UP-TO-DATE IMMUNIZATION COVERAGE AMONG INFANTS ATTENDING A CLINIC AT A TERTIARY HOSPITAL DURING THE SECOND WAVE OF COVID-19 PANDEMIC IN KATHMANDU, NEPAL

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ABSTRACT

This study aimed to evaluate the utilization and quality of routine immunization (RI) services at a tertiary hospital during the second wave of the COVID-19 pandemic period. An observational analytical study was carried out in the Immunization Clinic of a tertiary hospital in Kathmandu, Nepal. The infant cohort was enrolled over a period of 4 months and followed up for a year (April 2021 to August 2022). Up-to-date immunization (UTD) status, overall and vaccine specific drop-out rates were quantified and reasons for missed or delayed doses were elicited from caregivers. An infant who received BCG, 3 doses of Pentavalent (DPT-HEPB-HIB) and OPV containing vaccine, one dose of fractional IPV, 2 doses of Rotavirus vaccine, 3 doses of PCV and first dose of Measles-Rubella (MR1) vaccine prior to their first birthday was categorized as UTD. Dropout rates between early and later vaccine doses were defined as the percentage of children that started their immunization series, but did not complete it for some reason. Among 227 infants (44.1% female) enrolled in the study, about three-fourths (74.5%, 95% CL 68.3% to 80.0%) were identified as UTD. Among UTD infants (n=169), two-thirds of the infants (65.1%, 95% CL 57.4% to 72.3%) had received the vaccines at the recommended age milestones. Overall dropout rate (BCG-MR1) was about 19% with highest dropout between the first and third Pentavalent dose (10%). Maximum delay was seen for MR1 vaccine. Common reasons for missed or delayed visits were that the infant received vaccine at another health facility, or the infant was ill, caregivers had travelled to village/maternal home or were busy. In conclusion, three-fourths of the infant cohort had received all of the recommended vaccines as per the National immunization schedule at our immunization clinic. However, one third had delayed their visits to the clinic. While routine immunization reporting looks at the number of vaccine doses that have been administered at an immunization clinic, this study has documented a sustained utilization of RI services during the second wave of the pandemic period. The lower dropout rate for pentavalent vaccine indicates a qualitative improvement in RI services at the tertiary hospital. However, an ongoing scrutiny of immunization data recording with a progression to digital health records and provision of timely reminders to caregivers may further help to strengthen RI services at the institutional level.

KEYWORDS

Infant immunization, up-to-date status, COVID-19, Nepal

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INTRODUCTION

The novel coronavirus disease (COVID-19) pandemic has been declared as a public health emergency of international concern. It has received global attention with innovative and disruptive measures for containment and mitigation of transmission of SARS-Cov2 infection.

During the early phase of the Covid-19 pandemic, the World Health Organization (WHO) had warned of disruption of routine immunization (RI) services due to shifting of healthcare resources to COVID-19 response. Any disruption in the immunization services had the potential to widen gaps and inequities in immunization coverage and lead to secondary outbreaks of vaccine preventable diseases (VPDs). Hence, guidelines had been formulated to support the immunization services during COVID-19 pandemic.[1]

Nepal's national immunization program (NIP) has ensured social equity and provided access to complete immunization schedule to every child. It has achieved significant milestones with the elimination of poliomyelitis and maternal and neonatal tetanus. Moreover, NIP has contributed significantly to the decline in infant and child mortality in Nepal.[2]

However, there was a decline in RI coverage during the first wave of COVID 19 pandemic due to the imposition of the first lockdown that began on the 24th of March, 2020. Based on the WHO advisory alert, a directive was issued by the Ministry of Health and Population (MoHP), for resumption of RI services at various levels of health facilities. Consequently, during the lock down in the second wave that extended from April 29th to 1st of September 2021, RI services were maintained. RI was further strengthened during this period, through the introduction of the Rotavirus vaccine to the NIP schedule.[3,4]

As per the National Immunization schedule in Nepal, infants with up-to-date (UTD) immunization have received Bacille Calmette Guerin (BCG) containing vaccine at birth, 3 doses of Pentavalent (DPT-HEPB-HIB) vaccine and Oral Polio (OPV) containing vaccine at 6,10 and 14 weeks after birth), 1 dose of fractional Inactivated Polio (fIPV) containing vaccine at 14 weeks, 2 doses of Rotavirus vaccine at 6 and 10 weeks, 3 doses of Pneumococcal Conjugate vaccine (PCV) at 6 weeks, 10 weeks and 9 months and 1 dose of Measles-Rubella (MR) containing vaccine at 9 months, prior to their first birthday.[3]

According to the WHO immunization program guide, dropout rates between early and later doses are defined as the percentage of children that started their immunization series, but did not complete it for some reason. Dropout rates are used to evaluate the utilization and quality of routine immunization services.[5]

Kathmandu District is classified as low immunization coverage (<80%) for the first dose of DPT-HEPB-HIB containing vaccine with a low dropout rate (<10%) for first and third dose of Pentavalent vaccine.[3] Expert opinion in Nepal has suggested that immediate effects of decreased vaccination due to COVID-19 pandemic may not be evident due to herd effect protection. However, this protection may gradually decline and catch-up campaigns may be necessary in the post pandemic period.[6]

This study aimed to evaluate the utilization and quality of routine immunization services at a tertiary care hospital during the second wave of the pandemic period. We have quantified the up-to-date immunization status, overall and vaccine specific drop-out rates among infants and identified reasons for missed or delayed doses.

MATERIALS AND METHODS

A hospital based observational analytical study was carried out in the Immunization Clinic run by the Department of Community Medicine in Nepal Medical College Teaching Hospital from 1st April 2021 to 31st August 2022 (seventeen months) after ethical clearance from the Nepal Medical College Institutional Research Committee (NMC-IRC) Ref. No.: 059-078/079.

The estimated sample size was calculated assuming a 29% drop-out rate for the third dose of Pentavalent vaccine based on a study carried out in our clinic.[7] Within 95% confidence intervals and a 7% margin of error, the minimum sample size was calculated to be 161 infants. Infants who received BCG from 1st April 2021 to 31st July 2021 at the clinic with a minimum of two visits over a one-year period were included in the study. Infants receiving BCG prior to or after the specified dates, those with a single visit to the clinic and children older than 1 year were excluded from the study.

The cohort of infants receiving BCG vaccination during April, May, June and July 2021 were identified from the immunization records and their immunization status was followed up from April 2021 to July 2022. Purposive sampling technique was used to include infants with immunization records meeting inclusion and exclusion criteria. A self-constructed pretested tool was used to obtain

Socio-demographic information as follows: age, gender, birth weight, ethnicity, place of residence, immunization registration number of infant, telephone number of parents. Vaccine received and age at vaccination was recorded at each visit. At the end of the study period, parents whose infants have missed or delayed doses were contacted for eliciting the reasons. An Infant was defined as a child less than 12 months of age.

At the end of the study period an infant was categorized as having up-to-date (UTD) immunization if she/he had received BCG, 3 doses of Pentavalent vaccine and OPV vaccine, one dose of fIPV, 2 doses of Rotavirus vaccine, 3 doses of PCV and 1 dose of MR vaccine prior to their first birthday.

A cluster of vaccines received by the infant at the age milestones of 1.5, 2.5 and 3.5 months are termed as COMBO1, 2 and 3 respectively at the immunization clinic. COMBO-1 comprised of Rota-Polio-PCV-DPT-HEPB-HIB containing vaccines. COMBO-2 comprised of Rota-Polio-PCV-DPT-HEPB-HIB containing vaccines. COMBO-3 comprised of Polio-f IPV-PCV-DPT-HEPB-HIB containing vaccines.

Infants were identified as having received on time immunization if they had received the vaccines at the recommended age milestone as per NIP at birth, 6 weeks, 10 weeks, 14 weeks and nine months, respectively.

The dropout rate was calculated as follows:[5]

Overall dropout rate (BCG to MR1): No. of infants receiving BCG doses – No. of infants receiving MR1 doses / total number of infants receiving BCG * 100

Third dose Pentavalent vaccine dropout: No. of infants receiving DPT-HepB-HIB1 doses – No. of infants receiving DPT-HepB-HIB3 doses / No. of infants receiving DPT-HepB-HIB1 doses * 100

Third dose Pentavalent vaccine to MR1 dropout: No. of infants receiving DPT-HepB-HIB3 doses – No. of infants receiving MR1 doses / No. of infants receiving DPT-HepB-HIB3 doses * 100

Collected data was entered in MS Excel, cleaned and analysed with EPI-INFO ver. 7 and licensed Stata 15 statistical software. On-time and up to date immunization rates were reported within 95% confidence limits. Overall and vaccine specific dropout rates were reported. Up to date immunization was studied in relation to infant cohort characteristics using Chi-square and Fisher-Exact test.

RESULTS

Two hundred and twenty-seven infants (44.1% female) receiving BCG vaccine were enrolled as the study cohort. About two-thirds of the

Table 1: Baseline characteristics of infant cohort (n=227)

Variables	n	%
SEX		
Male	127	55.9
Female	100	44.1
ETHNICITY		
Hill Adibasi & Janajati	142	62.6
Khas-Aryan	56	24.7
Others	29	12.8
LBW (<2.5kg)		
Yes	15	6.6 (3.8 to 10.7)
No	212	93.4

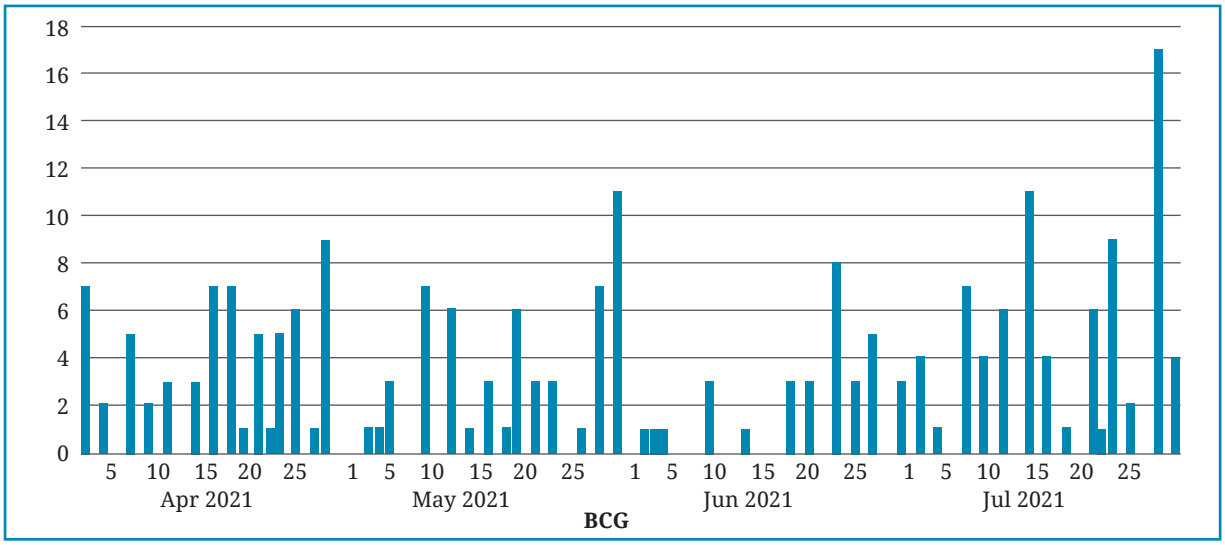

Fig. 1: Enrollment of infant cohort (n=227)

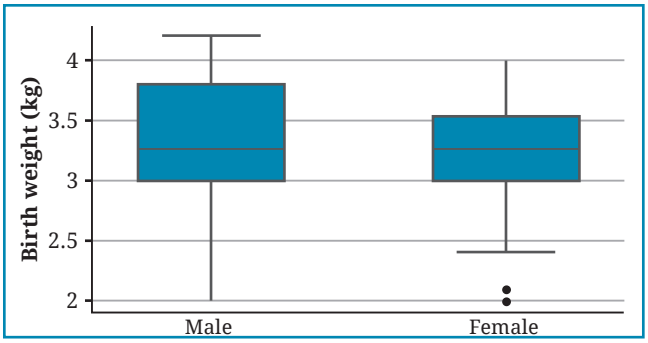

Fig. 2: Boxplot of birthweight categorized by sex among the infant cohort (n=227)

infants were identified as Hill *Adibasi* and *Janajati* ethnicity with about 7% (95% CL: 3.8% to 10.7%) born with low weight (<2.5 kg) (Table 1). The frequency of enrollment was sixty-four infants in April, fifty-four in May, thirty-two in June and seventy-seven in July 2021 (Fig. 1). The boxplot summary of birthweight showed mean birth weight among male (3.3 kg) and female infants (3.2 kg) did not differ significantly (Fig. 2).

During a year follow-up period, out of the 227 infants enrolled, 216 received COMBO1, 202

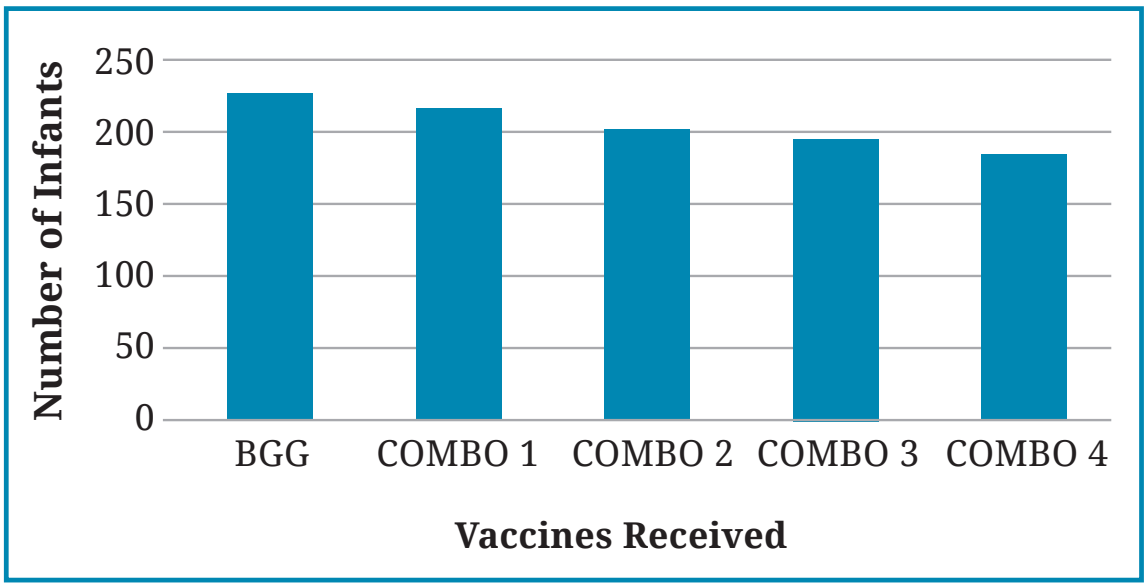

Fig 3: Vaccines received by infant cohort (n=227) during the study period

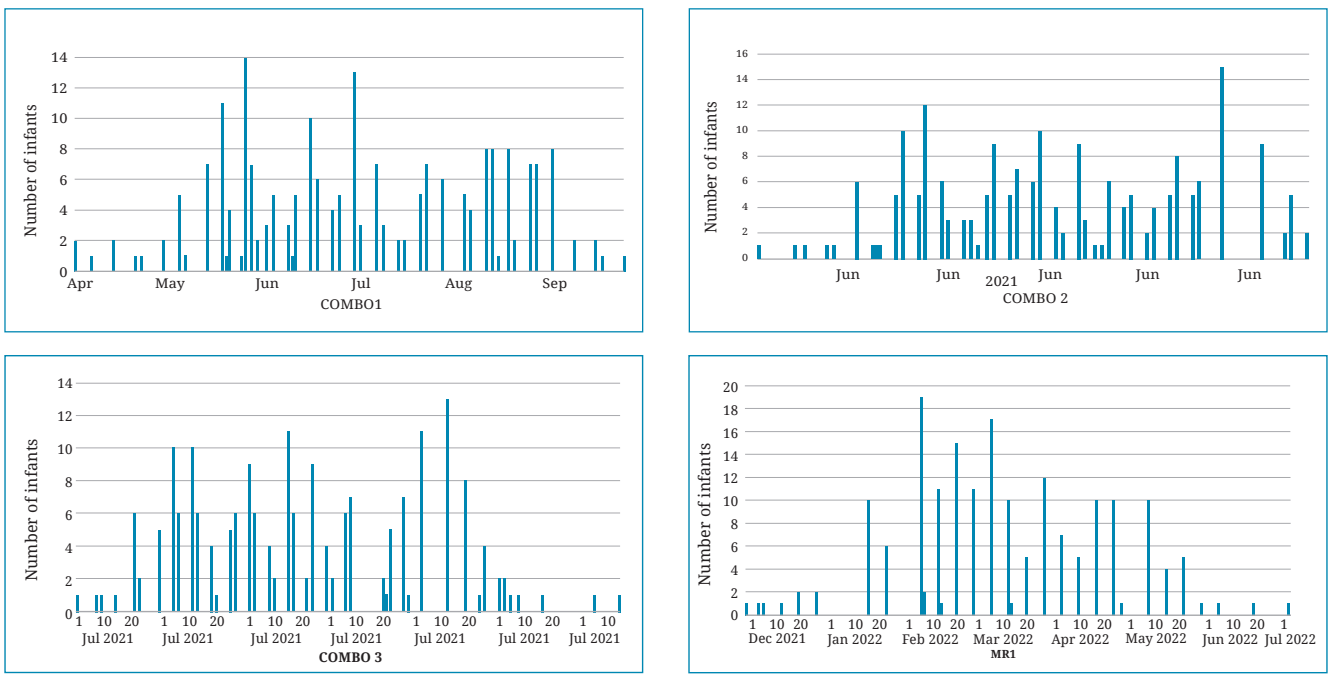

Fig. 4: Time trend for infant cohort receiving COMBO 1 (n=216), COMBO 2(n=202), COMBO 3(n=195) and MR1 (n=184) vaccines

Table 2: Median age of infants at immunization						
Age at immunization (months)	**n**	**Min**	**25%**	**Median**	**75%**	**Max**
BCG	227	0	0	0	0	2.5
Combo 1	216	1.5	1.5	1.5	1.5	3.5
Combo 2	202	2.5	2.5	2.5	2.5	4.5
Combo 3	195	3.5	3.5	3.5	4	5.5
MR 1	184	9	9	9.5	10	12

Table 3: Vaccination status outcomes among infant cohort population (n=227)				
Vaccination status	**n**	**%**	**Exact 95% LCL**	**Exact 95% UCL**
UpToDate				
Yes	169	74.5	68.3	80.0
No	58	25.5	20.0	31.7
On time (n=169)				
Yes	110	65.1	57.4	72.3
No	59	34.9	27.8	42.6

Table 4: Overall and vaccine-specific dropout rates in the infant cohort		
Vaccine	**Dropout rate**	**%**
Overall (BCG-MR1)	227-184/227 *100	18.9
BCG-Combo1	227-216/227*100	4.8
Third dose Pentavalent (Combo1-Combo3)	216-195/216 *100	9.7
Third dose to MR1 (Combo3-MR1)	195-184/195 *100	5.6

Table 5: Characteristics influencing UpToDate Immunization status				
Characteristic	**UTD Immunization**		**Chi-square value**	**P value**
Ethnicity	**No**	**Yes**		
Hill Adibasi & Janajati	33 (61.1)	109 (63.0)	0.457	0.796
Khas-Aryan	15 (27.8)	41 (23.7)		
Others	6 (11.1)	23 (13.3)		
Sex	**No**	**Yes**		
Male	28 (51.9)	99 (57.2)	0.482	0.487
Female	26 (48.1)	74 (42.8)		
LBW (<2.5 kg)	**No**	**Yes**	0.073	0.758*
Yes	4 (7.4)	11 (6.4)		
No	50 (92.6)	162 (93.6)		
Living residence distance from hospital	**No**	**Yes**		
Less than 30 min	39	126	1.16	0.28
More than 30 min	19	43		
Total	54	173		

*Fisher-Exact P value

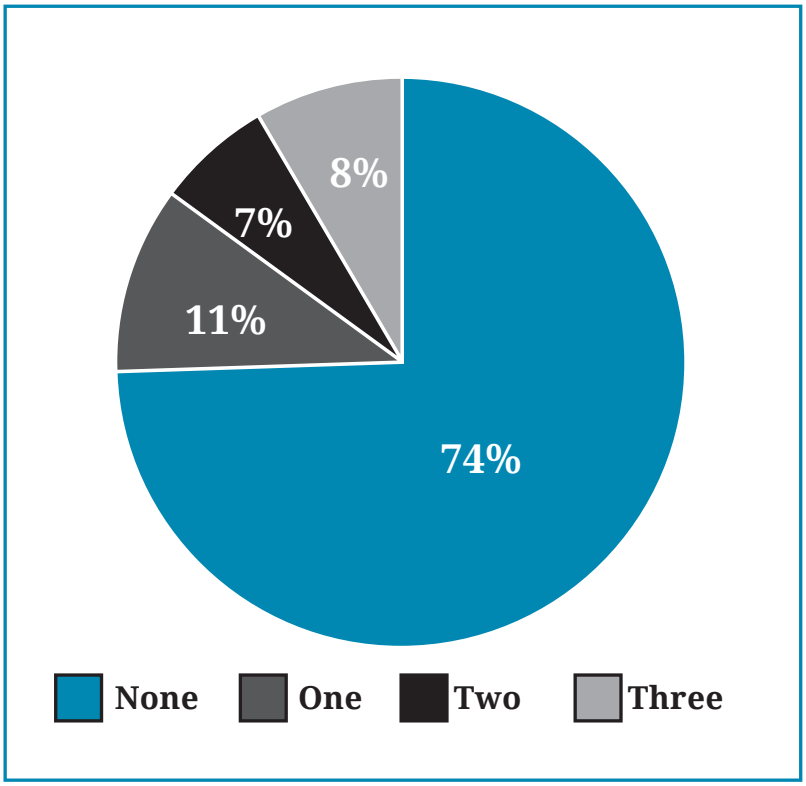

Fig. 5: Pattern of missed visits to the clinic (n=227)

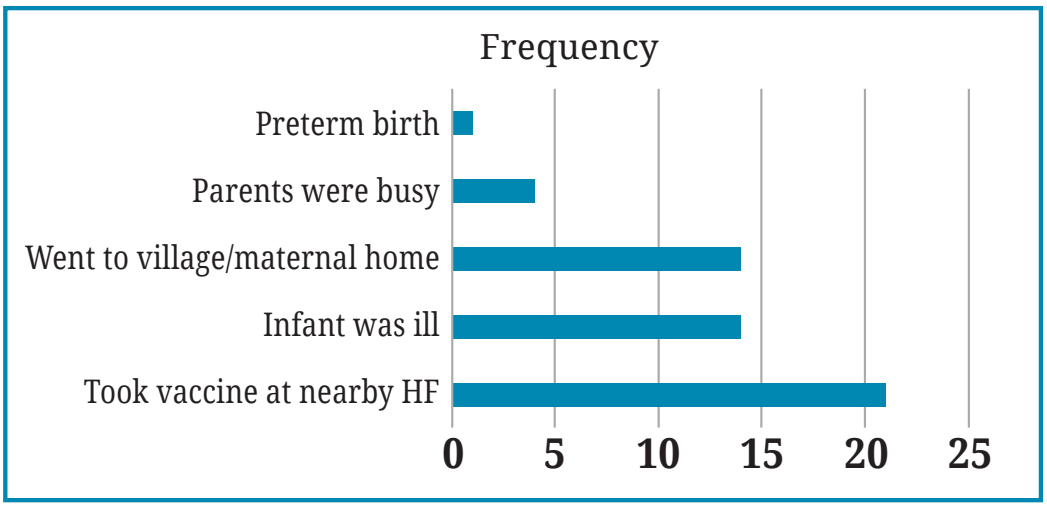

Fig. 6: Reasons for missed or delayed visits (n=54)

received COMBO2, 195 received COMBO3 and 184 received MR1 vaccine doses (Fig. 3).

As seen in Table 2, the median age at immunization corresponded to the recommended age milestone (birth, 6 weeks, 10 weeks, 14 weeks and 9 months) as per NIP schedule. However, some infants received BCG vaccine at 2.5 months rather than at birth. Two to four weeks of delay was seen for infants receiving the first dose of MR vaccine with a median age of 9.5 months (IQR 9-10 months).

About three-fourths (74.5%, 95% CL 68.3% to 80.0%) of the infant cohort (n=169) were identified as UTD for immunization.

Among those who were up to date (n=169), two-thirds (n=110) of the infants (65.1%, 95% CL 57.4% to 72.3%) had received the vaccines at the recommended age milestones as per the NIP schedule (Table 3). The overall dropout rate was calculated to be 18.9%. The highest dropout rate was found to be between the first and third combo dose at about 10% (Table 4). The time trend for vaccination visits was shown

in Fig. 4. Among the infant cohort (n=227), 11% missed a single visit, 7% missed two visits and 8% missed three visits to the clinic (Fig. 5).

UTD immunization status was not found to be significantly influenced by sex, ethnicity, low birth weight or distance of the residence from the health care institution (Table 5).

At the end of the study period, we tried to contact the parents/caregivers whose infants had either missed or delayed the visits to the clinic and found that 12 contact numbers were incorrect and 30 were missing. In all, a total of 54 parents whose infants had either missed or delayed the visits to the clinic were contacted. As shown in Fig. 6, the most common reasons for missed or delayed visits were that the infant had received the vaccine at a health facility that was close to their place of residence (n=21), or the infant was ill (n=14). An equal proportion of caregivers said that they had travelled to their village (n=7) or maternal home (n=7) and given the age-appropriate vaccine in that particular location. Another reason was that the parents were busy (n=4). Delay in the start of vaccination was attributed to the preterm birth of the infant (n=1).

DISCUSSION

The second wave during the COVID-19 pandemic period coincided with the lock down in Kathmandu that extended over five months (end of April 2021 to the beginning of September 2021). The infant cohort was enrolled during this period (April-July 2021). During recruitment, it was observed that a lower number of infants were enrolled during the months of May and June 2021. Female infants (44%) were found to comprise less than half of the infant cohort (n=227).

At the end of the study period, three-fourths of the infant cohort had received all of the recommended vaccines prior to their first birthday. However, only two-thirds of those with UTD immunization had received the vaccines at the NIP recommended age milestones (birth, 6 weeks, 10 weeks, 14 weeks and 9 months). When examined by baseline characteristics such as sex, ethnicity, birthweight status and place of residence, no sub-group of infants were differentially impacted in relation to their immunization status.

During the early COVID-19 pandemic period, electronic medical record data from Canada (a high income country) such as Canada (University of Toronto Practice-Based Research Network) showed that UTD immunization rate among children under two years of age was 71% in the pre-pandemic period. A 5% to 6% drop in overall UTD immunization was seen during the first wave of COVID-19 pandemic.[8]

Similarly, the Vaccine Safety Datalink in United States reported substantially lower rates of weekly vaccine administration across age groups during the early months of the COVID-19 pandemic, followed by an increase to near pre-pandemic levels from summer into fall 2020. Despite the return to more typical levels of vaccination, the proportion of children with UTD vaccinations was lower among the 7-month and 18-month children.[9,10]

Among middle income countries, a study in Colombia reported an immunization coverage of 76% in 2019. There was a 14.4% decline in 2020 with immunization coverage dropping more significantly among infants.[11]

In the present study, with an UTD immunization of 76.2%, we expected an overall dropout of about 24%. However, the actual overall (BCG-MR1) dropout rate was lower (18.9%). This lower dropout was attributable to some infants who had missed either the second or third COMBO doses but had returned to the clinic for the first dose of the Measles-Rubella containing vaccine (MR1).

The highest dropout among the infant cohort was seen between the first (6 weeks) and third COMBO (14 weeks) doses. However, when compared to a previous study carried out in the pre-pandemic period at the same clinic, a lower dropout rate (10% vs 29%) was seen.[7]

Several global reviews and country-level studies had reported a decline in the number of administered vaccine doses. Moreover, the largest decline (57%) was observed in the South-East Asia region in the number of administered doses of diphtheria–pertussis–tetanus-containing vaccine (DTP3) and Measles vaccine (MR1) in the first half of 2020. An approximately four-fold increase was observed in polio cases in polio endemic countries. Routine immunization services had begun to recover by mid-2020. These reviews highlighted the need for ongoing assessment of recovery, catch-up vaccination strategy implementation for vulnerable populations, and ensuring vaccine coverage equity and health system resilience.[12,13,14]

In South Asia, the Sindh province in Pakistan reported a 52.5% decline in the daily average

number of vaccinations administered during lockdown compared to baseline.[15] The highest decline was seen for BCG (40.6%), with infants missing immunization during the lockdown. The lowest rates were seen in rural areas, urban slums, and polio-endemic sub-districts. One out of every two children in Sindh province had missed their routine vaccinations during the COVID-19 lockdown. Higher maternal education, facility-based births, and early enrolment into the immunization program were significantly associated with immunization uptake during the lockdown period.[15] In India, there was a significant drop in the number of vaccine doses administered during the first wave with a sharp decline (-87%) during April, May (-67%) and June (-33%).[16]

As the study infant cohort were facility-based births with an early enrolment into the immunization program, this may have contributed to the UTD immunization rate (76.4%) which was comparable to that reported in the pre-pandemic period in previous studies (71% to 76%).

Intentional delay in vaccination has been identified during the early period of the COVID19 pandemic period. The Italian Paediatric Society have reported that one-third (34%) children had missed routine immunization visits during the first lockdown period (n=1474 respondents). The common reasons for reduced adherence were fear of contracting SARS-CoV-2-virus (44%) or due to postponement (42%) or closure of RI services (13%). [10]

Another cross-sectional study in Saudi Arabia, among 577 caregivers (90.8% mothers) of under two years' children reported a 37% prevalence of intentional vaccination delay. Fear of COVID19 infection and avoidance of exposure to persons with COVID19 were the most common reasons of intentional delay.[17]

A review conducted in India, reported significant declines in the vaccine coverage rates Some reported disruptions for all vaccines, while a few reported sparing of birth doses. Shortage of healthcare workers due for them being diverted to patient care services and their reduced movement due to lockdowns and non-availability of public transport were prominent causes. Parents avoided RI sessions as they feared them or their children getting infected. They also faced travel restrictions, just like the healthcare workers. Promptly identifying missed out children and scheduling catch-up sessions is required to sustain the gains made over the decades by the immunization program of India.[18]

In Nepal, a qualitative study (n=7 service providers, n=8 service users) found that some service providers mentioned facing disruptions in services. Some parents had intentionally decided to delay scheduled immunisation. However, most service providers showed high morale and determination to deliver the RI services. Most parents (service users) reported taking their children for immunisation. It was difficult to confirm up-to-date immunization among children whose families had migrated from urban to rural areas during the pandemic. Service providers also experienced lack of adequate guidance to deal with the pandemic and personal protective equipment to protect themselves and service users. Despite experiencing disruptions in childhood immunisation service due to the COVID-19 pandemic, service users and providers were determined to vaccinate the children.[19] Interestingly in the current study, when probed about the reasons for missed or delayed doses, none of the parents or caregivers spoke about fear of COVID 19 disease or disruptions related to the second lockdown as a reason for missing or delaying the vaccine.

During the pandemic, many hospitals were designated as COVID-19 hospitals and various measures taken by the government to contain the spread of infection have disrupted the provision of routine health-care services including immunization. A modelling study in Indonesia estimated the impact of the pandemic in reducing the basic childhood immunization coverage. The basic childhood immunization coverage would be 53%, 50%, and 43% for a 5%, 10% and 20% reduction in immunization coverage.[20]

Given the context of the COVID-19 pandemic period, the study results indicated that routine immunization services were sustained at our institutional level during the second wave. Moreover, all of the infants with missed or delayed doses whose parents we were able to contact had received the vaccines elsewhere. Hence, the overall and vaccine specific dropout rates among the infant cohort are health facility based rates and may not indicate a drop in immunization coverage at the community or district level in Kathmandu, Nepal.

This study has helped to identify several remedial measures that could be adopted at the health facility such as maintaining proper contact numbers and records. More importantly, messaging about the vaccines received and when they need to return to the clinic needs to be reinforced to parents and caregivers accompanying all of the infants.

Our immunization records are currently held in physical form. Perhaps digital immunization records may help us to track the infants and send timely reminders to parents/caregivers about the immunization visits to the clinic.

Limitations: As this was a health facility based study, it does not reflect the immunization coverage among infants at the community or district level. Due to time constraints, the follow-up period was restricted to a year and hence UTD immunization status was reported for infants rather than for children under two years of age. As, immunization services at the health facility were disrupted for a small period during the first lockdown period we have not compared UTD rates prior to and during the first wave of the COVID pandemic.

In conclusion, three-fourths of the infant cohort had received all of the recommended vaccines as per the National immunization schedule at our immunization clinic. However, one third had delayed their visits to the clinic. The maximum delay was seen with the first dose of the Measle-Rubella containing vaccine. The pentavalent vaccine dropout rate was lower than that reported during the pre-pandemic period. Routine immunization reporting only looks at the number of vaccine specific doses that have been administered at an immunization clinic. Hence, this study has documented a sustained utilization of RI services during the second wave of the pandemic period in Kathmandu, Nepal. The lower dropout rate for Pentavalent vaccine indicates a qualitative improvement in RI services. However, an ongoing scrutiny of immunization data recording with a progression to digital health records and provision of timely reminders to caregivers may further help to strengthen RI services at the institutional level.

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