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Retrospective Study

Survival and predictors of mortality among HIV-infected adults receiving ART in Hawassa comprehensive specialized hospital, Sidama regional state, Ethiopia

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Abstract

Background: Having claimed lives, HIV/AIDS is still a significant global public health concern. Antiretroviral therapy (ART) is now widely available, and this rapid expansion of access is dramatically improving HIV epidemic survival rates worldwide.

Objectives: The aim of this study was to identify the mortality risk factors and survival status of ART patients attending Hawassa Comprehensive Specialized Hospital in 2020.

Methods: In a five-year retrospective cohort research, all patients seen between January 2015 and December 2019 were analyzed. The data were analyzed with SPSS 25.0. The Kaplan-Meier Log-rank model was employed to gauge the survival time of ART patients based on explanatory variables. Both bivariate and multivariate Cox proportional hazards regression models were employed to identify the independent causes of mortality.

Results: Patients on ART had a 74% overall survival probability. With a median survival of 34 months, there are 0.135 deaths for every 100 person-years. Hemoglobin level (HR = 2.38; 95% CI = 3.3-6.3), WHO clinical stage III and IV (HR = 3; 95% CI = 2.2-9.5, p = 0.04), Age >=60 (HR = 1.6; 95% CI = 1.3-2, p = 0.04) and Functional status bed ridden (HR = 3.1; 95% CI = 1.2-9.4, p = 0.04) were all independent predictors of death among RVI patients.

Conclusion: In comparison to trials conducted in wealthy countries, the survival rate of ART patients in this study was low. Patients who are anemic; WHO advanced clinical stage; old age, and functional status bedridden should be closely followed and monitored.

More Information

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Introduction

Having taken approximately 33 million lives to date, HIV/AIDS continues to be a significant global public health burden. Despite this, HIV infection has developed into a manageable chronic health disease that enables individuals living with HIV to live long and healthy lives thanks to increasing access to effective HIV prevention, diagnosis, treatment, and care, including opportunistic infections. An estimated 38.0 million people were predicted to be HIV-positive as of the end of 2019 [1,2]. In 2019, the main population groups and their sexual partners were responsible for more than 60% (about 62%) of all new HIV infections worldwide among people aged 15 to 49.

These groups were responsible for more than 95% of new HIV infections in each of these regions, including Eastern Europe and Central Asia, Asia and the Pacific, Western and Central Europe and North America, and the Middle East and North Africa. The WHO African Region is home to 25.7 million HIV-positive individuals or more than two-thirds of the global total [1,3,4]. Ethiopia is one of the countries in Sub-Saharan Africa that has been most severely affected by the HIV pandemic. The number of HIV-positive Ethiopians is thought to be 738,976. [5]. According to the Ethiopian Demographic and Health Survey 2016, the overall HIV prevalence is 0.9% and the urban prevalence is 2.9%, which is seven times higher than the rural prevalence (0.4%) (EDHS 2016).

The World Health Organization guidelines, which

recommend early ART for all PLHIV, regardless of CD4 cell count, were based on a growing body of evidence demonstrating the increased risk of AIDS or death associated with delaying treatment, according to the 2016 EDHS reports that HIV incidence varies by area, ranging from less prevalent in [6]. Antiretroviral therapy (ART) availability is being quickly expanded, which is dramatically enhancing worldwide HIV epidemic survival and reducing AIDS-related mortality rates. Increased ART use has, to date, largely in developing and underdeveloped nations decreased the estimated 6.6 million AIDS-related deaths that occurred globally [3,7]. Service coverage has continuously risen as a result of concerted international efforts to prevent HIV. In 2019, 68% of adults with HIV around the globe were taking antiretroviral medications for the rest of their lives (ART).

Antiretroviral therapy (ART) enhances immune system performance while reducing HIV replication and new cell infection. ARV medication consequently enhances the survival and quality of life of HIV carriers [1,8]. In Ethiopia, antiretroviral treatment (ART) was first made available in 2005. Only 426,000 of the projected 738,976 HIV-positive Ethiopians who need antiretroviral medication (ART) are now receiving it [5,9].

A few studies on the mortality of HIV adults completed in Ethiopia and other nations demonstrate that prompt ART introduction among HIV/AIDS adults lowers mortality and has a favorable effect on survival for those particular study groups. Additionally, cotrimoxazole prophylaxis therapy (CPT), older age, male sex, baseline hemoglobin, CD4 count, WHO clinical stage and HAART use.

Materials and methods

Study setting and period

The research was done at the ART and IPT services offering Hawassa University Specialized Hospital. It is 273 kilometers south of Addis Ababa. A teaching hospital with basic facilities for HIV care and treatment, with an established clinical set-up and highly skilled medical staff, the hospital provides services for about two million individuals. Since July 2006, the hospital has been providing pre-ART and ART services.

Study design

An Institutional based retrospective study was conducted between January 2015 to December 2019 in Hawassa comprehensive specialized hospital to assess survival in PLWHA and those who are on ART.

Population

Source population: A person living with HIV/AIDS, age ≥ 15 years and started ART treatment in Hawassa comprehensive specialized hospital.

Study population: Those patients fulfilling the following criteria.

Inclusion criteria

- Positive adults aged 15 yrs or older who started ART
- HIV patients with the complete intake form, registers and follow-up form

Exclusion criteria

- Diagnosis is made outside of health institution
- Women who were pregnant at the time of ART initiation and lactating mother.

Sample size determination

The sample size was determined using double population proportion formula by considering CD4, functional status and WHO stage as the major predictor variables{Formatting Citation}. Moreover, CD4 is considered an independent predictor since it gives the maximum sample size. The sample size was calculated by using open Epi info version 7 statistical packages.

$$n_1 = \frac{\left[Z_{\frac{\alpha}{2}}\sqrt{(1+\frac{1}{r})p(1-p)} + Z_{\beta}\sqrt{\frac{p_1(1-p_1)+p_2(1-p_2)}{r}}\right]^2}{(p_1-p_2)^2}$$

$$Where,\ p = \frac{p1+rp2}{r+1},\ if\ \ r{=}1\ then\ p = \frac{p1+p2}{2}$$

P1: is the percent of completed with the outcome

P2: is the percent of non-completers. With the outcome

Z α/2: is taking CI 95%: 80% power

r: is the ratio of non-completers to completers1:1.

Sample size calculation was done by considering determinant

S.N	Variables	CI	Assumptions	Total sample size	Reference
1.	CD4	95%	P1=54% P2=7.5%	483	[10]
2.	WHO stage	95%	P1=65% P2=34%	92	[11]
3.	Bedridden functional status	95%	P1=66% P2=33%	88	[12]

P1: is the percent of completed with the outcome P2: is the percent of non-completed with the outcome	Z α/2: is taking CI 95% : 80% power

- r is the ratio of non-completers to completers 1:1

✓ Then the largest sample size (n = 483)

Sampling technique

Study participants were selected by using a systematic random sampling method using commands in Excel all 464 records of patients receiving ART in Hawassa comprehensive specialized hospital were listed in an excel spreadsheet, and a randomly selected 483 patients were studied.

Dependent and Independent variables

Time to the event in a month served as the primary outcome metric. The interval between the start of ART treatment and the event or censoring date was used to compute the time of survival in months. Socio-demographic traits and baseline clinical data were the independent determining variables. The ART patients were monitored up until the time of death, loss to follow-up, transfer out, or study conclusion. If a patient was lost for follow-up or transferred out, they were regarded as censored.

Data collection procedure and quality control

A form for gathering data was created using the ART clinic's entry and follow-up procedures. Reviewing the pre-ART register, laboratory request, and follow-up form allowed for the collection of the data. Prior to beginning ART, the most recent test findings served as the baseline value. By creating the necessary data collection tools and maintaining close supervision, data quality was managed. The accuracy of each filled-out data collection form was verified.

Entry and analysis

The data was cleaned and coded before being entered into Epidata 4.6.2. An analysis based on a 5 - year cohort follow-up was conducted. Finally, data was exported for processing into SPSS version 25.0. Interquartile range (IQR) was used in the presentation of descriptive statistics for numeric variables, whereas frequency and percentages were used for categorical variables. By using the Kaplan-Meier Log-rank model to calculate the TB Occurrence time based on explanatory variables, the TB-free survival time was calculated. To the independent determinants, bivariate and multivariate Cox proportional hazards regression models were run.

Operational definition

Lost to follow-up: If a patient discontinued ART for one to three months as recorded by the ART physician

Event: - PLWHIV on ART, who died during the study period

Survival: lack of experience with death.

Ethical considerations

Ethics approval and consent to participate: The research and ethics commission (REC) of Addis Abeba University's School of Nursing and Midwifery's College of Health Sciences granted its approval. The hospital's outpatient administrators provided a letter of authorization to view patient data. Since we are reporting on a retrospective analysis of medical records, the ethics committee waived the requirement for informed consent and completely anonymized all data before we had access to it.

Results

483 people in all were surveyed and 262 (54.2%) of them were men. The age range of the respondents was 18 to 68 years, with a mean age of 32.8 and 12.8 years (Mean SD). 56.1% of the 271 respondents, or more than half, were married. Regarding participant education, 271 (56.1%) of the respondents had secondary education or higher, while the remaining 212 (43.9%) had only primary education. Only 26 people, or 25.50% of the population, went to college. 51.1% of the 247 respondents, or nearly half, have used drugs or alcohol in the past.

By profession, 123 respondents (25.5%) worked in the government. Only 186 participants, or 38.5%, came from rural areas, with urban participants making up the majority. Regarding religion, 225 people (46.6%) identified as Orthodox believers (Table 1).

Table 1: Socio–demographic characteristics of HIV patients who were enrolled for ART care at Hawassa University Comprehensive Specialized Hospital Sidama, Ethiopia, from January 2015 to December 2020 (*n* = 483).

Characteristics	Status at last contact Death Censored		Total
Age in years [mean = 32.8, SD = 12.8]			
18 – 39	8(2.5%)	313(97.5%)	321(66.5%)
40 – 59	5(3.5%)	138(96.5%)	143(29.6%)
> = 60	13(68.4%)	6(31.6%)	19(3.9%)
Sex			
Male	10(4.5%)	211(95.5%)	221(45.8%)
Female	16(6.1%)	246(93.9%)	262(54.2%)
Marital Status			
Never Married	4(3.7%)	103(96.3%)	107(22.2%)
Married	15(5.5%)	256(94.5%)	271(56.1%)
Separated	3(8.6%)	32(94.1%)	35(7.2%)
Widowed	1(4.8%)	20(95.2%)	21(4.3%)
Divorced	3(6.1%)	46(93.9%)	49(10.1%)
Residence			
Urban	15(5.1%)	282(94.9%)	297(61.5%)
Rural	11(5.9%)	175(94.1%)	186(38.5%)
Religion			
Protestant	10(5.9%)	159(34.8%)	169(35%)
Orthodox	12(5.3%)	213(94.7%)	225(46.6%)
Muslim	3(5.8%)	49(94.2%)	52(10.8%)
Catholic	1(3.8%)	25(96.2%)	26(5.4%)
Other	0	11(100%)	11(2.3%)
Substance Use			
Yes	16(6.5%)	231(93.5%)	247(51.1%)
No	10(4.2%)	226(95.8%)	236(48.9%)
Educational Status			
No education	5(8.1%)	57(91.9%)	62(12.8%)
Primary	12(8%)	138(92%)	150(31.1%)
Secondary	6(3.4%)	171(96.6%)	177(36.6%)
More than Secondary	3(3.2%)	91(96.8%)	94(19.5%)
Occupation			
Farmer	10(17.5%)	47(82.5%)	57(11.8%)
Merchant/Trader	3(2.7%)	108(97.3%)	111(23%)
Government Employed	2(1.6%)	121(98.4%)	123(25.5%)
Non – Government	3(7.1%)	39(92.9%)	42(8.7%)
Day Laborer	1(2.3%)	43(97.7%)	44(9.1%)
Jobless	2(6.3%)	30(93.8%)	32(6.6%)
Driver	2(5.1%)	37(94.9%)	39(8.1%)
Retired/housewives/Student (other)	3(8.8%)	32(91.4%)	34(7%)

More than half 356 (73.7%) of the study participants were WHO clinical Stage I/II and medium of current CD4 count = 456 cells/μL. Seventy-six (76.2%) of respondents were in CPT prophylaxis and (93.8%) were IPT completed. Three hundred six (69.7%) of respondents' functional status was working and more than half of respondents' BMI were less than 18 kg/m^2 (Table 2).

Survival experience among different groups of ART patients in log-rank test 26 patients (5.4%) died during the follow-up period, with a death incidence rate of 0.135 per 100 person-years. The survival probability at the eleventh month of ART initiation was 99.8%. This proportion reduces to 99.6, in the 14th month and is preceded by 99.4%, 97.9%, 91.6%, and 76.4% in the second, third, fourth, and the end of the follow-up period, respectively (Figure 1). Baseline WHO clinical stages (Log-rank, $p \leq 0.01$), functional status (Log-rank, $p \leq 0.001$), age (Log-rank, $p \leq 0.001$base line hemoglobin (Log-rank, $p \leq 0.001$), and CD4 count (Log-rank, $p \leq 0.01$) were variables that showed the significant association with the survival of patients on ART within Log-rank test (Figure 2) (Table 3).

Table 2: Clinical characteristics of HIV patients who were enrolled for IPT care at Hawassa University Comprehensive Specialized Hospital, Sidama, Ethiopia from January 2015 to December 2020 (n = 483).

Characteristics	Status at last contact Death	Censored	Total
WHO clinical Stage	1		
I and II	6(1.7%)	350(98.3%)	356(73.7%)
III and IV	20(15.7%)	107(84.3%)	127(26.3%)
CD4 cell count (Cells/μL)			
< = 200	12(17.4%)	57(82.6%)	69(14.3%)
> 200	14(3.4%)	400(96.6%)	414(85.7%)
Medium of current CD4 count = 456 cells/ μL, (IQR, 314 – 661) and 231 cells/ μL (IQR, 105 – 400)			
BMI			
< 18 kg/m^2	19(7.1%)	248(92.9%)	267(55.3%)
> 18 kg/m^2	7(3.2%)	209(96.8%)	216(44.7%)
Medium BMI = 20.29 kg/m^2 (IQR, 18.49 – 22.36)			
CPT use			
Yes	18(4.9%)	350(95.1%)	368(76.2%)
No	8(7.0%)	107(93%)	115(23.8%)
IPT use			
Yes	23(5.1%)	430(94.9%)	453(93.8%)
No	3(10.0%	27(90%)	30(6.2%)
HIV/TB co – infection			
Yes	7(13.5%)	45(86.5%)	52(10.8%)
No	19(4.4%)	4106(95.6%)	429(89.2%)
Chronic illness			
Yes	11(47.8%)	12(52.2%)	23(4.8%)
No			
Hemoglobin			
> = 11 mg/dl(Normal)	16(4.1%)	374(95.9%)	390(80.7%)
< 11 mg/dl(Anemia)	10(10.8%)	83(89.2%)	93(19.3%)
Functional status			
Working	3(0.9%)	333(99.1%)	336(69.7%)
Ambulatory	7(6.9%)	99(93.4%)	106(22%)
Bed ridden	16(40%)	24(60%)	40(8.3%)

Modeling of risk factors that are effective in the survival rate of patients on ART by using the Cox regression model.

To identify the independent predictors of survival after initiation of ART, Bivariate and multivariate Cox regression models were used. Bivariate Cox regression model, baseline WHO clinical stage, CD4, age, hemoglobin and functional status and HIV/TB co-infection showed significant association with early mortality after initiation of ART (Table 2). After multivariate analysis, four baseline factors could be independently identified: hemoglobin level (HR **=** 2.38;95% CI = 3.3-6.3); WHO clinical stage III and IV (HR = 3; 95% CI = 2.2-9.5, p = 0.04**);** Age > = 60 (HR = 1.6; 95% CI = 1.3–2, p = 0.04)**;** Functional status bed ridden (HR = 3.1; 95% CI = 1.2-9.4, p = 0.04)**;** were independent predictors of mortality among RVI patients (Table 4).

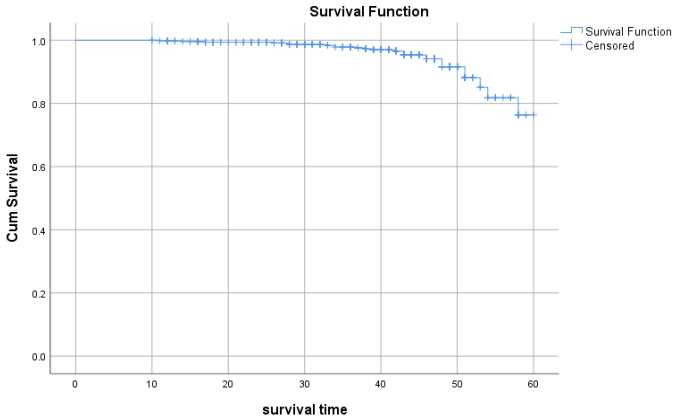

Figure 1: Shows the overall survival probability of patients on ART starting from the initiation of ART until the end of the study period among PLWHA, Hawassa town, Southern Ethiopia, November 2020.

Table 3: Baseline characteristics and probability of ART survival during 5 years of follow–up (Kaplan–Meier method) of HIV patients receiving ART, Hawassa University Comprehensive Specialized Hospital, Sidama, Ethiopia from January 2015 to December 2019. (n = 483).

Characteristics (Variables)	Mean survival time/ Probability in month over 5 yr (95% CI)	Log rank test	p – value
Age in years [mean = 32.8,SD = 12.8]			
18 – 39	58.89(57.95,59.85)	141	$p \leq 0.001$
40 – 59	56.68(55.01,58.36)		
> = 60	42.99(37.68,48.31)		
WHO clinical stage		40	$p \leq 0.01$
I & II	58.97(58.11,59.84)		
III & IV	51.61(49.50,53.72)		
CD4 cell count (Cells/μL)	51.81(48.41,55.22)	29.5	$p \leq 0.001$
< = 200	54.95(52.32, 57.59)		
> 200	39.85(35.43, 44.26)		
Functional status			
Working	58.37(57.62, 59.11)	120	$p \leq 0.001$
Ambulatory	57.34(55.43,59.26)		
Bed ridden	55.52(41.14,49.91)		
HIV/TB co – infection			
Yes	54.69(52.01, 57.38)	6.10	$p \leq 0.01$
No	57.88(56.79,58.97)		
Hemoglobin			
> = 11 g/dl(Normal)	57.94(56.86,59.01)	8.32	$p \leq 0.01$
<11 g/dl(Anemia)	55.11(52.99,57.23)		

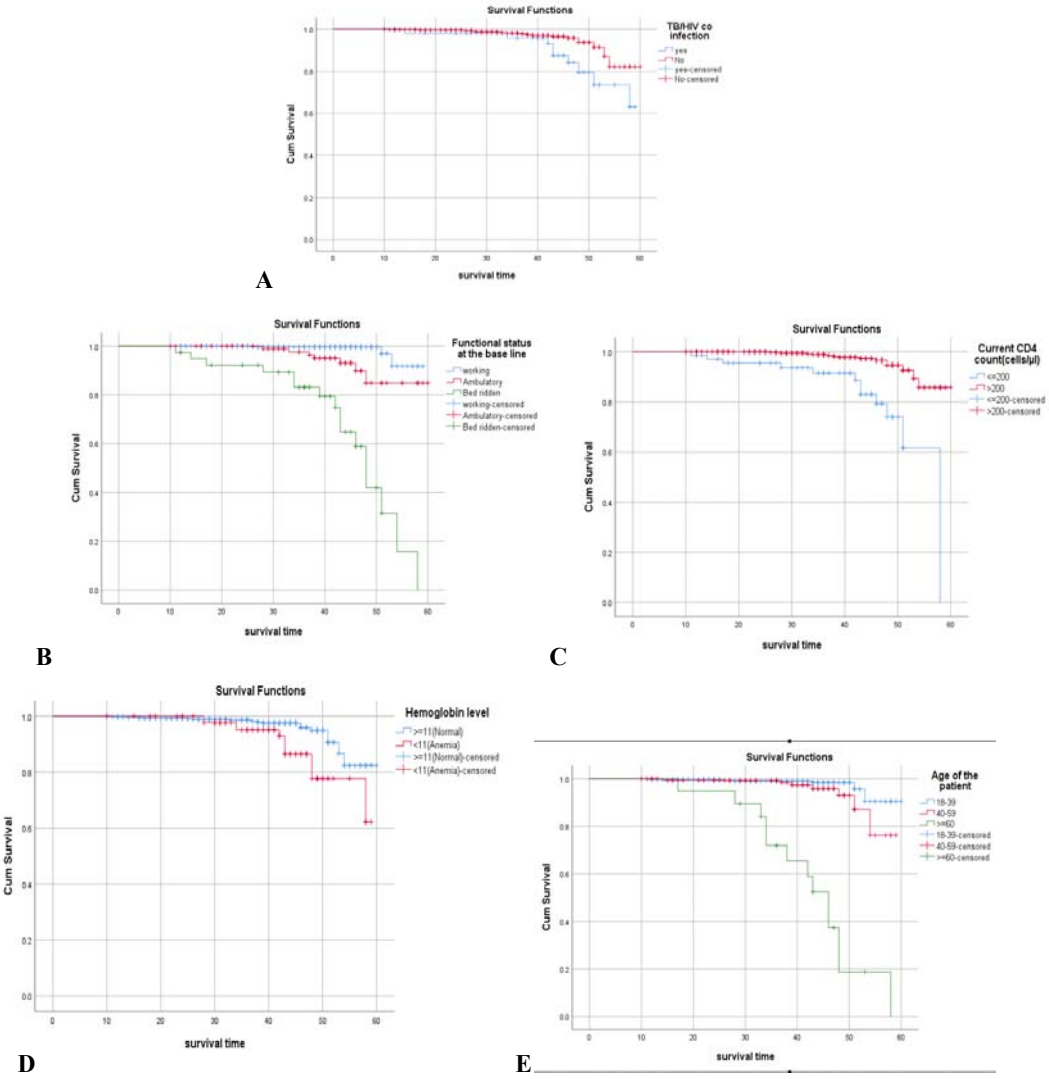

Figure 2: Kaplan-Meier survival curves show for comparison of (A) TB/HIV co-infection,(Log-rank test; $p \leq 0.01$); (B) Functional status, (Log-rank test; $p \leq 0.01$) (C) CD4 Cell count status, (Log-rank test, $p \leq 0.01$); (D) Hemoglobin count, (Log-rank test; $p \leq 0.01$) and (E) Age of the patients, (Log-rank test; $p \leq 0.01$) at baseline among PLWHA, Hawassa town, Southern Ethiopia, November 2020.

Table 4: Cox regression analysis of the determinants of the incidence of TB among adults, who completed IPT care at Hawassa university comprehensive specialized hospital in Sidama Regional State, January 2015 to December 2019 (n = 483).

Characteristics (Variables)	CHR (95% CI)	p – value	AHR (95% CI)	p – value
Age in years [mean = 32.8, SD = 12.8]				
18 – 39	1.00(Ref)		1.00(Ref)	
40 – 59	0.03(0.11 – 0.074)	$p \leq 0.01$	0.11(0.03 – 0.4)	0.061
> = 60	2.3(0.3 – 15)	$p \leq 0.01$	1.6(1.3 – 2)	0.04
WHO clinical stage				
I &II	1.00(Ref)	$p \leq 0.01$	1.00(Ref)	$p \leq 0.01$
III&IV	10.75(4.3 – 26.8)		3(2.2 – 9.5)	
CD4 cell count (Cells/µL)				
< = 200	1.00(Ref)	$p \leq 0.01$	0.59 (0.15 – .2.26)	0.44
> 200	0.15(0.07 – 0.33)	$p \leq 0.01$	1.00 Ref)	
Functional status				
Working	1.00(Ref)	$p \leq 0.01$	1.00 (Ref)	
Ambulatory	0.01(0.005 – 0.065)	$p \leq 0.01$	0.05(0.01 – 0.23)	$p \leq 0.01$
Bed ridden	1.4(1 – 3.5)	$p \leq 0.01$	3.1(1.2 – 9.4)	$p \leq 0.01$
HIV/TB co – infection				
Yes	2.73(1.19 – 6.26)	0.02	0.96(0.35 – 2.6)	0.93
No	1.00(Ref)	$p \leq 0.01$	1.00 Ref)	
Hemoglobin > = 11 g/dl(Normal)	1.00(Ref)	$p \leq 0.01$	1.00(Ref)	
<11 g/dl(Anemia)	3.34(0.15 – 0.73)	0.26	2.38(3.3 – 6.3)	$p \leq 0.01$

Discussion

In this retrospective cohort analysis, we found that CD4 cell count = 200 (Cells/L), advanced WHO staging (III and IV) and hemoglobin functional status were significant independent predictors of decreased survival in patients with HIV/AIDS following ART commencement. In univariate analysis, clinical AIDS stage at treatment initiation, baseline CD4 count, hemoglobin, age, HIV/TB co-infection and functional status were all substantially related to patient survival on ART. In a multivariate analysis, the only variables still significantly linked with survival were hemoglobin 11 g/dl (Anemia), WHO clinical stage, and functional level.

In 19194 PYO, there were 26 fatalities (5.4%) in our study, at a rate of 0.135 per 100 PYO. The cohort's estimated survival probability at 1 - 5 years was, respectively, 99.8%, 99.4%, 97.9%, 91.6% and 76.4%. Comparing this finding to other research in Africa shows that ART patients had a greater survival rate. The likelihood of remaining alive on ART at 6, 12 and 18 months, respectively, was 89.8%, 83.4% and 78.8%, according to the same study [13]. However, especially in the first six months, the mortality rate was equivalent to those of the majority of studies [12,14,15]. This may be explained by the fact that the majority of the study's participants had advanced diseases.

After correcting for confounding variables, our data corroborate the association between WHO staging (III and IV) and death, which is consistent with studies conducted in the north and west Ethiopia, which reveal comparable results of high mortality among advanced WHO clinical stage and correspondingly [2,6,8]. Another study, done in south Ethiopia and the Debremarkos referral hospitals, discovered that patients with WHO stages II and IV at the start of the study had a higher risk of death than people with WHO stages I and II who were mobile or bedridden. A five-year retrospective cohort research in Tanzania's Kagera Region produced similar findings as the prior study [16].

A study conducted in Cameroon's Far-North Province revealed that individuals with low hemoglobin levels upon diagnosis had nearly twice the chance of death as patients with high hemoglobin levels 2.38. (3.3 - 6.28). (0.0478) [17]. Our study results also suggest a similar trajectory, which could be attributed to hematologic difficulties, with patients progressing to AIDS at a faster rate and patients with hemoglobin levels less than 11 g/dl (Anemia) having a greater mortality rate in response to the viral killing. A South African study discovered that a decreased hemoglobin content of 8 g/dl was one of the key indications of higher mortality in HIV/AIDS patients. [18]. This outcome is identical to the current study. Similarly, a meta-analysis research in Adults Starting Antiretroviral Therapy (ART) in Low- and Middle-Income Countries.

In this study, the patient's functional status was used to determine their survival status. The patients' bedridden and ambulatory status was found as the key deciding factor. This is similar to the studies done in the Somali region with the result of a bedridden functional status. Other African researchers have found that functional level, particularly bedridden and ambulatory status, is a predictor of ART patient survival [8,19-23].

A comparable study conducted in the Far East and India reveals that the functional condition of ART patients was a major factor in mortality and survival over the study period [24-29].

Acknowledgment

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Availability of data and materials

The corresponding author will provide the datasets used in the current work upon reasonable request from individuals who are interested.

Ethics approval and consent to participate

The Research and Ethics Commission (REC) of Addis Ababa University's School of Nursing and Midwifery, College of Health Sciences, granted ethical approval. The hospital outpatient administration of Hawassa University specialized hospital granted permission to examine patients' data. Because we are reporting on a retrospective analysis of medical records, all data were fully anonymized before we obtained them and the ethics committee waived the informed consent requirement.

Funding

The research was funded by Addis Ababa University. The University does not have any role in the design of the study and data collection, analysis and interpretation of data and in writing the manuscript should be declared.

Limitations

Due to Incomplete records being eliminated from the data, it affected the strength of associations, so the death rate could be underestimated or overestimated. The study was retrospective, and there was a risk of bias due to uncertainty on previous data.

Authors' contribution

BB, and AF, conceived, designed and developed the data collection instruments. BB and AF performed the statistical analysis and wrote all versions of the manuscript. All authors critically revised and approved the final manuscript.

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