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Original Research

Loss to follow up after pregnancy among mothers enrolled on the option B+ program in Uganda

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ABSTRACT

Objective: Option-B+ programs in Uganda have reported high levels of loss to follow up (LTFU) after cessation of breastfeeding, and this remains unknown beyond this period. In this study, we assessed the incidence and factors associated with LTFU two to four years after delivery among Option-B+ mothers.
Study design: Retrospective cohort.
Methods: We reviewed files of 452 mothers who enrolled on Option-B+ between January 1st, 2013 and December 31st, 2014 at Kisenyi Health Centre IV in Kampala district. We assessed factors associated with LTFU using Cox proportional hazards regression. We also explored the reasons for LTFU using three focus group discussions, five in-depth and three key informant interviews.
Results: Of the 452 mothers, 131(29%) were LTFU after delivery. The incidence of LTFU after delivery was 17/1000 person months (95% CI, 14–30/1000) with a median follow up of 32 months. The risk of LTFU was higher among mothers who started ART on the day they tested HIV positive (aHR = 1.66, 95% CI; 1.25–2.20, p-value< 0.001). Reasons for LFTU included transport costs, stigma, poor human resource policies and non-disclosure.
Conclusion: LTFU after delivery among Option-B+ mothers is higher than the global target of 15%. ART initiation on the day a mother tests positive increases the risk of LTFU. The major reasons for LTFU were stigma and non-disclosure. To reduce the risk of LTFU, we recommend approaches that encourage disclosure to sexual partners and ongoing specific support to mothers who are initiated on ART-the day of positive test.

1. Introduction

Mother-to-child transmission accounts for over 90% of the paediatric HIV infections. Globally150,000 children were infected with HIV in 2018 [1]. In Uganda, there were 58,832 deliveries to HIV-positive mothers and 7500 children were newly infected with HIV in 2018 [1,2]. In 2012, Uganda adopted the option-B+ strategy to prevent mother-to-child HIV transmission (PMTCT) [3]. In this strategy, HIV-infected mothers are started on antiretroviral therapy (ART) and maintained on this therapy for life. This requires continued engagement with the healthcare system, but Option-B+ programs in Uganda have reported high (27%–37%) levels of loss to follow up (LTFU) after cessation of breastfeeding [4–7]. Mothers who are LTFU are at risk of drug resistance, virologic failure, have higher viral loads and are more likely to infect their sexual partners [8–10].

Life after birth presents multiple challenges which increase the risk of LTFU; caring for a newborn is hectic, leaving minimal time for self-care [9]. Some mothers don't disclose their HIV status to their partners [10] and find it difficult to attend clinic visits regularly. Sometimes, the motivation of mothers for remaining in care changes when they give birth to healthy babies. Mothers with high CD4 cell counts may not have experienced AIDS-related conditions and don't perceive themselves to be at risk of adverse outcomes, further increasing the risk of LTFU [11].

Studies on LTFU under the Option-B+ era conducted in Uganda have examined continued engagement up to cessation of breastfeeding [4,5,12], to the best of our knowledge none of them have looked at LTFU beyond this period. This study assessed the incidence and factors associated with LTFU two to four years after delivery among Option-B+ mothers attending a primary health care unit in Uganda.

Abbreviations: KIIs, Key Informant Interviews; IDIs, In-depth Interviews; FGDs, Focus Group Discussions; LTFU, Lost to Follow up and pmo-person months.

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2. Methods

We conducted the study at Kisenyi Health Centre (HC) IV, a primary health care unit in Kampala capital. It serves a semi-urban and slum population with over 1,330 HIV-positive pregnant mothers started on ART by December 2016. Between January 2013 and December 2014, Kisenyi HC IV initiated 705 pregnant mothers on ART. On average, six starts mothers on ART daily at the PMTCT clinics, where they receive HIV care services until confirmation of the exposed infant's final HIV status. Thereafter, mothers are transferred to the general HIV care unit for routine monitoring and follow up. The scheduled clinic visits ranges from two weeks to three months, depending on their medical condition. During clinic visits, mothers are provided with health education, family planning services, screening and treatment for other infections, and treatment adherence assessment. Those who miss an appointment are contacted by peer counsellors, and if they don't respond within a month, they are physically traced by community teams. This information is captured in HIV care cards and registers.

We used both qualitative and quantitative data collection methods in the study. For the quantitative data, Option B+ mothers' files were retrospectively reviewed and information on: follow up status by December 2016, demographic and clinical characteristics were extracted. We consecutively enrolled study participants until we acquired the required sample size.

For qualitative data, focus group discussions (FGDs), in-depth interviews (IDIs) and key informant interviews (KIIs) were conducted to explore reasons for the observed LTFU. The KIIs involved two clinical officers and one midwife obtained by purposive sampling based on their knowledge and role in the Option-B+ program at Kisenyi HC IV. In-depth interviews engaged five mothers who were LTFU during the study period, traced and currently in care. We held three FGDs with Option-B+ mothers who were active in care, each FGD composed of 6–8 members obtained by snowballing. The principal investigator moderated the interviews and FGDs using preset topic guides. Research assistants captured gestures and body language displayed during the focus group discussions.

LTFU in this study referred to a mother who has missed her last scheduled clinic visit for three consecutive months or more after delivery and was neither transfers-out or dead as per the ministry of health guidelines [13]. We defined the incidence of LTFU as the number of mothers missing clinic visits for three or more consecutive months after delivery divided by the total follow up time. Follow up time was censored for mothers who either died or transferred to other ART clinics.

Cochran method was used to estimate the sample size for incidence of LTFU [14]. The parameters applied in this calculation included: a standard normal (Z) value corresponding to 95% confidence interval (CI), ±5% level of precision, and an estimated LTFU of 58% [15]. After adjusting for missing records at the health facility, the estimated sample size was 578.

The Cox proportional hazard regression model was used to determine factors associated with LTFU. We considered variables with a p-value $<$ 0.20 at bivariate analysis for inclusion in multivariate analysis. We also assessed for interaction, confounding, and independent predictors in the regression model. Factors associated with incidence of LTFU were reported by adjusted Hazard Ratio (aHR) at 95% CI. We set statistical significance at a 95% CI and $p < 0.05$ in this analysis. We used STATA 13 (STATA Corp, College Station, TX, USA) for the analysis.

Qualitative data collection and the subsequent analysis followed an iterative process, informational redundancy established the last FGD, KII and IDI. Audio-taped interviews and focus group discussions were translated to English, transcribed verbatim, then edited to remove any identifiers. We analysed the data using content analysis, and a coding framework informed by literature, topic guides and emerging themes from transcripts. Qualitative analyses were conducted using Open code version 4.0.

3. Results

We traced and reviewed 656 files of the 705 pregnant mothers enrolled in Kisenyi HC IV during the study period. Of these, 27 had incorrectly documented appointment dates, 77 were LTFU and 100 transferred out before delivery. We excluded these from the study, thus leaving an analytical sample size of 452 (Fig. 1).

Majority of the Option-B+ mothers (84%; 348/452) started ART on the day they tested HIV positive. At the time of ART initiation, 215 (48%) mothers were below 25 years of age, 381 (84.3%) were married, 391(92%) had a baseline CD4 cell count $>$ 200 c/μl and 71 (16%) had one or more opportunistic infections. Most of the mothers 349 (77%) had HIV negative infants on discharge from the PMTCT clinic (Table 1).

Out of 452 mothers who initiated Option-B+, 131 (29%) were LTFU after delivery. The incidence of LTFU after delivery was 17/1000-person months (pmo) (95% CI, 14–30/1000-pmo) with a median follow up of 32 months (IQR, 13 months). The incidence of LTFU differed significantly among mothers below 25 years of age (27/1000-pmo, 95% CI, 27–36/1000-pmo) compared to older mothers (10/1000-pmo, 95% CI, 10–13/1000-pmo). The risk of LTFU was higher among mothers who started ART on the same day they tested positive compared to those who started later (aHR = 1.66, 95% CI; 1.25–2.20, p-value $<$0.001). See Table 2.

The commonly cited reasons for LFTU included, non-disclosure of HIV status, transport costs, stigma, poor human resource policies, misconception that the mother's health is unimportant once the HIV-exposed infant tests negative for HIV and no partner support.

1.) Partner support

In two FGDS, mothers acknowledged that their spouses' support is the reason they are still in care after birth as highlighted;

> "But mine (partner) knows.… When appointment day reaches, he reminds me and even sends me transport money." (FGD3)

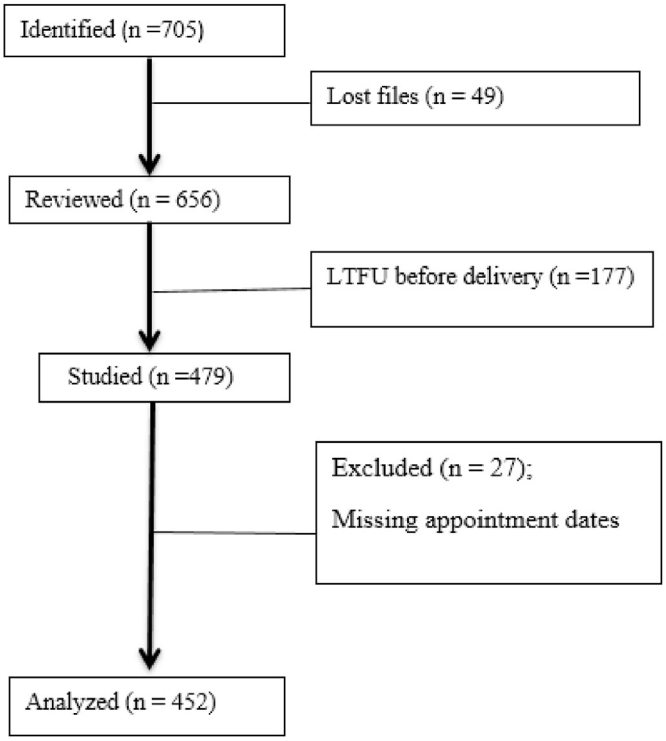

Fig. 1. A flow diagram describing the patients included in the study.

Table 1
Baseline characteristics of mothers enrolled on Option B+ program January 2013 to December 2014 at Kisenyi HC IV.

Variable	Number (N = 452)	Percentage (%)	Incidence rate per 1000 pmo	95% Confidence interval
Marital status				
Single	60	13.3	32	26–41
Married	381	84.3	15	14–17
Divorced/ Separated/ Widowed	11	2.4	26	14–48
Age at ART initiation				
17–24	215	47.6	27	27–36
25–42	237	52.4	10	10–13
Median [25], range (17,42)				
Tested positive and initiated ART on the same day				
Yes	380	84.1	33	30–37
No	72	15.9	05	04–06
Had a treatment supporter on enrollment into care				
Yes	441	97.6	17	15–28
No	11	2.4	38	21–49
Infections at ART initiation				
None	381	84.3	16	14–17
One or more	71	15.7	29	23–36
[a]**Gestation age at 1**st **ANC (N = 381)**				
1–24weeks 210 46.3 10 09-12				
25–38 weeks 181 63.7 32 28-37				
CD4 at ART initiation[a]**(N = 425)**				
Less than 200	34	8	16	14–17
Equal to or more than200	391	92	36	28–46
Exposed infant HIV status				
Negative	349	77.2	14	13–16
Positive	12	2.7	31	13–43
Unknown	91	20.1	47	38–58

[a] Missing data on variables; Gestation age at 1st ANC (44/452).

"My husband. He doesn't have the virus, but I do. He helps me —he encourages me to attend the clinic and swallow medicines so I can raise his kids –." (FGD2)

2) Disclosure of HIV status

Non-disclosure of HIV status is a major reason mothers were LTFU. One KI mentioned; *"disclosure is the biggest challenge, those who don't disclose find it difficult to get transport money."*

Another KI added. *"Some of these women have not disclosed. So they have to find ways of escaping from home".*

An FGD participant mentioned, *"Most of them are not accompanied by their spouses on the day they test positive and start ART. They fear disclosing later on and drop commitments they made when the baby tests negative." (FGD2).*

An IDI reaffirms *"I did not tell anyone I live with, so I have kept my hospital visits a secret. But sometimes it's difficult to hide and in such circumstances, I miss clinic appointments because I don't want anyone to find out,".*

3) Stigma

Stigma has contributed to non-disclosure and driven Option-B+ mothers away from seeking care. One FGD participant narrated;

"————when I told my relatives am HIV positive they mistreated me… …" (FGD2)

An IDI mentioned *"I have not disclosed to anyone, if I tell them my problems, they will gossip,".*

Another respondent added, *"mothers are afraid of finding village mates at the clinic. So they decide to just leave treatment in fear that people who know them may report to their husbands"* (FGDI).

Table 2
Factors associated with LTFU after pregnancy among Option B+ mothers enrolled at Kisenyi HC IV Jan 2013–Dec 2014.

	Bivariate			Multivariate		
Variable	Hazard ratio	95% CI	P-Value	Hazard ratio	95% CI	P-Value
Marital status						
Married	1					
Single	0.56	0.29-1.06	0.074			
Divorced/Separated/Widowed	2.22	1.03–4.76	0.041			
Age at ART initiation (categorized based on literature)						
17-24	1.18	0.84-1.64	0.337	1.18	0.84-1.67	0.337
25-41	1			1		
Tested positive and initiated ART on the same day						
Yes	1.68	1.25-2.29	0.001	1.66	1.25-2.20	<0.001
No	1.0					
Had a treatment supporter on enrollment into care						
Yes	1					
No	1.92	0.79- 4.70	0.153			
Infections at ART initiation						
None	1					
One or more	0.9	0.55-1.46	0.671			
Gestation age at 1st **ANC**(categorized at median)						
1–24 weeks	0.77	0.54-1.11	0.159	0.77	0.54-1.19	0.179
25–38weeks	1					
CD4 at ART initiation						
≥200	1					
Less than 200	0.84					
Exposed infant HIV status						
Negative	1					
Positive	2.34	0.57- 9.60	0.235			
Unknown	5.9	4.15- 8.39	0.241			

KIIs- Key Informant Interviews; IDIs - In-depth Interviews; FGDs- Focus Group Discussions; LTFU- Lost to follow up, pmo-person months.

A KI augmented *"… mothers stigmatised after disclosing to a friend relocated and didn't return in care"*.

4) Transport costs

The findings showed that mothers find it difficult to meet their transport costs and are forced to miss clinic appointments. An IDI reported *"I have never forgotten the day when I am supposed to pick my pills, the problem is transport"*.

A KI mentioned *"People don't work so they depend on others to give them transport to come"*.

An FGD participant cited *"Your appointment may approach when you don't have transport money, so you miss the clinic.,"* (FGD1).

5) Exposed infant HIV status

The misconception that the mother's health is unimportant once the exposed infant tests HIV negative jeopardises continuation in care as stated;

"I started ART when I was pregnant.… when the baby tested negative, I said to myself, if the baby is well, why bother taking the medicine? I abandoned treatment, but I fell sick, so I came back to the clinic …" (IDI)

"when the babies test negative, other mothers think they are cured of HIV and abandon care," (FGD1).

On the other hand, delivery of a healthy baby motivated mothers to stay in care as stated;

"I had lost the morale, but when I delivered a negative baby, I got motivated. — I have to be healthy for my baby's sake —I can't afford to miss a clinic visit anymore," (IDI).

6) Human resource policy and disclosure

Some human resource policies don't allow mothers time off to seek medical attention. These policies coupled with non-disclosure make adherence to HIV care difficult as cited;

"We have bosses who don't know our status. During immunisation, we use the baby as a reason to come, but after we have no excuse we can give for leaving work to attend a clinic," (FGD3).

"I had an appointment today, but when I asked for permission, he denied me. I just left, and the boss told me I won't receive a wage. He might suspend me," (FGD2).

4. Discussion

This study found higher LTFU of 29% after delivery among Option-B+ mothers, compared to the global target of 15% for ART clients [16]. The incidence of LTFU was 17/1000-pmo, higher among mothers with a baseline CD4 cell count ≥200 copies/μl and those below 25 years of age at ART initiation. ART initiation on the same day a mother tested HIV positive increased the risk of LTFU.

The LTFU of 17/1000-pmo is similar to that observed in urban clinics in central Uganda (15/1000-pmo) [7], but lower than that reported in rural settings in the region (30/1000-pmo) [4]. Evidence on the relationship between urban versus rural sites and LTFU remains inconclusive as some studies have found LTFU rates to be lower in smaller rural clinics [17]. These smaller rural clinics are resource-constrained, and health workers are not motivated to be vigilant about LTFU mothers(4). Mothers in rural areas travel long distances and need more time to reach health facilities, which could explain why there may be a higher LTFU rate in these settings [4,18].

LTFU was higher among mothers below 25 years compared with older mothers. These findings resonate with several studies in Sub-Saharan Africa [4,17,18]. Younger mothers may not understand the benefits of taking ART [5], are prone to internal stigma [19] and have less settled lifestyles, thus finding it difficult to engage with the health system [15].The Option-B+ program should integrate youth-friendly services to equip young mothers with the skills required to maintain HIV treatment [20].

Mothers with a baseline CD4 ≥ 200 copies/μl had a higher incidence of LTFU compared with those with lower baseline CD4 cell counts. Mothers with high baseline CD4 are often not ill and may not perceive themselves at risk of HIV/AIDS conditions, making their retention in care more difficult [6,17,18]. In our qualitative work, some mothers who were once LTFU only returned to care after feeling unwell.

Mothers started on ART on the day they tested positive are more likely to be LTFU after delivery than those started on ART at a later date. Our findings resonate with those reported in Sub-Saharan Africa [17,21]. These mothers may not be adequately counselled and have limited time to accept their diagnosis [10,18]. Our qualitative work showed that most mothers who start ART on the day they test positive are unaccompanied by their partners. The mothers fear disclosing their status and withdraw from treatment when the baby is confirmed HIV negative. Option-B+ programs should assess mothers' readiness to maintain treatment before ART initiation.

Study participants mentioned several reasons for LTFU after delivery, including; non-disclosure, transport costs, partner support, stigma, human resource policies, and exposed infant status. These reasons are like those published in literature [4,8,10,17,22,23]**.** Although negative HIV status of exposed infants was statistically insignificant, our qualitative data indicates it may explain the observed LTFU. Mothers' misconception that their health is not important once the baby turns negative, jeopardises continuation in care. Those starting ART when they are well see no reason to stay in care after delivering a healthy baby [24].

Non-disclosure of HIV status was a major contributor to LTFU after delivery. According to Kiwanuka et al., only 47.4% of Option-B+ mothers reveal their HIV status because disclosure threatens a woman's relationship with her spouse and family [4]. Her HIV-positive status questions her ability to be a wife, a mother and to care for her family [23]. Similarly, participants reported external stigma after revealing their status and others feared peoples' response to their HIV diagnosis so they did not disclose. Disclosure is a prerequisite for physical, financial and emotional support essential for retention in care [4,21].

Study participants acknowledged that mothers who do not disclose their status find it difficult to get transport and permission from work to attend clinic days. To alleviate these challenges, Option-B+ programs should consider flexible opening hours like evenings or weekends when most employees are free and employers' approval is not required.

Finally, mothers from the FGDs acknowledged that they are still in care because their husbands support them. In Sub-Saharan Africa, HIV-positive women are often economically dependent on their partners and the men provide transport needed to seek care [4,8]. So, mothers need their spouses' permission to initiate and stay in HIV care [8]. However, partner support is achieved after disclosure, yet few mothers feel comfortable to reveal their HIV status. Option B+ programs should promote couple HIV counselling and testing as it improves couple communication and facilitates disclosure [25].

The study has several limitations including use of secondary data that lacked information on some key variables such as education level, occupation and parity. However, information bias may be minimal considering the study incorporated qualitative findings which captured

reasons for the observed LTFU. Our sample size (452 versus 578) was relatively small to detect all factors associated with LTFU after delivery.

In summary, LTFU among Option-B+ mothers after delivery is high, and mothers starting ART on the day they test positive increases the risk of LTFU. The major reason for LTFU was non-disclosure, so we recommend approaches that promote disclosure to male partners. Further studies should be conducted to understand circumstances around same day ART initiation that hinders women from continuing in care. Providing interventions to support HIV- infected and newly diagnosed pregnant mothers is critical for improving long term retention in care.

Ethical approval

Makerere University School of Medicine Research and Ethics Committee approved the study and waived requirement for informed consent to review existing medical records. Kampala City Council Authority and the in-Charge of Kisenyi HC IV endorsed the study. We sought oral informed consent from study participants before start of discussion and audio recording of the dialogues during FGDs, KIIs and IDIs.

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Authors' contributions

Yerusa Kiirya: conceptualization, methodology, validation, formal analysis, investigation, data curation, writing original draft, reviewing and editing of manuscript, visualisation and project administration.

Joan Kalyango: conceptualization, methodology, validation, formal analysis, reviewing and editing of manuscript and supervision.

Philippa Musoke: conceptualization, methodology, validation, reviewing and editing of manuscript and supervision.

Gloria Adobea Odei Obeng-Amoako: conceptualization, methodology, formal analysis, data curation, writing original draft, reviewing and editing of manuscript and visualisation.

All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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