

Incidence and Predictors of Anti-Retroviral Treatment (ART) Failure among Adults Receiving HIV Care at Zewditu Memorial Hospital, Addis Ababa, Ethiopia

Chalachew Sisay^{1*}, Alemayehu Bekele², Abay Sisay³, Hana Mekonen¹, Kumera Terfa¹, Daniel Melese¹ and Boja Dufera¹

¹Addis Ababa Public Health Research and Emergency Management, Addis Ababa, Ethiopia

²Ethiopian Public Health Association, EPHA, Addis Ababa, Ethiopia

³Addis Ababa University, College of Health Sciences, School of Clinical Laboratory Science, Addis Ababa, Ethiopia

Abstract

Background: Despite availability of antiretroviral therapy, HIV is responsible for 2.7 million new infections and 2.0 million deaths from worldwide. Anti-Retroviral treatment failure is not a commonly diagnosis in healthcare facilities in Ethiopia and there is dearth of information on the extent and predictors of treatment failure among adults receiving HIV care in the study setting. The aim of the current study is to assess the incidence and predictors of Anti-Retroviral Treatment (ART) failure among adults receiving HIV care at Zewditu Memorial Hospital, Addis Ababa, Ethiopia.

Methods: Facility based retrospective cohort study design was employed on archived data from 2011 to 2016. Data compilation checklist was developed from intake card and ART follow-up card. The collected data were coded and entered using Epi Info 7 and analysed using Statistical Packages for Social Science (SPSS) version 20 software.

Results: The overall incidence rate of ART treatment failure were 4.91 cases per person months follow up with 2.1, 0.24 and 0.13 immunological, clinical and virological treatment failure cases per 100 person years of follow-up respectively

Conclusion: The incidence of Anti-Retroviral Treatment failure was considerable among the study participants. The predictors for ART failure were WHO stage 3 at start, CD4 count at base line, disclosure and opportunistic infections. Comprehensive interventions have to be in place to tackle treatment failure among adults on ART through rendering optimum care focusing on adults with advanced WHO stage, lower CD4 count at baseline, opportunistic infections and people who did not disclose their HIV status.

Keywords: Adults; HIV; Incidence; Predictors; Anti-retroviral treatment failure

Abbreviations: ART: Antiretroviral Therapy; AIDS: Acquired Immuno Deficiency Syndrome; cART: Comprehensive Anti-retroviral Treatment; CI: Confidence Interval; HAART- Highly Active Anti-retroviral Therapy; HIV: Human Immunodeficiency Virus; MTCT: Mother-To-Child Transmission; PMTCT: Prevention Mother-To-Child Transmission; SNNP: South Nation Nationality People; SPSS- Statistical Packages for Social Science; WHO: World Health Organization

Background

Human Immune Deficiency Virus (HIV) is responsible for a worldwide pandemic and also the cause of Acquired Immune Deficiency Syndrome (AIDS). More than 36.7 million persons worldwide are living with HIV, of which 15.7 million (4%) are women. In addition, there are 2.1 million new infections and 2.0 million deaths from AIDS worldwide, despite recent improvements in access to Antiretroviral Therapy (ART) [1].

The World Health Organization (WHO) estimated that nearly 11.7 million people living with human immunodeficiency virus (HIV) in low- and middle-income countries received antiretroviral therapy (ART) in 2013 [2]. Global ART scale-up has been made possible by the use of standardized and simplified treatment protocols and decentralized service delivery, with limited reliance on laboratory monitoring [3,4]. In order to enhance treatment monitoring, WHO recommended by 2013 that viral load measurements among people receiving ART be performed 6 months after initiating ART and every 12 months thereafter [5,6].

Sub-Saharan Africa remains the region most heavily affected by HIV. 1.9 million People living in sub-Sahara Africa become newly

infected with HIV, bringing the total number of people living with HIV to 22.4 million. Moreover an estimated 1.4 million AIDS related deaths occur in sub-Sahara Africa. But the rate of new HIV infections and death has slightly declined as a result of improved access to ART [7].

In resource deprived countries ART Treatment failure is determined by clinical, immunological and/or virological failures and also patient monitoring system is dependent on clinic-immunological methods, though they lack sensitivity/specificity to detect virological failures of ART, which is the gold standard for ART treatment failure. Such circumstances, whether attributable to virologic failure, stopping ART or loss to follow-up, has been shown to increase morbidity and mortality [8].

Despite the fact that ART drugs are effective in improving the health status of HIV positive individuals up to undetectable viral load level. In Ethiopia, the past ten years, there have been significant achievements in the response to the human immunodeficiency virus (HIV) epidemic. One of the achievements was massive scale-up of

***Corresponding author:** Chalachew Sisay, Addis Ababa public health research and emergency management, Addis Ababa, Ethiopia, Tel: 251924336220; E-mail: chalesisay19@gmail.com

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antiretroviral treatment (ART) access to in the country has brought tremendous benefit to populations affected by HIV/AIDS [9].

After antiretroviral treatment (ART) initiation for the client monitoring and evaluation of blood viramia is one of the key activity of health care providers by the help of CD4 count, clinical evaluation and viral load measurement. However, based on CD4 count has poor predictor of virological failure and test targeted to monitor adherence in first-line anti-retroviral therapy (ART) [10].

ART failure is not a regularly diagnosis in most health care facilities in Ethiopia. Very few patients among the needy are started on second line ART regimens [11]. Previous studies have evaluated the patterns associated with switching from first line ART regimes to second line ART regimes; however, studies that evaluate the first line ART regime failures in limited resource settings like Ethiopia and Africa at large are scarce [12]. Even if many HIV positive clients accessed ART, there was a treatment failure. Studies show that the magnitude of ART treatment failure in the public health sector in Ethiopia ranges from 20.4% to 33.3% [13,14]. By the end of June 2013 the number of people ever enrolled in chronic care reached 728,874 while the number ever started ART was 439,301 and 317,443 were currently receiving ART. Only 70.3% of individuals who ever started ART were currently on treatment indicating challenges in patients' retention [15-17].

Hence, this study was designed to disclose the incidence and predictors of ART treatment failure to inform healthcare professionals and the leadership of the health system to evaluate patients on ART in every visit for treatment failure and contributing factors to improve the quality of care and combat treatment failure to antiretroviral treatment.

Method

Facility based retrospective cohort study design, using facility records was employed. Data recorded from 2011 to 2016 were used to retrieve relevant information from patient ART intake card and follow up card and also from the hospital electronic database for ART program (Register Database) to address the objectives of the study. According to the annual report of the Addis Ababa City Administration Health Bureau for July 2015, there were a total of 125,994 HIV positive clients (94.4% adults) who ever enrolled to ART services, among which 74,986 (94.8% adults) had ever started ART and there were 53,677 (95.5% adults) currently on ART. The city in 2015, 11 public hospitals, 77 Government health centers, 14 private hospitals and 9 Non Government clinics provided ART services in Addis Ababa. So the present study was conducted at Zewditu Memorial Hospital, which is one of referral public hospital in Addis Ababa, with strong HIV /AIDS care and treatment center.

The Hospital is one of the largest health facilities providing a comprehensive HIV care and treatment in Ethiopia. It was selected as the first pilot location for HIV programs and grew into a model program. In July 2003, Ethiopia's first ART program started at this health facility with support of CDC-Ethiopia and served HIV positive patients from around the country for a nominal fee. Through PEPFAR's support, the hospital began a free ART program in March 2005. Since the Hospital, one of the referral hospitals for the catchment sub city with wide geographical area, most patients have follow up in this hospital. There are a total of 10,672 patients enrolled to HIV care at Zewditu Memorial Hospital since 2003. From December 2011 to December 30, 2016 there were 3,184 HIV positive patients ever enrolled in chronic care who have baseline CD4 measured. Patients are then followed based on the National guideline. Hence, this study was conducted on data

records of these clients (3184) enrolled to ART services from 2011 to 2016 in the hospital ART.

Sample size determination and sampling technique

Among the different predictors of treatment failure, baseline CD4 count <500 cells/mm³ yield the maximum sample size. A power of 80%, a 5% level of significance and ratio of 1:2 (exposed: Unexposed) were assumed. Moreover, a 15.8% treatment failure among patients with baseline CD4 count ≥500 cells/mm³ (exposure) and a 7.9% treatment failure among patients with baseline CD4 count 500 cells/mm³ were assumed [18].

The sample size of this study was determined using the following formula

$$n_1 = \frac{(Z_{\beta/2} + Z_{1-\beta})^2 p q (r+1)}{r(p_1 - p_2)^2}$$

$$\text{And } n_2 = r n_1$$

where

n_1 : number of exposed;

n_2 : number of unexposed;

1.96=value of the standard normal distribution corresponding to a significance level of α (1.96 for a 2-sided test at the 0.05 level);

0.84=value of the standard normal distribution corresponding to the desired level of power (0.84 for a power of 80%).

r =ratio of unexposed to exposed

p_1 =proportion of exposed with disease and $q_1=1-p_1$

p_2 =proportion of unexposed with disease and $q_2=1-p_2$

Based on the above assumptions, it was found that the sample size required was 531 with 12% of contingency (64) give 595 study participants included in study (Figure 1).

Operational definitions

Treatment failure: Is categorized as clinical, immunological and virological failure and defined as follows [19].

Clinical failure: New or recurrent WHO stage 4 condition OR new or recurrent WHO stage 3 with pulmonary TB and/or severe bacterial infections [19].

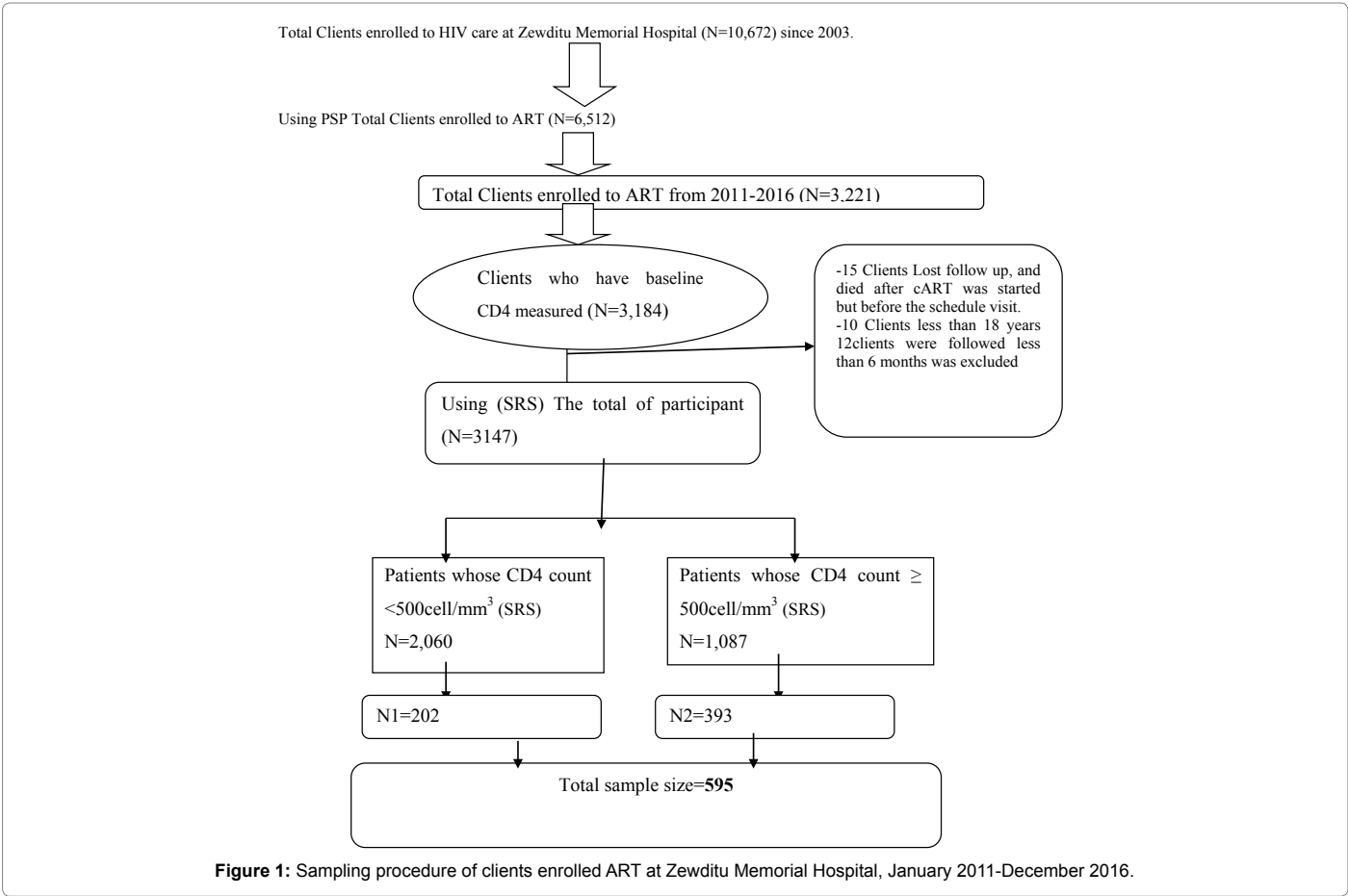
Immunological failure: Fall of CD4 count to baseline (or below) OR 50% fall from on treatment peak value OR Persistent CD4 levels below 100 cells/mm³[19].

Virologic failure: Viral failure is defined by a persistently detectable viral load exceeding 1000 copies/mL (that is, two consecutive viral load measurements within 3 months interval with adherence support between measurements) after at least 6 months of starting a new ART regimen [20].

Poor adherence: Is defined in terms of total missed appointments described by greater than three days per month [20].

Data quality control

To ensure the quality of data, standard data compilation tool were designed by referring previous studies. Before data collection, the data collectors were get a one day orientation by principal investigators. The data collectors were Hospitals data clerks. There was a regular supervision to data collectors by the principal investigators to maintain the data quality.



The required data was collected from electronic database for ART program (Register Database) by considering carefully all the variables stated in the tool with due attention to avoid any redundancy of the study participants. Completeness of the data was declared through periodic data collection. Finally data was analyzed employing appropriate statistical treatment following proper entry and cleaning.

Data processing and analysis

After the data was collected based on compilation tool developed entered to the excel sheet then cleaned, edited, coded and reentered and analyzed using SPSS version 20 statistical software package. Descriptive analysis using frequency and summary statistics was conducted to describe the study subject. Kaplan Meier survival analysis model were used to describe the time to treatment failure and Cox regression analysis has been used to determine the association between dependent variable and covariates with significant association (p value <0.05). Hazard Ratio with 95% CI was used to determine the predictors of treatment failure.

Results

Socio demographic characteristics study participants

From January 2011 to December 2016, a follow up study using record review was conducted. A total of 595 patients receiving ART treatment were enrolled. Of these, 352 (59.2%) were females. Most of the study participant 512 (89.1%) were in the age group 25-49 years and the mean age at the start ART was 39.6 ± 8.23 years. Most of the study participant had secondary education 241 (40.5%). Two hundred

Characteristics	Frequency N=595	(%)	95% Confidence Interval	
			Lower	Upper
Age				
18-24	19	3.2	1.8	4.7
25-49	512	89.1	83.2	88.9
>=50	64	10.8	8.2	13.3
Sex				
Female	352	59.2	55.7	63.4
Male	243	40.8	36.6	44.3
Marital status				
Never married	173	29.5	26.0	33.7
Married	233	39.7	35.4	43.8
Divorced	115	19.6	16.2	22.5
Widowed	66	11.2	8.7	14.0
Educational status				
No education	65	11.1	8.3	13.6
Primary	217	37.0	32.9	40.6
Secondary	241	41.1	37.5	45.2
Tertiary	64	10.9	8.3	13.3
Occupation/ Employment status				
Employed	359	64.6	60.6	68.7
Unemployed	197	35.4	31.3	39.4

Table 1: Baseline socio-demographic characteristics of adults enrolled for ART at Zewditu Memorial Hospital, from January 2011 to December 2016 (N=595).

thirty three (39.2%) were married while based on occupational status of participant three hundred fifty nine (64.6%) were employed (Table 1).

Baseline clinical characteristics study participant

The immunological, virological and clinical failures were 15.3%, 1.8% and 4.4% respectively. Based on WHO staging treatment failure observed within the group found, so that patients found WHO stage 1 is 17 (13.3%), stage 2 as 34 (26.6%), stage 3, 58 (45.3%) and stage 4,

(N=595) Characteristics	Frequency N=595	(%)	Bootstrap for percent	
			95% Confidence Interval	
			Lower	Upper
Regiment started				
1a=d4t-3TC-NVP	17	2.9	1.5	4.2
1b=d4t-3TC-FEV	9	1.5	0.7	2.7
1c=AZT-3TC-NVP	36	6.1	4.2	7.7
1d=AZT-3TC-EFV	31	5.2	3.4	7.1
1e=TDF-3TC-EFV	436	73.3	69.7	77.0
1f=TDF+3TC+NVP	58	9.7	7.5	12.4
1g=ABC+3TC+EFV	4	0.7	0.2	1.3
1h=ABC+3TC+EFV	4	0.7	0.2	1.4
WHO stage				
Stage I	343	58.2	54.0	62.0
Stage II	91	15.4	12.6	18.7
Stage III	118	20.0	16.8	23.1
Stage IV	37	6.3	4.4	8.3
Functional status				
Working	487	83.3	80.5	86.2
Ambulatory	70	12.0	9.4	14.5
Bedridden	28	4.8	3.2	6.5
Duration on ART in months				
6-12	5	0.8	0.2	1.7
13-25	22	3.7	2.2	5.4
26-48	50	8.4	6.2	10.8
49-61	41	6.9	4.9	9.1
>62	477	80.2	76.5	83.2
CD4 count at baseline (cells/mm³)				
0-49	83	13.9	11.3	16.8
50-99	119	20.0	16.8	23.2
100-199	139	23.4	19.8	26.7
200-349	202	33.9	30.1	38.2
350-999	52	8.7	6.4	11.3
Baseline Weight in Kg				
<50	101	17.6	14.4	20.7
>50	473	82.4	79.3	85.6
Disclosure				
Not disclosed	188	32.9	29.4	36.7
Disclosed	384	67.1	63.3	70.6

Table 2: Baseline clinical characteristics HIV infected patients enrolled for ART at Zewditu Memorial Hospital from January 2011 to December 2016. (N=595).

19 (14.8%). Of the participants 495 (94.3%) were no drug substitution similarly four hundred sixty two (78.2%) were not drug switch. About three hundred forty three (83.2%) were working in their functional status at the time of enrollment. The median baseline of CD4 counts were 157 cell/mm³ with inter quartile range (180: 27-289). The most common prescribed ART medication is TDF-3TC-EFV (1e) were 436 (73.3%). The median waiting time on ART in the hospital was 45 months with the inter quartile range of 35 months. At baseline 343 (58.2%) of the participants were found on WHO stage 1. One hundred forty two (23.9%) of study participant were diagnosed and confirmed HIV status more than five years. While One hundred forty nine (25%) respondent were found on ART treatment follows up for more than four years. Four hundred seventy four (82.4%) study participant were found greater than fifteen kilogram at baseline, in addition to this information, 384 (67.1%) disclosed their status at baseline (Table 2).

Treatment failure

Among the 595 study participants, 465(78.5%) were right censored (free of treatment failure). It was found that a total of 128 study participants (21.5%) have indication of treatment failure with the occurrence rate was 4.91cases per 1000 months follow up paired. Among the total 128 treatment failures 15.3%, 1.8% and 4.4% individual were categorized immunological, virological and clinical respectively. Among those patients who have treatment failure 19 (33.3%) had viral load measurement at the end of one year treatment follow up. In the meantime the total of 11 immunologic failure (57.9%) and 1 clinical (5.3%) were viral load test was done and confirmed treatment failure. On the other hand patients who had ART treatment failure were 3(42.9%), 9(72.5%), 17(29.8), 4(19.0%) and 95 (20.4%) were transfer out, death, drop, lost, alive respectively (Table 3).

Survival mean and median

Using the Kaplan Meier survival analysis method, the mean survival time (the expected time to event) was found to be 50.52 months with 95% CI (48.30,52.73) while the median survival time was 53.54 months with 95% CI (40.54,55.46). The overall incidence rate of treatment failure was 4.91 cases per 1000 person months of follow-up (Tables 4 and 5).

Findings on survival functions

The Log rank test showed that there was significant difference in survival times between the different categories of WHO stage, after recoding into two group, the comparison on the survival time of WHO stage 3 and 4 with WHO stage 1 and 2, until the first one year they have similar survival time. However, as time progressed, patients in WHO stage 3 and 4 at baseline had declined survival time. Adults in WHO stage 1 and 2 at baseline had sustained the survival time up until year five (Figure 2).

The other relevant finding in this study patients were adherence to treatment, the survival function of treatment adherence status of patient shows that at time zero all patients have similar adherence

Personal status category	Person time in months	Treatment failures	Treatment failure incidence rate	Case person-months
Transfer out	308.07	3	0.00973	9.73 case per 1000 person months
Death	1916.11	9	0.00469	4.69 case per 1000 person months
Drop	2078.58	17	0.00817	8.17 case per 1000 person months
Lost	871.09	4	0.00459	4.59 case per 1000 person months
Alive	20882.74	95	0.00474	4.74 case per 1000 person months
Overall	26056.59	128	0.00491	4.91 case per 1000 person months

Table 3: Person-time contributed by study participant and Incidence of treatment failure by status at the last visit in Zewditu Memorial Hospital in Addis Ababa, January 2011-December 2016.

	N	Minimum	Maximum	Sum	Median	Mean	Inter quartile range (IQR)	Std. Error of the mean	Std. Deviation
Age	595	18	65	23569	40	39.6	11	0.34	8.24
Weight	557	35	105	36333.12	65	65.2	19	0.57	13.47
Calculated months on ART	595	6	139	26056.59	45	13.8	35	0.85	20.73
Alive since HIVdiagnod grouped in months	595	6	150	34442.43	60	57.89	36	1.14	27.88
CD4 count at baseline	595	10	898	109408	157	183.88	180	5.49	133.90

Table 4: Survival characteristics of ART patients in Zewditu Memorial Hospital in Addis Ababa, 2011-2016.

VARIABLES	Mean	Std. Error of the mean	95% Confidence Interval of the mean		Median	Std. Error of the median	95% Confidence Interval of the median	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
Body mass index								
<18 kg/m ²	47.670	1.399	44.928	50.412	52.000	2.139	47.807	56.193
18.5-24.9 kg/m ²	45.096	1.833	41.503	48.689	45.260	3.203	38.982	51.538
25-29.9 kg/m ²	45.614	2.638	40.443	50.786	49.000	2.810	43.492	54.508
30-39.5 kg/m ²	76.175	4.780	66.807	85.544	67.000	1.070	64.903	69.097
Overall	50.518	1.127	48.309	52.727	53.000	1.257	50.537	55.463
TB Baseline								
Yes	52.236	2.553	47.232	57.239	53.000	4.254	44.663	61.337
No	49.749	1.231	47.336	52.162	53.000	1.261	50.528	55.472
Overall	50.340	1.135	48.114	52.565	53.000	1.221	50.608	55.392
Years since HIV diagnosed (months)								
6-12	18.889	6.229	6.681	31.098	9.200	0.820	7.593	10.807
12-24	17.489	0.581	16.351	18.628	17.250	0.458	16.352	18.148
24-36	28.121	0.871	26.413	29.828	26.660	1.798	23.136	30.184
36-48	39.972	0.859	38.288	41.657	42.000	1.596	38.871	45.129
48-60	48.299	1.356	45.641	50.958	53.000	1.024	50.993	55.007
60-72	59.458	0.990	57.518	61.398	63.000	1.523	60.015	65.985
>72	70.610	2.567	65.579	75.642	67.000	1.964	63.151	70.849
Overall	50.518	1.127	48.309	52.727	53.000	1.257	50.537	55.463
Duration on ART (in months)								
6-12	23.682	6.109	11.709	35.655	11.000	1.101	8.842	13.158
12-24	26.455	2.198	22.146	30.764	18.220	0.687	16.874	19.566
24-36	36.340	1.357	33.681	39.000	32.200	0.310	31.592	32.808
36-48	45.307	0.713	43.910	46.704	45.120	0.952	43.254	46.986
48-60	59.202	0.992	57.258	61.146	55.000	0.343	54.327	55.673
>60	73.453	1.801	69.923	76.983	67.000	0.291	66.431	67.569
Overall	50.518	1.127	48.309	52.727	53.000	1.257	50.537	55.463

Table 5: Survival characteristics of group of variables on ART patient in Zewditu Memorial Hospital, Addis Ababa, 2011-2016.

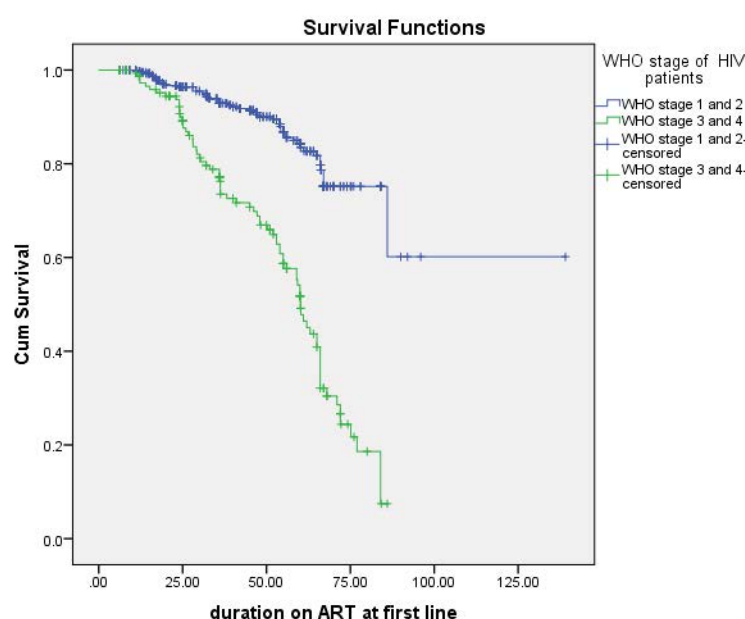


Figure 2: Survival functions of different groups of WHO stage of ART clients in Zewditu Memorial Hospital in Addis Ababa, January 2011-December 2016.

status while patients with poor adherence status to treatment as the time progress the odds of survival function declined while those with Good adherence status were sustained in the long paired (Figures 3 and 4) Patients at the beginning of ART started they have similar survival time until two years however when the time steps forward the survival staidly declined until six years (Figure 5).

Predictors of treatment failure

Cox regression analysis was done, among 595 study participant. In

this study except marital status all other socio demographic variables including age, educational status and employment condition were found to be significant predictors of Anti Retro viral Treatment (ART) failure. Accordingly, being unemployed, being old age (age ≥ 50 years) and primary and secondary education level of HIV patient more likely hazard risk of anti-retro-viral treatment failure by 1.57, 1.96, 1.42 and 1.27 times with 95% CI (AHR (1.096,2.293)), (AHR (1.308,2.958)), (AHR (1.010,2.022)) and (AHR (1.014,1.613)), respectively (Table 3). Similarly, clinical characteristics including WHO stage at baseline,

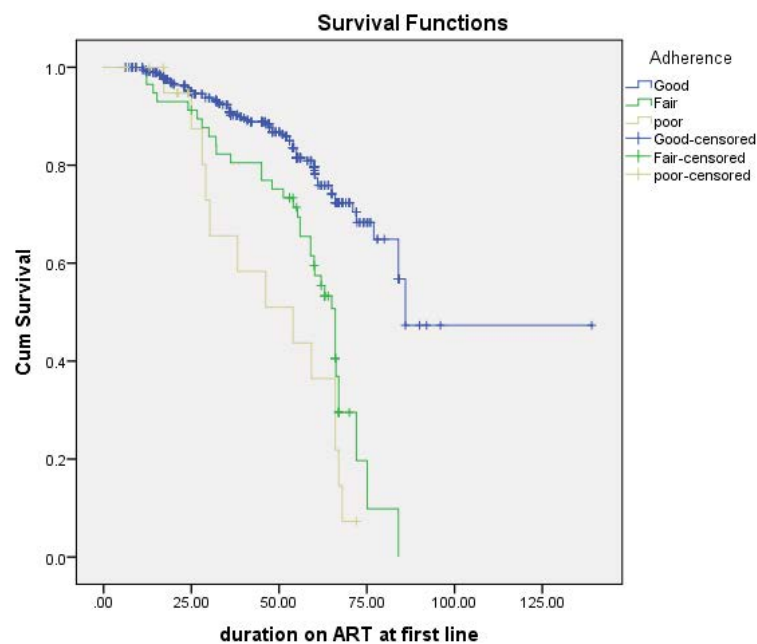


Figure 3: Survival functions of different groups of treatment adherence ART clients in Zewditu Memorial Hospital in Addis Ababa, January 2011-December 2016.

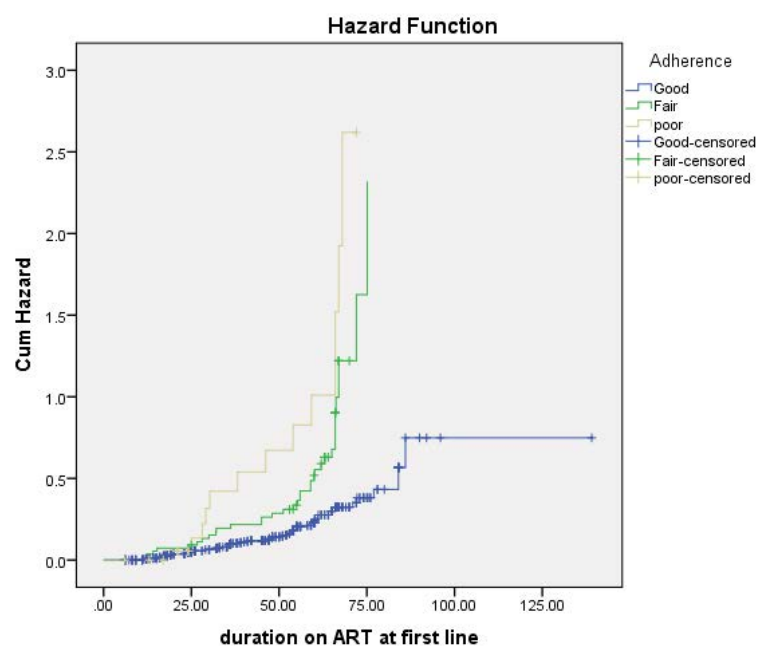


Figure 4: Hazard risk of different groups of treatment adherence of ART clients in Zewditu Memorial Hospital in Addis Ababa, January 2011-December 2016.

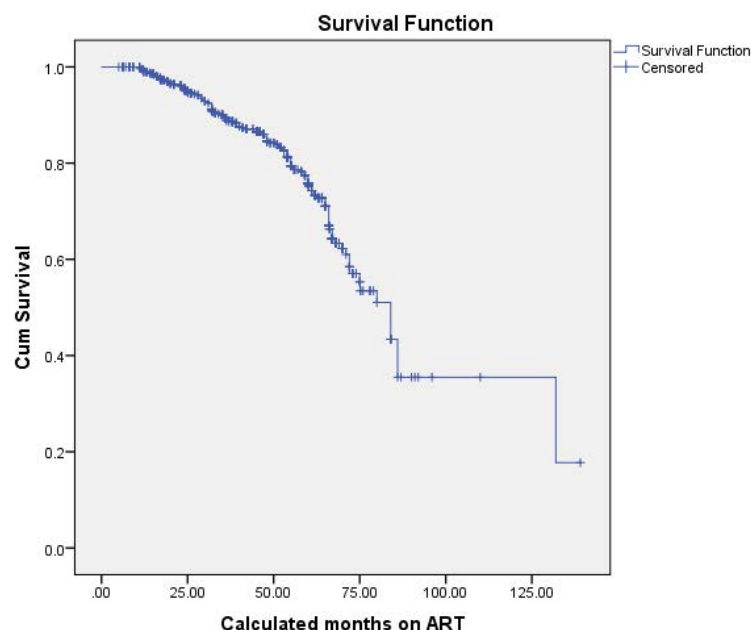


Figure 5: Survival functions of ART clients from six months of therapy to treatment failure in Zewditu Memorial Hospital in Addis Ababa, January 2011-December 2016

Disclosure, any opportunistic infection except TB, Adherence, CD4 count at baseline (cells/mm³) and, had significant relationship with treatment failure as predictors.

Patients who had CD4 count (0-49 cells/mm³) at baseline were 2.67 times more likely to have treatment failure than patients with CD4 count (350-999 cells/mm³) at 95% CI (AHR: 2.67; 95% CI (1.297-5.515)).

ART clients who had not disclosed their HIV status to any one had more likely to develop risk of treatment failure as compared with ART customers who disclosed their status (AHR: 1.49; 95% CI (1.172-1.900)).

Patients who have any opportunistic infection except TB, have risk of treatment failure as compared with no any opportunistic infection at baseline (AHR: 0.642; 95% CI (0.472-0.875)).

Forty eight percent (48%) of the treatment failure were detected patient who were found WHO stage 3 as compared to patients who were found WHO stage 1 (AHR: 0.52; 95% CI (0.294-0.954)). Similarly 48% of treatment failures was emanated from patients with fair adherence to the treatment as compared to Good treatment adherence (AHR: 0.52; (0.351-0.774) (Table 6).

Discussion

This study was designed to assess the incidence and predictors of ART treatment failure in Zewditu Memorial Hospital, Addis Ababa, Ethiopia from January 2011-December 2016.

The overall Incidence of treatment failure in the current study is 4.91 cases per 1000 person months of follow up. This is by far lower than the finding of another study conducted in private health facilities in Addis Ababa. This could be due to variation in the service quality including monitoring HIV Viral load is often not performed, the assays are costly and require sophisticated, expensive laboratory equipment and trained technicians private health facilities quality [18,21,22]. The incidence of immunological, virological and clinical failure

in this study is 2.1, 0.24 and 0.13 per 100 person years of follow-up respectively. As the sensitivity and specificity of immunologic and clinical failures were discussed to be low despite these limitations, in recent year the importance of HIV viral load testing is increasingly recognized; implying the relevance of diagnosing failure using viral load determination technique to obtain better yield of patients' status. Thus the assessment of progress in clinical condition has to be further accompanied by viral load tests to confirm true treatment failure and to take optimal decision of switching and avoiding misclassification [23]. However, viral load determination is not well accessible in resource meager settings like Ethiopia. Likewise, only 11 patients with immunologic failure (57.9%) and 1 clinical (5.3%) were further tested for viral load. Contrasting the findings from a study conducted in Kenya [24], where the clinical failure exceeded the virological and immunological failures, the results from this study showed that the treatment failure as defined by immunological criteria was high (15%); followed by the clinical failure (4.4%) and by virological failure (1.8%).

The hazard of developing treatment failure among patients age were ≥ 50 years was higher compared to age 18-24 years this is in contrast to the study conducted Myanmar [25]. This may be due to poor adherence, the differences in the medical attention given to the patients with advanced age.

Patients who had CD4 count greater than 50 cells/mm³ and weight greater than 50 Kg at baseline the hazard of treatment failure is 16.2% and 21.6%, respectively this is aligned with study conducted in Kenya [26].

The mean survival time (the expected time to event) in current study is 50.20 months however median survival time was similar to the 53.54 months study conducted in Addis Ababa [18]; the difference may be the health care practices and care that given matters.

By conducting Multivariate Cox analysis five significant predictors of treatment failure obtained. Among the predictors like opportunistic infection, adherence, WHO stage at baseline, CD4 count in cells/mm³ at baseline and disclosure status were statistically significant.

Covariate	Treatment failure (%)	Free of treatment failure (%)	Crude hazard risk (95% CI)	Adjusted hazard risk (95% CI)
Age				
18-24	0	12 (2.4)	1	
25-49	72 (76.6)	377 (75.2)	0.955 (0.537-1.699)	1.730 (0.945-3.168)
>=50	22 (23.4)	112 (22.4)	0.537 (0.300-0.997)	1.279 (1.014-1.613)**
Education				
Not educated	20 (21.5)	47 (9.5)	0.528 (0.354-0.787)*	1.171 (0.825-1.663)
primary	40 (43.0)	178 (35.8)	0.611 (0.455-0.821)*	1.429 (1.010-2.022)**
Secondary	30 (32.3)	211 (42.5)	0.725 (0.544-0.966)*	1.967 (1.308-2.958)**
tertiary	3 (3.2)	61 (12.2)	1	
Unemployed	34 (34.0)	163 (34.6)	1.583 (1.096-2.287)*	1.575 (1.096-2.293)**
Opportunistic infection (OI)				
None	65 (52.8)	400 (87.9)	1	1
Any OI except TB	37 (30.1)	45 (9.9)	1.720 (0.968-3.056)*	0.642 (0.472-0.875)**
TB (all types)	21 (17.1)	10 (2.2)	1.048 (0.555-1.979)	0.604 (0.340-1.073)
Adherence				
Good	75 (61)	409 (93.0)	1	
Fair	35 (28.5)	22 (5.0)	0.406 (0.245-0.600)*	0.522 (0.351-0.774)**
Poor	13 (10.3)	9 (2.0)	0.541 (0.279-1.047)	
WHO stage at baseline				
1	17 (13.3)	326 (70.7)	1	
2	34 (26.6)	57 (12.4)	0.088 (0.046-0.168)*	0.085 (0.044-0.166)
3	58 (45.3)	60 (13.0)	0.544 (0.309-0.996)*	0.529 (0.294-0.954)**
4	19 (14.6)	18 (3.9)	0.776 (0.461-1.308)	0.730 (0.423-1.260)
Baseline TB				
Yes	64 (50.8)	88 (19.3)	1	
No	62 (49.2)	369 (80.7)	0.386 (0.272-.549)	
CD4 count at baseline (cells/mm³)				
0-49	40 (31.2)	43 (9.2)	2.879 (1.399-5.924)*	2.673 (1.297-5.515)**
50-99	42 (32.8)	77 (16.5)	1.531 (0.743-3.154)	1.223 (0.592-2.529)
100-199	20 (15.6)	119 (25.5)	0.816 (0.371-1.795)	0.971 (0.439-2.144)
200-349	17 (13.3)	185 (39.6)	0.369 (0.164-0.829)*	0.393 (0.171-0.901)**
350-999	9 (7.0)	43 (9.2)	1	
Disclosure				
Not Disclosure	84 (67.2)	104 (23.3)	1.289 (1.040-1.598)	1.492 (1.172-1.900)**
Disclosure	41 (32.8)	343 (76.7)	1	

** indicates p<0.05

Table 6: Cox-regression analysis showing predictors of ART treatment failures in Zewditu Memorial Hospital from January 2011 to December 2016.

In the current study, WHO stage 3 at the base was found to increase the hazard risk of treatment failure. This is similar with studies conducted in Ethiopia and Mozambique [18,23].

As for the disclosure status, patients who do not disclose their HIV status were more likely to have treatment failure than those who disclose. This is in agreement with the findings of a study conducted at St. Luke and Tulu Bolo Hospitals, South West Shoa Zone, Oromia [18,27]. However, it is dissimilar with the findings from a study in Tanzania [23]. This may be explained by differences in perceived and enacted stigma and discriminatory attitudes between the two settings.

Limitation of the Current Study

Lack of completeness of independent variables might have affected the findings. In addition to this some other important behavioral and background data like educational, disclosure, individual income were not captured in the ART registers and/or follow up charts and electronic databases.

Conclusion

The treatment failure incidence rate in Zewditu Memorial hospital was considerable. The independent predictors of treatment failure are adherence, WHO stage 3 at baseline, CD4 count in cells/mm³ at baseline and disclosure status. Early Antiretroviral treatment failure detection is one of critical key improvement area of the health care providers with close follow up of ART clients and identifying the predictor factors of failure.

Recommendation

Based on the findings obtained, the following recommendations were put forward in the study area.

1. To solve treatment failure can be minimized by routinely following the patients viral load all HIV patients however; those patients were found the potential predictors of treatment failure including low CD4 count, WHO stage 3, opportunistic infection and not disclosure.

2. The clinicians should follow treatment failures early using the gold standard, viral load test, before and after switching second line generation.
3. Finally the ART treatment failure incidence rate should be researched in all other hospitals.

Ethics Approval and Consent to Participant

Ethical clearance was obtained from Addis Ababa public health research and emergency management core process Ethics and Research Committee and permission were obtained from Zewditu Memorial hospital where data is going to be collected.

Availability of Data and Material

The data sets during and/or analyzed during the current study available from the corresponding author on reasonable request.

Authors' Contributions

Chalachew sisay, Alemayehu Bekele conceived and designed the study and collected data, performed analysis, interpretation of data and also critically reviewed of this manuscript. Abay Sisay, Hana Mekonen, Kumera Terfa, Daniel Melese and Boja Dufera support data collection, perform analysis, interpretation of data and also critically reviewed of this manuscript.

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