



## Predictors of exclusive breastfeeding for six months among HIV-exposed infants in Uganda: Insights from a prospective cohort study, 2017–2019

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### Summary

**Background:** Exclusive breastfeeding is recommended for HIV-exposed infants (HEIs) for six months to lower the risk of mother-to-child HIV transmission and enhance HIV-free survival. We estimated the predictors of exclusive breastfeeding (EBF) for 6 months in mothers receiving routine prevention of mother-to-child HIV transmission (PMTCT) care in Uganda.

**Methods:** We conducted a secondary analysis of data from a prospective cohort study of Uganda's PMTCT impact evaluation, conducted at 152 randomly selected public and private facilities during 2017-2019. HEIs were defined as infants born to HIV-positive mothers who tested HIV-negative at baseline. Mother-HEI pairs were recruited  $\leq 3$  months postpartum and followed at 6, 9, 12, 15, and 18 months. Baseline data included the HEIs' and mothers' HIV status, while follow-up data included infant feeding practices. We excluded HEIs with missing feeding data at 6 months. Multivariate modified Poisson regression was used to determine predictors of EBF for six months.

**Results:** Among 1,527 eligible HEIs, 767 (50%, 95%CI 48-53%) were male, 464 (30%, 95%CI 28-32%) were exclusively breastfed for six months, and 310 (20%, 95%CI 18-22%) of their mothers received PMTCT services at a level IV health centre (HC) or hospital. Among 1,013 mothers with data on viral suppression, 890 (88%, 95%CI 86-90%) were virally suppressed at baseline. Of 1,278 mothers with data on HIV disclosure, 205 (16%, 95%CI 14-18%) disclosed their HIV status to their spouses. Having a mother who was virally suppressed (aRR=2.1, 95%CI 1.2-3.8), disclosed her HIV status to her spouse (aRR=1.4, 95%CI 1.0-2.0), and received PMTCT at a HC IV or hospital vs a lower-level health facility (aRR=1.4, 95%CI 1.1-1.9) were associated with increased likelihood of receiving EBF for 6 months among HEIs.

**Conclusion:** HEI six-month EBF rates were low. Factors that have been previously associated with adherence to ART (viral suppression, disclosing status to spouses) were also associated with EBF for 6 months. Further investigation is needed to understand the reasons for these, as well as the reasons for higher EBF rates among women attending PMTCT at higher-level facilities.



## Introduction

Globally, there has been a decrease in new HIV infections among children under five years from 320,000 in 2010 to 160,000 in 2021 [1]. However, this progress fell short of achieving the 2020 targets of fewer than 20,000 new infections set under the super-fast track framework to end AIDS by 2030 [2, 3]. Breastfeeding can be a route of mother-to-child HIV transmission (MTCT) accounting for about a quarter of the overall infant HIV infection rate [4, 5]. However, early cessation of breastfeeding can have detrimental effects on both mothers and infants [6, 7]. Premature weaning poses risks such as infant growth failure and increased HIV transmission during this vulnerable period. On the other hand, exclusive breastfeeding (EBF) for up to six months has been shown to reduce the risk of postpartum HIV transmission to HIV-exposed infants (HEIs) and increase HIV-free survival rates [4, 8-10]. Non-adherence to EBF poses a more than doubled risk of postpartum HIV transmission to the HEI [11-13]. For instance, in a study done in Cameroon, infants on mixed feeding had a 7-fold higher rate of HIV vertical transmission at 24 months compared to those on EBF, while infants on exclusive replacement feeding had a 1.5-fold higher transmission rates compared to those who had breastfeeding [14].

Breastfeeding is the optimal method of feeding infants, particularly in low-income countries, supporting their growth, development, and overall survival [15, 16]. Breastfeeding (EBF) provides vital protection against life-threatening conditions such as Pneumonia, Diarrhoea, and Malnutrition as breast milk contains anti-infective whey proteins [8, 16-19]. The World Health Organization (WHO) guidelines from 2016 recommend that mothers living with HIV, who consistently take antiretroviral therapy (ART), exclusively breastfeed their infants for the first 6 months and introduce complementary feeding while continuing to breastfeed until 12 months. These recommendations remain unchanged, even in situations where access to ART drugs may be uncertain, such as during acute emergencies, as it contributes to increased survival [8]. The Uganda 2010 national guidelines for prevention of mother to child transmission of HIV (PMTCT) and Infant Feeding in the Context of HIV recommended Mothers to exclusively breastfeeding until 6 months of age, and continue breastfeeding while introducing complementary feeds until 12 months of age [19-21].

Despite these guidelines, non-adherence to EBF has been reported among HIV-exposed infants (HEIs), particularly in developing countries [22-26]. Few studies have been done in Uganda to assess the predictors for EBF for 6 months among HEIs. We assessed the prevalence and predictors of exclusive breastfeeding up to 6 months among HIV exposed infants at routine PMTCT sites in Uganda: 2017-2019 to inform control and prevention interventions.



## Methods

### Study design, setting, and data source

We conducted a secondary analysis of data from a prospective cohort study of Uganda's PMTCT impact evaluation, conducted at 152 randomly selected public and private facilities during 2017-2019 [27].

In the baseline study conducted between September 2017 and March 2018, infants aged 4 to 12 weeks and their caregivers at selected healthcare facilities were enrolled. Participants were excluded if critically ill, caregivers were <18, or they declined infant HIV testing. Maternal HIV status was confirmed by documented ART use (e.g., ANC card, mother's medical record, infant's health card) or positive antibody test following the Ministry of Health national testing algorithm. Viral load tests were conducted for HIV-positive mothers. Infants were screened for HIV-1/2 antibodies using finger stick whole blood to determine maternal HIV status as well as infant HIV exposure status if the infant was accompanied by a caregiver. Confirmatory polymerase chain reaction (PCR) using Cobas Ampliprep/Taqman HIV-1 Qualitative Test Version 2.0 was performed for reactive infant results using dry blood. HIV negative infants and their HIV positive mothers were enrolled in the follow up study. HIV-positive infants were connected to ART care and excluded from the prospective study.

The prospective study had two cohorts. Cohort I: HIV-positive mothers with HIV-negative infants from the baseline study, and Cohort II: HIV-negative mothers with HIV-negative infants. Follow-up visits for both occurred at 6, 9, 12, 15, and 18 months postpartum, with  $\pm 6$  weeks flexibility. Cohort I additionally tracked infant HIV prophylaxis and maternal ART. All infants were assessed for HIV, <18 months via PCR and  $\geq 18$  months with on-site antibody testing. Cohort I mothers had viral load tests at 6- and 12-month visits. Follow-up visits for Cohort I focused on infant-related questions only including the infants feeding options measured as Exclusive breastfeeding (EBF), exclusive replacement feeding (ERF), and mixed feeding (MF). EBF was defined as breastfeeding with no added supplements except vitamins; ERF was defined as the administration of commercial formula feeding using bottles; and MF was described as a combination of both breastfeeding and formula feeding practices. At each visit, mothers in cohort II were screened for new HIV infection using on-site rapid antibody testing, following the MoH algorithm. If during follow-up visits, a mother in cohort II was identified as having HIV infection, the mother-infant pair became part of cohort I. However, by 6 months of follow up, we did not have any mother cross-over from cohort II to cohort I.

Tests were performed at the Central Public Health Laboratory in Kampala. Infants of mothers with HIV were tested for presence of HIV RNA by PCR using COBAS Ampli Prep/TaqMan HIV-1 Qualitative assay, version 2.0 (Roche Diagnostics, Branchburg, New Jersey) utilizing infant dried blood samples (iDBS) on Guthrie cards. All first positive or indeterminate results were confirmed by a second PCR test (Amplicor HIV-1 DNA, version 1.5, Roche Diagnostics). For maternal viral load measurement, maternal dried blood spots (mDBS) on Guthrie cards were tested using the Abbott real-time 1.0ml



HIV RNA DBS version 2.00 protocol. Left over iDBS and mDBS were stored at  $-80^{\circ}\text{C}$  at Central Public Health Laboratory after testing.

### **Study variables and data abstraction**

In this analysis, we abstracted data on Mother Infant pairs from cohort 1 defined as infants who were HIV negative and born to HIV infected mother at baseline. All HEIs in cohort I were eligible for the analysis. HEIs whose feeding information at six months was missing were excluded due to data quality issues.

We abstracted baseline data on predictor variables for EBF for six months. The independent variables at baseline included infant sex, infant age, infant birthweight, nevirapine prophylaxis, mother's age, mother's status, mother's education level, other's viral suppression, mother's HIV disclosure to spouse, mother's use of alcohol during pregnancy, ANC booking, mother's HIV diagnosis in relation to 1<sup>st</sup> ANC visit, number of ANC visits, delivery place, birth attendant, prophylaxis, initiation of breast feeding, and Level of PMTCT facility, nevirapine.

We also abstracted 6-month follow up data on the outcome variable. The outcome variable was exclusive breastfeeding for six months defined as infants breastfed at baseline and at six months.

### **Statistical analysis**

Using descriptive analysis, we computed the proportion of infants who received exclusive breastfeeding for 6 six months as the proportion of total HEIs (denominator) that were exclusively breastfed for six months (numerator). Multivariate modified poisson regression was used to estimate unadjusted and adjusted risk ratios, adjusting for potential confounders that would cause a significant difference in the risk ratios. To generate the model, we performed a backward stepwise elimination at  $p>0.05$ . All statistical tests were performed at 5% level of significance. The model was a good fit for the data. All statistical analyses were performed using STATA® version 14 (Stata Corp LP, Texas, USA).

### **Ethical approval**

The impact evaluation study obtained clearance from the ethical review boards of the Uganda Virus Research Institute (UVRI), Research Ethics Committee (FWA No.00001354), and the U.S. Centers for Disease Control and Prevention (CDC) Atlanta. It was cleared and registered by the Uganda National Council for Science and Technology (FWA No. 00001293). The secondary analysis was determined to be non-research by the Office of the Associate Director for Science at the CDC because the project did not involve collection of primary data from human subjects' research. The project was aimed at addressing a public health problem. In addition, we obtained permission from the Ministry of Health, Kampala, Uganda to access and utilize the data. Data accessed did not have personal identifiers.





## Results

### Demographic and clinical characteristics of HIV exposed infants and their mothers

Out of 17,520 infants enrolled in the impact evaluation study, 799 were excluded due to missing information on HIV exposure status at baseline. 1804 HEIs from cohort I were screened for eligibility and further 277 were excluded due to missing information on feeding at 6 months. 1,527 HIV-exposed infants (HEIs) were included in the analysis. Out of 1,523 HEIs with data on sex, 767 (50.4% 95% CI 47.8%-52.9%) were male. Out of 1,013 mothers with data on viral suppression, 890 (87.9% 95% CI 85.7%-89.7%) achieved viral suppression at baseline. Out of 1,278 mothers with data on HIV disclosure, 205 (16% 95%CI 14.1%-18.2%) disclosed their HIV status to their spouses. Out of 1527 mothers, 310(20.3% 95% CI18.4%-22.4%) received PMTCT services at HC IV or hospital.

### Proportion of HIV exposed infants that received exclusive breastfeeding for six months, Uganda, 2017–2019

Out of 1,527 HEIs, 464(30.4%, 95% CI 28.1-32.8%) were exclusively breastfed for 6 months, 1,012 (66.3%, 95% CI 63.8-68.6%) were on mixed feeding, and 51 (3.3%, 95% CI 2.8-4.4%) were on exclusive replacement feeding.

### Predictors of exclusive breast feeding for 6 months among HIV-exposed infants in Uganda, 2017–2019

At bivariate analysis, mothers who were virally suppressed at baseline, and mothers who attended PMTCT at HC IV or hospital were more likely to exclusively breast feed their HEIs for six months. Alcohol use during pregnancy, HIV disclosure, skilled birth attendant, mother's age, education level, marital status, ANC booking, number of ANC visits, place of delivery, birth weight, nevirapine prophylaxis, and initiation of breast feeding within 1 hour were not associated with EBF for six months.

In multivariate analysis, HEIs whose mothers had viral suppression at baseline (aRR=1.8, 95% CI 1.1-2.9) were more likely to be exclusively breastfed up to six months compared to those whose mothers were not virally suppressed. HEIs born to mothers who attended PMTCT at HC IV or hospital (aRR=1.4, 95% CI 1.1-1.9), were more likely to be exclusively breastfed for 6 months compared to those whose mothers attended PMTCT at a HC II or private clinic. HEIs born to mothers who disclosed their HIV status to their spouses (aRR=1.4, 95% CI 1.0-2.0) were more likely to be exclusively breastfed for 6-months compared to those whose mothers did not disclose the HIV status to their spouses. Not using alcohol during pregnancy cofounded on the on the association between VL suppression and EBF for 6-months and the HEI's birthweight equal to or more than 2.5 kg cofounded on the on the association between VL suppression and EBF for 6-months (Table 1).



**Table 1: Bivariate and multivariate analysis for predictors of exclusive breastfeeding for 6 months among HIV exposed infants, Uganda, 2017-2019**

Variable	EBF for 6-months, N=464		No EBF for 6-months, N=1,063		cRR (95%CI)	aRR* 95%CI
	n	(%)	n	(%)		
<b>Mother's Viral Load</b>						
Not suppressed	23	(7.6)	100	(14.0)	1.0	
Suppressed	279	(92.4)	796	(86.9)	1.6	(1.1-2.4)
<b>PMTCT facility level</b>						
II or Private clinic	198	(42.7)	451	(42.4)	1.0	
III	146	(31.5)	422	(39.7)	0.8	(0.7-1.0)
IV or Hospital	120	(25.8)	190	(17.8)	1.3	(1.0-1.6)
<b>Alcohol use</b>						
Yes	36	(8.3)	88	(9.2)	1.0	
No	398	(91.7)	870	(90.8)	1.1	(0.8-1.5)
<b>Disclosure to partner</b>						
No	322	(83.0)	751	(84.4)	1.0	
Yes	66	(17.0)	139	(15.6)	1.1	(0.8-1.4)
<b>Skilled birth attendant</b>						
No	30	(9.0)	101	(7.6)	1.0	
Yes	303	(91.0)	676	(87.0)	1.4	(0.9-2.0)
<b>Age of mother (years)</b>						
15-24	141	(30.5)	319	(30.3)	1.0	
≥25	321	(69.5)	735	(69.7)	0.99	(0.8-1.2)
<b>Marital status</b>						
Never married	51	(11.5)	107	(10.7)	1.0	
Cohabiting	46	(10.4)	110	(11.0)	0.91	(0.6-1.4)
Married	347	(78.2)	779	(78.2)	0.95	(0.7-1.3)
<b>Education level</b>						
None	48	(10.3)	141	(13.3)	1.0	
Primary	297	(64.0)	696	(65.5)	1.2	(0.9-1.6)
Secondary	119	(25.7)	226	(21.3)	1.4	(0.97-1.9)
<b>ANC booking</b>						
Late	286	(67.8)	629	(65.9)	1.0	
Early	136	(32.2)	326	(34.1)	0.9	(0.8-1.2)
<b>ANC visits</b>						
1-3	171	(40.6)	342	(36.1)	1.0	
≥4	250	(59.4)	606	(63.9)	0.9	(0.7-1.1)
<b>Place of delivery</b>						
Home	39	(8.6)	131	(12.7)	1.0	
Private clinic	86	(19.0)	220	(21.3)	1.2	(0.8-1.8)
Public facility	327	(72.4)	680	(66.0)	1.4	(1.0-2.0)
<b>Child's gender</b>						
Male	223	(48.2)	544	(51.3)	1.0	
Female	240	(51.8)	516	(48.7)	1.1	(0.9-1.3)
<b>Birth weight (kg)</b>						
<2.5	27	(8.2)	55	(7.2)	1.0	
≥2.5	304	(91.8)	710	(92.8)	0.9	(0.6-1.4)



<b>Infant number</b>				
>1	2 (0.4)	15 (1.4)	1.0	
1	462 (99.6)	1048 (98.6)	2.6 (0.6-10.4)	
<b>Nevirapine at birth</b>				
No	47 (14.2)	116 (14.9)	1.0	
Yes	285 (85.8)	664 (85.1)	1.0 (0.8-1.4)	
<b>Initiation of BF</b>				
>1 hour	106 (35.8)	116 (14.9)	1.0	
Within 1 hour	190 (64.2)	664 (85.1)	1.0 (0.8-1.4)	

cRR: crude Risk Ratio, aRR: adjusted Risk Ratio, EBF: Exclusive breastfeeding, BF: breastfeeding, ANC: antenatal care, PMTCT: prevention of mother to child HIV transmission \*adjusted for birthweight of infant and use of alcohol during pregnancy

## Discussion

This study estimated the prevalence of EBF at 6 months and assessed predictors for exclusive breast feeding for 6 months among HEIs at routine PMTCT sites in Uganda. The EBF rate among HEIs was 30%. Mothers virally suppressed at baseline, disclosed their HIV status to their spouses, and attended PMTCT at higher level health facilities were more likely to exclusively breastfeed for 6 months. The infant's birthweight equal or greater than 2.5 kg confounded on the association between VL suppression and EBF up to 6-months and disclosure and EBF up to 6-months. Not using alcohol during pregnancy confounded on the association between VL suppression and EBF up to 6-months.

The prevalence of EBF at 6 months was 30%. This is comparable to 43% EBF at 14 weeks reported in Northern Uganda [28], and the 32% prevalence of EBF at 6 months among HEIs in south Africa [29]. Another study in Western Uganda reported 29% of HIV positive mothers adhering with the recommended infant feeding practices[30]. However, the prevalence we found is twice lower than the 65% prevalence reported in Western Kenya [31] and three times lower than the 88% prevalence of EBF among HEI reported in Ethiopia[32]. The difference could be due to the differences in the study designs. The study in western Kenya and Northern Ethiopia were cross-sectional studies and mothers were requested to do a self-report for the periods they did exclusive breastfeeding while this was a prospective study design with 3-monthly follow-up. The 30% prevalence is low and the remaining close to three quarters of HEIs on non-exclusive breastfeeding especially MF up to 6 months could be exposed to killer child hood illness of pneumonia, diarrhoea, and malnutrition and could affect the survival of HEIs in Uganda [8, 16-18].

Mothers who were virally suppressed had 80% higher chances of exclusively breastfeeding HEIs for 6 months compared to mothers who were not virally suppressed. This finding agrees with findings reported in northern Uganda where HIV positive mothers who adhered to ART during pregnancy were more likely to exclusively breastfeed up to 14 weeks [28]. Further, the findings agree with another study in rural Tanzania [33]. This finding suggests that effective HIV treatment and viral suppression play a role in EBF for 6 months.



Mothers who disclosed their HIV status to their partners had 40% higher chances of exclusively breastfeed for 6 months compared to mothers who did not disclose. This is similar to findings in Ethiopia where HIV positive mothers who disclosed to their spouses were more likely to exclusively breastfeed their HEIs for 6 months[24, 25]. The mother's HIV disclosure to the partner could support the mother to minimize stigma of EBF reported among mothers[34, 35]. This suggests that open communication and support within the family may contribute to the successful practice of EBF.

Mothers who attended PMTCT at a higher-level health facility had 40% higher chances of exclusively breastfeed for 6 months compared to mothers who attended at level II or private facilities. This could be possibly explained by the comprehensive PMTCT package provided at higher level health facilities. This suggests that the quality of healthcare services and counseling at these facilities may positively influence EBF practices.

The birthweight equal to 2.5kg or more confounded on the association between disclosure and EBF and on the association between VL suppression and EBF. This is possibly due to the infant's health and feeding capabilities of low birthweight babies. This is supported by finding from other studies elsewhere that reported higher birthweight being associated with EBF of HEIs up to 6- months [36-38]. There are no recent studies showing relation between Viral suppression and infant birthweight. However, earlier studies reported low birthweight less than 2.5 kg as a complication of non-adherence with high viral load and poor CD4 response during pregnancy[39].

Not using alcohol during pregnancy confounded on the association between VL suppression and EBF up to 6-months. Studies elsewhere have reported use of alcohol were less likely to breast feed exclusively for 6 months[29, 40-43]. Studies have also reported the use of alcohol being associated with missing antiretroviral drugs which could result in non-viral suppression[44]. This indicates that alcohol consumption during pregnancy may be a factor affecting EBF practices among HIV-positive mothers. Therefore, efforts need to be intensified to support HIV positive mothers to abstain from using alcohol during and after pregnancy to improve their feeding practices.

### **Study limitations**

Out of the 17,520 infants enrolled in the impact evaluation, screened for eligibility, 799 (6.9%) were excluded due to missing information on HIV exposure status and further 277/1804 (15%) were excluded due to missing information on feeding option at 6 months. This exclusion may have led to a potential underestimation of the observed effect.

### **Conclusion**

HEI six-month EBF rates were low. Factors that have been previously associated with adherence to ART (viral suppression, disclosing status to spouses) were also associated with EBF for 6 months. In addition, mothers attending PMTCT at higher level health facilities were more likely to do EBF for the HEIs. Further investigation is needed to understand the reasons for these, as well as the reasons for higher EBF rates among women attending PMTCT at higher-level facilities.





### Conflict of interests

The authors declare that they have no conflict of interests.

### Authors' contributions

PCK developed the study concept, participated in its design, analysis, interpretation of the study and drafting of the bulletin. RA, and LN participated in design, analysis, interpretation, and review of the bulletin. TL, and BSN participated in the analysis, interpretation, and review of the bulletin. RM, BK, DK, LB, PM, and ARA participated in the interpretation and review of the bulletin to ensure intellectual content and scientific rigor. All authors read and approved the final bulletin.

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