PREVENTING PANDEMIC-INDUCED DISRUPTION IN ROUTINE IMMUNIZATION SERVICES IN SOUTH ASIAN COUNTRIES: A SYSTEMATIC REVIEW

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by

Dr. Akshaya Thakur
MPH - Cohort IX (2021-23)

Under the guidance of

Dr. Neetu Purohit, PhD
Professor, IIHMR University

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ABSTRACT

TITLE: Preventing Pandemic-Induced Disruption in Routine Immunization Services in South Asia: A Systematic Review

OBJECTIVE: The objective of this systematic review was to find out the magnitude of disruption of Routine Immunization coverage of children in South Asian countries due to COVID-19, the reasons for such disruptions, and measures taken/suggested by the literature to be prepared in case of occurrence of events of similar nature in future.

Methodology: A systematic review of published literature was performed. Three databases including Medline, EMBASE, and Scopus were searched. The literature searched included Medical Subject Headings (MeSH) terms “Routine Immunization”, “COVID-19”, and the “name” of any South Asian country. Primary studies, studies dealing with secondary data analysis, and expert opinions dealing with strategies for the prevention of disruption in RI services during the Covid-19 Pandemic times were included, however, studies based on reviews were excluded

RESULT: A total of 17 studies were finally selected for the identified for his systematic review. Routine immunization services in many counties of South Asia such as India, Bangladesh, Pakistan, and Afghanistan were disrupted and consequently, about 50% of children got their routine immunization delayed/missed. Major supply-side reasons like fear of infection among healthcare workers, lack of transportation facilities and travel restrictions imposed by authorities, issues related to the supply chain, absence of guidelines and SOPs to work in the COVID-19 pandemic, lack of personal protection equipment, and demand-side issues like travel restriction or restrictions to move outside, lock down, advisory to stay indoors, fear of infection, misconceptions

regarding vaccinations and vaccine hesitancy exacerbated by Covid-19 pandemic, misinformation about COVID-19, etc. were factors causing disruption of routine immunization services utilization. It is important to focus on the immediate response to mitigating the pandemic and its effect, simultaneously efforts should be ensured that essential services like RI are not disrupted. We also need to ensure adequate allocation of resources and full-fledged continuation of the RI services. COVID-19 has caused large-scale disruption in routine immunization services and given important lessons to scientific and medical communities about the grave dangers imposed by similar events in the future. We need to have an emergency preparedness plan available to us in preparation for similar events in the future.

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Dr. Akshaya Thakur

MBBS, AFIH, DTM&H

MPH-09

Preventing Pandemic-Induced Disruption in Routine Immunization Services in South Asia: A Systematic Review

1 INTRODUCTION

Immunization of children against vaccine-preventable disease (VPD) is one of the most successful public health interventions that has prevented life of millions of children who were able to live up a healthy life. It is also the most efficient intervention for saving life and suffering at a remarkably very low cost. Fully immunizing a child cost less than 35$, which includes the cost of vaccines and the cost of their administration in LMICs like India [1]. Children are immunized against most of the VPDs like Tuberculosis (TB), Polio, Diphtheria, Pertussis, Tetanus, Hepatitis, Pneumonia, Measles, Mumps, Rubella, and Rotavirus infection under the Routine Immunization (RI) Program of eight South Asian countries namely India, Pakistan, Afghanistan, Bangladesh, Nepal, Sri-Lanka, Bhutan, and the Maldives. Usually, vaccines are given at birth (BCG, OPV, and Hepatitis B), in the sixth week of life (Diphtheria, Pertussis, Tetanus, Hepatitis B, Hemophilus influenza, Polio, Rota Virus infection), the tenth week of life (Diphtheria, Pertussis, Tetanus, Hepatitis B, Hemophilus influenza, Polio, Rota Virus infection), the fourteenth week of life (Diphtheria, Pertussis, Tetanus, Hepatitis B, Hemophilus influenza, Polio, Rota Virus infection), at the ninth month of life (Measles) and the eighteenth month of life (Measles). Additionally, immunization against other diseases such as Japanese Encephalitis, Mumps, Rubella, Pneumococcal Pneumonia, and typhoid are provided sub-nationally by the public or by private providers. Table 1 shows trends in immunization in South Asian countries before the pandemic.

Table -1: Percentage of fully immunized children in South Asian countries prior to Covid-19

Country	Status of full immunization* coverage in percentage

India	62% 2015 [2] 76% 2019 [2]
Sri Lanka	>90% since 2004 [3]
Bangladesh	83% 2014 [4] 89% 2018 [5]
Nepal	78% 2018 [6]
Bhutan	About 95% since the past decade [7]
Maldives	> 95% 2019 [8]
Pakistan	74% 2017 [9]
Afghanistan	40.6% in 2015 [10]

*(*Full immunization is defined as giving all vaccination to children under the World Health Organization (WHO) immunization schedule up to Measles 1st dose i.e., the child should receive vaccine one dose of Bacilli Calmette Guerin (BCG), three doses of Diphtheria Pertussis and Tetanus (DPT), three doses of Oral Polio Vaccine (OPV), three doses of Hepatitis B Vaccine and one dose of Measles vaccine within the age of one year*.)

Several countries of the world faced disruption in essential health services including routine immunization services during the COVID-19 pandemic and it was estimated that full vaccination coverage of children dropped by at least 7-8% globally [11]. As per WHO and UNICEF data in South Asia, nearly 1.9 million more children missed essential vaccination coverage as compared to the year 2019 due to COVID-19 Pandemic [12]. As per UNICEF estimations, 3,038,000 children missed DTP-1 vaccination in India in the year 2020, this number was 1,403,000 in 2019, similarly in Pakistan 968,000 children missed DTP-1 vaccination in the year 2020 as compared to 567,000 in the year 2019 [13]. As per the WHO database, Bhutan suffered minor disruption in routine immunization services during the pandemic but recovered and scaled up immunization services in 2021 [14]. Sri Lanka, and Nepal, and the Maldives maintained their RI levels as par to year 2019 performance [15] [16] [17]. Any disruption in RI service is concerning as the schedule of childhood vaccination is required to be followed due to it being time sensitive as each vaccine is developed carefully to protect against a specific illness at a specific time and some vaccine requires more than one dose to develop a strong immune response [18] and thus even a small gap in the vaccination

coverage can put by decades of work in danger. Delayed and missed vaccination can lead the child to be vulnerable to diseases and serious complications [18]. This has direct and indirect effects on multiple sustainable development goals including ensuring healthy lives and promoting well-being for all and at all ages, reduction of poverty, and malnutrition, and achieving economic prosperity.

2. OBJECTIVE

Scientists and healthcare workers across the world were concerned about the effect of COVID-19 on routine immunization services all over the world. Due to a lack of sufficient resources, developing countries of the South Asian region are presumed to have long-term adverse effects due to disruption in routine immunization services. This has also raised issues and concerns related to future preparedness and management of RI services in case of infectious disease outbreaks with similar widespread impact potentials. This systematic review aims to find out the magnitude of disruption of Routine Immunization coverage of children in South Asian countries due to COVID-19, the reasons for such disruptions, and assessment of strategies, and measures taken/suggested by the literature to overcome such disruption in the case of occurrence of events of similar nature.

3 METHODOLOGIES

A systematic review of published literature was performed.

3.1 Search strategy

Three databases were searched: Medline, EMBASE, and Scopus. The data search was limited to studies published from March 2020 to September 2022 with English as the publishing language, Literature searched included Medical Subject Headings (MeSH) terms “Routine Immunization”, “COVID-19”, and the “name” of any South Asian country in the full text of the articles. Filters of

age up to 6 years from birth were applied to all searches. This limited the number of irrelevant results, such as those related to adult vaccinations and COVID-19 vaccines.

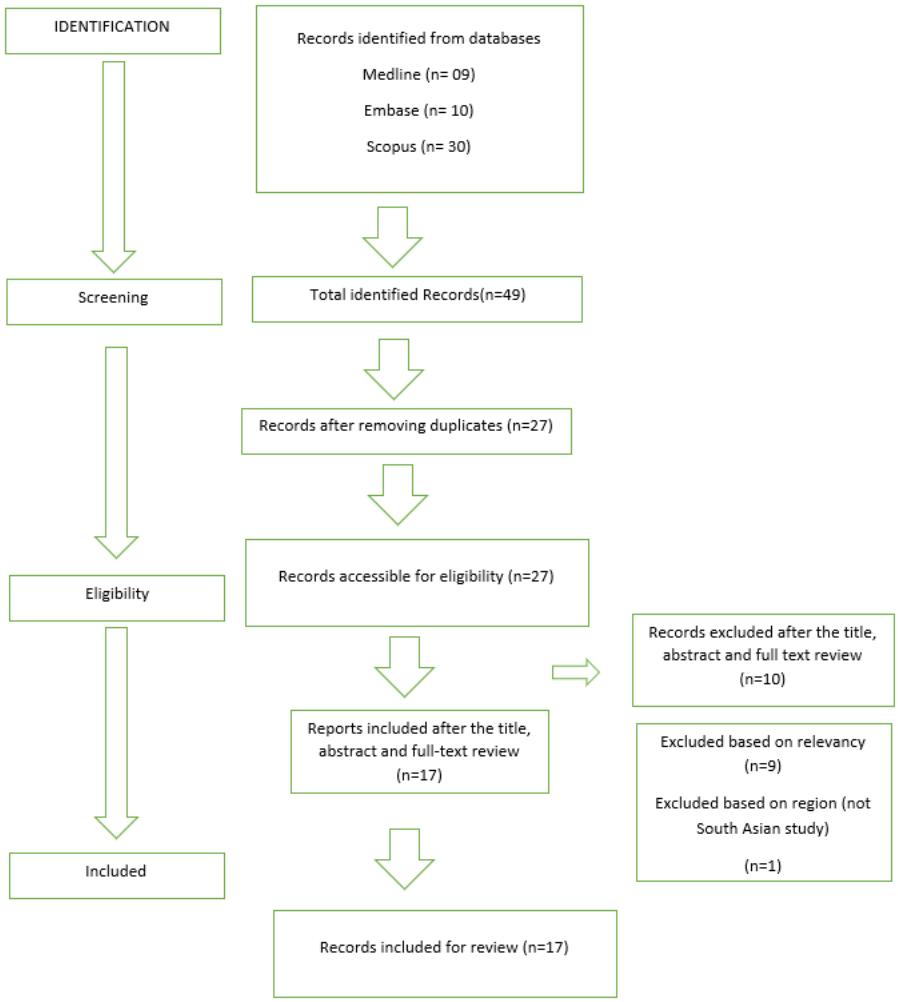
3.2 Inclusion and exclusion criteria

Studies dealing with the impact of the COVID-19 pandemic on routines immunization in any of eight South Asian countries namely India, Pakistan, Afghanistan, Bangladesh, Nepal, Sri Lanka, Bhutan, and the Maldives regarding the RI vaccines (Bacilli Calmette Guerin, Diphtheria Pertussis and Tetanus, Oral Polio Vaccine, Hepatitis B Vaccine, and Measles vaccine) universally recommended by the WHO, published from March 2020 onwards to Sept 2022 were included. Primary studies, Studies dealing with secondary data analysis, and expert opinions dealing with strategies for the prevention of disruption in RI services during the Covid-19 Pandemic times were included, however, literature reviews were excluded. All studies published in a language other than English were excluded.

3.3 Result screening and selection

Records were analyzed and de-duplication of studies was performed during the screening process. To shortlist initially identified studies, screening was performed by title to exclude irrelevant results, followed by abstract, and finally by a full-text review.

Fig 1 PRISMA flow diagram summarizing identification, screening, exclusion, and inclusion of studies



3.4 Data extraction and quality assessment

Data records were extracted in the pre-defined excel data sheet on Microsoft Excel, in following parameters: publication details like digital record number or digital object identifier, name of authors, the title of study, published year, study details such as design, source of data, sample size and methods, site of study, country, population type, funding agency, conflicts of interest, data in pre-COVID period, COVID periods, and post COVID period, vaccines included, results for each

outcome of interest (number of vaccines administered pre and during and post COVID-19 pandemic period), methods of analysis and conclusions. Vaccine coverage is defined as the number of children receiving a certain vaccine as a percentage of the total population in a specific time. Delay in vaccination is defined as a 2-week delay in the administration of the relevant vaccine as per schedule or after 2 weeks of the scheduled dose in the context of a prior dose of the same vaccine. Missed vaccination is defined as missing one or more doses of one vaccine or multiple vaccines..

Studies underwent quality and bias assessment using the quality assessment of observational and cross-sectional studies criteria provided by the National Heart, Lung, and Blood Institute (NHLBI) [19].

Table 2 Quality assessment based on the National Heart, Lung, and Blood Institute (NHLBI) checklist for observational studies

CRITERIA : YES/NO/Other*(CD, NR, NA)	Kazi A. M. et al.	Khan A. et al.	Manzoor A. et al.	Sahoo B. et al.	Bhadoria S. S. et al.	Siddiqi D. A. et al.	Emmanuel F. et al.	González P. A. et al.	Ali I.	Nguyen P. H. et al.	Rizwan W. et al.	Khan S. A. et al.	Rahman S. U. et al.	Dixit S. M. et al.	Hanifi S.M.A. et al.	Chandir S. et al.	Chandir et al.
1. Was the research question or objective in this paper clearly stated?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
2. Was the study population clearly specified and defined?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
3. Was the participation rate of eligible persons at least 50%?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	NA	NA	NA	NA	NA	Yes	NA	NA	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
5. Was a sample size justification, power description, or variance and effect estimates provided?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	No	No	NA	Yes	NA	Yes
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
10. Was the exposure(s) assessed more than once over time?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
12. Were the outcome assessors blinded to the exposure status of participants?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
13. Was loss to follow-up after baseline 20% or less?	NA	NA	NA	NA	NA	NA	NA	NA	NA	YES	NA	NA	NA	NA	NA	NA	NA
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Yes	NA	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes	NA	Yes	NA	Yes
*CD, cannot determine; NA, not applicable; NR, not reported	MEDIUM	CD	MEDIUM	MEDIUM	MEDIUM	GOOD	MEDIUM	MEDIUM	CD	MEDIUM	GOOD	MEDIUM	MEDIUM	CD	GOOD	CD	GOOD

3.5 Data synthesis and analysis

The Cochrane Handbook for Systematic Reviews of Interventions [20] was consulted and adapted as appropriate for the conduction of this systematic review.

4 ETHICAL CONSIDERATIONS

Not required.

5 FINDINGS AND DISCUSSION

A total of 17 studies were included after the screening procedure.

Table 3 Enumeration of literature considered in this systematic review based on the country of origin

Country	Literature belonging to the specific country
India	n=2 [21 22]
Sri Lanka	n=0, WHO Factsheet [15]
Bangladesh	n=2 [23 24]
Nepal	n=1 [25]
Bhutan	n=0, WHO Factsheet [14]
Maldives	n=0, WHO Factsheet [17]
Pakistan	n=11 [26 27 28 29 30 31 32 33 34 35 36]
Afghanistan	n=1 [37]

Due to the non-availability of relevant literature from Sri Lanka, Bhutan, and Maldives, WHO factsheets were considered.

Case-by-case analysis of the selected literature:

All the studies were analyzed by segregating them into tabulated criteria and disruption of RI services was analyzed in one table, causes of disruption as per the study and finally measures suggested by authors in each study were tabulated.

5.1 Disruption of RI services: On analysis of studies, it was found that during the lockdown period there was a significant delay in children receiving immunization with some specific vaccine administration getting delayed in up to 60% of cases. This delay was seen in the post-pandemic period as well and many children did not receive the vaccines at all. Table 4 gives details of such decline in RI of children in the studied regions and gives a comparison if available with the pre and post-pandemic period.

Table 4 Status of vaccination coverage during to COVID-19 pandemic times in different regions of South Asia.

Authors	**Site**	**Methodology used**	**Studied vaccine**	**Decline in vaccine coverage**
Kazi A. M. et al.	CHC of tertiary health center Aga khan hospital, Karachi, Pakistan	NA	NA	NA
Khan A. et al.	Pakistan	NA	NA	NA
Manzoor A. et al.	New City Teaching Hospital & Divisional Head Quarter Teaching Hospital, Mirpur, Azad Kashmir.	The questionnaire-based was study conducted from March to September 2021 by interviewing 1200 parents who visited OPDs and had children less than 2 years old.	Non-Specific	18% of children got delayed in getting vaccinated (by > 2 weeks) 2% completely missed getting vaccinated.
Sahoo B. et al.	Department of Pediatrics of Kalinga Institute of Medical Sciences,	Observational study of medical records of the Covid-19 period from March 2020 to August 2020 to pre Covid-19 period from March 2019 to August 2019	Non-Specific	43% decline in children attending immunization

	Tertiary care Hospital, Bhubaneswar, India			
Bhadoria S. S. et al.	Jaya Arogya Group Of Hospitals (JAH), tertiary care Hospital of Gajra Raja Medical College, Gwalior, India.	A cross-sectional study conducted from 1st Feb 2020 to 31st August 2020 analyzed OPD records.	Pentavalent-1, IPV-1 (Inactivated Polio Vaccine), PCV-1(Pneumococcal Conjugate Vaccine), OPV-1 (Oral Polio Vaccine-1) and Rotavirus-1. Pentavalent-2, Rotavirus-2 and OPV-2. Pentavalent-3, OPV-3, Rotavirus-3, PCV-2 and IPV-2. MR-1 includes (Measles Rubella). Booster-I included: MR-2, Diphtheria Pertussis Tetanus (DPT) booster-1 and OPV-booster dose and Booster-II Includes DPT-2 and OPV booster dose	The number of children visiting the hospital for Immunization declined from 22.4 % in the month of February to 17. 5% in March and to 11. 51% in June. About 6.2% of children were found to be delayed in vaccination as per schedule. The maximum delay in getting vaccinated was seen in the 4-to-6-month age group and the delay was seen maximum in the children who were supposed to get vaccinated in the month of June.
Siddiqi D. A. et al.	Sindh province, Pakistan	Secondary data analysis of the electronic immunization registry (Zindagi Mehfooz) of Sindh province, Pakistan from 12th Feb. 2020 to 20th April 2020	Non-specific	A decline of 74% during covid-19 lockdown to 6 months preceding covid-19 lockdown.
Emmanuel F. et al.	Primary and Secondary level public sector health facilities of Pakistan	Data from the District health information system of May 2020 and December 2020 is compared to data of May 2019 and December 2019.	Pentavalent 3rd dose	The number of recipients of Penta 3rd Dose declined by 35.9% in May 2020 as compared to May 2019 However, a gain of 1.3 % was seen in Dec. 2020 as compared to Dec 2019.

González P. A. et al.	Langham province of Afghanistan	Afghanistan EPI Health Management Information System database of April-July 2020 to April-July 2019 is compared	BCG OPV-0 Penta-1 OPV-1 PCV-1 Rota-1 DPT-2 OPV-2 PCV-2 Rota OPV-3 IPV PCV-3 DTP-3 Measles OPV-4 Hepatitis-B	BCG: Decline of 19% OPV-0: Decline of 18% Penta-1: Decline of 19% OPV-1: Decline of 19% PCV-1: Decline of 21% Rota-1: Decline of 20% OPV-2: Decline of 19% DPT-2: Decline of 22% PCV-2: Decline of 23% Rota: Decline of 23% OPV-3: Decline of 23% IPV: Decline of 23% PCV-3: Decline of 26% DTP-3: Decline of 23% Measles: Decline of 28% OPV-4: Decline of 28% Hepatitis-B: Decline of 6%
Ali I.	Pakistan	NA	NA	NA
Nguyen P. H. et al.	Dhaka, Bangladesh	Baseline survey data of 8 health facilities of Feb. 2020 compared with the lockdown period (26th March 2020 to 30th May 2020) and Sept-Oct 2020.	Non-Specific	Fewer parents sought immunization services for their children during the lockdown period and immunization fell by 61 percent during the lockdown period and 66.1 percent by September.
Rizwan W. et al.	Children Hospital Lahore and Allama Iqbal Memorial Hospital Salikot and Idress Teaching Hospital, Sialkot, Pakistan	analytical cross-sectional study with structured interviews with participants	BCG OPV 0 Penta 1 PCV 1 Rota 1 OPV1 Penta 2 PCV 2 Rota 2 OPV 2 Penta 3 PCV 3 Rota 3 OPV 3 IPV Measles 1 Measles 2	BCG missed by 4% OPV 0 missed by 4% Penta 1 missed by 9% PCV 1 missed by 9% Rota 1 missed by 9% OPV1 missed by 9% Penta 2 missed by 6% PCV 2 missed by 6% Rota 2 missed by 6% OPV 2 missed by 6% Penta 3 missed by 5.5% PCV 3 missed by 5.5% Rota 3 missed by 5.5% OPV 3 missed by 5.5% IPV missed by 5.5% Measles 1 missed by 4.6% Measles 2 missed by 3.4% Overall, 33.9% of children had delayed vaccination and 20.3% missed their vaccination.

Khan S. A. et al.	Pakistan	A cross-sectional study in which participants were selected from public and private sector vaccination centers.	Non-specific	36.4% of children had delayed vaccination.
Rahman S. U. et al.	Teaching Hospital of Khyber-Pakhtunkhwa, Pakistan	Data analysis of the hospital immunization registry of the teaching hospital, Khyber-Pakhtunkhwa, Pakistan in which 5 months of lockdown period (1st April 2020 to 31st Aug 2020), and 5 months of post-lockdown period (1st Sept. 2020 to 31st January 2020) is compared with pre-lockdown period (1st Nov 2019 to 31st March 2020)	Penta 1 PCV 1 Rota 1 OPV1 Penta 2 PCV 2 Rota 2 OPV 2 Penta 3 PCV 3 OPV 3 Measles 1 Measles 2	The decline in immunization coverage ranging from 30.7% to 49.6% during the lockdown period and a decline of 2.8% to 20.2% in post lockdown period was seen. Lockdown period: Penta 1 Decline of 33.8% PCV 1 Decline of 30.7% Rota 1 Decline of 31.3% OPV1 Decline of 30.7% Penta 2 Decline of 33.8% PCV 2 Decline of 33.6% Rota 2 Decline of 34.6% OPV 2 Decline of 33.6% Penta 3 Decline of 37.3% PCV 3 Decline of 35.0% OPV 3 Decline of 35.0% Measles 1 Decline of 40.7% Measles 2 Decline of 48.6% Post-lockdown period: Penta 1 Decline of 13.8% PCV 1 Decline of 12.3% Rota 1 Decline of 15.6% OPV1 Decline of 12.3% Penta 2 Decline of 10.5% PCV 2 Decline of 9.6% Rota 2 Decline of 9.6% OPV 2 Decline of 9.6% Penta 3 Decline of 5.2% PCV 3 Decline of 2.8% OPV 3 Decline of 2.8% Measles 1 Decline of 17.8% Measles 2 Decline of 20.2%
Dixit S. M. et al.	Nepal, Senegal and Liberia	NA	NA	NA
Hanifi S.M.A. et al.	Southeast Bangladesh	Data of Health and demographic surveillance system from 1st March to 31st may 2020 is compared with corresponding data from 2018 and 2019.	Non-specific	The decline in the expanded program of immunization outreach sessions to 74% in the month of March, 10% in April, and 3% in May. A total of 71% of sessions were suspended leading to 25.5% of children missing immunization in the month of March, 89.5% in the month of April, and 96.3% in the month of May.

Chandir S. et al.	Karachi, Pakistan	Data of the average daily number of children getting immunized as per the electronic immunization registry (Zindagi Mehfooz) of 6 months before the lockdown i.e., 23rd Sep 2019 to 22nd March 2020 was compared with 1st 6 weeks of lockdown (23rd March to 9th May 2020) and post lockdown period (10th May 2020 to 6th June 2020)	BCG OPV 0 Penta 1 PCV 1 Rota 1 OPV1 Penta 2 PCV 2 Rota 2 OPV 2 Penta 3 PCV 3 Rota 3 OPV 3 IPV Measles 1 Measles 2	27.2% decline in the mean vaccination visits. Lockdown period: BCG Decline of 58.6% OPV 0 Decline of 51.1% Penta 1 Decline of 60.7% PCV 1 Decline of 60.7% Rota 1 Decline of 60.4% OPV1 Decline of 60.9% Penta 2 Decline of 55.0% PCV 2 Decline of 55.0% Rota 2 Decline of 54.3% OPV 2 Decline of 54.9% Penta 3 Decline of 49.9% PCV 3 Decline of 52.3% OPV 3 Decline of 49.7% IPV Decline of 49.8% Measles 1 Decline of 48.9% Measles 2 Decline of 52.7% Post-lockdown period: BCG Decline of 30.0% OPV 0 Decline of 19.1% Penta 1 Decline of 38.9% PCV 1 Decline of 38.9% Rota 1 Decline of 38.8% OPV1 Decline of 39.1% Penta 2 Decline of 37.5% PCV 2 Decline of 37.5% Rota 2 Decline of 36.9% OPV 2 Decline of 37.3% Penta 3 Decline of 30.0% PCV 3 Decline of 32.9% OPV 3 Decline of 30.0% IPV Decline of 29.8% Measles 1 Decline of 14.8% Measles 2 Decline of 31.7%
Chandir S. et al.	Sindh province, Pakistan	Data of the average daily number of children getting immunized as per the electronic immunization registry (Zindagi Mehfooz) of 6 months before the lockdown i.e., 23rd Sep 2019 to 22nd March 2020 was compared with 1st 6 weeks of lockdown (23rd March to 9th May 2020)	BCG OPV 0 Penta 1 PCV 1 Rota 1 OPV1 Penta 2 PCV 2 Rota 2 OPV 2 Penta 3 PCV 3 Rota 3 OPV 3 IPV Measles 1	BCG Decline of 56.6% OPV 0 Decline of 51.6% Penta 1 Decline of 56.4% PCV 1 Decline of 56.4% Rota 1 Decline of 56.1% OPV1 Decline of 56.2% Penta 2 Decline of 51.0% PCV 2 Decline of 51.1% Rota 2 Decline of 50.7% OPV 2 Decline of 50.7% Penta 3 Decline of 49.5% PCV 3 Decline of 49.7% OPV 3 Decline of 49.2% IPV Decline of 51.6% Measles 1 Decline of 47.4% Measles 2 Decline of 48.2%

			Measles 2	

5.2 Reasons for Disruption in RI services: Table 5 analyses the demand side, supply side, and in some cases contextual reasons for the disruption of RI services. Most demand-side issues were related to lockdown policies and misconceptions prevalent due to the COVID-19 pandemic. Supply-side reasons were dominated by issues faced by health workers like the absence of guidelines, SOPs, and Personal protective equipment to carry out RI services during the pandemic along with the fear of getting infections.

Table 5 Reasons for disruption of RI services during the COVID-19 Pandemic period

Authors	**Site**	**Causes of demand side disruption**	**Causes of supply-side disruption**	**Context-Specific**
Kazi A. M. et al.	CHC of tertiary health center Aga khan hospital, Karachi, Pakistan	NA	NA	NA
Khan A. et al.	Pakistan	NA	NA	NA
Manzoor A. et al.	New City Teaching Hospital & Divisional Head Quarter Teaching Hospital, Mirpur, Azad Kashmir.	Fear of contracting Covid-19 and issue of transportation.	NA	NA
Sahoo B. et al.	Department of Pediatrics of Kalinga Institute of Medical Sciences,	NA	Na	NA

	Tertiary care Hospital, Bhubaneswar, India			
Bhadoria S. S. et al.	Jaya Arogya Group Of Hospitals (JAH), tertiary care Hospital of Gajra Raja Medical College, Gwalior, India.	Fear of covid-19 infection, restriction of movement, and lockdown policies, the delay appears to be planned rather than a lack of adherence	Changing priorities for covid-19, logistics delivery issues, and message issued by authorities for staying at home overwhelmed the message that childhood immunization is operating as usual	NA
Siddiqi D. A. et al.	Sindh province, Pakistan	NA	suspension of outreach services, distantly located areas from vaccination sites had a higher proportion of missed vaccination	NA
Emmanuel F. et al.	Primary and Secondary level public sector and facilities of Pakistan	Exacerbation of access-related challenges like seeking medical care, reaching to the facility, and receiving adequate care.	Imposition of strict lockdown, partial or complete closure of Outdoor Patient Department services of primary, secondary, and tertiary hospitals.	NA
González P. A. et al.	Langham province of Afghanistan	Fear of COVID-19 exposure in healthcare settings Fear of transmission of infection in general,	Reduction in health care provision, insecurity, disruption in global manufacturing and supply chains, border closure, and the global suspension by vaccine companies	Insecurity, and frequent armed conflicts between the government and the opposition
Ali I.	Pakistan	Limited outdoor movements, fear of getting the infection, Rumors conspiracy theories, vaccine refusal, and resentment.	Lockdown policies, Suspension of the massive vaccination drive	Vaccination is a western plot conceived as harmful to the local population
Nguyen P. H. et al.	Dhaka, Bangladesh	Fear of leaving home and getting infected with Covid-19, lack of availability of services and service providers, travel restrictions and lack of transport, family members non-allowance to leave home, non-availability of	Increased workload of healthcare workers during the pandemic, healthcare workers were scared to deliver service door-to-door, lack of transportation facilities for reaching vaccination centers causing longer walking distances, Apprehensions of family members of healthcare workers due to perceived risks which prevented healthcare workers to continue with their work, discomfort with PPE (personal	NA

		PPE (personal protective equipment).	protective equipment), sick family member, busy with COVID-19 work, no salary incentives, neighbors discomfort/hindrance	
Rizwan W. et al.	Children Hospital Lahore and Allama Iqbal Memorial Hospital Salikot and Idress Teaching Hospital, Sialkot, Pakistan	Fears of getting infected with Covid-19 after visiting vaccination center, transportation issues, fear of side effects.	NA	NA
Khan S. A. et al.	Pakistan	NA	Lockdown, Closure of expanded program of immunization, Decline in immunization in private sector	NA
Rahman S. U. et al.	Teaching Hospital of Khyber-Pakhtunkhwa, Pakistan	NA	NA	NA
Dixit S. M. et al.	Nepal, Senegal and Liberia	Restriction on movements outside of the residence and physical access to vaccination services due to social distancing policies and lockdown measures enacted to curb viral transmission, misinformation, and rumors about Covid-19 vaccine safety.	50% of immunization centers halted operation during the initial onset of the lockdown, Covid-19 infections among healthcare workers led to the abrupt closure of service, delayed shipment of vaccines stocks and key supplies due to travel restrictions and reduced flights, Reduced hours of operations and halted services, Inadequate PPE, sanitation supplies, infection control supplies, deployment of staff for COVID-19 response, staff shortage due to COVID-19 infection, fear of infection, fear of exposure, and burnout among health care workers, postponement or cancellation of vaccination campaigns at mass scale and vaccine introduction, fear of virus exposure at healthcare settings, individuals instructed to postpone or delay non-urgent healthcare services due to concerns about overburdening of healthcare facilities,	NA

Hanifi S.M.A. et al.	Southeast Bangladesh	The unwillingness of villagers to hold immunization sessions, and social distancing measures.	Absenteeism of vaccination staff, lack of guidance to vaccinators to continue vaccination outreach sessions, lack of PPE, overburdened healthcare services, and staff directed for another COVID-19 work	EPI sessions were held in a home of villagers and vaccinators were not sure if the homeowner will allow their homes for the conduction of vaccination sessions during the pandemic. Vaccination staff perceived the pandemic to be temporary and did not continue vaccination.
Chandir S. et al.	Karachi, Pakistan	Restriction of movements, Concerns about Covid-19 transmission	Fear of infection among the vaccinators and lack of preparedness of healthcare workers	NA
Chandir S. et al.	Sindh province, Pakistan	Reluctance from parents due to fear of exposing their children to COVID-19 infection, myths, rumors, and misinformation during pandemic times increased vaccine hesitancy, restriction on movement by authorities, unavailability of public transportation, and increase in commuting costs.	Strict restrictions on the movement faced vaccinators for outreach sessions, health workers' issues about the possibility of infection through engaging with clients in the absence of clear guidelines and proper PPEs	NA

5.3 Suggestions to overcome disruption in RI services: Table 6 gives some of the authors' suggested measures to overcome disruption in RI services faced in the region of studies.

Table 6 Measures suggested for preventing disruption in the routine immunization services during the COVID-19 Pandemic.

Authors	Site	Demand side	Supply-side	Context-Specific
Kazi et al.	CHC of tertiary health center Aga khan hospital, Karachi, Pakistan	The development of a mobile application that has the capacity to Monitor and track information. Information needs to be authentic reliable and useful. Apps should be able to share personalized reminders.	Development of Smartphone application (Mobile Health Application) to bridge gaps between accessibility to health information and service provision.	Religious contents supporting immunization services and behavior change.
Khan A. et al.	Pakistan	Developing strategies to increase public awareness directed towards increasing coverage of vaccination.	Telehealth services by both private and public providers at an affordable rate. Supplementation of telehealth services by door-to-door vaccination of children who missed vaccination. Organization of immunization campaigns and conduction of mass vaccination at low cost and to cover large populations even in challenging areas or parts of the country. Drive-through vaccination services by prior appointments.	NA
Manzoor A. et al.	New City Teaching Hospital & Divisional Head Quarter Teaching Hospital, Mirpur, Azad Kashmir.	Home vaccination and dedicated health centers for admission	NA	NA
Sahoo B. et al.	Department of Pediatrics of Kalinga Institute of Medical Sciences, Tertiary care Hospital, Bhubaneswar, India	NA	NA	NA
Bhadoria S. S. et al.	Jaya Arogya Group Of Hospitals (JAH), tertiary care Hospital of Gajra Raja Medical College, Gwalior, India.	NA	NA	NA
Siddiqi D. A. et al.	Sindh province, Pakistan	NA	Utilization of data from electronic immunization registries for policies and implementation strategies Routine use of data from electronic immunization registries for supply	NA

			chain, monitoring and evaluation process, etc.	
Emmanuel F. et al.	Primary and Secondary level public sector and facilities of Pakistan	NA	NA	NA
González P. A. et al.	Langhman province of Afghanistan	NA	Strategies of maintaining routine immunization services by following WHO guidelines, strengthening outreach and fixed services, ensuring supplies, capacity building of healthcare workers, massive campaigns, and strategies to promote access control fear and anxiety provoked by pandemic and media.	NA
Ali I.	Pakistan	NA	Employment of a multidisciplinary approach to create an advanced preparedness program for dealing with the pandemic after-effects on the vaccination program, Social and behavior change campaigns to counter conspiracy theories, rumors, and misconceptions, use anthropological experts who can comprehend and guide regarding the interplays of Socio-cultural, economic, political, and psychological factors. Door-to-door vaccination programs, well-capacitated and adequately-paid vaccination staff, Adequate monitoring, and supervision, Surveillance of vaccination campaigns, and focus on the remote and rural areas.	NA
Nguyen P. H. et al.	Dhaka, Bangladesh	NA	Adaptation of healthcare workers like coordination with their supervisors and colleagues for the arrangement of vaccination drives, phone calls to parents to schedule immunization appointments, sending reminders to mothers via messages and WhatsApp or phone call	NA
Rizwan W. et al.	Children Hospital Lahore and Allama Iqbal Memorial Hospital Salikot and Idress Teaching Hospital, Sialkot, Pakistan	NA	Deployment of qualified doctors for alleviating the fears of parents at the vaccination centers.	NA
Khan S. A. et al.	Pakistan	NA	NA	NA
Rahman S. U. et al.	Teaching Hospital of Khyber-Pakhtunkhwa, Pakistan	NA	NA	NA

Dixit S. M. et al.	Nepal, Senegal and Liberia	NA	Leveraging current or setting up systems to track missed children and catch-up efforts Catching up routine immunization services as soon as the risk of transmission is mitigated	NA
Hanifi S.M.A. et al.	Southeast Bangladesh	NA	NA	NA
Chandir S. et al.	Karachi, Pakistan	NA	Use of Electronic Immunization registry for supply chain issues, monitoring and evaluation of immunization process	NA
Chandir S. et al.	Sindh province, Pakistan	NA	Use of virtual engagements and learning platforms for training vaccinators and access to essential information related to standard operating procedures (SOPs) in the COVID-19 context, creative and innovative interventions such as messaging services, communication, and online chatbots, mobile immunization vans, generation of defaulter list on EIR for cat-up sessions, enhanced outreach, and mop-up sessions	NA

5.4 Country-wise specifics of disruption in RI services:

5.4.1 Impact of the COVID-19 pandemic on routine immunization services in India

Sahoo B. et al [21] reported a decline of about 43% of children attending immunization sessions during the lockdown period from March to August 2020 as compared to March to August 2019. Singh S. et al. [22] reported a 6.2 % delay in immunization of children reporting to OPD services in a tertiary hospital in Gwalior They reported a maximum delay during the month of June. In India Fear of covid-19 infection, restriction of movement, and lockdown policies are major reasons for demand-side disruptions of RI services and changing priorities for covid-19, logistics delivery issues, and the messages issued by authorities for staying at home overwhelmed the message that childhood immunization is operating as usual.

5.4.2 Impact of the COVID-19 pandemic on routine immunization services in the Maldives

Study selection for this systematic review failed to retrieve any relevant studies from the Maldives, but as per data from WHO and UNICEF, the island country was successful in immunizing more than 95% of children [17] against VPDs as par with its historical trends and did not suffer the impact of COVID -19 on its routine immunization program.

5.4.3 Impact of the COVID-19 pandemic on routine immunization services in Nepal

Study selection for this systematic review failed to retrieve any relevant studies from Nepal, but as per data from WHO and UNICEF, the landlocked country was successful in immunizing more than 85% of its children [16] against VPDs in 2020 and 2021, with measles and DPT (3^{rd} dose) vaccine coverage more than 90%, hence it can be assumed that Nepal did not suffer the impact of COVID -19 on its routine immunization program.

5.4.4 Impact of the COVID-19 pandemic on routine immunization services in Bhutan

Study selection for this systematic review failed to retrieve any relevant studies from Bhutan but as per data from WHO and UNICEF, the landlocked country was successful in immunizing more than 95% of children [14] against VPDs as par with its historical trends and did not suffer the impact of COVID -19 on its routine immunization program.

5.4.5 Impact of the COVID-19 pandemic on routine immunization services in Sri-Lanka

Study selection for this systematic review failed to retrieve any relevant studies from the Sri-Lanka, but as per data from WHO and UNICEF, the island country was successful in immunizing more than 95% of children [15] against VPDs as par with its historical trends and did not suffer the impact of COVID -19 on its routine immunization program.

5.4.6 Impact of the COVID-19 pandemic on routine immunization services in Bangladesh

Nguyen P. et al. performed a data comparison from the already conducted survey for program evaluation of maternal, infant, and young child nutrition services in urban maternal neonatal and child health (MNCH) facilities and compared Baseline survey data of 8 health facilities of Feb. 2020 with the lockdown period (26th March 2020 to 30th May 2020) and Sept-Oct 2020. They found that routine immunization uptake fell by 61 percent during the lockdown period and 66.1 percent by September.

Major demand side causes of disruption identified in Bangladesh include fear of leaving home and getting infected with Covid-19, lack of availability of services and service providers, travel restrictions and lack of transport, family members' non-allowance to leave home, non-availability of PPE (personal protective equipment).

Major supply-side causes of disruption identified in Bangladesh were increased workload of healthcare workers during the pandemic, healthcare workers were scared to deliver service door-to-door, lack of transportation facilities for reaching vaccination centers causing longer walking distances, Apprehensions of family members of healthcare workers due to perceived risks which prevented healthcare workers to continue with their work, discomfort with PPE (personal protective equipment), sick family member, busy with covid-19 work, no salary incentives, neighbors discomfort/hindrance

5.4.7 Impact of the COVID-19 pandemic on routine immunization services in Pakistan

Siddiqi D. A. Et al. [29] performed Secondary data analysis of the electronic immunization registry (Zindagi Mehfooz) of Sindh province, Pakistan from 12th Feb. 2020 to 20th April 2020 and

found a decline of 74% during covid-19 lockdown to 6 months preceding covid-19 lockdown. Data analysis was further scaled up to the country level by Chandir S. et al. [35] and they similarly saw a decline in RI services in the range of 30% to 61% and even in post lockdown period catch-up of vaccination services cannot be achieved and vaccination remained 40% lower than the corresponding period in the year 2019. Reman S. et al. [34] also reported a decline in immunization coverage ranging from 30.7% to 49.6% during the lockdown period and a decline of 2.8% to 20.2% in the post-lockdown period was seen overall. Is estimated that about 1 out of every 2-child missed vaccination in the Pakistan because of the pandemic.

Major demand side causes of disruption identified in Pakistan were the fears of getting infected with Covid-19 after visiting the vaccination center, transportation issues, limited outdoor movements, fear of side effects rumors conspiracy theories, vaccine refusal, and resentment. COVID-19 Exacerbated existing access-related challenges like seeking medical care, reaching the facility, and receiving adequate care.

Major supply-side causes of disruption identified in Pakistan were the imposition of strict lockdowns, and partial or complete closure of Outdoor Patient Department services of primary, secondary, and tertiary hospitals, suspension of the massive vaccination drive, fear of infection among the vaccinators, and lack of preparedness of healthcare workers.

5.4.8 Impact of the COVID-19 pandemic on routine immunization services in Afghanistan

González P. A. et al.[37] used the health information management system (HIMS) database of Laghman province and compared records from April-July 2020 to April-July 2019 and they found a decline in vaccination in the range of 6% to 28% of various vaccines administered.

Major demand-side causes of disruption identified were the fear of COVID-19 exposure in healthcare settings and the fear of transmission of infection in general.

Major supply-side causes of disruption identified were the reduction in the provision of health care services, insecurity, issues related to global manufacturing and supply chains, closure of international borders, and the global suspension by vaccine companies. The important contextual cause was insecurity and frequent armed conflicts between the government and the opposition.

5.5 Measures to prevent disruption in RI services during the event like COVID-19 pandemic

In a situation like the COVID-19 pandemic, prioritization of routine immunization services holds great importance in the prevention of outbreaks of VPDs. Small nations such as Shri-Lanka, Nepal, Bhutan, and the Maldives were able to strategize routine immunization services and have performed well in terms of the percentage of children receiving complete immunization, Countries like India, Pakistan, Bangladesh, and Afghanistan suffered severe disruption in the uptake of routine immunization services. These countries represent a population with higher infant and under-5 mortality rates [38]. Due to multiple challenges faced by the health systems of these countries which led to disruption in routine immunization services, it's a necessity to develop guidelines and SOPs to prevent supply and demand side reasons of disruptions impacting routine immunization services during events like COVID-19. This reduction in immunization of VPDs raises concerns about future increased mortality and morbidity of children hence routine immunization services should be maintained even in a pandemic situation.

Cardoso P et al. [39] also identified the Southeast Asia region as one of the impacted W.H.O. regions for Disrupted immunization services by the COVID-19 pandemic Similar causes of disruption

were identified by Sharma M. et al. [40] in a similar systematic review dealing with disruption in immunization services in India and other developing countries.

Governments can consider important strategies suggested in the studies of this literature review

A) Development of a user-friendly mobile health application dedicated to routine immunization services with the aim to bridge gaps between accessibility to health information and service provision. The app can guide and inform users about the importance of children's vaccination, send personalized reminders, have the ability to track missed children, provide readily accessible training materials and supervisory support to healthcare workers, etc.
B) Telehealth services by both private and public providers and supplementation of telehealth services by door-to-door vaccination of children who missed vaccination.
C) Real-time utilization of electronic immunization data and organization of vaccination campaigns in areas with a higher number of children with missed vaccination, and for supply chain management, monitoring, and evaluation process, etc.
D) Employment of a multidisciplinary approach with intersectoral collaboration to create an advanced preparedness program for dealing with the pandemic after-effects on the vaccination program.
E) Catching up on routine immunization services as soon as the risk of transmission is mitigated by organizing special vaccination sessions, mobile immunization vans to reach remote communities, etc.
F) Development of strategies to promote access to immunization sessions, and control fear and anxiety provoked by the pandemic and media misinformation.

6 CONCLUSIONS

The COVID-19 pandemic was one of the most challenging times for health services and public health in the 21st century. It is important to focus on the immediate response to mitigating the pandemic and its effect, simultaneously efforts should be ensured that essential services like RI are not disrupted. We also need to ensure adequate allocation of resources and full-fledged continuation of the RI services. We can learn lessons from developed countries and countries like Bhutan, Maldives, and Sri Lanka which performed relatively well in the continuation of RI services during the pandemic. COVID-19 has caused large-scale disruption in routine immunization services and given important lessons to scientific and medical communities about the grave dangers imposed by similar events in the future. We need to have an emergency preparedness plan available to us in preparation for similar events in the future. Additionally, more research is needed to fully develop protocols and strategies to overcome the short and long impact of pandemics on RI services and other health programs.

7 CONFLICTS OF INTEREST

There are no conflicts of interest.

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