

Asian Pacific Journal of Tropical Disease

journal homepage: <http://www.apjtc.com>Infectious disease research <https://doi.org/10.12980/apjtd.7.2017D6-295> ©2017 by the Asian Pacific Journal of Tropical Disease. All rights reserved.

Mortality predictors of HIV-infected patients on antiretroviral therapy in Debre Tabor General Hospital and Woreta Health Center, South Gondar Zone, Northwest Ethiopia

Mekonnen Assefa Ahunie^{1*}, Endris Assen Ebrahim²¹Department of Social and Public Health, College of Health Sciences, Debre Tabor University, Debre Tabor, Ethiopia²Department of Statistics, Faculty of Natural and Computational Sciences, Debre Tabor University, Debre Tabor, Ethiopia

ARTICLE INFO

Article history:

Received 29 Aug 2016

Received in revised form 11 Oct, 2nd revised form 24 Oct, 3rd revised form 26 Oct 2016

Accepted 15 Nov 2016

Available online 21 Dec 2016

Keywords:

HIV

Antiretroviral therapy

Mortality

Antiretroviral adherence

ABSTRACT

Objective: To investigate the mortality predictors of HIV-infected individuals who were receiving antiretroviral treatment.**Methods:** Data were extracted from medical records of 698 antiretroviral therapy (ART) users enrolled at Debre Tabor General Hospital and Woreta Health Center from January 2005 to June 2014 and sociodemographic, clinical and ART-related data were collected. Mortality was compared by using time-to-event Kaplan-Meier method and log rank test and Cox regression analysis were used to identify the predictors of mortality.**Results:** The overall mortality rate was 1.5 per 100 persons per year. Ambulatory and bedridden patients had four- and seven-fold higher risk of death [adjusted hazard ratio (HR) = 4.2, 95% confidence interval (CI): 1.7–10.7 and adjusted HR = 6.5, 95% CI: 2.0–20.7, respectively] as compared to those patients who had worked functional status. Patients who had poor antiretroviral drug adherence had five times higher risk of death (adjusted HR = 5.1, 95% CI: 1.6–16.3) than patients who had good antiretroviral adherence.**Conclusions:** Mortality rate was highly observed in the early phase of antiretroviral treatment. Poor ART adherence, being ambulatory and bedridden functional status was independent predictors of mortality.

1. Introduction

One of the most destructive epidemics in our world is AIDS. Worldwide, 36.7 and 35 million people were living with HIV and died from AIDS-related illnesses since the start of the epidemic, respectively. Since December 2015, HIV-infected people accessing antiretroviral therapy (ART) were 17 million up from 15.8 million in June 2015 and 7.5 million in 2010[1]. In low- and middle-income countries, an estimated over 1.4 million people were receiving ART in 2011 than in 2010[2]. The most dramatic progress on treatment coverage has been made in Sub-Saharan Africa where treatment

has been increased by 19% between 2010 and 2011. In addition, at least 745 000 people in high-income countries were receiving ART. As a result, more lives are being saved. Globally, since 1995, ART has saved 14 million lives per year in low- and middle-income countries, with more than 9 million of these in Sub-Saharan Africa. In Sub-Saharan Africa, an estimated more than quadrupled number of cumulative lives per year were saved between 2008 and 2011[3].

The annual AIDS-related deaths have decreased by 43% since the first global treatment target was set in 2003. In Eastern and Southern Africa, the world's most affected region, the number of people receiving treatment has reached nearly 10.3 million which was more than doubled since 2010 and AIDS-related death has been decreased by 36% since 2010. However, there were 2.1 million new HIV infections worldwide in 2015 adding up to a total of 36.7 million people living with HIV[4]. By 2010, universal access to treatment for HIV/AIDS for all those who need it is one of the targets of the millennium development goal[5]. Even though 5 million people in the low- and middle-income countries have accessed to ART, only one third out of those who get the treatment and access to ART still remain a major barrier in these parts of

*Corresponding author: Mekonnen Assefa Ahunie, Department of Social and Public Health, College of Health Sciences, Debre Tabor University, Debre Tabor, Ethiopia.

Tel: +251912873043

E-mail: mekonnen.as@gmail.com, mekidelat@yahoo.com

The study protocol was performed according to the Helsinki declaration and approved by Research and Ethics Committee of Debre Tabor University. Informed written consent was obtained from Debre Tabor General Hospitals and Woreta Health Center.

The journal implements double-blind peer review practiced by specially invited international editorial board members.

the world[6]. Sub-Saharan Africa, a region with only 12% of the global population, remains the most heavily affected region by HIV. In 2011, about 69% of all people living with HIV and more than 50% of deaths from AIDS-related illnesses in adults and children occurred in this region[7].

Over the last decade, ART has become more readily available with some countries even achieving universal ART access. Early initiation of ART has been reported to reduce HIV transmission besides its effect on reducing mortality and morbidity[8]. Early mortality was higher in low-income settings due to the advanced stage of the disease at initiation of ART and large proportion of occurrence of opportunistic infections[9]. There is a well established clinical benefit of ART for AIDS patients in terms of mortality reduction and improvement of life quality though there is regional variation. Life quality and expectancy of people living with HIV and AIDS have been significantly improved with highly active ART[3]. Suppressing HIV viral replication and restoring immune function are the primary goals of initiating highly active ART for HIV-infected individuals[10].

Several studies have reported predictors of mortality among HIV-infected people but mainly among those with advanced immune suppression and those who were receiving ART. In Ethiopia, a retrospective cohort study reported that 10% weight loss, advanced World Health Organization (WHO) clinical stage, bedridden functional status at baseline and CD4 cell count ≤ 200 cells/mm³ were independent predictors of death[11,12]. In Thailand study, anemia and severe immune suppression at baseline were predictors of early mortality, whereas the increase of CD4 (a baseline of CD4 < 50 cells/mm³), persistent anemia and virological response at 6 months were identified as predictors of long-term mortality[13]. Population-based study in Uganda evidenced that ART-naïve for HIV-infected individuals with CD4 cell count of 350 cells/mm³ had higher mortality than that of the general population. Likewise to developed countries, developing countries should aim to initiate ART at higher CD4 cell counts than the current threshold on their ART guideline to avert this preventable death. As a result, there is a need to allocate more resources for the expected increase in patients initiating ART at the higher CD4 threshold[14]. When ART is initiated at advanced stage of immune suppression denoted by low serum albumin level and CD4 cell count, risk of mortality is increased. This highlights the importance of timely initiation of ART drugs, namely, early detection of HIV infection and early managements of opportunistic infection including tuberculosis in the resource limited countries[15]. Similarly, the current study aimed to supplement the available evidences of mortality of patients on ART program in Ethiopia. In the study area, predictors of mortality of HIV-infected patients on ART treatment are not well investigated yet. Likewise, mortality among adult HIV-infected patients who were receiving ART and its predictors were investigated in this study.

2. Materials and methods

2.1. Study design, setting and period

A retrospective cohort study design was employed from January 2005 to June 2014 in Debre Tabor General Hospital and Woreta

Health Center in South Gondar zone. Debre Tabor General Hospital was the only hospital serving for catchment area population of South Gondar zone. With an estimated 16% increasing form in 1994 census report, there was an estimated total of population of 2 051 738 including 1 041 061 men and 1 010 677 women with a population density of 145.56, and 195.619% or 9.53% were urban inhabitants. South Gondar zone has an area of 14 095.19 km²[16]. At ART clinic of Debre Tabor General Hospital and Woreta Health Center, a total of 8 357 patients were enrolled until June 2014. By excluding the 4 541 pre-ART patients, patient's records enrolled between January 2005 to June 2014 were reviewed by using patients' ART unique identification number and age of 15 years and above as a reference.

2.2. Sample size and sampling procedures

All HIV-infected individuals who were receiving ART program and aged ≥ 15 years were included in this study. However, patients who were transferred in after starting of ART were excluded. The required sample size was determined by using two population proportion formulas by taking into account of the following assumptions: 5% level of significance, 80% power and a ratio of unexposed to exposed of 1:1. Estimated proportion of mortality in Ethiopia was taken as 4.1% for non-exposed group (WHO Stage I and II) and 10.1% for exposed group (WHO Stage III and IV)[17]. Therefore, the calculated total sample size was used to obtain the final sample size by considering 10% of incomplete data. However, in practice, total 698 patients' medical records were retrieved.

To recruit the predetermined sample size, simple random sampling technique was used for the ART clinic computerized registry and randomly selected study subjects were generated from the Computer registry among the eligible cards after registration number was identified. A total of 8 357 HIV infected patients were enrolled for care and treatment in Debre Tabor General Hospital and Woreta Health centre. A total of 4 378 patients who were enrolled from January 2005 to June 2014 for care and treatment were included to follow them for at least 9 years. As a result, a total of 698 patient registration cards were randomly selected. Any HIV infected individuals who were receiving ART treatment program having known and unknown follow up status on ART treatment program were included in this study but those who transferred it after starting ART treatment were excluded from this study.

2.3. Ethical considerations

Research and Ethics Committee of Debre Tabor University has offered the ethical approval. Following the approval, Debre Tabor General Hospitals and Woreta Health Center were informed through an endorsement which was a support letter from Debre Tabor University. Following the endorsement provided by Debre Tabor University, information about the objectives of the study was delivered into the selected health facilities through a support letter and oral permission was obtained from the respected health

facilities administration. Since the study was conducted through review of patients' medical record with kept confidentiality, none of the individuals were not subjected to any harm. Individual person who happened in the hospital during record review was requested to give consent. To maintain the confidentiality of the patients, nurses who were working in Art Clinic of the selected health facilities had been used to retrieve the data from the medical records. In addition, the data extraction form didn't include the personal identifiers. We extended our appreciation for Research and Ethics Committee of Debre Tabor University for the approval and ethical clearance.

2.4. Data collection tools and procedures

Data collection form which helped to extract necessary information from ART registration book and patients' cards were prepared by the principal investigator. The questionnaire was composed of sociodemographic, patient clinical condition and ART drug adherence and English version questionnaire was used. The questionnaire was pretested and then applicability and acceptability of the procedures and tools were evaluated. Six clinical nurses and two health officers were recruited as data collectors and supervisors, respectively. Data collectors and supervisors have taken a two-day training. All filled questionnaires were checked for accuracy, completeness and consistency by the supervisors and the primary investigator.

2.5. Data management and analysis

Epi Info™ for window version 3.5.3 software was used for data entry and SPSS version 16 statistical software was used for cleaning and analysis. *Chi-square* test was used for assessing the difference between WHO clinical Stage I and II and WHO clinical Stage III and IV with respect to various variables. Independent sample *t*-test statistics was used to compare the respondents' age between the two categories. Mortality of the two groups was compared by using time-to-event Kaplan-Meier methods and survival time was compared among subjects with WHO clinical Stage I and II and WHO clinical Stage III and IV, with the use of the log-rank test.

Before adjusting the covariates, the association between mortality and WHO clinical stages was done by using bivariate Cox proportional hazards regression analysis. Multivariate Cox regression analysis was performed to see the independent effects of determinant factors after the Cox proportional hazard assumption was checked. All variables with $P < 0.2$ during the bivariate Cox regression analysis were included on the multivariate Cox regression model. Hazard ratios with 95% confidence interval (CI) were used to test the significance of the association after multivariate Cox regression analysis.

3. Results

3.1. Sociodemographic characteristics

Data were retrieved from 698 (99.4%) of 702 records with the

mean \pm SD of age of the respondents that were (34.4 ± 8.9) years among alive group and (37.6 ± 10.8) years among dead group. Majority of the 487 (93.7%) patients in alive group and 33 (97.1%) in dead group were orthodox and 261 (50.4%) and 14 (43.8%) of patients were married in alive and dead group, respectively. In both groups, the majority of patients were urban resident, 380 (73.5%) in alive and 25 (73.5%) in dead group, respectively (Table 1).

Table 1

Sociodemographic characteristics of the patients in Debre Tabor General Hospital and Woreta Health Center in South Gondar zone from January 2005 to June 2014.

Variables	Alive [n (%)]	Dead [n (%)]	χ^2	df	
Age (mean \pm SD)	34.48 \pm 8.90	37.6 \pm 10.8			
Sex	Male	222 (42.4)	14 (40.0)	0.07	1
	Female	302 (57.6)	21 (60.0)		
Religion	Orthodox	487 (93.7)	33 (97.1)	0.60	3
	Muslim	31 (6.0)	1 (2.9)		
	Catholic	1 (0.2)			
	Others	1 (0.2)			
Marital status	Never married	71 (13.7)	8 (25.0)	3.80	4
	Married	261 (50.4)	14 (43.8)		
	Separated	46 (8.9)	2 (6.2)		
	Divorced	84 (16.2)	6 (18.8)		
	Widowed	56 (10.8)	2 (6.2)		
Level of education	No education	227 (44.0)	19 (57.6)	3.80	3
	Primary	133 (25.8)	5 (15.2)		
	Secondary	113 (21.9)	8 (24.2)		
	Tertiary	43 (8.3)	1 (3.0)		
Employment status	Working full time	275 (61.8)	9 (36.0)	46.10	4
	Working part time	65 (14.6)	3 (12.0)		
	Not working due to ill health	43 (9.7)	10 (40.0)		
Occupation	Unemployed	61 (13.7)	1 (4.0)	0.60	5
	Others	1 (0.2)	2 (8.0)		
	Daily laborer	101 (23.8)	6 (25.0)		
	Farmer	53 (12.5)	4 (16.7)		
	Housewife	84 (19.8)	4 (16.7)		
Place of residence	Government employee	62 (14.6)	3 (12.5)	0.00	1
	Non government employee	12 (2.8)	1 (4.2)		
	Others	112 (26.4)	6 (25.0)		
	Urban	380 (73.5)	25 (73.5)		
Rural	137 (26.5)	9 (26.5)			

*: Significant at $P = 0.0001$; $\alpha = 0.05$.

3.2. Clinical characteristics of patients

From the total 698 patients who were receiving ART, 527 (75.4%) of them were alive, 35 (5.0%) were dead, 39 (5.6%) were dropout, 88 (12.6%) were transferred out, and 9 (1.3%) of them were lost. Approximately half percentage of the patients were in clinical Stage I and II and Stage III and IV, 266 (52.1%), 245 (47.9%) in alive cohort and 16 (48.5%) and 17 (51.5%) in dead group, respectively. A total of 516 (97.9%) alive patients and 33 (94.3%) dead individuals had a hemoglobin level of more than 10 mg/dL at the start of ART. Most of the patients had a good antiretroviral (ARV) drug adherence, 486 (97.8%) and 22 (84.6%) in alive and dead cohort, respectively. From 283 alive patients, 119 (42.0%) and 36 (12.7%) of their partners had unknown and negative HIV status and 7 (46.7%) and 1 (2.9%) of their partner of dead individuals had unknown and negative HIV status, respectively (Table 2). From 698 patients who were receiving ART, 527 (75.4%) of them were alive, 35 (5.0%) were dead, 39 (5.6%) were dropout, 88 (12.6%) were transferred out, and 9 (1.3%) of them were lost.

3.3. Cumulative risk of death

All 698 study subjects had contributed to a total of 2 801.6 person years, of which 1 283.59 person per year were from WHO clinical Stage I and II and 1 518.036 were from WHO clinical Stage III and IV HIV patients. The cumulative probabilities of surviving in the first 48 months in WHO clinical Stage I and II cohort were 93% and 94% in WHO clinical Stage III and IV cohort, respectively.

The cumulative probability of survival for 9 years in non-exposed and exposed categories of patients who were receiving ART were 93% and 88%, respectively. And the cumulative probabilities of the compliment of survival for 9 years *i.e.* death was 7% and 12% on WHO clinical Stage I and II, III and IV, respectively.

Table 2

Clinical characteristics of patients in Debre Tabor General Hospital and Woreta Health Center in South Gondar zone, January 2005 to June 2014.

Variables	Alive [n (%)]	Dead [n (%)]	χ^2	df	P	
Patient functional status	Working	409 (81.3)	15 (44.1)	28.7	2	0.0001
	Ambulatory	74 (14.7)	13 (38.2)			
	Bedridden	20 (4.0)	6 (17.6)			
TB smear result at enrollment	Not determined	205 (52.8)	15 (65.2)	6.3	2	0.0400*
	Negative	155 (39.9)	4 (17.4)			
	Positive	28 (7.2)	4 (17.4)			
TB treatment at enrollment	Yes	41 (9.6)	7 (26.9)	7.7	1	0.0050*
	No	385 (90.4)	19 (73.1)			
Ctrimoxazole adherence	Good	430 (99.3)	21 (100.0)	0.1	1	0.7000
	faire	3 (0.7)	0 (0.0)			
HIV test result of partner	Not asked	7 (2.5)	1 (97.1)	2.5	3	0.4000
	Negative	36 (12.7)	1 (2.9)			
	Positive	121 (42.8)	6 (40.0)			
	Unknown	119 (42.0)	7 (46.7)			
Number of causal sexual partner	One	246 (91.4)	16 (84.2)	2.5	3	0.4000
	Two	5 (1.9)	1 (5.3)			
	Three	13 (4.8)	2 (10.5)			
	More than three	5 (1.9)	0 (0.0)			
Use of condom	Always	30 (7.6)	10 (0.0)	5.8	4	0.2000
	Sometimes	94 (23.9)	3 (17.6)			
	Rarely	17 (4.3)	1 (5.9)			
	Never	202 (51.3)	13 (76.5)			
	Others	51 (12.9)	0 (0.0)			
ARV adherence	Good	486 (97.8)	22 (84.6)	16.9	2	0.0001*
	Faire	1 (0.2)	0 (0.0)			
	Poor	10 (2.0)	4 (15.4)			
ART adherence barrier	Stigma	31 (44.3)	1 (16.7)	12.6	5	
	Afraid of medication	14 (20.0)	3 (50.0)			
	Doubt on medication	1 (1.4)	0 (0.0)			
	Depressed	1 (1.4)	1 (16.7)			
	Forgot medication	2 (2.9)	1 (16.7)			
	Others	21 (30.0)	0 (0.0)			
Health condition of partner	Healthy	110 (38.6)	3 (25.0)	7.7	3	
	Chronically ill	65 (22.8)	1 (8.3)			
	Dead	39 (13.7)	5 (41.7)			
	Unknown	71 (24.9)	3 (25.0)			

*: Significant at $\alpha = 0.05$; TB: Tuberculosis.

There was a no statistical significant difference between the two groups on their survival time (log rank test statistics = 0.014, $df = 1$, $P = 0.9$). There was an increase risk of hazard among those HIV- infected patients on ART whose hemoglobin count was less than 10 mg/dL, but

there was no statistically significant difference on survival probability between the two arms (log rank test statistics = 2.1, $df = 1$, $P = 0.1$) (Figures 1 and 2).

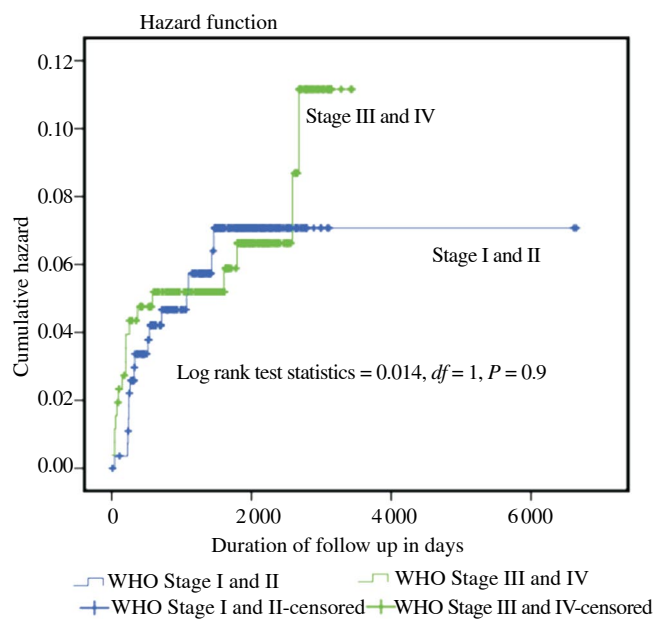


Figure 1. Kaplan-Meier estimate of survival among WHO clinical Stage I and II and Stage III and IV patients during their ART follow up in the ART clinic in Debre Tabor General Hospitals and Woreta Health Center from January 2005 to June 2014.

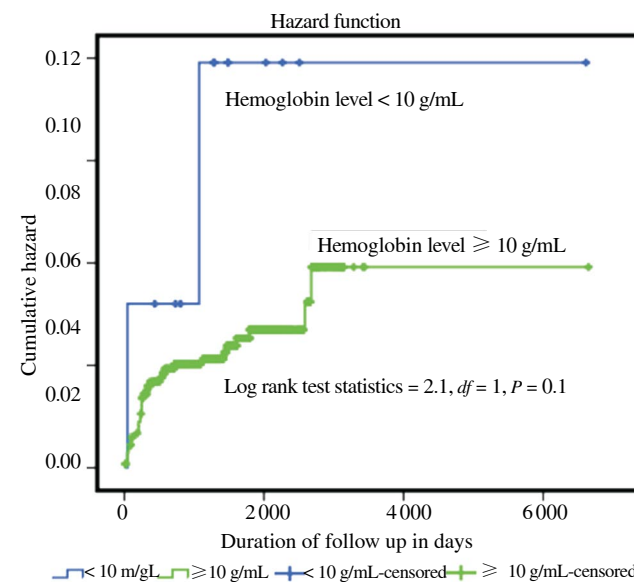


Figure 2. Kaplan-Meier estimate of survival among HIV-infected patients whose hemoglobin level was below 10 mg/dL and above 10 mg/dL during their ART follow up in the ART clinic in Debre Tabor General Hospitals and Woreta Health Center from January 2005 to June 2014.

3.4. Predictors of mortality

Before fitting the covariate into the model, Cox proportional hazard assumption was checked by schoenfield residuals test and graphically by $-\ln(-\ln)$ survival probability. Those variables with $P < 0.2$ on the bivariate Cox regression analysis were fitted to the multivariate Cox regression analysis model.

Based on the multivariate Cox regression analysis, ambulatory patients had four folds higher risk of death (adjusted hazard ratio

= 4.2, 95% CI: 1.7–10.7) as compared to patients of working functional status, and bedridden patients had six times higher hazards of death (adjusted hazard ratio = 6.5, 95% CI: 2.0–20.7). Relative to patients who had good ARV drug adherence, those patients who had poor ARV drug adherence had 5.1 times more hazards of death (95% CI: 1.6–16.3) (Table 3).

Table 3

Predictors of mortality of selected clinical characteristics of the respondents on Debre Tabore General Hospital and Woreta Health Center in South Gondar zone from January 2005 to June 2014.

Variables		Alive (n)	Dead (n)	Adjusted hazard ratio (95% CI)	P
Patient functional status	Working	409	15	1	
	Ambulatory	74	13	4.2 (1.7–10.7)	0.002*
	Bedridden	20	6	6.5 (2.0–20.7)	0.002*
ARV adherence	Good	486	22	1	
	Fair	1	0	0.0 (0.0)	0.900
	Poor	10	4	5.1 (1.6–16.3)	0.006*
ART regimen	1a(30)	126	10	1	
	1a(40)	4	0	0.0 (0.0)	0.900
	1b(30)	78	2	0.2 (0.02–1.5)	0.100
	1b(40)	12	0	0.0 (0.0)	0.900
	1c	115	9	1.2 (0.4–3.2)	0.700
	1d	33	5	1.2 (0.3–3.4)	0.800
	1e	128	9	1.0 (0.3–3.4)	0.900
	1f	23	0	0.0 (0.0)	0.900
CD4 count	< 200	313	24	0.6 (0.2–2.4)	0.500
	200–350	144	5	0.5 (0.1–2.3)	0.400
	> 350	70	6	1	
Hemoglobin level	< 10 mg/dL	11	2	2.5 (0.3–20.8)	0.300
	>10 mg/dL	516	33	1	

*: Significant at $\alpha = 0.05$, 1a(30) = d4t(30)+3TC+Nvp; 1b(40) = d4t(40)+3TC+Efv; 1e = TDF+3Tc+Efv; 1a(40) = d4t(40)+3TC+Nvp; 1c = Azt+3Tc+Nvp; 1f = TDF+3Tc+Nvp; 1b(30) = d4t(40)+3TC+Efv; 1d = Azt +3Tc+Efv.

4. Discussion

In our study, mortality of HIV-infected patients and predictors of mortality were assessed for those who were enrolled on ART program. As a result, a total of 35 (5.0%) deaths were observed and in the first year of ART initiation, majorities (71.4%) of the patients died. There was an overall mortality rate of 1.5 per 100 person per year with the proportion of 5.7% of death in WHO clinical Stage I and II and 6.5% among WHO clinical Stage III and IV with their respective incidence rate of 12.5 per 1000 person per year and 11.2 per 1000 person per year, respectively. These findings were lower than the research finding of 46 (8.85%) total deaths with an overall mortality rate of 3.2 per 100 person per year reported from Aksum Hospital. Likewise, one-third (45/136) of all deaths and 89 of the deaths (65.4%) occurred in the first 3 months and 12 months on ART, respectively according to the study conducted in Nigerian Hospital. And majority (72.8%) of the death occurred over the first 36-month follow-up period. At one year of starting ART, more than 50% of death occurred within three months of ART initiation with an overall mortality rate of 7.66 death per 100 patients per year and this early treatment death was due to the advanced immune deficient status at enrollment

and independents response of ART that defines the late death. In addition, tuberculosis was found to be the most important cause of death and it caused 48% of the total death and other studies also showed greater estimate than this current findings[15,18-23]. Though the exact cause of high mortality was not explained by any of the observational studies at the initial phases of ART, there were different estimates of mortality probably due to both early and recent phases of treatment including in the study period and initiation of ART for most patients at early stage of the disease that were relatively surviving longer and patients were required treatment in relatively less advanced disease stage because their awareness has been increased.

Functional status of patients during the ART initiation was considered as a statistically significant predictor of mortality. As a result, ambulatory and bedridden patients were 4.2 and 6.5 times higher risk of death than patients in working functional status, respectively, which is in line with other studies conducted in Ethiopia. Like an Eastern Ethiopia study showed that as compared to working functional status counterpart, bedridden patients had 4.09 times higher risk of mortality, and ambulatory patients were 2.38 and 2.72 times at higher risk of death than patients in working functional status, respectively[21,24]. Others studies also showed that there was 55% lower risk of death among patients of working functional status than bedridden patients during initiation of ART[22]. The risk of mortality for bedridden patients was 2.7 times higher risk of death as compared to ambulatory patients in urban slums of Kenya[12]. Similarly, relative to patients of working functional status, ambulatory and bedridden patients had 2.87 and 6.90 times higher risk of death, respectively[25]. Likewise, those bedridden clients at initiation of ART were more likely to die compared to working functional status clients. In this regard, studies from Ethiopia and Nepal reported supporting evidences that being bedridden was a predictor of mortality during ART care[11,21,26,27].

Therefore, due attention should be given for ambulatory and bedridden patient to reduce high risk of mortality rate. In the current findings, patients with poor ART adherence had 5.1 times more risk of death than patients of good adherence. Consistently with this, the study conducted in Addis Ababa showed that patients with poor ART adherence were 3.92 folds more risk of death than those who have good ART adherence and study conducted in Debre Markos Hospital showed that there were 2.16 and 1.88 times higher risk of death for patients of fair and poor ART adherence than those with good adherence respectively[21,28]. Even though ART adherence was a statistically significant predictor of mortality, since the current study used documents review, adherence assessment technique was not as such reliable. In the current study, unlike other studies, predictors like WHO

clinical stage, base line hemoglobin level and CD4 cell count were not significant predictors of mortality. In the contrary, there are other studies which showed that the effects of those predictors on mortality for example for clinical care, late presentation of patients at WHO clinical Stages III and IV had 2.16 times higher hazard of death than Stages I and II patients and Tanzanian study showed that WHO clinical Stage IV patients had 4.16 times risk of death in advanced WHO stages (odds ratio = 4.3; 95% CI: 2.6–6.8)[21,29].

Our study showed that the base line CD4 cell count doesn't have any statistically significant association with death which is in line with study done in Debre Markose Hospital[21]. In the contrast, a case control study conducted in Jimma and Mettu Karl Hospitals showed that CD4 count below 200 cells/mm³ had 9.8 times higher risk of death than the reference group (odds ratio = 9.8, 95% CI: 5.5–17.5) and after adjusting it for confounding, baseline CD4 count (odds ratio = 2.71; 95% CI: 1.51–6.21; *P* = 0.02) remained significant predictors of mortality[29]. Study done in Axum Hospital showed that risk of mortality was two-fold more in patients who had a CD4 cell count below 50 cell/mL than those patients who had CD4 count of 200 cell/mL. The likelihood of death was increasing because of increased occurrence of opportunistic infections due to advanced immunodeficiency marker. There were two-fold increased risk of mortality for anemic patient at the baseline of treatment than those who doesn't have anemia[18].

Unlike this study, several studies showed that baseline hemoglobin level as independents predictor of death for example study conducted in Debre Markose Hospital revealed that patients were at high risk of death where there hemoglobin level was below 10 g/dL at baseline of treatment[21]. And patients have high risk of mortality when the hemoglobin level was below < 11 g/dL at the base line of treatment[18]. The findings of this study were interpreted by revising its strengths and limitations. This study might be taking both clinical and non clinical characteristics, larger sample size and long period of retrospective follow-up. Due to many unreported/home deaths, using routinely collected data might have been introduced under estimation of mortality. In addition to this since, we collected secondary data of deaths which might be occurred due to opportunistic infections secondary to poor adherence to ART regimen and prophylactic antibiotics, so authors fail to ascertain that all recorded deaths were AIDS-related deaths. These were considered as the limitation of this study. Therefore, this limitation should be considered into account for our findings and interpretation.

The cumulative risks of death during ART follow up period were not statistically significantly different between WHO clinical stages. As a result, the cumulative probability of survival for 9

years was more or less comparable between WHO clinical Stage I and II and Stage III and IV. The majority of death occurs in the early period of ART follows up duration before 12 months. Ambulatory and bedridden patients had more hazard of death than patients who were on working functional status and patients who had poor ARV drug adherence had more risk of death than those patients who had good ARV drug adherence.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

We are very grateful to Debre Tabor University for the technical and financial support of this study. At last but not least, we also would like to thank head of the respective health facilities and staffs of those facilities for their hospitality, patience and giving their precious time to support us.

References

- [1] The Joint United Nations Programme on HIV and AIDS. Global statistics – 2015. Geneva: The Joint United Nations Programme on HIV and AIDS; 2016. [Online] Available from: http://www.unaids.org/sites/default/files/media_asset/20150901_FactSheet_2015_en.pdf [Accessed on 15th June, 2016]
- [2] United Nations General Assembly. Political declaration on HIV/AIDS: intensifying our efforts to eliminate HIV/AIDS. New York: United Nations General Assembly; 2011. [Online] Available from: http://www.unodc.org/documents/southeastasiaandpacific/2012/02/hlm-hiv/20110610_UN_A-RES-65-277_en.pdf [Accessed on 15th June, 2012]
- [3] The Joint United Nations Programme on HIV and AIDS. Together we will end AIDS. Geneva: The Joint United Nations Programme on HIV and AIDS; 2012. [Online] Available from: https://www.unicef.org/aids/files/aids_togetherwewillendaids_en.pdf [Accessed on 15th June, 2016]
- [4] The Joint United Nations Programme on HIV and AIDS. Global AIDS Update. Geneva: The Joint United Nations Programme on HIV and AIDS; 2016. [Online] Available from: http://www.who.int/hiv/pub/arv/global-AIDS-update-2016_en.pdf?ua=1 [Accessed on 15th July, 2016]
- [5] United Nations. Millennium declaration. New York: United Nations; 2000. [Online] Available from: <http://www.un.org/en/development/devagenda/millennium.shtml> [Accessed on 15th June, 2016]
- [6] World Health Organization. Report on the global AIDS epidemic. Geneva: World Health Organization; 2010. [Online] Available from:

- http://www.who.int/hiv/pub/global_report2010/en/ [Accessed on 10th June, 2011]
- [7] The Joint United Nations Programme on HIV and AIDS. World AIDS day report. Geneva: The Joint United Nations Programme on HIV and AIDS; 2011. [Online] Available from: http://files.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/JC2216_WorldAIDSday_report_2011_en.pdf [Accessed on 15th June, 2016]
- [8] World Health Organization. Towards universal access: scaling up priority HIV/AIDS interventions in the health sector. Geneva: World Health Organization; 2010. [Online] Available from: <http://www.who.int/hiv/pub/2010progressreport/en/> [Accessed on 15th June, 2016]
- [9] The Joint United Nations Programme on HIV and AIDS. AIDS epidemic updates. Geneva: The Joint United Nations Programme on HIV and AIDS; 2010. [Online] Available from: <http://search.unaids.org/search.asp?lg=en&search=AIDS%20epidemic%20update%202010> [Accessed on 15th June, 2016]
- [10] Federal Ministry of Health. Guideline for management of opportunistic infections and antiretroviral treatment in adolescents and adults in Ethiopia. Abuja: Federal Ministry of Health; 2008. [Online] Available from: http://www.who.int/hiv/pub/guidelines/ethiopia_art.pdf [Accessed on 15th June, 2016]
- [11] Biadgilign S, Reda AA, Digaffe T. Predictors of mortality among HIV infected patients taking antiretroviral treatment in Ethiopia: a retrospective cohort study. *AIDS Res Ther* 2012; **9**: 15.
- [12] Muhula SO, Peter M, Sibhatu B, Meshack N, Lennie K. Effects of highly active antiretroviral therapy on the survival of HIV-infected adult patients in urban slums of Kenya. *Pan Afr Med J* 2015; **20**: 63.
- [13] Fregonese F, Collins IJ, Jourdain G, Lecoecur S, Cressey TR, Ngo-Giang-Houng N, et al. Predictors of 5-year mortality in HIV-infected adults starting highly active antiretroviral therapy in Thailand. *J Acquir Immune Defic Syndr* 2012; **60**: 91-8.
- [14] Masiira B, Baisley K, Mayanja BN, Kazooba P, Maher D, Kaleebu P. Mortality and its predictors among antiretroviral therapy naïve HIV-infected individuals with CD4 cell count ≥ 350 cells/mm³ compared to the general population: data from a population-based prospective HIV cohort in Uganda. *Glob Health Action* 2014; **7**: 21843.
- [15] Bhowmik A, Bhandari S, De R, Guha SK. Predictors of mortality among HIV-infected patients initiating anti retroviral therapy at a tertiary care hospital in Eastern India. *Asian Pac J Trop Med* 2012; **5**: 986-90.
- [16] United Nations Population Fund. Summary and statistical report of the 2007 population and housing census. New York: United Nations Population Fund; 2008. [Online] Available from: http://ecastats.uneca.org/aicmd/Portals/0/Cen2007_firstdraft.pdf [Accessed on 15th June, 2016]
- [17] Tsegaye E, Worku A. Assessment of antiretroviral treatment outcome in public hospitals, South Nations Nationalities and Peoples Region, Ethiopia. *Ethiop J Health Dev* 2011; **25**(2): 102-9.
- [18] Tadesse K, Haile F, Hiruy N. Predictors of mortality among patients enrolled on antiretroviral therapy in Aksum Hospital, Northern Ethiopia: a retrospective cohort study. *PLoS One* 2014; **9**(1): e87392.
- [19] Assefa Y, Kiflie A, Tesfaye D, Mariam DH, Kloos H, Edwin W, et al. Outcomes of antiretroviral treatment program in Ethiopia: retention of patients in care is a major challenge and varies across health facilities. *BMC Health Serv Res* 2011; **11**: 81.
- [20] Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health. Version 3.01. [Online] Available from: www.OpenEpi.com [Accessed on 15th June, 2016]
- [21] Abebe N, Alemu K, Asfaw T, Abajobir AA. Predictors of mortality among HIV positive adults on antiretroviral therapy in Debreworkos Referral Hospital, Northwest Ethiopia. *J AIDS HIV Res* 2014; **6**(1): 19-27.
- [22] Amuron B, Levin J, Birunghi J, Namara G, Coutinho A, Grosskurth H, et al. Mortality in an antiretroviral therapy programme in Jinja, South-East Uganda: a prospective cohort study. *AIDS Res Ther* 2011; **8**: 39.
- [23] Odafe S, Idoko O, Badru T, Aiyenigba B, Suzuki C, Khamofu H, et al. Patients' demographic and clinical characteristics and level of care associated with lost to follow-up and mortality in adult patients on first-line ART in Nigerian Hospitals. *J Int AIDS Soc* 2012; **15**: 17424.
- [24] Solomon T, Worku A. The effect of HAART on incidence of tuberculosis among HIV infected patients in Hawassa University Referral Hospital, South Ethiopia: a retrospective cohort study [dissertation]. Addis Ababa: Addis Ababa University; 2011.
- [25] Mageda K, Leyna GH, Mmbaga EJ. High initial HIV/AIDS-related mortality and -its predictors among patients on antiretroviral therapy in the Kagera Region of Tanzania: a five-year retrospective cohort study. *AIDS Res Treat* 2012; **2012**: 843598.
- [26] Setegn T, Takele A, Gizaw T, Nigatu D, Haile D. Predictors of mortality among adult antiretroviral therapy users in Southeastern Ethiopia: retrospective cohort study. *AIDS Res Treat* 2015; **2015**: 148769.
- [27] Bhatta L, Klouman E, Deuba K, Shrestha R, Karki DK, Ekstrom AM, et al. Survival on antiretroviral treatment among adult HIV-infected patients in Nepal: a retrospective cohort study in far-western region, 2006–2011. *BMC Infect Dis* 2013; **13**: 604.
- [28] Kebebew K. Determining factors that affect the survival rate of HIV-infected patients on art: the case of Armed Forces General Teaching Hospital, Addis Ababa, Ethiopia [dissertation]. Addis Ababa: Addis Ababa University; 2011, p. 54-6.
- [29] Yesuf KM, Melese ZT. Prevalence of toxoplasmosis in HIV/AIDS patients in Mettu Karl Hospital. *Am J Health Res* 2015; **3**(3): 183-8.