

Effect of Universal Test and Treat Strategy on Treatment Outcomes and Patient Survival Among HIV Patients in Addis Ababa, Ethiopia: A Retrospective Cohort Study

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Abstract

Background

In 2013 world health organization revised the antiretroviral therapy treatment initiation protocol which became under practice since 2016 in Ethiopia from CD4 cell count < 500 mg/dl to “Universal test and treat” approach, following models suggest that moving to rapid antiretroviral therapy initiation regardless of CD4 cell count is cost-effective in wide variety of settings. This study aimed to assess the effect of universal test and treat strategy on treatment outcomes and patient survival among HIV patients.

Methods

Institutional based retrospective cohort study was conducted on 527 patients on antiretroviral therapy at selected public hospitals in Addis Ababa, Ethiopia from January to February 2024. Data were collected using a standardized checklist on randomly selected patients’ treatment records recorded over a period of ten years (2013–2023). Systematic sampling technique was employed to collect the data. The collected data then cleaned, edited and entered into Epi info version 7 and analysed using SPSS version 26. Cox model was built to estimate survival and predictors.

Result

From all participants, 468 (88.8%) were alive on antiretroviral therapy at the end of the follow-up. Nine (1.7%) participants were dropped out, 50 (9.5%) participants died, 14 (5.3%) from exposed and 36 (13.7%) from the unexposed group. Patients were followed for total of 2594.6 person-year of observation with the overall incidence density rate of death in the cohort 0.02 person-year which was equal to 2 people per 100 peoples. Participants enrolled in the universal test and treat strategy survived longer than participants enrolled in the CD4 based treatment program (log rank X2 test = 3.91, p value = 0.048). Factors associated with patient mortality among exposed and unexposed include; baseline CD4 count, baseline world health organization stage, baseline weight, drug form type, drug adherence, opportunistic infections prophylaxis, new opportunistic infections and treatment failure were identified as independent factors associated with mortality with p-value of < 0.05.

Conclusion

Mortality was reduced and patients survived longer after universal test and treat strategy implementation. Therefore, application of universal test and treat strategy should be strengthened in all public and private health facilities throughout the country.

BACKGROUND

Human immunodeficiency virus (HIV) infection remains the leading cause of morbidity and mortality throughout the world. Since the start of the epidemic, around 76.1 million people have become infected and 35.0 million people have died from AIDS (acquired immunodeficiency syndrome) related illnesses (1). The global HIV epidemic has had the greatest impact on Sub-Saharan Africa (SSA). An estimated 67% of the 38.4 million people living with HIV (PLWH) globally in 2021 were from SSA. SSA was responsible for 670,000 of the 1.5 million new infections and 280,000 of the 650,000 AIDS-related deaths reported globally in 2021 (2).

As one of the sub-Saharan countries, the case in Ethiopia is not different. It is characterized by a low-intensity, mixed epidemic and self-sustaining transmission with a prevalence of 1.1%. Universal test and treat strategy (UTT) is a program which the population at risk is screened for HIV infection and diagnosed HIV infected individuals receive early treatment, aiming to eliminate HIV as it reduces the rate of spreading the virus to other people. This strategy is particularly concerned for public interest (3). The very first test-and-treat model by Granich and his colleagues has excellently resulted in conceptualizing a landmark of global health policy (4), inducing the world to be motivated to universally or at least radically screen HIV infected individuals in the population and promote their early treatment, not only for their own suppression from progression of HIV infection but also for the public benefit (3).

This evidence for the effectiveness of treatment for prevention has led to new world health organization (WHO) guidelines for a 'test and treat' strategy – increasing testing and treatment coverage by initiating all people diagnosed with HIV on antiretroviral therapy (ART) immediately regardless of their CD4 (Cluster of differentiation 4) count or viral load, thereby decreasing community viral load and reducing the rate of new HIV infections.

Although the health care system has accepted the public health benefit of test and treat strategy for the prevention of new transmission, assuring the individual level benefit of the program in terms of disease progression, long term outcome, drug adherence and resistance development, morbidity, mortality and other progress indicator is very important. It seems mean survival times in early initiation of the treatment is higher than the one who initiated later or differed until the standard CD4 count is achieved. The different treatment outcomes have been reported differently in different studies; mostly stated as higher survival time, higher resistance, higher immune reconstitution syndrome rate, lower mortality and longer survival (5, 6, 7).

Despite the implementation of WHO's recommendation, evidence on the clinical effect of "test and treat strategy" is scarce (8). Also, the optimal timing for initiating ART has not yet concluded. Recent two randomized studies showed that ART initiated immediately after HIV diagnosis and irrespective of the CD4 + T cell count leads to a significant reduction of morbidity and mortality. Several studies assessing ART during acute HIV infection show beneficial effects on laboratory progression markers. Potential positive effects of initiation of ART during acute HIV infection include reduction of viremia, lower viral set point, lower probability of transmission and a reduced number of infected cells which might allow for the preservation of HIV-specific immune responses and preserving the ability to control viral replication.

Furthermore, it is fundamental to avoid transmission in this critical period of high viremia and thus, high infectivity (9, 10, 11, 12).

UTT program or early initiation of treatment can also improve the treatment outcome of HIV infected patients. Rapid ART could improve uptake of the therapy by reducing the number of PLWH lost to follow-up in the period of linkage from HIV diagnosis to ART commencement (13, 14).

Generally, the effect of UTT is particularly beneficial for public level programs. However, its real effect on the treatment outcome and patient survival was not evaluated well. Therefore, this study was aimed to assess the effect of the UTT program on treatment outcome and patient survival, by recruiting a cohort of ART users in the new UTT approach and the previous (differed treatment/CD4 based) programs at selected public health institutions in Addis Ababa, Ethiopia. Factors associated with patient mortality among exposed and unexposed HIV patients were also assessed. The results of this study will have implications for policy makers, health care providers and other concerned bodies to improve or strengthen policies related to UTT program. The finding of this study will also be used as a baseline for other studies.

METHODS

Study Area and Period

This study was conducted in Addis Ababa, Ethiopia, the capital city of the country. It was chosen because Addis Ababa has the highest HIV prevalence in the country and proportional to population, and more ART attendees were found in this area than anywhere else in the country. The study was conducted on HIV-positive clients who were on ART in selected governmental hospitals of Addis Ababa, i.e. Yekatit 12 hospital medical college, Minilik compressive specialized hospital and Tikur Anbesa compressive specialized hospital from January to February 2024. The study was approved by the Research Review Committee of Yekatit 12 Hospital Medical College Research and Publication Office (Ethics approval protocol numbers for each hospital: Minilik 249/23, Black lion 250/23, Yekatit 263/23). The approval from Yekatit 12 hospital medical college covered all three participating institutions. All methods were performed in accordance with the relevant guidelines and regulations. Given the retrospective cohort design utilizing de-identified medical records, the requirement for individual informed consent was waived by the Research Review Committee of Yekatit 12 Hospital Medical College Research and Publication Office.

Study Design

Institutional based retrospective cohort study was conducted at selected hospitals in Addis Ababa.

Study Population

All adult HIV-positive people who were enrolled in HIV care and treatment service at Yekatit 12 hospital medical college, Minilik compressive specialized hospital and Tikur Anbesa compressive specialized hospital comprised the source population. Selected HIV-positive people who started ART in Yekatit 12 hospital medical college, Minilik compressive specialized hospital and Tikur Anbesa compressive specialized hospital constituted the study population.

The study population consisted of two groups: a group of HIV-Positive clients who were not exposed to the test and treat strategy (unexposed), specifically clients who started ART before the implementation of the test and treat strategy (between January 2013 and July 2016), and a group of HIV-positive clients exposed to the test and treat strategy (exposed), specifically clients who started ART between August 2016 and February 2023.

Inclusion criteria

All ART users in the selected three hospitals over a period of 10 years (from 2013 to 2023) who were enrolled or on ART at least for 6 months. A 10-year period was analysed, encompassing several years both prior to and following the initiation of UTT since UTT was initiated in Ethiopia by the year 2016.

Exclusion criteria

All ART users before January 2013 and After February 2023 were excluded from the study. Incomplete records for the basic outcome variables were excluded.

Sample size determination

To determine the appropriate sample size for this study by considering a variety of factors that are significantly related to the outcome variable; under the Cox proportional hazards model/log rank test considering the following assumptions: hazard ratio of 0.77, a 95% level of confidence, power of 80%, and 0.05 significance level (11).

The sample size determination formula proposed by Schoenfeld (22) is given by

$$n = (Z_{\alpha} + Z_{\beta})^2 / (((\log(RH))^2 q_0 q_1)) = 7.8489 / 0.0164 = 479$$

The initial sample size was calculated to be 479, by adding 10% for incompleteness, the final sample size was 527.

Sampling technique

Three hospitals among 12 hospitals which have been utilizing UTT strategy in Addis Ababa, were selected by lottery method. The number of study units was selected based on the population in

proportion to the sample size of the total ART users in the hospitals. Systematic sampling technique was used to select patient records. The sampling interval (k) of patient records in each hospital was determined by dividing the total number of patient records (N) to the allocated sample size (n). Then the next patient record was selected every k^{th} interval. In the cases where the selected patient records were incomplete, patient records next to the incomplete ones were considered.

For instance, $N = 837$ ART users and the minimum sample size being $n = 527$ an interval of $K = N/n = 1.6$ the first study record was selected by using lottery method and then every 2 units were taken till the sample size sufficed.

The sample was allocated proportionally for the three selected hospitals and records were selected randomly. The sample was divided into exposed (264) and unexposed (263) categories in selected hospitals.

Study Variables

Dependent variable

Effect of Universal test and treat strategy on HIV treatment

Independent variables

Socio- demographic characteristics: Age, sex, educational status, residence, occupation, marital status.

Clinical condition of the patient: baseline CD4 count, new OIs, comorbidities

Enrolment status: before UTT, after UTT

Treatment regimen, side effect, complication, treatment failure etc.

Data Collection Tools/Instruments

Data were collected using a structured checklist for records review developed from the registers and follow up charts. Since the registers were prepared in English, the checklist was also prepared in English. The sources of data for this study were the Pre-ART register, the ART register and the patients' ART follow up and medical charts. In those registers and follow up charts, clients' socio demographic, clinical and laboratory information, treatments being provided, the follow up status of each client were recorded.

Data Collection Procedure

Data were collected from client charts using a structured checklist for records review developed from the registers and follow up charts. Three data collectors experienced in data collection and one supervisor who had a bachelor degree in health science and working in ART were recruited for data collection and assigned other than their current working area. To maintain the quality of data,

appropriate training was given to data collectors about the check list in order to get common understanding and make aware of the context of each question. Before the actual data collection, the check list was pretested on 5% of sample size in one of non-selected hospitals in Addis Ababa, and the data in the pretest were not included in the actual data. Daily supervision was made at each facility throughout the data collection period. Selected client charts with incomplete information were substituted by charts immediately next to them.

Data Processing and Analysis

Data were cleaned, coded and entered into Epi-info version 7 and exported to SPSS version 26, then exploratory data analysis were carried out to check the levels of missing values, presence of influential outliers, multi-collinearity, normality and proportionality of hazards over time. Bivariate analysis was done to identify associations between dependent and independent variables. Hazard ratio with 95% CI and P-value were used to assess the strength of association and statistical significance. Kaplan Meier survival curve together with log rank test were fit to test for the presence of difference in incidence of death, progression of disease, change in CD4 cell count, immunological/clinical failure and other outcomes among the comparison groups (test and treat vs differed treatment). Cox-regression analysis was carried out to identify independent predictors of death in both groups. Variables significant at $P < 0.25$ level in the bivariate analysis were included in the final multivariate regression analysis, to identify independent predictors of some relevant outcomes' treatment like failure and mortality. The forward stepwise regression method was applied and level of significance was used at p-value less than 0.05. Model fitness checked by graphing residual plots with Cox-Snell residual plot. Goodness of fit of the final model was checked by Nelson Aalen cumulative hazard function against Cox Snell residual. Association was summarized by using adjusted hazard ratio (AHR) and statistical significance tested with 95% CI.

RESULTS

The study consists of two groups: Half of them (263) were a group of HIV positive clients who started ART based on eligibility criteria between January 2013 and July 2016, before the commencement of the test and treat strategy (unexposed), and the rest half (264) were a group of HIV-positive clients exposed to the test and treat strategy (exposed), specifically clients who started ART between August 2016 and February 2023.

Socio demographic Characteristics

The mean age of the study participants was 42.5 (median 41 years) with a standard deviation of 11.45 years. Among all the studied participants, 93 (35.2%) exposed participants were between 25–34 years in age, followed by 90 (34.1%) between age 35–44 years. On the other hand, 83 (31.6%) of unexposed participants were between age 35–44 years, followed by 72 (27.4%) between age 45–54 years. Slightly greater than half, 146 (55.3%) exposed and 134 (51%) unexposed were female participants. Almost all, 260 (98.5%) exposed and 255 (97%) unexposed study participants were urban dwellers. Majority, 130 (49.2%) exposed and 205 (77.9%) unexposed study participants were married. Again, majority of both

136 (51.5%) exposed and 119 (45.2%) unexposed participants attended secondary school, and more than half, 162 (61.4%) exposed and 177 (67.3%) unexposed were unemployed (Table 1).

Table 1
Socio demographic characteristics of participants, Addis Ababa, Ethiopia,
2024.

Variables	Exposed (#264)		Unexposed (#263)	
	Frequency	Percent	Frequency	Percent
Age				
20–24 years	6	2.3	5	1.9
25–34 years	93	35.2	41	15.6
35–44 years	90	34.1	83	31.6
45–54 years	54	20.5	72	27.4
55–64 years	20	7.6	38	14.4
65–72 years	1	0.4	24	9.1
Sex				
Female	146	55.3	134	51.0
Male	118	44.7	129	49.0
Residence				
Urban	260	98.5	255	97.0
Rural	4	1.5	8	3.0
Marital status				
Single	65	24.6	20	7.6
Married	130	49.2	205	77.9
Divorced	43	16.3	18	6.8
Widowed	26	9.8	20	7.6
Educational status				
No formal education	8	3.0	5	1.9
Primary	66	25.0	42	16.0
Secondary	136	51.5	119	45.2
Tertiary	54	20.5	97	36.9
Employment				
Employed	102	38.6	86	32.7

Variables	Exposed (#264)		Unexposed (#263)	
	Frequency	Percent	Frequency	Percent
Unemployed	162	61.4	177	67.3

The table illustrates a socio demographic characteristic of both exposed and unexposed PLWH for UTT.

Baseline Characteristics of Study Participants

The baseline CD4 count of majority of both exposed 177 (67%) and unexposed 199 (75.7%) study participants were between 200–350 cells/mm³. With regard to baseline opportunistic infections, 139 (52.7%) of exposed participants did not have OIs whereas 175 (66.5%) unexposed participants did. The vast majority of exposed 246 (93.2%) and majority of unexposed 192 (73%) were at stage I of HIV at the initial baseline assessment (Table 2).

Table 2
Baseline characteristics of study participants, Addis Ababa, Ethiopia, 2024.

Variables	Exposed (#264)		Unexposed (#263)	
	Frequency	Percent	Frequency	Percent
Baseline CD4 count				
< 200 cells/mm ³	10	3.8	51	19.4
200–350 cells/mm ³	177	67.0	199	75.7
350–500 cells/mm ³	77	29.2	13	4.9
Baseline functional status				
Working	252	95.5	235	89.4
Ambulatory	8	3.0	10	3.8
Bedridden	4	1.5	18	6.8
Baseline opportunistic infection				
Yes	125	47.3	175	66.5
No	139	52.7	88	33.5
Baseline OIs treatment given?				
Yes	125	47.3	175	66.5
No	139	52.7	88	33.5
Baseline WHO stage				
I	246	93.2	192	73.0
II	9	3.4	33	12.5
III	7	2.7	22	8.4
IV	2	0.8	16	6.1
Baseline weight				
< 50 kg	49	18.6	79	30.0
> 50 kg	215	81.4	184	70.0

The table illustrates a baseline information of both exposed and unexposed PLWH for UTT before they got ART.

Antiretroviral Therapy of Study Participants

From the total participants, all 264 (100%) exposed and the majority 201 (76.4%) unexposed were already started ART because of test and treat strategy and immunologic condition respectively. Majority, 180 (68.2%) of exposed participants were on 1j, whereas, almost all 257 (97.7%) unexposed participants were on 1e. Similarly, majority of both exposed 248 (93.9%) and unexposed 222 (84.4%) participants had good adherence of ART drugs. Fifteen (5.7%) of exposed and 56 (21.3%) of unexposed participants treatment were failed because of clinical, immunologic and virologic reasons each 5 (1.9%) in exposed participants and most importantly immunologic 30 (11.4%) reason in unexposed participants. Thirteen (4.9%) in exposed and 49 (18.6%) in unexposed groups of participants switched to second line treatment. (Table 3).

Table 3
Antiretroviral therapy of study participants, Addis Ababa, Ethiopia, 2024.

Variables	Exposed (#264)		Unexposed (#263)	
	Frequency	Percent	Frequency	Percent
Reasons for initiating ART				
WHO stage			1	0.4
Immunologic			201	76.4
Virologic			13	4.9
Both WHO stage and immunologic			48	18.3
Test and treat	264	100		
ART regimen				
1e	84	31.8	257	97.7
1j	180	68.2		
Other			6	2.3
Drug form type				
Fixed dose combination	228	86.4	185	70.3
Separate	11	4.2	27	10.3
Both used previously	25	9.5	51	19.4
Drug adherence				
Good	248	93.9	222	84.4
Fair	13	4.9	27	10.3
Poor	3	1.1	14	5.3
TB-screen				
Positive	10	3.8	198	75.3
Negative	254	96.2	65	24.7
OIs prophylaxis				
Cotrimoxazole	106	40.2	207	78.7
INH	13	4.9	23	8.7
Citri and IHN	138	52.3	31	11.8
None	7	2.7	2	0.8

Variables	Exposed (#264)		Unexposed (#263)	
	Frequency	Percent	Frequency	Percent
New OIs				
Yes	16	6.1	44	16.7
No	248	93.9	219	83.3
Treatment failure				
Yes	15	5.7	56	21.3
No	249	94.3	207	78.7
Reasons for treatment failure				
Clinical	5	1.9	21	8.0
Immunologic	5	1.9	30	11.4
Virologic	5	1.9	5	1.9
Not failed	249	94.3	207	78.7
Switch to second line				
Yes	13	4.9	49	18.6
No	251	95.1	214	81.4
Other comorbidities				
Yes	29	11.0	47	17.9
No	235	89.0	216	82.1

The table illustrates the antiretroviral therapy of both exposed and unexposed PLWH for UTT.

Treatment Outcome

From the total participants, 468 (88.8%) were active (alive on ART) at the end of the follow-up (Censored). Nine (1.7%) participants were dropped out, 3 (1.1%) from exposed and 6 (2.3%) from unexposed group. Totally, 50 (9.5%) participants died (Event), 14 (5.3%) from exposed and 36 (13.7%) from the unexposed group (Fig. 1).

Patient Survival Analysis

Five hundred twenty-seven patients were followed for different periods of time with a total of 2594.6 person-year of observation with the overall incidence density rate (IDR) of death in the cohort was 0.02 per person-year which was equal to 2 people per 100 peoples within 1 year of observation. It was

significantly different for the two comparison groups, 0.03 person-year in unexposed group that was equal to 3 people per 100 peoples, and 0.01 in exposed group that was 1 people per 100 peoples. The cumulative probability of survival at the end of 1st, 2nd, 3rd, and 4th years of enrolment to treatment for the group of clients who started ART before the implementation of the universal test and treat strategy (unexposed group) was 98.1%, 96.2%, 90.1% and 89.4% respectively, and for the group of clients who started ART based on test and treat strategy (exposed group) at the end of 1st, 2nd, 3rd, 4th, 5th and 6th years of enrolment was 100%, 100%, 97%, 94.7%, 94.7% and 94.7% respectively, with significant difference between the two groups.

The log rank test and Kaplan–Meier survival curve indicated that a survival difference between the two groups is significant. However, the median survival time was undetermined. Because the largest observed analysis time was censored; the survivor function does not go to zero. The relative risk of death among unexposed groups was about 2.8 times higher than their counterparts (OR = 2.83: 95% CI: 1.49, 5.39). Participants enrolled in the UTT program survived longer than participants enrolled in the CD4 based treatment program (log rank X2 test = 3.91, p value = 0.048) (Fig. 2)

Factors Associated with Mortality among Study Participants

Marital status, baseline CD4 count, baseline functional status, baseline OIs, baseline WHO stage, baseline weight, drug form type, drug adherence, OIs prophylaxis, new OIs, treatment failure and other comorbidities were the candidate variables selected for multivariable cox regression analysis with p-value of ≤ 0.25 .

In the multivariable cox regression model, after controlling for the effect of other confounding factors, eight variables: baseline CD4 count, baseline WHO stage (Stage III and IV), baseline weight (Being less than 50 kg), drug form type (Separate), drug adherence (Poor), OIs prophylaxis (Cotrimoxazole or INH), new OIs and treatment failure were identified as independent factors significantly associated with mortality with p-value of < 0.05 .

Study participants with baseline CD4 count < 200 cells/mm³ were 17 times more likely to die than those with baseline CD4 count 350–500 cells/mm³ (AHR = 17.10: 95% CI: 4.11, 78.66). Similarly, participants with baseline CD4 200–350 cells/mm³ were 7 times more likely to die than those with baseline CD4 count 350–500 cells/mm³ (AHR = 7.30: 95% CI: 3.42, 15.60). Study participants with baseline WHO stage III were 4 times more likely to die than those with WHO stage I (AHR = 4.72: 95% CI: 1.14, 19.64). Likewise, participants with baseline WHO stage IV were 4 times more likely to die than those with WHO stage I (AHR = 4.90: 95% CI: 1.12, 21.38). Baseline weight among participants with < 50 kg were almost 2 times more likely to die than their counterparts (AHR = 1.84: 95% CI: 1.00, 3.37). With regard to drug form type, participants who used separate form were 6 times more likely to die than those who used fixed dose combination (AHR = 6.15: 95% CI: 2.30, 16.43). Participants with poor drug adherence were nearly 7 times more likely to die than those with good adherence (AHR = 6.64: 95% CI: 1.26, 35.01). The OIs

prophylaxis among study participants who took cotrimoxazole were nearly 26 times less likely to die than those who took nothing (AHR = 25.77: 95% CI: 4.43,149.87). Likewise, participants who took INH were 22 times less likely to die than those who took nothing (AHR = 22.08: 95% CI: 3.24,150.54). Participants with new OIs were 3 times more likely to die than their counterparts (AHR = 3.21: 95% CI: 1.11,9.29). Study participants with treatment failure were 3 times more likely to die than their counterparts (AHR = 3.13: 95% CI: 1.15,8.47) (Table 4).

Table 4
Factors associated with mortality among participants, Addis Ababa, Ethiopia 2024

Variables	Exposed (#264)		Unexposed (#263)		CHR (95%CI)	AHR (95%CI)
	No	%	No	%		
Marital status						
Single	65	24.6	20	7.6	1	
Married	130	49.2	205	77.9	5.13(2.97,8.86)**	
Divorced	43	16.3	18	6.8	1.36(0.65,2.86)	
Widowed	26	9.8	20	7.6	2.50(1.16,5.39)*	
Baseline CD4 count						
< 200 cells/mm ³	10	3.8	51	19.4	30.21(12.32,74.09)**	17.10(4.11,78.66)**
200–350 cells/mm ³	177	67.0	199	75.7	6.66(3.58,12.40)**	7.30(3.42,15.60)**
350–500 cells/mm ³	77	29.2	13	4.9	1	1
Baseline functional status						
Working	252	95.5	235	89.4	1	
Ambulatory	8	3.0	10	3.8	1.34(0.52,3.45)	
Bedridden	4	1.5	18	6.8	4.83(1.61,14.47)*	
Baseline opportunistic infection						
Yes	125	47.3	175	66.5	2.21(1.56,3.15)**	
No	139	52.7	88	33.5	1	
Baseline WHO stage						
I	242	91.7	180	68.4	1	1
II	10	3.8	21	8.0	2.82(1.30,6.14)*	1.27(0.40,4.04)
III	7	2.7	37	14.1	7.11(3.10,16.31)**	4.72(1.14,19.64)*
IV	5	1.9	25	9.5	6.72(2.53,17.90)**	4.90(1.12,21.38)*
Baseline weight						
< 50 kg	49	18.6	79	30.0	1.88(1.25,2.83)*	1.84(1.00,3.37)*
Note: 1 = Reference category, * significantly associated, ** highly significantly associated						

Variables	Exposed (#264)		Unexposed (#263)		CHR (95%CI)	AHR (95%CI)
	No	%	No	%		
> 50 kg	215	81.4	184	70.0	1	1
Drug form type						
Fixed dose combination	228	86.4	185	70.3	1	1
Separate	11	4.2	27	10.3	3.03(1.46,6.26)*	6.15(2.30,16.43)**
Both used previously	25	9.5	51	19.4	2.51(1.50,4.21)**	1.92(0.96,3.81)
Drug adherence						
Good	248	93.9	222	84.4	1	1
Fair	13	4.9	27	10.3	2.32(1.17,4.61)*	0.83(0.23,2.97)
Poor	3	1.1	14	5.3	5.21(1.48,18.38)*	6.64(1.26,35.01)*
Ols prophylaxis						
Cotrimoxazole	106	40.2	207	78.7	2.28(0.75,6.95)*	25.77(4.43,149.87)**
INH	13	4.9	23	8.7	2.06(0.57,7.46)*	22.08(3.24,150.54)*
Citri and INH	138	52.3	27	10.3	0.13(0.07,0.73)	1.01(0.18,5.61)
None	7	2.7	6	2.3	1	1
New Ols						
Yes	16	6.1	44	16.7	3.11(1.71,5.68)**	3.21(1.11,9.29)*
No	248	93.9	219	83.3	1	1
Treatment failure						
Yes	15	5.7	56	21.3	4.49(2.47,8.17)**	3.13(1.15,8.47)**
No	249	94.3	207	78.7	1	1
Other comorbidities						
Yes	29	11.0	47	17.9	1.76(1.07,2.90)*	
No	235	89.0	216	82.1	1	
Note: 1 = Reference category, * significantly associated, ** highly significantly associated						

DISCUSSION

The treatment outcome of this study revealed that the overall incidence of death was 9.5%, which was in line with the study done in Gurage zone 9.6% (15) and Jinka hospital 10% (16), but slightly higher than the studies done in Nepal 7% (17) and Tigray 7.5% (18). On the other hand, the finding of this study was slightly lower than the study done in Debre-Markos Hospital 13.56% (19). The discrepancy might be due to difference in socio-demographic characteristics of the study participants, study area and study period differences.

The incidence of death among exposed and unexposed patients for UTT, participants who were not exposed to universal test and treat strategy was significantly higher 13.7% than the exposed one 5.3%. This finding was similar with a study done in Gurage zone with the incidence of death in CD4 based treatment and UTT 12.2% and 5.9% respectively (15).

Concerning the effect of UTT program on patient survival among exposed and unexposed HIV patients, in the current study the overall incidence density rate (IDR) of death in the cohort was 0.02 per person-year which was equal to 2 people per 100 peoples within 1 year of observation. The finding of this study was almost similar to a study done in Gurage zone with the overall incidence density rate of death in the cohort was 0.03 per person-year which is equal to 3 people per 100 peoples within 1 year of observation (15).

The cumulative probability of survival at the end of 1st, 2nd, 3rd, and 4th years of enrolment to treatment for the group of clients who started ART before the implementation of the universal test and treat strategy (unexposed group) was 98.1%, 96.2%, 90.1% and 89.4% respectively, and for the group of clients who started ART based on test and treat strategy (exposed group) at the end of 1st, 2nd, 3rd, 4th, 5th and 6th years of enrolment was 100%, 100%, 97%, 94.7%, 94.7% and 94.7% respectively. This finding was almost similar to a study done in Gurage zone with the cumulative probability of survival at the end of 1st, 2nd, 3rd, and 4th years of enrolment to treatment was 98%, 90.2%, 89.2% and 88% respectively (15). The finding was also similar with a study conducted at Debre-Markos Hospital that revealed the survival probability for the total cohort at the end of 3 months was 96%; at the end of 6 months was 92%; at the end of 9 months was 89%; and that of the probability of surviving at the end of follow-up was 88% (19).

On the other hand, the finding of this study is slightly different from a study done in Nepal, the survival probability of HIV patients on ART at 3 months, 6 months, 1 year, 2 years, 5 years and at 8 years were 89.6%, 87.1%, 84.8%, 81.7%, 77.7% and 73.6% respectively (17). The discrepancy might be due to difference in socio-demographic characteristics of the study participants, study area and study period differences.

The relative risk of death among unexposed groups was about 2.8 times higher than their counterparts (OR = 2.83: 95% CI: 1.49,5.39). Participants enrolled in the UTT program survived longer than those enrolled in the CD4 based treatment program (log rank X2 test = 3.91, p value = 0.048). This finding was similar to a study done in Gurage zone that the log rank test and Kaplan–Meier survival curve indicated patients enrolled in the UTT program survived longer than patients enrolled in the differed treatment program (log rank X2 test = 4.1, p value = enrolment) (15).

With regard to factors associated with patient mortality among exposed and unexposed patients, baseline CD4 count (CD4 count < 200 cells/mm³ and CD4 200–350 cells/mm³), baseline WHO stage (Stage III and IV), baseline weight (Being less than 50 kg), drug form type (Separate), drug adherence (Poor), OIs prophylaxis (Cotrimoxazole or INH), new OIs and treatment failure were identified as independent factors significantly associated with mortality with p-value of < 0.05. The finding was similar to a study done in India which indicated that mortality was significantly associated with CD4 count, clinical stage and functional status (20). The finding was also similar to a study done in Gurage zone that base line CD4 count, program of enrolment, development of new OIs and treatment failure were predictors associated with patient mortality (15).

On the other hand, the finding of this study was different from the studies conducted in different areas: in Nepal, ART center, male gender, residence outside the ART district, bedridden, lower bodyweight/kg and treatment not switched to second-line regimen (17), at Jinka Hospital, non-disclosure of HIV status, history of tuberculosis, functional status and substance abuse (16), at Wolaita Sodo University, widowed, history of substance uses and history of IV drug use (21), in Central Zone Tigray, patients with late diagnosis of HIV, rural residence, unemployment, bedridden patients, ambulatory patients and baseline haemoglobin level (18), were factors independently predicted the mortality of patients. The discrepancy might be due to difference in socio-demographic characteristics of the study participants, study area and study period differences.

LIMITATIONS AND RECOMMENDATIONS FOR FUTURE STUDIES

Because the study was retrospective, missing data and incompleteness of information were the concerns of the study. Hence, selection bias may be introduced since the data is obtained from record review. Any systematically selected patient chart with missing data or incomplete information was managed by substituting it with patient chart with complete information immediately next to the missed or incomplete one. Other incidental causes of death could not be ruled out in some cases specially if the patient was not admitted in the hospital because of advanced stage of HIV/AIDS during his/her final life time and if the information of his/her death only obtained from the family after his/her loss of ART follow-up. Facility related factors should be assessed in the future.

CONCLUSIONS

The relative risk of death among unexposed groups for UTT was higher than the exposed one. Participants enrolled in the UTT program survived longer than participants enrolled in the CD4 based treatment program. Variables like baseline CD4 count, baseline WHO stage (Stage III and IV), baseline weight (Being less than 50 kg), drug form type (Separate), drug adherence (Poor), OIs prophylaxis (Cotrimoxazole or INH), new OIs and treatment failure were identified as independent factors significantly associated with mortality with p-value of < 0.05.

The implementation of “Universal Test and Treat strategy” should be strengthened in all public and private health facilities throughout the country. Clients should start ART as early as possible if they are diagnosed as HIV positive. Further studies should be under taken to assess facility related factors that will have an impact on treatment outcomes and patient survival among HIV patients.

Abbreviations

ART: Antiretroviral Therapy, AIDS: Acquired Immune Deficiency Syndrome, AHR: Adjusted Hazard Ratio, CHR: Crud Hazard Ratio, DHS: Demographic and Health Surveys, FHAPCO: Federal HIV/AIDS Prevention and Control Office, HAART: Highly Active Antiretroviral Therapy

HIV: Human Immune Deficiency virus, HIVDR: HIV Drug Resistance, IDR: Incidence Density Rate, PLWHA: People living with HIV/AIDS, PMTCT: Prevention of Mother To Child Transmission of HIV, RCT: Randomized Controlled Trial, UNAIDS: United Nations Program on HIV/AIDS, UNDP: United Nations Development Program, UNICEF: United Nations Children's Fund, UTT: Universal Test and Treat, WHO: World Health Organization

Declarations

Ethics approval and consent to participate:

Ethical approval was obtained from Research Review Committee of Yekatit 12 Hospital Medical College Research and Publication Office: (Ethics approval protocol numbers for each hospital: Minilik 249/23, Black lion 250/23, Yekatit 263/23). The approval from Yekatit 12 hospital medical college covered all three participating institutions. Given the retrospective cohort design utilizing de-identified medical records, the requirement for individual informed consent was waived by the Research Review Committee of Yekatit 12 Hospital Medical College Research and Publication Office.

Consent for publication:

Not applicable

Competing interests:

The authors declare that they have no competing interests.

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Author Contribution

TFL, YMW and AWT developed the study objective, data management and analysis. TFL wrote the first draft of the manuscript. Additionally, TFL contributed to the study design, interpreted the results, and drafted and revised the manuscript. The authors have read and approved the final manuscript.

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Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figures

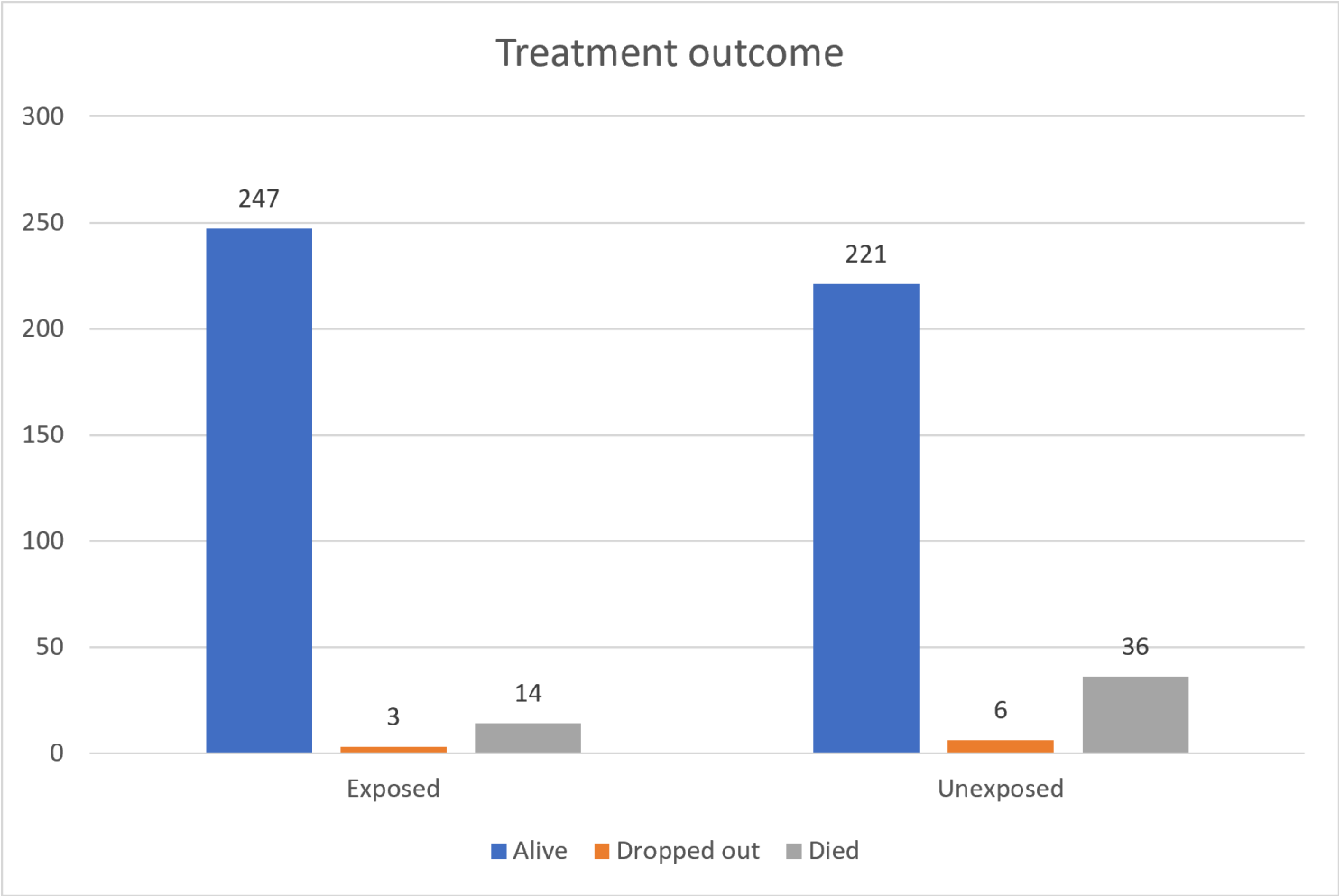


Figure 1

Treatment outcome of study participants, Addis Ababa, Ethiopia, 2024. Most of the participants in both categories remain alive, some died and a very few of them in both categories dropped out from the therapy.

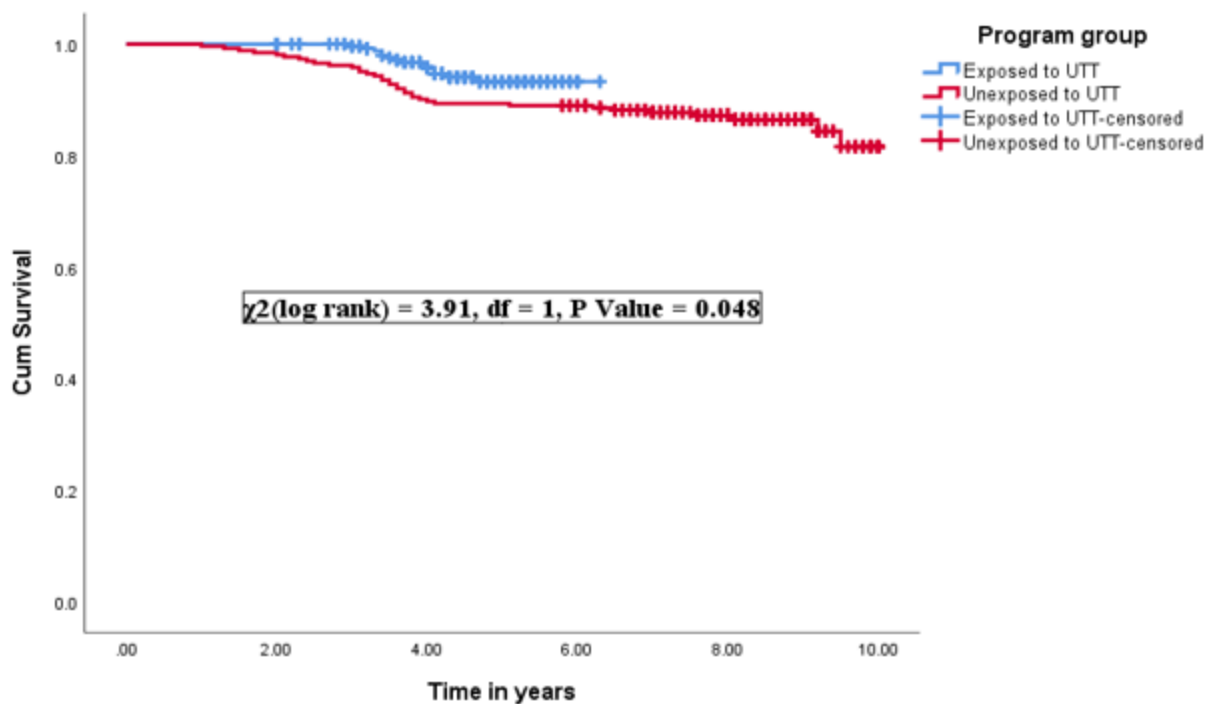


Figure 2

Kaplan–Meier survival estimate of study participants, Addis Ababa, Ethiopia, 2024.

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