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Research Article

Assessment of Loss to Follow-Up (LTFU) and Associated Factors among Pregnant Women Initiated Antiretroviral Under Option B+ in Selected Health Facilities of West Zone Oromia, Ethiopia

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Abstract

Introduction: Antiretroviral therapy (ART) is effective for elimination of mother-to-child transmission (eMTCT) of human immunodeficiency virus (HIV) infection, reducing infant mortality and ensuring maternal virologic suppression. Evidence shows that LTFU among HIV positive pregnant women on option B+ is high compared to their non-pregnant counterparts. Moreover, LTFU is more likely to occur when ART is initiated rapidly as in the case of option B+. The women who are LTFU are more likely to get lost due to psychosocial issues such as fear of HIV disclosure, stigma, and insufficient social support and non-acceptance of HIV status. Additionally, the earlier months of ART initiation and LTFU among Ethiopia HIV pregnant on option B+ are critical for ensuring that women are retained in care.

Methods: A quantitative prospective cohort descriptive design was followed to conduct the study. Five randomly selected Hospitals providing Option B+ services with routine viral load assessment by Oromia regional Laboratory (ORL) since January 2016 to January 2017 was randomly selected. Bivariate and multivariable analyses were conducted to determine factors affecting the time to ART initiation following an HIV test and logistic regression used to determine the correlation between time and treatment outcomes.

Result: The study results revealed that 319 respondents, 81.8% were active and 18.2% were loss to follow-up no clinical contact for 18 months. The proportion of respondents that were LTFU was highest among pregnant women on ART for > 38 months on ART, 9.4% compared to ≤ 37 months (8.8%).

Therefore, in this study identified that factors associated with LTFU were missing appointments ($p < 0.001$), time on ART ($p = 001$) and weight at ART start (0.018) were independently associated with LTFU status among HIV positive pregnant women that initiated lifelong ART on option B+ in Ethiopia.

Conclusion: The results also revealed that maternal weight at ART start was an important predictor of LTFU among Ethiopia HIV pregnant on option B+. The study results suggested that duration on ART is an important predictor of LTFU among women on option B+ in West shoa, Oromia, Ethiopia. Additionally, the earlier months of ART initiation are critical for ensuring that women are retained in care.

Keywords: *ART Initiation Pregnant Women Option B +; Loss to Follow-Up*

Abbreviations

ANC: Antenatal Care; ART: Antiretroviral Therapy; AZT: Zidovudine; DNA: Deoxyribonucleic Acid; EFV: Efavirenz; eMTCT: Elimination of Mother-to-Child Transmission; HBM: Health Belief Model; HIV: Human Immunodeficiency Virus; MoH: Ministry of Health; MTCT: Mother-to-Child Transmission; NNRTI: Non-Nucleoside Reverse Transcriptase Inhibitor; NVP: Nevirapine; PCR: Polymerase Chain Reaction; PMTCT: Prevention of Mother-to-Child Transmission; TDF: Tenofovir Disoproxil Fumarate; UNAIDS: Joint United Nations Programme on HIV/AIDS; WHO: World Health Organization; 3TC: Lamivudine

Introduction

According to LTFU excludes patients that have died, transferred out, or stopped ART and who are more than 60 days late for their first follow-up visit and the cumulative incidence of LTFU by the second year is 24.5% (95% CI, 23.2% - 25.8%) among women who start ART during pregnancy and 20.2% (95% CI, 18.3% - 22.2%) among those who start ART while breastfeeding in 13 Malawian health facilities [1]. In Cameroon reports that among 65 (24.3%) women on option B+ that discontinued treatment 44.6% were LTFU and 55.8% actively stopped treatment [2]. Other findings revealed that 17.7% was due to LTF stopped treatment [3]. A systematic review suggest that overall, the proportion of women who are lost after ART initiation reached 23.9% (95% CI 22.6 - 25.3%) in all option B+ patients with 29.4% (95% CI 27.6 - 31.3%) loss among B+ pregnant women [4]. The Overall 24.3% women discontinued treatment, either defined by LTFU 44.6% or actively stopped treatment 55.8% [5]. In Northeast Ethiopia, 11.9%, 15.7% and 22.6% of women on option B+ were LTFU at 6, 12 and 24 months respectively [6].

Findings in South Africa revealed that at 6 months following ART initiation, pregnant women 28.1% are more likely to get LTFU compared to 16.9% of non-pregnant women with a 1.3 times greater attrition risk among pregnant cohorts (RR 1.29; 95% CI 1.09 - 1.54; p = 0.009). Therefore, previous findings suggest that LTFU is higher among HIV pregnant women compared to the non-pregnant or breastfeeding women [1,4,7].

According to reasons for reduced retention in option B+ programmes in Lilongwe Malawi included religious related issues, community related stigma, lack of transport and clinic related challenges. Evidence shows that LTFU among HIV positive pregnant women on option B+ is high compared to their non-pregnant counterparts. Moreover, LTFU is more likely to occur when ART is initiated rapidly as in the case of option B+ [8]. The women who are LTFU are more likely to get lost due to psychosocial issues such as fear of HIV disclosure, stigma, and insufficient social support and non-acceptance of HIV status. Women who initiate ART on option B+ do so when they are healthy with high CD4 counts and less advanced WHO stage 1 or 2. This protects them from acquiring HIV related opportunistic infections like TB which may lead to ill health and mortality. Therefore, the research statement for this study is "What is the correlation between the time to antiretroviral therapy initiation following an HIV test and Lost to follow up among HIV pregnant women that initiated ART on Option B+ for at least 12 months in healthcare facilities of Ethiopia?"

Materials and Methods

Study setting and design

The research design for this study quantitative prospective cohort descriptive design was conducted from January 2017 to March 2017, at ART clinics of governmental hospitals in west Shoa zone, Oromia Regional State, Ethiopia. Ambo town which is the capital of the zone is located 112 kilometers to the west of Addis Ababa the capital of the country. According to information from the zonal health office the total population in zone is estimated to be 2,381,079 of which 1,214,350 of them are female. Currently the health system of the zone consists of 6 hospitals, 90 health centers and 447 health posts with 98% of potential health service coverage.

There are different governmental and non-governmental organizations working on HIV/AIDS in the zone. There are 5 hospitals namely Ambo hospital, Enchini Primary Hospital, Gedo Hospital, Gindaberet Hospital, Guder Primary Hospital and21 health centers are ART sites currently, there 8,439 clients on ART in west shewa zone (Data from west shewa zone health office, November 2016).

For the study, three public hospitals (Ambo General Hospital; 3000 clients, Gedo Hospital; 485 clients, Enchini Primary Hospital; 976 client) and were selected based on the load of the clients served in the facilities that conduct routine viral load assessment for patients on option B+ PMTCT by Oromia regional laboratory during January 2016 to January 2017. HIV positive pregnant women that initiated ART received option B+ services for 12 months and had viral load assessment will be targeted in these heath facilities during the study. All Sampled pregnant HIV positive women that initiated ART under Option B+ services for at least 12 months from selected healthcare facilities in west shoa zone.

The selection criterion were include HIV positive pregnant women that initiated ART and received Option B+ services for at least 12 months with viral load assessment selected from 3 Hospital in west shoa Zone of Oromia region that conducted viral load assessment for patients on ART by Oromia regional laboratory during January2017 to March 2017.

Sample size determination and sampling procedure

The required sample size was determined using Statecalc program of the EPI INFO version 7.1.0 statistical package with a 50% rate of viral suppression based on limited data with a precision of +/- 5% and Confidence limits as % of 95. By considering correction formula, since the total population was less than 10000 which as was 1860, the final sample size was 318. The final size with non-response rate of 5% was 334. All hospitals found in west shoa Zone of Oromia region that providing ART services was identified and randomly selected by computer generated methods to be included in the study. The number of study respondents were be allocated proportionally for the five Health centers, based on their total number of ART clients'positive pregnant women who initiated ART under option B+ for at least 12 months to participate in the study.

Operational definitions

Lost to follow up: Treatment interruption (> 90 days) since initiated ART.

Data collection tools and procedures

The data collection tool will include a structured questionnaire (translated) and chart or medical records abstraction tool adopted from similar surveys and modified for the study. Questions in the chart abstraction were adopted from the HIV care card used for clinical management of clients receiving HIV care and treatment. Data on both the questionnaires and abstraction forms were collected by trained research assistants and data abstractors. At the completion of abstraction at the health facilities, tools were checked for completeness and completed tools were collected by the team leaders and stored in safe and locked cabinets accessed only by the researcher.

Data management and analysis

The returned questionnaires were checked for completeness, cleaned manually, coded and entered into EPI INFO 7.1.0 version and then transferred to SPSS windows version 20.0 for further analysis. Frequencies mean and standard deviation was used to summarize descriptive statistics of the data and text, tables and graphs were used for data presentation. Bivariate analysis were used primarily to check which variables have association with the dependent variable individually. Variables which are found to have association with the dependent variables were then entered in to Multiple Logistic regression for controlling the possible effect of confounders and finally the variables which have significant association was identified on the basis of AOR, with 95%CI and p-value to fit into the final regression model.

Result

The respondents' mean age was 30.78 years (n = 319) with a standard deviation (SD) of **±** 6.56 years.

Their age ranged from 18 to 50 years; 77.4% of them were ≤ 35 years.

In table 1 out of 319 respondents that completed information about their marital status, 233 (73.0) respondents reported that they were married and 24 (7.5%) were divorced/Separated.

In table 1, Orthodox and Protestants had the highest proportion 48.6 and 45.8% and ethnicity the majority 246 (77.1%) were Oromo followed by Amhara 46 (14.4%).

Of the respondents, 116 (36.4%) were not attained formal education and 18 (5.6) achieved were diploma and above (see table 1).

Variable		Frequency (%)
Age	**Age in years (n = 319) Mean 30.78 (SD) (6.56)**	
	<= 26	99 (31.0)
	27 - 30	62 (19.4)
	31 - 35	86 (27.0)
	36+	72 (22.6)
Marital status	Single	41 (12.9)
	Married	233 (73.0)
	Widow/widowed	21 (6.6)
	Divorced/Separated	24 (7.5)
Religion	Orthodox	155 (48.6)
	Protestant	146 (45.8)
	Muslim	18 (5.6)
Ethnicity	Oromo	246 (77.1)
	Amhara	46 (14.4)
	Tigray	14 (4.4)
	Gurage	13 (4.1)
Education	Illiterate	116 (36.4)
	Read and Write	62 (19.4)
	1 - 8th grade	93 (29.2)
	9 - 10th grade	30 (9.4)
	Diploma and above	18 (5.6)
Employment	Gov't	31 (9.7)
	Merchant	53 (16.6)
	Private	47 (14.7)
	Housewife	123 (38.6)
	Farmers	65 (20.4)
Residence	Urban	193 (60.5)
	Rural	126 (39.5)

Table 1: *Sociodemographic characteristics of HIV+VE pregnant women initiated ART under Option B+ in selected health facilities of West Zone Oromia, Ethiopia 2017.*

Clinical characteristics of respondents

Out of 319 respondents that had WHO stage at ART start documented, 35.7% (n = 114) were staged as WHO stage 1 and 45.6% (n = 146) as stage 2. Out of the total respondents had CD4 counts less than (≤ 350 cells/μL were 61.4% at baseline and 85.3% had > 350 cells/μL during data collection on current recent CD4 counts.

The mean CD4 at ART start was 349.68 cells/μL and IQR (1 - 1012). The majority of the respondents were initiated on the recommended ART regimen for option B+ with 65% (n = 207) TDF+3TC+EFV.

Other respondents were initiated on AZT+3TC+EFV 3.8% (n = 12). None of the respondents were initiated on 2nd line regimen.

Variable		Frequency (%)
Time to ART from HIV testing	Same day (0 day)	218 (68.3)
	Delay 1 thru 8 days	101 (31.7)
WHO Clinical stage at ART start	Clinical Stage 1	114 (35.7)
	Clinical Stage 2	146 (45.8)
	Clinical Stage 3	37 (11.6)
	Clinical Stage 4	22 (6.9)
WHO Treatment stage (WHO- T)	T-Stage 1	309 (96.9)
	T-Stage 2	10 (3.1)
Clinical Adherence	Schedule	309 (96.9)
	Unscheduled	10 (3.1)
Adherence to medication	Good	306 (95.9)
	Poor/ Fair	13 (4.1)
ART Regimen	TDF+3TC+EFV-1e	207 (64.9)
	AZT+3TC+NVP-1c	93 (29.2)
	TDF+3TC+NVP-1f	7 (2.2)
	Azt+3tc+EFV-1d	12 (3.8)
ART regimen of the mother on Maternal PMTCT intervention during recent pregnancy	Yes	315 (98.7)
	No	4 (1.3)
Newly diagnosed and started on ART during recent pregnancy	Yes	87 (27.3)
	Know HIV +ve on ART	232 (72.7)
Of Newly diagnosed and started on ART during recent pregnancy		
ANC		67 (21)
Labour @Delivery		15 (4.7)
Post-Partum (FP, EPI, U5yr OPD)		6 (1.9)
Loss to follow-up no clinical contact for 18 months	Yes	58 (18.2)
	No	261 (81.8)
Treatment interruption (> 90 days) since initiated ART	Yes	59 (18.5)
	No	260 (81.5)

Table 2: *Respondents' clinical characteristics HIV+VE pregnant women initiated ART under Option B+ in selected health facilities of West Zone Oromia, Ethiopia 2017.*

Loss to follow-up (LTFU)

Of 319 respondents, 81.8% were active and 18.2% were loss to follow-up no clinical contact for 18 months. The proportion of respondents that were LTFU was highest among pregnant women on ART for ≤ 37 months (8.8%) compared to > 38 months on ART, 9.4% and almost similar numbers of mothers were interrupted for at least greater than 90days since initiated ART. Loss to follow up.

Variable	Frequency (%)
Loss to follow-up (LTFU)	
Yes	58 (18.2)
No	261 (81.8)
Treatment interruption (> 90 days) since initiated ART	
Yes	59 (18.5)
No	260 (81.5)

Table 3: *Treatment outcomes (Loss to follow-up (LTFU) of pregnant women initiated ART under Option B+ in selected health facilities of West Zone Oromia, Ethiopia 2017.*

Association factors with Loss to follow-up (LTFU)

In the final model N = 319 (p < 0.001), attending hospitals (OR 6.997, 95% CI; 1.321 to 37.061, p = 0.022) compared to HCIII and IV; missing appointments (OR 4.266, 95% CI; 1.951 to 9.331, p < 0.001); weight at ART start (OR 0.899, 95% CI; 0.824 to 0.982, p = 0.018) and time on ART (OR 0.109, 95% CI; 0.031 to 0.386, p = 0.001) were independently associated with increased LTFU among HIV pregnant women that start ART on option B+. The study results suggest that time to ART following HIV testing was associated to LTFU among HIV positive pregnant women that initiate on lifelong ART. Attending hospitals compared to lower health facilities, missing appointments, weight at ART start and time on ART were independently associated with LFTU.

Variable	Odds Ratio	95 CI	p-value
Time on ART	0.109	0.031 to 0.386	0.001
Health facility			
Hospital (Gudeo+ Gindbert)	1.000		
Hospital (Ambo General)	6.997	1.321 to 37.061	0.022
Missed appointments	4.266	1.951 to 9.331	0.000
Weight at ART start	0.899	0.824 to 0.982	0.018

Table 4: *Association between independent factors and LTFU of HIV+VE pregnant women initiated ART under Option B+ in selected health facilities of West Zone Oromia, Ethiopia 2017.*

Discussion

Time on ART is an important predictor of treatment outcomes among women who initiate ART under option B+. Most importantly, the initial period during ART initiation is associated with poor outcomes like reduced viral suppression. The proportion of suppressed respondents with VL < 1000 copies/ml was lowest 57.14% (4/7) among those on ART for < 37 compared to those on ART for 38 - 70 months (92.05%), 25 - 36 months (92.31%) and > 36 months (96.88%). Detectable VL or none suppression is highest among women that enroll on option B+ with ≤ 4 months of ART [9]. The results of this study emphasized the need to intensify support for HIV pregnant women on option B+ during the early months of ART initiation. Concerning LTFU, the in this study results showed that overall 18.2% were loss to follow-up no clinical contact for 18 months. The proportion of respondents that were LTFU was highest among pregnant women on ART for ≤ 37 months (8.8%) compared to > 38 months on ART, 9.4%. In Zimbabwe, 17.7% of women on option B+ in 34 health facilities get LTFU [3]. Previous study revealed that higher proportion 44.6% among women on option B+ is due to LTFU and in a systematic review also reported that overall 23.9% (95% CI 22.6 - 25.3%) of women on option B+ get lost following ART initiation and of these 29.4% (95% CI 27.6 - 31.3%) loss is among pregnant women and 16.1% (95% CI 14.3 - 18.0) in breastfeeding women [2,4]. Among women 65 (24.3%) women that discontinue treatment 44.6% are due to LTFU [5].

In 13 Malawian health facilities, the cumulative incidence of LTFU by the second year is 24.5% (95% CI, 23.2% - 25.8%) among women who started ART during pregnancy [1] and in Western Cape Town, SA 28.1% pregnant women are more likely to get LTFU compared to

16.9% among non-pregnant women at 6 months following ART initiation [7]. In Northeast Ethiopia, 11.9%, 15.7% and 22.6% of women on option B+ are LTFU at 6, 12 and 24 months respectively [6]. According to some previous [2,3] and [6] both pregnant and breast feeding women on option B+ were assessed for LTFU. Other studies [4] and indicated high LTFU among HIV positive pregnant women compared to non-pregnant women. This study however, only concentrated on HIV pregnant women that initiated lifelong ART under option B+ [7].

The study results suggested that duration on ART is an important predictor of LTFU among women on option B+ in West shoa, Oromia, Ethiopia. Additionally, the earlier months of ART initiation are critical for ensuring that women are retained in care. Health facility level ($p = 0.022$), missing appointments ($p < 0.001$), time on ART ($p = 001$) and weight at ART start (0.018) were independently associated with LTFU status among HIV positive pregnant women that initiated lifelong ART on option B+ in Ethiopia. The study results demonstrated that HIV positive pregnant women initiate ART with a relatively high weight. The results also revealed that maternal weight at ART start was an important predictor of LTFU among Ethiopia HIV pregnant on option B+. A set of reliability and validation rules were applied and all associated factors were taken after indication of significance in the "goodness of fit" for the models. Even though this study also had a few limitations: This study was facility-based among PLHIVs' that results were not generalizable to the general population in the community and cause and effect relation was not assured because of cross-section study deign.

Conclusions

Of 319 respondents, 81.8% were active and 18.2% were loss to follow-up no clinical contact for 18 months. The proportion of respondents that were LTFU was highest among pregnant women on ART for ≤ 37 months (8.8%) compared to >38 months on ART, 9.4%.

Therefore, in this study identified that factors associated with viral load response were poor/fair adherence missing doses in the past month, missing appointments, baseline CD4 and maternal months on ART were statistically significant.

This study however, only concentrated on HIV pregnant women that initiated lifelong ART under option B+. The proportion of them that were LTFU presented in most of the studies was much higher compared to the one in the study. This could be attributed to the fact that only HIV positive women that had a viral load were included in the study as an inclusion criterion which was not the case with the other studies.

Loss to follow up among HIV positive women who initiate on ART is of great concern since this could predispose them to discontinuing their treatment as well as increasing the risk of MTCT in option B+ program.

The significant results included factors that hindered the process of ART initiation and compliance to medication such as minimal male participation during PMTCT; missing clinic appointments due to traveling away from home or taking a trip and work related issues; missing doses due to traveling away from home, forgetting and lack of food.

The study results suggested that duration on ART is an important predictor of LTFU among women on option B+ in West shoa, Oromia, Ethiopia. Additionally, the earlier months of ART initiation are critical for ensuring that women are retained in care.

The results of this study was also guide policy and current protocol modification in the area of Option B+ implementation especially in low-resourced countries that face challenges due to weak health systems and to contextualise it.

Therefore, strategies aimed at improving adherence among women on option B+ are to ensure that these women achieve adequate immunological outcomes.

Prospective studies that aim at further understanding the factors associated with treatment outcomes like viral change, LTFU, and immunological outcomes among women who initiate on lifelong ART including the outcomes among children is beneficial in developing strategies to further support women on option B+.

Ethical Consideration

Ethical clearance was obtained from the Ethical review committee of Ambo University CMHSs. Formal letter of cooperation was written to respective hospitals/health centers. The right to refuse was respected and information collected from this research project was kept confidential and the collected information was stored in a file, without the name of study participant.

Competing Interests

The author(s) declare that they have no competing interests.

Authors' Contributions

Dereje Bayissa Demissie, Maru Mossisa and Michael Tamene Haile conceptualized the study, designed the study instrument and conducted the data analysis and wrote the first draft and final draft of the manuscript. DBD Approved the research proposal with some revisions, participated in data analysis, revised subsequent drafts of the paper and involve in critical review of the manuscript. All authors read and approved the final manuscript.

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