

## Research Article

# Time to Attrition and Associated Factors among Adults Enrolled In Pre-Anti- Retroviral Therapy Care in Tepi General Hospital, Ethiopia

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**Background:** Pre-antiretroviral therapy (Pre-ART) patient attrition is a growing concern in Ethiopia. Nevertheless, there is little information that assesses the magnitude and its contributing factors.

**Objective:** This study assessed time to attrition and associated factors among adults enrolled in pre-ART care at Tepi General Hospital in South West Ethiopia.

**Methods:** Records of adult pre-ART patients enrolled at Tepi General Hospital from October 2010 to September 2013 were reviewed to identify factors associated with time to attrition. Time to attrition was defined as the period a patient was enrolled in pre-ART care until lost to follow up or death. Kaplan Meir curve was used to estimate survival time, and log-rank test was used to compare the time to event among different groups of patients. Cox proportional hazard model was used to assess factors associated with time to attrition.

**Results:** We followed 652 pre-ART patients for 337.6 person years of observation from enrolment to pre-ART outcomes. Of these, 179 patients were lost to follow up and 37 patients died, contributing to an overall attrition of 33.13%. In the first six months the attrition rate was 89.8%. Not starting cotrimoxazole prophylaxis (AHR=1.51, 95% CI, 1.02-2.25), being co-infected with tuberculosis (TB) (AHR=2.16, 95% CI, 1.35-3.45), living further than 10 km away from the hospital (AHR=1.44, 95% CI, 1.07-2.0), and undisclosed HIV status (AHR=3.04) were found to be associated with time to attrition.

**Conclusion:** Pre-ART patient attrition rate was high among patients not using cotrimoxazole prophylaxis, TB/HIV co-infected, living >10 km from a health care facility and with undisclosed HIV status. Close follow-up of patients during the first six months' period is highly recommended.

**Keywords:** Attrition; Death; South West Ethiopia; Loss to Follow-Ups

**Abbreviations**

AIDS: Acquired Immuno-Deficiency Syndrome, ART: Anti-Retroviral Therapy, LTFU: Lost to Follow Up, PYOs: Person Years of Observations

**Introduction**

Globally 36.7 million people were living with HIV at the end of the year 2015, of which 46% had started antiretroviral therapy (ART) [1,2]. Greater than 60% of the global cases were located in sub-Saharan Africa [1,3-5]. In settings with limited resource and high disease burden not all patients who present at earlier stage of their illness are eligible for ART [6,7]. Even when they are eligible for ART, early initiation of treatment will depend on several factors [3,7,8]. Distance to healthcare facility, social stigma, being in a less advanced disease stage, feeling healthy, occupation, and level of literacy were factors that contributed to late presentation for ART care [4,9-12]. It is likely in settings with limited resources and high disease burden, some patients will either die or loss to follow up before they are

started on ART [3,4]. A literature review of patient attrition in sub-Saharan Africa showed that less than one-third of patients remain continuously in care between testing HIV-positive and starting ART [13].

Attrition pre-ART in sub-Saharan Africa has been insufficiently described leaving major research gaps, especially regarding long-term retention rates and socio demographic, economic, clinical and programmatic logistic determinants [6], it has only recently began to be documented in literatures [13]. Ethiopian ART hospitals are facing challenges of pre-ART attritions due to high loss to follow up and death [3,7,13,14,16].

Significant pre-ART attrition is an alarm for inadequate uptake of interventions. Previously, strategies and resources to address attritions have focused on the ART period but, Pre-ART attrition given lesser attention [16-20].

At Tepi General Hospital, the annual HIV progress report showed that remarkable numbers of patients who testsero-positive failed

**Table 1:** Baseline selected socio-demographic and clinical characteristics of 652 adult pre-ART patients enrolled to pre-ART care at Tepi General Hospital, Sheka Zone, South West Ethiopia, during 2010-2013.

Selected Variables		N (%)
Age(in years) (n=650)	15-24	161(24.5)
	25-34	296 (45.5)
	35-44	124 (19.1)
	44+	69 (10.6)
Sex	Male	265 (40.6)
	Female	387 (59.4)
Occupation (n=650)	employed	174 ((26.7)
	Unemployed	280 (43.1)
	Merchants	160 (24.5)
	Other	35 (5.4)
Educational status (n=651)	No education	112 (17.2)
	Primary	254 ((39.0)
	Secondary	149(22.9)
	Tertiary and above	136(20.9)
Religion (n=649)	Orthodox	428(67.5)
	Muslim	104(16.0)
	Protestant	88(13.6)
	Other	19(3.0)
CPT provision at enrolment	Yes	360 (55.2)
Service available within≤10km	yes	444 (68.1)
WHO clinical staging	Early stage presenters	385 (59.0%)
	Late stage presenters	267 (41.0%)
Disclosure status (n=250)	Family members	349 (53.7)
	To other relatives	36 (5.5%)
	Not at all	265 (40.8%)

\*\*Pre-ART: pre-Antiretroviral Therapy; CPT: Cotrimoxazole prophylaxis Therapy; WHO: World Health Organization.

to start pre-ART and linked to pre-ART were undergoing attrition during the pre-ART care continuum before ART initiation [21].

Knowing when and why attrition occurs in Ethiopia could be useful to develop pertinent intervention strategies against pre-ART patient attritions. We aimed to assess attrition times and associated factors before ART initiation among adult pre-ART patients in Tepi General Hospital, South West Ethiopia.

## Methods

### Study design, setting and population

We conducted a retrospective cohort study among all 652 adult HIV positive clients  $\geq 15$  years old enrolled into Pre-ART care from October 01, 2010 to September 30, 2013 in Tepi General Hospital, South West Ethiopia, which is located at approximately 610 kilometers [15] from the capital, Addis Ababa. Pre- ART and ART services were started in the study area during 2006. Other services including provider-initiated counseling and testing (PICT), voluntary counseling and testing (VCT), prevention of mother-to-child transmission (PMTCT), and condom promotion are delivered integrally. According to WHO and Ethiopian Ministry of

**Table 2:** The estimated attritions of adult pre-ART patients at the end of 3, 6, 12, 24 and 36 month's observation periods at Tepi General Hospital, South West Ethiopia, during 2010-2013.

Observation period in months	Attrition		Total	Cumulative attritions	Cumulative attritions in %
	LTFUs	death			
At 3	137	16	153	153	70.83
At 6	30	11	41	194	89.8
At 12	5	4	9	203	93.98
At 24	7	5	12	215	99.54
At 36	0	1	1	216	100
Total	179	37	216		

Health guidelines [8,24], patients who test positive should be linked to pre-ART care on the same day of testing. Linked patients are continuously followed on pre-ART care until they are eligible to start HIV treatment (ART). CD4 of linked patients' is measured as early as possible, in the same day of testing.

### Operational definitions

In this study time to attrition was defined as time between enrollment and lost to follow up or death. Lost to follow up was defined as when patients miss their appointments 90 days after the last schedule. Death was considered as the death of people on pre-ART in the reporting period due to any cause. Patients who are active on pre-ART care or transferred out to other services were considered as censored. Transfer out is the official transferring of the patient to another ART clinic within or outside a catchment area [12].

Those patients' transferred to other health facilities, active on pre-ART follow-up and treatments initiated were considered as censored cases at the end of observation period.

Patients who started ART, transferred to other facility or active at the end of observation period were considered censored.

### Data Source and assessment of attrition

Tepi General Hospital patient information is recorded and kept confidentially both in hard copies and electronic formats. Except for those in clinical urgency and chronic management, Pre-ART patients are appointed for care and follow-up at every three months. Information related to patient is taken by adherence supporters and case managers. Patient related data coding, entry and analysis is done by trained data clerks.

### Sample size

Ever enrolled pre-ART patients since the start of service during 2006 were 2215 up to time of data collection. There were 652 adult HIV positive patients enrolled into pre-ART care in Tepi General Hospital from October 2010 to September 2013 and all of them were included in this study.

### Variables and measurements

The major pre-ART outcome variable was time to attrition. Age, sex, religion and residence were among the demographic information's recorded for each patient. Baseline WHO clinical stage, number of CD4 cells count, Cotrimoxazole (CPT) provision, opportunistic infections, baseline functional status of the patient, TB status, BMI, mode of patient referral system and availability of ART

**Table 3:** Comparisons of pre-ART patient attritions segregated by CPT status and HIV status disclosure at enrolment, Kaplan Meir Table.

Baseline variable	Time in month	Status	Cumulative proportion surviving at time T	N of cumulative attritions	N of remaining cases
<b>CPT provision</b>					
<b>Yes</b>	at 3 month	attrition	0.9	36	324
	at 6 month	attrition	0.82	46	104
<b>No</b>	at 3 month	attrition	0.6	117	175
	at 6 month	attrition	0.46	148	104
<b>Disclosure</b>					
<b>Family</b>	at 3 month	attrition	0.92	28	321
	at 6 month	attrition	0.86	37	120
<b>Not at all</b>	at 3 month	attrition	0.56	117	148
	at 6 month	attrition	0.4	145	71

CPT: cotrimoxazole prophylaxis.

clinic within 10km distance were also recorded.

### Data collection

Electronic files of patients enrolled to pre-ART care between October, 2010 to September, 2013 were reviewed to identify those who failed to keep scheduled appointments for more than 90 days. A list of these “LTFUs” patients was generated from medical register by observing the last appointment date.

Data were extracted from both electronic data base and standard registries using checklist developed from WHO and national treatment guideline for pre-ART care [11,33].

### Data management and analysis

The data were entered to Epi Data 3.1, cleaned and exported to SPSS 20 for analysis. First, descriptive analysis was done, followed by bivariate analysis to identify factors associated with time to attrition. Those variables in the bivariate analysis with P -value < 0.25 were considered as candidates to be included in the multivariable Cox regression model. Using back ward variable selection method the final Cox regression model was fitted.

Attrition, mortality, and LTFU rates were calculated by summing the number of patients’ who experienced the event (attrition, death, or LTFU) during a particular period of time divided by the total number of years of follow-up during this period. Attrition experiences of pre-ART patients segregated by significant predictor variables at enrolment were compared by using Kaplan-Meier survival table. The proportional hazard assumption was checked by using log-log survival curves based on Schoenfeld residuals. We calculated incidence density for mortality and LTFUs using person years of contribution to the cohort.

## Results

### Patient characteristics

We identified a total of 711 clients enrolled into pre-ART care during the study period. Among these, 652 were eligible for this study as per the inclusion criteria. Virtually all the remaining Pre-ART patients (n=59) were excluded from the study due to being from neighboring province (Gambella) and being children.

The mean age of participants was 30.59 (SD, 9.8) years and 59.4% were females. From the total study participants, 58.0% were married,

34.4% of the clients had dependent children below 15years, 39.3% had primary level education, and 67.2% were orthodox Christians. More than half (50.8%) were from the rural communities and 34.4% were Amhara by their ethnicity.

From a total of 652 study participants enrolled to pre-ART care, about two third (65.6%) were linked to care with baseline CD4 count >350 cells/ml and 59.0% were early stage presenters.

The majority (99.8%) of patients were screened for TB, of which 17% were positive.

Among 79.9% of patients with history of at least one type of opportunistic infections during presentation to care, 55.2 % had been started with cotrimoxazole prophylaxis.

Related to participants’ body mass index (BMI), 36.3% were underweight (BMI<=18.5), 60.1% were normal (BMI=18.5<BMI<24.9) and 0.9% were overweight.

Of all the patients, 92.6% were at working conditions and 3.8% were ambulatory and 3.2% were bedridden. With regard to distance from the hospital, 68.1% were located within 10km. With regard to HIV status disclosure, 40.8% had not disclosed at all for any one (Table1).

### Patient attritions during follow up period

We followed up a total of 652 clients for median of 8.9 (IQR, 4.57-13.23) months in pre-ART care from 2010 to 2013 for 337.6 person years of observation (PYOs) for an overall attrition rate of 33.13%. The minimum and maximum follow up time was 2 and 1080 days (36 months) respectively. From the overall attritions (31.13%), the highest attritions (89.8%) occurred within 6 months’ follow-up period and increased to (93.98%) at the end of 1year of observation period (Table 2). At the end of follow up time, of the total patients who were registered to pre- ART care 22 (3.4%) were transferred to other facility, 282 (43.3%) had initiated treatment, 179 (27.5%) were lost to follow up, 37 (5.7%) died and 132 (20.2%) were being active on pre-ART care. Overall patient attrition was 33.13%.

The mean estimate of attrition time for patients who started cotrimoxazole prophylaxis (CPT) at pre-ART care during enrolment was 25.43 (95% CI, 22.80-28.06) months. For patients who were not started on CPT it was 13.94 (95% CI, 12.06-15.83) months. The observed difference in attrition time between these two categories of

**Table 4:** Bivariate and multivariable cox regression findings at Tepi General Hospital, Sheka Zone, South West Ethiopia, during 2010-2013.

Variables	Crude HR	95% CI	p-value	AHR	95.0% CI AHR
<b>CPT at enrolment</b>					
<b>CPT provided **</b>				<b>1</b>	
CPT not provided	2.28	1.67-3.14	0	<b>1.51</b>	<b>1.02--2.25</b>
<b>Baseline function</b>					
<b>Working**</b>				<b>1</b>	
Ambulatory	0.69	0.33-1.47	0.337	0.73	0.33-1.62
Bedridden	2.04	1.14-3.67	0.016	1.68	0.91-3.12
<b>CD4 category &lt;350**</b>				<b>1</b>	
<b>&gt;=350</b>	2.23	1.41-3.54	0.001	1.45	0.87-2.42
<b>Disclosure status</b>					
<b>To Family members**</b>				<b>1</b>	
To other relatives	2	1.09-3.67	0.025	1.6	0.86-3.00
No disclosure at all	4.05	2.86-5.72	0	<b>3.04</b>	<b>2.07-4.45</b>
TB result : positive	1.3	0.84-2.00	0.238	<b>2.16</b>	<b>1.35-3.45</b>
<b>negative**</b>				<b>1</b>	
<b>Service availability Within &lt;10km**</b>				<b>1</b>	
<b>&gt;=10km</b>	2.05	1.57-2.68	0	<b>1.44</b>	<b>1.07-2.0</b>
OI category					
<b>No OI at all**</b>				<b>1</b>	
At least one OI	1.6	1.19-2.16	0.002	1.13	0.75-1.71
<b>&gt;=2 OI</b>	1.19	0.82-1.74	0.354	0.83	0.59-1.17
<b>Dependent children Yes</b>	1.2	0.90-1.61	0.214	1.2	0.89-1.62
<b>No **</b>				<b>1</b>	

\*\*Reference category CPT cotrimoxazole prophylaxis, AHR, adjusted Hazard Ratio, CI Confidence Interval

patients was statistically significant ( $P < 0.001$ ).

Similarly, the mean estimate of attrition time for patients who disclosed their HIV status to their family member's was 27.07 (95% CI, 24.82-29.33) months whereas for patients who did not disclose their HIV status at all to any one during enrolment to care was, 10.83 (95% CI, 8.94-12.72) months. The difference in attrition time between different categories of disclosure status was also statistically significant ( $P < 0.001$ ).

At enrolment, the cumulative proportions of patients retained were higher for patients who started CPT, disclosed their HIV status for their family members, were negative for TB and lived within 10km from the general hospital when compared to their counter parts (Table 3).

### Predictors of attrition attributed to lost follow up and death in pre-ART

The following explanatory variables with p-values  $< 0.25$  were selected for multivariate Cox regression model during the bivariate analysis of time to attrition. Baseline functional status of the patient, CPT, service availability, Cluster of Differentiation 4 (CD4) category, TB screening result, opportunistic infections, dependent children in the home and HIV status disclosure. Of these, CPT at enrolment, positive TB screening result, distance from the ART clinic and HIV status disclosure were found to be independent predictors of time to

attrition (Table 4).

## Discussion

Nowadays, the need to focus on attaining United Nation's target (90-90-90) on HIV/AIDS (90% of people who are HIV infected will be diagnosed, 90% of people who are diagnosed will be on antiretroviral treatment and 90% of those who receive antiretroviral will be virally suppressed by 2020), will be emphasized by retaining patients both on pre-ART and ART care [5,7,19,25,24].

In this study, the rate of attrition in pre-ART care was one in every third patients. This finding is higher [19,27,28] compared to different settings. This could be due to variations in study design, patient follow-ups and definitions of LTFU. Unlike our study, which defined pre-ART patients as all newly enrolled HIV patients regardless of their clinical stage and CD4 count, studies conducted in different settings [18,26,29] focused on pre ART patients with an advanced disease stage and low CD4 cell counts.

The incidence of pre-ART attrition was highest in the first year of study. Approximately 94% of attrition cases occurred in the first year and all attritions occurred at the end of the two-year observation period. This is higher by nearly 6% when compared to findings from Nigeria that showed that 88.0% of attritions cases occurred in the first year and all deaths occurred in the first six months of pre-ART care [13]. This variation may be due to poor monitoring and tracking



of defaulting patients observed during early periods of pre-ART care [7,13,17]. Thus enhancing retention strategies in pre-ART care like community based ART distribution and home based nursing interventions are highly recommended [41].

Over three-quarter of pre-ART patients (83.8%) who did not start CPT at enrolment were lost to follow up compared to about 16% lost to follow up reported among those who started CPT at enrolment. The time to attrition for patients who were started on CPT at pre-ART care enrolment was nearly 2-fold higher than those patients who were not started on CPT. Furthermore, the patients on CPT had over 35% reduction in risk of attrition at six month and increased retention time after adjustment for the other explanatory variables compared to those who did not start CPT at enrolment; and the difference was statistically significant. In another study from Kenya, treatment of ART ineligible patients with cotrimoxazole improved the 12-month retention in care from 63% to 84%; this can suggest that patients may have perceived more benefit from cotrimoxazole treatment. These data indicate that the provision of free medicines or nutrition can improve the usefulness perception of the visits to the clinic and, therefore, the retention in pre-ART care [7,13,30,31].

In this study, HIV status disclosure was found to be significantly associated with time until attrition among pre-ART patients. Compared to those patients who disclosed their HIV status to their family members, those who did not disclose it to anyone had a nearly three times higher risk of attrition. In one study, disclosure status did not show a significant association [37] and this could be due to differences in methodological variations. But, a study in Ethiopia indicated that HIV positive people experience both discriminatory exclusion and isolation from society, which further discourages disclosure of their HIV status. As a result, status disclosure and health-seeking behavior could be negatively affected. Similarly, among interviewed pre ART patients from Addis Ababa, 50% had not disclosed their HIV status due to fear of rejection from household members, thus they attrited from care [37]. Another systematic review of 34 studies supports the notion that HIV status disclosure can improve access to HIV/AIDS care and, therefore, the retention in pre-ART care [38]. Part of the underlying explanation for undisclosed HIV status can be fear of stigma and rejection from household members and the community at large [38,39].

Pre-ART patients who were positive for TB at enrolment to care were at high risk of attrition from care (AHR=2.16) compared to those TB negative at enrolment to care. This is in line with the high mortality observed in HIV patients with tuberculosis in a study cohort from India [35]. Another perspective can be patients are dying being reluctant to take both ART and anti-tuberculosis as indicated from Soweto, South Africa [36,42]. This may be also explained from, according to 2013 global TB report, even though Ethiopia has met TB incidence rate falling, 82% of HIV positive TB patients are on HIV care continuum and only 38% of people living with HIV and enrolled in to care were given isoniazid preventive therapy (IPT) [40]. But, in this study setting no data was found about patients' treatment status with IPT. It is important to offer both HIV testing to TB patients and TB diagnosis in HIV patients. Early detection and effective treatment are essential to preventing TB-associated deaths [43].

Regarding to the patient attrition in connection with service

availability, patients who lived  $\geq 10$ km from the center had higher risk of early attrition (AHR=1.44) when compared to those who lived within 10km. This study is in line with finding from Durban, South Africa that, nearly half of HIV infected patients (45%) enrolled in to pre-ART care was lost from care due to attritions and patients who lived  $\geq 10$  km from the service provision area had higher risk of early attrition (ARR=1.37). But, the time to attrition is a little bit late in this cohort.

Similarly a study from India indicated that, patients who lived near the service area were retained more on care as compared to those living abroad (ARR=1.09) [35].

The study has the following limitations; -first, the power of this study could be limited as number of deaths might be underestimated. This could be due to lost to follow up patients dying at home without reported. Using data with incomplete information might have introduced bias. Second, the outcome of pre-ART among transferred out patients is unknown. This could affect the estimated number of pre-ART outcomes.

## Conclusion

Attrition from pre-ART care was observed among more than a third of our study patients with the highest attrition being in the first year of pre-ART care. Analysis of predictor variables indicated that, these high and early patient attritions were associated with no cotrimoxazole uptake, being a TB patient, living  $\geq 10$ km from the center and disclosure status.

Close monitoring and improved tracking of patients is recommended during the early periods of pre-ART care.

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