Current Tropical Medicine Reports (2022) 9:225–233
https://doi.org/10.1007/s40475-022-00273-6

COVID-19 Impact on Disparity in Childhood Immunization in Low- and Middle-Income Countries Through the Lens of Historical Pandemics

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Accepted: 24 September 2022 / Published online: 19 December 2022

Abstract

Purpose of Review The COVID-19 pandemic, since 2020, has affected health care services and access globally. Although the entire impact of COVID-19 pandemic on existing global public health is yet to be fully seen, the impact of COVID-19 pandemic on global childhood immunization programs is of particular importance.

Recent Findings Disruptions to service delivery due to lockdowns, challenges in vaccination programs, vaccine misinformation and hesitancy, and political and social economic inequalities all posed a threat to existing childhood immunization programs. These potential threats were especially critical in LMIC where childhood immunization programs tend to experience suboptimal implementation.

Summary This review provides an overview of childhood immunizations and discusses past pandemics particularly in LMIC, factors contributing to disparities in childhood immunizations, and reviews potential lessons to be learned from past pandemics. Vaccine hesitancy, social determinants of health, and best practices to help lessen the pandemic's influence are also further elaborated. To address current challenges that hindered the progress made in prevention of childhood illnesses through vaccination campaigns and increased vaccine availability, lessons learned through best practices explored from past pandemics must be examined to mitigate impact of COVID-19 on childhood immunization and in turn conserve health and improve economic well-being of children especially in LMIC.

Keywords COVID-19 · Vaccine hesitancy · Childhood immunizations · Pandemics

Introduction

Since COVID-19 was officially declared a global pandemic in March 2020, more than 531 million confirmed cases and more than six million COVID-19-related deaths have been reported to the World Health Organization [67]. The COVID-19 pandemic not only caused significant direct morbidity and mortality but has had a broader impact on child health. Existing disparities between high-income countries and low- and middle-income countries (LMIC) were exacerbated by disruption of public health infrastructures and delivery of important services such as childhood immunization [2, 11]). By May 2020, GAVI, the Vaccine Alliance; WHO; and UNICEF warned that 80 million children were at risk for vaccine-preventable diseases from COVID-19 disruptions in childhood immunization programs [2, 46]. Not only has the development of pediatric COVID-19 treatments and vaccines lagged [2], the distribution of existing vaccines among adults in LMIC is far behind that in HIC, with only 7.7% of individuals in 50 of the least wealthy countries being totally vaccinated [55]. Certain contributing factors in LMIC, such as social determinants of health (SDoH) and vaccine hesitancy, further complicate vaccine disparities. Beyond the direct effects

This article is part of the Topical Collection on *Pediatric Global Health*

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of disruption of health care services, the full impact on children's health is yet to be seen.

The scale of the COVID-19 pandemic also threatens progress made by childhood immunization programs, necessitating examination of the impact of the pandemic and an urgent global multi-sectorial and specific health response to preserve childhood vaccinations. This review highlights the history of childhood immunizations, the most pressing impact on immunization of children living in LMIC, the factors contributing to disparities in childhood immunizations, and best practices from history for application to the COVID-19 pandemic.

History of Childhood Immunization and Pandemics

Vaccine development dates to 1796, when Edward Jenner pioneered the smallpox vaccine [47]. Immunization has been widely acclaimed as one of the greatest interventions in public health, and childhood immunization has significantly decreased pediatric morbidity and mortality in modern society [8, 32, 45]. Immunizations may play a role in the reduction of poverty and improvement of economic well-being, especially for children living in LMIC [1, 56]. Efforts such as those from GAVI, the Vaccine Alliance, have significantly improved access to childhood vaccines in these regions, thereby improving children's quality of life [1].

As the impact of the COVID-19 pandemic on childhood vaccinations continues to reverberate, one may wonder how its impact compares to other pandemics. The world has experienced approximately 21 pandemics, most recently the influenza pandemics, H1N1 causing the influenza of 1918–1920 (Spanish flu) and its viral descendants causing the Asian flu of 1957 (H2N2), Hong Kong flu of 1968 (H3N2), Swine flu of 2009 (H1N1), and the AIDS pandemic [53]. Efforts made to combat previous historical pandemics included specific treatments and vaccines that decreased the number of cases and fatalities [53].

The geographic scope, time distribution, and mortality of these diseases vary. Commonly referred to as the "greatest medical holocaust in history," the Spanish flu of 1918 was the last pandemic that caused global disruption, spreading first through trade routes, and impacting LMIC from India to distant islands in the southern Pacific [52•]. The Spanish flu was often misdiagnosed and ignored in the early stages until it became widespread and hard to contain [33]. Effective vaccines and treatment modalities were not available. Therefore, efforts to control outbreaks relied largely on non-pharmaceutical interventions, such as quarantines, school closures, banning public gatherings, and infection-prevention practices (e.g., minimizing respiratory transmission with facemasks) [33]. The waves of COVID-19 variants along with its global impact render the ongoing COVID-19 more like the Spanish flu than any other pandemic [33].

When attempting to appreciate the impact of COVID-19 on childhood immunization in contrast to other pandemics, it is important to point out that the advancements in science and public health have accelerated at a faster pace during the last century [52•]. Many of the previously fatal pandemics such as the Black Death, New World smallpox outbreaks, and Spanish flu all took place prior to the discovery and implementation of therapeutics and public health surveillance [52•]. There were no standardized childhood immunization programs during previous pandemics that would provide comparable circumstances for measuring past and present impacts [52•].

The Spanish flu of 1918 caused a temporary decline in the global population growth during the outbreak. In contrast, the COVID-19 pandemic is not anticipated to affect global population growth, but it is anticipated to have public health impacts that may reduce life expectancy [52•]. One consequence is the lack of access to immunization services or underutilization of childhood vaccines for preventable diseases. During the 2010–2019 period, which saw the emergence of Swine flu (H1N1), Ebola, and MERS, routine vaccination coverage was high though stagnant [44]. The lack of comparable historical perspective of pandemics, therefore, calls for an analysis of COVID-19 impacts on childhood immunizations.

Impacts of COVID-19 Pandemic on Childhood Immunization in LMIC

The WHO created the Expanded Program on Immunization (EPI) in 1974 to protect all infants from tuberculosis, diphtheria, tetanus, pertussis, poliomyelitis, and measles through access to the BCG, DPT, Polio, and MCV vaccines, respectively (see Table 1) [44]. Additional vaccines added subsequently include pneumococcal conjugate vaccine (PCV), rotavirus, RCV, Hep B, Hib, MCV2, and HPV (see Table 1) [44].

The COVID-19 pandemic disrupted all health services, but childhood immunization was among the hardest hit in 2020 [12]. This interruption affected approximately 80 million children younger than the age of 1 year [25]. From 2019 to 2020, coverage for most vaccines had declined globally, with LMIC the most affected [21, 44]. The impact was most notable on the African continent, where immunization before COVID-19 was already substandard; WHO statistics indicated that many African countries were significantly behind in child mortality targets for Sustainable Development Goals [4]. South Africa, for example, had been struggling to achieve optimal immunization coverage since 2014 due to political factors and socioeconomic inequalities [45].

Table 1 Childhood immunizations acronyms defined

BCG	Bacille Calmette-Guerin
DPT	Diptheria, pertussis, and tetanus
Polio (OPV/IPV)	Oral polio vaccine, inactivated polio vaccine
MCV1	Measles-containing-vaccine first-dose
PCV	Pneumococcal conjugate vaccine
RV	Rotavirus vaccine
RCV	Rubella-containing vaccine
HepB	Hepatitis B
Hib	Hemophilus influenza type B
MCV2	Measles-containing-vaccine second dose
HPV	Human papilloma virus

Child and Adolescent Immunization Schedule. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html. Accessed September 20, 2022

Vaccines and Immunization. https://www.who.int/health-topics/vaccines-and-immunization#tab=tab_1. Accessed September 20, 2022

Coverage of the third dose of DPT vaccine by 12 months of age is used as a proxy for immunization program performance [44]. Lack of access to immunizations is defined by children who do not receive their first dose, DPT1 (i.e., zero dose children), whereas underutilization of immunization services among children with access are reflected by those who receive their first dose but do not finish the 3-dose series, DPT3 [44]. The number of zero-dose children increased: middle-income countries accounted for the largest increase (12.1 M; 71%), followed by low-income countries (4.5 M, 26%) [44]. Nearly two-thirds (11 M; 65%) of zero-dose children hailed from ten countries: Angola, Brazil, Democratic Republic of the Congo, Ethiopia, India, Indonesia, Mexico, Nigeria, Pakistan, and the Philippines [44]. The South-East Asia and Eastern Mediterranean regions experienced the largest decrease in DPT3 coverage [44].

With immunization coverage affected around the world, a rise in the risk of new outbreaks of vaccine preventable illnesses occurred [21]. COVID-19 negatively impacted polio vaccinations globally and to a much greater extent in LMIC. In 2020, 46 poliovirus immunization campaigns in 38 countries, predominantly in Africa, were suspended [21]. Polio outbreaks were reported in more than 30 countries, where a new mutated, vaccine-derived strain of poliovirus was discovered [21]. In 2020, human polio and environmental cases increased: "959 human cases of circulating vaccine-derived poliovirus type 2 (cVDPV2) and 411 cVDPV2-positive environmental samples were reported globally from 27 countries" compared to 2019 when only "366 cVDPV2 cases and 173 cVDPV2-positive environmental samples were reported" [13••]. The polio outbreaks during COVID-19 were associated with low immunization rates and non-immunized populations [13••]. A similar scenario was described in Pakistan, which faced polio eradication challenges even prior to 2020 [20]. The pandemic led to approximately 40 million children missing their polio vaccinations [20]. Although administrations of vaccinations have resumed, the potential consequences and the urgency needed to reach these children are pressurizing an already overburdened health care system [20].

LMIC are more vulnerable due to weak health systems, economic limitations, and diminished capacity to deal with the demands of the pandemic while maintaining essential health services [12]. Existing deficiencies before COVID-19, such as higher death rates among unvaccinated children in LMIC compared to HIC, are exacerbated by pandemic pressures [12]. The pandemic further exposed pre-existing, gender-based inequities, whereby boys were vaccinated more than were girls [12]. A hospital in India noted that the least affected group was composed of children receiving vaccines at birth, due to a Ministry of Health and Welfare policy in 2020 to continue birth dose vaccines during the pandemic [5]. However, of concern, parents chose to avoid routine immunization for older children, placing them at greater risk for vaccine-preventable diseases [5].

Reasons for interrupted and delayed immunizations were COVID-19 restrictions such as lockdowns, limited movements, and infection-control measures; parental fears and misinformation about vaccines and their side effects; availability of health care personnel; individual characteristics such as socioeconomic status, cultural traits, and household size; and vaccine logistic issues [6, 21, 43, 44]. The WHO recommended continuing routine immunizations while maintaining COVID-19 infection control measures, and previously interrupted immunization services were resumed with provision for catch-up vaccinations [21]. In a study by Abbas et al., it appeared to be far more advantageous to continue routine child immunization despite the risk of acquiring SARS-CoV-2 in the African region [1].

Contributing Factors Impacting Childhood Immunization in LMIC

History of Hesitancy Towards Disease Prevention

The advent of social media has amplified this recurring, hesitant human response. The immediate availability and pervasive access have enabled both factual and false information to be disseminated globally with ease and credibility and at unprecedented speeds [52•, 68]. Social media have transformed patterns and expectations of communication, largely contributing to the infodemic of misinformation and disinformation accompanying the COVID-19 pandemic.

Before the development of vaccines, hesitancy to other measures of disease prevention existed during outbreaks of diseases. It is, then, no surprise that vaccine hesitancy continues as an outgrowth of this human response. The WHO cited vaccine hesitancy as one of the top ten threats to global health in 2019 [63]. During recent years, vaccine hesitancy trends are increasing, with larger numbers of people unwilling to receive recommended vaccinations [68].

Drivers of COVID-19 Vaccine Hesitancy

The global initiative to vaccinate all populations against COVID-19 is one way to prevent the rise of new variants and control this disease [7]. Both COVID-19 vaccinations and routine childhood vaccinations in LMIC are hindered by vaccine hesitancy. Inadequate vaccine uptake contributes to the development of new SARS-CoV-2 variants and vaccine-preventable childhood illnesses [48]. Studies reveal vaccine hesitancy rates between 10 and 30% among parents in HIC [15, 41, 57], comparable to individuals in LMIC, where approximately 20% indicated an unwillingness to take the COVID-19 vaccine between June 2020 and January 2021 [61]. Despite the vaccine hesitancy trend in LMIC, a study in Brazil revealed that some parents were willing to vaccinate [7].

The reasons for vaccine hesitancy are complex, depend on geographical location and culture, and are heightened by misinformation from anti-vaccine groups, social media, and public figures [26, 36, 61]. Sometimes, official health communications can inadvertently act as a driver of vaccine hesitancy. One early example was the WHO communication in July 2021 that considered children and adolescents at low risk of contracting COVID-19 compared to adults and people with a chronic illness, which contributed to vaccine hesitancy among parents [29]. When interpreted without nuance and pushed through many layers of social media, health messages can be poorly distilled by the public and undermine public trust. This can be problematic because COVID-19 vaccination compliance increases with trust in health authorities and reduction in vaccine myths and beliefs [7].

Myths and misconceptions are other drivers that intensify parental fears and perceptions about the safety of COVID-19 vaccinations, resulting in delays or refusal to get children vaccinated for COVID-19 [30]. General myths about vaccines play a role in COVID-19 vaccine hesitancy, including vaccines can overwhelm the immune system and affect neurological development, certain vaccines cause autism, vaccines increase the risk of autoimmune diseases, and the administration of vaccines early in pregnancy increases the risk of miscarriage [26].

Vaccine safety concerns specific to COVID-19 also drive the lack of vaccine confidence [16, 26, 36]. "…the most described fears are that adjuvants like aluminum, preservatives like mercury, inactivating agents like formaldehyde, manufacturing residuals like human or animal DNA fragments, and the sheer number of vaccines might be overwhelming, weakening or perturbing the immune system [26]." The interpretation of study results in siloes or without full context, such as the surveillance studies of the Pfizer–BioNTech mRNA vaccine in children 12–15 years that reported transient myocarditis in some young adults, can also drive vaccine hesitancy [29, 42].

Pandemic othering, when a disease is stigmatized and marginalized groups are targeted, is another driver of vaccine hesitancy [18]. Othering has a long history, stretching from the stigmatization of Spanish and Portuguese soldiers during the 1918 influenza to immigrants in South Africa, homosexual men, and Haitians in the USA during the early days of the HIV/AIDS pandemic [18]. During the COVID-19 pandemic, Chinese and Asian descendants of various nationalities were targeted, and subsequent divisions were sowed among socioeconomic and political groups. Significant consequences of othering affect policies, politics, and, importantly, public health: people try to avoid being stigmatized and may not cooperate with public health authorities during an emergency due to mistrust [18]. Social exclusion can increase vaccine hesitancy and can lead to messages about preventive measures and vaccines falling on distrustful and deaf ears.

However, patients and communities do tend to trust health providers when providers engage in informed discussions with them about vaccinations, increasing vaccine uptake [48, 59]. Increased health worker-community engagements can reduce vaccine hesitancy through strong, presumptive language that ensures effective communication on vaccination uptake [28].

Social Determinants of Health

Social determinants of health (SdoH), "the conditions in which people are born, grow, live and work," have implications on children's access to life opportunities, health, and life expectancy [35]. SDoH not only impact health outcomes but also facilitate or hinder health behaviors such as choosing to be vaccinated. Therefore, SDoH should be considered when developing customized approaches to address factors contributing to immunization [24, 48, 62].

Much like pandemics of the past, the burdens of COVID-19 are not equally distributed. SDoH have influenced the effects of COVID-19, affecting those in LMIC more than those in HIC [60•]. Populations that generally had negative SDoH outcomes appeared to be most afflicted by COVID-19 [35]. Lockdowns further affected these groups' quality of life for various reasons, including inability to work from home, inability to socially distance, and lack of proper access to soap, water, or sanitizers [40, 60•]. School closures aggravated the problems further [60•]. Approximately 80% of children globally were affected by the pandemic, with increased instances of mental health disturbances such as anxiety, depression, irritability, boredom, and erratic sleep patterns being reported [60•]. Incidences of child abuse and violence against children also increased due to the restrictive measures [60•]. Furthermore, the benefits of children attending school (e.g., school meals, a safe environment for intellectual, and emotional development) were temporarily lost, leading to a rise in negative psychological symptoms [60•]. According to UNESCO, 91% of school-going children stopped their education in April 2020 [21]. This discontinuance affected school-based programs including school meals and vaccination campaigns, in turn complicating the existing hardships facing children in LMIC [10, 37].

These effects were more profound among poorer communities due to pre-existing challenges, lack of resources, and comorbidities [35, 60•]. In 2011, some 800 million people were living in extreme poverty, and approximately 20% in low-income countries were declared as being extremely poor. The pandemic created global economic strain, and LMIs experienced the brunt of it through increased debts and poorer health outcomes, especially with the negative impact on childhood vaccinations [51, 56]. COVID-19 mortality rates among children in LMIC have been low so far, but they face other challenges that exacerbate poor outcomes from experiencing malnutrition, poor sanitary environments, nutritional anemia, and infections [10, 37].

SDoH also influenced vaccine hesitancy, which is more pronounced among caretakers of children with low education levels compared to those with high education levels in LMICs compared to HICs [65]. Similarly, an association exists between vaccine refusal and young parental age, low education levels, and low household incomes [19, 34, 57].

Best Practices to Mitigate COVID-19 Impact on Childhood Immunization

Vaccines have proven significantly successful in protecting children from infectious diseases. Smallpox, which ravaged hundreds of millions of lives over centuries, was eradicated in 1980 through the success of WHO's Operation Smallpox Zero [31]. Global mass vaccination efforts since the 1960s have placed polio on a similar trajectory for eradication, though the setbacks due to COVID-19 have led to outbreaks in endemic regions [27]. The following lessons and best practices can be gleaned from these historical experiences to guide contemporary efforts to mitigate morbidity and mortality from COVID-19 and its impact on childhood immunization that threatens global child health.

Catch-up Strategies for Routine Childhood Vaccinations

Though some routine immunization programs of vaccine-preventable diseases have begun to recover, others in certain geographical regions continue to be negatively impacted by COVID-19 [58]. Catch-up strategies, aimed at vaccinating individuals missing doses for which they are eligible per national guidelines, are critical to reverse the immunization disruptions [38]. These strategies should be tailored specifically to each country's circumstances and include a combination of immediate activities (e.g., mass vaccination) and a framework within routine immunization (e.g., screening children for vaccination status at any health encounter) [44]. Catch-up vaccination programs would be particularly beneficial if they were incorporated into schools and clinics where unvaccinated children may be followed [44]. These programs, however, require additional resources such as additional health care workers, training to implement these strategies, and early and efficient implementation to help lessen the task at hand [44].

Childhood Mass Vaccination Programs for COVID-19 Vaccines

The importance of mass vaccination of children and adults cannot be overstated for its role to confer herd immunity within a population [31]. The routine pediatric use of the PCV13 vaccine in the USA achieved herd immunity and has had a greater impact on reducing invasive pneumococcal disease than has merely routine immunization in immunocompetent adults [39]. In some HIC, modern outbreaks of measles, mumps, and pertussis have resulted from increased vaccine hesitancy and decrease in childhood vaccinations [31]. In addition to the eradication of smallpox and near eradication of polio, vaccines have resulted in upwards of 90% decrease in morbidity for most other vaccine-preventable illnesses due to herd-immunity protection [49]. With respect to COVID-19, vaccines for all are the best option to confer herd immunity and protect naïve populations [17].

Restoring Parental Vaccine Confidence and Generating Vaccine Demand

Several key factors contribute to the ability of mass vaccination programs to achieve herd immunity. One strategy is generating a population's demand for the vaccine [31, 66], which requires a multifaceted approach, including addressing vaccine hesitancy [66]. Evaluating the root cause of vaccine hesitancy in specific communities and determining a tailored approach are key [66]. Recommendations to address vaccine hesitancy and increase parental vaccine confidence in the context of COVID-19 in LMIC require concerted efforts such as ensuring inclusive health policies that prioritize child vaccinations; addressing COVID-19 vaccine misinformation and safety through community sensitization programs; enhancing provider approval for communities to get vaccinated; scaling up COVID-19 health authority-led campaigns; increasing education levels; and using multisectoral approaches to address SDoH. Strong leadership, role models from all segments of society (e.g., popular culture, local community, religious institutions), and political will are needed to encourage greater acceptance of vaccines [31, 66].

Equitable and Effective Delivery of COVID-19 Vaccines

Beyond vaccine demand, allocation and distribution of the vaccine are the other critical factors necessary for equitable and effective delivery of vaccines [31, 66]. As with most scarce resources, COVID-19 vaccine allocation was a contentious debate. More privileged populations received the vaccines first and in steady supply [66]. Though global collaboration efforts have been made to ensure equitable access and distribution through the Access to COVID-19 Tools (ACT) Accelerator and the COVAX mechanism, vaccine nationalism and politics have undermined its progress [66]. It is reminiscent of what happened in 2009 soon after the WHO announced H1N1 a pandemic: three HIC purchased scarce vaccines for their citizens, leaving limited supply for LMIC that needed it [23]. During emergency situations such as pandemics, existing inequalities are exposed and further exacerbated. Vaccine allocation needs to be determined by what will stop the pandemic, regardless of who has the leverage to pay for it; collaborative, targeted international efforts and the injection of appropriate funds are required [66].

Advocacy for Child Vaccine Equity and Global Child Health

Children are a vulnerable population often overlooked with regard to care and treatment of diseases. Diagnostics, medications, and vaccines for children usually are an afterthought when compared to adults [22, 29], thus requiring lifesaving machines and medicines to be secured in health facilities for increased positive outcomes [3] and improved access to care and treatment, as in the case of HIV/AIDS [50]. Similar debates about children and vaccines have ensued during the COVID-19 pandemic (i.e., should children even be vaccinated?) [9, 69]. This debate is ongoing, but what is important is that children globally, and especially in LMIC, be proactively considered for equitable and optimized health outcomes.

Conclusion

The COVID-19 pandemic generated a tremendous cost on global health, with substantial morbidity and mortality [55] and unprecedented disruptions in delivery of essential health services [11, 54]. The long-term effects of these service disruptions on children's health have yet to be fully realized. Vaccination programs were hindered, and pervasive misinformation campaigns promoted vaccine hesitancy or avoidance [30]. These threats to childhood immunizations are of urgency in LMIC, which have a tendency toward fragile health systems and suboptimal vaccination rates [12, 45]. To address these obstacles, we must learn from past pandemics and safeguard the progress that has been made in reducing vaccine preventable illnesses in children globally.

Acknowledgements Dr. Lee Ligon and Dr. Satid Thammasitboon for their mentorship and editorial comments on the paper.

Declarations

Conflict of Interest Diane Nguyen is the Pediatric Global Health section editor for the Current Tropical Medicine Reports. The author has no relevant financial or other non-financial interests to disclose. All other authors have no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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•• Of major importance

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