

Review Article

Children and COVID-19 Vaccine: A Public Health Ethics Perspective

*Nurunnabi ASM¹, Ashique SS², Jahan A³, Sweety AA⁴, Sharmin S⁵

Abstract

As COVID-19 cases were in rise all over the world and the World Health Organization declared a pandemic, there was an increasing focus on availability of new vaccines and drugs against the virus. Meanwhile, we already have several vaccines in COVID-19 vaccination programmes across the globe. During the process of development and clinical trials of the vaccines, several questions were popped up by multiple stakeholders about child vaccination against COVID-19. Most of the queries focused on safety of COVID-19 vaccines, the clinical trial process, priority criteria of getting a vaccine, why and why not children be included in the vaccination programme. In adult population of the country, COVID-19 vaccination programme is being carried out in an unequalled state; the focus is now on paediatric population, as some countries have already started to vaccinate children. At the time of writing this paper when Government of Bangladesh has not yet decided to vaccinate children in the country but initiatives has been taken by health department for above 12 years children vaccination. However, this paper aims to discuss potential ethical dilemmas related to COVID-19 vaccination in children especially in low-resource settings and dig into effective strategies to implement COVID-19 vaccination programme properly in the field of public health.

Keywords: COVID-19 vaccine, children, clinical trial, ethical issues, public health

1. *Dr. Abu Sadat Mohammad Nurunnabi, Graduate Student, Dalla Lana School of Public Health, University of Toronto, ON, Canada; Email: abu.nurunnabi@mail.utoronto.ca
2. Dr. Shamsi Sumaiya Ashique, Assistant Professor, Department of Paediatrics, National Center for Control of Rheumatic Fever & Heart Disease, Sher-E-Bangla Nagar, Dhaka-1207, Bangladesh
3. Lt. Col. (Dr.) Asmay Jahan, Associate Professor, Department of Paediatrics, Army Medical College Bogura, Bogura Cantonment, Bogura-5801, Bangladesh
4. Dr. Afroza Akbar Sweety, Assistant Professor, Department of Virology, Dhaka Medical College, Dhaka-1000, Bangladesh
5. Dr. Saida Sharmin, Associate Professor, Department of Community Medicine, International Medical College, Tongi, Gazipur-1711, Bangladesh

* For correspondence

INTRODUCTION

During the global coronavirus disease 2019 (COVID-19) pandemic, which has resulted in considerable illness and death around the world,¹ the incidence among adolescents between 12 and 17 years of age was very less in the beginning.^{2,3} However, the rate of infected children and their absolute numbers seem to be increasing day by day.⁴ Since illness was found generally milder in children than adults, children can have severe disease leading to hospitalization.^{5,6} Approximately one third of adolescents hospitalized because of COVID-19 needed an intensive care unit (ICU) support; among them, mechanical ventilation was ensued to 4.9% cases.⁶ Moreover, it is evident that long-term complications, such as multisystem inflammatory syndrome in children (MIS-C) may follow primary infection as occurred in many cases.^{7,8} School-age children represent a high proportion of COVID-19 cases in recent times in many countries, and played an important role in the transmission of infection including spread of the highly transmissible variants.⁹⁻¹² Meanwhile, in Bangladesh, people of the country are experiencing the third COVID-19 wave, as fueled by the delta variant first detected in neighbouring country, India.¹³ It has hit fast on the heels of a springtime second wave, and during a shortage in vaccine doses. In some of the low-income countries with low vaccination rates, e.g., Bangladesh, coronavirus cases are surging. As COVID-19 cases were in rise around the world, there was availability of new vaccines and drugs against the virus. Meanwhile, we have got several vaccines in our vaccination program against COVID-19 around the world and so many are still in the pipelines.¹⁴ During the process of development and clinical trials of the vaccines, several questions were popped up by multiple stakeholders about child vaccination. Most of the queries focused on safety of COVID-19 vaccines, the clinical trial process, priority criteria of getting a vaccine, why and why not children be included in the vaccination. This paper aims to discuss potential ethical dilemmas related to COVID-19 vaccination in children especially in low-resource settings and dig into effective strategies to implement COVID-19 vaccination programme properly in the field of public health.

ETHICAL ISSUES

The very first issue came up is that the approval procedure for COVID-19 vaccine is quite different in comparison to any typical vaccine. Because of severity of this pandemic situation, the FDA adopted an Emergency Use Authorization (EUA) for this vaccine, which bypasses the standard protocol or steps to vaccine licensing and termed as “Biologics License Application (BLA) process”. Interestingly, this rigorous process also requires “comprehensive data on the vaccine's safety and efficacy” but not as comprehensive as needed in the standard process; however, it is authorized after multiple review by the advisory committees.¹⁵ Thus, BLA promotes trust and confidence among clinicians and public as well. However, EUA focuses on a reasonable balance between availability of a vaccine in a short time and vaccine's safety and effectivity.^{15,16}

The second issue is that usually children do not take part in any clinical research until phase-3 trial, where a vaccine is tested for its efficacy and safety by administering it to thousands of people. Typically, this was done in adults COVID-19 vaccines, which are already approved and in the waitlist.¹⁷ However, scientists demanded more compelling safety data of those vaccines before any paediatric trial.¹⁷⁻²⁰ As children are vulnerable and heterogeneous population, we hardly calculate paediatric doses by simply measuring body weight in all cases, and some drugs may affect children badly despite their proven safety in adult population. Hence, it is important to weigh the risks and benefits while designing any vaccine research in paediatric population.²⁰⁻²⁴

Nevertheless, in terms of public health measures, to ensure safety, control the spread of infection, and maximize benefit for overall population, children should be vaccinated. Hence, scientists argued in favour of gathering safety and efficacy related data of all ongoing COVID-19 vaccine trials in different countries. Looking at those data that are available to date, they supported enrollment of children in vaccine trials. However, they urged that teenagers would be enrolled at first, and after proper observation of adverse effects, outcome and follow-up, inclusion of younger children and infants would be justifiable.^{17,22,25}

At the time of writing this paper, in different countries, only approved vaccine for children (i.e., 12-18-year old), is the “Pfizer-BioNTech BNT612b2 vaccine”.²⁶ To set priority, based on proportion of severity of infection with SARS-CoV-2 and further complications, children with comorbidities and physically/mentally challenged are

allowed to get vaccines first comparing with normal healthy children.²⁷ Moreover, it is crucial to allow more time to gather safety and efficacy data of any vaccine that will ultimately show grounds for approval to use in children.^{17,22}

The American Academy of Pediatrics has also advocated for the inclusion of children in paediatric COVID-19 vaccine testing.²⁸ However, we know that enrollment of children in biomedical research involves weighing risks and benefits, i.e. a balance between access (to experimental but potentially life-saving therapeutics) and protection (from unsafe or ineffective therapeutics).^{21,22,24} As noted, children under the age of 12 years have yet to be enrolled in COVID-19 vaccine trials.^{17,29} This omission can be justified ethically by the need to ensure adequate safety data are obtained in adults who can give a voluntary and informed consent to participate in such trials, particularly since adults bear the major burden of disease.^{22,24} To date, multiple real-world effectiveness studies from the United States and other countries demonstrate that recommended two-dose mRNA COVID-19 vaccine is estimated 64-99% effective against infection, and able to reduce 87-97% risk of hospitalization.²⁹ Another reason for child vaccination is to consider protection of the wider population, as we do in case of any preventable infectious disease. When any child or adult is infected with the coronavirus, it may get a chance to mutate and create a variant in the host body that might come up being more virulent and resistant to all available therapies. Hence, the more we can reduce infections and re-infections in the population, the more we will bar to emergence of new variants and ultimately reduction of costs in healthcare during this pandemic.³⁰⁻³² However, the paediatric trial participants must be protected from unnecessary harms and must be provided with medical attention during or after the study, either because they suffer either for participation in the study or aggravating pre-existing illness.²⁰⁻²⁴

VACCINATION STRATEGIES

The World Health Organization (WHO) assesses the quality, safety, and efficacy of COVID-19 vaccines. The U.S. Food and Drug Administration (FDA) and the U.S. Centers for Disease Control (CDC) have granted emergency use authorization (EUA) for several COVID-19 vaccines. Some national regulators have also assessed other COVID-19 vaccine products for use in their countries. However, when we are writing this article, for children aged 12 years and above, the only recommended is the Pfizer COVID-19 vaccine.³³ However, in Bangladesh, paediatric vaccination has not been approved

at the time, which may be due to shortage of vaccine. Based on projections, it is inevitable that number of cases will increase substantially in the settings of low vaccination rates and high variant transmissibility.³² Moreover, we support fair access to healthcare for every child like every adult citizen of the society by ensuring efficient use of our limited resources.^{19,31,34} Hence, we recommend a fair, equitable policy to vaccinate children ages 12 and up. For Bangladesh, any vaccination programme tends to be successful as it has a long-standing history, infrastructure, manpower and community support for EPI programme, even in hard-to-reach areas.³⁵ However, monitoring and surveillance are needed to maintain the priority list and prevent vaccine misuse.^{36,37} The number of available doses likely will initially be constrained and will increase over time, necessitating phased implementation.¹⁹ Safe and efficacious vaccines are needed for all. Health departments and regulatory bodies within a government have ethical responsibilities to monitor vaccines for safety after they are licensed, which is an important means of fostering public trust.^{17,28,38} Moreover, the vaccine must be widely available and easily accessible to all.^{31,34,37}

Despite WHO guidance many low-income and middle-income countries (LMICs) like Bangladesh have not yet introduced COVID-19 vaccination for children. WHO guidance from July 14, 2021, states that "... children and adolescents tend to have milder disease compared to adults, so unless they are part of a group at higher risk of severe COVID-19, it is less urgent to vaccinate them than older people, those with chronic health conditions and health workers".³³ In another recent declaration of WHO's Strategic Advisory Group of Experts (SAGE) has confirmed the suitability of the Pfizer-BioNTech vaccine for children aged 12 years and above. They also suggested that children aged between 12 and 15 years screened as high risk may get priority in vaccination programme. WHO also assured of instant update of any change in policy recommendation based on evidence (results of ongoing trials on children in some countries) or epidemiological surveillance and situation as well as emergence of new variant.³³

Meanwhile, with progression of COVID-19 vaccination programme in adult population, the Ministry of Health and Family Welfare of Government of the People's Republic of Bangladesh with consultation of the COVID-19 Task Force is preparing for an extension of this programme to school children. We assumed that this consideration is based on evidence that showed reductions in transmissibility of the virus, incidence of hospitalization, and risks of complications and deaths following

vaccination in different population.³² Another important consideration might be preventing outbreaks in educational institutions, as we have already experienced that disruption of educational activities for months ultimately causes several "medium to long term impacts on public health" alongside this pandemic's effects.³⁹ We assume that policy makers will also consider all other potential benefits against the risks of vaccination in children.

CONCLUSIONS

Closure of educational institutions in our country was one of the biggest challenges during this pandemic situation. However, now reopening of schools has become necessary for our children, as "schools are integral part of social-emotional learning, formative relationships with peers and adults, opportunities for play, and other developmental progression".³⁹ A mass vaccination among eligible children will facilitate reopening schools and help reduce devastating toll that it has taken on children. To create and uphold public trust and confidence in COVID-19 vaccination in children, a uniform, transparent, proactive, and culturally sensitive communication strategy is needed,^{17,38} through which government public health agencies along with their private collaborators will inform public on a regular basis about the status of the vaccination process in children all over the country.

REFERENCES

1. World Health Organization (WHO). WHO Coronavirus Disease (COVID-19) Dashboard. 2021. Retrieved from: <https://covid19.who.int/> (Accessed April 11, 2021).
2. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, Tong S. Epidemiology of COVID-19 among children in China. *Pediatrics*. 2020;145(6):e20200702.
3. Posfay-Barbe KM, Wagner N, Gauthey M, Moussaoui D, Loevy N, Diana A, et al. COVID-19 in children and the dynamics of infection in families. *Pediatrics*. 2020;146(2):e20201576.
4. Centers for Disease Control and Prevention (CDC). COVID-19 update, 2020. Available: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html> (Accessed September 11, 2021).
5. Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics

- and outcomes of children with Coronavirus Disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr.* 2020;174(9):868-73.
6. Havers FP, Whitaker M, Self JL, Chai SJ, Kirley PD, Alden NB, et al. Hospitalization of adolescents aged 12-17 years with laboratory-confirmed COVID-19 - COVID-NET, 14 States, March 1, 2020 – April 24, 2021. *MMWR Morb Mortal Wkly Rep.* 2021; 70(23): 851-7.
 7. Centers for Disease Control and Prevention. Information for healthcare providers about multisystem inflammatory syndrome in children (MIS-C). 2021 Available at: <https://www.cdc.gov/mis/hcp/index.html> (Accessed April 12, 2021).
 8. Antúñez-Montes OY, Escamilla MI, Figueroa-Uribe AF, Arteaga-Menchaca E, Lavariega-Saráchaga M, Salcedo-Lozada P, et al. COVID-19 and Multisystem Inflammatory Syndrome in Latin American Children: A Multinational Study. *Pediatr Infect Dis J.* 2021; 40(1):e1-e6.
 9. Lam-Hine T, McCurdy SA, Santora L, Duncan L, Corbett-Detig R, Kapusinszky B, et al. Outbreak Associated with SARS-CoV-2 B.1.617.2 (Delta) Variant in an Elementary School – Marin County, California, May-June 2021. *MMWR Morb Mortal Wkly Rep.* 2021;70(35):1214-9.
 10. National Centre for Immunisation Research and Surveillance. COVID-19 in Schools – The Experience in NSW. New South Wales, Australia: National Centre for Immunisation Research and Surveillance; 2020.
 11. Posfay-Barbe KM, Wagner N, Gauthey M, Moussaoui D, Loevy N, Diana A, et al. COVID-19 in children and the dynamics of infection in families. *Pediatrics.* 2020;146(2):e20201576.
 12. Davies NG, Klepac P, Liu Y, Prem K, Jit M; CMMID COVID-19 working group, Eggo RM. Age-dependent effects in the transmission and control of COVID-19 epidemics. *Nat Med.* 2020; 26(8): 1205-11.
 13. Novelli G, Colona VL, Pandolfi PP. A focus on the spread of the delta variant of SARS-CoV-2 in India. *Indian J Med Res.* 2021;153(5&6):537-41.
 14. World Health Organization (WHO). WHO lists additional COVID-19 vaccine for emergency use and issues interim policy recommendations. May 7, 2021. Retrieved from: <https://www.who.int/news/item/07-05-2021-who-lists-additional-covid-19-vaccine-for-emergency-use-and-issues-interim-policy-recommendations> (Accessed May 11, 2021).
 15. Zuckerman DM. Emergency Use Authorizations (EUs) Versus FDA Approval: Implications for COVID-19 and Public Health. *Am J Public Health.* 2021 Jun;111(6):1065-9.
 16. Shah A, Marks PW, Hahn SM. Unwavering Regulatory Safeguards for COVID-19 Vaccines. *JAMA.* 2020;324(10):931-2.
 17. Opel DJ, Salmon DA, Marcuse EK. Building trust to achieve confidence in COVID-19 vaccines. *JAMA Netw Open.* 2020;3(10):e2025672.
 18. Kumar J, Meena J. COVID-19 Vaccine in children: where do we stand? *Indian Pediatr.* 2021;58(2):194-5.
 19. Bell BP, Romero JR, Lee GM. Scientific and ethical principles underlying recommendations from the Advisory Committee on Immunization Practices for COVID-19 Vaccination Implementation. *JAMA.* 2020;324(20):2025-6.
 20. Baker JP, Katz SL. Childhood vaccine development: an overview. *Pediatr Res.* 2004;55(2):347-56.
 21. Nurunnabi ASM, Rahman E, Ashique SS, Jahan A. Ethical considerations in conducting paediatric research. *Community Based Med J.* 2020;9(2):54-8.
 22. Kulkarni, P. Current topics in research ethics in vaccine studies. *Perspect Clin Res.* 2013;4(1):80-3.
 23. Bangladesh Medical Research Council (BMRC). Ethical guidelines for conducting research studies involving human subjects. Dhaka: BMRC; 2013.
 24. Sammons HM, Starkey ES. Ethical issues of clinical trials in children. *Paediatr Child Health (Oxford).* 2012;22(2):47-50.
 25. Cooper DM, Afghani B, Byington CL, Cunningham CK, Golub S, Lu KD, et al. SARS-CoV-2 vaccine testing and trials in the pediatric population: biologic, ethical, research, and implementation challenges. *Pediatr Res.* 2021; 90:966-70.
 26. Health News: NPR. Pfizer Gets FDA Approval to Enroll Kids as Young As 12 in COVID-19 Vaccine Trial: Shots. 2020. Retrieved from: <https://www.npr.org/sections/health-shots/2020/10/1>

- 3/923248377/will-kids-get-a-covid-19-vaccine-pfizer-to-expand-trial-to-ages-12-and-up. (Accessed May 19, 2021).
27. Hadjipanayis A, Dornbusch HJ, Grossman Z, Theophilou L, Brierley J. Mandatory vaccination: a joint statement of the Ethics and Vaccination working groups of the European Academy of Paediatrics. *Eur J Pediatr.* 2020;179(4):683-7.
 28. American Academy of Pediatrics (AAP). Include children in COVID-19 vaccine trials. 2020. Retrieved from: <https://www.aappublications.org/news/2020/11/17/covidvaccinetrials111720>. (Accessed September 19, 2021).
 29. Centers for Disease Control and Prevention (CDC). Science Brief: COVID-19 Vaccines and Vaccination. September 15, 2021. Retrieved from: <https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/fully-vaccinated-people.html> (Accessed September 11, 2021).
 30. Rodrigues CMC, Plotkin SA. Impact of vaccines; health, economic and social perspectives. *Front Microbiol.* 2020;11:1526.
 31. Dawson A. Vaccination ethics. In: *Public health ethics*. Cambridge: Cambridge University Press; 2011. p.143-53.
 32. Rella SA, Kulikova YA, Dermitzakis ET, Kondrashov FA. Rates of SARS-CoV-2 transmission and vaccination impact the fate of vaccine-resistant strains. *Sci Rep.* 2021 11(1):15729.
 33. World Health Organization (WHO). WHO COVID-19 advice for the public: getting vaccinated. July 14, 2021. Retrieved from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/advice> (Accessed September 22, 2021).
 34. Isaacs D, Kilham H, Leask J, Tobin B. Ethical issues in immunisation. *Vaccine.* 2009;27(5):615-8.
 35. Nurunnabi ASM, Mozaffor M, Hossain MA, Sony SA. Mass vaccination programme: Public health success and ethical issues – Bangladesh perspective. *Bangladesh J Bioethics.* 2018;9(3):11-5.
 36. Cooper LZ, Larson HJ, Katz SL. Protecting public trust in immunization. *Pediatrics.* 2008; 122(1): 149-53.
 37. Williamson L. The ethical impact of mandating childhood vaccination: The importance of the clinical encounter. *Clin Ethics.* 2021;16(4):271-7.
 38. Opel DJ, Diekema DS, Ross LF. Should we mandate a COVID-19 vaccine for children? *JAMA Pediatr.* 2021;175(2):125-6.
 39. World Health Organization (WHO). Considerations for school-related public health measures in the context of COVID-19. September 14, 2020. Retrieved from: <https://www.who.int/publications/i/item/considerations-for-school-related-public-health-measures-in-the-context-of-covid-19> (Accessed September 22, 2021).