Original Article

Systematic Review On Covid Vaccination In Children- Assessment Of Safety, Immunogenicity, Efficacy And Adverse Effects

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Abstract

Introduction: The recent pandemic outbreak Covid-19 has led to substantial illness and ultimate mortality across the globe and children are highly are in the verge of being in a critical role as vectors in the transmission of SARS-CoV-2 in the community. There are quite a few studies which have observed that the vaccinated individuals who become infected again are on the side fewer side to transmit the virus due to reduced viral load and the duration of virus shedding and as a result, transmission from vaccinated individual to household contacts is significantly lower. This systemic review was thus undertaken with the objective of analysing the literature that were available on the safety, immunogenicity, efficacy and if any adverse effects of covid vaccination in children.

Material and Methods: We conducted both a systematic review. This review was solely based on the predefined protocol and it was conducted in concordance with PRISMA guidelines.

Conclusion: The available data reports similar efficacy and safety in children as of adults. Therefore, more clinical trials are needed to be conducted and published for evaluation of safety and if any long-term effects of Covid vaccines.

Keywords: Covid vaccine in children; covid vaccine efficacy; Corona vaccine

INTRODUCTION

The recent pandemic outbreak Covid-19 has led to substantial illness and ultimate mortality across the globe[1] and the observed incidence of Covid-19 among adolescents aged 12 to 17 years from April 1 through June 11, 2021 was reported to be approximately 900 per 100,000 population.[2] The global morbidity, mortality, and societal disruption caused by the coronavirus disease 2019 (Covid-19) pandemic prompted accelerated clinical vaccine development and regulatory interventions to mitigate some of its consequences.[3]

Inadvertent and prolonged school closures and long-term quarantine have created a havoc with the psychosocial health of children.[4] Children are greatly playing a significant role as vectors in the transmission of SARS-CoV-2 among the communities.[5]

Therefore, decrease in virus transmission has been observed in children who area vaccinated and thus will help in reducing severe cases in adults and will also tend to reduce the risk of developing certain new variants of virus.[6] There are quite a few studies which have observed that the vaccinated individuals who become infected again are on the side fewer side to transmit the virus due to reduced viral load and the duration of virus shedding and as a result, transmission from vaccinated individual to household contacts is significantly lower.[7-9]

The factors that are to be taken into account is that efficacy and safety of the vaccine among the given population.[10] This systemic review was thus undertaken with the objective of analysing the literature that were available on the safety, immunogenicity, efficacy and if any adverse effects of covid vaccination in children.

MATERIAL AND METHODS

Data sources and search strategy

This review was solely based on the predefined protocol and it was conducted in concordance with PRISMA guidelines. We were sought to conduct a systematic search based on the Web of Science (www.webofknowledge.com), PubMed (www.ncbi.nlm.nih.gov/pubmed), Google Scholar (scholar.google.it) and Scopus (www.scopus.com) databases for

publications. The following terms were searched 'covid vaccine in children', 'covid vaccine efficacy', 'Corona vaccine', 'Covid-19 pandemic' and safety of covid vaccine' and 'immunogenicity of covid vaccine' as keywords for literature search which was limited to only reports published in the English language.

Study selection and eligibility criteria

The study protocol basically includes various observational studies, non-randomized clinical studies and randomized controlled trials (RCTs) with a collection of data being recorded from trials of covid vaccine in children aged between 2-17 years. One of the most important criteria for the initial selection of studies was the evaluation of the safety, immunogenicity, efficacy and if any adverse effects of covid vaccination in children.

Exclusion criteria

The exclusion criteria included studies that were duplicate, studies with small, studies that do not provide useful information, case reports, reviews or editorials, only adult cases- based studies.

Data extraction, Process of screening and selection of articles:

All the citations along with the title and abstract was added to a specified endnote library and final list of studies to be screened for inclusion in the study was prepared by removing the duplicates. Articles were carefully screened by assessment of the title and thorough reading the abstracts to shortlist the studies which are likely to satisfy the inclusion criteria of the review. Attempts were made to obtain full-text articles for the satisfaction of inclusion and exclusion criteria. Studies not satisfying inclusion criteria was excluded further.

RESULTS:

Almost over a total of 250 articles were recognised and identified from the search of major databases and manual screening of the list of references of related data generated after the articles. Based on titles and abstracts, 27 full texts articles were retrieved among them 21 articles were excluded. So, a total of 6 articles were excluded in the review. Across 6 studies providing relevant data, were analysed. There is one ongoing study that had been carried out among Indian children titled phase II/III, open label, multicenter study to assess the safety and immunogenicity of the whole-virion inactivated SARS-CoV-2 vaccine (COVAXIN®) in a healthy volunteers age ≤18 to ≥2 years with a total sample size of 525 healthy volunteers but could not enroll it into analysis as it was in recruiting phase still to be published. Table 1 summarizes the local and systemic reactions, efficacy and immunogenicity of Covid vaccination in children and adolescents.

Table 1: Local and systemic reactions, efficacy and immunogenicity of Covid vaccination in children and adolescents

Author (year)	Local reactions	Systemic reactions	Efficacy	Immunogenicity
Walter EB et al[11] (2022)	Injection-site pain (71 to 74%) Lymphadenopathy (0.9%) and in placebo recipient (0.1%) (as reported 7 days after injection)	Severe fatigue (0.9%), headache (0.3%), chills (0.1%), and muscle pain (0.1%) (as reported 7 days after injection)	90.7%	-
Olson SM et al[12] (2021)			106 case-patients aged 12–15 years (VE = 91%)	-
Glatman-Freedman A et al[13] (2021)	Not reported	Not reported	For 16 year old individuals, at the 15- 21 days period after the second dose, ranged between 97.7% (95% CI: 95.9 98.7%) for deaths and 98.6% (95% CI: 97.8 99.1%) for severe/critical disease.	-
Frenck Jr RW et al[14] (2021)	injection-site pain [in 79 to 86% of participants]	fatigue [in 60 to 66%], and headache [in 55 to 65%])	100% (95% CI, 75.3 to 100).	The geometric mean ratio of SARS-CoV-2 50% neutralizing titers after the 2nd dose in 12-to-15-year-old participants related to 16-to-25-year-old participants was 1.76 (1.47 to 2.10)
Ali K et al[15] (2021)	mRNA-1273 group: injection-site pain (in 93.1% and 92.4%, respectively); placebo group: injection-site pain (in 34.8% or 30.3%, respectively)	mRNA-1273 group: headache (in 44.6% and 70.2%) and fatigue (in 47.9% and 67.8%); placebo group: headache (in 38.5% and 30.2%) and fatigue (in 36.6% and 28.9%)	The immune response was similar to that in young adults, and the vaccine was efficacious in preventing Covid-19.	98.8% serologic response is being identified among adolescents; absolute difference in serologic response between the adolescents and young adults was observed as 0.2percentage (95% CI, −1.8 to 2.4).
Han B et al[16] (2021)	73 [13%] of 550 participants developed pain at the injection site, occurring in 36 (16%) of 219 participants in the 1·5μg group, 35 (16%) of 217 in the 3 μg group, and two (2%) in the alum-only group	-	-	In phase 2,180 of 186 participants experienced sero-conversion (96·8% [93·1–98·8]) in the 1·5μg group and 180 of 180 participants (100·0% [98·0–100·0]) in the 3·0μg group, with the geometric mean titres of 86·4 (73·9–101·0) and 142·2 (124·7–162·1)

DISCUSSION

The present meta-analysis of the literature found that the efficacy of vaccine is 90.7% to 100% in children and Ali K et al[15] revealed that the immune response is equivalent to that in young adults, and the vaccine was efficient in preventing Covid-19. Glatman-Freedman A et al[17] reported that the rate of reduction of hospital stay, severe to critical disease and deaths of 16-years aged individuals who became SARS-CoV-2-positive for 14- 20 days after the first vaccine dose were 44.2% (95% CI:27.3 57.3%), 46.8% (95% CI: 32.9 57.9%) and 36.4% (95% CI: 8.6 50.4%), respectively. Individuals aged 16 years experienced the highest VE against the incidence of new cases and for all the outcomes that were reached at the 15 to 21 days period after the second dose, ranging from 97.7% (95% CI: 95.9 98.7%) of mortality and 98.6% (95% CI: 97.8 99.1%) for debilitating disease injection-site pain [in 79 to 86% of participants] fatigue [in 60 to 66%], and headache. 14 to 20 days after the first dose, the VE estimated to be in the range between 54.3% (95% CI: 50.6 57.8%) for infection and 77.3% (95% CI: 71.2 82.1%) for severe/critical disease. Similarly, Frenck Jr RW et al[14] reported that BNT162b2 had favorable safety and adverse effect profile among those participants who are without evidence of previous history of SARS-CoV-2 infection, no Covid-19 cases with an onset of 7 or more days after dose 2 were noted among BNT162b2 recipients, and 16 cases occurred among placebo recipients. The efficacy of vaccine was observed to be 100% (95% CI, 75.3 to 100).

In contrast to that, Xiaohui Zou et al[18] found that COVID-19 vaccination among adults cannot assure the same effective performance in children as that of adults. Post vaccination COVID-19 illness observed among adults was identified by the onset of symptoms in acute respiratory illness; but mostly in children, many of the COVID-19 cases are observed mild and asymptomatic and therefore the parents might not be aware of the infection since children might fell sick more often when compared to adults (such as with common colds), which would make the infection rate highly underestimated and efficacy overestimated. Similarly, Frenck Jr RW et al[14] reported that BNT162b2 found that adverse effects were mild-to-moderate reactogenicity observed for short-term (predominantly injection-site pain [in 79 to 86% of participants], fatigue [in 60 to 66%] and headache [in 55 to 65%]);but there were no serious adverse events and few overall severe adverse events after vaccination. Precaution should be taken to assess the long-term effect of vaccine on children's who are younger than 12 years.[18]

R.W. Frenck Jr et al[14] conducted research in ongoing phase III trial, in which 2260 adolescents aged between 12 to 15 years, BNT162b2 was observed to be safe and highly effective (efficacy 100% (95% CI, 75.3 to 100)). Sinovac's mRNA vaccine CoronaVac is available for commercial use in children aged ≥ 3 years in China, on the basis of a phase I/II trial revealed acceptable safety and a very strong immune responses in 100% of participants in the higher dose group.[19] BNT162b2 (Pfizer; BioNTech) was the first COVID-19 to be approved in children (aged 12–15), initially in Canada and later in several other countries.[20] Moreover, after obtaining the emergency approval of COVID-19 vaccines for children aged between 12 and 15 years old, it was recently obtained in the United States and Europe, it is important to evaluate the interest to vaccinate children with a COVID-19 vaccine among the lower- and middle-income countries (LMICs). In view of this, Bono SA et al[21] launched an online cross-sectional survey in several LMICs and found that of the 6571 participants, among them 64.0%, 72.6%, and 92.9% were made to vaccinate children at 50%, 75% and 95% effectiveness levels. Among the applicants who were undergraduates and those who were worried/fearful about COVID-19, had increased knowledge scores with respect to COVID-19 and a higher belief that COVID-19 vaccination is meticulous to protect others showed more interest to accept COVID-19 vaccination of children. Children who are constituted under COVID-19 vaccination will actually limit the spread of the virus, particularly in schools which may eventually decrease the need for school closures which has a potent negative effect on child development. Ruggiero KM et al[22] undertook a study on parents' attitude to effectively vaccinate their children against COVID-19 and observed that only 21.93% of the subjects had observed with overall vaccine hesitancy (VH). Half of parents included in the study (49.45%) informed that they want the COVID vaccine for their child whereas 44.17% had other plans to vaccinate against COVID once the vaccine becomes commercially available all over. There are few parents who are hesitant about vaccine due to their concern for vaccine side effects (61.5%) and vaccine safety (48.96%). Additionally, a correlation between parents who were planning to vaccinate their child against the flu and being less VH about a COVID-19 vaccine for their child.

The efficacy of vaccine is reported to be about 100% as per the reports announced from Moderna's mRNA-1273 in adolescents in the age range between 12–17 years and its approval at this age group is highly anticipated among the parents and caretakers. Moderna vaccine have also displayed a trial in children aged between 6 months to 12 years.[23] Moreover it has been established those vaccinating children is mandatory to attain herd immunity and limit the severity of COVID-19 and safety should be taken into account as the paramount factor before COVID-19 vaccine being rolled out in younger age group children. Upon consideration of the unique host immunity response and stage of children development, surveillance of the vaccine in the commercial market its safety should be considered and should be constantly observed for a longer period than that seen in adults.[18]

CONCLUSION

The available data reports similar efficacy and safety in children as of adults. Therefore, more clinical trials are needed to be conducted and published for evaluation of safety and if any long-term effects of Covid vaccines.

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