JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Coronavirus Pandemic

Impact of the COVID-19 pandemic on routine immunization services in Yerevan and vaccinations against COVID-19 in Armenia

Naira Melkonyan[1], Arman Badalyan[1], Hasmik Hovhannisyan[1], Karine Poghosyan[2]

[1] Epidemiology Department, Faculty of Public Health, Yerevan State Medical University, Yerevan, Armenia
[2] Infectious and Non-Infectious Diseases Department, National Center for Disease Control and Prevention, Ministry of Health of the Republic of Armenia, Yerevan, Armenia

Abstract

Introduction: The coronavirus disease (COVID-19) has led to millions of deaths around the world. The indirect effects of the pandemic, include disruption of routine immunization services.

Methodology: We conducted a retrospective review to assess the impact of the pandemic on routine immunization in Yerevan and the vaccinations against COVID-19 in Armenia. We compared the number of administered doses of DPT/VHB/HIB/IPV1,2,3, Pneumococcal1,2,3, Rotarix1,2, and MMR1 vaccines in target groups in 2020 and 2021 and the total vaccination coverage in 2019, 2020, and 2021. We also analyzed the number of COVID-19 vaccines administered in Armenia from 17 May 2021 to 6 February 2022.

Results: There was a decline in the number of administered doses of vaccines at the beginning of the pandemic due to restrictive quarantine measures: 16 ± 4.5 (95% CI, 11.8-20.2), $p < 0.05$, during the second wave 18 ± 2.6 (95% CI, 15.6-20.4), $p < 0.05$ and during the interruption due to COVID-19 vaccine delivery 16 ± 7.4 (95% CI, 9.1-22.9), $p < 0.05$. There was no significant decrease in the number of vaccinations during the first, third, and fourth pandemic waves ($p > 0.05$) Overall, the COVID-19 vaccination process was slow and only 30% of the population were vaccinated.

Conclusions: The COVID-19 pandemic led to disruptions in the routine immunization process, but there was no significant decrease in the total vaccine coverage due to rapid scaling up of the vaccination services and catch-up vaccinations. Thus, the restrictions imposed during the pandemic did not affect the overall progress of vaccination.

Key words: COVID-19; vaccination; vaccine-preventable disease; epidemic wave; coronavirus; pandemic.

J Infect Dev Ctries 2022; 16(11):1687-1695. doi:10.3855/jidc.17028

(Received 27 June 2022 – Accepted 03 September 2022)

Introduction

Since its emergence in Wuhan, China in late 2019, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) that causes coronavirus disease (COVID-19) has spread rapidly to nearly all the countries of the world and has become a pandemic. This led to a crisis and social disruption on a global scale [1,2]. Millions of lives were lost around the world as a direct result of the pandemic. As of 25 March 2022, about 478 million confirmed coronavirus cases and about 6.1 million deaths have been recorded globally [3,4]. The indirect effects of the pandemic on healthcare programs are equally important. As governments across the world attempted to contain the epidemic by implementing lockdowns, closing borders and halting mass gatherings, experts started worrying about the indirect health impacts including disruptions of routine immunization services [4,5,6]. According to the World Health Organization (WHO), the main challenges that the immunization services could face due to the COVID-19 pandemic included fewer people visiting health facilities for immunization due to fear of coronavirus infection, concerns among health workers for their own safety while delivering immunization services, and shortage of qualified health workers due to diversion of resources to COVID-19 response [4,7]. Disruptions of routine health services are likely to increase morbidity and mortality, particularly in risk groups [4,8,9]. This has led to challenges in the case of vaccine-preventable infections [10]. Health systems have been overstretched and unable to operate effectively due to the rapidly increasing demand on health facilities [11]. Previous epidemics have demonstrated that when health systems are overwhelmed, mortality from vaccine-preventable diseases can also increase dramatically. COVID-19 has triggered a similar breakdown of immunization systems and the future of a hard-fought struggle to prevent

mortality from vaccine-preventable diseases is at stake. Thus, there will be challenges in the future with preventing deaths from vaccine-preventable diseases [7,12,13]. According to the data collected by the WHO, United Nations International Children's Emergency Fund (UNICEF), Global Alliance for Vaccines and Immunization (GAVI) and the Sabin Vaccine Institute, provision of routine immunization services is substantially hindered in at least 68 countries (developed and developing) and is likely to affect approximately 80 million children under the age of 1 living in these countries [14-16].

In Armenia, 18 vaccine-preventable diseases are included in the national schedule of immunization, for routine vaccinations. Before the COVID-19 pandemic, these vaccines had at least 90% uptake at the national level. As a result of the successful implementation of the National Immunization Program vaccine-preventable diseases have significantly decreased in Armenia and cases of pertussis, tetanus, and mumps have been rare. The incidence of bacterial meningitis decreased by 2.4 times among children under 5 years of age between 2009 and 2019 due to *Haemophilus influenzae* type B and pneumococcal vaccines. Cases of viral hepatitis B have not been registered among children under 14 years of age after the introduction of hepatitis B vaccine (1999). Endemic cases of measles and rubella have been eliminated (data from 2007) and poliomyelitis and diphtheria have been eradicated (data from 2002) [17]. Despite the successes of the immunization program there is vaccine hesitancy in Armenia, especially in the case of new vaccines and this can influence routine vaccination programs [18].

The first case of COVID-19 was registered in Armenia in March 2020. Since then, there have been five COVID-19 waves that caused 422,423 confirmed coronavirus cases and 8,607 deaths as of March 25, 2022 [19]. In this study we aimed to assess the influence of the COVID-19 pandemic on routine vaccinations in Yerevan city, and vaccinations against COVID-19 in Armenia.

Methodology

Our analysis involved two stages. In the first stage, we analyzed the impact of the pandemic on routine immunization services. In the second stage, we studied the COVID-19 vaccination program.

Impact of the pandemic on routine immunization services

We used the National Center for Disease Control (NCDC) of Armenia database to collect data on the number of COVID-19 cases and deaths by month and then calculated the COVID-19 incidence and mortality rates per 100,000 population during the pandemic waves between March 2020 and December 2021.

We calculated the total number of routine immunization doses administered per month to children aged 0–12 months and 12-24 months at the clinic of "Heratsi" Hospital Complex №1 of Yerevan State Medical University at Mkhitar Heratsi. We included the first, second, third administered doses of the diphtheria – tetanus – pertussis - hepatitis B - *Haemophilus influenzae* type B - poliomyelitis vaccine (hexavalent combination vaccine: DPT/VHB/HIB/IPV1,2,3), the first, second, and third administered doses of a pneumococcal vaccine (Pneumococcal1,2,3), the first and second administered doses of a rotavirus vaccine (Rotarix1,2) in children aged 0–12 months in 2020 and 2021, and the first administered dose of the measles – mumps - rubella vaccine (MMR1) for children aged 12-24 months in 2020 and 2021. We calculated the number of administered doses of the above stated vaccines according to the pandemic waves and compared the mean values of the administered doses of vaccines between months on a quarterly basis (three months) during the COVID-19 pandemic from 2020 to 2021.

We compared the total vaccination coverage of children aged 0–12 months and 12-24 months in 2019 (before the COVID-19 pandemic), and in 2020, and 2021 (during the COVID-19 pandemic) in Heratsi" Hospital Complex №1 of Yerevan State Medical University at Mkhitar Heratsi. We compared this data with the total vaccination coverage in the same target groups in Armenia.

COVID-19 vaccination status

During the second stage, we collected data on the number of COVID-19 vaccinations per week in Armenia from 17 May 20221 to 6 February 2022 using the database of the National Center for Disease Control of Armenia.

Statistical analysis

Descriptive statistics including the mean value ($\bar{X}$), standard deviation (SD), and population mean ($\mu \pm \sigma$) with 95% confidence interval (CI) for continuous parameters (the numbers of the administered doses of routine vaccinations in children aged 0-12 months: DPT/VHB/HIB/IPV1,2,3 vaccine, Pneumococcal1,2,3 vaccine, Rotarix1,2 vaccine) were calculated using Microsoft Office Excel. T-test (two tailed, independent samples) was used to compare the mean values of the number of vaccinations by month in 2020 compared

with 2021 to assess the impact of factors disrupting routine vaccinations. Null and alternative hypotheses were employed to determine statistical significance.

H_0: There was no association between the two studied variables.

H_a: There was an association between the two studied variables.

p values of less than 0.05 were considered statistically significant when the null hypothesis was rejected and the alternative hypothesis was conformed.

In addition, the frequency (percentage) for categorical variables (total vaccination coverage of children aged 0-12 months and 12-24 months) was also calculated. Chi-square test was used to compare the categorical variables before the pandemic (2019) and during the pandemic (2020-2021). *p* values less than 0.05 were considered statistically significant.

Ethical compliance

This research did not involve the use of human subjects or animal experiments and does not require ethical approval.

Figure 1. Dynamics of the COVID-19 incidence rates and COVID-19 mortality rates per 100,000 people in Armenia from March 2020 to December 2021.

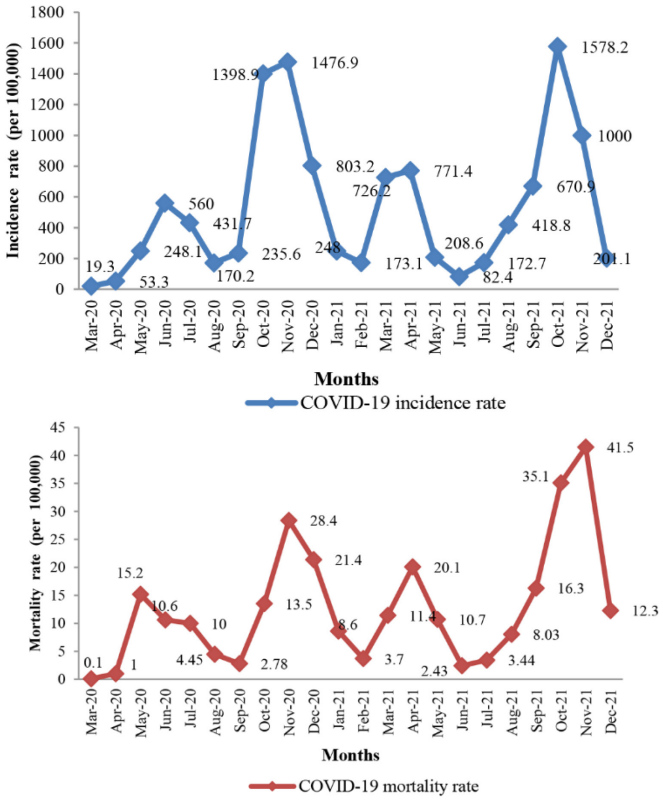
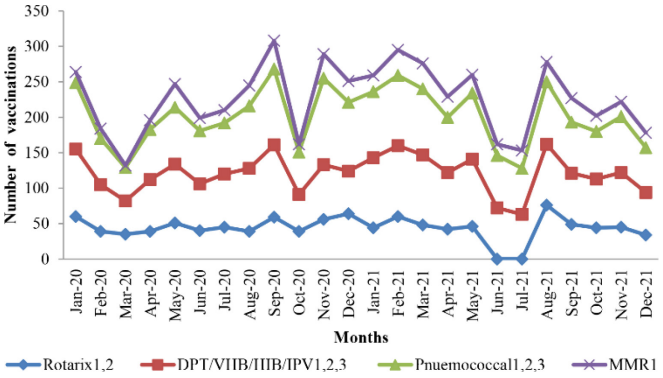


Figure 2. Dynamics of the number of vaccinations of DPT/VHB/HIB/IPV1,2,3, Pneumococcal1,2,3, and Rotarix1,2 vaccines in children aged 0–12 months, and MMR1 vaccine in children aged 12-24 months in the clinic of "Heratsi" Hospital Complex №1 of Yerevan State Medical University (2020-2021).



Results

Prevalence of COVID-19 disease during COVID-19 waves in Armenia

The first case of COVID-19 was registered in Armenia on March 1, 2020. The disease spread rapidly, and by April, 571 cases and 3 deaths were reported. COVID-19 cases and deaths continued to increase until June (16,573 cases, 450 deaths), and was characterized as the first coronavirus pandemic wave in Armenia. The number of cases decreased by August (5,037 cases, 428 deaths), after which it began to slightly increase in September (6972 cases, 82 deaths). There was a sharp increase in cases and deaths in October (41,404 cases, 400 deaths) and November (43,713 cases, 830 deaths) and this led to the second wave of coronavirus infection. Later, the number of cases decreased until February 2021, but deaths continued to increase (5,128 cases, 1002 deaths). There was again an increase in the number of cases in March (21,520 cases, 338 deaths) and in April (22,860 cases, 595 deaths) and this was the third epidemic wave. The fourth epidemic wave was in October 2021 (46,766 cases), and was more severe than the previous ones during which the highest number of coronavirus cases and deaths were recorded due to the B.1.617 "Delta" type coronavirus; 1,040 deaths in October and 1,231 deaths in November.

All cases were confirmed in the laboratory by real time polymerase chain reaction (RT-PCR) test provided in the reference laboratory of NCDC of Armenia.

The number COVID-19 cases and deaths are presented in Figure 1. We assessed the dynamics of COVID-19 incidence rates and COVID-19 mortality rates per 100,000 population in Armenia between March 2020 and December 2021.

Impact of the pandemic on routine immunization services

Figure 2 shows the variation in numbers of administered doses of DPT/VHB/HIB/IPV1,2,3, Pneumococcal1,2,3, and Rotarix1,2 vaccines in children 0-12 months and MMR1 vaccine in children 12-24 months in the clinic of "Heratsi" Hospital Complex №1 of Yerevan State Medical University at Mkhitar Heratsi from 2020 to 2021. A decrease in the number of vaccinations can be observed and this coincides with the early stage of the pandemic and with some COVID-19 waves. This decrease in vaccination was observed in both the age groups. The differences in the number of individual vaccines in the same target group (children aged 0-12 months) was due to the refusal of specific vaccines.

Table 1 summarizes the means and standard deviation (SD) of the total number of vaccines administered to children aged 0–12 months in the clinic of "Heratsi" Hospital Complex №1 of Yerevan State Medical University on quarterly bases and population mean values with 95% confidence interval during the early stage of the pandemic and the peaks of the waves. The mean 16 ± 4.5 (95% CI, 11.8-20.2) of administered doses of vaccines declined at the beginning of pandemic in March 2020 compared to February and increased in April ($p < 0.05$). During the first pandemic wave, in June 2020, the mean was 23 ± 2.9 (95% CI, 20.3-25.7), which is lower compared to the mean in May and July. However, this decrease was not statistically significant ($p > 0.05$). In October 2020, during the second wave, the mean 18 ± 2.6 (95% CI, 15.6-20.4) was significantly lower than September and November ($p < 0.05$). During the third pandemic wave, in April 2021, the mean declined to 25 ± 4.5 (95% CI, 20.5-29.2) in comparison with March and May of the same year. However, this decline was not statistically significant ($p > 0.05$). Finally, the fourth wave in October 2021 had a relatively non-significant decline ($p > 0.05$) in mean [22 ± 1.6 (95% CI, 21-24)].

The sharp decline in vaccinations registered in June and July 2021 [mean 18 ± 9.01 (95% CI, 9.6-26.4) and 16 ± 7.4 (95% CI, 9.1-22.9)] were significantly lower than in May and August. There was no increase in the number of the coronavirus cases during this time. This was associated with the over-stretched immunization services and medical workers due to the launch of COVID-19 vaccinations. The delivery of Rotarix vaccine was also interrupted during these months.

In order to assess the interruption of routine vaccinations during the pandemic, we compared the total vaccination coverage of children aged 0-12 months and 12-24 months during the pandemic phase in the clinic of "Heratsi" Hospital Complex №1 of Yerevan State Medical University in 2020, 2021, and before the pandemic in 2019. This analysis showed that in 2020 there was a slight decline in the total coverage of vaccinations in children up to the age of 1 year, from 84% to 83%, $p > 0.05$. In 2021, the coverage rate increased from 83% to 87%. In 2020, the total coverage

Table 1. Number of routine total vaccinations among children aged 0–12 months in the clinic of "Heratsi" Hospital Complex №1 of the Yerevan State Medical University during the COVID-19 pandemic (2020-2021).

Risk factors for disruption of routine vaccinations	Period of time	Mean number of vaccinations ($\bar{X}$ ± SD) 95% CI	Population mean of the number of vaccinations (μ ± σ) 95% CI	Statistical significance*
Beginning of the pandemic, March 2020	February 2020	21 ± 1.8	19.4-22.6	$p < 0.05$
	March 2020	16 ± 4.5	11.8-20.2	
	April 2020	23 ± 3.4	19.8-26.2	
First pandemic wave, June 2020	May 2020	27 ± 3.7	23.6-30.4	$p > 0.05$
	June 2020	23 ± 2.9	20.3-25.7	
	July 2020	24 ± 3.7	20.6-27.4	
Second pandemic wave, October 2020	September 2020	34 ± 3.2	31-37	$p < 0.05$
	October 2020	18 ± 2.6	15.6-20.4	
	November 2020	37 ± 4.3	33-41	
Third pandemic wave, April 2021	March 2021	30 ± 6.9	23.5-36.5	$p > 0.05$
	April 2021	25 ± 4.5	20.5-29.2	
	May 2021	29 ± 3.7	25.5-32.5	
Fourth pandemic wave, October 2021	September 2021	24 ± 1.4	22.7-25.3	$p > 0.05$
	October 2021	22 ± 1.6	21-24	
	November 2021	25 ± 2.7	22.5-27.5	
Launch of COVID-19 vaccinations, June, July 2021	May 2021	29 ± 3.7	25.5-32.5	$p < 0.05$
	June, July 2021	18 ± 9.01, 16 ± 7.4	9.6-26.4, 9.1-22.9	
	August 2021	31 ± 5.7	25.7, 36.4	

*T-test was used to compare the mean values of the numbers of routine vaccinations administered to children aged 0-12 months in a given month in the presence of disruption factors of vaccination with the mean values of months before and after disruption.

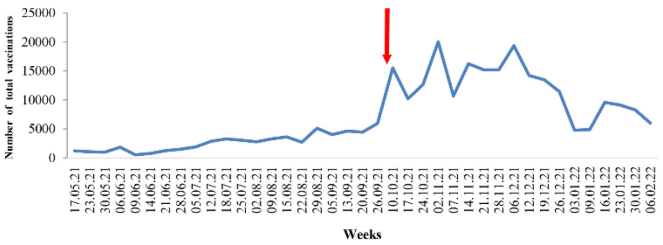
of vaccination in children aged 12-24 months decreased from 84% to 80%, $p > 0.05$, but it increased to 83% in 2021 (Table 2). However, these fluctuations in coverage were not statistically significant. Next, we compared these values with the total coverage of vaccinations in the same target groups in Armenia: 92% in 2019, 86% in 2020, 92% in 2021 among children aged 0-12 months and 95% in 2019, 94% in 2020, 94% in 2021 among children aged 12-24 months.

In order to catch up on the routine vaccinations, the Ministry of Health of Armenia introduced the guidelines on the implementation of immunization measures during the pandemic and these guidelines were adopted in April 2020. The guidelines included recommendations on routine vaccinations during the pandemic, maintenance of strict anti-pandemic regime in medical institutions and public awareness. These measures have led to increase in vaccinations and restoration of total coverage in children aged 0–12 months and 12-24 months in the clinic of "Heratsi" Hospital Complex №1 at the Yerevan State Medical University and in Armenia.

Progress of COVID-19 vaccination

We also studied the progress of vaccination against COVID-19 in Armenia. Mass vaccinations against COVID-19 have been carried out since April 2021 with the Sputnik V and AstraZeneca vaccines. Later on, CoronaVac, Moderna, Sinopharm, and Pfizer-BioNTech vaccines were also provided. Total vaccinations in Armenia reached 1,925,556 by February 6, 2022, out of which 1,054,178 were first dose, and 858,981 were second dose, and 12,397 were booster dose. A total of 29% of the population were vaccinated with at least one dose of the COVID-19 vaccine. However, the vaccination rate was rather low from April to September 2021 (Figure 3), involving an average of about 1900 people daily, which is 0.08% of the target population (>18 years). In October 2021, the Armenian Government introduced restrictions on unvaccinated people to speed up the vaccination process. These restrictions included mandatory presentation of a vaccination certificate or a RT-PCR

Figure 3. Dynamics of the total number of vaccinations against COVID-19 in Armenia (17.05.2022-06.02.2022).



negative test every 14 days for Government employees. This restrictive measure led to an increase in the participation of the population in vaccination programs in October ($p < 0.05$) compared to the previous months (April to September). An average of 14,700 people received the COVID-19 vaccine daily which represents 0.67% of the target population. This relative activation of the vaccination process continued until December 2021, but it did not contribute to the development of significant immunity in the population.

To ensure high vaccination coverage, the Armenian Government continued to tighten measures in December 2021, changing the 14-day period of the PCR-negative test of unvaccinated workers to 7 days. However, this measure did not contribute to an increase in the number of vaccinations ($p > 0.05$). The increase in number of vaccinations was not affected by other restrictions imposed by the Armenian Government in January 2022 and there was a decrease in the number of vaccinations compared to October-December ($p < 0.05$) (Figure 3).

Thus, analysis of vaccinations in different age groups indicated low vaccination rates in the age group ≥ 65 years, which is the primary risk group for the coronavirus disease. The primary changes in vaccination rates in response to Government restriction and guidelines occurred in lower age groups (35-64 and 18-34 years) (Table 3).

Discussion

Our data indicate that there were four COVID-19 waves from March 2020 to December 2021. The

Table 2. Total vaccination coverage among children aged 0–12 months and 12-24 months in the clinic of "Heratsi" Hospital Complex №1 of Yerevan State Medical University (2019, 2020, 2021).

Years	Children aged 0–12 months			Statistical significance	Children aged 12-24 months			Statistical significance
	Size of target group	Total number vaccinated	Vaccination coverage (%)		Number of target group	Total number vaccinated	Vaccination coverage (%)	
2019	351	295	84%		348	292	84%	
2020	335	277	83%	$p > 0.05$	363	292	80%	$p > 0.05$
2021	332	290	87%		346	286	83%	

decrease in the number of vaccinations in March 2020 was associated with incidence of coronavirus cases, restrictive quarantine measures which included restrictions on the movement of people, and panic among people who limited contact with others. Armenia, and some other countries, adopted guidelines to catchup the routine vaccinations in April 2020. The guidelines set up unified prevention and control mechanisms for the COVID-19 pandemic and mobilized awareness programs through local health establishments, community (marz) centers with weekly meetings and discussions to inform parents of children regarding vaccination, and strengthened and encouraged staff safety and protection. In addition, the guidelines promoted maintenance of strict pandemic protocols in medical institutions that provide routine vaccination services, and established a reasonable vaccination catch-up process by identifying individual children in need of catch-up vaccinations. Pre-examination and consultation on vaccinations and activation of vaccination services according to dynamically-adjusted coronavirus risk levels were encouraged; measures were taken to avoid crowds at vaccination clinics by using appointments, Mobile vaccination centers were established, daily service hours were increased and vaccination services were offered during the weekends, and the number of accompanying persons were reduced [20,21]. This led to the resumption of the pace of vaccination process and the number of vaccinations began to rise. In June 2020, during the first wave of the pandemic, there was no significant decrease in the number of vaccinations while there was a rapid increase in cases. In October 2020, during the second COVID-19 wave, a significant decrease in the number of vaccinations was observed, which was the result of a crisis in the country caused by a significant spread of coronavirus cases and a tense military situation. As a result, the healthcare system was overloaded, and there was a high demand for medical workers. However, this situation was adjusted in the next month and the vaccination process resumed. During the third COVID-19 wave in April 2021, an increase in the number of cases did not significantly affect the vaccination process, and in October (the fourth wave) a higher number of COVID-19 cases was registered, which also did not impact on the vaccination process. A considerable decrease in vaccination was observed in June-July 2021 when there was a significant decrease in COVID-19 cases (Figure 1). This situation was associated with the interruption due to the Rotarix vaccine delivery, and the increase in COVID-19 vaccination during this time led to an overload of immunization services (Table 1).

The study shows that rapid activation of the routine vaccinations after disruptions led to catch up vaccinations and total coverage in children aged 0–12 months and 12-24 months was restored in the healthcare facility and in Armenia. In 2020, the coverage rate was slightly reduced; however, this was not associated with the pandemic. In 2020, total coverage of vaccination in children aged 12-24 months decreased, but it increased and was restored in 2021 (Table 2).

Similar findings have been presented in previous studies. A decline in the number of administered doses of diphtheria–pertussis–tetanus-containing vaccine (DTP3) and the first dose of the measles vaccine (MCV1) in the first half of 2020 was noted. The lowest number of vaccine doses administered was observed in April 2020, when 33% fewer DTP3 doses were administered globally, ranging from 9% in the WHO African region to 57% in the South-East Asia region. Recovery of vaccinations began by June 2020, and continued into late 2020. WHO regional office reported substantial disruption to routine vaccination services in April 2020, related to interrupted vaccination demand and supply, including reduced availability of the healthcare workforce. It has been reported that 45 (69%) of 65 countries showed disruption in outreach services compared with 27 (44%) of 62 countries with disrupted fixed-post immunization services [4].

Slowing or stopping the immunization process, even in the short term, can lead to an increase in the susceptibility of the population and increase the risk of vaccine-preventable infection outbreak [7,13,22]. Outbreaks can lead to an increase in morbidity and mortality, especially among children and high-risk

Table 3. Vaccination rates by age groups among Armenian population.

December 2021 to March 2022 (Month/week)	Age groups			
	> 65	35-64	18-34	12-17
	Vaccination rates (%)			
01.12.2021 - 13.12.2021	15.2	60.5	24	0.01
13.12.2021 - 20.12.2021	15.2	60.1	24.6	0.07
20.12.21 - 17.01.2022	15.2	58.9	25.7	0.1
17.01.2022 - 31.01.2022	15.2	58.5	26.2	0.1
31.01.2022 - 02.02.22	15.2	58.4	26.3	0.1

groups, and cause additional strain on the health system, which is already overloaded by the COVID-19 pandemic [10]. In 2021-2022 a mutated strain of poliovirus was reported in more than 30 countries including Afghanistan, Pakistan, and Congo [22,23], and in 2020 diphtheria cases were reported in Pakistan, Bangladesh and Nepal [22]. Measles cases are being reported around the globe, including in Bangladesh, Brazil, Cambodia, Central African Republic, Iraq, Kazakhstan, Nepal, Nigeria and Uzbekistan [22,24]. GAVI estimated that more than 117 million children in 37 countries have not been vaccinated against measles in 2020 due to the COVID-19 pandemic. Measles immunization campaigns in 24 countries have already been delayed [24].

In contrast to routine catch-up vaccinations, COVID-19 vaccinations were rather slow in Armenia, despite the widespread COVID-19 infections. However, vaccine hesitancy is not universal to all vaccines and people do not have the same underlying concerns with regard to every vaccine; thus, refusal of one vaccine does not necessarily indicate complete vaccine denial. The vaccines against COVD-19 were new and had been developed more quickly than is usual for new pharmaceuticals [18], possibly resulting in vaccine hesitancy. Similar hesitancy had been observed in the case of the vaccine against human papillomavirus (Gardasil), which was introduced in Armenia in 2017.

The restrictions introduced by the Government of the Republic of Armenia in October 2021 were a stimulus that encouraged unvaccinated people to get vaccinated. The relative activation continued until December 2021. Unfortunately, the restrictions applied at the later stage were not as effective; as a result, only about 30% of the population was vaccinated against COVID-19 as of February 6, 2022, which is much lower than the expected vaccine coverage, and also lags behind the vaccination coverage in other countries (Table 4) [25]. There were low vaccination rates (15.2%) in the main risk group of the population (≥ 65 years) which can lead to a high risk of severe disease and death. Since November 2021, a new type of coronavirus BA.1 "omicron" has spread in the world, which, as is known, has a high rate of infectivity and ability to bypass the human immune system [26-28]. Since the effectiveness of the two doses of vaccines decrease in the case of the new subtypes of coronavirus, it is necessary to administer booster doses [29,30]. The administration of booster doses of theCOVID-19 vaccine has also been slow in Armenia.

Conclusions

Our study showed that the COVID-19 pandemic has had substantial impact on the routine immunization process in Yerevan during some periods of the pandemic. The main risk factors for disruption of immunization services were during the initial stage of the COVID-19 pandemic, and were linked to the establishment of restrictive quarantine measures. During the second COVID-19 wave, the risk factors were associated with the crisis situation in the country, including the tense pandemic and military situations, overload of the healthcare system, launch of the COVID-19 vaccine and the demand on medical workers resulting in the interruption of vaccine delivery. The activation of immunization services lead to recovery of the vaccination process and there was no significant decrease in the total vaccination coverage among children aged 0-12 months and 12-24 months.

However, this was not the case with the COVID-19 vaccinations. The restrictions introduced by the Armenian Government during the pandemic did not affect the vaccination process against COVID-19 in general. We have had a low coverage of COVID-19 vaccinations.

In consideration for the limited healthcare resources, it is necessary to implement catch-up immunization strategies, especially for the most

Table 4. Total vaccinations against COVID-19 in other countries (data collected on 06.02.2022).

Country	Number of doses administered (×1,000,000)	Fully vaccinated (%)	Booster dose (%)	Daily rate of doses administered (×1,000)
China	3.01 (billion)	86.8	-	7,600
Portugal	9.2	90	52	77
Singapore	4.8	85	57	20
USA	542.0	63.4	26.6	460.1
Russia	155.7	48.1	7.1	214.9
Turkey	142.8	62.8	39.3	164.7
Azerbaijan	12.2	47.2	21.8	30.8
Iran	134.8	64.7	22.9	537.2
Georgia	2.8	33.0	-	6.5
Armenia	1.9	29	0.4	6.0

vulnerable populations who were already at high risk before the pandemic, create flexible mechanisms for simultaneous mass vaccination against COVID-19 and routine vaccinations in medical institutions, strengthen health information systems to routinely record immunization coverage and ongoing vaccine-preventable disease surveillance, and educate the population to change their attitude towards vaccination.

Limitations

The study on the number of routine vaccinations was based on only one medical institution in Yerevan; other medical institutions of the provinces were not included. Therefore, results may not represent the situation in the entire country.

During the study, only laboratory confirmed COVID-19 cases were considered, and suspected cases were not included.

Acknowledgements

We thank the National Center for Disease Control and Prevention of the Ministry of Health of RA for providing access to the database and the Clinic of "Heratsi" Hospital Complex №1 of Yerevan State Medical University at Mkhitar Heratsi for giving access to the immunization data. The authors did not receive any financial support for the research, collection, analysis and interpretation of data, writing and publication of this article.

Authors' Contributions

Naira Melkonyan: methodology, data curation, investigation, writing original draft, software, formal analysis. Arman Badalyan: methodology, data curation, formal analysis, conceptualization, writing, review and editing. Hasmik Hovhannisyan: writing, review and editing, project administration, supervision. Karine Poghosyan: data curation, writing original draft.

References

1. Van Damme W, Dahake R, Delamou A, Ingelbeen B, Wouters E, Vanham G, Van de Pas R, Dossou JP, Ir P, Abimbola S, Van der Borght S, Narayanan D, Bloom G, Van Ag, Engelgem L, Ahmed MA, Kiendrebeogo JA, Verdonck K, De Brouwere V, Bello K, Kloos H, Aaby P, Kalk A, Al-Awlaqi S, Prashanth NS, Muyembe-Tamfum JJ, Mbala P, Ahuka-Mundake S, Assefa Y. (2020) The COVID-19 pandemic: diverse contexts; different epidemics—how and why? BMJ Glob Health 5: e003098.
2. WHO (2020) WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Available: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. Accessed: 31 July 2020.
3. Worldmeter (2020) COVID live - coronavirus statistics. Available: https://www.worldometers.info/coronavirus/. Accessed: 31 July 2020.
4. Shet A, Carr K, Danovaro-Holliday MC, Sodha VS, Prosperi C, Wunderlich J, Wonodi C, Reynolds HW, Mirza I, Gacic-Dobo M, O Brien KL, Lindstrand A (2022) Impact of the SARS-CoV-2 pandemic on routine immunization services: evidence of disruption and recovery from 170 countries and territories. Lancet Glob Health 10: e186–194.
5. Oyo-Ita, A, Wiysonge, CS, Oringanje C, Nwachukwu CE, Oduwole O, Meremition MM (2016) Interventions for improving coverage of childhood immunization in low-and middle-income countries. Cochrane Database Syst Rev 7: Cd008145.
6. Nelson R (2020) COVID-19 disrupts vaccine delivery. Lancet Infect Dis 20: 546.
7. Danovaro C, Gurung S, Ho LL, Linstrand A (2020) Understanding the disruption to programmes through rapid polling. WHO Global Immunization News (GIN) Newsletter, March–April 2020. Available: https://www.who.int/immunization/GIN_March-April_2020.pdf?ua=1. Accessed: 9 June 2021.
8. Menendez C, Gonzalez R, Donnay F, Leke RGF (2020) Avoiding indirect effects of COVID-19 on maternal and child health. Lancet Glob Health 7: e863–e864.
9. Zar HJ, Dawa J, Fischer GB, Castro-Rodriguez JA (2020) Challenges of COVID-19 in children in low-and middle-income countries. Paediatr Respir Rev 35: 70–74.
10. Pan American Health Organization (PAHO), WHO (2020) Summary of the status of national immunization programs during the COVID-19 pandemic. Available: https://www.paho.org/en/documents/summary-status-national-immunization-programs-during-covid-19-pandemic-july-2020. Accessed 28 July 2020.
11. WHO (2020) Pulse survey on continuity of essential health services during the COVID-19 pandemic. Interim report. Aug 27, 2020. Available: https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS_continuity-survey-2020.1. Accessed: 20 September 2021.
12. Sun X, Samba TT, Yao J, Yin W, Xiao L, Lui F, Lui X, Zhou J, Kou Z, Fan H, Zhang H, Williams A, Lansana PM, Yin Z (2017) Impact of the Ebola outbreak on routine immunization in western area, Sierra Leone - a field survey from an Ebola epidemic area. BMC Public Health 17: 363.
13. Lassi ZS, Naseem R, Salam RA, Siddiqui F, Das JK (2021) The impact of the COVID-19 pandemic on immunization

campaigns and programs: a systematic review. Int J Environ Res Public Health 18: 988.
14. WHO (2020) At least 80 million children under one at risk of diseases such as diphtheria, measles and polio as COVID-19 disrupts routine vaccination efforts, warn GAVI, HO and UNICEF. Available https://www.who.int/news/item/22-05-2020-at-least-80-millionchildren-under-one-at-risk-of-diseases-such-as-diphtheria-measlesand-polio-as-covid-19-disrupts-routine vaccination-effrts-warn-gaviwho-and-unicef. Accessed: 20 September 2021.
15. Causey K, Fullman N, Sorensen RJD, Galles NC, Zheng P, Aravkin A, Danovaro-Holliday MC, Martinez-Piedra R, Sodha SV, Velandia-González MP, Gacic-Dobo M, Castro E, He J, Schipp M, Deen A, Hay AI, Lim SS, Jonathan F Mosser JF (2021) Estimating global and regional disruptions to routine childhood vaccine coverage during the COVID-19 pandemic in 2020: a modeling study. Lancet 398: 522–534.
16. UNICEF (2020) Rapid assessment on the social and economic impacts of COVID-19 on children and families in Viet Nam. Hanoi. Available: https://www.unicef.org/vietnam/reports/rapid-assessment-social-and-economic-impacts-covid-19-children-and-families-viet-nam. Accessed: 10 August 2020.
17. Government of the Republic of Armenia Decision No 2129 (2020) National Program of Immunization 2021-2025. Available: http://armvaccine.am/uploads/Binder1.[1].pdf. Accessed: 10 August 2020.
18. Badalyan AR, Hovhannisyan M, Ghavalyan G Ter-Stepanyan MM, Cave R, Cole J, Farlow AWK, Mkrtchyan HV (2021) Knowledge attitude, and practice of physicians regarding vaccinations in Yerevan, Armenia: a case study of HPV. Vaccines 9: 1188.
19. National Center for Disease Control and Prevention of Armenia (nd) Available: https://ncdc.am. Accessed: 10 August 2020.
20. Wu J, Yu W, Cao L, Cao L, Rodewald L, Ye J, Song Y, Li L, Lui X, Wen N, Wang F, Hao L, Li Y, Zheng H, Li K, Ma C, Mu D, Liu Y, Zang G, An Z, Wang H, Yin Z (2020) Effectiveness of catch-up vaccinations after COVID-19 containment - China, 2020. China CDC Wkly 2: 968-974.
21. Ministry of Health Armenia Guidelines of Minister of Health of the Republic of Armenia (2020) Implementation of immunization activities during COVID-19 pandemic. Order No 1313–A, April 2020. Available: http://armvaccine.am/am/ra-health-minister-orders. Accessed: 10 August 2020.
22. Hoffman J, Maclean R (2020) Slowing the coronavirus is speeding the spread of other diseases. New York Times. Available: https://www.nytimes.com/2020/06/14/health/coronavirus-vaccines-measles.html. Accessed: 5 August 2020.
23. This Week GPEI (2020) Polio this week as of 13 January 2020. Available: http://polioeradication.org/polio-today/polio-now/thisweek. Accessed: 5 August 2020.
24. Statement by the Measles and Rubella Initiative of American Red Cross, U.S. CDC, UNICEF, UN Foundation and WHO (2020) More than 117 million children at risk of missing out on measles vaccine, as COVID-19 surges. Available: https://measlesrubellainitiative.org/measles-news/more-than-117-million-children-at-risk-of-missing-out-on-measlesvaccines-as-covid-19-surges/. Accessed: 31 July 2020.
25. Bloomberg (2020) COVID vaccine tracker. Available online: https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/. Accessed: 31 July 2020.
26. Reardon S (2022) How well can omicron evade immunity from COVID vaccines? Nature. Available: https://doi.org/10.1038/d41586-022-00283-4. Accessed: 2 February 2022.
27. Chaguza Ch, Coppi A, Earnest R, Ferguson D, Kerantzas N, Warner F, Young HP, Breban MI, Billig K, Koch RT, Pham K, Kalinich CC, Ott IM, Fauver JR, Hahn AM, Tikhonova IR, Castaldi Ch, De Kumar B, Pettker ChM, Warren JL, Weinberger DM, Landry ML, Peaper DR, Schulz W, Vogels Ch B.F., Grubaughet ND (2022) Rapid emergence of SARS-CoV-2 omicron variant is associated with an infection advantage over delta in vaccinated persons. MedRxiv. Available: https://www.medrxiv.org/content/10.1101/2022.01.22.22269660v1. Accessed: 25 January 2022.
28. Kannan RS, Spratt NA, Sharma K, Chand HS, Byrareddy SN, Singh K (2022) Omicron SARS-CoV-2 variant: unique features and their impact on pre-existing antibodies. J Autoimmun 126: 102779.
29. European Medicine Agency (2022) Preliminary data indicate COVID-19 vaccines remain effective against severe disease and hospitalization caused by the Omicron variant. Available: https://www.ema.europa.eu/en/news/preliminary-data-indicate-covid-19-vaccines-remain-effective-against-severe-disease-hospitalisation. Accessed: 25 January 2022.
30. UK Health Security Agency (2021) SARS-CoV-2 variants of concern and variants under investigation in England. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf. Accessed: 25 January 2022.

Corresponding author

Naira Melkonyan MD
Department of Epidemiology, Faculty of Public Health, Yerevan State Medical University,
2 Koryun St. Yerevan, 0025, Armenia.
Tel: +37491375860
Email: nmelkonyan01@gmail.com

Conflict of interests: No conflict of interests is declared.