facility.

The parent or guardian were invited to participate in a self-administered survey via a Google form link 2 weeks after the children received their second vaccine dose. The survey was conducted in Bahasa Malaysia and consisted of the following domains: demographic details, underlying comorbidities, allergy history and description of side effects after vaccination. Participation for consent was obtained through an "I agree" checkbox in the Google form survey, signifying informed consent. Participants who selected "I disagree" would be allowed to withdraw from the study.

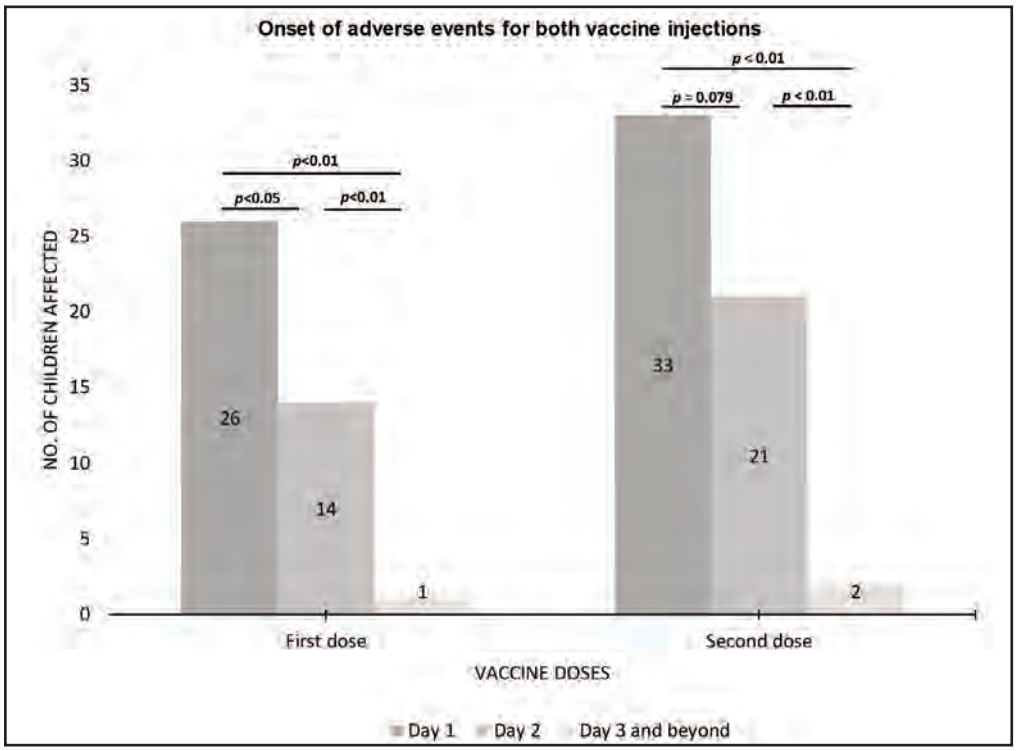

Fig. 1: Comparison of onset of side effects for both vaccine doses. *(p-values were computed via Chi-squared tests).*

The primary outcome measures were the proportion of children experiencing side effects from either vaccine dose. These side effects were reported directly by the parents or guardians, providing first-hand accounts of their child's reactions to the vaccine. Additionally, we described the vaccine's side effects and analysed sociodemographic differences between children who developed side effects from those who did not.

Data analysis was performed using descriptive statistics. Categorical variables were presented as frequencies and percentages, and continuous variables as means with standard deviations (SD). Categorical variables were compared using Chi-squared tests and Fisher exact tests, depending on whether the assumptions for the Chi-square test were met. The independent t-test was used for comparing means of continuous variables. Statistical significance was set based on a p-value of <0.05.

Ethical Approval for the Study

This study was approved by the Medical Research and Ethics Committee (MREC), and was granted the approval ID: NMRR ID-22-00987-QOQ (IIR). The survey was anonymous and ensured the confidentiality of the participant's information. No personal or identifiable data were collected during the course of the study.

RESULTS

The study included 195 participants who completed the survey. Detailed baseline characteristics of the study population are provided in Table I. The mean age of the study participants was 9 years old (SD 2.0), and 43.1% were males. The predominant ethnic group was Malays (80.0%), a representation of the hospital's workforce demographics. Nearly a quarter of the participants (24.1%, n=47) had underlying comorbidities, with respiratory disorders being the most prevalent (13.3%). A history of allergy was present in 20.5% of the participants, with dust and seafood allergies being the most common.

Our data revealed approximately one-third of the participants (31.8%, n=62) experienced side effects following immunisation with the COVID-19 vaccine (Table II). Pain at the injection site (29.7%, n=58), fever (15.9%, n=31), localised inflammation/redness (15.9%, n=21) and arthralgia/myalgia (9.2%, n=18) were the most frequently reported side effects. Although a larger proportion of participants reported these side effects after the second dose than the first, these differences were not statistically significant. Two (1.0%) of the 195 participants were hospitalised after receiving the second vaccine dose; one due to chest pain but tested positive for COVID-19, and another a child with pre-existing eczema who developed generalised rash one day after receiving the second dose of vaccine. Both cases had uneventful hospital stays. Otherwise, there were no reported severe side effects such as anaphylaxis, myocarditis or deaths.

We further investigated the onset of post-vaccination side effects. Among the subjects who developed side effects after the initial dose, 97.6% (n= 40) reported experiencing them within the first two days post-vaccination (Figure 1). The frequency of participants experiencing side effects was significantly higher on the day following vaccination

compared to the second and third days. A similar pattern was observed with the second dose, with 96.4% (n=54) developing side effects within two days.

Subsequent analysis compared the characteristics of individuals who did and did not experience side effects (Table III). We observed that the proportion of participants who experienced side effects was higher among those with underlying comorbidities compared to those without (33.9% vs. 19.5%, p=0.029). A sub-analysis of the various comorbidities showed no specific comorbidity was associated with a higher proportion of side effects. Otherwise, no significant differences were observed based on age, weight, sex, ethnicity and the presence of allergies between both groups. We also examined the potential effect of premedication on post-vaccination side effects. Premedication regimens included common drugs such as paracetamol, antihistamines, non-steroidal anti-inflammatory drugs (NSAIDs) and steroids. There were no significant differences in the proportion of participants developing side effects between the premedicated and non-premedicated groups.

In our study, 17.4% (n=34) were diagnosed with COVID-19 following the first dose of vaccination, prior to the administration of the second dose. Following the second dose, this proportion decreased significantly to 4.6% (n=9), a change which was statistically significant (p<0.001). Notably, none of the participants who developed COVID-19 following vaccination required hospitalisation.

DISCUSSION

In Malaysia, a remarkable 3,312,886 doses of COVID-19 vaccines have been administered to children aged 5 to 11 years as of 31 December 2022, according to the National Pharmaceutical Regulatory Agency (NPRA).[15] National data revealed 523 adverse events following immunisation (AEFI) reports in this age group, translating to a rate of 158 AEFI per 1,000,000 doses administered. The AEFI rates in children were lower than the overall AEFI reporting rate (369 per 1,000,000 doses), with the vast majority (94%) being non-serious effects. This data highlights the vaccine's favourable safety profile.

In line with this national data, our study found that approximately one-third of the participants reported mild, self-limiting side effects post vaccination. These findings are consistent with data from other international vaccine safety reporting platforms and the NPRA, as well as our previous publication among the adult population.[15-17] Myocarditis was notably absent in our cohort, a risk often associated with COVID-19 vaccination in adult and adolescent populations.[18,19] The disparity may be due to differences in vaccine dosage and scheduling. The children vaccine contains lower doses and are spaced eight weeks apart, as opposed to the three-week interval used in adults during the pandemic. This regimen likely contributed to a lower incidence of severe adverse events in children.

Our findings reveal that most side effects appeared soon after vaccination and predominantly within the first 2 days. This pattern remained consistent across both doses of the vaccine, and tally with the findings from other studies.[17,20] Notably, some children did contract COVID-19 following vaccination. However, none of them required hospitalisation, suggesting the vaccine mitigated the disease severity. We also observed a decrease in the number of reported COVID-19 following the second dose of the vaccine. However, drawing definitive conclusions about the vaccine role in prevention of COVID-19 is challenging, due to the coincidental decline in COVID-19 incidence during this period.

In our analysis, a higher proportion of participants with pre-existing comorbidities experienced side effects when compared to their healthy counterparts. This observation could be due to the more attentive health monitoring by their parents, leading to them being more likely to report any perceived side effects following vaccination. However, it is important to clarify that this observation does not imply the vaccine poses increased risk for children with pre-existing conditions. The presence of comorbidities are recognised risk factor for severe outcomes in paediatric COVID-19.[21] The WHO's Strategic Advisory Group of Experts on Immunisation (SAGE) recommended that these children should be given a medium to high priority in receiving COVID-19 vaccines.[22] This recommendation highlights the significant benefits of vaccination, which outweigh the potential risks of side effects. Prior studies have identified a history of allergy as a risk factor for side effects following vaccination, potentially due to the heightened immune system responses to certain substances.[23,24] The COVID-19 vaccine adverse reactions have been thought to be related to an ingredient called polyethylene glycol (PEG), a component of lipid nanoparticle used to encase and stabilise the mRNA, aiding its delivery into the cells.[25] However, our data did not show any significant differences in the occurrence of side effects between children with pre-existing allergies and those without. Additionally, the proportion of participants who experienced side effects was comparable between those who received premedication and those who did not, suggesting that premedication may not be necessary for COVID-19 vaccination.

This study has several limitations. First, the single-centre nature of this study limits the ability to generalise our findings to the general population. However, focusing on our local community allowed for a detailed exploration of vaccine side effects, capturing specific details which are potentially overlooked in broader national data. Our study's results on the onset of adverse effects and the analysis of factors such as age, weight, comorbidities, allergy history and premedication usage add valuable information, complementing the broader data reported by the NPRA. Second, participation in the study was voluntary and dependent on the willingness of the vaccine recipient's parents to respond to our invitation. This may have introduced a degree of selection bias, as parents of children who experienced side effects may have been more inclined to participate in the study. Third, our study had a lower-than-expected response rate. While the low response rate can impact the representativeness of our findings, it does not undermine the valuable insights gathered from those who chose to participate. Lastly, as the Pfizer-BioNTech (Comirnaty) vaccine was the only one administered to the target population, a comparison with other vaccine types was not possible.

CONCLUSION

In conclusion, our findings demonstrate the generally mild and manageable side effects experienced by children following COVID-19 vaccination. This study adds to the body of evidence supporting the safety of COVID-19 vaccines in the paediatric population and serves as a historical record of the vaccine safety during this unprecedented pandemic that deeply impacted our nation. Additionally, our study offers crucial insights into the patterns of these side effects and their influencing variables. This data would aid in informed decision-making and parenteral counselling processes. Future research involving a larger and more diverse sample size and comparison across different types of COVID-19 vaccines would be beneficial for a more comprehensive understanding of paediatric COVID-19 vaccination.

ACKNOWLEDGEMENT

We thank the Director-General of Health Malaysia for permission to publish this article. We would also like to acknowledge Dr Essazul Imran bin Mohd Aris and all staffs from the Occupational Safety and Health Unit (UKKP) of Hospital Tuanku Ja'afar Seremban for their valuable contributions and support for this project.

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