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COVID-19 Vaccination and COVID-19 Complication: Multisystem Inflammatory Syndrome in Children (MIS-C) What Parents Should Know?

First published on 22 February 2022 by Nur Aazifah, Nurul Iman Hafizah and Boon-How Chew for the Pandemic Scientific Response team.

Caution: Summary is a preliminary report of work by Pandemic Scientific Response team. It will be continuously updated in accordance to the unfolding of events and emerging of scientific evidence.

In Brief

- The rates of COVID-19 infection among children aged 5 to 11 years old in Malaysia is alarming following the emergence of new virus variant, Omicron.
- Despite high infection rates, the vaccination rate is still slow with only 12% of children has received their first dose which could be attributed by parents' hesitancy towards the vaccine.
- Due to high infection rates of COVID-19, there is an increased risk of getting COVID-19 complications especially among unvaccinated children. As such, myocarditis, respiratory failure, neurological complications and multisystem inflammatory syndrome (MIS-C) are among post-COVID-19 complications that raised concern among medical practitioners.
- Data have shown that there were 174 cases of MIS-C following COVID-19 infection reported since June 2020 until December 2021, with 7 deaths recorded (4%). This trend shows higher mortality rate as compared with data from other countries such as in the United Kingdom and United States.
- To date, only Pfizer-BioNTech Comirnaty vaccine has been approved and proven safe and effective against COVID-19 infection for children.
- Common side effects of vaccination are fever, fatigue, headache, vomiting, diarrhoea, muscle pain and joint pain. Out of 8.7 million doses of COVID-19 administered, only 2.4% (100/4239) reported serious events that either requires urgent medical attention, life-threating illness, permanent disability, congenital anomaly or birth defect or death.
- Latest data shows that vaccine offers up to 90% protection against COVID-19 infection among children.
- This response draws current published data on efficacy of COVID-19 vaccine against COVID-19 infection and post-infection complications among children aged 5 to 11 years old.

Summary

The vaccination uptake among children (5-11 years old) at Malaysia is in much slower trend since its launch at the early February 2022 under the National COVID-19 Immunisation Programme for Children (PICKids), as compared to the teenager and adult gr oups. Up until now, only 12.8% [2] children had received their first dose of the COVID-19 vaccine as of (20 February 2022)). An online survey done by a group of researchers from UM and UMS to assess the willingness of parents to vaccinate their children under 12 years old found that the hesitancy of the parents is attributed to the uncertainty towards the new vaccine in terms of the long-term effect of vaccine, doubt about the content of the vaccine as well as having a belief that the vaccine is unsafe for their children [14].

However, different concern raised among medical practitioners whereby vaccination against COVID-19 should be highly considered for children in order to prevent further complications related to COVID-19 infection such as MISC, myocarditis, respiratory failure, neurological complication as well as post COVID conditions [17, 18]. Initially, previous studies have shown that children are less susceptible from COVID-19 complications compared to adult [12]. However, since April 2020 there has been reports on a newly recognized syndrome related to SARS-CoV-2 infection characterised by hyperinflammation and muti-organ involvement in children called MIS-C.

What is MIS-C?

MIS-C is characterised by a severe illness requiring hospitalisation, usually presented with fever, elevated inflammatory markers and multisystem dysfunction in the setting of recent proven or probable COVID-19 infection, in the absence of alternative diagnosis[5]. MIS-C generally occurred 2-6 weeks after a typically asymptomatic and mild infection with COVID-19[6-10]. The MIS-C cohort of patients are younger than the severe COVID-19 patients (median age 6 years versus 13 years old) and associated with vascular injury and cardiac disease[5].

How Dangerous It Is?

Up to 68% of the patients with MIS-C require intensive care, while inotropic support was required in 40% and the mechanical ventilation was required in 15% of MIS-C cases [11]. The fatality rate was reported at 1.7% in US and 1.4% in Europe [11]. In Malaysia, there were **174** cases of MIS-C reported since June 2020 until December 2021, which the largest proportion from 5 to 9 years old age group, with **7** deaths recorded (4%). This indicates higher mortality rate as compared with US and Europe studies, as mentioned previously. However, the surveillance of long-term complications of MIS-C in world-wide is still ongoing.

COVID-19 Vaccination for Children

To date, only Pfizer-BioNTech Comirnaty vaccine has been both approved by the US Food and Drug Administration (FDA) and the National Pharmaceutical Regulatory Agency (NPRA) and proven safe and effective to be used as a COVID-19 vaccine for children. In a recent published trial by E.B Walter et al (2021) showed that common adverse reactions of COVID-19 vaccination in Phase 2 and Phase 3 randomised clinical trial among children 5-11 years old are fever, fatigue, headache, chills, vomiting, diarrhoea, muscle pain as well as joint pain. The adverse reaction more commonly observed after the second dose injection. Table 1 showed the frequency of adverse reaction following vaccination on phase 2 and 3 trial as well as the comparison with placebo.

Table 1: Adverse events related to COVID-19 vaccination

Adverse Reaction	Recipient (N = 1517)		Placebo N=751	
	First dose	Second dose	First dose	Second dose
Local event				
Redness	15	19	6	5
Swelling	10	15	3	3
Pain at the injection Site	74	71	31	29
Systemic events and use of medication				
Fever	3	7	1	1
Fatigue	34	39	31	24
Headache	22	28	24	19
Chills	5	10	5	4
Vomiting	2	2	1	1
Diarrhoea	6	5	4	5
Muscle pain	9	12	7	7
Joint Pain	3	5	5	4
Use of antipyretic medication	14	20	8	8

Source: E.B Walter et al. (2022). Evaluation of the BNT162b2 Covid-19 Vaccine in Children 5-11 years of age. *N Engl J Med*;386:35-46

The study, however, did not have enough power to detect the rare events and severe side effects of the vaccination. In addition, Centres for Disease Control and Prevention (CDC) reviewed the post licencing surveillance through Vaccine Adverse Event Reporting System (VAERS) as well as v-safe found out that from an approximate 8.7 million doses of Pfizer-BioNTech COVID-19 administered, there were 4249 (0.0005) reports of adverse reaction following vaccination. Of such, 97.6% of the reports were not serious adverse reaction while there remaining 2.4% (N=100) was classified as serious event. Adverse event is considered serious if the either one of the following is reported: **hospitalisation, life-threatening illness, permanent disability, congenital anomaly or birth defect or death**.

The most commonly reported conditions among the 100 reports of serious events were fever (29; 29.0%), vomiting (21; 21.0%), and increased troponin (15; 15.0%). Among 12 serious reports of **seizure**, one child experienced **syncope** (not seizure) and another child potentially experienced syncope, two children experienced **febrile seizure**, one child had a history of seizures, two children had a potentially evolving seizure disorder, and five children experienced new-onset seizures. Among 15 preliminary reports of **myocarditis** identified during the analytic period, 11 were verified and met the case definition for myocarditis of these 11 children, seven recovered, and four were recovering at time of the report. The occurrences of serious adverse reaction more common to occur in male with mean age of 9.

Most of the adverse reaction is mild and tolerable consistent with the trial conducted by E.B Walter et and most serious event able to recover with in short period of time.

What is the Dose of COVID-19 Vaccine for Children Aged 5 to 11 Years Old?

The dose allowed for children is only 10-µg with 8 weeks apart between the two doses as compared to the recipients of 12 years and above, with approved dose of 30-µg and 4 weeks apart between injections.

Why mRNA Vaccine?

Infection-induced antibody response is lower and less consistent compared with mRNA vaccine-induced antibody response.

Facts About COVID-19 mRNA Vaccines

1. **COVID-19 mRNA vaccines cannot give someone the virus that causes COVID-19 or other viruses.**

   mRNA vaccines do not use the live virus that causes COVID-19 and cannot cause infection with the virus that causes COVID-19 or other viruses.

2. **They do not affect or interact with our DNA in any way.**

   mRNA never enters the nucleus of the cell where our DNA (genetic material) is located, so it cannot change or influence our genes.

3. **The mRNA and the spike protein don't last long in the body.**

   Our cells break down mRNA and get rid of it within a few days after vaccination. Scientists estimate that the spike protein, like other proteins our bodies create, may stay in the body up to a few weeks.

Why Do Children Need to be Vaccinated Against COVID-19?


Photo source: Adib Rawi Yahya from The Sun

The rapidly increasing positive COVID-19 cases among paediatric population is alarming. Data from COVIDNOW [3] showed almost 15 % from the total case are from the age 0-11 years old. Up till date, COVID-19 cases increased from average of 500 cases (baseline since January 2022) daily to almost 3500 cases daily (7-fold increment) which may be attributed by school opening as well as the emergence of omicron variant. According to Director General of Health Malaysia [16,17], the total number of children below 12 years old contracted COVID-19 were more than 50 000, and 32 from that figure develop COVID category 4 and 5 (1 in 1588). This figure was recorded only since January 2022 until mid-February. With the increasing number of cases, hospitalisation rate is expected to increase and the likelihood for a child to get MIS-C from COVID-19 infection will increase as well. Approximately 1 in 3200 COVID-19 infection among paediatric will develop MIS-C and 1-2 percent will die [6-9].

Currently, the observed vaccine efficacy in the trial is 90.7% (95% CI, 67.7-98.3) which means the recipient of vaccine have 90% protection from infected with COVID-19. By reducing the number of COVID-19 infection the proportion of severe complication cases arise especially MIS-C will reduce as well.

Can Vaccine Prevent Children from Developing MIS-C if the Child is Infected with COVID-19?

Pfizer-BioNTech vaccine is highly effective (Vaccine effectiveness is 91% (95 CI 78%-97%)) in preventing MISC for age 12-18 years old[4]. The study showed 95% patient affected with MISC were unvaccinated and the outcome for 5% vaccinated child with MISC is better were none of them require ventilatory or cardiovascular support[4]. Unfortunately, since the vaccination for 5-11 years old just started, there was currently no published data to investigate such outcomes.

Conclusion

The main question arises whether the benefits of vaccination against COVID-19 infection outweighs the long-term adverse reaction associated with the vaccination. Thus, the long-term surveillance post vaccination is utmost important.

However, parents need to be aware that vaccination for the young children are not only protective against COVID-19, but also to protect against severe infection related to undiscovered impacts of new variants as well as protection against post COVID conditions or previously known as long COVID complications.

In the community level, children vaccination will be able to reduce community transmission which further lead to avoidance of isolation, quarantine, school closure and other possibilities towards lockdowns.

Precaution is greatly needed to anticipate more cases with newly found variant called Omicron which can spread much faster and more infective than the Delta variant.

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