

INEQUALITIES IN ACCESS TO COVID-19 VACCINES AND POTENTIAL SOLUTIONS FOR LOW- AND MIDDLE-INCOME COUNTRIES

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Abstract: Despite approved vaccines against Coronavirus Disease 2019 (COVID-19) having been available for more than a year, low- and middle-income countries (LMICs) have been unequally affected by low vaccination coverage. The overarching goal of the COVID-19 Vaccine Global Access (COVAX) mission is to ensure that all countries can secure enough doses to vaccinate 20% of their population before any one country vaccinates more than 20% of their population. However, limited resources, poor infrastructure and constrained financial capabilities have contributed to challenges in producing, acquiring, and distributing vaccines amongst developing nations. This review was aimed at identifying inequalities and proposing mitigation measures to minimize disparities in access and distribution of COVID-19 vaccines in LMICs. A narrative literature review of scientific papers published during 2020-2022 was carried out accessing databases including Google Scholar and Medline (PubMed). Factors affecting access to COVID-19 vaccine research, manufacturing, procurement, and deployment capabilities were studied. The results revealed that the combined populations in LMICs that make up 84% of the global population were able to secure only 30% of the COVID vaccine doses produced in 2021. Alternatively, high-income countries make up 16% of the global population and had purchased 70% of vaccine doses produced in 2021. The causes were multifactorial and included challenges involving production, procurement and allocation, deployment, accessibility, and vaccine hesitancy. Mitigation measures include better manufacturing or procurement capabilities based on shared intellectual property and aid as well as better storage systems for temperature-sensitive vaccine deployment. Vaccine hesitancy can be mitigated by leveraging the influences of well-informed health care workers, social workers, political, religious and community leaders who can help dispel misinformation and improve vaccine acceptance among the masses. Reducing disparities in vaccination coverage of LMICs is an important step towards the global progress in combating the pandemic and especially in preventing the spread of potential viral variants.

Keywords: COVID-19, Vaccine, Low- and Middle-Income Countries (LMICs), Disparities

Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic has illuminated numerous global public health disparities. As the global scientific community has collaborated to accelerate funding, research, and

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intellectual property for the development of safe and effective vaccines against COVID-19, low- and middle-income countries (LMICs) have disproportionately struggled to access disease prevention and treatment. Throughout the course of the pandemic, they have suffered high case rates, along with difficulty securing doses and delivering vaccines to their citizens. (So et al., 2021)

The COVID-19 Vaccine Global Access (COVAX) Facility, in partnership with other global health organizations, was developed to provide a global solution to the COVID-19 pandemic. COVAX is the vaccines pillar of the Access to COVID-19 Tools (ACT) Accelerator. The ACT Accelerator is a ground-breaking global collaboration to accelerate the development, production, and equitable access to COVID-19 tests, treatments, and vaccines (Acquah, N., 2021). COVAX aimed to accelerate funding, research and manufacturing of COVID-19 vaccine candidates while also negotiating low vaccine costs and equitable distribution across the globe. COVAX identified 92 low- and middle-income countries as eligible to access COVID-19 vaccinations at the same time as high-income countries through advanced market commitments. In accordance with principles of global equality, the overarching COVAX mission is to ensure that all countries can secure enough doses to vaccinate 20% of their population before any one country vaccinates more than 20% of their population (Duke Global Health Innovation Center, 2022).

While approved vaccines against the COVID-19 virus offer hope for combatting the pandemic, failure to ensure global access to vaccines and acquire herd immunity leads to prolonged pandemic states throughout the world. A 2022 technical report on ‘Accelerating COVID-19 Vaccine Deployment’ was published by the WHO and the World Bank in collaboration with the IMF and WTO as members of the Multilateral Leaders Task Force on COVID-19 as well as Gavi and UNICEF as members of the CoVDP. As per this report, for the first time since the pandemic began, the global supply of vaccines is not currently a binding constraint. Through coordinated efforts between global, regional, and bilateral vaccine suppliers and manufacturers, LMICS are now in a better position to match their own country specific demand for doses with the supply of vaccines arriving in country. Minor issues including trade bottlenecks are being tackled and export restrictions being rolled back. However, exports of some vaccination-related products continue to remain restricted indicating persistent global shortages.

Currently the overarching challenge revolves around vaccine delivery and getting people immunized. To achieve the global targets, a sustained and concerted country-led push to deliver against nationally defined vaccination strategies can lead to better achievements of global targets. An efficient strategy has been prioritizing full vaccination and boosters for high-risk populations including older adults, healthcare workers, persons with co-morbidities including immunocompromised persons. Strengthening and building long-term capacity through strong leadership engagement and commitment is an important goal. Additionally, as people’s risk perception of the virus wanes, careful risk communication and community engagement is needed to keep people motivated to get vaccinated (WHO publication, 2022).

The WHO, UNICEF, and Gavi with international partners including the World Bank launched the COVID-19 Vaccine Delivery Partnership, a collective international effort with ‘One Country

Team’, ‘One Plan’, and ‘One Budget’. However, despite an initial incremental success, low and lower-middle income countries are facing difficulties to get a step change in vaccination rates. As this

poses a threat to the fragile economic recovery and increases the risk of serious disease and death in populations with low vaccination coverage, it is important to accelerate the delivery of other COVID-19 tools and treatments to help the world build up multiple layers of protection against the virus (Booming-WHO publication, 2023).

While approved vaccines against the COVID-19 virus offer hope for combatting the pandemic, failure to ensure global access to vaccines and acquire herd immunity leads to prolonged pandemic states throughout the world. There are several factors that contribute to vaccine disparities including research, manufacturing, procurement, as well as deployment capabilities for COVID-19 vaccines especially in LMICs.

Paucity of comprehensive reviews on different aspects of this topic and the relevance of knowing the factors responsible for these disparities prompted us to carry out this research. The findings of this narrative review would be relevant in understanding the mitigation measures to create better and sustainable vaccination drives for combating future reemergence of the pandemic or the emergence of new ones in the future.

Aims and Objectives

The overarching goal of this narrative review is to compile information for better future vaccine preparedness during possible recurrences of the COVID-19 pandemic or for future occurrence of pandemics. The study objectives include analyzing the complexities and factors leading to inequalities pertaining to COVID-19 vaccine research, manufacturing, procurement, as well as deployment capabilities in LMICs. Additional objective is to analyze the major gaps and shortcomings in different aspects of vaccine procurement, availability, and administration and to discuss effective mitigation measures to reduce vaccine disparities in LMICs.

Materials and Methods

A narrative review on the COVID-19 vaccine inequalities and potential solution in LMICs was carried out by obtaining scientific papers published as research articles and various technical reports published by WHO and its various partnerships. Various electronic databases including Google Scholar, Medline (PubMed) and WHO websites were included in the search. The key search terms “COVID-19 vaccine inequality” OR “COVID-19 inequity” AND “income” were used. A total of 62 papers were identified using search criteria. Primary research reporting scientific data or peer-reviewed articles citing primary research were included. Additional references were acquired through cross-referencing. Summary reports published on the WHO website were also included as data source for secondary data. Exclusion criteria included commentary, opinion pieces, editorials, and news articles. References were collected over a two-year period from the time COVID-19 was declared a public health emergency of international concern on January 30, 2020, through January 31, 2022. In total, 25 articles were reviewed, out of which 18 were journal papers and seven were documents published by WHO and other organizations.

Results

Our review of important publications yielded the following important information:

Production

As per a report of the WHO, 58% of the world's population has had primary vaccination with 11.3 billion doses of COVID-19 vaccines having been administered worldwide. Yet only 11% of the population in low-income countries are vaccinated, compared with 73% of those in high income countries (WHO report, 2022).

Among different factors responsible for these disparities, the important ones included disruptions to global supply chains, export restrictions applied to vaccine-related inputs and finished products, manufacturing challenges, intense competition for vaccines and delays to regulatory approvals. These led to a severe lagging behind of LMICs as vaccine deliveries increased in higher income countries. This in turn disrupted plans to test and implement their delivery systems.

Vaccine candidates must undergo clinical trials to be approved by stringent regulatory bodies and subsequently produced at a scale to meet the global population requirements (Wouters et al., 2021). Over \$39 billion USD have been committed to vaccine development globally. Unable to invest financial or technological resources in vaccine development, LMICs must rely on shared knowledge, technology, or doses (Sheikh et al.,2021).

Due to lack of financial and technological resources, many developing nations are incapable of investing in vaccine development and hence cannot ramp up their vaccine production. This puts them in a state of dependency on other nations and on global cooperation. (Sheikh et al.,2021). There have been major challenges for efforts at knowledge sharing through temporary waivers.

Countries that lack the domestic capacity to mass produce vaccines and ensure coverage for their citizens are forced to make purchase agreements or accept donated doses to procure COVID vaccines. In the early stages of vaccine production, Africa and South America suffered from vaccine manufacturing droughts (Choi et al.,2021). In October 2020, South Africa and India filed a joint proposal to the World Trade Organization (WTO) requesting temporary waiver of intellectual property rights to improve knowledge sharing in the public domain (Peacocke et al.,2021). Large scale vaccine manufacturers like China and India met the demand for doses in low- and middle-income countries by scaling up their production and export of vaccines (Choi, 2021).

Purchase and Allocation

The development of vaccine nationalism, in which most wealthy countries compete to purchase or stockpile vaccine doses, has led more vulnerable countries to contend for a limited supply of remaining vaccines. (Choi, 2021). Pandemic vaccine supply chain differs from traditional distribution due to individual governments directly purchasing vaccines from manufacturers, bypassing wholesalers, and distributors. Additionally, the total volume of vaccines needed to vaccinate the entire world population is far greater than any prior vaccine campaign (Alam et al., 2021).

A large part of the global vaccine availability has been purchased by wealthier nations pushing the developing world to the back of the queue regarding vaccine supply and delivery. Although high-income countries represent only 16% of the world's population, they have purchased more than half of all COVID-19 vaccine doses (Sheikh et al.,2021).

China successfully built a cold-chain air bridge for transporting vaccines to African countries while maintaining ultra-cold temperatures. As the largest vaccine manufacturer in the world, India donated 1 million vaccine doses to COVAX and 10 million doses to African countries (Choi et al.,2021). However, in March 2021 India faced a second wave of COVID cases spreading from cities to small towns and rural regions. India then began reporting a shortage of vaccines, leading to a temporary halt on vaccine exports to cover domestic needs (Koller et al., 2021).

The efforts of COVAX have been undermined by bilateral agreements between high-income countries and vaccine manufacturers for the pre-purchase of COVID vaccines. While their combined populations make up only 16% of the global population, high-income countries have purchased 4.2 billion doses of COVID vaccines from five leading candidates, securing over 70% of the doses (figure 1) expected to be produced by the end of 2021(Wouters et al., 2021).

A study performed six months after the deployment of approved vaccines analyzed the association between country income level and vaccination coverage, represented by the number of vaccine doses administered per 100 people. It was found that only 11.95 doses/100 people and 1.26 doses/100 people had been administered in lower-middle- and low-income countries respectively. This contrasts with high-income countries where 58.49 doses/100 people had been administered (figure 2) (Duan et al., 2021)

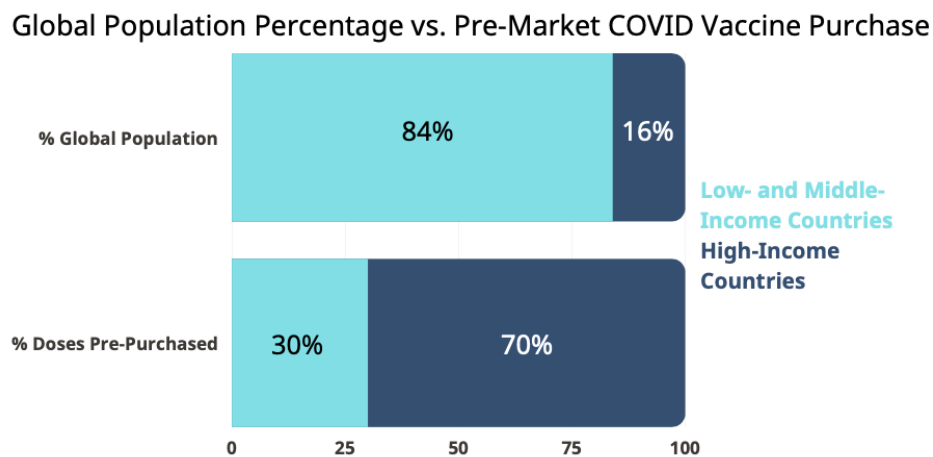


Figure 1: Global Population Percentage vs Pre-Market COVID-19 Vaccine Purchase (Wouters et al., 2021)

Combined populations in low- and middle-income countries (light blue) make up 84% of the global population but have only been able to secure 30% of the COVID vaccine doses expected to be produced by the end of 2021. Alternatively, high-income countries (dark blue) make up 16% of the global population and have purchased 70% of vaccine doses to be produced in 2021.

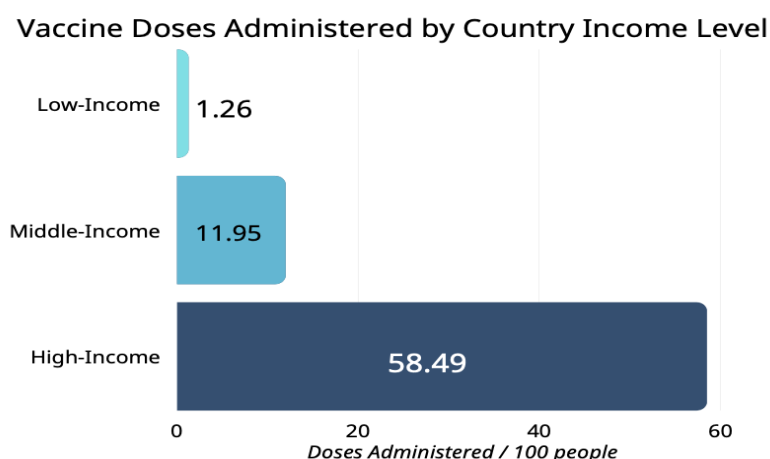


Figure 2: Vaccine Doses Administered by Country Income Level (Duan et al., 2021)

Association between country income level and vaccination coverage, represented by the number of doses administered per 100 people. Data collected 6 months after the deployment of approved vaccines. Low- and middle-income countries had administered 1.26 doses/100 people and 11.95 doses/100 people, respectively. In contrast, high-income countries had administered 58.49 doses/100 people.

Deployment

There have been several deterrents to the deployment of vaccines:

One of the main reasons for an unequal global vaccine scenario has been a slow domestic vaccine rollout, a reflection of domestic health inequality and weak state capacity. Despite availability of vaccines, the machinery for vaccine rollout in several countries has been weak. Factors causing constraints such as inadequately trained staff and lack of storage and logistic infrastructure have been mainly responsible. Based on this analysis, an important mitigation measure is massive expansion of vaccination capacity through huge investments and radical new public health approaches (UNDP technical document, 2023).

Once doses have been secured for LMICs, they must be distributed to and accepted by their citizens. Many countries have been faced with delayed acceptance or refusal as a barrier to vaccination. The results of a survey of 23 countries with 23,000 respondents showed that the overall willingness to accept vaccination was at 79.1%. Hesitancy increased in eight countries, however, ranging from 1.0% (United Kingdom) to 21.1% (South Africa) (Lazarus et al., 2021). In Bangladesh, it was found that vaccine resistance was highest among rural, semi-urban, slum, elderly, and low-educated populations (Tagoe et al., 2021).

It was interesting to note that the behavioral determinants of COVID vaccine acceptance among participants from all surveyed countries included perceived social norms, belief in divine will, trust in COVID vaccines, trust in sources of safety information, and vaccine safety as reasons for both accepting and rejecting the COVID vaccine. In many places, participants were more willing to accept vaccines when close family members, friends, religious or community leaders, and healthcare representatives were also recommending vaccination. Alternatively, those rejecting the vaccine had

very low trust in COVID vaccine information, stating it is “not safe at all” (Davis et al., 2022). One in eight (12.1%) vaccinated respondents were hesitant about booster doses. Main factors leading to vaccine hesitancy included illiteracy, mistrust in science and governments and health authorities, misinformation, and concerns around vaccine safety and in some countries, age and minority race or ethnicity (Lazarus et al., 2021).

Another important factor is the limited efficacy of current COVID-19 vaccines in preventing infection against new circulating variants. Introducing updated vaccine formulations and regular boosters could also influence acceptance, making it challenging for convincing individuals and communities to accept new vaccines to maintain protective immunity, especially as the risk perception of COVID-19 infection has decreased (Petherick et al., 2021). A vaccine acceptance survey was conducted by Solice Arce et al, across 15 survey samples covering 10 LMICs in Asia, Africa, and South America and HICs like Russia and the United States. The study revealed that there was a higher willingness to take a COVID-19 vaccine in their LMIC samples (mean 80.3%; median 78%; range 30.1 percentage points) compared with the United States (mean 64.6%) and Russia (mean 30.4%) (Solice Arce et al., 2021).

In several LMICs, information, knowledge and communication barriers were important reasons for vaccine hesitancy. For lay audiences, there is a need to continuously disseminate new information on the usefulness and efficacy and safety of existing and newly formulated ones. As per Chokou et al., the ongoing ‘infodemic’ of voluminous, high-speed information—accurate or not—further impedes vaccine literacy. (Chokou et al., 2022)

Other major challenges influencing vaccine administration especially in Bangladesh and Ghana were concerns about monitoring and controlling vaccine temperatures, lack of trained healthcare professionals to administer doses, accessing remote areas and difficulty adhering to a prioritization framework. Further limitations in technology and internet connectivity impeded the monitoring of vaccine programs to track uptake and administration in real-time (Tagoe et al., 2021).

It was challenging for remote locations in many LMICs to have optimum storage systems for temperature-sensitive vaccines. Hence recommended temperatures while transferring or storing large quantities of doses could not be controlled and monitored well (Alam et al., 2021). Although, single dose vaccines by Johnson & Johnson could be stored at normal refrigerator temperatures and make it a viable option, undesired complications of the vaccine like unexplained illness and coagulopathy created a setback for the acceptance of this vaccine (Sheikh et al., 2021).

Discussion

Based on the important findings of the various scientific papers and articles reviewed, there are major disparities in various aspects of the COVID-19 vaccination in the LMICs. In this discussion we highlight the most important factors causing disparities and discuss the mitigation measures for the same.

Previous vaccine campaigns against communicable diseases such as polio, Hepatitis B, and others have been successful in many countries. Such programs set up a framework for approaching mass

vaccination against COVID-19. Vaccination efforts must be supported by surveillance networks, trained personnel, and operation centered infrastructure (Sheikh et al., 2021).

The major disparity seen was that by April 2021, although more than 500 million people the world over had received at least one dose, most High-Income Countries (HICs) had administered at least one dose to over 20 percent of their populations, and a few outliers had provided at least one dose to well over 50 percent (Hall et al., 2021). On the other hand, several of LMICs were yet to administer an initial dose to 1 percent of their populations as of the same time. This posed a risk not only to the residents of the country but also to the emergence and potential global spread of possible viral variants. As the global initiative on COVID-19 Vaccines Global Access (COVAX) stated: “With a fast-moving pandemic, no one is safe, unless everyone is safe”.

Considering the supply challenges, this has proven to be a bottleneck for the smooth supply of vaccines in LMICs. The following critical factors need to be addressed to mitigate these challenges:

1. Efficient centers that drive targets set by policy makers, scenario planning, roadmap development, and oversee decision making, implementation and manage uncertainty.
2. Effective strategies to ensure effective roll out by ensuring availability, administration, accessibility, acceptability, affordability, and accountability.
3. Leverage existing experience gained by implementing immunization programs in the past and because COVID-19 vaccine rollout strategies could potentially disrupt ongoing immunization programs.
4. Build better health system capacities and resiliency via better investment in delivery infrastructure including digital systems.

One of the solutions to overcome the short supply of vaccines is for the Middle Income Countries to become self-sufficient, ramp up vaccine production and supply to other LMICs. As was noted during the pandemic, to counter the global inefficiency and lack of solidarity that was threatening the management of the pandemic, homegrown vaccines and local manufacturing in middle-income countries was the best option for low-income countries. While China signed contracts to supply 24 countries, India obtained approval from AstraZeneca to manufacture their vaccine in the largest vaccine factory in the world, the Serum Institute. Millions of vaccine doses were manufactured and this enabled them to deliver 20 times more doses than China to COVAX. India sent vaccine doses free of charge to neighbouring countries of Nepal, Bangladesh, Myanmar, the Maldives, Sri Lanka, the Seychelles, and Afghanistan. To some other countries India provided vaccines at a low prices of US\$3 to US\$5 at no profit (Garnier S, 2021).

Another major factor that led to disparities in vaccination was the inability to maintain optimum cold chains for temperature sensitive vaccines. As the vaccine immunogenicity and effectiveness are highly dependent on the storage in cold temperatures, monitoring the cold chain continuity and using up of the vaccines within critical timeframes after being removed from the cold chain or after a puncture in the multidose vial are important practical issues (Holm et al., 2021). The issues regarding accidental interruption of the cold chain and hence vaccine instability can be avoided by allocating funds for the equipments to ensure the maintenance of cold chains as well as having appropriately trained managers who are tasked to manage and monitor cold chains (Fahrni et al., 2022)

Vaccine hesitancy is a significant factor which acts as a hurdle for mass immunizations and creation of herd immunity. Understanding the drivers of COVID-19 vaccine acceptance is of global concern because a lag in vaccination in any country may result in the emergence and spread of new variants that can overcome immunity conferred by vaccines and prior disease.

It was noteworthy that parental hesitancy to vaccinate children younger than 18 years remained high in many High-Income Countries, including France, Germany, Sweden, the United Kingdom, the United States and South Korea (Lazarus et al., 2023). In LMICs, such as Kenya and Nigeria, there was low perception of vaccine safety and younger parental age, which may have led to less experienced parenting and parents themselves not getting vaccinated.

Solice et al. concluded that the most stated reason for vaccine refusal is concern about safety concern over side effects which was fueled by intensive media coverage of adverse events? (Solice Arce et al., 2021). As misrepresentation and misinformation can derail progress in COVID-19 vaccination coverage, it is important for stake holders such as health care workers, social workers, political, religious and community leaders to be educated regarding the benefits of vaccine so they can help dispel misinformation and improve vaccine acceptance in LMICs. Trusted leaders are held in high regard and are very influential in molding the opinions of their followers (Davis et al., 2022).

Conclusion

This narrative review gave us a deep insight into the existing inequalities in COVID-19 vaccine accessibility amongst the LMICs. When compared to developed countries, low- and middle-income countries have faced difficulty producing, acquiring, and deploying COVID-19 vaccines. Failure to achieve herd immunity in such countries poses a worldwide public health risk due to the potential emergence of more virulent strains and uncontrolled spread of disease.

Limited resource availability and infrastructure means that low- and middle-income countries are unable to manufacture enough vaccines to protect their populations. Although many low- and middle-income countries have been able to secure dose deliveries, they remain challenged to distribute them amongst their citizens. Various barriers to equitable deployment have been identified based on logistical vaccine transport and stability challenges via maintenance of cold chains. Vaccine misinformation and hesitancy are other factors that have led to low vaccination rates. To overcome the inequality in COVID-19 vaccine access among LMICs, mitigation strategies must be implemented. Global cooperation is required to overcome low vaccination rates in LMICs by mobilizing shared doses and ensuring safe, equitable distribution. Future studies can be targeted on specific reasons for COVID-19 vaccine inequities and practical mitigation measures based on lessons learned during the pandemic.

Declaration of Interest Statement

The authors declare that they have no conflict of interests.

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