

Pediatric Covid Vaccination: A Jab in Time Could Save Little Ones in Their Prime!

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The Covid-19 pandemic has been no less than a savage of sorts. Since the identification of the mystery virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Wuhan, China in December 2019¹, there has been an alarming rate at which it has transcended continental barriers and affected swathes of populations irrespective of ethnic, socioeconomic, and tropical differences. There emerged not only mounting evidence on the burden of disease but also its impact across age groups and vulnerable strata. Within six months of identification of the virus, by mid June 2020, the pandemic is estimated to have affected more than 6.8 million people with almost 380,000 deaths.² Unfortunately children have not been spared from the devastating direct consequences thereof. Children usually contract the infection owing to close contact with household adults who are in turn more exposed to the virus due to the latter's occupation. The earliest pediatric Covid-19 reports from United States were from a consortium of 41 pediatric intensive care units as a cross sectional report over 2 weeks in March-April 2020 with a 2 week follow-up assessing outcomes.³ Assessing 48 children contracting the infection, it was inferred that though the severity of illness was far lesser than adults, almost 83% of those requiring admission had pre-existing comorbidities. Later in the year, by May 2020, the game changed with the Centre for Disease Control issuing a warning in form of the newly described entity multisystem inflammatory syndrome in children (MIS-C), with severe inflammation, multi-organ failure and in turn high mortality.⁴ This came as a red alert for proponents of childhood Covid-19 being mild as against adult disease. It mainly stemmed from multiple reports from Europe describing a sudden rise in cases of a Kawasaki Disease (KD) like illness with severe cardiac involvement and macrophage activation syndrome.^{5,6} Overall meta-analyses suggest about one-fifths (21%) children have no symptoms while 3.8% may have severe disease.⁷

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Concordant to previous epidemics of coronaviruses, pediatric Covid-19 accounts for less than 2% of total reported cases.⁸ It had earlier been speculated that children have lesser susceptibility to the SARS-Coronavirus by virtue of differences in their innate immune system. However contact tracing studies, retrospective seroprevalence studies and population based infection surveys have demonstrated a flat attack rate irrespective of age, emphasizing a novel pathogen with no prior immunity across age groups.⁷ Hence attention needs to be paid to certain questions in a pragmatic and evidence based manner:

1. How will the pandemic affect unvaccinated children and what are the challenges in managing pediatric and neonatal covid-19?
2. How effective has vaccination been in adults?
3. Should Covid vaccine be given to children at all? Are there enough trials: efficacy and safety issues.
4. How vaccinating children will influence the pandemic curve?
5. Will vaccination provide additional confidence in restoring early school reopening and interactive sessions for children?

6. Future aspects like Covid-19 endemicity and how to brace up for the challenge with respect to pediatric vaccination: the India perspective.

Covid-19 is primarily a respiratory disease with pneumonia and consequent hypoxia being the most common cause of mortality. In an ideal situation, respiratory physicians and intensivists are best equipped to treat this condition. But the sheer magnitude of the disease has prompted doctors irrespective of their specialty to be pressed into service for Covid care in adults. The same is difficult to apply in treating pediatric patients who demand special care and the need for medical professionals trained in handling newborns and children, an additional strain for the already overstretched medical framework. In addition to the existent social distancing norms and Covid appropriate hygiene, vaccines are the new weapon in the anti-Covid armamentarium.

Since late last year, various vaccines have been rolled out against Covid-19. Moderna's mRNA-1273,⁹ Pfizer's mRNA based BNT162b2,¹⁰ Oxford university-Astra Zeneca's vaccine¹¹ and the Indian adaptation thereof (Covishield) based on the simian adenovirus and a home grown, whole virion inactivated vaccine COVAXIN, apart from the Chinese Sinovac and

Russia's Sputnik V¹² all having shown promise. Emergency use authorization by various national drug regulating bodies has already been granted.^{13,14} Vaccines have shown efficacy to the tune of >90% (mRNA vaccines) for infection prevention and >95% in preventing severe disease in adult trials and also deemed effective in real world studies on front line workers.¹⁵ Most have been authorized for use in age more than 16-18 years, till the recent approval granted to Pfizer's BNT162b2, for children more than 12 years.¹⁶

Until recently, the strategy has largely been to enforce "prevent exposure to prevent infection and hence disease". Coupled with the general belief that children are not affected as severely as adults, restraint was the most logical thing to do or so it was believed. In terms of schooling for children, a total cessation of in-person learning ensued, which soon enough got substituted by online academic sessions as a desperate measure to ensure no deprivation of learning. Not everyone in a low-medium income country has access to such privileges, thereby putting undue financial burden on families desiring internet based schooling for their children. Thankfully, research started pouring in citing schools may not be so bad a transmission site, if basic Covid hygiene is followed.^{17,18} However fear ruled, schools continued to remain shut and the effects started showing up in scholastic performances,¹⁹ mental health issues,²⁰ and a decrease in physical activity levels in this age group²¹. All of these can easily be traced back to the "restraint" policy. Such an extreme measure probably was the need of the hour then. However a vision of easing norms can be realized if one can offer a substantial level of first line protection from disease in this age group. Vaccinating all adults would render vulnerable the pediatric population, which will then act as a selective or preferential host to the virus and in fact help in perpetuating the cycle and genesis of novel mutations, a reversal of sorts with onward transmission from pediatric index cases.^{22,23} Hence the submission, vaccinating children is essential. This would in turn lead to the best mode of "source control" in the post adult vaccination scenario and help in flattening the pandemic curve. It is worthwhile noting that children of all age groups are susceptible, with highest severity in infants and younger children as also ones with comorbidities.²⁴ Prioritization of groups may be a choice when there is enough literature available on long term effects and natural history of asymptomatic or milder infections and a retrospective risk benefit analysis. In its absence and with a long productive lifespan ahead inoculation of all children is strongly favored, albeit with sequential prioritization but not denying others. Vaccines approved elsewhere like the Pfizer's BNT162b2 should be imported and reserved for this age group. It is heartening to note that COVAXIN, a vaccine developed jointly by Bharat Biotech and National Institute of Virology under Indian Council of Medical Research has already begun trials in children 2-18 year old in May 2021 with an estimated primary completion by August 15th this year.²⁵ An emergency use authorization after completion of trials will boost India's effort in self-reliance and ease school re-opening among other activities essential for a child's mental and physical development.

A vision of integrating India's fight against Covid-19 can be considered complete and comprehensive if Covid-19 vaccination for children can be merged with India's Universal

Immunization Program (UIP).²⁶ Trials in Newborns and younger infants are the way to go forward with possibly 2 doses of Covid-19 vaccine given at 6 and 10 weeks of the UIP schedule. This will enable us to visualize Covid-19 immunization not as a privilege but as a right for children.

Further Reading:

1. Du Z, Wang L, Cauchemez S, et al. Risk for Transportation of Coronavirus Disease from Wuhan to Other Cities in China. *Emerg Infect Dis.* 2020;26(5):1049-1052. doi:10.3201/EID2605.200146
2. Hoang A, Chorath K, Moreira A, et al. COVID-19 in 7780 pediatric patients: A systematic review. *EClinicalMedicine.* 2020;24:100433. doi:10.1016/j.eclinm.2020.100433
3. Shekerdemian LS, Mahmood NR, Wolfe KK, 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):868-873. doi:10.1001/jamapediatrics.2020.1948
4. HAN Archive - 00432 | Health Alert Network (HAN). Accessed August 7, 2021. <https://emergency.cdc.gov/han/2020/han00432.asp>
5. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. *Lancet.* 2020;395(10239):1771-1778. doi:10.1016/S0140-6736(20)31103-X
6. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet (London, England).* 2020;395(10237):1607-1608. doi:10.1016/S0140-6736(20)31094-1
7. Gaythorpe KAM, Bhatia S, Mangal T, et al. Children's role in the COVID-19 pandemic: a systematic review of early surveillance data on susceptibility, severity, and transmissibility. *Sci Reports* 2021 11. 2021;11(1):1-14. doi:10.1038/s41598-021-92500-9
8. CDC COVID-19 response team. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) - United States, February 12-March 16, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(12):343-346. doi:10.15585/MMWR.MM6912E2
9. Baden L, El Sahly H, Essink B, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. *N Engl J Med.* 2021;384(5):403-416. doi:10.1056/NEJMOA2035389
10. Polack FP, Thomas SJ, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *N Engl J Med.* 2020;383(27):2603-2615. doi:10.1056/nejmoa2034577
11. Knoll MD, Wonodi C. Oxford-AstraZeneca COVID-19 vaccine efficacy. *Lancet.* 2021;397(10269):72-74. doi:10.1016/S0140-6736(20)32623-4
12. Ella R, Vadrevu KM, Jogdand H, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial. *Lancet Infect Dis.* 2021;21(5):637-646. doi:10.1016/S1473-3099(20)30942-7
13. Cavaleri M, Enzmann H, Straus S, Cooke E. The European Medicines Agency's EU conditional marketing authorisations for COVID-19 vaccines. *Lancet.* 2021;397(10272):355-357. doi:10.1016/S0140-6736(21)00085-4
14. Krause PR, Gruber MF. Emergency Use Authorization of Covid Vaccines — Safety and Efficacy Follow-up Considerations. *N Engl J Med.* 2020;383(19):e107. doi:10.1056/NEJMP2031373
15. Kaur U, Ojha B, Pathak BK, et al. A prospective observational safety study on ChAdOx1 nCoV-19 corona virus vaccine (recombinant) use in healthcare workers- first results from India. *EClinicalMedicine.* 2021;0(0):101038. doi:10.1016/J.ECLINM.2021.101038
16. Frenck RW, Klein NP, Kitchin N, et al. Safety, Immunogenicity, and Efficacy of the BNT162b2 Covid-19 Vaccine in Adolescents. *N Engl J Med.* 2021;385(3):239-250. doi:10.1056/nejmoa2107456
17. Li X, Xu W, Dozier M, et al. The Role of Children in the Transmission of SARS-CoV2: Updated Rapid Review. *J Glob Health.* 2020;10(2):1-11. doi:10.7189/jogh.10.021101
18. Falk A, Benda A, Falk P, Steffen S, Wallace Z, Høeg TB. COVID-19 Cases and Transmission in 17 K-12 Schools — Wood County, Wisconsin, August 31–November 29, 2020. *MMWR Morb Mortal Wkly Rep.* 2021;70(4):136-140. doi:10.15585/mmwr.mm7004e3

19. Engzell P, Frey A, Verhagen MD. Learning loss due to school closures during the COVID-19 pandemic. *Proc Natl Acad Sci U S A*. 2021;118(17). doi:10.1073/PNAS.2022376118
20. Meherali S, Punjani N, Louie-Poon S, et al. Mental health of children and adolescents amidst covid-19 and past pandemics: A rapid systematic review. *Int J Environ Res Public Health*. 2021;18(7). doi:10.3390/ijerph18073432
21. Chaffee BW, Cheng J, Couch ET, Hoeft KS, Halpern-Felsher B. Adolescents' Substance Use and Physical Activity Before and During the COVID-19 Pandemic. *JAMA Pediatr*. 2021;175(7):715-722. doi:10.1001/JAMAPEDIATRICS.2021.0541
22. Jiehao C, Jin X, Daojong L, et al. A case series of children with 2019 novel coronavirus infection: Clinical and epidemiological features. *Clin Infect Dis*. 2020;71(6):1547-1551. doi:10.1093/cid/ciaa198
23. Park Y, Choe Y, Park O, et al. Contact Tracing during Coronavirus Disease Outbreak, South Korea, 2020. *Emerg Infect Dis*. 2020;26(10). doi:10.3201/EID2610.201315
24. Preston LE, Chevinsky JR, Kompanyets L, et al. Characteristics and Disease Severity of US Children and Adolescents Diagnosed With COVID-19. *JAMA Netw Open*. 2021;4(4):e215298-e215298. doi:10.1001/JAMANETWORKOPEN.2021.5298
25. COVAXIN in a Pediatric Cohort - Full Text View - ClinicalTrials.gov. Accessed August 9, 2021. <https://clinicaltrials.gov/ct2/show/NCT04918797>
26. Kumar VM, Pandi-Perumal SR, Trakht I, Thyagarajan SP. Strategy for COVID-19 vaccination in India: the country with the second highest population and number of cases. *npj Vaccines*. 2021;6(1). doi:10.1038/s41541-021-00327-2